Departamento de Farmacología y Terapéutica

Facultad de Medicina

Universidad Autónoma de Madrid

Interferon-stimulated gene 15 (*ISG15*) and myeloid G protein-coupled receptor kinase 2 (GRK2) are novel mediators of vascular dysfunction induced by hypertension and obesity.

DOCTORAL THESIS

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CERTIFICAN, que **Doña María González Amor** ha realizado bajo su dirección el presente trabajo: ***"Interferon-stimulated gene 15 (ISG15) and myeloid G protein-coupled receptor kinase 2 (GRK2) are novel mediators of vascular dysfunction induced by hypertension and obesity"***, como Tesis para alcanzar el grado de Doctor por la Universidad Autónoma de Madrid.

Para que conste a efectos oportunos, firman la presente en Madrid a 10 de mayo de 2021.

Dra. Ana María Briones Alonso **Dra. Ana Belén García Redondo**

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Nada en la vida debe ser temido,
solamente comprendido.
Es hora de comprender más
para temer menos.
Marie Curie (1867-1934)

No entiendes realmente algo a menos que
seas capaz de explicárselo a tu abuela.
Albert Einstein (1879-1955)

A mis padres y abuelos.

A Sari y Pablo.

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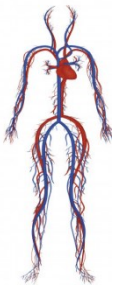

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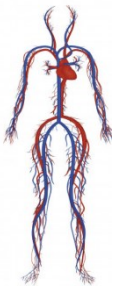


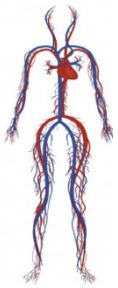
Abbreviations

AA	aortic aneurysm
AAA	abdominal aortic aneurysm
AC	adventitial cells
ACE	angiotensin converting enzyme
ACh	acetylcholine
ACN	acetonitrile
ADRF	adipocyte-derived relaxing factor
Ang	angiontensin
AP-1	activator protein 1
AT_1R	angiotensin II receptor type 1
BMI	body mass index
CAGE	chymostatin-sensitive angiotensin II-generating enzyme
CDR	cell danger response
CM	calmodulin
CNP	natriuretic peptide C
COX	cyclooxygenase
cPGES	cytosolic PGE_2 synthase
CRP	C-reactive protein
CSA	cross-sectional area
CVD	cardiovascular diseases
CXCL	chemokine (C-X-C motif) ligand
Cys	cysteines
DAG	diacylglycerol
DBP	diastolic blood pressure
DHE	dye dihydroethidium
ECs	endothelial cells
ECM	extracellular matrix
EDHF	endothelium-derived hyperpolarizing factor
EET	epoxyeicosatrienoic acids
EGF	epidermal growth factor
eNOS	endothelial nitric oxide synthase

EPR	electron paramagnetic resonance
ER	endoplasmic reticulum
ET-1	endothelin-1
FDR	false discovery rate
GPCRs, G_q-R	G protein-coupled receptors
GRK2	G protein-coupled receptor kinase 2
HAECs	human aortic endothelial cells
HFD	high fat diet
HMEC-1	human microvascular endothelial cells 1
ICAM-1	intracellular adhesion molecule 1
IFIH1	interferon-induced helicase C domain-containing protein 1
IFNs	interferons
IGF-1	insulin-like growth factor 1
ILs	interleukins
IMT	intima-media thickness
IP_3	inositol 1,4,5-triphosphate
IRS1	insulin receptor substrate 1
ISG15	Interferon-Stimulated Gene-15
JAK1/2	Janus Kinase 1/2
KHS	Krebs Henseleit Solution
LFA-1	leukocyte function-associated antigen-1
LOX	lipoxygenase
MAC1	macrophage antigen 1
MCP-1	monocyte chemoattractant protein 1
MLC	myosin light chain
MLCK	myosin light chain kinase
MMPs	matrix metalloproteinases
mPGES	membrane bound PGE_2 synthase
MRA	mesenteric resistance arteries
NADP	nicotinamide adenine dinucleotide phosphate
ND	normal diet

NE	norepinephrine
NEFA	non-esterified fatty acids
NFAT	nuclear factor of activated T cells
NFκB	nuclear factor kappa-light-chain-enhancer of activated B cells
nNOS	neuronal nitric oxide synthase
NOX	NADPH oxidase
Nrf2	nuclear factor (erythroid-derived 2)-like 2
$O_2^{\cdot-}$	superoxide anion
$ONOO^-$	peroxynitrite
PBMCs	peripheral blood mononuclear cells
PDGF	platelet derived growth factor
PFA	paraformaldehyde
PG	prostaglandin
Phe	phenylephrine
PI3K	phosphoinositide 3-kinase
PKC	protein kinase C
PLC	phospholipase C
PPAR	peroxisome proliferator-activated receptor
PRR	pattern recognition receptor
PVAT	perivascular adipose tissue
PVNs	perivascular nerves
RAS	renin-angiotensin system
RAAS	renin-angiotensin-aldosterone system
rISG15	recombinant ISG15
ROS	reactive oxygen species
SBP	systolic blood pressure
SHR	spontaneously hypertensive rats
SMCs	smooth muscle cells
SOCS	suppressor of cytokine signaling
SODs	superoxide-dismutases

SR	sarcoplasmic reticulum
STAT	signal transducer and activator of transcription
TAA	thoracic aortic aneurysm
Tempol	4-hidroxi-2,2,6,6-tetrametilpiperidin-1-oxilo
TGF-β	transforming growth factor β
TLR	Toll-like receptors
TNFs	tumor necrosis factors
TXA2	thromboxane A2
UPR	unfolded protein response
VCAM-1	vascular cell adhesion molecule 1
VEGF	vascular endothelial growth factor
VSM	vascular smooth muscle
VSMCs	vascular smooth muscle cells
WKY	Wistar Kyoto
WT	wild-type or wall thickness



Abstract

Hypertension and obesity are significant health problems worldwide with remarkable consequences on morbidity and mortality. In fact, both hypertension and obesity are major risk factors for cardiovascular diseases (CVD). Endothelial dysfunction, vascular remodelling and altered vascular mechanics are common features of vascular damage in hypertension and obesity. During the last decades, it become evident the importance of low-grade inflammation in the vascular alterations associated to these diseases. This inflammatory status is characterized by accumulation of inflammatory cells in the vasculature and other tissues such as the perivascular adipose tissue (PVAT), and enhanced local and circulating proinflammatory cytokines. Therefore, the identification of novel inflammatory mediators involved in the vascular damage associated to hypertension and obesity has become an area of active research.

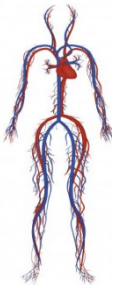
Earlier studies identified interferon-γ (IFNγ) and tumor necrosis factor-α (TNFα) as important cytokines involved in vascular damage in hypertension. Moreover, TNFα has been recognized a key mediator involved in insulin resistance and vascular damage in obesity. In the first chapter of this PhD Thesis we studied the implication of Interferon-stimulated gene 15 (ISG15), an ubiquitin-like protein that induces a reversible post-translational modification (ISGylation) and can also be secreted as a free form, in the development of vascular damage associated with hypertension. On the other hand, previous evidence found a role for G-receptor kinase 2 (GRK2), a serine/threonine kinase that desensitizes multiple G protein-coupled receptors, in adiposity insulin sensitivity and in the vascular alterations associated to hypertension and obesity. However, whether GRK2 expressed in a specific subset of inflammatory cells might have a role in the vascular damage associated to obesity, is unknown. The second chapter of this PhD Thesis explores the contribution of myeloid GRK2 to the vascular alterations associated with obesity. For this, we used multidisciplinary approaches in cell-based systems, animal models of hypertension and obesity in transgenic mice and samples from patients, to explore changes in vascular function, structure and mechanical properties, as well as underlying molecular mechanisms. The main results were as follows:

1. Bioinformatics analysis identified ISG15 as a mediator of hypertension-associated vascular damage. *ISG15* expression in human peripheral blood mononuclear cells positively correlated with systolic blood pressure and carotid intima-media thickness. Consistently, *Isg15* expression was enhanced in aorta from hypertension models and in angiotensin II (Ang II)-treated vascular cells. ISG15$^{-/-}$ mice were protected against Ang II-induced hypertension. Proteomics revealed differential expression of proteins implicated in cardiovascular function and remodelling, and vascular redox state in aorta from Ang II-infused ISG15$^{-/-}$ mice. In fact, ISG15$^{-/-}$ mice were protected against Ang II-induced vascular stiffness, elastin remodelling, endothelial dysfunction

and expression of inflammatory and oxidative stress markers. Conversely, mice with excessive ISGylation ($USP18^{C61A}$) showed enhanced Ang II-induced hypertension, inflammation and reactive oxygen species (ROS) generation along with elastin breaks, aortic dilation and rupture. Accordingly, human and murine abdominal aortic aneurysms showed augmented *ISG15* expression. Mechanistically, ISG15 induces vascular ROS production, while antioxidant treatment prevented ISG15-induced endothelial dysfunction and vascular remodelling.

2. *GRK2* levels showed a positive correlation with myeloid- (CD68) and lymphoid-specific (CD3, CD4, and CD8) markers and with leptin in PVAT from patients with abdominal aortic aneurysms. In addition, using a mouse model of myeloid-specific GRK2 deletion (LysM-$GRK2^{+/-}$), we showed that decreasing GRK2 levels in myeloid cells prevents the PVAT-induced impairment of endothelium dependent relaxations to acetylcholine and insulin in animals fed a high fat diet (HFD). Moreover, downregulation of GRK2 in myeloid cells attenuated HFD-mediated upregulation of pro-inflammatory cytokines such as TNFα, the expression of the NADPH oxidase (NOX)1 subunit and infiltration of macrophages and T lymphocytes in PVAT. Pharmacological blockade of TNFα or NOX1 pathways restored the impaired vasodilator responses to insulin in arteries with PVAT from HFD-fed animals.

In conclusion our results suggest that ISG15 and myeloid GRK2 are novel mediators of vascular damage in hypertension and obesity through oxidative stress and inflammation.



Resumen

La hipertensión y la obesidad son importantes problemas de salud en todo el mundo con notables consecuencias sobre la morbilidad y la mortalidad. De hecho, tanto la hipertensión como la obesidad son importantes factores de riesgo para el desarrollo de enfermedades cardiovasculares. La disfunción endotelial, el remodelado vascular y las alteraciones en la mecánica vascular son aspectos comunes del daño vascular en hipertensión y obesidad. Durante las últimas décadas, se ha demostrado la importancia de la inflamación de bajo grado en el daño vascular asociado a las enfermedades cardiovasculares. Dicha inflamación se caracteriza por la acumulación de células inflamatorias en la vasculatura y en otros tejidos como el tejido adiposo perivascular (PVAT, del inglés *perivascular adipose tissue*) así como con el aumento de citoquinas proinflamatorias locales y circulantes. Por tanto, la identificación de nuevos mediadores inflamatorios implicados en el dicho daño se ha convertido en un área de investigación muy importante.

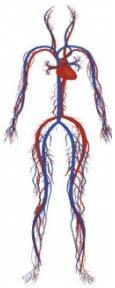
Estudios previos identificaron el interferón-γ (IFNγ) o el factor de necrosis tumoral-α (TNFα) como importantes citoquinas implicadas en el daño vascular asociado a la hipertensión. Además, se acepta que TNFα es un mediador clave implicado en la resistencia a la insulina y el daño vascular observados en obesidad. En el primer capítulo de esta Tesis Doctoral se estudia la implicación del gen 15 estimulado por interferón (ISG15), una proteína similar a la ubiquitina que induce una modificación postraduccional reversible (ISGilación) y que también puede secretarse como forma libre, en el desarrollo de daño vascular asociado a la hipertensión. Por otro lado, estudios anteriores demostraron que la quinasa de receptores acoplados a proteínas G (GRK2), una serina/treonina quinasa que desensibiliza múltiples receptores acoplados a proteína G, juega un papel importante en el control de la adiposidad, la sensibilidad a la insulina, y las alteraciones vasculares asociadas a la hipertensión y la obesidad. Sin embargo, se desconocía el papel de GRK2 procedente de células inflamatorias en el daño vascular asociado a la obesidad. El segundo capítulo de esta Tesis Doctoral explora la contribución del GRK2 presente en células mieloides en las alteraciones vasculares asociadas a la obesidad. Para ello, se han utilizado enfoques multidisciplinares en sistemas celulares, modelos de hipertensión y obesidad en ratones transgénicos y muestras de pacientes, para explorar los cambios en la función, la estructura y las propiedades mecánicas vasculares, así como los mecanismos moleculares subyacentes. Los principales resultados fueron los siguientes:

1. Un análisis bioinformático identificó a ISG15 como un mediador del daño vascular asociado a la hipertensión. La expresión de *ISG15* en células mononucleares de sangre periférica humana correlacionó positivamente con la presión arterial sistólica y el grosor íntima-media carotídeo. De acuerdo con estos datos, la expresión de *Isg15* incrementó en la aorta de modelos animales

de hipertensión y en células vasculares tratadas con angiotensina II (Ang II). Los ratones ISG15$^{-/-}$ mostraron protección frente a la hipertensión inducida por Ang II. Además, estudios proteómicos revelaron una expresión diferente de proteínas implicadas en la función y remodelado cardiovascular, así como de proteínas implicadas en el estado redox vascular, en la aorta de ratones ISG15$^{-/-}$ infundidos con Ang II. De hecho, los ratones ISG15$^{-/-}$ estaban protegidos de la rigidez vascular inducida por Ang II, el remodelado de la elastina, la disfunción endotelial y la expresión de marcadores de inflamación y de estrés oxidativo. Por el contrario, ratones con excesiva ISGilación (USP18^{C61A}) mostraron un aumento en la hipertensión inducida por Ang II, la inflamación y la generación de especies reactivas de oxígeno (ROS, del inglés *reactive oxygen species*), junto con alteraciones en la elastina y dilatación y rotura de la aorta. De acuerdo con estos resultados, se observó un aumento en la expresión de *ISG15* en aneurismas aórticos abdominales humanos y murinos. En cuanto a los mecanismos, nuestros resultados demuestran que ISG15 induce la producción vascular de ROS y que el tratamiento antioxidante previene la disfunción endotelial y el remodelado vascular inducidos por ISG15.

2. Los niveles de GRK2 mostraron una correlación positiva con marcadores mieloides (CD68) y linfoides (CD3, CD4 y CD8) y con leptina, en el PVAT de pacientes con aneurisma aórtico abdominal. Además, utilizando un modelo de ratón con deleción específica de GRK2 en células mieloides (LysM-GRK2$^{+/-}$), demostramos que la disminución de los niveles de GRK2 en las células mieloides previene el deterioro de las relajaciones dependientes de endotelio a acetilcolina e insulina inducido por el PVAT en animales alimentados con una dieta rica en grasa. Además, la disminución de GRK2 en células mieloides atenuó el incremento de la citoquina proinflamatoria TNFα, la expresión de la subunidad 1 de la NADPH oxidasa (NOX) 1 y la infiltración de macrófagos y linfocitos T en PVAT, inducidos por la dieta alta en grasa. Finalmente, el bloqueo farmacológico de las vías de TNFα o NOX1 restauró las respuestas vasodilatadoras a insulina en las arterias con PVAT de animales alimentados con dieta alta en grasa.

Como conclusión, nuestros resultados sugieren que ISG15 y GRK2 mieloide son nuevos mediadores del daño vascular en la hipertensión y la obesidad a través del estrés oxidativo y la inflamación.



Introduction

1. General concepts

It is well accepted that cardiovascular diseases (CVD) are the main cause of mortality worldwide (World Health Organization, 2019). Both hypertension and obesity are the most important risk factors for developing a future cardiovascular event. In addition, particularly hypertension, is a major risk factor for aneurysms.

Hypertension is a chronic pathology characterized by high levels of blood pressure continued over time, which significantly increases the risk of developing CVD. It is estimated that 1.13 billion people worldwide suffer from hypertension, while only less than 20% having blood pressure under control. Furthermore, hypertension is associated with high morbidity and mortality rates and is the leading cause of premature death worldwide (World Health Organization, 2019). The etiology of this disease is not entirely clear, however, it is known that hypertension is a multifactorial disease resulting from the interaction between genetic, physiological, and environmental factors (Kumar, 2010).

Hypertension can be primary or secondary. In primary or essential hypertension there is not a specific cause that explains the increase in blood pressure. Essential hypertension accounts for about 90-95% of the total (Carretero and Oparil, 2000; Kakar and Lip, 2006). The term *essential* comes from the initial belief that the increase in blood pressure was essential to maintain a sufficient tissue perfusion (Rang and Dale, 2012). One of the main characteristics of essential hypertension is the increase in peripheral resistance (Bund and Lee, 2003), explained more detailed below. In secondary hypertension there is a specific cause of blood pressure elevation (blood vessels malformation, steroids or catecholamines secreting tumors in the adrenal cortex, coarctation of the aorta, kidney disease or endocrine problems such as primary aldosteronism) (Rang and Dale, 2012).

Optimal blood pressure values for an adult are <120 mm Hg for systolic blood pressure (SBP) and <80 mm Hg for diastolic blood pressure (DBP) (120/80). Hypertension is referred to a SBP equal or greater than 140 mm Hg and a DBP equal or greater than 90 mm Hg, although these limits may vary depending on age or the presence of other concomitant problems such as kidney disease or diabetes. Values between 120/80 mm Hg and 129/84 mm Hg are considered as “normal”, while values between 130/85 mm Hg and 139/89 mm Hg are known as “normal-high”. In this state above optimal bool pressure, the subjects' probability of suffering a cardiovascular event also increases, in addition to a high risk of developing hypertension over time (ESC and ESH, 2019)

Obesity is also a significant health problem worldwide with important consequences on morbidity and mortality (Regan and Shah, 2020). Indeed, it is well accepted that the risk of CVD increases with body mass index (BMI, in kg/m^2) (World Health Organization, 2020). BMI greater than or equal to 25 indicates overweight while BMI greater than or equal to 30 points defines obesity. For children, age needs to be considered when defining overweight and obesity.

The excessive accumulation of fat in the body is known as *increased adiposity*. According to World Health Organization, in 2016, 13% of adults were obese, and 39% of adults were overweight with a high probability of developing obesity or at least of suffering from the damages caused by an excess of fat (World Health Organization, 2020). Childhood obesity also remains a matter of serious concern, with 38 million children under the age of 5 being overweight or obese in 2019 and which prevalence has dramatically risen from 4% in 1975 to over 18% (World Health Organization, 2020). Lifestyle factors are major contributors but there is an increasing knowledge about genomic and metabolomic pathways involved with obesity (Regan and Shah, 2020) and with the complications derived from it (Sanghera et al., 2019).

Both hypertension, obesity and CVD have some degree of genetic background. They share some polymorphisms within genes that enhance expression of proteins that influence CVD. There are at least 5 genes (*FTO, ADCY3, BDNF, MC4R, TBX15-WARS2*) with different genetic variants which belong to obesity and hypertension at the same time (**Figure 1**, Sanghera et al., 2019). Among other functions, these genes are implicated in fat mass and insulin levels regulation, adipogenesis, and energy homeostasis. In addition, other diseases sharing some polymorphisms with obesity and hypertension are type 2 diabetes and dyslipidemia (**Figure 1**).

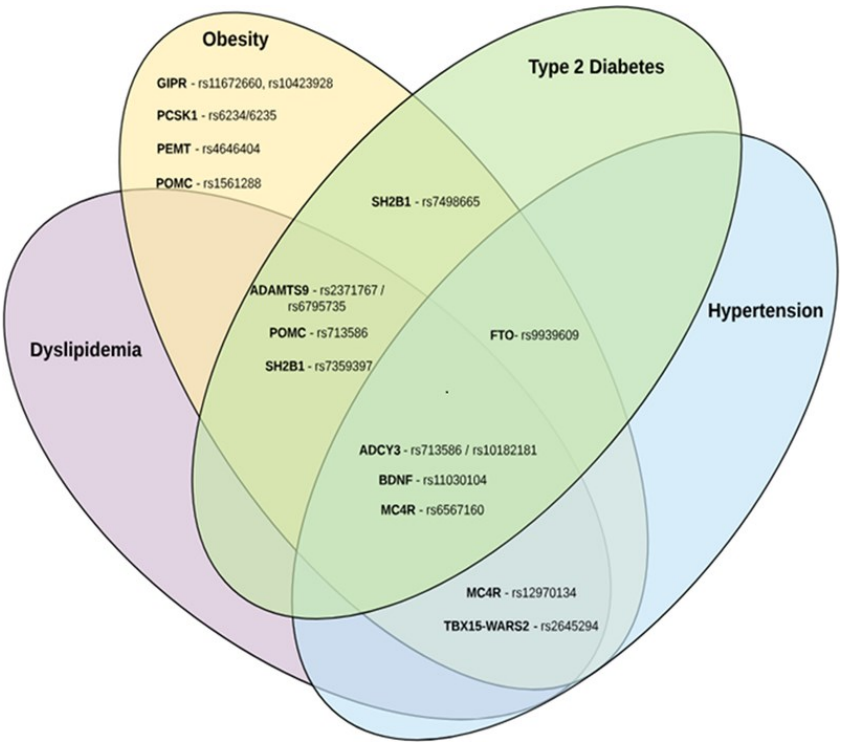


Figure 1. Venn diagram of common genetic variants identified by GWAS for obesity, classified based on the results of the pleiotropic association reported of the same loci/variants with other cardiovascular-related diseases. Each colour in the Venn diagram (yellow, purple, green, blue) corresponds to each of the cardiovascular traits (obesity, dyslipidemia, type 2 diabetes, hypertension), respectively. Taken from Sanghera et al., 2019.

Aortic aneurysm (AA) is a potentially lethal vascular pathology characterized by a permanent dilation of the aorta. AA is prevalent among older adults and can cause significant morbidity and mortality if not addressed on time (Anagnostakos and Lal, 2021). For the diagnosis in patients, a dilation in the aorta of more than 3 cm is needed (Chaikof et al., 2018). Without treatment, the vessel wall continues to weaken and can become unable to compensate the pressure exerted by the intraluminal blood, arising the rupture of the aorta. Due to the lack of clinical symptoms in AA patients, death due to rupture of the aorta is common and it occurs in approximately 80% of the patients suffering from AA (Chaikof et al., 2018). Aneurysms can be abdominal AA (AAA) or thoracic AA (TAA) (Kuivaniemi et al., 2015). The aorta, regardless of the location, depends on fibromuscular layers (lamellar units) to distribute stress and provide elasticity. The media of the thoracic aorta is composed of around 60 lamellar units, while the abdominal aorta consits of 30 lamellar units (Wolinsky and Glagov, 1969). This difference in the number of lamellar units is, probably, one of the causes that make the abdominal aorta more prone to aneurysmal degeneration (Kuivaniemi et al., 2015).

The etiology of AAA remains under continuous investigation but some causes include inflammatory disorders, infections, and trauma. Risk factors associated with AAAs include

hypertension, dyslipidemia, family history of AAA, peripheral artery disease, advanced age, male gender, and smoking (Chaikof et al., 2018; Anagnostakos and Lal, 2021). The pathophysiology of this disease is related to an initial arterial injury causing a cascade of inflammation and extracellular matrix (ECM) protein disruption leading to arterial wall weakening (Anagnostakos and Lal, 2021). However, TAAs are usually the result of genetic mutations in rare diseases and degenerative processes such as Marfan syndrome (Davis et al., 2014). When identified early, aneurysms are monitored for size, growth rate and presence of aberrant biomechanical properties of the aneurysmal sac, factors with high probability of increasing the risk of rupture (Anagnostakos and Lal, 2021).

We will next review different concepts of arterial function, structure and mechanical properties, and how hypertension, obesity and AAs influence these parameters. In the last decades, it has become evident the relationship between hypertension, obesity, AAA, and inflammation. We will revise the role of the immune system and some specific cytokines such as interferon γ (IFNγ) in the vascular alterations associated with these pathologies. In this sense, we will focus in one IFN stimulated gene (***ISG15***) and the post-translational modification that this protein produces (*ISGylation*). Moreover, we will discuss the importance of G protein-coupled receptor kinase 2 (**GRK2**) in vascular signalling and its physiopathological functions in inflammatory cells in the context of adiposity and insulin resistance. Finally, we will briefly discuss pharmacological aspects for the treatment of hypertension, obesity and aneurysms.

2. Structure and function of the vascular system.

The cardiovascular system is a closed system that has three main components: the heart, the blood vessels and the blood itself. There are two main different blood vessels depending on the type of blood they are carrying on: arteries transport the oxygenated blood from the heart to the capillaries, while veins transport the blood back to the heart to be oxygenated again inside the lungs.

2.1. Structure of the arterial wall.

The different types of arteries are distinguished by their structure and specific innervation and this is adapted to the specific function they fulfil. The basic organization of arteries consist of three well-differentiated layers or *tunica*: the inner layer (*tunica intima*), middle layer (*tunica media*) and adventitia layer (*tunica externa*). These layers are organized into cellular components and ECM (**Figure 2**).

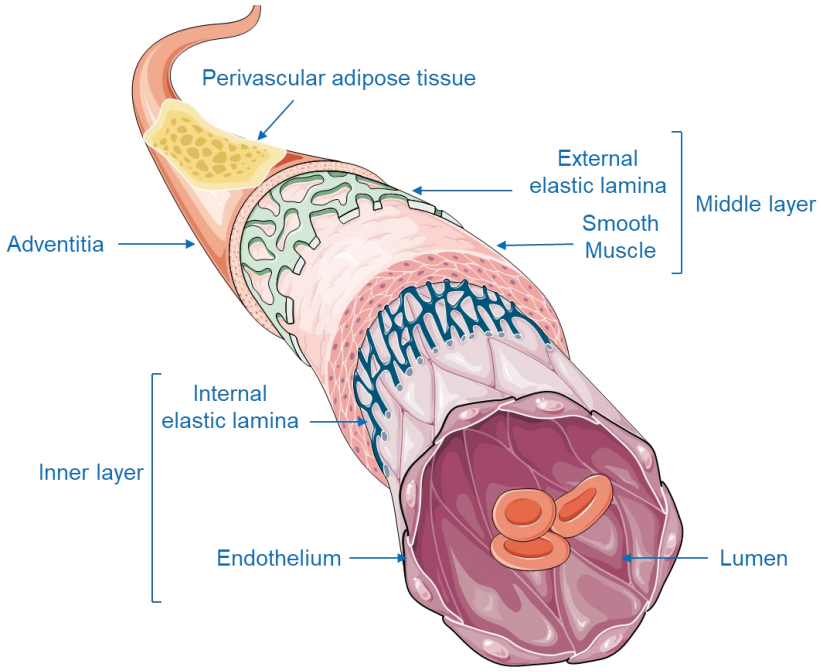


Figure 2. Basic structural organization of the arteries. Modified from smart.servier.com.

- **Inner layer** (***Tunica intima***): it is directly in contact with the circulating blood and consists of a monolayer of **endothelial cells** (ECs) and the basement membrane that is rich in collagen, fibronectin, laminin, and proteoglycans (Sumpio et al., 2002). This layer is separated from the media layer by the internal elastic lamina, which is a very thin and fenestrated elastic sheet (Lee, 1995; Briones et al., 2003). This inner layer has an important role in the control of vascular function and structure because ECs are an important source of vasoconstrictor and vasodilator factors, as well as proliferative and antiproliferative substances. Additional functions of EC are preventing coagulation, controlling blood flow and facilitating exchange of proteins between blood and tissues. Moreover, ECs have a key role in the regulation of inflammatory processes (Pober and Sessa, 2007).

- **Middle layer** (***Tunica media***): it is the thickest layer and consists of **vascular smooth muscle cells** (VSMCs) arranged circularly or helically, as well as variable amounts of ECM, rich in elastin and collagen. VSMCs carry the contractile apparatus of the arteries, made up of fine actin filaments and thick myosin. VSMCs are in continuous contact with ECs through the fenestrae of the internal elastic lamina (Rhodin, 1980). The proportion of ECM in the middle layer varies according to the diameter of the vessel and its function. The middle and the external layer or adventitia, are separated by a second sheet of elastic fibers, the external elastic lamina. This layer also regulates vascular tone and structure since VSMCs respond to multiple vasoactive and

mitogenic factors and hemodynamic forces. Moreover, different substances are produced by VSMC.

- **Adventitia layer** (***Tunica externa***): it is mainly formed by **fibroblasts** but in some conditions, it may also contain macrophages, lymphocytes, mast cells and different components of the ECM. Initially, it was thought that this layer only served as a support for the vessel, but it has become evident that adventitia also participates in the regulation of vascular tone and structure by releasing various factors (González et al., 2001; Stenmark et al., 2013).

The **extracellular matrix** (**ECM**) is a viscoelastic gel that support vascular cells, determining the elasticity and mechanical properties of the vessels. Its components are synthesized by different cell types of the vascular wall. The main components of the ECM are collagen and elastin: collagen confers strength while elastin gives elastic properties to vessels (Wagenseil and Mecham, 2009).

Collagen is a very rigid protein whose main function is to limit the distension of the vessel produced by pressure. Type I and III collagens are the major collagens detectable in vessels, representing 60% and 30% of vascular collagens, respectively. The remaining 10% includes type IV, V, VI, VIII, XII and type XIV collagens (Jacob, 2003). The blood vessels contain enzymes that degrade collagen (mainly matrix metalloproteinases, MMPs), allowing an active balance between degradation and synthesis (Galis and Khatri, 2002; Newby, 2005).

Elastin is the most abundant protein in the wall of the large arteries. However, elastin is also present in the resistance arteries, mainly in the internal and external elastic lamina. Elastin constitutes 90% of the elastic fibers; the other compounds of elastic fibers are microfibrillar glycoproteins such as fibrillins and microfibrillar-associated glycoproteins (MAGPs). Fibrillin-1 has been deeply investigated since mutations in the *FBN1* gene were found in patients suffering from Marfan´s syndrome (Dietz and Mecham, 2000). These fibers form fenestrated sheets allowing cell contact. The function of elastin is to distribute stress across the arterial wall. Elastin is also degraded by MMPs and by endogenous vascular elastase (Jacob, 2003; Arribas et al., 2006).

Although less abundant, other proteins of the ECM include glycoproteins, proteoglycans and integrins. Proteoglycans provide the properties of turgor and resistance to compression, in addition to containing receptors for enzymes and cytokines. Main proteoglycans in the vascular wall are hyaluronan, decorin, versican and perlecan (Jacob, 2003). Integrins are the principal receptors used by animal cells to bind to the ECM. They are heterodimers and they function as transmembrane linkers between the ECM and the actin cytoskeleton. Many matrix proteins in

vertebrates are recognized by several integrins. For example, at least 8 integrins bind fibronectin and 5 bind laminin. Human integrin heterodimers are formed from at least 9 types of β subunits and 24 types of α subunits (Alberts et al., 2002).

Perivascular adipose tissue (**PVAT**) is in very closed contact with the adventitia layer, surrounding blood vessels. Microvessels, nerves and migratory cells connect the perivascular space with the adventitia. PVAT contains not only adipocytes, but also immune cells such as macrophages, T cell subsets, NK cells and dendritic cells, lymphatic vessels, perivascular nerves (PVNs) and stromal cells (Guzik et al., 2007; Omar et al., 2014; Moore et al., 2015; Wensveen et al., 2015). During the last few decades, it has become evident that signals originated from perivascular cells also play essential roles in the regulation of vascular development, physiology, artery wall remodelling, immune surveillance and vascular disease (Majesky et al., 2011; Hu and Xu, 2011; Omar et al., 2014; Psaltis and Simari, 2015). It has been described that PVAT participate in CVD, such as atherosclerosis in mice and human (Henrichot et al., 2005; Gustafson, 2010; Rajsheker et al., 2010; Manka et al., 2014;), in part, through the release of pro-inflammatory cytokines, deeply explained below.

2.2. Types of arteries.

For the efficient functioning of the arterial system, it is necessary to maintain an adequate pressure and a continuous blood flow, which is achieved through the existence of various types of arteries. The primary classification of the arteries is based on the external diameter, lumen diameter, arterial wall thickness and the composition of their layers, especially the middle layer:

- **Elastic or conductance arteries**: this group includes the largest arteries, such as the aorta, the pulmonary artery or the iliac artery. Their middle layer is formed by lamellar units composed of several elastin sheets and VSMCs, so they have a very distensible wall: depending on the artery, they expand above 10% of their diameter after each heartbeat, in order to accommodate for the arrival of blood (Levick, 2003). In the aorta, the most elastic artery, this distensibility represents its ability to dampen the pulsatility of ventricular ejection and to transform a pulsatile pressure and flow at the site of the ascending aorta into a continuous pressure and flow at the site of arterioles (Laurent and Boutouyrie, 2015).

- **Muscular or distribution arteries**: they have medium and small caliber. Some examples include the radial, femoral, cerebral and coronary arteries. The middle layer contains more VSMCs than the elastic arteries and they transport blood from an elastic artery to the resistance vessels. Their function is to distribute the blood to the different portions of the body (Levick, 2003).

- **Resistance arteries or arterioles**: they are small arteries (between 100 and 300 µm in diameter) and they have a narrow lumen and thick muscular wall. These arteries are responsible for the regulation of blood pressure (Levick, 2003). In detail, mean arterial pressure (MAP) is proportional to cardiac output (CO) and peripheral vascular resistance (R):

MAP=CO x R.

CO is directly proportional to stroke volume and heart rate, parameters that do not depend greatly on different types of arteries.

R is the frictional resistance produced by all vessels to blood flow. It is determined by arteries and arterioles with diameters less than 500 µm, which contribute approximately 70% (Christensen and Mulvany, 2001). According to Poiseuille's law, the resistance (R) that a vessel offers to the passage of blood depends on the viscosity of the blood (ŋ), the length of the vessel (L) and, mainly on the radius (r):

$R = 8\eta L/\Pi r^4$.

Therefore, the resistance is inversely proportional to r^4, and thus the radius of the vessels is the main determinant of peripheral vascular resistance. The radius can change due to altered function, decreased distensibility, or truly modified wall structure.

2.3. Vascular remodelling.

Vascular remodelling refers to the process that occurs when the vascular wall changes its structure in order to maintain the adequate vascular resistance. Remodelling is usually an adaptive process that occurs in response to long-term changes in hemodynamic conditions, but it may also contribute to the pathophysiology of vascular diseases and circulatory disorders (Gibbons and Dzau, 1994). Physiological vascular remodelling is observed during pregnancy or aging. However, vascular remodelling is found in many pathological situations including hypertension, obesity or aneurysms. Vascular remodelling is an active process that involves changes in cell growth, death, or migration, and in the synthesis, reorganization, or degradation of ECM (Renna et al., 2013).

In general terms, vascular remodelling can be classified as *hypertrophic remodelling* that is associated with vascular growth, *hypotrophic remodelling* with decreased vessel wall area or *eutrophic remodelling* where no changes in the amount of material of the vascular wall are observed. In addition, *inward remodelling* associates with smaller diameters whereas *outward*

or compensated remodelling are associated with greater or similar vessel size, respectively (Mulvany, 1999; van Varik et al., 2012) (**Figure 3**). More specifically:

- **Hypertrophic remodelling**: it is generally associated with increased media thickness due to changes in either cell growth or number. Concomitantly, media/lumen ratio and vascular cross-sectional area (CSA) increase (Mulvany, 1999). This type of remodelling is characteristic of elastic arteries with aging and hypertension (Schiffrin, 2012), obesity (Briones et al., 2014), atherosclerosis and restenosis (Renna et al., 2013) and predominates in secondary hypertension (Mulvany, 2008)

- **Hypotrophic remodelling**: it is characterized by a decrease in the amount of material in the vascular wall (smaller CSA) (Mulvany, 1999). Hypotrophic remodelling can occur due to apoptosis or a rearrangement of the material of the vascular wall (Intengan and Schiffrin, 2001). It has been observed in renal afferent arterioles of spontaneously hypertensive rats (SHR) (Norrelund et al., 1994) and in mesenteric resistance arteries of ouabain-induced hypertensive rats (Briones et al., 2006).

- Eutrophic remodelling: it is associated with a decrease in the external and internal diameters and an increase in the media thickness and in the media/lumen ratio without changes in CSA (Mulvany, 1999). The processes underlying this type of remodelling are less known but a combination of inward vascular wall growth and apoptosis in the peripheral area have been suggested. Also, eutrophic remodelling may be the consequence of a prolonged vasoconstriction of vascular cells embedded in an expanded ECM (Bakker et al., 2002; Schiffrin, 2012). Resistance arteries from patients with essential hypertension, rat genetic models of hypertension such as the spontaneously hypertensive rat (SHR), or mice models of Angiotensin II (Ang II) infusion exhibit predominantly eutrophic inward remodelling, although the latter can also associate to hypertrophic remodelling (Briones et al., 2010). Moreover, some arteries from diabetic or obese animal models can also show this type of remodelling (Briones et al., 2014).

Likewise, **outward remodelling** occurs in aneurysms, in conductance arteries during hypertension and in some vessels from some models of obesity, while **inward remodelling** can be observed in obesity, atherosclerosis, restenosis, or resistance arteries in hypertension (Renna, de las Heras, 2013; Briones et al., 2014; Dorrance et al., 2014) (**Figure 3**).

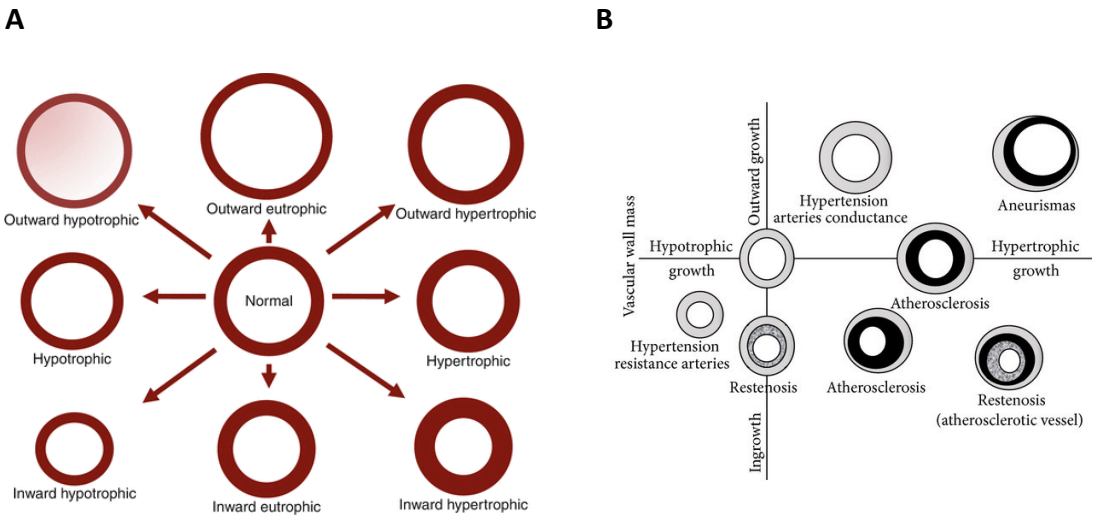


Figure 3. A. Types of vascular remodelling. B. Schematic representation of remodelling adaptation in different pathologies. Taken from (A) Touyz and Montezano, 2015; (B) Renna et al., 2013.

2.4. Vascular stiffness.

The components of arteries that account for the majority of its mechanical properties are collagen and elastin deposited in the medial layer (Wagenseil and Mecham, 2009). At physiological pressure, less than 10% of collagen fibers are engaged, whereas at higher pressures, the vessel becomes progressively less distensible as collagen fibers are recruited to support passive wall tension and restrict aortic distension. With additional increases in wall strain or stretch ratio, there is little further change in radius as additional collagen fibers are recruited, accounting for the nonlinear nature of vascular elasticity (Wagenseil and Mecham, 2009).

Vascular stress is the force applied to an artery divided by the surface area over which that force is applied. Shear stresses from the blood flow, longitudinal stress from surrounding tissue, and circumferential stress from the blood pressure are responsible for the stresses imparted on the vessel wall. The forces that generate stresses also induce deformations in the vessel wall that can be converted into strains. Strain relates the deformed dimensions of an object to the undeformed dimensions and quantifies deformation regardless of the original geometry (Wagenseil and Mecham, 2009). The stress-strain relationship is a measure of vascular stiffness.

Arterial stiffness changes vessel wall properties. Arterial stiffness has an independent predictive value for cardiovascular morbidity and mortality and is responsible, at least in part, for hypertensive vascular remodelling in hypertension (Laurent et al., 2001; Briones et al., 2010). An increase in stiffness of the resistance vasculature, contributes at least in part, for increased

peripheral resistance observed in hypertension (Briones et al., 2010). Changes in arterial stiffness are determined by quantitative and qualitative alterations in vascular ECM due to hemodynamic, genetic, or humoral factors (Briones et al., 2010; Laurent and Boutouyrie, 2015).

2.5. Endothelial dysfunction.

A quiescent healthy endothelium continuously releases potent vasodilators in response to blood flow (Brandes, 2014). Endothelial function is considered a 'barometer' of cardiovascular health and is useful in disease evaluation and in therapeutic patient management. Cardiovascular risk factors but also several immunometabolic and neuroendocrine diseases switch the endothelial phenotype from health to disease-causing endothelial dysfunction (Dal Lin et al., 2015). Endothelial dysfunction associates with an imbalance in the bioavailability of active substances, resulting in the predisposition to inflammation and vasoconstriction. But endothelial dysfunction is not a condition comprising only attenuated endothelium-dependent vasodilation, it also comprises endothelial inflammatory activation (Watson et al., 2008). In fact, the endothelium orchestrates vascular remodelling processes and inflammation; conversely, inflammation induces endothelial dysfunction (Brandes, 2014).

The molecular mechanisms underlying the disruption of endothelial homeostasis remain unclear (Dal Lin et al., 2019). The dysfunction of ECs is considered an early event before the development of serious vascular diseases such as atherosclerosis, thrombosis, or vascular leaks in the capillaries (Simionescu, 2007; Husain et al., 2015). When endothelial dysfunction appears, it can be usually considered as a systemic condition (Anderson et al., 1995), affecting both the peripheral vasculature and the coronary arteries. But, although it is well accepted that endothelial dysfunction is a predictor of atherosclerosis development and it is early observed in obesity, its role in blood pressure elevation is less understood. In this sense, the exact contribution of attenuated release of vasodilator substances to hypertension has not been fully stablished, and we cannot forget that metabolic and local nervous factors, and also renal and central mechanisms can directly control blood pressure. In addition to peripheral resistance, the endothelium affects other aspects as vascular stiffness (Duprez et al., 2013).

3. Physiological factors that regulate vascular tone.

Several vasodilator and vasoconstrictor substances regulate vascular tone. Main vasodilator factors include nitric oxide (NO), prostaglandin I_2 (PGI_2) and prostaglandin E_2 (PGE_2, acting on specific receptors), endothelium-derived hyperpolarizing factor (EDHF) and some reactive

oxygen species (ROS). Main vasoconstrictor factors are thromboxane A_2 (TXA_2) and other prostanoids, endothelin-1 (ET-1), some components of the renin-angiotensin-aldosterone system (RAAS) and some ROS. Most of these factors can be generated by the three layers of the vascular wall.

3.1. Mechanisms involved in contraction and relaxation of the vascular smooth muscle.

Vascular smooth muscle contraction is mainly regulated by the concentration of intracellular free calcium $[Ca^{2+}]_i$. In response to different stimuli, $[Ca^{2+}]_i$ increases after Ca^{2+} entry from the extracellular space through L-type Ca^{2+} channels or the release of Ca^{2+} from the sarcoplasmic reticulum (SR) (**Figure 4,** pathway 1). Ca^{2+} binds to calmodulin (CM) and the Ca^{2+}-CM complex activates the myosin light chain kinase (MLCK) that catalyzes the phosphorylation of the myosin light chain (MLC), thus increasing the ATPase activity of myosin, which interacts with actin and induces contraction (Hirano, 2007) (**Figure 4**, pathway2).

The increase in $[Ca^{2+}]_i$ can also occur through the activation of several families of G protein-coupled receptors (GPCRs). G_q-R triggers an increase in the activity of phospholipase C (PLC), which generates diacylglycerol (DAG) and inositol 1,4,5-triphosphate (IP_3) (**Figure 4**, pathways 3 and 4). DAG stimulates protein kinase C (PKC), which decreases the activity of the myosin light chain phosphatase (MLCP), promoting contraction (**Figure 4**, pathway 3). IP_3 promotes the release of Ca^{2+} from the SR (**Figure 4**, pathway 4). In addition, there are other two types of GPCRs, G_s-R and G_i-R that modulate cAMPC levels. G_s-R contribute to increase cAMP levels that at vascular level produce vasodilation by inhibition of MLCK, while G_i-R activation reduces cAMP thus increasing the activity of MLCK and produces contraction at vascular level (Horowitz A et al., 1996) (**Figure 4**, pathway 5).

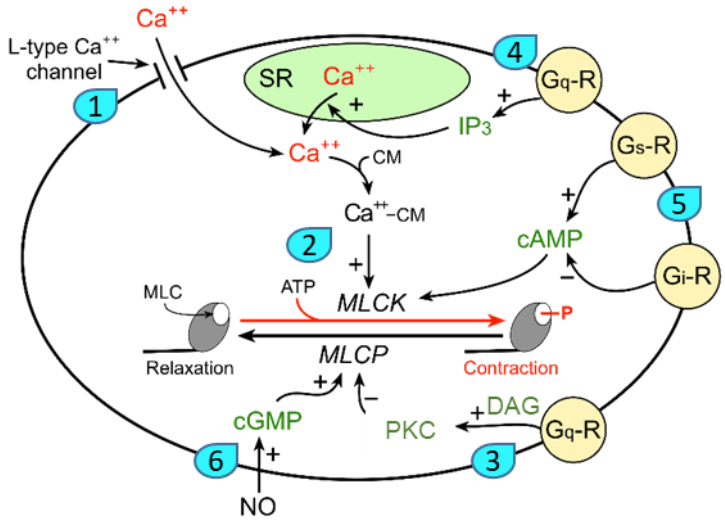


Figure 4. **Mechanisms involved in vascular smooth muscle contraction.** Modified from Klabunde, 2012.

Vascular relaxation can be achieved by reducing the levels of free cytoplasmic Ca^{2+}, increasing cAMP or by reducing the phosphorylation rate in the presence of Ca^{2+}-CM (Godfraind and Miller, 1985). Physiological antagonism of contraction can occur through the interaction of a compound (either endogenous or exogenous) with a specific membrane receptor that mediates the relaxation of the smooth muscle. These membrane receptors include β2-adrenoreceptors, histamine receptors, bradykinin receptors or M_3 muscarinic receptors in undamaged endothelium of blood vessels (Godfraind and Miller, 1985). Specifically, activation of M_3 receptors in the endothelium of healthy blood vessels produces an increase in the synthesis of NO, which diffuses to the adjacent VSMCs, activating soluble guanylate cyclase and cGMP production that causes VSM relaxation through different mechanisms including activation of MLCP and K^+ channels, Ca^{2+} store in the sarcoplasmic reticulum, and others (**Figure 4**, pathway 6). When vascular endothelium is damaged, vasoconstriction or decreased relaxation are observed after direct stimulation of the M_3 muscarinic receptor.

3.2. Physical forces: wall stress and shear stress.

As mentioned, blood vessels are under constant mechanical loading from blood flow and pressure, which cause endothelial shear stress and circumferential wall stress and strain (stretch), respectively. Under physiological situations there is a laminar flow, which sometimes turns to turbulent flow provoking pathological changes. These mechanical forces cause morphological changes of endothelium and blood vessel wall, but also trigger biochemical events. There is considerable evidence that physiological forces are required and exert vasoprotective roles via NO, providing a homeostatic oxidative balance (Lu and Kassab, 2011). As mentioned, a perturbation of tissue stress and strain, for example in hypertension (Agabiti-Rosei and Rizzoni, 2010) and diabetes (Sachidanandam et al., 2009; Paneni et al., 2013), can disturb biochemical homeostasis and lead to vascular remodelling and possible dysfunction (e.g., altered vasorelaxation, stiffness, etc.).

How the vessel wall senses and transduces the mechanical stretch shared to various haemodynamic perturbations remains a central topic of mechanobiology. Indeed, a variety of receptors, integrins and ECM components have been studied (Davies, 2009; Chiu and Chien, 2011). Common molecules may be activated by laminar shear stress or circumferential stretch. For example, shear stress activates integrins on the endothelium surface to upregulate endothelial NO synthase (eNOS) activity. In contrast, stretch-mediated integrin activation on smooth muscle cells (SMCs) is modulated by ECM interactions and results in actin polymerization. Also, shear stress may inactivate Ang II receptor type 1 (AT_1R) via the NO-

dependent pathway whereas circumferential stretch can activate AT_1R in a ligand-independent manner leading to superoxide production, and endothelial and SMC dysfunction (Lu and Kassab, 2011).

3.3. Vascular innervation.

The peripheral circulation is regulated to distribute cardiac output to the organs and tissues according to their individual metabolic or functional needs while maintaining arterial blood pressure within a relatively narrow range. As mentioned, regional blood flow can be efficiently regulated at local level by the intrinsic ability of vessels to respond to various mechanical forces (e.g., wall tension and shear stress) as well as chemical stimuli (e.g., tissue metabolites and O_2). Superimposed on this system of local control is another level of regulation governed by changes in central neural activity that adjust cardiovascular function to meet the needs of the body as a whole: the autonomic nervous system, which is responsible for involuntary control of most visceral organs, including the heart and blood vessels, effecting rapid changes in blood pressure, in the amount and distribution of cardiac output, and in the distribution of blood volume (Thomas, 2011). PVNs release adrenergic, cholinergic, peptidergic, purinergic, and nitrergic neurotransmitters that lead to SMC arterial contraction or relaxation via their actions on SMCs, ECs, or other PVNs. Meshworks of PVNs are often found in the adventitia (Westcott and Segal, 2013).

Neural control of the cardiovascular system is governed mainly by the activity of the **sympathetic nerves**, with a limited but important cardiac effect of the parasympathetic nerves. Sympathetic nerves increase cardiac rate and contractility, cause constriction of arteries and veins, cause release of adrenal catecholamines, and activate the RAAS (Thomas, 2011; Westcott and Segal, 2013). Postganglionic sympathetic fibers release norepinephrine (NE), which at vascular level binds to α-adrenoceptors to produce vasoconstriction or to β-adrenergic receptors that, in general, facilitate vasodilation.

The presence of **sensory PVNs** has been characterized in a wide variety of vascular beds across several animal species. While calcitonin gene-related peptide is the primary neurotransmitter, substance P and ATP are released as cotransmitters (Brain and Grant, 2004).

Nitrergic nerves are present in many vascular beds, including mesenteric or femoral, and contribute to PVN-mediated vasodilation via NO produced within nerve terminals that contain neuronal NO synthase (nNOS) (Burnstock, 2009), including some sensory and parasympathetic PVNs. Nitrergic nerves can also modulate vasomotor activity through interacting with other PVNs. For example, in rat mesenteric arteries, nitrergic nerves localize with sympathetic nerves

and NO release inhibits adrenergic vasoconstriction, presumably by diminishing NE release (Hatanaka et al., 2006; Koyama et al., 2010).

3.4. Vascular mediators.

Several humoral factors affect the vascular system and act like endocrine/paracrine signals, regulating vascular tone. The vascular endothelium acts as a source of several potent chemical mediators (**Figure 5**), which mostly inhibit the contraction of the contiguous smooth muscle and avoid excessive leukocyte adhesion, VSMC growth, and platelet aggregation. Many other cell types can produce these mediators and affect vascular tone.

3.4.1. Prostanoids.

Prostanoids are critical modulators of vascular tone and platelet aggregation under physiological and pathological conditions. Biosynthesis of prostanoids depends on the action of cyclooxygenases 1 and 2 (COX-1 and COX-2, respectively) on arachidonic acid released by phospholipases from the membrane phosphoglycerides. Both COX isoforms transform arachidonic acid into two very unstable endoperoxides, PGG_2 and PGH_2, that are then transformed in specific prostaglandins (PGE_2, PGI_2, PGD_2, $PGF_{2\alpha}$) and TXA_2 by the action of specific isomerases. Prostaglandin I_2 (PGI_2 or prostacyclin) was the first component discovered of this group, by Bunting, Gryglewski, Moncada and Vane (Moncada et al., 1976).

COX requires low levels of lipid peroxides for activation and the activated state continues auto-catalytically, through new PGG_2. Unlike COX-1, COX-2 protein is not normally present, although constitutive COX-2 is found in some organs like the kidney. It is an immediate-early response gene, and its expression can be regulated by transcriptional and post-transcriptional mechanisms. COX-2 promoter contains a TATA box, with several binding sites for transcription factors such as nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB), cyclic AMP-responsive binding protein (CREB), nuclear factor of activated T cells (NFAT) or activator protein-1 (AP-1) that are the responsible for its expression under pathological conditions. COX-2 is induced by lipopolysaccharide and inflammatory cytokines such as interleukin (IL)-1 and tumor necrosis factor α (TNFα), among others. In addition, in the last years it has been shown that other factors like Ang II, ET-1 or ROS can induce its expression at the cardiovascular level (Rang and Dale, 2012; Hernanz et al., 2014).

As mentioned, the production of the different prostanoids depend on the activity of specific synthases. PGE_2 is the most abundant prostanoid in the human body. There are three PGE synthases, cytosolic PGE_2 synthase (cPGES) and two different membrane bound synthases

(mPGES-1 and mPGES-2). cPGES and mPGES-2 are constitutive, while mPGES-1 is inducible by inflammatory stimuli similarly to COX-2 (Hernanz et al., 2014).

Prostanoids bind to specific GPCRs. PGE_2 is able to bind to four receptor subtypes (EP_1-EP_4), where EP_1 and EP_3 induce vasoconstriction whereas EP_2 and EP_4 mediate vasodilation. EP receptors are also implicated in platelet aggregation, monocyte and macrophage migration, SMC proliferation and migration, vascular cytokine production or MMP activation (Félétou et al., 2011). PGI_2 is the main PG released by vascular endothelium, and it acts on type I prostanoid (IP) receptors, inducing vasodilation and inhibiting platelet activation (Hernanz et al., 2014). The thromboxane receptor (TP) is involved in platelet aggregation, smooth muscle contraction, expression of adhesion molecules and infiltration of monocytes/macrophages. The unstable endoperoxide intermediates PGG_2 and PGH_2 are constricting factors derived from the endothelium and specifically, PGH_2 can also activate TP receptors (**Figure 5**) (Nakahata, 2008; Hernanz et al., 2014).

3.4.2. Nitric oxide (NO).

In 1980, Furchgott and Zawadzki discovered an endothelium-derived relaxing factor, which was later identified as NO (Ignarro et al., 1987; Palmer et al., 1987). There are different NO synthases (NOS), two constitutive and one inducible. Constitutive eNOS is mostly present in ECs from vessels, and can be regulated by shear stress, chronic exercise or pregnancy, constitutive nNOS is expressed in the brain and peripheral nervous system, and inducible NOS (iNOS) is activated by immunological or inflammatory stimuli such as lipopolysaccharide of IL-1β. NO is continuously released from the vascular endothelium and it diffuses to the underlying VSMCs where activates guanylate cyclase and cGMP production that produces vasodilation by decreasing intracellular calcium concentration through a number of mechanisms and intervenes in the physiological control of blood pressure (**Figure 5**). In addition, NO inhibits VSMC proliferation, platelet adhesion and aggregation, and monocytes adhesion and migration, so NO greatly protects blood vessels from the development of atheromas and thrombosis (Alderton et al., 2001; Rang and Dale, 2012).

3.4.3. Endothelin-1 (ET-1).

ET-1 is a vasoconstrictor factor secreted by ECs. ET-1 binds GPCRs ETA and ETB (**Figure 5**). ETA and ETB in the SMCs produce contraction and cell proliferation, while ETB in ECs triggers relaxation by stimulating the release of endothelial PGI_2 and NO (Marasciulo et al., 2006). VSMCs, cardiomyocytes and fibroblasts express ETA that activates PLC, leading to generation of IP3 and DAG. Secretion of ET-1 is enhanced by physical factors such as shear stress, or stimuli

including thrombin, IL-1, endotoxin, epinephrine, Ang II, growth factors, cytokines, and ROS. By contrast, the release of endogenous ET-1 is reduced by mediators such as NO, cGMP, atrial natriuretic peptide, and PGI_2. Under physiological conditions, the effects of ET-1 are carefully regulated through inhibition or stimulation of ET-1 release from the endothelium. Thus, dysregulation of the ET-1 system in important in the pathogenesis of several diseases such as hypertension and insulin resistance (Marasciulo et al., 2006).

3.4.4. Endothelium-derived hyperpolarizing factors (EDHF).

The exact nature of EDHF is not known and several factors have been suggested. These include epoxyeicosatrienoic acids (EET, derivatives of cytochrome P450 enzymes), various products of lipoxygenase (LOX), hydrogen peroxide (H_2O_2), carbon monoxide (CO), hydrogen sulfide (H_2S) and C natriuretic peptide (CNP). These substances cause vasodilation by hyperpolarisation of VSMCs through activation of K^+ channels (**Figure 5**). In addition, EDHF also produces hyperpolarisation of ECs, which increases intracellular [Ca^{2+}]. The improvement in the EDHF pathway contributes to the beneficial effect of some therapeutic interventions such as angiotensin-converting enzyme (ACE) inhibitors, AT_1R blockers and phosphodiesterase 3 inhibitors (Félétou and Vanhoutte, 2009).

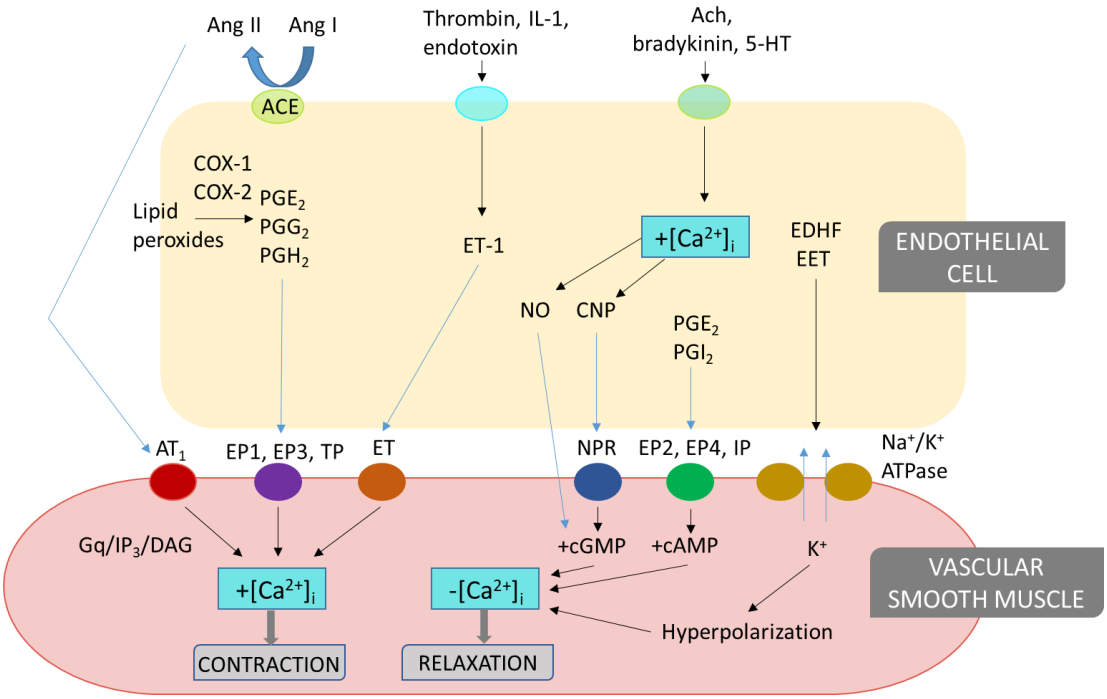


Figure 5. Vasoconstrictor and vasodilator mediators derived from the endothelium. Under physiological situations or after the activation of endothelial cells (ECs) with different stimuli such as angiotensin II (Ang II), thrombin, interleukin-1 (IL-1), endotoxin, acetylcholine (Ach), bradykinin or 5-hydroxytryptamine (5-HT), EC can release several chemical factors such as prostaglandins (PGs), NO, endothelin-1 (ET-1) or

endothelium-derived hyperpolarizing factors (EDHF), which bind to their receptors in the vascular smooth muscle cells (VSMCs), or activates K+ channels triggering relaxation or contractile responses. ACE, angiotensin-converting enzyme; AT_1, angiotensin 1 receptor; CNP, C natriuretic peptide; DAG, diacylglycerol; EET, epoxyeicosatetraenoic acid; ET, endothelin receptors; EP, prostanoids P receptor; Gq, G proteins; IP, prostanoids I receptor; IP_3, inositol 1,4,5-triphosphate; NPR, natriuretic peptide receptor; TP, prostanoids T receptor. Modified from Rang and Dale, 2012.

In addition to secreting vasoactive mediators, ECs express many enzymes, transport mechanisms and receptors that bind circulating hormones and other substances, that contribute to the different functions of the endothelium, but this will not be discusses in this manusript.

3.4.5. Renin-angiotensin system (RAS).

The RAS acts synergistically with the sympathetic nervous system and has a fundamental role in the development of several cardiovascular pathologies mainly through the regulation on Na^+ excretion and vascular tone (Touyz and Sciffrin, 2000). Hyperactivation of this system has been described in atherosclerosis (Hammoud et al., 2007), diabetes (McGuire et al., 2008), obesity (Cabandugama et al., 2017) and hypertension (Boos and Lip, 2006; Ruiz-Ortega et al., 2006; Kobori et al., 2007). The RAS was initially considered as a strictly circulating system, however, it is now accepted that there are local RAS members in the brain, kidney, adrenal cortex, adipose tissue or the vascular wall itself (Touyz and Sciffrin, 2000; Bader et al., 2001; Engeli et al., 2003; Kobori et al., 2007).

The main peptide of this system is Ang II, which is synthesized by the consecutive action of two enzymes: renin and ACE. Furthermore, the conventional system is becoming more complex due to the emergence of other enzymes capable of participating in Ang II synthesis, such as the chymostatin-sensitive Ang II-generating enzyme (CAGE chymase) (Lorenz, 2010) (**Figure 6**). Renin is produced in the kidney, specifically in the juxtaglomerular apparatus, in response to different physiological stimuli, such as a decrease in renal perfusion pressure or a decrease in the [Na^+] in the fluid of the distal tubule. Moreover, β-adrenergic receptor agonists and PGI_2 stimulate renin secretion directly, while Ang II acts as an inhibitor of the pathway by self-regulation. The substrate for renin is circulating angiotensinogen produced by the liver, to form angiotensin I (Ang I), a 10 amino acid peptide without biological activity. ACE, produced mainly in the pulmonary endothelium and in the kidney, acts on this Ang I, to produce Ang II, a powerful vasoconstrictor (**Figure 6**). The limiting step of this pathway is the production of renin in the granular cells of the juxtaglomerular apparatus (Gradman and Kad, 2008). Furthermore, there is a second ACE (ACE 2) capable of performing the hydrolysis of Ang I to Ang 1-9 and the hydrolysis of Ang II to Ang 1-7. The formation of Ang 1-9 from Ang I by ACE 2 is considerably slower than the hydrolysis of Ang II to give Ang 1-7 by the same enzyme. Ang 1-7 can also be formed from

Ang 1-9 by the action of ACE (Rüster and Wolf, 2006; Ocaranza and Jalil, 2012) (**Figure 6**). Ang II can be transformed into Ang III and Ang IV through the action of two enzymes (aminopeptidases A and N, respectively), and Ang II can also be transformed into Ang 1-9 by the action of endopeptidases (**Figure 6**).

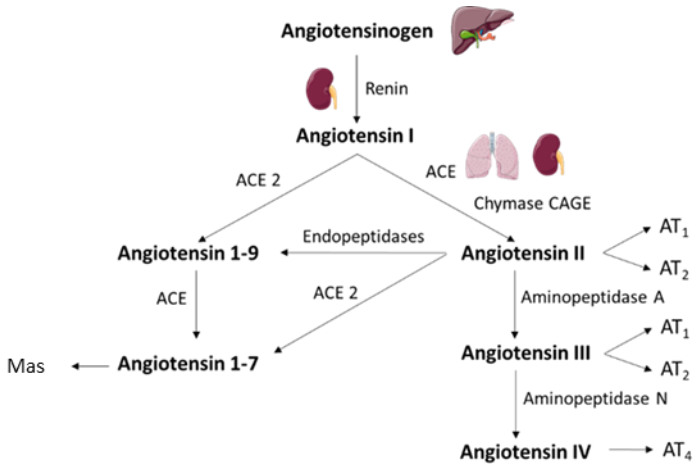


Figure 6. Scheme of renin-angiotensin system (RAS). Modified from Rüster and Wolf, 2006.

Ang II is essential for the functional and structural integrity of the vascular wall, and plays an important role in the physiological processes that regulate blood pressure and in the pathological processes that are involved in vascular diseases (Touyz and Schiffrin, 2000). Specifically, among the many effects of Ang II at the vascular level are modulation of vasomotor tone, regulation of cell growth and apoptosis, regulation of cell migration and deposition of the ECM, stimulation of ROS generation by nicotinamide adenine dinucleotide phosphate (NADPH) oxidases, stimulation of the production of specific growth factors such as platelet derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor β (TGF-β), insulin-like growth factor (IGF-1), basic fibroblast growth factor or platelet activator factor, and synthesis of vasoconstrictor factors like ET-1, adhesion molecules like intracellular adhesion molecule, (ICAM-1), E-selectin, integrins or cytokines such as TNFα, IFNγ or ILs (Forrester et al., 2018).

The main actions of Ang II are mediated by GPCRs AT_1 or AT_2 (**Figure 6**). The effects of AT_1 receptors include generalized vasoconstriction, increased release of NE that enhances the sympathetic effects, stimulation of proximal tubular reabsorption of Na^+, aldosterone secretion in the adrenal cortex, and cell growth in the heart and arteries through intracellular phosphorylation pathways, such as Jak/Stat or ERK1/2. It is also a recognized source of oxidative

stress in the cardiovascular system (Touyz et al., 2003). AT_2 receptors are mostly expressed during fetal life and in certain areas of the adult brain. They participate in growth, development, and programmed cell death. The cardiovascular effects of AT_2 receptors include inhibition of cell growth, decrease in blood pressure and vasorelaxation, but these effects are relatively weak, especially compared to the effects of AT_1 receptor (Forrester et al., 2018). Interestingly, emerging evidence clearly demonstrates protective effects of a selective non peptide AT_2 receptor agonist at the vascular level through different mechanisms (Sumners et al., 2019).

Ang III and IV have been considered of less importance, but Ang III also binds to AT_1 and AT_2 receptors, triggering similar physiological responses as Ang II (**Figure 6**), while Ang IV stimulates the release of plasminogen activator inhibitor I by the endothelium. Ang IV receptors (AT_4) have a peculiar distribution, which includes the hypothalamus (Forrester et al., 2018). Meanwhile, Ang 1-7 binds to the Mas receptor (**Figure 6**) and has opposite actions to Ang II: it induces vasodilation, through an increase in the production of NO, EDHF and vasodilator prostanoids, and it has antiproliferative effects (Forrester et al., 2018).

3.4.6. Reactive oxygen species (ROS).

ROS are produced by almost all cell types and specifically, all cells in the vascular wall including VSMCs, ECs and adventitial cells, together with circulating cells such as platelets, leucocytes, and red blood cells can generate ROS. They act as intracellular second messengers interacting with multiple signalling pathways, and affecting basic cellular functions such as proliferation, migration, cell death, ECM modulation and degradation, NO inactivation, stimulation of certain kinases, and expression of proinflammatory genes (Paravicini and Touyz, 2008). The term *ROS* encloses reactives derived from oxygen, among which superoxide anion ($O_2^{\cdot-}$), hydrogen peroxide (H_2O_2) and peroxynitrite ($ONOO^-$) stand out for their biological implications. Others are hydroxyl radical (OH) and hypochlorous acid (HOCl).

$O_2^{\cdot-}$ is formed by the univalent reduction of molecular oxygen. Main sources of $O_2^{\cdot-}$ include NADPH oxidase (NOX), xanthine oxidase, LOX, COX, CYP450 isoforms, monoxygenases and uncoupled eNOS. $O_2^{\cdot-}$ can also be generated non-enzymatically by the mitochondrial electron transport chain, the endoplasmic reticulum (ER), and peroxisomes (Martín-Ventura et al., 2017).

$O_2^{\cdot-}$ has a fundamental role in redox biology because apart from having numerous functions, is the precursor of the other ROS. For example, $ONOO^-$ is formed after the chemical reaction of $O_2^{\cdot-}$ with NO, also reducing the bioavailability of the NO (Drummond et al., 2011). The majority of $O_2^{\cdot-}$ generated is rapidly converted to H_2O_2 by the three superoxide dismutases (Mn-, extracellular-, Cu-Zn-SOD) which, in contrast to $O_2^{\cdot-}$, penetrates cell membranes easily, and

functions as a second messenger that activates multiple signaling pathways (Martín-Ventura et al., 2017).

Regarding $O_2^{\cdot-}$ functions, it is capable of activating different signalling pathways such as Akt or MAPK, which lead to the activation of proinflammatory transcription factors such as AP-1 and NFκB (Lee and Yang, 2012; Tsai et al., 2012), and it is involved in the synthesis of proinflammatory genes such as chemokine monocyte chemoattractant protein 1 (MCP-1) or the adhesion molecules ICAM-1 and vascular cell adhesion molecule 1 (VCAM-1), among many others (Lee and Yang, 2012).

The misbalance between ROS generation and elimination determines oxidative stress. It is now accepted that oxidative stress is involved in many cellular and tissue processes in relation to CVD. In fact, all established cardiovascular risk factors such as hypercholesterolemia, hypertension, diabetes mellitus, obesity and smoking enhance ROS generation. In the context of CVD, not only vascular cells produce and release ROS. Inflammatory cells infiltrated at the (peri)vascular level are now recognized as a potential source of ROS in different CVD including atherosclerosis, hypertension, obesity and AAA (Drummond et al., 2011; Martín-Ventura et al., 2017).

3.4.6.1. NADPH oxidase.

The NOX family is the main source of ROS in the vascular wall, both in physiological and pathological conditions (Drummond et al., 2011; Lassègue et al., 2012; Montezano and Touyz, 2014). The main catalytic activity of NOX is the production of ROS ($NADPH + 2\ O_2 \rightarrow O_2^{\cdot-} + NADP^+ + H^+$), while the rest of ROS-generating enzymes have another main function and only produce ROS as a by-product or when malfunctioning. The NOX is an enzymatic complex consisting of different cytosolic and one or two transmembrane subunits. The transmembrane subunits are $p22^{phox}$ and a catalytic subunit that, in mammals, can be found in 7 different isoforms: NOX1-5 and DUOX1-2, also called NOX6-7. NOX5 and DUOX lack additional subunits (Zhang et al., 2020) (**Figure 7**). The NOX subunits are responsible for transporting electrons through the biological membranes, reducing O_2 to $O_2^{\cdot-}$, and using NADPH as an electron donor. The cytosolic subunits (NOX organizer 1 (NOXO1), NOX activator 1 (NOXA1), Rac1/2, $p67^{phox}$, $p47^{phox}$ and $p40^{phox}$) are involved in the assembly of the complex to the membrane and in the activation of the enzyme (Touyz et al., 2011).

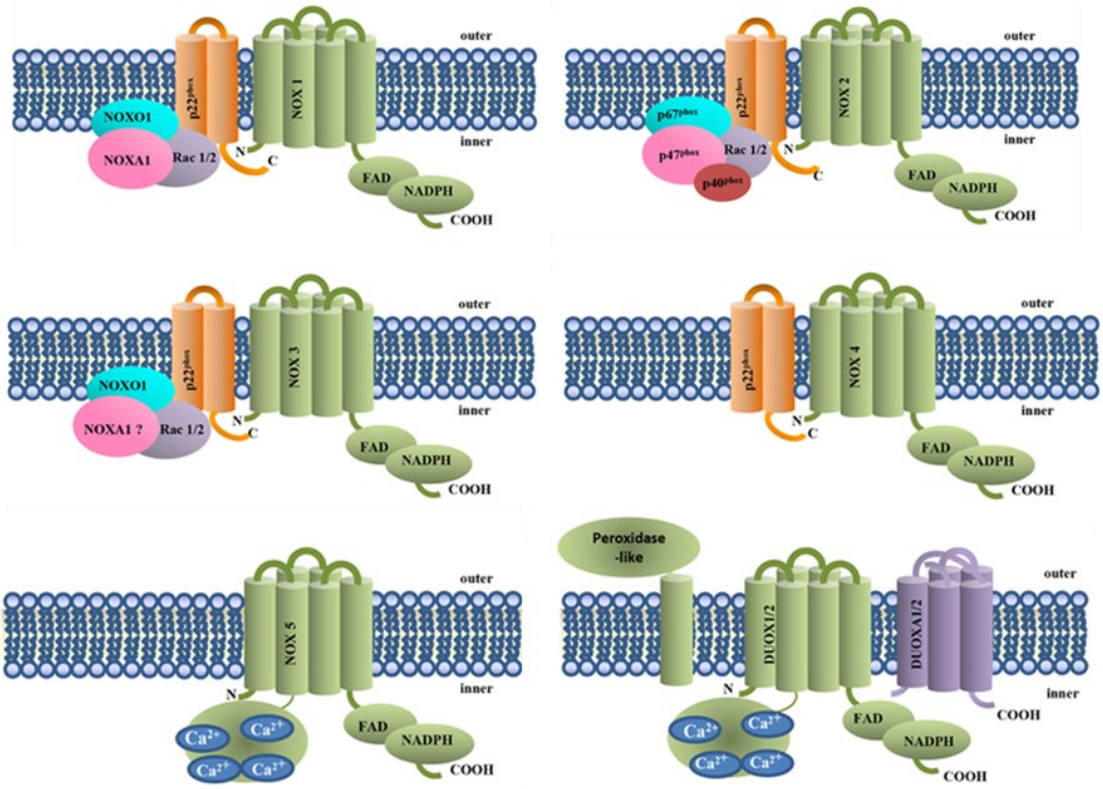


Figure 7. Structure of the different NADPH oxidases. Modified from Santillo et al., 2015.

NOX2 was the first to be characterized in phagocytes. NOX1, NOX2, NOX4 and NOX5 are expressed in the cardiovascular system including ECs and VSMCs. Furthermore, NOX1, NOX2 and NOX4 are found in adventitial fibroblasts (Drummond et al., 2011). All isoforms produce $O_2^{\cdot-}$ in vascular cells with the exception of NOX4, which preferably produces H_2O_2. NOX5 is present in lower forms and higher mammals, but not in rodents (Zhang et al., 2020).

At the vascular level, basal NOX1/2 expression is usually low but several stimuli such us mechanical stress, Ang II, ET-1 or aldosterone increase their expression (Touyz et al., 2011). NOX4 is involved in constitutive ROS production but certain stimuli such as hypoxia, TGF-β1, Ang II or mechanical stress can also increase its expression (Cucoranu et al., 2005; Lee et al., 2013). Notably, it has become evident that in some conditions, NOX4 has a protective role at vascular level, preventing cell activation or proliferation (Touyz and Montezano, 2012). Unlike other NOXs, NOX5 is regulated by intracellular Ca^{2+} concentration since this subunit consists of 4 calmodulin-like domains with the ability to bind Ca^{2+} (Drummond et al., 2011). It is tightly regulated through numerous post-translational modifications and is activated by vasoactive agents, growth factors and pro-inflammatory cytokines (Touyz et al., 2019). For example, vascular NOX5 is activated by thrombin, PDGF and ionomycin through PKC and cAMP (Serrander

et al., 2007; Jay et al., 2008). Moreover, in human ECs, Ang II and ET-1 induce redox signalling and MAPK activation in a NOX5-dependent manner (Montezano et al., 2010).

The different functions of NOXs are very complex and depend on the different physiopathological conditions. In general, data from patients with coronary artery disease or hypertension, and animal models of hypertension, diabetes or atherosclerosis, suggest that NOX1 and NOX2 promote endothelial dysfunction and inflammation, while NOX4 might have a vasoprotective role in certain situations by increasing the bioavailability of NO and by suppression of cell death pathways (Drummond and Sobey, 2014). Moreover, especially NOX-1 and NOX4 are involved in vascular remodelling in different pathological conditions such as hypertension, restenosis, atherosclerosis, aortic dilation or pulmonary hypertension (García-Redondo et al., 2016). NOX5 is involved in the regulation of different vascular functions including vascular contraction and relaxation and vascular remodelling, although because it is not expressed in rodents, less information on this NOX isoform is available (Touyz et al., 2019).

3.4.6.2. Antioxidant systems.

A good vascular function depends on the balance between oxidative and antioxidant mechanisms. Several antioxidant systems regulate ROS levels. Enzymes include catalase, SODs, glutathione peroxidase, glutathione S-transferases, thioredoxin reductase and epoxide hydrolase 2 (Snezhkina et al., 2019). SODs are the most important ones and as mentioned, their main function is to transform $O_2^{\cdot-}$ into H_2O_2. There are 3 isoforms of SOD (Cu/Zn-SOD, Mn-SOD and extracellular-SOD), which differ in the cofactor they use and in their cellular location. Catalase, glutathione peroxidase or thioredoxin reductase catalyze the conversion of H_2O_2 into H_2O and O_2 (Martín-Ventura et al., 2017).

Increased levels of ROS activate nuclear factor (erythroid-derived 2)-like 2 (Nrf2), a master regulator of the antioxidant response, which is activated to counteract oxidative stress. Nrf2 controls the expression of about 250 genes including those encoding antioxidant enzymes such as glutathione and thioredoxin systems, SODs, catalase, and hemoxygenase-1, among many others. In addition to enzymatic degradation of ROS, various low molecular weight compounds can directly react with ROS. These molecules can be endogenously synthesized or obtained from diet and include vitamins C and E, uric acid, glutathione, flavonoids and thiols (Martín-Ventura et al., 2017).

3.4.7. Vasoactive factors released by PVAT.

Experimental studies performed over the last two decades identified vasoactive factors released by PVAT as important regulators of vascular tone, arterial growth, and remodelling (Fernández-Alfonso et al., 2017). Under physiological situations, PVAT exhibits a net anticontractile effect. It was observed for several GPCR agonists, such as phenylephrine, Ang II, serotonin and noradrenaline in PVAT-mounted arteries or after incubation with PVAT conditioned media (Fernández-Alfonso et al., 2017).

Among PVAT relaxing factors, adipocyte-derived relaxing factor (ADRF) has received particular attention. ADRF was the first factor suggested to be released and transferred from PVAT to the underlying vascular wall to exert a paracrine anticontractile effect (Löhn et al., 2002). Although ADRF has not yet been identified, it can produce arterial relaxation by opening VSMC voltage-gated K^+ channels. ADRF release and action is dependent on the external [Ca^{2+}] without involvement of ECs (Löhn et al., 2002). In addition, there are other PVAT-derived relaxing factors that cause relaxation through endothelial mechanisms (Fernández-Alfonso et al., 2017). The precise nature of intracellular signaling pathways responsible for production of PVAT-derived relaxing factors is largely unknown. However, it is recognized that numerous vasoactive factors derived from adipose tissue act *via* the phosphoinositide 3-kinase (PI3K) pathway that is involved in NO synthesis (Zhang et al., 2014). Interestingly, PI3K-signaling has been also implicated in insulin resistance and inflammatory signaling in obese adipose tissue (Fernández-Alfonso et al., 2017).

Leptin and adiponectin are the best known PVAT-derived adipokines and have been also proposed as PVAT-derived relaxing factors in different vascular beds, such as coronary arteries and mesenteric arteries. Other adipokines, such as omentin, visfatin, irisin, and apelin have been suggested as putative PVAT-derived relaxing factors, since they are also able to relax blood vessels involving mainly endothelium-dependent pathways (Gollasch, 2017). However, evidence of their paracrine influence from PVAT is more limited. Importantly, a growing list of studies suggest that PVAT may also be a source of contractile substances, such as noradrenaline, Ang II, adipokines, or ROS especially in a pathological state (Fernández-Alfonso et al., 2017). This will be discussed in more detail in other sections of this introduction.

4. GPCRs and G protein-coupled receptor kinase 2 (GRK2).

As mentioned earlier, GPCRs expressed in VSMCs and ECs are responsible for maintaining the balance between contraction and relaxation of vessels and their modulation has been a primary target of therapeutic treatments. Upon agonist stimulation, GPCRs activate heterotrimeric G-proteins, leading to the dissociation of the G protein into activated subunits (**Figure 8A**). This dissociation promotes downstream signaling through specific effectors proteins and second messengers (**Figure 8B**) (Brinks and Echart, 2010). There are four main classes of heterotrimeric G-proteins based on the Gα component. Activation of different Gα subtypes leads to diverse intracellular signaling cascades that modify vascular tone. $G\alpha_s$ promotes the activation of adenylyl cyclase (AC) resulting in the conversion of ATP to cAMP, inducing relaxation; $G\alpha_q$ activates PLC that hydrolyzes IP2 into IP3 and DAG, resulting in calcium mobilization, PKC activation and vascular contraction; $G\alpha_i$ inhibits AC, producing contraction; $G\alpha_{12/13}$ and $G\alpha_{q/11}$ activate Rho kinase, which inhibits MLCP, finally activating the MLC and initiating vasoconstriction (**Figure 8B**) (Barnes et al., 2005; Bregeon et al., 2009; Brinks and Echart, 2010).

G protein-coupled receptor kinases (GRKs) are serine/threonine kinases that, together with arrestins, desensitize several members of the GPCRs family, the largest superfamily of membrane receptors with central roles in physiology and target of around the 35% of the prescription drugs (Sriram and Insel, 2018). The classical way used by GPCR to transduce extracellular signals inside the cell is through activation of heterotrimeric G proteins. Upon agonist binding, GRKs phosphorylate GPCR in their intracellular domains, promoting the association of arrestins (**Figure 8A**), which are a small family of proteins very important for regulating signal transduction at GPCRs. Arrestins bind to the phosphorylated receptor, leading to uncoupling from heterotrimeric G proteins provoking receptor desensitization, inhibiting further interactions with G proteins. As a result of arrestin binding, phosphorylated receptors are also targeted for clathrin-mediated endocytosis, a process to re-sensitize and recycle receptors back to the plasma membrane (Premont and Gainetdinov, 2007; Penela et al., 2010). Arrestins can also act as scaffold proteins for main signalling mediators such as c-Src, MAPK cascades, Akt and the NFκB signalling pathway, among others (Kovacs et al., 2009; Luttrell and Gesty-Palmer, 2010). In addition, GRKs can regulate other cellular signalling pathways independently of G-proteins, such as tyrosine kinase receptors for IGF-1, insulin, PDGF or EGF (Mayor et al., 2011; Murga et al., 2019).

Seven GRK genes have been discovered in mammals and are subdivided into three groups: visual GRK subfamily (GRK1 and GRK7), the β-adrenergic receptor kinase subfamily (GRK2/GRK3)

and the GRK4 subfamily (GRK4, GRK5 and GRK6). Apart from visual GRKs and GRK4, GRKs are almost ubiquitously expressed (Penela et al., 2010). GRK2 has major importance because homozygous GRK2-deficient mice are lethal (Jaber et al., 1996). GRK2 participates in basic cellular processes such as differentiation/development (Molnar et al., 2007), cell migration (Penela et al., 2008) and cell cycle progression (Penela et al., 2010), among others. Moreover, GRK2 levels are tightly controlled by very complex mechanisms that differ depending on the pathological situations (Penela et al., 2003; Salcedo et al., 2006; Murga et al., 2019), showing the relevance of GRK2 in cell biology and physiology. For example, changes in GRK2 expression and activity occur during the onset or progression of several relevant inflammatory and CVD, suggesting that its alteration might have a key role triggering or developing these pathologies (Penela et al., 2006; Vroon et al., 2006; Dorn, 2009; Murga et al., 2019).

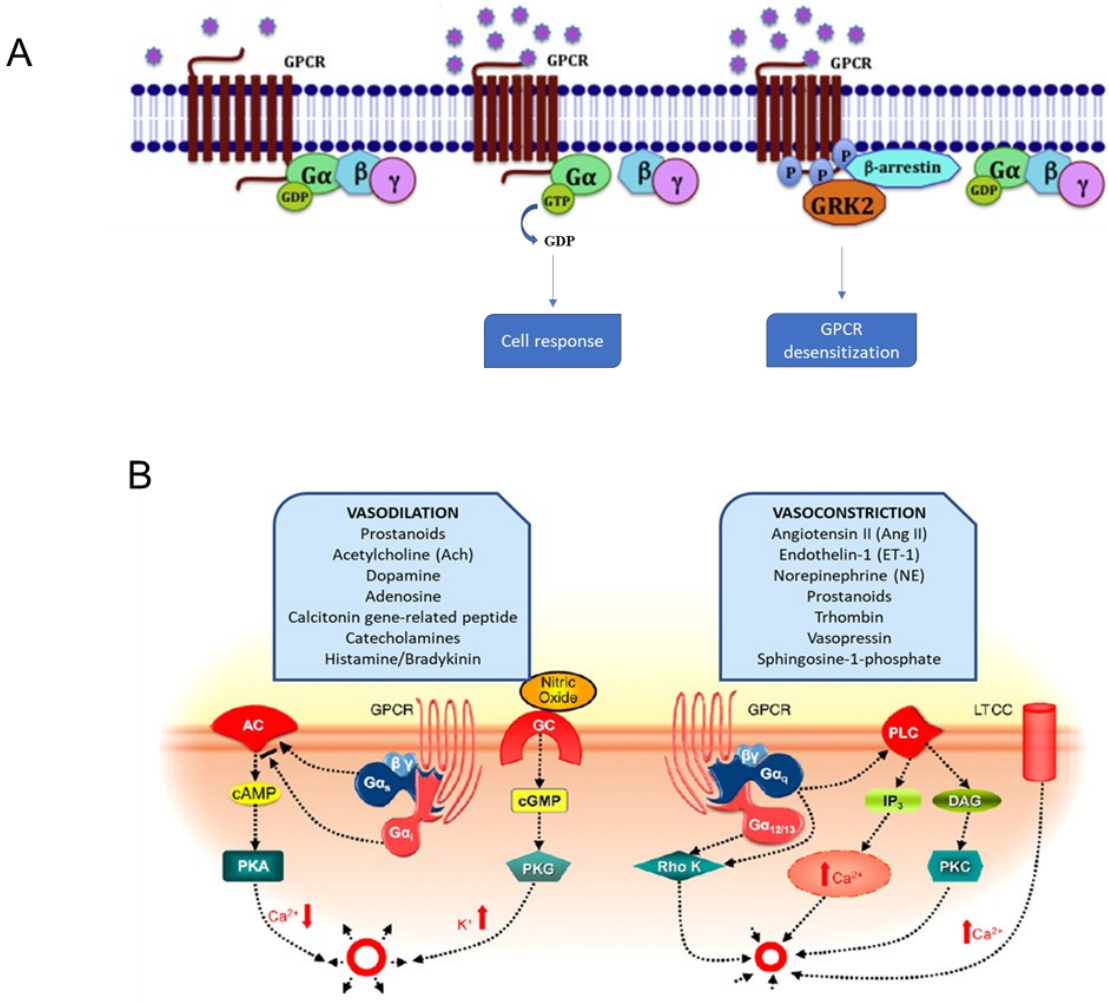


Figure 8. (**A**), **Desensitization of GPCR by GRK2.** Agonists activate the GPCR and induce a conformational change in the receptor that allows to its G_{α} subunit to hydrolyze the attached GTP to GDP, triggering cell responses. Activated G-protein is also a substrate for phosphorylation by GRKs. GRK phosphorylation promotes β-arrestin binding, causing G-protein uncoupling and GPCR desensitization. Modified from Rudomanova and Blaxall, 2017. (**B**), **Role of GPCR signalling cascade in vasodilation and vasoconstriction.**

Vasodilation occurs after activation of GPCRs by a wide range of agonists that leads to activation of adenylyl cyclase (AC) and guanylate cyclase (GC), increasing 2nd messenger concentrations and activation of protein kinase A (PKA) or PKG that reduce intracellular [Ca^{2+}] or activate potassium channels. Vasoconstriction occurs after activation of GPCRs by several agonists that leads to smooth muscle contraction via protein kinase C (PKC), Rho kinase (Rho K) or by increases in Ca^{2+}. PLC, phospholipase C; IP3, inositol 1,4,5-triphosphate; DAG, diacylglycerol; LTCC, L-type calcium channel. Modified from Brinks and Echart, 2010.

GRK2 seems to have an important role in the cardiovascular system. It is known that heart failure is associated with sympathetic nervous system hyperactivity. In this context, enhanced GRK2 levels would be initially beneficial to compensate β-adrenergic overstimulation. However, over time, this would become maladaptative finally leading to decrease cardiac contractility and survival (Murga et al., 2019). Moreover, changes in GRK2 levels and/or activity can mediate important effects in vascular function and structure that have been classically explained by GRK2-dependent desensitization of different GPCRs such as Ang II, ET-1, or adrenergic receptors (Brinks and Eckhart, 2010; Murga et al., 2019). Indeed, upregulated GRK2 levels were found in vessels in human and murine hypertension (Eckhart et al., 2002; Izzo et al., 2008, Avendaño et al., 2014). More recently, a role for GRK2 in insulin signalling have also been described (Murga et al., 2019). Specific aspects on the role of GRKs in the context of hypertension and obesity will be discussed in other sections of this manuscript.

5. Immune system.

Immune system is classically known for being able to discriminate between self and non-self and then fight against pathogen microorganisms. The cells of the immune system origin, and some also mature, in the bone marrow, and then, they migrate to different peripheral tissues. The hematopoietic pluripotent stem cells of the bone marrow can transform into two more specialized cells: the common myeloid progenitor and the common lymphoid progenitor (**Figure 9**) (Janeway et al., 2001).

Apart from being precursors of all the cellular elements of blood, including platelets and erythrocytes, the **myeloid progenitor** is the precursor of granulocytes (including neutrophils, eosinophils and basophils), macrophages, dendritic cells and mast cells of the immune system (**Figure 9**) (Janeway et al., 2001). **Granulocytes** are relatively short-lived and their levels increase when they leave the blood to migrate to the sites of infection or where an inflammation process is taking place. **Neutrophils** are phagocytic granulocytes and they represent the most numerous cellular component of the innate immune response, the faster but simple response of the immune system. **Eosinophils** and **basophils** are also granulocytes with an important role in

defence against parasitic infections and allergic inflammation. **Dendritic cells** are responsible of presenting the antigen for recognition by lymphocytes. **Mast cells** mainly reside near small blood vessels and they can release substances that affect vascular permeability, although they are best known for their role in allergic responses. They can recruit eosinophils and basophils, which are also exocytic.

Macrophages are phagocytes that are widely distributed in the body tissues, playing a critical role in innate immunity. They can also recruit other phagocytic cells from the blood. Macrophages are the mature form of monocytes, which circulate in the blood and continuously differentiate into macrophages after migration to different tissues. In general terms, in response to cell/cell or cell/molecule interaction, macrophage functionality within the hosting tissues can polarize to M1-like (pro-inflammatory) and/or M2-like (anti-inflammatory), although it is now accepted the existence of a sophisticated framework of functional and phenotypic differentiation (Harwani, 2018). M1 macrophages activate and guide Th1 T-lymphocytes and M2 macrophages are associated with induction of Th2 T-lymphocyte responses (Harwani, 2018). Moreover, M1 macrophages are able to produce ROS, which can limit NO bioavailability. Classically, IFNγ induces the differentiation of M1-macrophages, while IL-4 induces the anti-inflammatory M2 macrophages (Harwani, 2018). Apart from this classical stimuli, novel stimuli for macrophage polarization are being described, including some closely related with CVD (see below).

The **lymphoid progenitor** produces lymphocytes, the cells responsible for adaptive immunity (**Figure 9**) (Janeway et al., 2001). There are two major types of lymphocytes: **B cells**, which after activation differentiate in the bone marrow into plasma cells that secrete antibodies; and **T cells**, which differentiate in the thymus into effector T cells with a variety of functions. Once they have completed their maturation, both types of lymphocytes enter the bloodstream, to finally migrate to the peripheral lymphoid organs. There are two major types of T-cells, differentiated by their membrane proteins, T helper cells are CD4+ while cytotoxic T lymphocytes are CD8+. **Natural killer cells** are part of the innate immune system. They are able to recognize and kill some abnormal cells, as tumor cells and virus-infected cells.

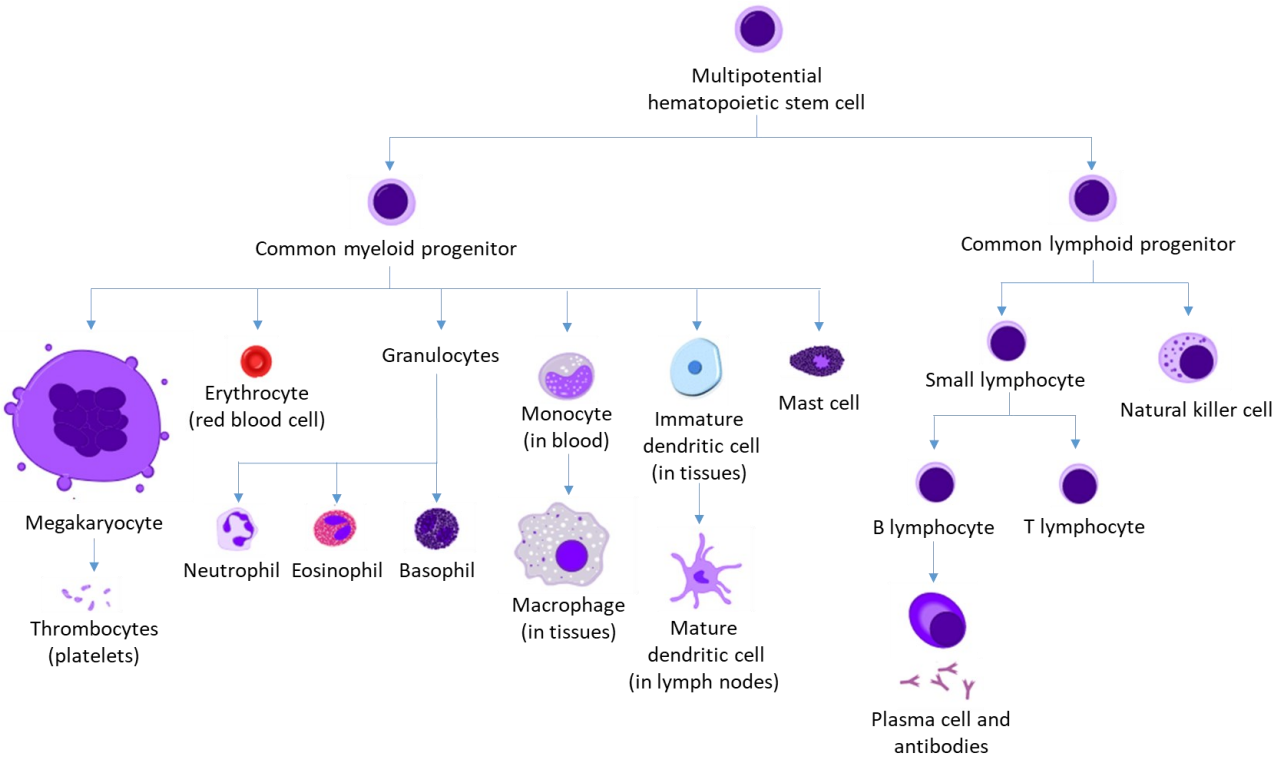


Figure 9. Myeloid and lymphoid cells. Modified from A. Rad and Mikael Häggström, M.D. Hematopoiesis (human) diagram.

Our understanding of the immune system has evolved over the past decades until the recognition that it is a dynamically regulated organ that plays a pivotal role in several physio-pathological processes, including organ development, tissue homeostasis and repair (Sattler and Kennedy-Lydon, 2017). Stressed tissues release alarm signals that activate antigen-presenting cells. Danger signals are recognized by the innate immune system through different receptors (pattern recognition receptors (PRR)) such as Toll-like receptors (TLR), which activate the production of cytokines and attract leukocytes to the site of lesion (Dal Lin et al., 2015). During the cellular response to stress (called universal cell danger response (CDR)), damaged cells and the immune system activate a sterile inflammation (or inflammosome), which is responsible for the activation of inflammatory processes. The onset of chronic diseases can be explained because of the abnormally activation of the CDR beyond the injury resolution, altering whole-body metabolism, leading to multiple organ dysfunction (Ehlers and Kaufmann, 2010; Cho and Blaser, 2012; Naviaux, 2014; Tang et al., 2017) and fibrosis (Sattler and Kennedy-Lydon, 2017). In this sense, there is increasing evidence about a continuous flow of molecular exchange between the cardiovascular and the immune system. However, how this communication takes place it is not fully understood (Dal Lin et al., 2019).

The role of innate immune cells (monocytes, macrophages and neutrophils) together with lymphocytes in the onset and development of atherosclerosis has been well explored by their

contribution to plaque instability (Sattler and Kennedy-Lydon, 2017). In addition, accumulating evidence supports a role for tissue macrophages and lymphocytes in hypertension (Harwani, 2018; Drummond et al., 2019) and obesity-associated metabolic diseases, such as insulin resistance (Chawla et al., 2011). Moreover, neutrophils have recently emerged as important modulators of CVD (Kossmann et al., 2014; Silvestre-Roig et al., 2020).

In general terms, the increase in inflammation usually begins after the endothelial activation by immune system and the expression of various adhesion molecules to attract different immune cells (Libby, 2006). These immune cells, as well as tissue resident cells, amplify the inflammatory signal by the augmented expression of cytokines (Kofler et al., 2005; Libby, 2006) which encompasses a broad category of small soluble proteins, such IFNs, ILs, chemokines, lymphokines, and TNFs. Interestingly, these cytokines are mainly produced by B and T lymphocytes, but also by activated ECs, VSMCs, fibroblasts, neurons or adipocytes (Trayhurn and Wood, 2004), Main pro-inflammatory cytokines include IFNγ, TNFα, IL-1, IL-6, IL-8 or IL-12 whereas anti-inflammatory compounds are TGF-β, IL-4, IL-10, IL-11 or IL-13, among others (**Figure 10**). A disbalance between pro- and anti-inflammatory mediators is considered as a pathophysiological mechanism common to different CVD, and this seems to be closely related to endothelial dysfunction (Kofler et al., 2005; Vicenová et al., 2009; Karbach et al., 2014) (**Figure 10**). Main transcription factors involved in cytokine generation at the vascular level are NFκB and NFAT. Besides classical inflammatory stimuli, they are activated by Ang II or ET-1 and participate in endothelial dysfunction and vascular remodelling observed in CVD (Esteban et al., 2011; Su et al., 2021). The role of specific cytokines in vascular damage in hypertension and obesity will be discussed in sections 7.2. and 8.2., respectively.

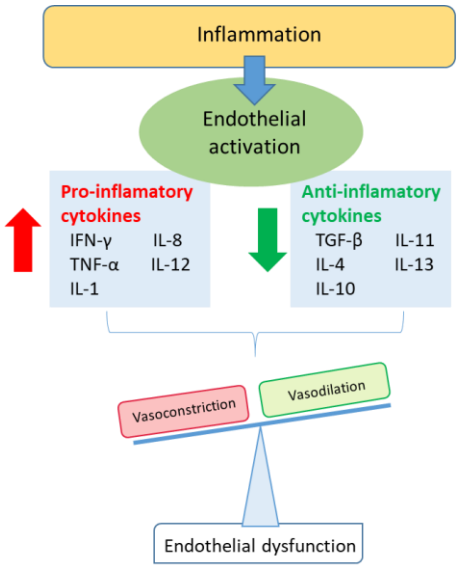


Figure 10. Effect of the decompensation between pro- and anti-inflammatory cytokines after endothelial activation in an inflammatory situation.

6. Interferon-stimulated gene-15 (ISG15).

IFNs-stimulated gene-15 (ISG15) encodes an ubiquitin-like protein that is produced as a 17 kDa precursor with two ubiquitin-like domains (**Figure 11**). So far, ISG15 has only been found in vertebrates (Zhang and Zhang, 2011). It is expressed mainly in monocytes, lymphocytes, and neutrophils, but also in dendritic cells, NK cells, epithelial-derived cell lines, fibroblasts and in several cell tumors (Knight and Cordova, 1991; Bogunovic et al., 2012; Tecalco Cruz and Mejía-Barreto, 2017; Albert et al., 2018). ISG15 expression was also observed in human microvascular endothelial cells (HMECs) after infection with Rickettsia conorii, the causative agent of Mediterranean spotted fever (Colonne et al., 2011) and in cardiomyocytes, where ISG15 expression was increased in patients with viral cardiomyopathy (Rahnefeld et al., 2014). However, to date very little is known on the role of the ISG15/USP18 system at the vascular level.

The ISG15 protein can be found in two different states: as a free protein (either intracellular or extracellular) or conjugated to substrate proteins, a post-translational modification termed *ISGylation* (**Figure 11**). Both ISG15 and enzymes involved in ISGylation, are induced in response to different IFNs, mainly type I (α and β) but also type II (IFNγ), and type III (IFNλ), as well as in response to lipopolysaccharides or TNFα (Levy et al., 1990; Jeon et al., 2010; Zhang and Zhang, 2011; Chairatvit et al., 2012; MacParland et al., 2016; Albert et al., 2018; Lertsooksawat et al., 2019).

ISGylation is a reversible post-translational protein modification, carried out on *de novo* synthesized proteins. ISGylation requires a cascade of enzymatic reactions to bind ISG15 to a lysine residue of the substrate protein (Zhang and Zhang, 2011; Albert et al., 2018) (**Figure 11**). ISGylation resembles ubiquitination and requires an E1 activating enzyme (UbE1L), an E2 conjugating enzyme (UbCH8), and E3 ligases (HERC5 in humans, HERC6 in mice) (Durfee and Huibregtse, 2012). Moreover, the ISG15 system operates in a similar way or even overlapping with the ubiquitin system (Dastur et al., 2006; Zou and Zhang, 2006). Although ISG15 does not target its substrates for degradation, there seems to be an interaction with proteasome, since increased ISG15 conjugates are observed after inhibition of the proteasome (Liu et al., 2003a). ISGylation is a reversible modification, carried out by USP18, an ISG15-specific protease (Honke et al., 2016). In addition, USP18 acts as a negative regulator of type I IFN-induced responses (Basters et al., 2018) (**Figure 11**). Human **intracellular ISG15** acts as a stabilizer for this action of USP18, since lack of intracellular ISG15 leads to unstable levels of USP18 (Francois-Newton et al., 2012; Zhang et al., 2015). This results in a persistent signalling of the pathways triggered by

type I IFN receptor, specially the JAK-STAT (Stark and Darnell, 2012). At the clinical level, this increase in type I IFN signalling due to the lack of intracellular ISG15 seems to be the responsible for cerebral calcifications (Zhang et al., 2015) and ulcerating skin lesions (Martín-Fernández et al., 2020) observed in some patients with inherited human ISG15 deficiency. The USP18 protein is expressed in liver, spleen, thymus, bone marrow, adipose tissue, and lungs. Furthermore, peritoneal macrophages and monocyte-derived macrophages express high levels of USP18 (Honke et al., 2016).

As noted above, **free ISG15** is secreted from cells and it has been detected in blood and urine (D'Cunha et al., 1996a; Hoan et al., 2016). This occurs even though ISG15 lacks a signal peptide for secretion. The mechanisms involved in ISG15 secretion are unknown although some specific determinants for secretion, including identification of specific aminoacids (L72A, S83A and L85F), has been shown (Swaim et al., 2020). Moreover, it has been observed that in Mycobacterium tuberculosis-infected macrophages, ISG15 can be released in microvesicles (Hare et al., 2015) and, in the context of HIV infection, the ISG15 protein was found in exosomes released by TLR3-activated microvascular brain ECs (Sun et al., 2016). More recently, it has been reported that NS1B, a protein that binds to ISG15 and ISGlated proteins (Yuan and Krug, 2001; Zhao et al., 2016), was involved in blockade of ISG15 secretion because the binding of NS1B occludes L72, one of the residues that are critical for ISG15 secretion (Swaim et al. 2020). Interestingly, ISG15 secretion is increased in M2 macrophages and in tumor-associated macrophages (Sainz et al., 2014). Moreover, lymphocytes and epithelial cells are also able to secrete ISG15 (Swaim et al., 2020), suggesting that the ISG15 secretion mechanism is operating in a wide range of cell types and conditions.

Free extracellular ISG15 protein acts as a modulator of neutrophils, monocytes, NK cells and dendritic cells (**Figure 11**), facilitating the release of cytokines such as IL-8 and IFNγ, or the anti-inflammatory IL-10, thus generating a positive feedback on the expression of ISG15 although the receptor involved was largely unknown (Dos Santos and Mansur, 2017).

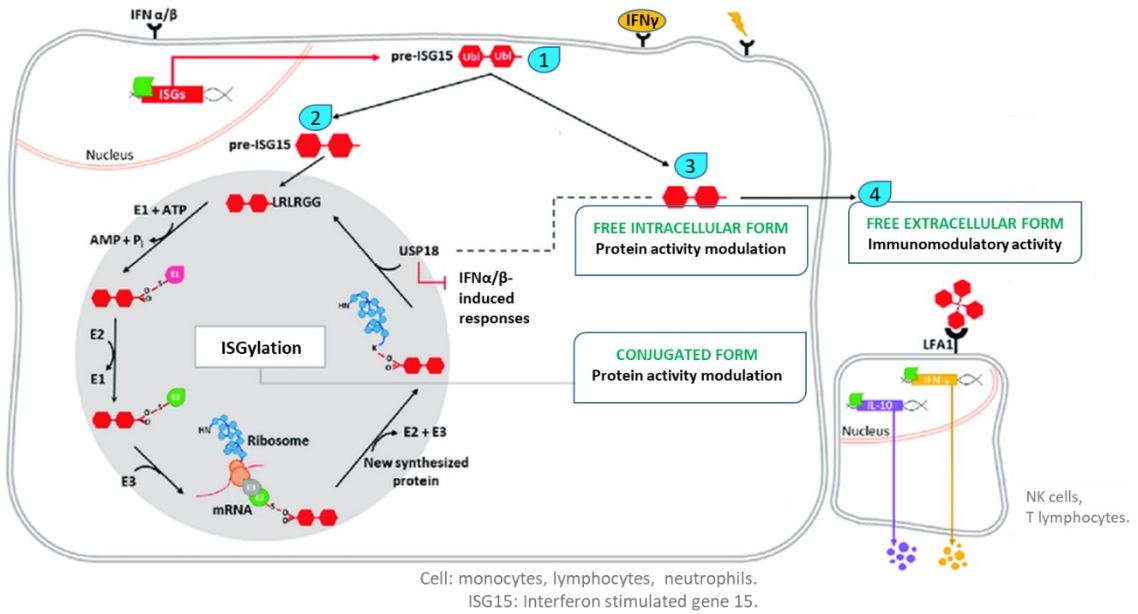


Figure 11. ISGylation process and intracellular/extracellular ISG15. Different stimuli such as IFNs trigger the expression of ISG15, which is produced as a 17 kDa precursor with two ubiquitin-like domains (1). The intracellular ISG15 protein can be free (3) or conjugate with *de novo* synthesized proteins in the process called ISGylation (2). ISGylation can be reversible by the action of the USP18 protease, which also regulates IFN-mediated signalling (2). The free form can also be secreted from the cell and it acts as a cytokine, binding to the LFA-1 integrin receptor on the surface of NK cells or T lymphocytes, causing the release of IFNγ and IL-10 (4). This extracellular form of ISG15 can form dimers or multimers with the aim of modulating cytokine levels. Modified from Albert et al., 2018.

6.1. Receptor for free ISG15.

A receptor for free ISG15 was recently discovered. This is the leukocyte function-associated antigen-1 (LFA-1), the classic receptor for ICAM-1 (Swaim et al., 2017), which is involved in the recruitment and adhesion of immune cells and is mainly expressed in T and B lymphocytes, macrophages, neutrophils, and NK cells (Abram and Lowell, 2009). Specifically, in NK cells and T lymphocytes free ISG15/LFA-1 pathway promotes the secretion of IFNγ and IL-10 (**Figure 11**) through Src-family kinase activity (Swaim et al., 2017). Similar results were observed in tumour associated macrophages (Chen et al., 2020) where ISG15 induced M2-like phenotype through interaction with LFA-1, engagement of Src- family kinase signal, and the subsequent secretion of CCL18. Also, ISG15/LFA pathway has a role in susceptibility of mouse corneas to P. aeruginosa infection (Gao et al., 2020). The identification of LFA-1 as one ISG15 receptor revealed the basis of ISG15 signalling, but further investigation is still warranted to identify the cell types and immunologic signals that are implicated on the ISG15-mediated responses in the extracellular space. Particularly, there is a paucity of information on the role of ISG15 in non-immune cells.

6.2. Functions of ISG15.

The biological functions of ISG15 appear to be very complex and diverse. In general, ISG15 has been extensively studied in viral infections where it has a protective role (Kunzi and Pitha, 1996; Yuan and Krug, 2001; Lenschow et al., 2007; Guerra et al., 2008; Hsiang et al., 2009). Moreover, ISGylated proteins seem to have an important role in the formation of tumors (Zhang and Zhang, 2011) and more recently, a role for ISG15 in obesity was found (Yan et al., 2021). ISG15 can bind hundreds of proteins, but the biological consequence of this interaction is only known for a small number of these interactions (Dos Santos and Mansur 2017; Albert et al., 2018). For example, the first molecular target of ISGylation that was identified is serine protease inhibitor 2a, which has an important role regulating intracellular proteases in antigen-presenting cells (Hamerman et al., 2002), thus providing information on the relationship of ISG15 with inflammation. Moreover, ISGylation can inhibit or activate the function of many proteins involved in viral infection but also in the progression of cancer, in the response to hypoxia or in the secretion of exosomes, among other processes (Villarroya-Beltri et al., 2017; Albert et al., 2018). At the cellular level, ISGylated proteins affect aminoacid, protein and carbohydrate metabolism, cell cycle, cell proliferation and differentiation, cell structure and motility, muscle contraction, intracellular protein trafficking, protein translation, ubiquitination or autophagy (Giannakopoulos et al., 2005, Villarroya -Beltri et al., 2017). Identification of ISGylated proteins require specific mass spectrometry studies. Thus, some proteins conjugated to ISG15 include proteins induced by type I IFNs, such as PKR and RIG-I, and some regulatory proteins involved in IFN signaling, such as Jasus Kinase 1/2 (JAK1/2) and STAT1 (Hsiao et al., 2010; Jeon et al., 2010). Interestingly, in the cardiovascular system, the JAK-STAT pathway is activated by Ang II, mediating several of its deleterious effects (Satou and González-Villalobos, 2012). As mentioned, there is little information on the role of ISG15 pathway at the cardiovascular level. ISGylation was described as a critical mechanism in the response of the innate immune system of cardiomyocytes against viral infections, decreasing inflammatory cardiomyopathy, cardiac damage and mortality (Rahnefeld et al., 2014). Moreover, cardiomyocyte-specific expression of constitutively active IκB kinase 2 was sufficient to activate the ISG15 pathway and caused widespread protein ISGylation in a NFκB-dependent manner, but the pathophysiological implication of this process was not reported (Maier et al., 2012).

The role of free ISG15 protein is less known. As mentioned earlier, in humans, the intracellular free ISG15 protein ensures the regulation of USP18-dependent IFNα/β and the prevention of IFNα/β-dependent autoinflammation (Zhang et al., 2015). Regarding extracellular ISG15, previous studies defined this secreted form as an IFNγ inducing molecule, specifically in

peripheral blood mononuclear cells (PBMCs), especially CD4+ and CD8+ lymphocytes (Knight and Cordova, 1991; Recht et al., 1991; D'Cunha et al., 1996a, 1996b), and this IFNγ production is independent of ISGylation (Bogunovic et al., 2012). Importantly, the lack of secreted ISG15 in patients with ISG15 deficiency accounts for their low levels of IFN-γ secretion ex vivo, and, thus, for their Mendelian susceptibility to mycobacterial disease phenotype in vivo (Bogunovic et al., 2012). More recently, the same effect was observed in NK cells (Bogunovic et al., 2012; Swaim et al., 2017) and human PBMCs, where ISG15 releases relevant proinflammatory cytokines such as CXCL1, CXCL5, CXCL8, CCL20, IL1, IL6, TNF, and IFNγ (Ostvik et al., 2020). Additionally, in HIV infected patients, the ISG15 protein released in exosomes from activated brain microvascular EC appeared to be involved in the transport of antiviral molecules (Sun et al., 2016).

Several viral de-ISGylases were found to reverse intracellular ISGylation, thus enhancing extracellular ISG15 secretion. Known viruses to use this mechanism include coronaviruses (such as SARS-CoV2), nairoviruses and foot-and-mouth disease viruses, suggesting that extracellular ISG15 secretion and further ISG15 signalling associated to the release of IL-8 and IFNγ could be the responsible, at least in part, for the cytokine release syndrome or 'cytokine storm' observed upon SARS-Cov2 infection causing COVID-19 (Swaim et al., 2020). The simplest explanation for the fact that intracellular ISG15-conjugation inhibits secretion, is that ISGylation limits the pool of free ISG15 available for secretion (Swaim et al., 2020). Notably, the role of the ISG15 pathway in hypertensive CVD remains completely unknown.

7. Hypertension and functional and structural vascular alterations.

Hypertension induces alterations in the function and the structure of the vasculature that in turn can contribute to the increase in blood pressure.

These alterations mainly include vascular remodelling, endothelial dysfunction and increased vasoconstrictor responses (Schiffrin, 2012), which have prognostic value for CVD (Perticone et al., 2001; Rizzoni et al., 2003).

The classic hypertensive aortic phenotype is characterized by vascular wall degeneration and calcification and increased aortic diameter (Schiffrin, 2012), but vascular changes with hypertension are more complex and depend on the vascular bed. In primary hypertension, large artery remodelling is characterized by an increase in intima–media thickness (IMT) (about +15–40%). Moreover, in proximal elastic arteries is common a lumen enlargement, and no changes in the lumen diameter of distal muscular arteries are usually observed (Laurent and Boutouyrie,

2015). During hypertension, in large arteries, there is an acceleration of the outward hypertrophic remodelling and increased stiffness is also observed with aging (Mitchell et al., 2003; Schiffrin, 2012). In advanced hypertension, the elastic laminae of large arteries undergo duplication and fragmentation, with increased collagen and fibronectin deposition, contributing to increased stiffness. Moreover, VSMC hypertrophy has been reported in the aorta (Laurent and Boutouyrie, 2015). In resistance arteries, hyperplasia, hypoplasia or no changes of VSMCs embedded in a thicker vascular wall is found in different arteries from different models of hypertensive rodents (Briones et al., 2009; Schiffrin, 2012; Roque et al., 2013).

As mentioned earlier, eutrophic remodelling is usually found in primary hypertension, both in humans, SHRs and mesenteric arteries from Ang II-infused mice probably due to inward growth with peripheral apoptosis or from vasoconstriction embedded in an expanded ECM (Bakker et al., 2002; Briones et al., 2009; Schiffrin, 2012; Marchesi et al., 2013; García-Redondo et al., 2016). Indeed, there is deposition of collagen and fibronectin with increased collagen:elastin ratio in small vessels from hypertensive humans and rodents (Schiffrin, 2012) which can be induced by ET-1 (Pu et al., 2003), Ang II and aldosterone (Neves et al., 2003; Avendaño et al., 2018). Hypertrophic remodelling has been described in secondary hypertension such as in renovascular hypertension, primary aldosteronism, or in pheochromocytoma, but also in hypertension associated with diabetes mellitus. In mineralocorticoid hypertension in rodents and in salt-sensitive Dahl rats, in both of which the ET system is activated, remodelling of small arteries is also hypertrophic (Schiffrin, 2012). Small artery remodelling may be the first manifestation of target organ damage, at least in human hypertension, because in a serie of patients, 100% of stage I hypertensive subjects show small artery remodelling, whereas only 60% have endothelial dysfunction (Park and Schiffrin, 2001).

Dysfunction of the endothelium is often associated with elevation of blood pressure but it is not entirely clear whether this is a cause or a consequence of blood pressure elevation. There is overwhelming evidence that in hypertension, endothelial dysfunction is manifested as reduced endothelium-dependent vasodilation with no general modifications of vascular responses to exogenous NO (Brandes, 2014). Endothelial dysfunction is also characterized by an inflammatory phenotype of ECs with increased proliferation, programmed cell death, altered morphology, production of C-reactive protein (CRP), and other inflammatory and thrombogenic mediators, including MCP-1 and plasminogen activator inhibitor 1, upregulated adhesion molecules, and enhanced thrombogenicity and adhesiveness for circulating cells (Endemann and Schiffrin, 2004). This endothelial dysfunction parallels with enhanced responses to various vasoconstrictor agonists including alpha adrenergic or TP agonists among others, although this

clearly depends on the vascular bed and animal model studied (Martínez-Revelles et al., 2013; Wang et al., 2020a).

It is now accepted that activation of RAS, proinflammatory processes, activation of the sympathetic nervous system, and alteration of signalling pathways mediated by GPCRs contribute to the functional and structural alterations associated with hypertension (Belmonte and Blaxal, 2011; Savoia et al., 2011; Xiao and Harrison, 2020). This will be discussed in detail in the next sections.

7.1. Role of ROS in vascular function and remodelling in hypertension.

Several factors of the hypertensive milieu, including Ang II, increased sodium, catecholamines, and altered mechanical forces, enhance the cellular production of ROS (Xiao and Harrison, 2020). Increased levels of ROS have been observed in hypertensive patients (Redón et al., 2003; Minuz et al., 2004; Ahmad et al., 2013; Carrizzo et al., 2013; Higashi et al., 2014), and in plasma and vessels from animal models of hypertension such as SHR rats, deoxycorticosterone acetate (DOCA)-salt rats and C57Bl6 mice infused with Ang II (Álvarez et al., 2007; Viel et al., 2008; Agarwal et al., 2009; Martínez-Revelles et al., 2013; Griendling et al,. 2021).

As mentioned earlier, Ang II is able to induce ROS production mainly through NOXs and these oxygen species activate signaling pathways such as kinases (MAPK, Akt, c-Src or ERK1/2), transcription factors (NFκB, AP-1, STAT3 or Nrf2), MMP, ion channels (Ca^{2+} channels or Na^{+} channels) or several genes that codify cytokines, chemokines or growth factors. These signaling pathways have important roles in cell growth, angiogenesis, migration, proliferation promoting vascular dysfunction (Griendling et al., 2021). Apart from NOX, the mitochondria produce excess of ROS in hypertensive patients and animal models, and there are feedforward mechanisms whereby ROS from NOX can stimulate radical formation in the mitochondria and viceversa (Dikalov and Dikalova, 2019). A reciprocal relationship between ROS and COX-2 was also previously described by our group and this had consequences on vascular dysfunction in hypertension (Martínez-Revelles et al., 2013). Moreover, uncoupled NO synthase and xanthine oxidase have also been implicated in the ROS formed in hypertension (Xiao and Harrison, 2020).

There is overwhelming literature showing that ROS are involved in the functional alterations of the vasculature observed in hypertension. Thus, studies using pharmacological approaches with antioxidants or inhibitors of the different sources of ROS, and studies using transgenic mouse models for NOX subunits and other enzymes involved in ROS generation, seem to demonstrate that, in general, these strategies normalize either the enhanced vasoconstrictor responses, the impaired endothelium-dependent vasodilation or both (Daiber and Chlopicki, 2020; Touyz et al.,

2020; Griendling et al., 2021). For example, our group previously demonstrated in *ex vivo* and *in vivo* studies with animal models of hypertension that ROS blockers such as apocynin, tempol or mito-tempo, reduced the augmented vasoconstrictor responses induced by phenylephrine or serotonin and/or improved endothelial function in SHR or Ang II-infused mice (Álvarez et al., 2008; Martínez-Revelles et al., 2013; Hernanz et al., 2015; Avendaño et al., 2018). Also, a number of studies suggest that ROS produced by NOX1 and NOX5 decrease endothelial relaxation, with NOX5 also increasing vasoconstriction (Griendling et al., 2021). Interestingly, ROS from NOX4 might increase endothelial relaxation, attributable to H_2O_2 production (Griendling et al., 2021). Mechanistically, the most accepted theory assumes that excessive $O_2^{\cdot-}$ reacts with NO facilitating ONOO- formation that reduces NO bioavailability and produces nitrosative stress at the vascular level (Lyle and Griendling, 2006; Paravicini and Touyz, 2008).

As discussed, ROS activate cellular pathways responsible for the proliferation and migration of VSMCs, the generation of matrix proteins, and the activation of MMPs (Hernanz et al., 2014). This impact in vascular remodelling and altered vascular mechanics as has been shown in many studies again using pharmacological or genetic strategies (Touyz et al., 2003; Li et al., 2013; García-Redondo et al., 2016; Griendling et al., 2021). For example, in response to Ang II, NOX-$1^{-/-}$mice showed a marked reduction in aortic media hypertrophy, and this reduction was due to a marked decrease in ECM accumulation and not to changes in the number of VSMCs (Gavacci et al., 2006). In general, NOX1-derived ROS facilitate vascular remodelling by eliciting dedifferentiation of VSMCs and by inducing its proliferation and migration. However, NOX4 seems to preserve smooth muscle phenotype although a role in proliferation and migration has also been described. Thus, depending on the disease model or the specific cell location, beneficial or deleterious effects of NOX4 can be found (García-Redondo et al., 2016).

7.2. Role of inflammation in vascular function and remodelling in hypertension.

During the last decades convincing evidence have demonstrated the role of different components of the innate and adaptive immune systems as factors that contribute to the development of hypertension. Specifically, the role of T lymphocytes in hypertension, as well as in the accompanying endothelial dysfunction, has been demonstrated (Seaberg et al., 2005; Guzik et al., 2007; Harrison et al., 2010; Drummond et al., 2019). Using murine models of hypertension, Guzik et al. were the first to demonstrate dependence of Ang II hypertension on the presence of T-lymphocytes (Guzik et al., 2007). Moreover, Ang II-induced hypertension was reduced by around 50% in $CD8^{-/-}$ mice (Trott et al., 2014), and in a small study of 45 hypertensive patients, Ji et al demonstrated a significant increase in circulating Th1 and Th17 T-lymphocytes,

in contrast to a dramatic decrease in Th2 T-lymphocytes (Ji et al., 2017). The mechanism by which T cells promote vascular damage in hypertension is being actively investigated. It is known that CD4+ T cells, are activated by various hypertensive stimuli such as high salt concentration, ROS, or Ang II (Harrison et al., 2010). In general, once these cells have been activated, they differentiate into T-helper phenotypes 1 or 2 (TH1 or TH2). Cells polarized towards the TH1 phenotype produce proinflammatory cytokines IFNγ, IL-2, TNFα, and TNFβ (Harrison et al., 2010). In this sense, various studies have shown that Ang II infusion in mice is associated with high IFNγ expression in vascular lesions (Harrison et al., 2010), heart (Han et al., 2012; Markó et al., 2012), vascular endothelium (Kossmann et al., 2013), smooth muscle (Kossmann et al., 2013), and kidney (Kamat et al., 2015) with important functions in the damage caused by hypertension. Furthermore, IFNγ induces oxidative stress and endothelial dysfunction (Mikolajczyk et al., 2016) and IFNγ knockout mice are protected against cardiac damage and endothelial dysfunction induced by Ang II (Han et al., 2012; Markó et al., 2012; Kossmann et al., 2013). Increased TNFα is observed in many pathophysiological conditions, including hypertension (Zhang et al., 2009) and it has a role in vascular function since a neutralizing antibody to TNFα decreased the formation of ROS and improved NO-mediated vasodilation (Zhang et al., 2009). These findings highlight the role of IFNγ and TNFα in cardiovascular damage associated with hypertension. The relationship between ROS and inflammation at the vascular level is accepted, non only because these proinflammatory cytokines induce oxidative stress in vascular tissues but also because ROS released from inflammatory cells can affect vascular homeostasis. For example, it has been recently described that NOX2 in regulatory T cells promotes Ang II-induced cardiovascular remodelling (Emmerson et al., 2018). The contribution of different subsets of T cells or specific cytokines has been studied using transgenic animal models or neutralizing antibodies (Drummond et al., 2019). Moreover, administration of recombinant cytokines has been used as a research strategy. For example, in a recent study we found that IL-17 infusion increased blood pressure and produced inward remodelling of small mesenteric arteries, and that treatment with an IL-17A neutralizing antibody diminished vascular remodelling in a model of Ang II infusion (Orejudo et al. 2020). Additionally, although less studied, several evidence suggests a role for B cell activation and IgG production in the vascular remodelling and endothelial dysfunction that contribute to vascular stiffening and exacerbation of hypertension (Drummond et al., 2019).

Enhanced M1 markers were found in vascular tissues from mice infused with Ang II for two (Qian et al., 2014) and four weeks (Qi et al., 2019; Ye et al., 2019). A causal role for monocytes and macrophages in the development of hypertension, vascular remodelling, and endothelial

dysfunction has been demonstrated in mice deficient in macrophage colony stimulating factor, which renders them deficient in macrophages (De Ciuceis et al., 2005; Ko et al., 2007), and after selective ablation of lysozyme M-positive (LysM(+)) myelomonocytic cells by low-dose diphtheria toxin in mice with inducible expression of the diphtheria toxin receptor (LysM(iDTR) mice) (Kossmann et al., 2014; Wenzel et al., 2011). Moreover, we recently reported that macrophage-conditioned media from Ang II infused mice induced endothelial dysfunction through the release of IL-1β and prostaglandins derived from COX-2 (Olivencia et al., 2021). M2-like macrophages were also found within the vascular wall after Ang II infusion (Moore et al., 2015) and they seem to promote vascular stiffening and ECM remodelling, including collagen deposition, adventitial fibrosis, and elastin loss (Moore et al., 2015), confirming that either M1- or M2-like macrophages have a role in vascular dysfunction in hypertension.

One big family of receptors whose activation leads to inflammatory cytokine production through NFκB, is the PRR family. Within this family, TLR4 stands out, because its expression is augmented in several models of hypertension and its inhibition with a neutralizing antibody prevents hypertension associated vascular remodelling, stiffness, hypercontractility and endothelial dysfunction, through inhibition of oxidative stress (De Batista et al., 2014; Hernanz et al., 2015).

In response to a variety of stimuli, including ROS, inflammatory cytokines, mechanical forces, and catecholamines, EC express increased levels of chemokines, selectins, and adhesion molecules, including ICAM-1 and VCAM-1 which are produced not only by ECs, but also by VSMCs. Monocytes possess ligands, including very late antigen 4 (VLA4), LFA-1 and the macrophage antigen 1 (MAC1) that bind to the receptors on the surface of EC and promote initially rolling, then adhesion, and ultimately transmigration. Transmigrated monocytes can transform to inflammatory macrophages, monocyte-derived dendritic cells, or can exist in a minimally differentiated but activated state and can re-emerge as activated circulating monocytes (**Figure 12**) (Xiao and Harrison, 2020). Ang II-induced hypertension was associated with an increase in vascular ICAM-1 expression, and this was attenuated by inhibiting NOX (Liu et al., 2003b). Recently, Lang et al. reported that an ICAM-1 neutralizing antibody markedly reduced hypertension, improved vascular function, reduced vascular hypertrophy and attenuated vascular inflammation in mice infused with Ang II (Lang et al., 2020), confirming the role of these adhesion molecules in hypertensive vascular damage. The endothelial expression of VCAM-1 is stimulated by ROS and altered mechanical forces, and it is inhibited by NO (Xiao and Harrison, 2020). Therefore, it would be conceivable that VCAM-1 expression by ECs is also increased in hypertension. Indeed, correlations between blood pressure and circulating levels of VCAM-1 have been reported in humans (Zhang et al., 2016; Ciobanu et al., 2019). However,

the specific role of VCAM-1 in vascular damage in hypertension has not been elucidated experimentally likely because embryonic deletion of VCAM-1 is lethal (Xiao and Harrison, 2020).

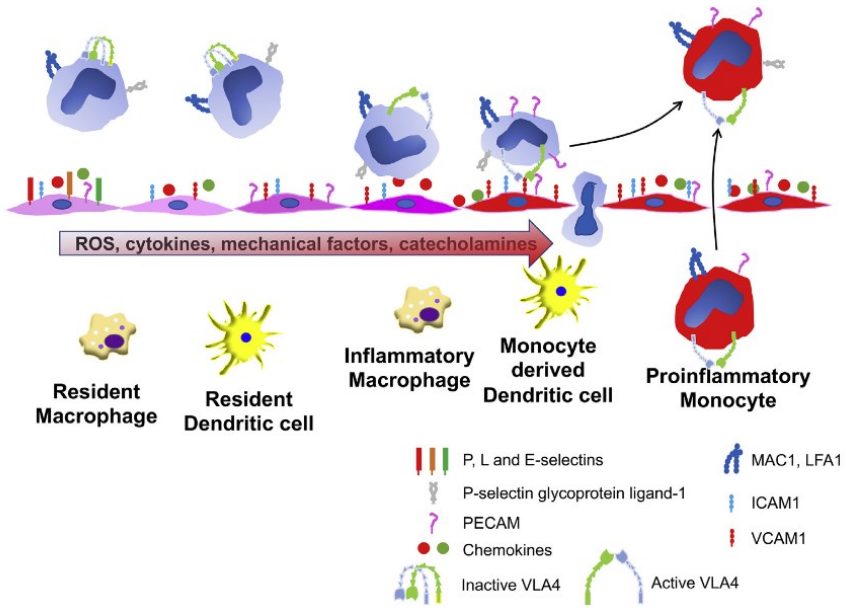


Figure 12. Endothelial leukocyte interactions. Rolling of leukocytes on the endothelium is an early event of inflammation mediated by the interaction of vascular selectins (including E-selectin, L-selectin and P-selectin) with leukocyte glycoprotein ligands (such as P-selectin glycoprotein ligand-1). This is followed by interaction of cell adhesion molecules (CAMs), including the intracellular adhesion molecules (ICAMs) 1-5 and the vascular CAM 1 (VCAM-1), with leukocyte integrins including the leukocyte function-associated antigen 1 (LFA-1), the very late antigen 4 (VLA4) and the macrophage antigen 1 (MAC1). VLA4 undergoes a transformational change that enhances its ability to interact with VCAM-1. After the rolling, adhesion and transmigration occur. Transmigrated monocytes can transform to pro-inflammatory macrophages, monocyte-derived dendritic cells, or can re-emerge as activated circulating monocytes. Resident macrophages and dendritic cells are also present in the interstitium of tissues and have major roles in tissue repair and immune surveillance. PECAM, platelet/endothelial cell adhesion molecule. Taken from Xiao and Harrison, 2020.

7.3. Role of GRK2 in vascular function and remodelling associated with hypertension.

As mentioned earlier, changes in GRK2 levels and/or activity can mediate important effects, which have been classically explained by GRK2-dependent desensitization of different GPCRs (Brinks and Eckhart, 2010). However, GRK2 is implicated in non-GPCR dependent pathways. One example is the described interaction of GRK2 with Akt that inhibits Akt-dependent activation of NO synthase, thus impairing NO production (Liu et al., 2005).

GRK2 expression is increased at the vascular level in animal models of hypertension including chronic Ang II infusion in C57Bl6 mice (Avendaño et al., 2014). We found that partial deletion of GRK2 improved endothelial dysfunction observed in hypertensive mice by restoring the impaired Akt/eNOS pathway and finally NO availability (Avendaño et al., 2014). However, some

reports demonstrated that global GRK2 knockdown may be detrimental due to enhanced renin- and AT_1R-mediated ROS production that can cause renal damage (Tutunea- Fatan et al., 2018) and the development of hypertension with age (Tutunea-Fatan et al., 2015), suggesting that reducing rather that completely abolishing GRK2 levels might be a more suitable strategy to prevent vascular damage in hypertensive disease.

Regarding vascular structure, it is known that activation of many GPCRs controls proliferation/migration of VSMCs and ECM deposition (Althoff and Offermanns, 2015), but the role of GRK2 in the vascular structural and mechanical alterations in hypertension has been poorly explored, and it might depend on the cell-specific location or the experimental model. Thus, partial overall GRK2 deletion prevents vascular hypertrophy and vessel stiffness induced by Ang II (Avendaño et al., 2014), whereas endothelial-specific GRK2 depletion triggers vascular structural abnormalities depending on ROS (Ciccarelli et al., 2013). Underlying mechanisms remain unexplored, but it has been suggested that GRK2 and β-arrestins participate of agonist-stimulated VSMC migration through activation of proliferative and promigratory MAPK such as ERK1/2 (Morris et al., 2012).

8. Obesity and functional and structural vascular alterations.

The risk of CVD increases with BMI (World Health Organization, 2020). Dyslipidemia, glucose intolerance, insulin insensitivity, hypertension, and pro-thrombotic and pro-inflammatory environments play an important role in the pathophysiology of obesity (Stapleton et al., 2008). A high proportion of obese patients develop hypertension, endothelial dysfunction and vascular remodelling (Martínez-Martínez et al., 2021) (**Figure 13**).

Endothelial dysfunction is one of the earliest vascular alterations observed in obesity. Numerous studies have described endothelial dysfunction in different obesity models, including genetic obesity, diet-induced obesity or induction of neuroendocrine alterations (reviewed at Martínez-Martínez et al., 2021). In obese patients, endothelial dysfunction has been observed together with hyperglycemia, inflammation, and oxidative stress (Dimassi et al., 2016). Indeed, most of the studies convey on oxidative stress and inflammation as underlying mechanisms. This topic will be discussed below. Endothelial dysfunction has been demonstrated even in adolescents and children with obesity. Moreover, this altered endothelial function affects not only conduit arteries, such as aorta, but also small arteries including mesenteric, coronary, renal or penile arteries. In the endothelial dysfunction caused by obesity there in an imbalance between

vasodilator (such as NO, EDHF, PGI_2) and vasoconstrictor factors (such as Ang II, ET-1, TXA_2) and also a reduction in eNOS levels or activity (**Figure 13**), which seems to be improved in response to exercise or diet supplements (Prieto et al., 2014; Martínez-Martínez et al., 2021). Furthermore, a recent study showed that endothelial dysfunction and wall thickening observed in aorta of mice fed with high-fructose were associated with a reduction of gut microbiota diversity and a reduction in the abundance of beneficial bacteria (Wang et al., 2020b). All these data support the complexity of the mechanisms involved in the vascular functional alterations that occur in obesity.

Obesity is associated with vascular remodelling, mainly characterized by media thickening and arterial stiffness, not only in conduit arteries such as aorta, but also in small ones such as mesenteric, renal and coronary arteries (Briones et al., 2014; Martínez-Martínez et al., 2014; Gil-Ortega et al., 2016; Martínez-Martínez et al., 2021). In this sense, IMT, a marker of vascular remodelling, is a good predictor of cardiovascular events in obese adults (Heiss et al., 1991; Ciccone et al., 2001;). Vascular remodelling is also observed in subcutaneous small arteries from overweight or obese hypertensive patients, which is accompanied by an increase in fibrosis or a reduction in elasticity (Elfimova et al., 2018). The alteration in vascular structure involves different mechanisms including ECM remodelling or SMC hyperplasia (Briones et al., 2014; Martínez-Martínez et al., 2021). In fact, proliferation of VSMCs is a common characteristic reported in vessels in the context of obesity (Gil-Ortega et al., 2016). This excessive proliferation can contribute to media thickening and it seems to be facilitated by the synthetic phenotype of the VSMCs (characterized by a high proliferation rate and synthesis of ECM and vasoactive factors) (Martínez-Martínez et al., 2021). In this sense, vascular fibrosis is also a common feature associated with obesity that results from the accumulation of type I collagen (Martínez-Martínez et al., 2021). No changes in elastin levels were associated with obesity, but changes in 3D elastin structure with a reduction in fenestra number in the internal elastic lamina has been reported in mesenteric arteries from obese mice (Gil-Ortega et al., 2016). This alteration affects vascular mechanical properties, thereby producing vessel stiffness (**Figure 13**) (Briones et al., 2003; González et al., 2006).

Obesity induces profound changes in PVAT. In obese animals and humans, both PVAT volume and adipocytes size increase in all vascular beds. Also, stromal fraction of this tissue changes towards a more inflammatory profile (Fernández-Alfonso et al., 2017). This obese phenotype shifts the secretory profile of PVAT affecting vascular function (**Figure 13**). While there might be some differences in the different vascular beds, probably, the most common effect of PVAT disfunction in obesity is a loss of the anticontractile effects induced by PVAT, and a greater

proinflammatory phenotype (Fernández-Alfonso et al., 2017). Moreover, an impairment in the endothelium-dependent vasodilator responses has been described in obese aortas in the presence of PVAT (Ketonen et al., 2010). Interestingly, it has been suggested that during initial steps of diet-induced obesity, the increase in leptin levels leads to an overproduction of NO in PVAT, which might preserve vascular function. However, in a long-term diet-induced obesity mouse model the increase in leptin levels correlates with a loss in PVAT-derived NO and eNOS expression, probably due to the development of leptin resistance (Gil-Ortega et al., 2014). Underlying mechanisms responsible for the lack of beneficial effects of PVAT in obesity are enhanced production of proinflammatory cytokines as discussed below.

8.1. Role of ROS in vascular damage in obesity.

ROS has a key role in the vascular damage caused by obesity, affecting both endothelial dysfunction and vascular remodelling and stiffness (**Figure 13**). Upregulation of ROS might be an early event before the development of vascular functional alterations. Thus, in an animal model of HFD for six weeks, obese rats presented aortic fibrosis and vascular inflammation even in the absence of vascular functional alterations, and these structural alterations were accompanied by an increase in $O_2^{\cdot-}$ levels (Martínez-Martínez et al., 2014).

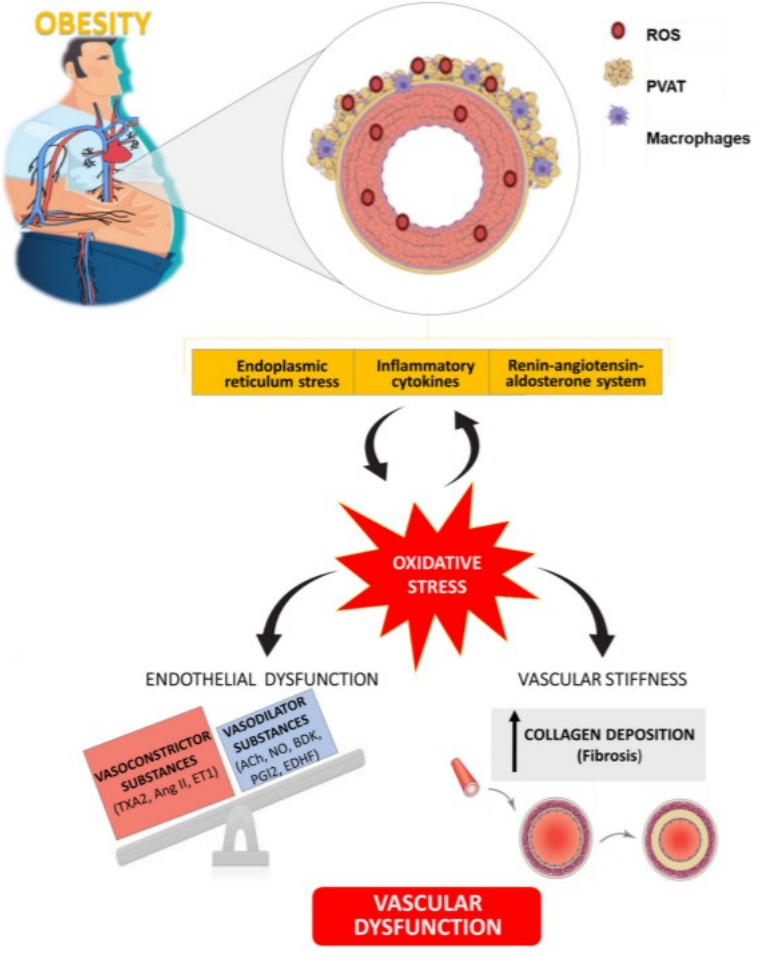


Figure 13. Role of oxidative stress in different mechanisms involved in vascular alterations associated with obesity. Under obesity conditions, an increase in perivascular adipose tissue (PVAT), reactive oxygen species (ROS) and macrophages is observed in vessels. This leads to enhanced endoplasmic reticulum stress, inflammatory cytokines and renin-angiotensin-aldosterone system activation that contribute to endothelial dysfunction and vascular stiffness. TXA2, Thromboxane A2; Ang II, Angiotensin II; ET1, Endothelin 1; Ach, Acetylcholine; NO, Nitric Oxide; BDK, Bradykinin; PGI2, Prostaglandin I2; EDHF, Endothelium-Dependent Hyperpolarizing Factor. Taken from Martínez-Martínez et al., 2021.

A large body of experimental and human evidence has documented that obesity is associated with endothelial dysfunction in different vascular territories and this is mainly due to compromised bioavailability of NO due to oxidative stress from upregulation of all main sources (Prieto et al., 2014; Virdis et al., 2019; Muñoz et al., 2020; Martínez-Martínez et al., 2021). This oxidative stress in obesity might also participates on vascular remodelling and fibrosis although literature on this topic is less abundant (Briones et al., 2014; Martínez-Martínez et al., 2021). Although locally generated ROS can clearly affect vascular function and structure, in the last two decades it has become evident that in obesity, PVAT surrounding all types of arteries is a major source of ROS that deteriorate NO signalling pathways. In fact, studies using PVAT-mounted arteries, PVAT-derived conditioned media and molecular phenotyping of obese PVAT, have clearly shown that PVAT-derived oxidative stress participates in vascular dysfunction in obesity (Fernández-Alfonso et al., 2017; Nosalski and Guzik, 2017). For example, animals treated with HFD showed uncoupling of eNOS and reduction in NO production and increasing $O_2^{\cdot-}$ generation in PVAT, that induced pro-contractile effects (Gil-Ortega et al., 2014; Xia et al., 2016). *Ex vivo* incubation with SOD and catalase restores the anticontractile function of PVAT from obese individuals (Aghamohammadzadeh et al., 2013, 2015). Other study found that PVAT from obese mice showed increased formation of H_2O_2 and $O_2^{\cdot-}$ that impact on the vascular endothelium, since PVAT-induced impairment of endothelium-dependent vasodilation in obese aortas was restored after incubation with the antioxidant Tiron or the H_2O_2 scavenger polyethylene-glycol-catalase (Ketonen et al., 2010). On top of this effect, TNFα derived from PVAT seems to have a key role. Thus, a recent study found that PVAT from obese rats induced endothelial dysfunction that was mediated through increased production of TNFα that activated NOX2 activity (DeVallance et al., 2018), suggesting an interplay between inflammation and oxidative stress in PVAT-dependent vascular damage.

8.2. Role of inflammation in vascular damage in obesity.

Obesity and other states of malnutrition are known to alter the immune function, modifying leukocyte populations and cell-mediated immune responses. In 2003 two studies simultaneously reported that obesity induces macrophage infiltration in adipose tissue in both

mice and humans (Weisberg et al., 2003; Xu et al., 2003). In fact, adipose tissue from lean individuals contains only 5% to 10% macrophages, but these cells represent up to 60% of all adipose tissue cells in diet-induced overweight patients (Berg and Scherer, 2005). Obesity not only increases macrophages infiltration in adipose tissue but causes a shift of macrophage subtypes from M2 to M1, leading to increased levels of proinflammatory cytokines (such as TNFα and IL-6) and ROS, which induce insulin resistance (Lumeng et al., 2007). Indeed, Hotamisligil and colleagues described that adipose tissue from obese mice secretes TNFα, which has a direct role in obesity-induced insulin resistance (Hotamisligil et al., 1993). This was the first functional link between obesity and inflammation, evolving into the concept of metabolic inflammation, which has been widely accepted as an important mechanistic connection between obesity and its complications (Hotamisligil, 2006). After TNFα, it was demonstrated that adipose tissue produces an array of cytokines and chemokines such as IL-6 and MCP-1, among many others, regulating systemic glucose and lipid metabolism (Cao, 2014). Since then, nearly every major type of immune cell has been identified in adipose tissue and found to be involved in metabolic regulation (Feuerer et al., 2009; Liu et al., 2009; Wu et al., 2011).

Local production of adipokines parallels with increased circulating levels of pro-inflammatory proteins in adults, adolescents and children (Weiss et al., 2004; Wärnberg et al., 2007; Gøbel et al., 2012). Specifically, in overweight and obese adults, enhanced levels of TNFα, IL-6 or CRP, have been reported (Festa et al., 2001; Bulló et al., 2003). Several mechanisms seem to contribute to the disbalance of immune system/inflammation in obesity (**Figure 14**). For example, obesity associates with deterioration in the production of adipokines, with increased levels of pro-inflammatory leptin and a reduction of anti-inflammatory adiponectin (**Figure 14**). Non-esterified fatty acids which can be released in response to lipolysis, can also induce inflammation through various mechanisms such as modulation of adipokine production, or activation of TLR or peroxisome proliferator-activated receptors (PPAR) (**Figure 14**). Specifically, the activation of TLR induces the synthesis of inflammatory markers in macrophages and aggravates insulin resistance (Fessler et al., 2009).

Nutrient excess and adipocytes expansion trigger ER stress. That activates a security mechanism known as the unfolded protein response (UPR), which is associated with increased ROS production and expression of different cytokines such as IL-8, IL-6, MCP-1 and TNFα (**Figure 14**) (Gregor and Hotamisligil, 2007). Moreover, adipose tissue expansion in obesity eventually occurs to a point where the development of local vasculature and oxygen supply is insufficient for tissue demands promoting a hypoxic milieu. It was hypothesized that the hypoxic adipocytes would produce inflammatory signals with the purpose of stimulate angiogenesis (Trayhurn and

Wood, 2004; Trayhurn et al., 2010). Moreover, hypoxia response fails to increase adipose tissue vascularization, but it triggers a situation of local fibrosis, contributing to adipose tissue dysfunction (Halberg et al., 2009) (**Figure 14**).

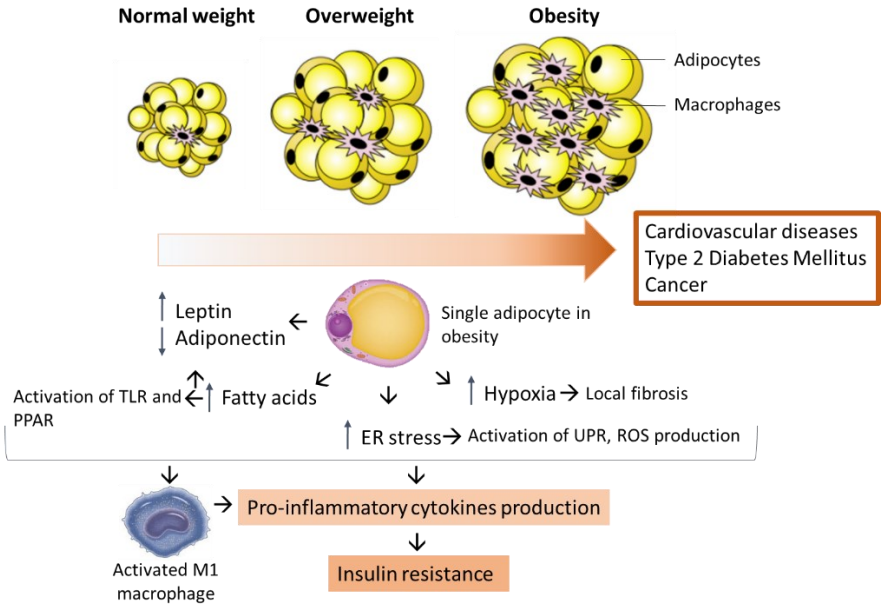


Figure 14. Proposed mechanisms implicated in the immune alterations in obesity. With obesity, the amount and size of adipocytes but also the number of immune cells like macrophages, increase. Hypertrophied adipocytes show altered secretion of adipokines and fatty acids, accompanied by increases in ER stress and hypoxia. In this scenario, macrophages increase their activity releasing pro-inflammatory cytokines that provoke insulin resistance. ER, endoplasmic reticulum; TLR, Toll-like receptors; PPAR, peroxisome proliferator activated receptors; UPR, unfolded protein response; ROS, reactive oxygen species.

This chronic inflammatory status is also reflected locally by the continuous presence of T-lymphocytes and pro-inflammatory macrophages in PVAT and subsequently, by the elevation in proinflammatory cytokines, affecting vascular physiology (Fernández-Alfonso et al., 2017). For example, Apovian et al. found that macrophage infiltration in subcutaneous adipose tissue is associated with systemic endothelial dysfunction and insulin resistance in obese patients (Apovian et al., 2008). As with oxidative stress, extensive literature has shown a deleterious role of inflammation in endothelial dysfunction and vascular remodelling in obesity (Prieto et al., 2014; Gil-Ortega et al., 2016; Virdis et al., 2019; Muñoz et al., 2020; Martínez-Martínez et al., 2021). Because as mentioned, TNFα is the most important cytokine released from obese PVAT, we will only discuss here some studies on this specific cytokine. There is a positive correlation between circulating TNFα levels and endothelial dysfunction in obese patients (Winkler et al., 1999). Importantly, hypoxia induced PVAT dysfunction that affected vascular function, and this effect was normalized by *in vitro* incubation with an anti-TNFα antibody (Greenstein et al., 2009).

In agreement, ex vivo incubation with the anti-TNFα antibody infliximab improves NO production in small arteries isolated from obese patients and this effect is more pronounced in PVAT-containing vessels than in PVAT-free arteries (Virdis et al., 2015). Also, as mentioned, TNFα can activate ROS in PVAT and induce endothelial dysfunction (DeVallance et al., 2018). Therefore, it is necessary to uncover the mechanisms responsible for increased inflammation and ROS production in PVAT in obesity.

8.3. Role of GRK2 in obesity.

As mentioned earlier, GRK2 can act as signal transducer beyond GPCR (Murga et al., 2019). Augmented GRK2 levels have been found in different tissues from patients and/or animal models of obesity and insulin resistance (Murga et al., 2019). Indeed, expression of GRK2 was increased in PBMCs from patients with diverse degrees of insulin resistance compared to control individuals (García-Guerra et al., 2010). Total GRK2 targeting or downregulation prevent and even reverses excessive weight gain and insulin resistance in different animal models of disease (Anis et al., 2004; Mayor et al., 2011; Vila-Bedmar et al., 2015). GRK2 affects insulin sensitivity in several cell types. For example, GRK2 inhibits insulin-mediated glucose transport in 3T3L1 adipocytes, independently of its kinase activity (Usui et al., 2004). Similarly, an inhibition of insulin-stimulated glucose uptake and insulin-dependent signalling was observed in adipocytes and myoblasts after overexpression of GRK2, again in a kinase-activity independent manner (García-Guerra et al., 2010), Moreover, similar results were observed *in vivo* in adipose tissue from wild-type and GRK2-hemizygous mice (Jiménez-Sainz et al., 2006; Kleibeuker et al., 2008). Underlying mechanisms seems to include the ability of GRK2 to modify insulin signals through binding to Gαq, the phosphorylation of insulin receptor substrate 1 (IRS1) by GRK2 modulating IRS1 stability or the altered GPCR-mediated transmodulation (**Figure 15**) (Mayor et al., 2011).

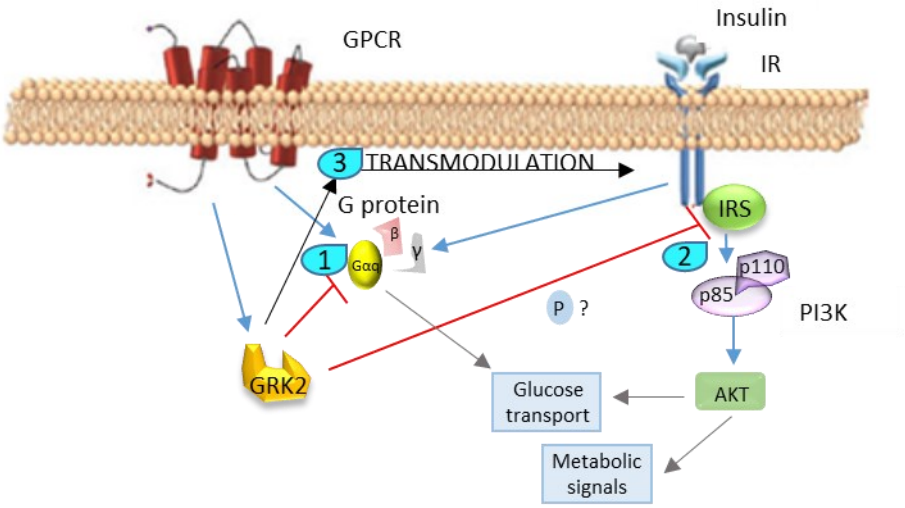


Figure 15. Modulation of insulin pathway by GRK2. Insulin binds to its receptor (IR), which recruits insulin receptor substrate (IRS) to activate the phosphatidyl-inositol 3-OH kinase (PI3K)/Akt pathway, or alternatively, heterotrimeric Gq proteins (G protein). GRK2 protein can bind to Gq (1) or to IRS (2), impairing downstream insulin signals. Insulin pathway signals can be also modified by a transmodulation of GPCR, which can be regulated by GRK2 levels (3). Modified from Mayor et al., 2011.

Increased expression of GRK2 has been observed in vessels from different mouse models of metabolic diseases (Taguchi et al., 2011, 2012). Moreover, the altered cytokine expression pattern observed in states of insulin resistance also contributes to enhance GRK2 expression levels (Vroon et al., 2006; García-Guerra et al., 2010). Partial deletion of GRK2 improved the endothelial dysfunction observed in obese/diabetic animal models by restoring the impaired Akt/eNOS pathway and finally NO availability in a process where glucose homeostasis seems to be implicated (Taguchi et al., 2011, 2012). These results suggest that modulation of GRK2 levels might be a promising strategy to fight against obesity-induced endothelial dysfunction, as suggested above for hypertension.

GRK2 is expressed in myeloid and lymphoid cells and it is known that its levels and activity change in these cells with different pathological conditions, including metabolic diseases or cancer (Vroon et al., 2006; Mayor et al., 2011; Murga et al., 2019; Cheng et al., 2020). GRK2 from lymphoid cells can function as a tumor suppressors (Cheng et al., 2020). It was also recently reported that reducing GRK2 levels in myeloid cells attenuates pro-inflammatory activation of macrophages and preserves physiological features of adipose and hepatic tissues, preventing the development of glucose intolerance and hyperglycemia after HFD (Vila-Bedmar et al., 2020). However, whether GRK2 expressed in myeloid cells might affect obesity associated-PVAT inflammation and thus impact on obesity-induced vascular dysfunction is unknown.

9. Abdominal aortic aneurysms (AAA).

AAA is a permanent enlargement and weakening or aortic wall. The development of AAA requires a first step of increased inflammation and ECM protein disruption leading to arterial wall weakening. Different studies demonstrate that the walls of aneurysmal arteries have less elastin and type I collagen than normal arteries. The development of AAA begins with neovascularization of the tunica media via the *vasa vasorum*. This could be initiated by hypertension, smoking, or genetic factors, causing injury to the aortic wall. Following neovascularization, inflammatory cells, such as macrophages, migrate into the vessel wall releasing proinflammatory cytokines and MMP that stimulate SMCs to produce more MMP and other proteinases. This leads to breakdown of collagen and elastin that stimulate the migration of more inflammatory cells, thereby setting up a cascade of aortic wall catabolism associated to contractile dysfunction of VSMCs, abnormal mechanical behaviour and endothelial dysfunction (Vorp, 2007; Wu et al., 2017; Anagnostakos and Lal, 2021). Molecular mechanisms underlying AAA formation are not clearly known, but experimental evidence demonstrate an important role for increased oxidative stress by NOX (Fan et al., 2014; Siasos et al., 2015), and enhanced production of inflammatory mediators (Wang et al., 2008; Yuan et al., 2021), as will be discussed below.

Some reports have implicated a dysregulated RAS in the formation and progression of AAA, through AT_1 receptor (Malekzadeh et al., 2013; Silverberg et al., 2014). In fact, the most widely used animal model for AAA is Ang II infusion into hyperlypidemic mice probably because of its technical simplicity and some degree of similarity to human AAA, including marked up-regulation of inflammation and extracellular matrix remodelling (Trollope et al., 2011; Golledge et al., 2020a). However, in some genetic mouse models or experimental conditions, Ang II leads to aortic dilation and dissection without coexisting with ApoE or LDLR deletion (Police et al., 2009; Villahoz et al., 2018), which provide great potential for research into the cellular and molecular mechanisms involved in AAA.

9.1. Role of ROS in vascular damage in AAA.

Both augmented production of ROS from different sources and dysregulation of antioxidants systems in human and experimental animal models, have been proposed as responsible for augmented oxidative stress in AAA (Emeto et al., 2016; Quintana and Taylor, 2019). Stimuli for ROS generation in AAA pathology are not entirely defined and they probably act in combination to augment vascular oxidative stress. Thus, classical risk factors for AAA such as smoking, advanced age, prohypertensive and proinflammatory factors such as Ang II or mechanical forces,

might trigger enzymatic reactions to produce ROS. In addition, proinflammatory cytokines, which are abundant in the context of AAA, are a well-known stimuli for ROS generation at the vascular level.

In general, it is accepted that dysregulation of ROS leads to widespread changes in the arterial wall that are central in the process of AAA development. These include increased expression of pro-inflammatory gene products, smooth muscle apoptosis, increased expression and activation of MMPs, and other key events in the pathogenesis of AAA (Emeto et al., 2016; Quintana and Taylor, 2019). More importantly, different approaches targeting ROS have been effective in preventing AAA formation in experimental animal models. For example, administration of antioxidant vitamins (Gavrila et al., 2005), deletion of NOX isoforms (Thomas et al., 2006), reversal of eNOS uncoupling (Gao et al., 2012), deletion of neutrophil myeloperoxidase (Kim et al., 2017) or catalase overexpression (Maiellaro-Rafferty et al., 2011), among many others, have been effective in preventing AAA formation (Emeto et al., 2016). However, there is limited information of the effectiveness of these treatments in established AAAs and more importantly, to date no beneficial effects of antioxidant treatments have been reported in well-designed clinical trials.

9.2. Role of inflammation in vascular damage in AAA.

Aortic wall inflammation is a multicellular-participating process including mononuclear cell infiltration, immunoglobulin (Ig) secretion and cytokine production, suggesting that both innate and adaptive immune responses are involved (Yuan et al., 2021). Despite of being a key aspect, the role of infiltrated inflammatory cells in AAA is not completely understood. T cells, macrophages, dendritic cells, neutrophils, B cells and mast cells infiltrate AAA wall (Yuan et al., 2021). The interactions among these cells provide the inflammatory microenvironment of aortic walls. For example, cytokines secreted by T cells are essential for macrophage activation, while dendritic cells and macrophages can present antigens to T cells to stimulating primary T cell responses (Guerriero, 2019). Also, there is no consensus on which are the key inflammatory cytokines involved in AAA, although increased presence of proinflammatory IFNγ, IL-6, TNFα, IL-17 or anti-inflammatory IL-10 cytokines has been shown (Liao et al., 2015). There are many studies showing beneficial effects of genetic deletion of different inflammatory cells subtypes or cytokines in prevention of AAA formation (Takahashi, 2021; Yuan et al., 2021), although unfortunately, in general, regression of AAA is challenging and not successfully achieved. This will not be reviewed here in detail. Instead, we will focus on the role of IFNγ on AAA pathology.

Sharma et al. showed high IFN-γ expression in aneurysms of the elastase infusion model (Sharma et al., 2012). Similarly, Zhou et al. demonstrated the key role of IFNγ produced by CD8+ T cells in the same model and results of several articles including two meta-analyses (Lindeman et al., 2008; Golledge et al., 2009; Zhou et al., 2013; Stather et al., 2014), showed increased expression of IFNγ in human aneurysms. However, decreased (Liao et al., 2015) or unaltered (Wang et al., 2018) circulating levels of IFNγ have been described in patients. Additionally, a protective role of IFNγ has been suggested in aneurysm formation and rupture (King et al., 2009). However, a lack of effect after IFNγ blockade in the Ang II-infused ApoE$^{-/-}$ mouse aneurysm model has also been described (Wang et al., 2010). Reasons for this variability are unknown but differences in animal models, patients or detection of local or circulating cytokine should be considered. On the other hand, recent studies seem to suggest a possible role for type I IFNs in aneurysm pathology, both in animal models and humans (Yan et al., 2016).

As discussed earlier, upon initial vascular damage, there is an upregulation of inflammatory factors such as resistin, leptin, cytokines and chemokines, which induce infiltration of inflammatory cells in PVAT (Nosalski and Guzik, 2017). Recent studies highlight the contribution of PVAT inflammation to AAA pathology. Sagan et al. found that T cells, rather than macrophages, are the major leukocyte subset in AAA and that their greatest accumulations occur in PVAT. Interestingly, they found that only PVAT T cell infiltration was strongly related to tertiles of AAA size (Sagan et al., 2019). In another study, Meekel and collages described that PVAT from patient with AAA shows increased MMPs and pro-inflammatory (*PTPRC*, *CXCL8*, *LCK* and *CCL5*) gene expression as well as a decreased in *PPARG* gene expression, an anti-inflammatory gene (Meekel et al., 2021). Despite of the abundant literature, more studies are still needed to fully understand the relationship between aneurysms and inflammation.

10. Pharmacological treatment of hypertension, obesity and AAA.

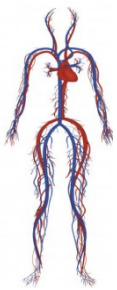
The efficacy of the main antihypertensive drugs (diuretics, ACE inhibitors, AT_1 antagonists, calcium channel blockers and beta-blockers) to decrease blood pressure in hypertensive patients is established. More importantly, many of these pharmacological approaches decrease cardiovascular risk in the long term (Williams et al., 2018). However, despite of the extensive knowledge about the mechanisms responsible for hypertension development and its relationship with aneurisms, obesity or even heart attack and stroke, there is still a massive number of hypertensive patients that do not have blood pressure under control, many are resistant to the blood-pressure lowering effects of the aforementioned drugs, and there seems

to be a residual cardiovascular risk in these patients. Moreover, there is not direct univocal relationship between blood pressure elevation and target organ damage. Up to date, there are not pharmacological treatments to slow or regress the development of aneurysms, although targeting the RAAS or using hydroxymethylglutaryl-CoA reductase inhibitors (statins), or beta-blockers in these patients is currently in the clinics. RAAS inhibitors and statins non only decrease blood pressure and lipid levels, but they might also confer some degree of vascular protection probably through attenuation of inflammation (Hackam et al., 2006; Oesterle et al., 2018). Beta-blockers apart from lowering blood pressure and heart rate, seem to have a positive effect by increasing the resistance of the aorta to stretching (Slaiby et al., 1994). Similarly, no pharmacological approaches are currently existing to treat obesity, and cardiovascular protection is elicited in selected patients with classical cardiovascular drugs. Taken together these studies suggest that there might be additional mechanisms that are not being efficiently targeted by the current pharmacological treatments.

It is interesting that even though numerous preclinical studies show the participation of ROS in hypertension (Sinha and Dabla, 2015), obesity (DeVallance et al., 2019) and AAA (Emeto et al., 2016), the use of substances to reduce oxidative stress as a treatment for these diseases has not been proven to be effective so far. Different epidemiological studies concluded that individuals with higher antioxidant intake have lower incidence of cardiovascular risk (Moran et al., 1993; Nawrot et al., 2007), and positive effects were also observed when combining antioxidants with another antihypertensive treatment (Barrios et al., 2002; On et al., 2002). However, a clear antihypertensive effect is not observed in most of the studies that analyze the effect of antioxidants in long term (Hajjar et al., 2002; Juraschek et al., 2012). Reasons for these discrepancies include lack of consistency, poor selection criteria, no information on concomitant diseases, flawed methodology used to measure oxidative stress, and the omission of necessary scientific aspects such as the pharmacokinetic properties or bioavailability of the antioxidants used (Ginter, 2000; Antoniades et al., 2003; Rodrigo et al., 2007). In fact, currently there are no clinically approved NOX/ROS inhibitors or antioxidants for use in the treatment of hypertension or other vascular diseases. Moreover, uncomplete knowledge on the molecular mechanisms underlying oxidative stress and the benefits of inhibiting ROS formation versus augmenting ROS detoxification, need to be clarified. In any case, it has been suggested that although it is necessary to carry out more well-conducted studies to obtain conclusive results on the efficacy of antioxidants in CVD, clinical utility of agents that reduce oxidative stress to manage hypertension and target organ damage is promising (Griendling et al., 2021).

As discussed in this PhD Thesis, growing evidence in animal models and in patients point to a possible role of inflammation as an additional mechanism of initiation and maintenance of CVD. Specific cytokines such as TNFα or IL-1 are associated with a high cardiovascular risk, supporting the theory that anti-inflammatory drug treatments may be a promising strategy to reduce cardiovascular risk in the field of traditional medical therapy (Golia et al., 2014). In fact, some of the therapies used currently in clinics, for example, statins and AT_1 antagonists, have antinflammatory effects that might contribute to their protective effects in the cardiovascular system. However, the results from clinical trials with anti-inflammatory drugs are variable. Early studies using a monoclonal antibody against TNFα (infliximab, ATTACH trial) or a soluble TNF receptor (etanercept, RECOVER and RENAISSANCE trials) showed lack of effect or even deleterious effects in patients with heart failure (Chung et al, 2003). However, recent results from the CANTOS trial have provided encouraging results. In this study, patients with a history of myocardial infarction and elevated levels of CRP were treated with an anti-interleukin-1β antibody (canakinumab). Authors showed a clear reduction in cardiovascular events rates that were not attributed to changes in blood pressure or incident hypertension (Ridker et al., 2017; Rothman et al., 2020).

Targeting inflammation might be a challenging approach because the overwhelming amount of proinflammatory pathways and mediators described. On the one hand, inhibition of one specific mediator will not likely be efficient. On the other hand, general anti-inflammatory drugs might produce immunosuppression and susceptibility to infections. In this sense, we cannot dismiss the essential role of inflammation fighting against pathogens. Proof of this complexity is the fact that non-steriodal antinflammatory drugs, which inhibit the activity of the COX-2 isoform involved in the synthesis of the proinflammatory mediator PGE_2, are associated with higher cardiovascular risk (Khan et al., 2019). Then, clearly identifying specific molecular mechanisms involved in CVD in relation with inflammation might contribute to more rational drug development.



Hypothesis and objectives

Hypothesis

Augmented infiltration of immune cells and enhanced levels of local proinflammatory cytokines such as IFNγ, TNFα and many others, are common hallmarks of vascular damage in many CVD including hypertension and obesity. This inflammatory milieu increases oxidative stress and reduces NO availability that is responsible for the endothelial dysfunction and vascular remodelling observed in these pathologies.

Because of the well-known role of IFNγ in hypertension-associated vascular damage, we hypothesized that ISG15 (an interferon stimulated gene) could be a novel mediator of vascular dysfunction and blood pressure elevation. In addition, given the previously described role of GRK2 in hypertension-associated vascular alterations and the role of macrophages in obesity-related vascular complications, we hypothesized that myeloid cells GRK2 may contribute to the development of obesity-induced vascular dysfunction. In both pathological conditions, underlying mechanisms responsible for vascular damage might be related with enhanced inflammation and oxidative stress.

Main objective

To study the involvement of ISG15 and myeloid GRK2 in the vascular damage associated with hypertension or obesity and the contribution of inflammation and oxidative stress as possible underlying mechanisms.

Specific objectives

1. To analyze the relationship between ISG15, hypertension and vascular damage in humans.

2. To evaluate the expression of the ISG15/USP18 system in vascular tissues of animal models of hypertension.

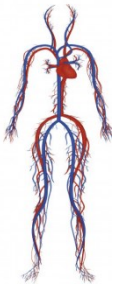
3. To analyze the role of ISG15/USP18 pathway in the alterations in vascular function, structure and mechanical properties associated with hypertension.

4. To study the role of inflammation and oxidative stress as underlying mechanisms responsible for the role of ISG15 in vascular damage in hypertension.

5. To determine the relationship between GRK2 levels and inflammation in PVAT from patients

6. To evaluate the role of myeloid GRK2 in the alterations in vascular function associated with obesity.

7. To analyze the role of inflammation and oxidative stress as underlying mechanisms responsible for the role of myeloid GRK2 in obesity-induced vascular dysfunction.



Materials and Methods

1. Bioinformatics analysis.

A dataset of proteins related to hypertension was created from Public Health Genomics and Precision Health Knowledge Base (V5.2) 'Phenopedia' (https://phgkb.cdc.gov/PHGKB/startPagePhenoPedia.action), using the term "Hypertension". We analyzed this dataset using the Upstream Regulator Analysis of Ingenuity Pathways Analysis (IPA@, Quiagen) software that identifies proteins included or not in the dataset, which may be potential master regulators. This tool defines an overlap p-value to measure the enrichment of the different master regulators in the database. In addition, a protein-protein interaction network was created by introducing ISG15 into the list of proteins obtained from 'Phenopedia' by STRING V 11.0 (https://string-db.org/). Finally, the results were visualized using Cytoscape (Shannon et al., 2003). Bioinformatics analysis were performed by Drs. Ana García Redondo and Inmaculada Jorge.

2. Human studies.

2.1. Isolation of peripheral blood mononuclear cells and detection of superoxide production from patients.

The study was carried out in accordance with the Declaration of Helsinki and Title 45, U.S. Code of Federal Regulations, Part 46, Protection of Human Subjects, Revised November 13, 2001, effective December 13, 2001. The Ethical Committee of the University Clinic of Navarra approved the protocol. Subjects were aware of the nature of the study and gave informed consent. The study was performed in a group of 175 asymptomatic subjects in whom global risk assessment was performed at the institution in the course of a general health check-up after a 12-hour overnight fast. In all subjects, absence of history of coronary disease, stroke, or peripheral arterial disease was recorded. Conventional cardiovascular risk factors, including arterial hypertension, obesity, smoking and diabetes were defined as previously described (Madrigal-Matute et al., 2015). Carotid ultrasonography was performed to determine intima-media thickness (IMT), as previously described (Madrigal-Matute et al., 2015). Patients were recruited from May 2002 until June 2005. Characteristics of the studied population are summarized in **Table 2**, from Results section.

In all 175 subjects, PBMCs were isolated from venous blood samples with Lymphoprep with a high purity and immediately used for enzymatic and molecular measurements, as previously described (Moreno et al., 2014).

The superoxide anion production was measured by chemiluminescence in a plate reader luminometer (Luminoskan Ascent, Labsystem), in isolated $4x10^5$ cells PBMCs stimulated with phorbol myristate acetate (3.2 µmol/L; Sigma-Aldrich, San Louis, MO, USA) in the presence of 5 µmol/L lucigenin, as previously published (Moreno et al., 2014). Luminescence measurements were recorded along an interval of 1 hour, and the value of the area under the curve was used to quantify chemiluminescence. In these PBMCs, *ISG15* gene expression was also measured by qRT-PCR, as explained later at section "7. qRT-PCR assay". These experiments were performed in Universidad de Navarra (Pamplona, Spain) by Dr. Guillermo Zalba.

2.2. Abdominal aortic aneurysms patients.

This study was approved by the Hospital de la Santa Creu i Sant Pau (HSCSP; Barcelona, Spain) Ethics Committee (12/031/1316) and was conducted according to the Declaration of Helsinki. Participation of patients and control subjects in the study was based upon informed consent of patients or legal representatives. Inclusions were carried out between January 2012 and December 2015. Human aneurysmal samples were collected from patients undergoing open repair for AAA at the HSCSP; while healthy aortas were obtained from multi-organ donors as previously described (Orriols et al., 2016; Alonso et al., 2016). From both groups, abdominal aorta segments were obtained following strict standard operating procedures and ethical guidelines. Patients with infectious or inflammatory aneurysms, or pseudoaneurysms were excluded from the study. Biopsies, devoid of intraluminal thrombi if present, were systematically obtained from the anterolateral wall of the mid-infrarenal aorta at the level of the inferior mesenteric artery. Healthy non-atherosclerotic aortas from multiorgan donors were also taken from the same region of the infrarenal abdominal aorta (Orriols et al., 2016). Samples of control subjects had no *post-mortem* evidence of AAA, atherosclerotic plaques or other medical conditions that could affect the study. Control patients included 88.2% male, 11.8% female, 64% smoker or ex-smoker, mean age 64±4 years; AAA patients include 100% male, 67% smoker or ex-smoker, mean age: 71±1 years ($P>0.05$ vs control). Samples were rapidly collected and stored at −80°C until the gene expression measurements by qRT-PCR, as explained later at section 7. These experiments were performed in Institut de Recerca Hospital de la Santa Creu i Sant Pau (Barcelona) by Drs. Cristina Rodríguez and José Martínez González.

2.3. Human fibroblasts culture.

Studies were conducted under ethics approval obtained from the West of Scotland Research Ethics Service (WS/12/0294). Subjects knew about the nature of the research study and gave informed consent. Small arteries were dissected from surplus surgical tissue of patients

receiving elective craniofacial surgeries at the Craniofacial/Oral & Maxillofacial Unit, Queen Elizabeth University Hospital, Glasgow. Cleaned arteries were cut into small pieces, 4-5 mm maximum, and they were transferred to a 25 cm tissue culture flask containing 3 mL of complete F12 medium. Flasks with explants were incubated at 37 °C/5% CO_2. After 24 h, medium was carefully changed to DMEM with 20% FBS. After a few days, fibroblasts started to grow out of the explants. Explants were removed from the fibroblasts culture after 10 days. For experiments, fibroblasts were plated in 6-well plate, until semi confluent. Before the experiments, cells were maintained in DMEM with 0.5% FBS over-night. After incubation with human recombinant ISG15 (rISG15; 10 ng/mL, Sino Biological, Life Technologies, Carlsbad, CA, USA, Cat. No. 12729-HNAE), these fibroblasts were frozen at -80˚C and then we studied NADPH oxidase activity or H_2O_2 production on them, as explained at sections 15 and 16, respectively.

2.4. Aortic perivascular adipose tissue from patients.

Aortic PVAT was obtained from 42 patients with AAA during open surgery in the Angiology and Vascular Surgery Unit of the Hospital Universitario La Princesa (Madrid) by Dr. Rosa Moreno Carriles. The study was carried out in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Hospital Universitario la Princesa (PI-825). Patients were diagnosed of AAA by computed tomography angiography and they gave informed consent. Inclusion criteria included having symptomatic or asymptomatic AAA with transverse or antero-posterior diameter ≥5.5 cm in men or ≥5 cm in women. Exclusion criteria included endovascular aortic reconstructive therapy, inflammatory aneurysm, active neoplastic conditions, human immunodeficiency virus (HIV) positive serology, and pregnancy. Clinical and demographic characteristics of the studied population are included in **Table 5**, from Results section. Samples were rapidly collected and stored at −80°C for subsequent RNA extraction and gene expression's study by qRT-PCR, as explained later at section 7.

3. Animal studies.

All animal experimental procedures were approved by the Ethical Committee of Research of the Universidad Autónoma de Madrid and Dirección General de Medio Ambiente, Comunidad de Madrid, Spain (PROEX 345/14 and PROEX 048/15) and Institut de Recerca Hospital de la Santa Creu i Sant Pau-Programa ICCC local ethical committee (Law 5/June 21, 1995), Generalitat de Catalunya). Animals were taken care of and used according to the Spanish Policy for Animal Protection RD53/2013, which meets the European Union Directive 2010/63/UE on the

protection of animals used for experimental and other scientific purposes and experiments were conducted in accordance with the National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals. All mice and rats were bred at the Animal Care Facility of the Faculty of Medicine, Universidad Autónoma de Madrid (UAM), of the Centro de Biología Molecular Severo Ochoa (Madrid, Spain), and at the Institut de Recerca Hospital de la Santa Creu i Sant Pau-Programa ICCC, under controlled conditions at 22 ±2 ˚C in a 12h light/dark cycle with *ad libitum* access to water and food.

3.1. Ang II-infused WT, ISG15$^{-/-}$ and USP18^{C61A} mice model.

Three-four-month-old male mice on C57Bl/6J genetic background were used. Ang II (1.44 mg/kg/day, 2 weeks; Sigma-Aldrich) was infused into wild-type mice (WT), ISG15 knockout mice (ISG15$^{-/-}$) and USP18^{C61A} knock-in mice, which have a mutation of the USP18 protein within the Cys at position 61 (substitution by alanine) that completely abolishes the isopeptidase activity leading to excessive ISGylation (Ketscher et al., 2015). The Ang II-infusion was achieved using subcutaneously implanted Alzet osmotic minipumps (model 2002, Alzet; Durect Corp., Cupertino, CA, USA). This is a good model for hypertension that resembles some forms of human hypertension. The RAS is usually activated in human primary hypertension and the level of blood pressure elevation achieved with this long-term subcutaneous infusion of Ang II in mice is on par with that observed in uncontrolled stage 2 hypertension (Lerman et al., 2019). For the implantation of osmotic minipumps, mice were anaesthetized with isofluorane inhalation (2%). ISG15$^{-/-}$ mice, and USP18^{C61A} transgenic mice were originally described elsewhere (Osiak et al., 2005; Ketscher et al., 2015) and they were kindly provided by Dr. Susana Guerra. ISG15$^{-/-}$ mice and WT littermate controls originated from the offspring of ISG15$^{-/-}$/WT x ISG15$^{-/-}$/WT mice. USP18^{C61A} and WT littermate controls originated from the offspring of USP18^{C61A}/WT x USP18^{C61A}/WT mice. Once the initial stocks were generated, the maintenance of the colony was generated by successive cross breeding of ISG15$^{-/-}$ with ISG15$^{-/-}$, ISG15$^{+/+}$ with ISG15$^{+/+}$ or USP18^{C61A} with USP18^{C61A} mice, in house breeding pairs.

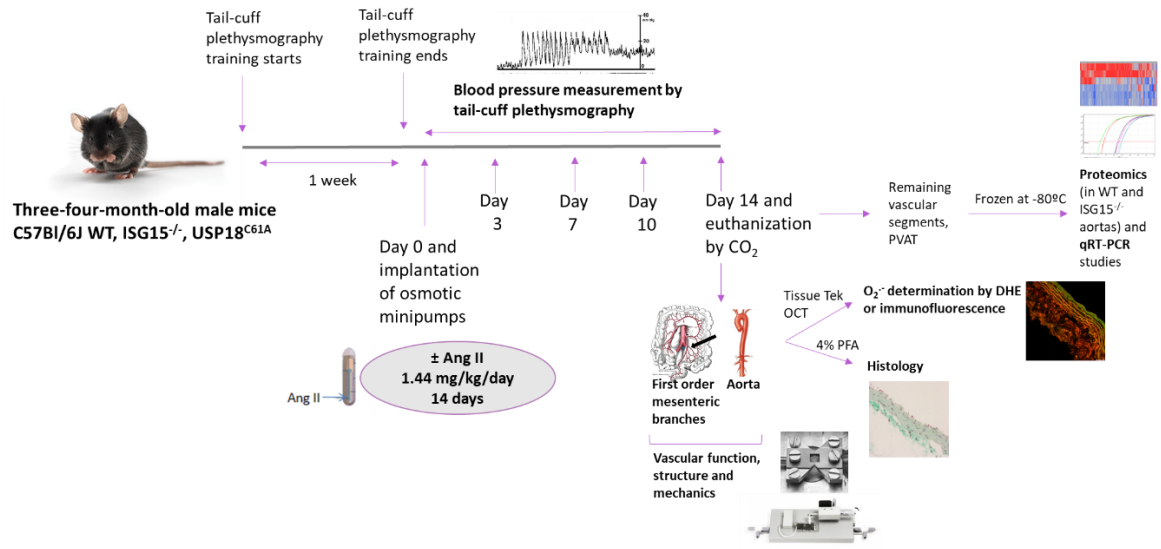


Figure 16. Ang II-infused WT, ISG15$^{-/-}$ and USP18^{C61A} mice model.

In another set of experiments, some USP18^{C61A} mice were daily treated with the antioxidant superoxide dismutase mimetic 4-hidroxi-2,2,6,6-tetrametilpiperidin-1-oxilo (Francischetti et al., 2014) (Tempol, 0.288 nmol/kg/day; Honeywell Fluka, Thermo Fisher Scientific, Waltham, MA, USA, Cat. No. GA12207) and Ang II.

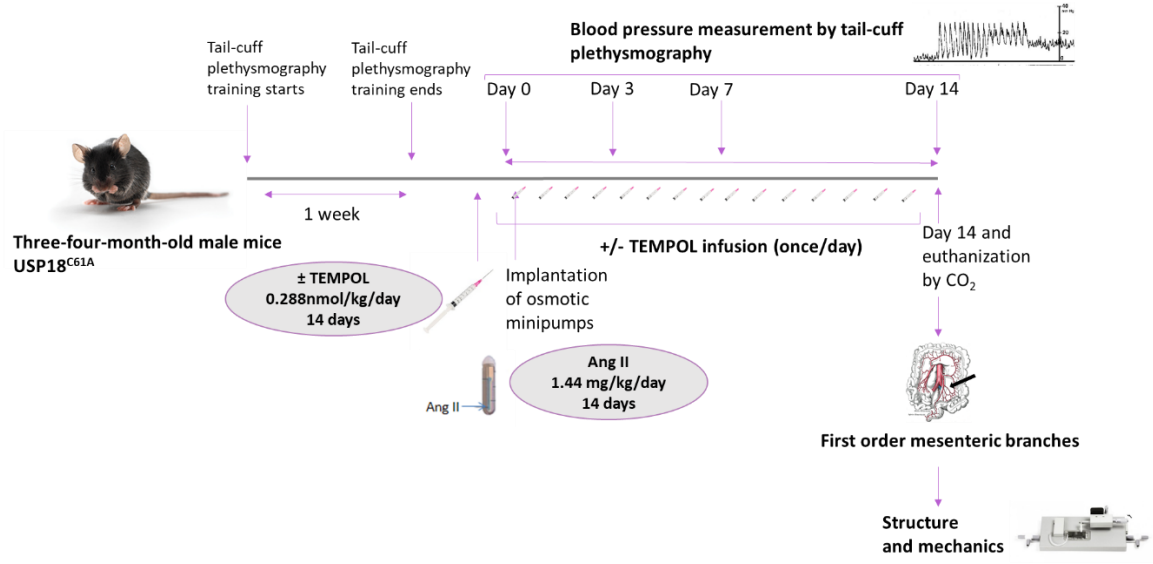


Figure 17. Model of Ang II-infusion and tempol-treatment in USP18^{C61A} mice.

In all groups, blood pressure was measured by tail-cuff plethysmography. Animals were trained for one week prior to final blood pressure measurements. Final measurements were done at

several days after Ang II osmotic minipumps implantation (**Figure 16** and **Figure 17**). At least six individual observations were performed and averaged for each animal.

At day 14, animals were euthanized by CO_2. Aorta and first-order mesenteric branches were dissected free of fat and connective tissue and placed in cold Krebs Henseleit Solution (KHS) (115 mmol/L NaCl, 25 mmol/L $NaHCO_3$, 4.7 mmol/L KCl, 1.2 mmol/L $MgSO_4 \cdot 7H_2O$, 2.5 mmol/L $CaCl_2$, 1.2 mmol/L KH_2PO_4, 11.1 mmol/L glucose, and 0.01 mmol/L Na_2EDTA). Vessels were divided in segments for analysis of vascular function (explained at section 4), structure and mechanics (explained at section 5) that was done on the same day of euthanasia (**Figure 16** and **Figure 17**). For histology, aortic segments were fixed in 4% paraformaldehyde (PFA). Aortic segments used for $O_2^{\cdot-}$ determination (as explained at section 13) or immunofluorescence (detailed at section 18) were placed in KHS containing 30% sucrose for 20 min, transferred to a cryomold containing Tissue Tek OCT embedding medium (Sakura Finetek, Netherlands, Europe) and then immediately frozen in liquid nitrogen for storage at -80˚C. Remaining vascular segments and PVAT were immediately frozen in liquid nitrogen and kept at -80˚C until the day of gene expression studies by qRT-PCR, as explained at section 7 (**Figure 16**).

3.2. Ang II-infused ApoE$^{-/-}$ mice model.

Three-month-old male Apolipoprotein-E-deficient mice (ApoE$^{-/-}$) (B6.129P2-Apoetm1Unc/J) were obtained from Jackson Laboratory (Bar Harbor, Maine, USA) and acclimated 1 week prior to the study. Mice were randomly distributed into Ang II or saline-infused animals. Ang II (1.44 mg/kg/day; Sigma-Aldrich) was infused via osmotic minipumps (model 1004, Alzet; Durect Corp.) for 28 days as previously described (Galán et al., 2016). At day 28, animals were euthanized by isofluorane overdose. Aorta was dissected free of fat and frozen at -80˚C until gene expression studies (**Figure 18**) by qRT-PCR as later explained at section 7. These experiments were performed in Institut de Recerca Hospital de la Santa Creu i Sant Pau (Barcelona) by Drs. Cristina Rodríguez and José Martínez González.

Figure 18. Ang II-infused ApoE$^{-/-}$ mice model.

3.3. High fat diet in LysM-GRK2$^{+/-}$ mice model.

Experiments were performed on five-month-old male control mice and mice with a reduction of around 50% in GRK2 levels in myeloid cells (LysM-GRK2$^{+/-}$) (Vila-Bedmar et al., 2020). To obtain these mice, transgenic male mice overexpressing a nuclear-localized Cre recombinase inserted into the first coding ATG of the lysozyme 2 gene (Lyz2) (B6.129P2-Lyz2tm1(cre)Ifo/J), obtained from Jackson Laboratories, were mated to floxed homozygous GRK2 (GRK2$^{f/f}$) female mice. GRK2$^{f/\Delta}$LysM-Cre$^{-/-}$ controls (referred to as control mice) and GRK2$^{f/\Delta}$LysM-Cre$^{+/-}$ (referred to as LysM-GRK2$^{+/-}$) offsprings were used and genotyped as described (Vila-Bedmar et al., 2020).

At 8 weeks of age (2 months), mice from both genotypes were separated into two groups: one group continued a normal diet (ND) (Harlan-Teklad Cat. No. 2018S, 12% calories from fat) and the other group was exposed to an HFD (Envigo (formerly Harlan) Cat. No. TD.07011, 54.4% calories from fat) for 12 weeks (**Figure 19**). This HFD model has been selected based on previous studies as it resembles some of the features of human obesity (Buettner et al., 2007) and it was performed in Centro de Biología Molecular Severo Ochoa (Madrid) by Drs. Rocío Vila Bedmar and Cristina Murga.

After 12 weeks, mice were euthanized by CO_2. Aorta from control and LysM-GRK2$^{+/-}$ mice were placed in cold KHS, and abdominal and thoracic aortic segments of around 2 mm in length were left with PVAT (PVAT+) or cleaned (PVAT-) to be mounted in a wire myograph in order to study vascular reactivity by isometric tension recording, as explained at section 4. Remaining PVAT from aorta was immediately frozen in liquid nitrogen and kept at -80˚C until the day of gene expression studies by qRT-PCR as explained at section 7 (**Figure 19**).

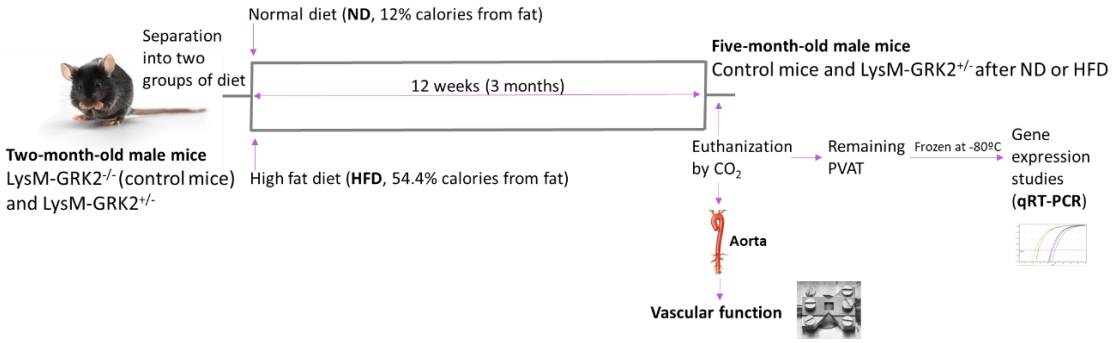


Figure 19. High fat diet (HFD) in LysM-GRK2$^{+/-}$ mice model.

3.4. Normotensive and hypertensive rats.

Aortas from one- and six-month-old male Wistar Kyoto (WKY) and SHR rats were also removed from adipose tissue and frozen to study *Isg15* gene expression. All rats were bred at the Animal Care Facility of the Faculty of Medicine, UAM, as indicated at the beginning of this section 3.

3.5. Aortic ex vivo incubation studies.

For some experiments, aortic segments from WT mice were incubated with Ang II (1 µM, 6h; Sigma-Aldrich) in the presence and in the absence of an anti-IFNγ antibody (5 µg/mL; Thermo Fisher Scientific, Cat. No. 16731181) and they were kept at -80˚C until the day of gene expression studies, as explained at section 7.

In other experimental set, aortic segments from male C57Bl/6J mice (3-month-old) were incubated for 20 h in DMEM-low glucose medium (Sigma-Aldrich) supplemented with 4 mmol/L glutamine, 1% FBS, 100 U/mL of penicillin and 100 µg/mL of streptomycin; at 37˚C and 5% CO_2, in the absence or in the presence of mouse rISG15 (10 ng/mL; CircuLex MBL International, Woburn, MA, USA, Cat. No. CY-R2274). Additionally, some *ex vivo* cultured segments were co-incubated with the selective NADPH oxidase 1 inhibitor NoxA1ds (10 µmol/L; Calbiochem-Merck, Cat. No. 5327610001), the selective cyclooxygenase 2 inhibitor celecoxib (1 µmol/L; Pfizer, NY, USA, Cat. No. SC58635), the non-selective integrin receptor inhibitor RGDS (Arg-Gly-Asp-Ser) (1 µmol/L; Cayman Chemical, Ann Arbor, MI, USA, Cat. No. 15359) or an anti-IFNγ antibody (5 µg/mL; Thermo Fisher Scientific, Cat. No. 16731181) in the presence of rISG15 (**Figure 20**). These drugs were added 30 min before overnight incubation with rISG15. Vascular reactivity was studied in a wire myograph as described at section 4. Control arteries were incubated in the same culture conditions (**Figure 20**).

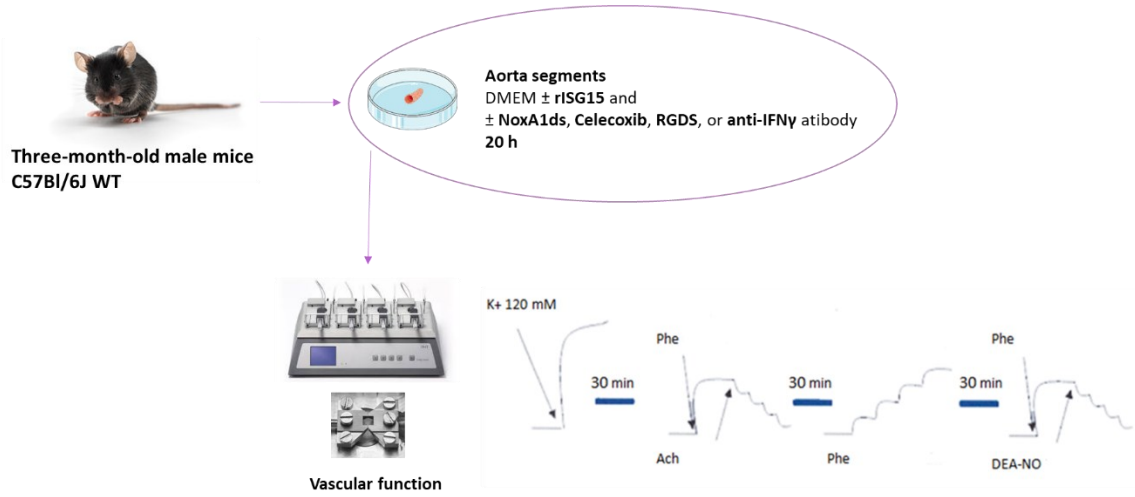


Figure 20. Vascular function study of rISG15-incubated (10 ng/mL) aortic segments. Co-incubated with the selective NADPH oxidase 1 inhibitor NoxA1ds (10 µmol/L), the selective cyclooxygenase 2 inhibitor celecoxib (1 µmol/L), the non-selective integrin receptor inhibitor RGDS (Arg-Gly-Asp-Ser) (1 µmol/L) or an anti-IFNγ antibody (5 µg/mL).

4. Vascular reactivity studies.

Aortic and mesenteric resistance arteries (MRA) were dissected and segments, 2 mm in length, were mounted in a wire myograph for isometric tension recording. After a 30-min equilibration period in oxygenated (with a mixture of 95% O_2 and 5% CO_2) KHS at 37°C and pH 7.4, segments were stretched to their optimal lumen diameter for active tension development. This was determined based on the internal circumference/wall tension ratio of the segments by setting their internal circumference, Lo, to 90% of what the vessels would have if they were exposed to a passive tension, which is equivalent to that produced by a transmural pressure of 100 mm Hg. Segments were washed with KHS and left to equilibrate for 30 min; then, contractility of the segments was tested by an initial exposure to a high K^+ solution (K^+-KHS, 120 mmol/L). After an equilibration period, aortic segments were precontracted with phenylephrine (Phe) at ~50% K^+-KHS contraction in order to perform a concentration–response curve to increasing concentration of Ach (1 nmol/L-10 µmol/L). For the study with $GRK2^{+/-}$ aorta segments, after washing the arteries and a 30 min equilibration period, aortic segments were precontracted again, and a concentration-response curve to increasing concentration of insulin (10 nmol/L–3 µmol/L) was carried out. For all the experimental protocols, after washing, a concentration-response curve to increasing concentration of Phe (1 nmol/L-30 µmol/L) was performed. Finally, a concentration-response curve to the NO donor Diethylamine NONOate (DEA-NO, 1 nmol/L-10 µmol/L) was performed in Phe precontracted arteries. Phe responses were stable and concentration response curves were performed after reaching a steady-state.

Some segments from HFD GRK2$^{+/-}$ mice were incubated with the specific inhibitor of NOX1, NOXA1ds (10 µmol/L; Calbiochem-Merck, Darmstadt, Germany, Cat. No. 5327610001) or with an anti-TNFα antibody (10 µg/mL; InVivoMAb, BioXcell, Lebanon, NH, USA, Clone XT3.11, Cat. No. BE0058) 1 h before the concentration-response curve to insulin. Vasodilator responses were expressed as a percentage of the previous tone generated by Phe. Vasoconstrictor responses were expressed as a percentage of the tone generated by K^+-KHS or in mN per mm of length for each segment.

5. Study of the structural and mechanical properties of mesenteric arteries.

5.1. Pressure myography studies.

The structural and mechanical properties of mesenteric arteries were studied using a pressure myograph (Danish Myo Tech, Model P100, J.P. Trading I/S, Aarhus, Denmark). Vessels were placed on two glass microcannula and secured with surgical nylon suture. During these experiments, vessels were submerged into calcium-free KHS ($0Ca^{2+}$-KHS; omitting calcium and adding 1 mmol/L EGTA). After any small branches were tied off, vessel length was adjusted until vessel walls were parallel without stretch. The segment was then set to a pressure of 45 mm Hg and allowed to equilibrate for 60 min at 37°C in $0Ca^{2+}$-KHS extravascular and intravascularly perfused, gassed with a mixture of 95% O_2 and 5% CO_2. Intraluminal pressure was then reduced to 3 mm Hg. A pressure-diameter curve was obtained by increasing intraluminal pressure in 20 mm Hg steps from 3 to 120 mm Hg. Finally, the artery was set to 45 mm Hg in $0Ca^{2+}$-KHS and then pressure-fixed with 4% PFA, pH 7.2-7.4 at 37°C for 60 min and kept in 4% PFA at 4°C for confocal microscopy studies.

Internal and external diameters were continuously measured under passive conditions (D_{i0Ca}, D_{e0Ca}) for 2 min at each intraluminal pressure. The final value used was the mean of the measurements taken during the last 30 s when the measurements reached a steady state. From internal and external diameter measurements in passive conditions, the following structural and mechanical parameters were calculated:

Wall thickness (WT) = $(D_{e0Ca} - D_{i0Ca})/2$

Circumferential wall strain (ε) = $(D_{i0Ca} - D_{00Ca})/D_{00Ca}$, where D_{00Ca} is the internal diameter at 3 mm Hg and D_{i0Ca} is the observed internal diameter for a given intravascular pressure, both measured in $0Ca^{2+}$ medium.

Circumferential wall stress (σ) = (P × D_{i0Ca})/(2WT), where P is the intraluminal pressure (1 mm Hg = 1.334 × 10^3 dynes·cm^{-2}) and WT is wall thickness at each intraluminal pressure in $0Ca^{2+}$-KHS.

Arterial stiffness independent of geometry is determined by the Young's elastic modulus (E =stress/strain). The stress-strain relationship is non-linear; therefore, it is more appropriate to obtain a tangential or incremental elastic modulus (E_{inc}) by determining the slope of the stress-strain curve (E_{inc} = δσ/δε). E_{inc} was obtained by fitting the stress-strain data from each animal to an exponential curve using the equation: $\sigma = \sigma_{orig}e^{\beta\varepsilon}$, where σ_{orig} is the stress at the original diameter (diameter at 3 mm Hg). Taking derivatives on the equation presented earlier, we see that E_{inc} = βσ. For a given σ-value, E_{inc} is directly proportional to β. An increase in β implies an increase in E_{inc}, which means an increase in stiffness.

5.2. Confocal microscopy study of nuclei distribution.

Pressure fixed intact arteries were incubated with the nuclear dye Hoechst 33342 (0.01 mg/mL; Thermo Fisher Scientific) for 15 min. After washing the arteries, they were mounted on slides using silicon-made wells to avoid artery deformation. They were viewed using a Leica TCS SP2 confocal system (Leica Microsystems, Wetzlar, Germany) fitted with an inverted microscope and Argon and Helium-Neon laser sources with x40 oil immersion lens (excitation wavelength 351-364 nm and emission wavelength 400-500 nm). At least two serial optical sections (stacks of images) of 0.5 µm thick serial optical slices, were taken from the adventitia to the lumen in different regions along the artery length. Metamorph image analysis software (Molecular Devices Corp. Downingtown, PA, USA) was used for quantification. The nuclei numbers were measured in Z axis as previously described (Briones et al., 2007) with minor modifications.

To allow comparison among the different groups, the following calculations were performed on the basis of 1-mm-long segments: artery volume (in mm^3) (volume = wall cross sectional area (mm^2) x 1 mm), total number of adventitial and smooth muscle cells (cell n = n of nuclei per stack x n of stacks per artery volume).

5.3. Organization of internal elastic lamina.

The elastin organization within the internal elastic lamina was studied on intact pressure-fixed segments of small mesenteric arteries, using fluorescence confocal microscopy (Leica TCS SP2; Leica Microsystems) based on the auto-fluorescent properties of elastin (excitation wavelength 488 nm and emission wavelength 500–560 nm), as previously described (Briones et al., 2003). Briefly, serial optical sections from the adventitia to the lumen (z step = 0.5 µm) were captured with a x40 oil objective (Zoom 4), using the 488 nm line of the confocal microscope. A minimum

of two stacks of images of different regions were captured in each arterial segment. Quantitative analysis of the internal elastic lamina was performed with Metamorph Image Analysis Software (Molecular Devices Corp.), as previously described (Briones et al., 2003). From each stack of serial images, individual projections of the internal elastic lamina were reconstructed and mean fenestrae area was measured.

6. Cell culture.

The human microvascular endothelial cells line (**HMEC-1**, ATCC®, Middlesex, UK; Cat. No. CRL-3243™) was used. Cells were cultured according to manufacturer instructions with MCDB131 medium (Corning, NY, USA, Cat. No. 702564) supplemented with 10 ng/mL epidermal growth factor (Sigma-Aldrich), 1 µg/mL hydrocortisone (Sigma-Aldrich), 10 mmol/L glutamine (Sigma-Aldrich), 10% FBS (Sigma-Aldrich), 100 U/mL of penicillin and 100 µg/mL of streptomycin. At 80% confluence, cells were serum-deprived for 24 hours before stimulation.

Human aortic endothelial cells (**HAECs**, ATCC®, Cat. No. PCS-100-011™) were also used. HAEC were cultured according to manufacturer instructions in Endothelial Cell Growth Medium (PromoCell, Heidelberg, Germany, Cat. No. C22010), enriched by Endothelial Cell Growth Medium Supplement (PromoCell, Cat. No. C39215) and penicillin/streptomycin (50 µg/mL). For functional studies, confluent cells were made quiescent by changing medium to DMEM with 0.5% FBS and penicillin/streptomycin (50 µg/mL) for 24 hours. Before stimulation, HAEC were fully serum-deprived.

Both types of ECs were treated with Ang II (0.1-100 nmol/L, for 2-24h; Sigma-Aldrich) or human rISG15 (10 ng/mL; Sino Biological, Life Technologies, Cat. No. 12729-HNAE) (Sainz et al., 2014) at times indicated in figure legends. Some of the HAEC, incubated with rISG15, were used to study $O_2^{\cdot-}$ production, as further explained at section 14. In other experiments, HMEC-1 were co-incubated with different inhibitors that were added 30 min before stimulation. Inhibitors included: the Ang II receptor 1 antagonist losartan (10 µmol/L; Merck, Darmstadt, Germany, Cat. No. USPH1370462), the non-specific AT_2 blocker PD 123177 (1 µmol/L; Sigma-Aldrich, Cat. No. P5749), the toll-like receptor 4 inhibitor CLI-095 (1 µmol/L; Invivogen, San Diego, CA, USA, Cat. No. TLRL-CLI95), the NFκB inhibitor parthenolide (1 µmol/L; Sigma-Aldrich, Cat. No. P0667) or the calcineurin inhibitor cyclosporine A (200 ng/mL; Sigma-Aldrich, Cat. No. 30024). Control cells were stimulated with vehicle. After the incubations, ECs were usually frozen at -80˚C to study gene or protein expression (explained at sections 7 and 17, respectively) and NADPH oxidase activity (explained at section 15).

Primary cultures of vascular smooth muscle cells (**VSMCs**) were obtained from aorta of three-month-old C57Bl/6J mice as described (Adhikari et al., 2015). Cells were grown in DMEM-high glucose medium (Sigma-Aldrich) supplemented with 20% FBS, 5 mmol/L glutamine, 100 U/mL of penicillin and 100 µg/mL of streptomycin. At 80% confluence, cells were serum-deprived for 24 hours and then they were stimulated with IFNγ (50 U/mL, 2h; PeproTech, Rocky Hill, NJ, USA, Cat. No. 31505) and Ang II (1-10 nmol/L for 3-24h; Sigma-Aldrich). Control cells were stimulated with vehicle. VSMCs were used to study *Isg15* gene expression, as indicated at section 7.

Peritoneal macrophages were obtained from control and Ang II-infused WT mice as described (Zhang et al., 2008). Briefly, 10 mL of PBS were injected into the peritoneal cavity of the mice. PBS was recovered, centrifuged (800 rpm, 5 min) and pellet was resuspended in DMEM-low glucose (Sigma-Aldrich) with 5 mmol/L glutamine, 10% FBS and 100 U/mL of penicillin and 100 µg/mL of streptomycin. Macrophages were plated in 60-mm dishes and medium was changed after 2h. After that, macrophages were cultured for 24h. At the end of the incubation time, macrophages were frozen at -80˚C until mRNA extraction for gene expression studies by qRT-PCR, as explained at the next section.

7. qRT-PCR assay.

Total RNA was isolated from human PBMCs and PVAT and from cells and mouse samples using TRIzol Reagent (Invitrogen, Carlsbad, CA, USA) and from human AAA tissue with TRIsure™ (Bioline, London, UK), according to manufacturers' protocols. RNA (0.5-1 µg) was reverse-transcribed with SuperScript™ VILO™ cDNA Synthesis Kit (Invitrogen) for PBMCs samples and with the High Capacity cDNA Archive Kit (Applied Biosystems, Foster City, CA, USA) when other cells and tissues were processed. Quantification of mRNA levels was performed by real-time PCR using specific primers and probes provided by the Assay-on-Demand system (Applied Biosystems) or PrimeTime® qPCR probe assays (Integrated DNA Technologies, Illinois, USA). Alternatively, forward and reverse primers were designed for real-time PCR (**Table 1**). Depending on the assay used in each case, we used the IQ SYBR Green supermix kit (Bio-Rad, Hercules, CA, USA) (for forward and reverse primers assays) or the NZYSpeedy qPCR Probe Master Mix (2x) ROX plus (Nzytech, Lisbon, Portugal) (for probe assays). *18S*, *ACTB* or *B2m* were used as housekeeping genes (**Table 1**). To calculate the relative index of gene expression, we employed the $2^{-\Delta\Delta C_T}$ method.

Table 1. Primers and probes used in qRT-PCR assays.

GENE NAME	Human (h)	Mouse (m) or Rat
ISG15 (h)/ *Isg15* (m)	FS: 5´AGGAATAACAAGGGCCGCAG RS: 5´GAAGGTCAGCCAGAACAGGT HS00192713_m1	Mm.PT.58.41476392.g FS: 5'GACGGTCTTACCCTTTCCAGT RS: 5'CCTTTCGTTCCTCACCAGGAT
		Rat: Rn.PT.58.18125348
USP18 (h)/ *Usp18* (m)	Hs00276441_m1	Mm.PT.58.28965870
Ifng (m)	-	FS: 5´ATCTGGAGGAACTGGCAAAAG RS: 5´TGTTGCTGATGGCCTGATTG
UBA7 (h)/ *Uba7* (m)	Hs00163295_m1	Mm.PT.58.31404401
UBE2L6 (h)/ *Ube2L6* (m)	Hs.PT.58.110053	FS: 5´CAACGTCAGGGAGGATGGTC RS: 5´ACTCACCAGCACATTGAGGG
HERC5 (h)/ *Herc6* (m)	Hs00180943_m1	FS: 5´TTTGCTCTGTCTCTCACGGG RS: 5´CTCTTTGTCCACTCCTGGG
PTGS2 (h)/ *Ptgs2* (m) (COX-2)	FS: 5´GCTCAGCCATACAGCAAATCC RS: 5´CCAAAATCCCCTTGAAGTGGG	FS: 5´TTCGGGAGCACAACAGAGT RS: 5´TAACCGCTCAGGTGTTGCAC
Mcp1 (m)	-	FS: 5´CATCCACGTGTTGGCTCA RS: 5´GATCATCTTGCTGGTGAATGAGT
Adgre1 (m) (F4/80)	-	FS: 5´TGCTCTAACTCTGTGGGAAGC RS: 5´GTTCAGGGCAAACGTCTCG
Cd3e (m)	-	FS: 5´TGGCTACTACGTCTGCTAA RS: 5´TATGGCTACTGCTGTCAGGT
NOX1 (h)/ *Nox1* (m)	Hs01071088_m1	FS: 5'CAACAGCACTCACCAATGCC RS: 5'ACATCCTCACTGACTGTGCC
NOX5 (h)	Hs00225846_m1	-
Lfa-1 (m)	-	Mm.PT.58.10215887
GRK2 (h)	Hs00176395_m1	-
TNFA (h)/ *Tnfa* (m)	Hs.PT.58.45380900	FS: 5'CCACGCTCTTCTGTCTACTG RS: 5'TGAGGGTCTGGGCCATAGA
Il6 (m)	-	FS: 5'TGATGGATGCTACCAAACTGG RS: 5'TTCATGTACTCCAGGTAGCTATGG

Ptges (m) (mPGES-1)	-	FS: 5'AGGATGCGCTGAAACGTGGAG RS: 5'CCGAGGAAGAGGAAAGGATAG
LEP (h) (Leptin)	Hs.PT.58.38591248.g	-
ADIPOQ (h)/ *Adipoq* (m) (Adiponectin)	Hs.PT.58.26002735	FS: 5'TGATGGCAGAGATGGCACTC RS: 5'CTGTCTCACCCTTAGGACCA
CD68 (h)	FS: 5'TAGCTGGACTTTGGGTGAGG RS: 5'CCAGTGCTCTCTGCCAGTA	-
CD3G (h)	FS: 5'TCTACCAGCCCCTCAAGGAT RS:5'AGGAGGAGAACACCTGGACTA	-
CD4 (h)	Hs00181217	-
CD8A (h)	Hs00233520	-
ACTB (h) (β-actin)	FS: 5´AGAGCTACGAGCTGCCTGAC RS: 5´AGCACTGTGTTGGCGTACAG Hs99999903_m1	-
B2m (m)	-	FS: 5´ACCCTGGTCTTTCTGGTGCTT RS: 5´TAGCAGTTCAGTATGTTCGGCTT
18S rRNA (h, m)	4310893E FS: 5'GTAACCCGTTGAACCCATT RS: 5'CCATCCAATCGGTAGTAGCG	4310893E

FS: Forward sequence; RS: Reverse sequence

8. Measurement of secreted ISG15.

Secreted ISG15 was measured in supernatant from aortic segments (2 mm in length) from WT mice treated or not with Ang II (1.44 mg/kg/day, 2 weeks;). After segments incubation for 6h in 150 µL of Krebs-HEPES buffer (in mmol/L: 130 NaCl, 5.6 KCl, 2 $CaCl_2$, 0.24 $MgCl_2$, 8.3 HEPES, 11 glucose, pH = 7.4) we used CircuLex Mouse ISG15 ELISA Kit (MBL International, Cat. No. CY-8091), following the manufacturer´s instructions. Specificity of the kit was confirmed using arteries from $ISG15^{-/-}$ mice that showed no detectable values (data not shown). Values were normalized per total amount of protein.

9. Proteomics study.

9.1. Protein digestion and peptide labeling and fractionation.

Aorta samples from mice were homogenized and then, protein extracts were prepared using ceramic beads (MagNa Lyser Green Beads instrument, Roche, Germany) in extraction buffer (50 mM Tris-HCl, 10 mM DTT, 4% (w/v) SDS, 50 mM iodoacetamide, pH 8.5) and boiled 5 min. After this point, samples were centrifuged and the supernatant was collected. Protein concentration in each sample was measured using RC/DC Protein Assay (Bio-Rad), and they were stored at -80˚C until tryptic digestion.

For tryptic digestion, we used filter-assisted sample preparation technology (FASP, Expedeon, San Diego, CA, USA) according to previously published method (Wisniewski et al., 2009). Briefly, 100 µg of each protein extract was diluted in urea sample solution (8 M urea in 100 mM Tris-HCl, pH 8.5) and loaded on filters. After centrifugation and a wash step with the same buffer, reversible oxidized protein thiol groups were reduced with dithiothreitol and then alkylated using methyl methanethiosulfonate, as described in the FASOLX method (Bonzon-Kulichenko et al., 2020). Proteins were digested overnight at 37°C using sequencing grade trypsin (Promega, Madison, WI, USA) in a 1:40 ratio (µg of trypsin:µg of protein) in 50 mM ammonium bicarbonate, pH 8.8. Eluted peptides were desalted on Waters Oasis HLB C18 cartridges (Waters Corp, Milford, MA, USA).

The resulting peptides were labeled with iTRAQ 8plex reagents (AB Sciex, Framingham, MA, USA), according to the manufacturers protocol. We performed 2 iTRAQ experiments, each one containing samples from 8 individuals (2 WT, 2 ISG15$^{-/-}$, 2 WT Ang II, and 2 ISG15$^{-/-}$ Ang II). Labeled peptides were mixed, desalted and separated into 5 fractions using high pH reversed-phase peptide fractionation (Thermo Fisher Scientific) by graded concentration of acetonitrile (ACN) prepared in triethylamine: (1) 12.5% ACN; (2) 15% ACN; (3) 17.5% ACN; (4) 20% ACN; (5) 50% ACN. Finally, eluted fractions were dried and stored at −20°C until LC-MS/MS analysis.

9.2. LC-MS/MS and data acquisition.

The tryptic peptide mixture was subjected to nanoLC-MS/MS. High-resolution analysis was performed on a nano-HPLC Easy nLC 1000 liquid chromatograph coupled to a QExactive HF-Orbitrap (Thermo Fisher Scientific) mass spectrometer. Peptides were suspended in 0.1% formic acid, loaded onto a C18 reverse phase nano-precolumn (Acclaim PepMap100, 75-µm internal diameter (I.D.), 3-µm particle size and 2-cm length, Thermo Fisher Scientific), and separated on an analytical C18 reverse phase nano-column (75 µm I.D. and 50 cm, Acclaim PepMap100,

Thermo Fisher Scientific), in a continuous gradient (9–30%B for 300 min, 30–90%B for 3 min, 90%B for 10 min, 90-2%B for 2 min and 2%B for 30 min, where A is 0.1% formic acid in HPLC water and B is 90% ACN, 0.1% formic acid in HPLC grade water).

Spectra were acquired using full ion-scan mode over the mass-to-charge (m/z) range 390–1600 and 60,000 (Full Width at Half Maximum, FWHM) FT-resolution. MS/MS was performed on the top fifteen ions in each full MS scan in data-dependent acquisition mode with 45s dynamic exclusion enabled. High collision energy dissociation (HCD) induced fragmentation was set to 30% normalized collision energy (NCE). MS/MS scan resolution was set to 17,500 and the first mass in fragmentation spectrum range was fixed at 100 m/z. A total of 22 MS data sets, four from unfractionated material and eighteen from the corresponding fractions, were registered with 125h total acquisition time.

9.3. Protein identification, quantification and statistics.

Proteins were identified in the raw files using the SEQUEST HT algorithm integrated in Proteome Discoverer 2.1 (Thermo Finnigan, Thermo Fisher Scientific). MS/MS scans were matched against a mouse protein database combined with human keratins and pig trypsin (UniProtKB/Swiss-Prot 2019_01 Release). For database searching, parameters were selected as follows: trypsin digestion with 2 maximum missed cleavages allowed, precursor mass tolerance of 800 ppm and a fragment mass tolerance of 0.02 ppm (Bonzon-Kulichenko et al., 2015). The N-terminal and lysine iTRAQ-8plex modifications were chosen as fixed modifications, whereas methionine oxidation, cysteine carbamidomethylation and cysteine methylthiolation were chosen as variable modification. The false discovery rate (FDR) was calculated based on the results obtained by database searching against the corresponded inverted database using the refined method (Martínez-Bartolomé et al., 2008; Navarro and Vázquez, 2009). Quantitative information was extracted from the intensity of the iTRAQ reporter ions in MS/MS spectra.

For comparative analysis of protein abundance changes, we used the Weighted Scan-Peptide-Protein (WSPP) statistical model (Navarro et al., 2014) under the SanXoT software package (Trevisan-Herraz et al., 2019). This model provides a standardized variable, Zq, defined as the mean-corrected $\log_2$-ratio expressed in units of standard deviation at the protein level. For the analysis of coordinated protein changes we used the Systems Biology Triangle (SBT) statistical model (García-Marqués et al., 2016), which estimates functional category averages (Zc) from protein values by performing the protein-to-category integration. Proteins were annotated based on DAVID bioinformatics tool (Huang et al., 2009a, 2009b) using Gene Ontology terms database. Data integration was calculated by the comparison of results from the ratio ISG15$^{-/-}$

Ang II/ISG15$^{-/-}$ with respect to the ratio WT Ang II/WT, both at Zq and Zc levels. Results of oxidized peptides abundance changes were tested for significance using the Kolmogorov-Smirnov test. These proteomics analyses were performed in Centro Nacional de Investigaciones Cardiovasculares by Drs. Inmaculada Jorge and Jesús Vázquez.

10. Masson´s trichrome staining.

Collagen was stained in paraffin-embedded aorta sections. They were dewaxed (at 60˚C 1h and xylol 5 min), and hydrated through EtOH (100% 5 min, 70% 5 min) to H_2O. Finally, they were stained with Masson-Goldner staining following the instructions of the manufacturer (Merck, Cat. No. 100485). After dehydration (through increasing concentrations of EtOH to xylol), slides were coverslipped using DPX Mountant for hystology (Sigma-Aldrich) and tissues were observed using an inverted microscope (Inverted microscope Axio Vert. A1, Zeiss, Oberkochen, Germany) and a camera (Axiocam 105 color, Zeiss) at x20 magnification. Finally, the media thickness of each aorta was measured.

11. In vivo ultrasound imaging.

Aortic images were taken in isoflurane-anesthetized mice (2% isoflurane) by high-frequency ultrasound with a VEVO 2100 echography device (VisualSonics, Toronto, Canada) at 30-µm resolution. Maximal internal diameter was measured at systole using VEVO 2100 software, version 1.5.0. These measurements were taken before Ang II administration to determine baseline diameters, and they were repeated at the indicated time points after Ang II-infusion. These experiments were carried out in Centro Nacional de Investigaciones Cardiovasculares by Dr. Ana García Redondo and Mª Jesús Ruiz.

12. Verhoeff-Van Gieson staining.

Aorta's elastic fibers were stained with a modified Verhoeff-Van Gieson staining. Paraffin-embedded aorta sections were dewaxed and hydrated (through 60 ˚C 1h, xylol 5 min, 100% EtOH 5 min, 70% EtOH 5 min and H_2O) before they were submerged in Verhoeff´s solution for 1 hour, differentiated in 2% ferric chloride for 1-2 minutes, treated with 5% sodium thiosulfate for 1 minute and finally counterstained in Van Gieson´s solution for 3-5 minutes. After dehydration (through EtOH increasing concentrations to xylol), slides were coverslipped using DPX and

images were obtained using an inverted microscope (Inverted microscope Axio Vert. A1, Zeiss) and a camera (Axiocam 105 color, Zeiss) at x40 magnification. Finally, elastic lamina breaks were counted in the medial layer of six sections per mouse and the mean number of breaks was calculated.

13. In situ detection of vascular $O_2^{\cdot-}$ production.

Incubation with the oxidative fluorescent dye dihydroethidium (DHE, Sigma-Aldrich) was used to evaluate $O_2^{\cdot-}$ production *in situ*. OCT-frozen aorta sections were washed once with Krebs-HEPES buffer and they were equilibrated for 30 min at 37˚C in the same buffer. Fresh buffer containing DHE (2 µM) was topically applied onto each tissue section. These aorta sections were incubated for 30 min in a light-protected humidified chamber at 37˚C, dried off, coverslipped using Prolong (Thermo Fisher Scientific) and viewed with a fluorescent laser scanning confocal microscope (Leica TCS SP5 equipped with x63 objective; Leica Microsystems). Fluorescence was detected with a 568 nm long-pass filter, using the same imaging settings for all experimental conditions. For quantification, three-four rings per animal were observed and averaged. The mean fluorescence densities in the target region were calculated. To minimize laser fluctuations from one day to another, all experimental groups were imaged every day and data were expressed as % of signal in control arteries.

14. Superoxide measurement by electron paramagnetic resonance.

Superoxide production in EC homogenate was measured by electron paramagnetic resonance (EPR) in samples containing 10 µg of protein and using the spin probe cyclic hydroxylamine 1-hydroxy-3- methoxycarbonyl-2,2,5,5-tetramethylpyrrolidine (CMH, 1 mM; Enzo Life Sciences, Exeter, UK; Cat. No. ALX-430-117) in a total volume of 100 µL of Krebs-HEPES buffer containing deferoximine (25 µM) and DETC (5 µM). After homogenization, EPR samples were placed in 50 µl glass capillaries and measurements were performed by Bruker BioSpin's e-scan EPR (Bruker® Biospin Corp., Southborough, MA, USA) equipped with a super-high Q microwave cavity at room temperature. The EPR instrument settings for experiments were as follows: field sweep, 50 G; microwave frequency, 9.78 GHz; microwave power, 20 mW; modulation amplitude, 2 G; conversion time, 656 ms; time constant, 656 ms; 512 points resolution and receiver gain, 1×10^5. Results were normalized by protein content.

15. NADPH oxidase activity assay.

The $O_2^{\cdot-}$ production generated by NADPH oxidase was determined by a chemiluminescence assay. Briefly, ECs were rinsed with PBS and maintained in phosphate buffer (50 mmol/L KH_2PO_4, 1 mmol/L EGTA, 150 mmol/L sucrose, pH 7.4). The reaction started with the addition of lucigenin (5 µmol/L) and NADPH (100 µmol/L; Sigma-Aldrich) mixture to the protein sample in a final volume of 250 µL. Chemiluminescence was determined every 2.4 seconds for 3 min in a microtiter plate luminometer (Enspire Perkin Elmer, Waltham, MA, USA). Basal activity in the absence of NADPH was subtracted from each reading and the result was normalized to protein concentration.

16. Measurement of H_2O_2 levels.

Hydrogen peroxide (H_2O_2) levels were measured in fibroblasts by amplex red fluorescence assay kit (Life Technologies, Paisley, UK, Cat. No. A22188) according to the manufacturer´s instructions. Fluorescence was measured in a 96-well plate at Ex/Em=530/590 nm. Finally, H_2O_2 production was normalized to protein concentration.

17. Western blot.

Cultured ECs were homogenized in lysis buffer [(in mmol/L) sodium pyrophosphate 50, NaF 50, NaCl 5, EDTA 5, EGTA 5, HEPES 10, Na_3VO_4 2, PMSF 50, Triton 100 0.5%, and leupeptin/aprotinin/pepstatin 1 mg/mL]. Proteins (10 µg) were separated by electrophoresis on 12% SDS polyacrylamide gel and transferred to a nitrocellulose membrane. Non-specific binding sites were blocked with 5% non-fatty dried milk in Tris-buffered saline solution with Tween (TBS-T) for 1h at room temperature. Different membranes were probed with anti-NOX1 (Sigma-Aldrich, Cat. No. SAB4200097, rabbit, 1:1000), anti-NOX4 (Abcam, Cambridge, UK, Cat. No. ab133303, rabbit, 1:1000), anti-NOX5 (kindly provided by Dr. David Harrison, rabbit, 1:1000) and anti-β-actin (Sigma-Aldrich, Cat. No. A2228, mouse, 1:1000) overnight at 4˚C. Next, membranes were washed with TBS-T and incubated with secondary fluorescence-coupled antibodies goat-anti-rabbit-IRDye 800 or goat-anti-mouse-IRDye 680 (LI-COR, Cambridge, UK) 1h, at room temperature in the dark and visualized by an infrared laser scanner (Odyssey Clx, LI-COR). Western blotting images were quantified using the software Image Studio™ Lite free version (LI-COR). Protein expression levels were normalized to loading controls and expressed as percentage (%) of the control.

18. Immunofluorescence.

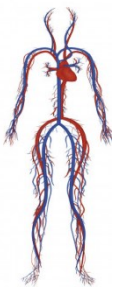
OCT-embedded aortic segments from mice were blocked with FBS 5% and incubated with primary antibody anti-LFA-1 (1:100) (Abnova, Taiwan, Cat. No. MAB7916) overnight at 4°C. After washing, slides were treated with the corresponding fluorescent antibody (Amersham Bioscience, Amersham, UK). Sections were counterstained with DAPI (Sigma-Aldrich) and mounted with Prolong (Thermo Fisher Scientific). The specificity was checked by omission of primary antibodies. Images were obtained with a Leica TCS SP2 confocal system (Leica Microsystems). Serial optical sections (z step=0.5 µm) were captured with a x40 oil objective.

19. Data analysis and statistics.

Statistical analysis was done by GraphPad Prism Software (v7.04) or by SPSS 15.0. All data are expressed as mean values±SEM and dot plots or *n* represents the number of animals, different cultures or patients studied. To choose the appropriate statistical test, we studied data distribution (by Shapiro-Wilk normality test). Results were analyzed by the Mann-Whitney non-parametric or Student's t-tests when appropriate (two-tailed) or one-way or two-way Anova followed by Bonferroni's, Tukey's or Sidak's multiple comparison tests. For survival analysis a Log rank (Mantel-Cox test) was calculated. Statistical analysis for the human PVAT study was also performed by GraphPad Prism. Univariate association was performed by Spearman correlation test. A $p < 0.05$ was considered significant.

Statistical analysis for the population used for the isolation of peripheral blood mononuclear cells were performed by SPSS 15.0. Univariate association was performed by Pearson correlation test. Multivariate linear regression analysis was conducted with carotid-IMT as dependent variable, including in the model the traditional risk factors and those variables that were significant in the univariate analysis. A $p < 0.05$ was considered significant.

Statistical analysis for proteomic studies is explained at section "9.3. Protein identification, quantification and statistics".



Results

CHAPTER 1

Hypertension is considered a low-grade inflammatory disease with increased local and circulating levels of proinflammatory cytokines, like TNFα and IFNγ, and infiltration of inflammatory cells in the vasculature and the contiguous PVAT. This inflammatory milieu can modify the structure and the function of the arteries. In the first chapter, we investigate the role of one IFN stimulated gene in the vascular alterations associated to hypertension.

1. Interaction network analysis uncovers a role for ISGylation and ISG15 with hypertension and vascular damage.

To date, there is no information of the possible relationship of the ISG15 pathway with vascular damage in CVD and specifically in hypertension. We then first performed a bioinformatic analysis to test this putative relationship. To identify the common proteins involved in hypertension, we searched for the term "Hypertension" in Phenopedia, and 2206 proteins were retrieved (**Annexed Table 1**). We then applied Upstream Regulator Analysis tool from Ingenuity Pathways Analysis software. Among the Upstream Regulators, we found cytokines like TNF, IL-1β, TGF-β1, IFNγ, or IL-6, and transcription factors such as signal transducer and activator of transcription 3 (STAT3) or NFκB as the most important master regulators for the dataset (*Upstream Regulator For Hypertension* in **Annexed Table 2**, only in electronic format). We then focused on IFNγ that was connected with 932 proteins from the dataset, among which 410 were directly connected (*IFNG Network* in **Annexed Table S2A,** only in electronic format). Interestingly, the ISGylation-related protein UBA7 and the de-ISGylation protein USP18 also appeared among the master regulators (*Upstream Regulator For Hypertension* in **Annexed Table 2**, only in electronic format), evidencing a possible role for ISGylation in the development of hypertension. In detail, UBA7 interacts with cytokines such as TNF or the anti-inflammatory cytokine IL-10 among other interleukins (**Figure 21A**), and USP18 directly interacts with several interleukins but also with IFNγ and proteins related to IFN signaling pathways such as interferon-induced helicase C domain-containing protein 1 (IFIH1), suppressor of cytokine signaling (SOCS) 1/3, and with the transcription factor NFAT (**Figure 21B**; *UBA7 and USP18_Network* in **Annexed Table 2B and 2C,** respectively, only in electronic format).

To explore the specific relationship of ISG15 with hypertension, we created a protein-protein interaction network with the 2206 hypertension-related proteins and ISG15 by STRING/Cytoscape. We found that ISG15 could be related with 60 proteins in the network

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Bioinformatics analysis were performed by Drs. Ana García Redondo and Inmaculada Jorge.

(**Figure 21C**). Some of these proteins, such as NFκB, C-C chemokine ligand 2 (CCL2), TNF, IFNγ, STAT3 or TLR4, are closely related to endothelial dysfunction and vascular remodelling (**Figure 21C**; **Annexed Table 3**), suggesting that ISG15 could be a new hypothetical mediator of vascular damage associated with hypertension.

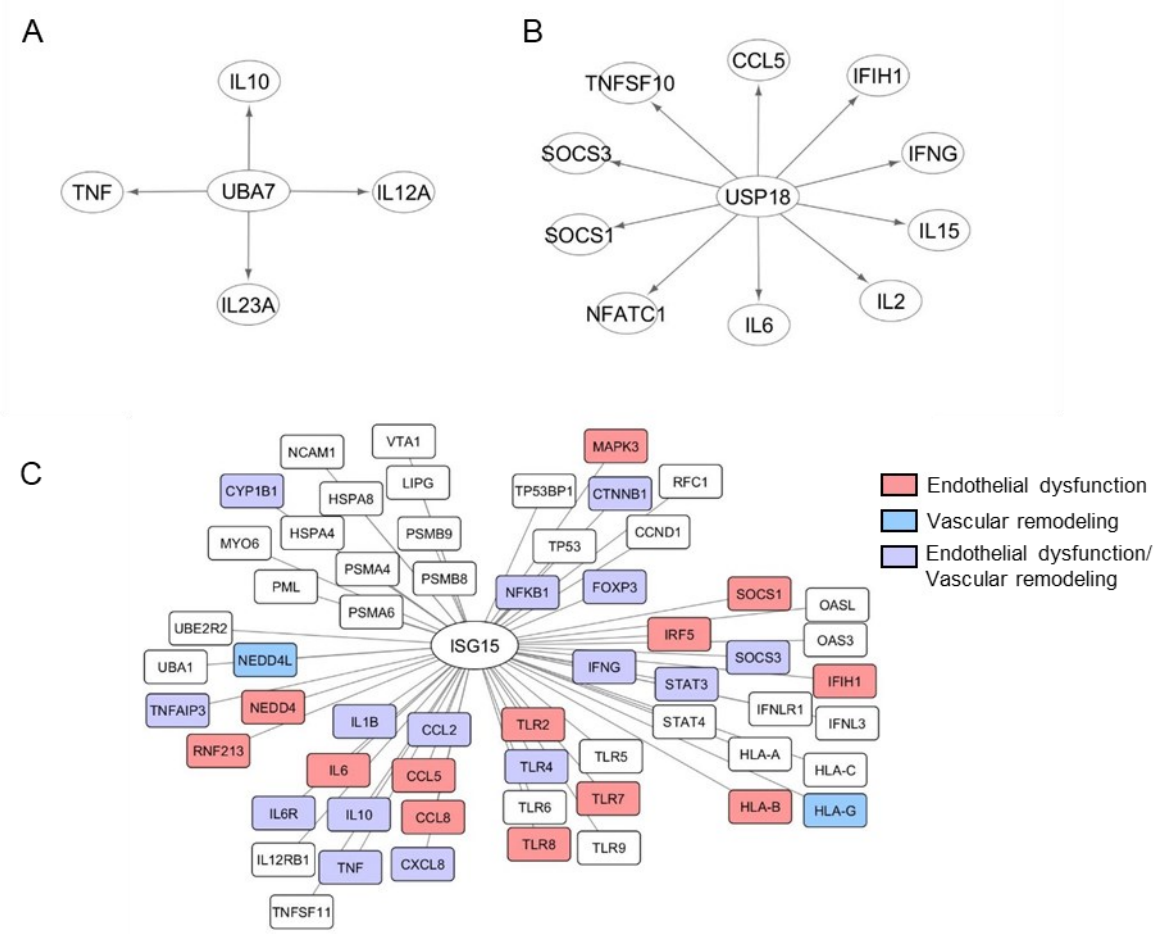

Figure 21. ISG15 is a potential mediator of vascular damage. Interactions between UBA7 (**A**) or USP18 (**B**) with other proteins involved in hypertension, obtained with Ingenuity Pathways Analysis software. (**C**), Protein-protein interaction network between hypertension-related proteins and ISG15 by STRING/Cytoscape.

2. ISG15 mRNA expression in PBMCs correlates with systolic blood pressure and with a marker of vascular remodelling in patients.

Because ISG15 is mainly expressed in immune cells in different physiological and pathological contexts and because of the key role of inflammatory cells in vascular damage, we measured *ISG15* mRNA in PBMCs from a population of 175 asymptomatic patients with cardiovascular risk factors, and its relationship with blood pressure or carotid-IMT, a marker of vascular remodelling. Characteristics of the studied population are summarized in **Table 2**.

Univariate analysis showed a positive correlation between *ISG15* mRNA and systolic blood pressure (**Figure 22A**; **Table 3**), and between *ISG15* mRNA and carotid-IMT (**Figure 22B**; **Table 3**).

Importantly, the association between carotid-IMT and *ISG15* mRNA levels (**Table 4A**) and between systolic blood pressure and *ISG15* mRNA levels (**Table 4B**) remained significant after adjusting for traditional risk factors. These results point to a relationship between *ISG15*, hypertension and vascular alterations in patients.

Table 2. Clinical characteristics of the studied population for the isolation of peripheral blood mononuclear cells and the detection of superoxide production.

Total population (n=175)	
Age, years	53.2±0.9
Gender, female/male	28/147
Body mass index, Kg/m^2	28.7±0.3
Blood pressure	
Systolic blood pressure (SBP), mm Hg	131.7±1.4
Diastolic blood pressure (DBP), mm Hg	82.7±0.7
Glucose, mg/dL	106.7±2.4
Smoking, no/yes	118/57
Arterial hypertension, no/yes	75/100
Diabetes mellitus, no/yes	149/26
Total cholesterol, mg/dL	224.2±3.3
HDL-cholesterol, mg/dL	46.2±0.9
LDL-cholesterol, mg/dL	152.7±2.9
Triglycerides, mg/dL	127.5±5.0
Superoxide production, RLU/s	18.4±1.2
ISG15, AU	3.22±0.15
Carotid-IMT, mm	0.71±0.01
Medication	
Antihypertensives, %	32
Oral hypoglycemics, %	7
Statins, %	10

Values are expressed as mean±SEM, number of subjects or percentages.

Table 3. Correlation coefficients of left carotid intima-media thickness (IMT) and *ISG15* with clinical and laboratory parameters in the studied population.

	ISG15		carotid IMT	
	r	p-value	r	p-value
Age, years	0.070	0.356	0.400	<0.001
Body mass index, kg/m^2	0.155	0.041	0.145	0.055
Systolic blood pressure, mmHg	0.274	<0.001	0.384	<0.001
Diastolic blood pressure, mmHg	0.219	0.004	0.276	<0.001
Glucose, mg/dL	0.161	0.033	0.120	0.115
Total cholesterol, mg/dL	-0.047	0.535	-0,046	0.543
HDL-cholesterol, mg/dL	0.037	0.630	0.026	0.733
LDL-cholesterol, mg/dL	-0.037	0.648	0.013	0.870
Triglycerides, mg/dL	0.005	0.951	-0.033	0.662
Superoxide production, RLU/s	0.065	0.392	0.375	<0.001
ISG15, A.U	-	-	0.274	<0.001
Carotid IMT, mm	0.261	<0.001	-	-

Correlations and p-values from Pearson correlation coefficient. A.U: arbitrary units; RLU: relative light units.

Table 4A. Multiple linear regression analysis with carotid intima-media thickness as dependent variable.

Independent variable	*β*	p-value	Partial r^2 (%)
ISG15, A.U	0.179	0.009	6.8
Age, years	0.327	<0.001	14.6
Gender, female/male	0.249	<0.001	6.5
Smoking, no/yes	0.045	0.501	0.1
Body mass index, kg/m^2	0.034	0.618	0.6
Systolic blood pressure, mmHg	0.217	0.004	3.4
Glucose, mg/dL	-0.058	0.391	0.3
Total cholesterol, mg/dL	-0.053	0.412	0.3

B, standardized regression coefficient; r^2, partial correlation after adjustment. Adjusted for age, gender, smoking, body mass index, systolic blood pressure, glucose and total cholesterol. r^2 for the total population was 32.6%. A.U: arbitrary units.

Data from PBMCs were obtained by Dr. Guillermo Zalba at Universidad de Navarra.

Table 4B. Multiple linear regression analysis with systolic blood pressure as dependent variable.

Independent variable	*β*	P-value	Partial r^2 (%)
ISG15, A.U	0.145	0.039	7.1
Age, years	0.207	0.006	9.8
Gender, female/male	-0.059	0.391	0.1
Smoking, no/yes	-0.028	0.684	0.2
Body mass index, kg/m^2	0.220	0.001	5.9
Glucose, mg/dL	0.043	0.531	0.1
Total cholesterol, mg/dL	0.086	0.188	0.6
Carotid intima-media thickness, mm	0.241	0.002	4.1

B, standardized regression coefficient; r^2, partial correlation after adjustment. Adjusted for age, gender, smoking, body mass index, glucose, total cholesterol and carotid intima-media thickness. r^2 for the total population was 27.8%. A.U: arbitrary units.

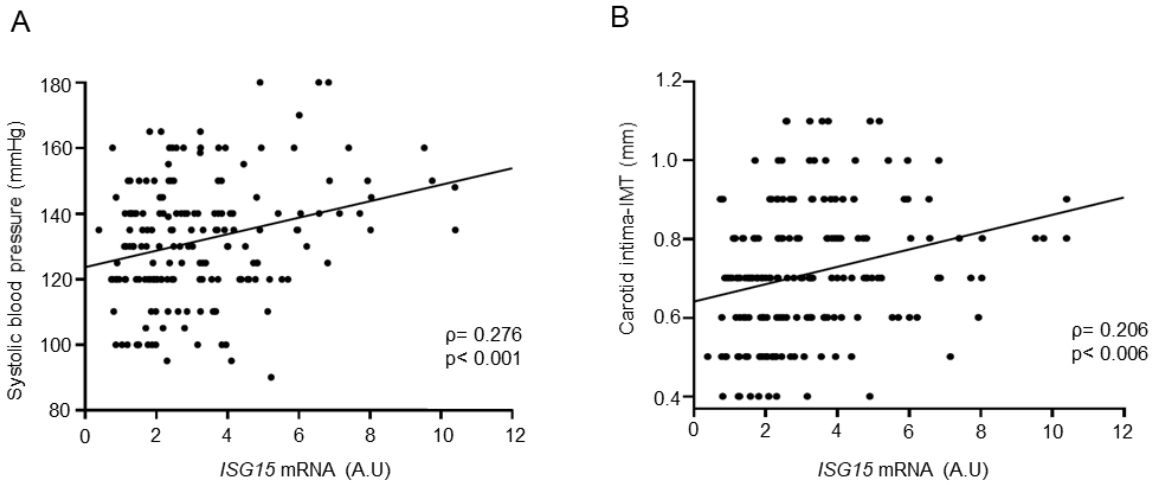

Figure 22. Positive correlation between *ISG15* mRNA and systolic blood pressure (**A**) or carotid-intima media thickness (IMT) (**B**) in human peripheral blood mononuclear cells of 175 asymptomatic patients. Univariate association was performed by Pearson correlation test. A.U indicates arbitrary units.

3. Angiotensin II induces ISG15 expression at the vascular level. Mechanisms involved.

By using cell-based systems and animal models of hypertension, we evaluated possible underlying mechanisms responsible for the role of ISG15 in vascular damage.

3.1. Angiotensin II increases IFNγ that induces Isg15 mRNA expression.

In cultured mice VSMCs IFNγ increased *Isg15* mRNA expression (**Figure 23A**) demonstrating the ability of type II IFN to stimulate *Isg15* expression at the vascular level. Previous studies have

shown that Ang II increased *Ifng* mRNA expression in aorta (Kossmann et al., 2013). This was also confirmed in our experimental model of hypertension induced by two weeks of Ang II infusion (**Figure 23B,** blood pressure levels shown in **Figure 29**). Moreover, acute *ex vivo* incubation of aorta with Ang II increased *Ifng* (data not shown) and *Isg15* mRNA expression, and this was prevented by co-incubation with an anti-IFNγ antibody (**Figure 23C**).

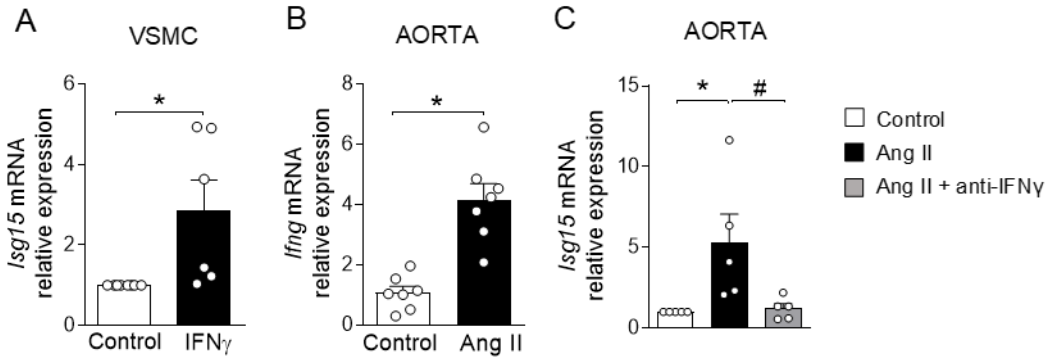

Figure 23. Ang II increases *Isg15* expression at the vascular level through IFNγ. (**A**), *Isg15* mRNA levels in vascular smooth muscle cells (VSMCs) from C57Bl6 mice treated or not with IFNγ (50 U/mL, 2h). (**B**), *Ifng* mRNA relative expression in aortas from Ang II-infused mice (1.44 mg/Kg/day, 2 weeks). (**C**), *Isg15* mRNA levels in aorta from C57Bl6 mice incubated or not with Ang II (1 µmol/L, 6h) in the absence or presence of anti-IFNγ antibody (5 µg/mL). *p<0.05 vs. Control, #p<0.05 vs. Ang II by Student t-test or one-way Anova and Sidak's multiple comparisons test. Dots in bars represent the number of cell cultures or animals.

3.2. Expression of the ISG15 system is increased in animal models of hypertension and in vascular cells and tissues in response to Ang II.

Aorta from hypertensive Ang II-infused mice showed increased *Isg15* mRNA expression (**Figure 24A**) and ISG15 protein secretion (**Figure 24B**). *Isg15* transcript was also increased in aorta from adult SHR, compared to WKY (**Figure 24C**), but not in aorta from one-month-old pre-hypertensive rats (**Figure 24D**), suggesting that high blood pressure might be a stimulus for *Isg15* expression.

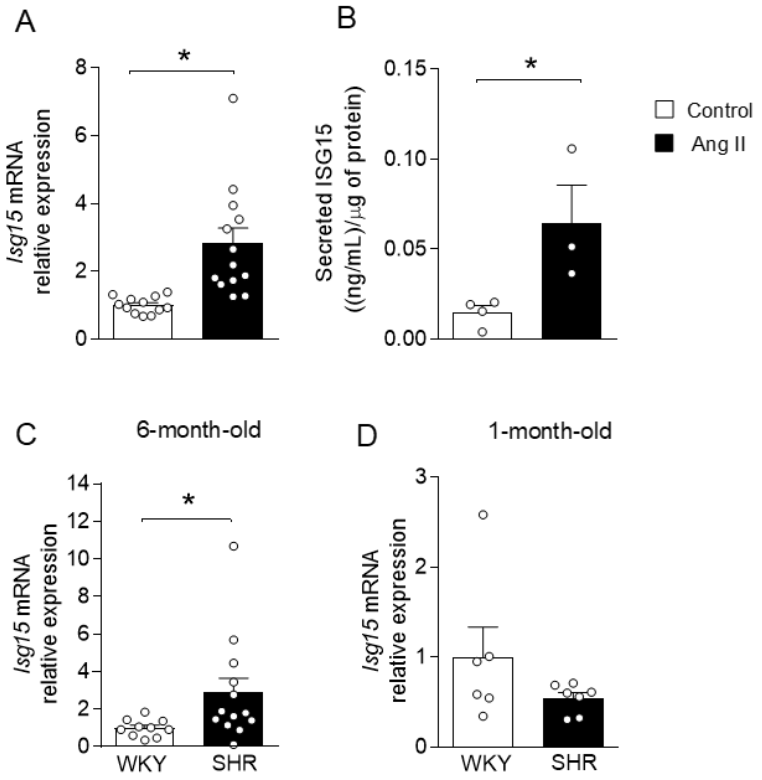

Figure 24. *Isg15* expression is increased in aorta from animal models of hypertension. *Isg15* mRNA expression (**A**) and secreted ISG15 protein (**B**) in aorta from C57Bl6 mice untreated (control) and treated with Ang II (1.44 mg/Kg/day, 2 weeks). (**C, D**) *Isg15* transcript levels in aorta from six- (hypertensive) and one-month-old (pre-hypertensive, data for blood pressure not shown) normotensive (Wistar Kyoto, WKY) and spontaneously hypertensive rats (SHR). *p<0.05 vs. Control, or vs. WKY by Student t-test. Dots in bars represent the number of animals.

We then evaluated the ability of Ang II to increase *ISG15* expression in different vascular cells. In cultured mice VSMCs, Ang II increased *Isg15* transcript (**Figure 25A**). Ang II also increased *ISG15* expression in HMEC-1 and HAEC, with the highest increase observed at the dose of 1 nmol/L (**Figure 25B**, **25C**). Similarly, Ang II increased the expression of ISGylation enzymes (*UBA7, UBE2L6 and HERC5 or Herc6*) in HMEC-1 (**Figure 25D**), and aorta from Ang II-infused mice (**Figure 25E**).

Regarding the de-ISGylation enzyme *USP18*, Ang II increased its mRNA levels in HMEC-1 but not in aorta (**Figure 25D, 25E**).

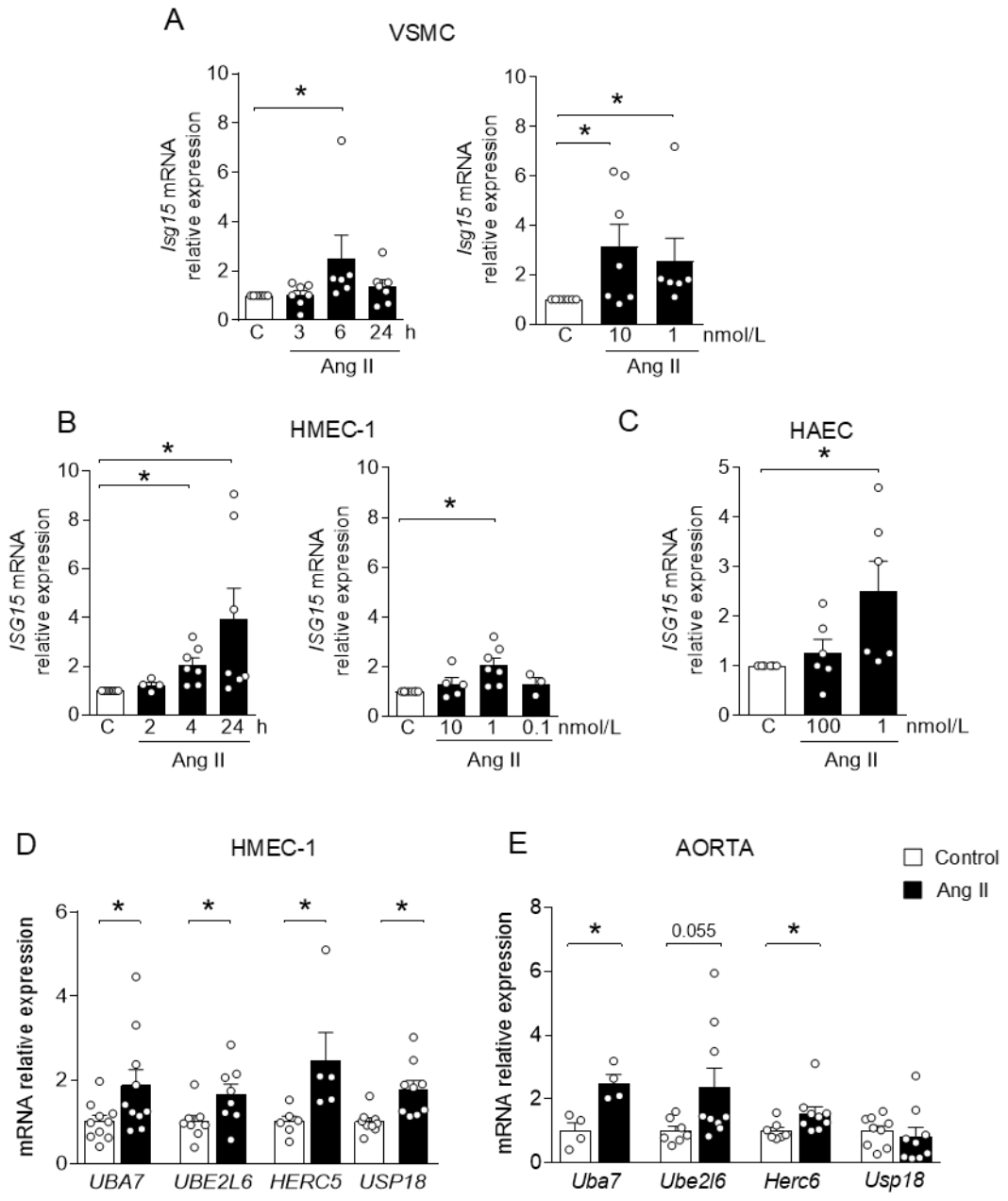

Figure 25. Ang II induces ISG15 pathway in vascular cells and aorta. *ISG15* mRNA levels in mice vascular smooth muscle cells (VSMCs) (**A**), human microvascular endothelial cells (HMEC-1) (**B**), and human aortic endothelial cells (HAEC) (**C**) incubated or not with Ang II at different times (1 nmol/L, 2-24 h) or doses (0.1-100 nmol/L, 4h). mRNA levels of ISGylation enzymes (*UBA7*, *UBE2L6* and *HERC5* or *Herc6*) and de-ISGylation enzyme *USP18* in HMEC-1 treated or not with Ang II (1 nmol/L, 4h) (**D**), and in aorta from Ang II-infused mice (1.44 mg/Kg/day, 2 weeks) (**E**). *p<0.05 vs. Control (C) by one-way Anova and Sidak's multiple comparisons post-test or unpaired Student t-test. Dots in bars represent the number of animals or cell culture experiments in each case.

We then investigated possible intracellular mechanisms that could be responsible for Ang II-induced *ISG15* expression in ECs.

3.3. NFκB is involved in Ang II-induced ISG15 expression.

The inflammatory and hypertensive effects of Ang II are mediated via AT_1 receptors. The AT_1 blocker losartan, but not the AT_2 blocker PD-123177, decreased Ang II-induced *ISG15* expression (**Figure 26A**).

It has been described that, in macrophages, TLR4 seems to be an important receptor inducing protein ISGylation (Kim et al., 2005). In addition, in a model of IκB kinase 2 activation, ISGylation of proteins in cardiomyocytes is dependent of NFκB (Maier et al., 2012). Moreover, Ang II increased TRL4 expression and activation of the transcription factor NFκB (Hernanz et al., 2015) and NFAT (Esteban et al., 2011) at the vascular level.

We found that neither the TLR4 inhibitor CLI-095 nor the NFAT inhibitor cyclosporine A prevented the Ang II-induced *ISG15* expression (**Figure 26A**, **26B**). However, the NFκB inhibitor parthenolide abolished the Ang II-induced *ISG15* mRNA in ECs (**Figure 26B**).

Altogether, these results demonstrate that Ang II increases vascular *ISG15* expression likely via AT_1/IFNγ/NFκB activation.

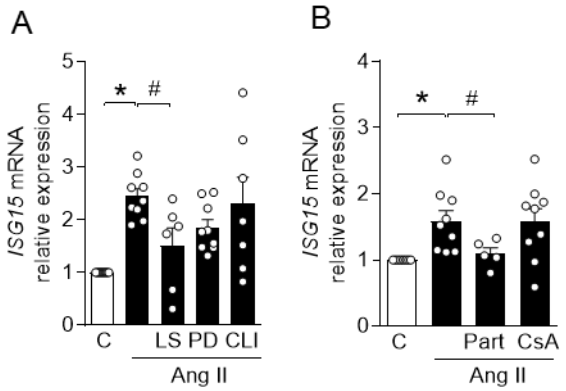

Figure 26. Ang II increases *ISG15* mRNA expression via AT_1 and NFκB activation. *ISG15* mRNA levels in human microvascular endothelial cells (HMEC-1) treated or not with Ang II (1 nmol/L, 4h) in the absence or presence of losartan (AT_1 blocker, LS, 10 µmol/L), PD-123177 (AT_2 blocker, PD, 1 µmol/L), CLI-095 (TLR4 inhibitor, CLI, 1 µmol/L) parthenolide (NFκB inhibitor, Part, 1 µmol/L) or cyclosporine A (NFAT inhibitor, CsA, 200 ng/mL). Inhibitors were added 30 min before Ang II and stimulation and inhibition experiments were performed in different sets of cells in different periods. *p<0.05 vs. Control (C), #p<0.05 vs. Ang II by one-way Anova and Sidak´s multiple comparisons post-test. Dots in bars represent the number of different cell culture experiments.

3.4. Enhanced levels of Isg15 in immune cells from hypertensive mice.

We then questioned whether Ang II might modify the expression of *Isg15* in macrophages and in PVAT, the main site from immune cells infiltration in Ang II-induced hypertension (Mikolajczyk et al., 2016). As shown in **Figure 27** Ang II-infusion increased *Isg15* mRNA expression in peritoneal macrophages (**Figure 27A**) but not in aortic PVAT (**Figure 27B**).

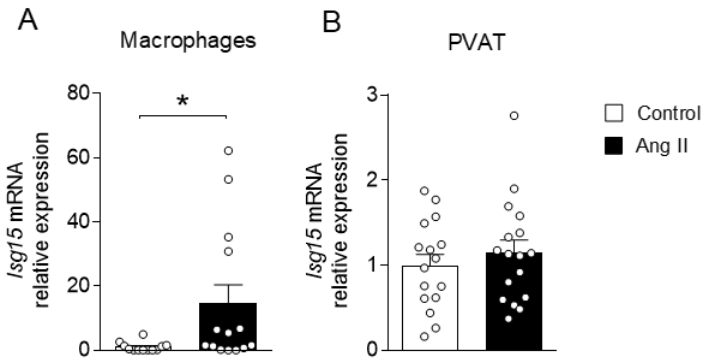

Figure 27. Ang II-infusion induces *Isg15* mRNA expression in peritoneal macrophages but not in aortic perivascular adipose tissue (**PVAT).** *Isg15* mRNA levels in peritoneal macrophages (**A**) or PVAT (**B**) from C57Bl6 mice untreated (Control) and treated with Ang II (1.44 mg/Kg/day, 2 weeks). *p<0.05 vs. Control by Student t-test. Dots in bars represent the number of animals.

4. ISG15 pathway is involved in the vascular alterations associated with hypertension.

4.1. ISG15 deletion modifies abundance of proteins involved in vascular function and remodelling in hypertension.

In order to get a comprehensive overview of the effects of ISG15 deletion at the vascular level, we carried out a multiplexed quantitative proteomics approach in aorta from WT and ISG15$^{-/-}$ mice untreated or infused with Ang II. We identified a total of 1,538 proteins (FDR<0.01) of which 52 proteins were differentially expressed between WT and ISG15$^{-/-}$ mice in response to Ang II (FDR<0.05). The complete list of these proteins is shown in **Annexed Table 4**. With this quantitative protein information, we built functional categories using a database of 428 GO terms from DAVID repository. After applying Systems Biology Triangle method (García-Marqués et al., 2016), we observed coordinated protein abundance changes at functional category level (**Annexed Table 5**).

To simplify interpretation, we manually grouped these categories into functional clusters. The *Cardiovascular remodelling* cluster included proteins that belong to 13 GO terms: skeletal

system development, positive regulation of endothelial cell proliferation, regulation of systemic arterial blood pressure, angiogenesis, blood vessel development, blood vessel remodelling, tissue homeostasis, positive regulation of cell-matrix adhesion, glycosaminoglycan biosynthetic process, heart morphogenesis, epithelial to mesenchymal transition, ventricular septum development and cardiac septum development (**Figure 28A, Annexed Table 6**). This cluster was significantly decreased (FDR<0.01) in the absence of ISG15 (**Figure 28D**), which suggests a negative effect of Ang II on the *Cardiovascular remodelling* in the aorta from ISG15$^{-/-}$ compared to WT mice. The *Cardiovascular function* cluster involved proteins that belong to 5 GO terms: regulation of heart rate, regulation of the force of heart contraction, regulation of membrane depolarization, skeletal muscle contraction and positive regulation of heart rate by epinephrine (**Figure 28B, Annexed Table 6**). This cluster was significantly increased in the absence of ISG15 (FDR<0.05) (**Figure 28D**), indicating a positive effect of Ang II on the *Cardiovascular Function* in the aorta from ISG15$^{-/-}$ compared to aorta from WT mice. Because ISG15 is an immune response protein, we also analyzed the *Immune System* cluster, represented with 14 GO terms: antigen processing and presentation of peptide antigen via MHC class I, positive regulation of defense response to virus by host, neutrophil homeostasis, hematopoietic progenitor cell differentiation, monocyte chemotaxis, positive regulation of cytokine production, prostaglandin biosynthetic process, negative regulation of inflammatory response to antigenic stimulus, adaptive immune response, immune system process, positive regulation of leukocyte migration, antigen processing and presentation of exogenous peptide antigen via MHC class I, neutrophil mediated immunity and myeloid cell homeostasis. We found a tendency to decrease (FDR=0.076) in the *Immune system* cluster in the absence of ISG15 (**Figure 28C, 28D, Annexed Table 6**).

These results provide evidence that ISG15 might play a relevant role in the vascular functional and structural alterations produced by hypertension.

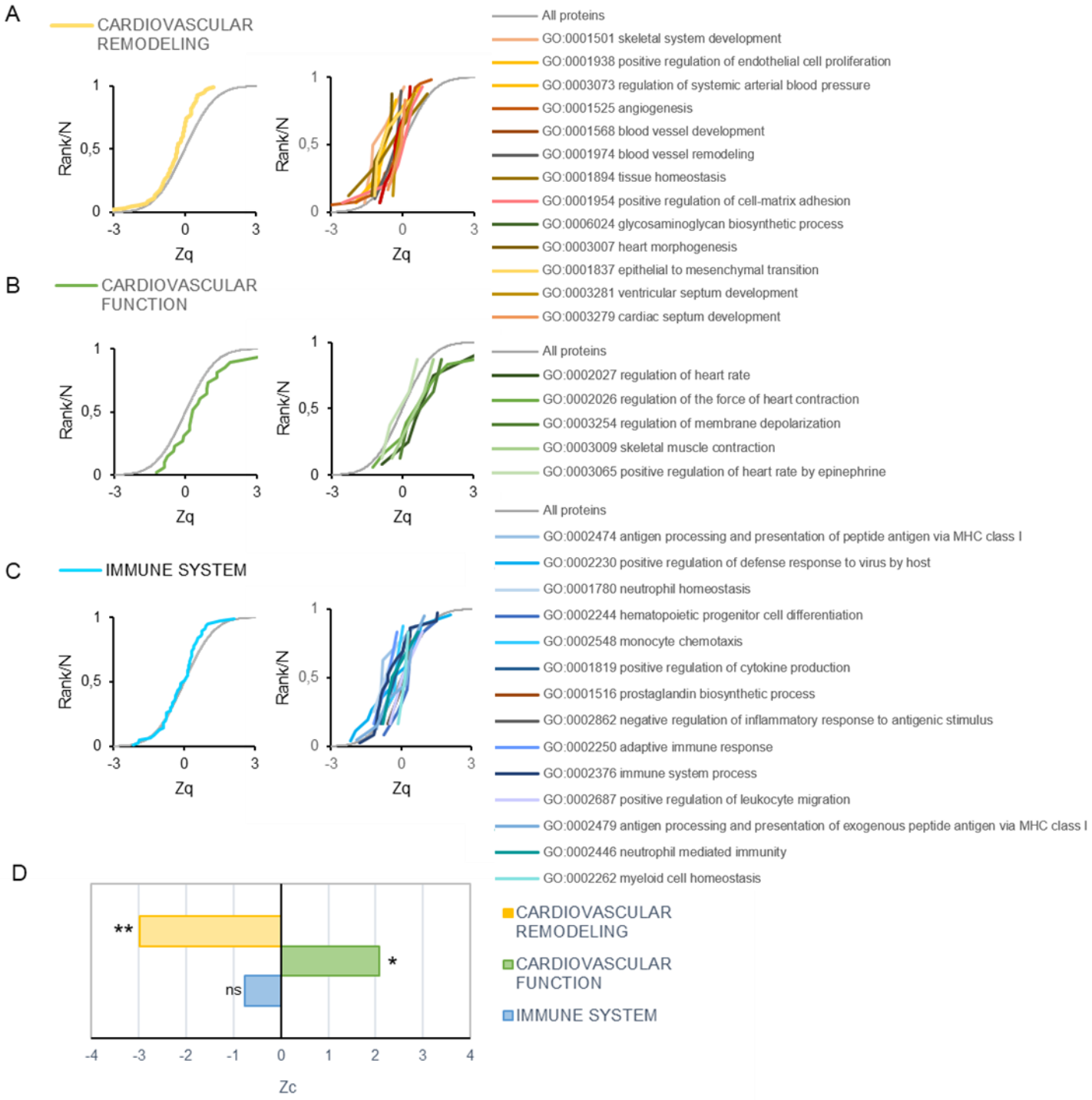

Figure 28. ISG15 promotes an alteration of *Cardiovascular remodelling* and *Cardiovascular function* categories identified by proteomics. Aortic tissue samples from WT and ISG15$^{-/-}$ treated or not with Angiotensin II (Ang II) were subjected to quantitative proteomics. The quantitative data were analyzed using the SBT model to detect coordinated protein changes in functional categories. The distributions of quantitative protein values (Zq) are plotted for three clusters (**A**) *Cardiovascular remodelling*, (**B**) *Cardiovascular function* and (**C**) *Immune system*. Panels on the left display the cumulative distribution of Zq from proteins belonging to each cluster. Panels on the right display the protein values belonging to the

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Data from proteomics analysis were obtained by Drs. Inmaculada Jorge and Jesús Vázquez at Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid.

related GO terms which compose each cluster. Protein values (Zq) are log_2 fold changes in Ang II-treated ISG15$^{-/-}$ compared to Ang II-treated WT, normalized with respect to untreated samples, expressed in units of standard deviation. (**D**) Standardized log_2 fold changes (Zc) of the three category clusters (*: FDR<0.05; **: FDR<0.01). The complete set of proteins belonging to each cluster is listed in **Annexed Table 6**.

4.2. ISG15 participates in hypertension, vascular stiffness and endothelial dysfunction in Ang II infused mice.

Since our bioinformatic analysis found a relationship between ISG15, hypertension and vascular damage, and the proteomics study identified different expression pattern of proteins involved in cardiovascular remodelling and function in response to Ang II in WT and ISG15$^{-/-}$ mice, we analyzed the physiopathological consequences of this regulation by analyzing blood pressure responses and vascular function and structure in response to Ang II in WT and ISG15$^{-/-}$ mice.

We did not find changes in systolic blood pressure in untreated WT and ISG15$^{-/-}$ mice (**Figure 29**). However, ISG15 deletion partially prevented the increase in systolic blood pressure induced by Ang II infusion (**Figure 29**).

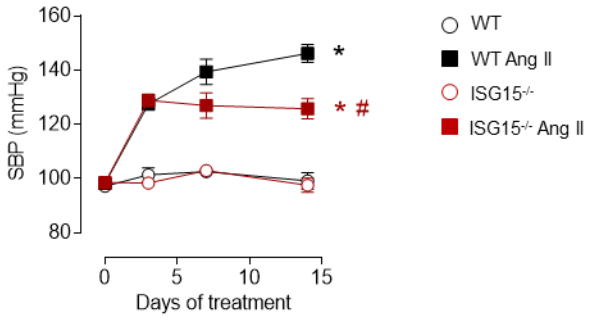


Figure 29. ISG15 is involved in Ang II-induced hypertension. Systolic Blood Pressure (SBP) in WT and ISG15$^{-/-}$ mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=8-12). *p<0.05 vs. untreated (WT or ISG15$^{-/-}$), # p<0.05 vs. WT Ang II by two-way Anova.

Vascular structure of aorta and SMA was similar in untreated WT and ISG15$^{-/-}$ mice (**Figure 30**). Meanwhile, Ang II augmented wall thickness and decreased lumen diameter in a similar manner in arteries from WT and ISG15$^{-/-}$ mice (**Figure 30A-C**). Ang II decreased the number of VSMC in mesenteric arteries from WT and ISG15$^{-/-}$ mice (**Figure 30D**). Nevertheless, the number of adventitial cells (AC) was significantly decreased only in ISG15$^{-/-}$ mice after Ang II treatment (**Figure 30D**). Regarding arterial mechanics, Ang II increased vascular stiffness in SMA from WT mice (reflected by the leftward shift of the stress-strain curve and the increased β value) but not in ISG15$^{-/-}$ mice (**Figure 30E**). This effect may be due to an altered 3D elastin structure in the

internal elastic lamina with smaller fenestrae in arteries from WT Ang II-infused mice, effects that were prevented in ISG15$^{-/-}$ Ang II-treated mice (**Figure 30F**).

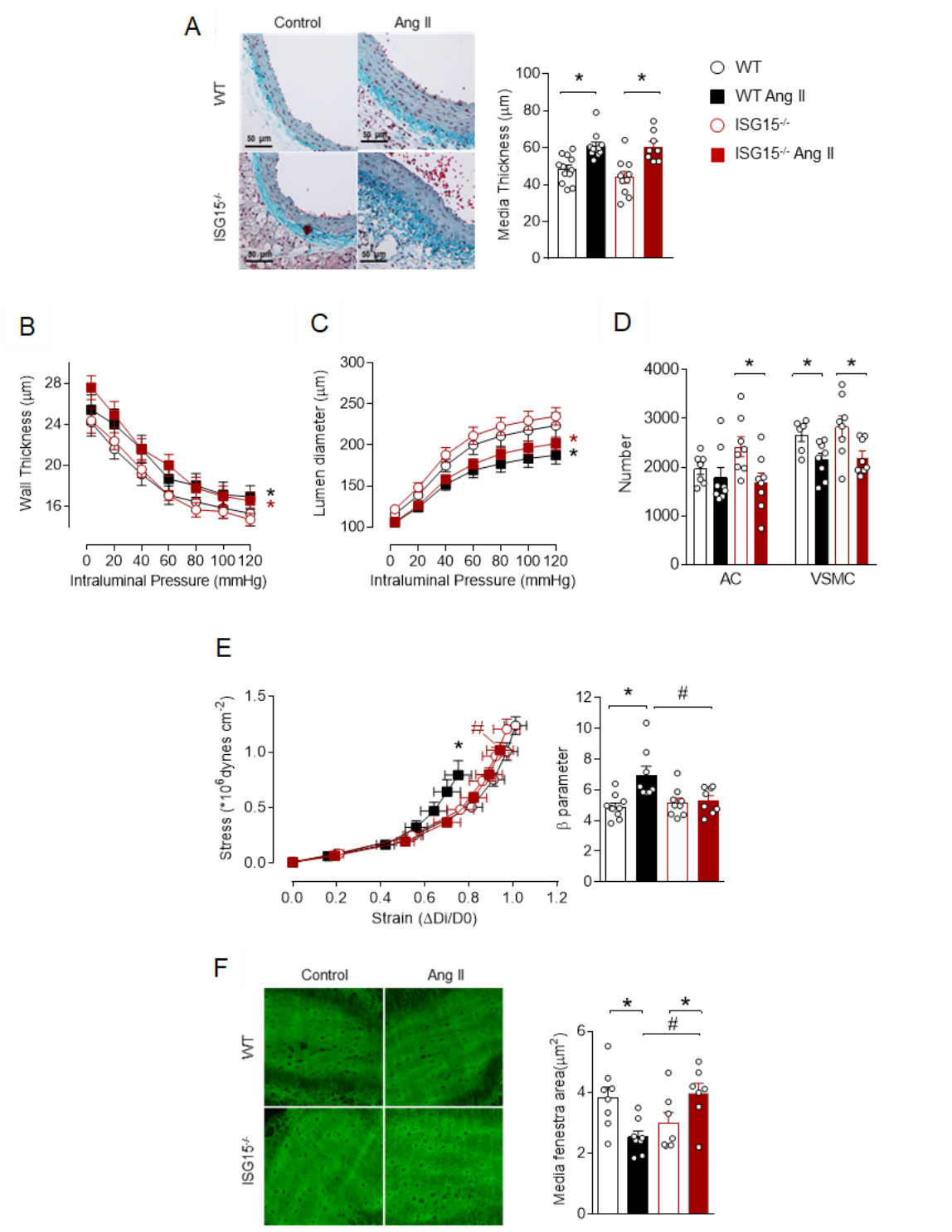


Figure 30. ISG15 is involved in Ang II-induced vascular stiffness. (**A**), Aortic Masson staining and media thickness quantification. (**B-D**) Structural and (**E**) mechanical parameters and (**F**) representative images and quantification of internal elastic lamina structure of small mesenteric arteries from WT and ISG15$^{-/-}$ mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=7-12). *p<0.05 vs. untreated (WT or

ISG15$^{-/-}$), # p<0.05 vs. WT Ang II by two-way Anova or one-way Anova and Sidak's multiple comparisons post-test. Elastin image size: 59.5×59.5µm. Dots in bars represent the number of animals.

Regarding the role of ISG15 in vascular function, endothelium-dependent or -independent relaxation and vasoconstrictor responses were similar in aorta and SMA from untreated WT and ISG15$^{-/-}$ mice (**Figure 31**). Ang II worsened endothelium-dependent relaxation to acetylcholine in aorta and SMA from WT mice but this effect was not observed in ISG15$^{-/-}$ mice that showed vascular protection (**Figure 31A, 31D**). No effect of Ang II or genotype was observed in the vascular response to exogenous added NO (**Figure 31B, 31E**), ruling out that changes in VSMC sensitivity to NO underlie the differences observed in endothelium-dependent relaxation. Ang II increased phenylephrine contractile responses similarly in aorta from WT and ISG15$^{-/-}$ mice (**Figure 31C**). Moreover, in SMA, no changes in vasoconstrictor responses were observed in the four experimental groups (**Figure 31F**).

Together, these findings point to ISG15 as a novel mediator involved in Ang II-induced hypertension, vascular stiffness and impaired endothelial function of conductance and resistance arteries.

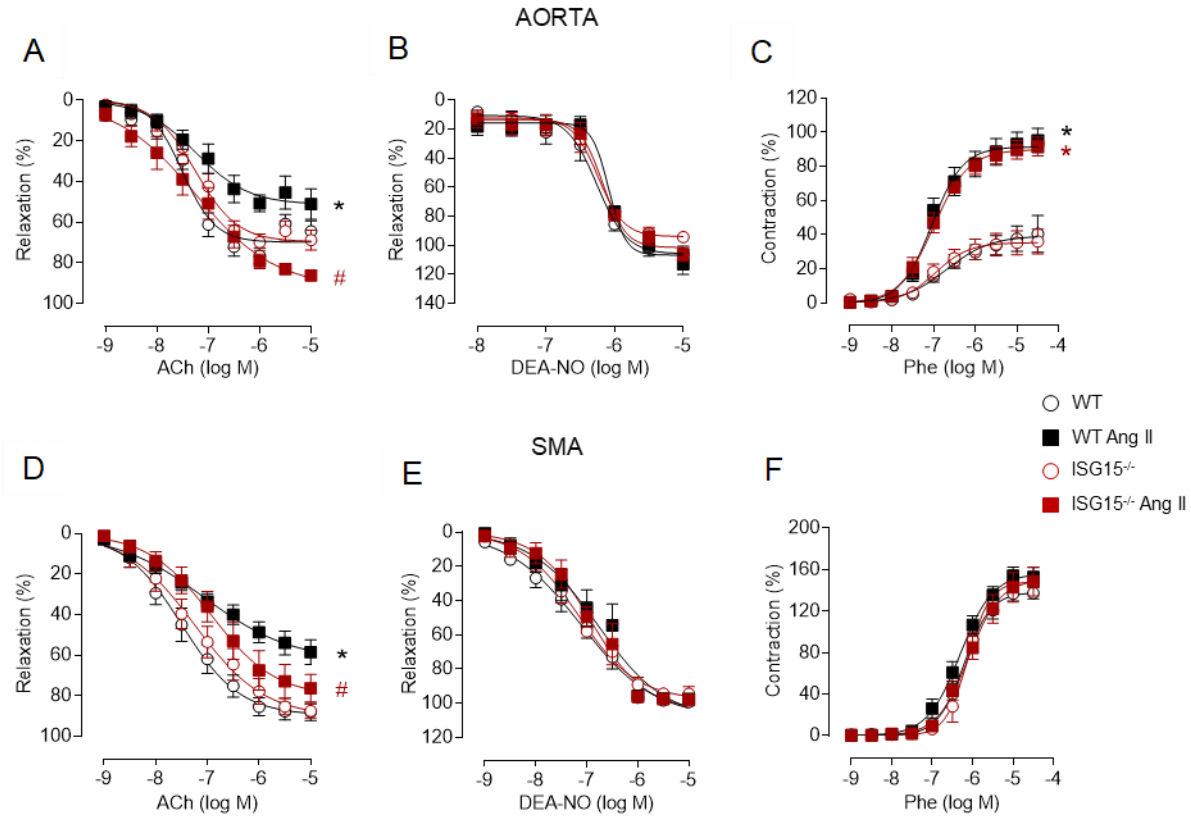


Figure 31. ISG15 is involved in Ang II-induced endothelial dysfunction. Concentration-response curves to Acetylcholine (ACh; **A**, **D**), diethylamine NONOate (DEA-NO; **B**, **E**) and phenylephrine (Phe; **C**, **F**) of aorta (**A**, **B**, **C**) and small mesenteric arteries (SMA) (**D**, **E**, **F**) from WT and ISG15$^{-/-}$ mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=7-12). *p<0.05 vs. untreated mice (WT or ISG15$^{-/-}$), #p<0.05 vs. WT Ang II by two-way Anova.

4.3. ISGylation plays a role in Ang II-induced hypertension and vascular remodelling.

As mentioned earlier, ISG15 can be found free intracellular or extracellular or conjugated to lysine residues of *de novo* synthesized target proteins, a process known as *ISGylation* that is reversible by the action of the protease USP18. To study the role of ISGylation in hypertension and vascular injury, we used a gain of function approach evaluating the effect of Ang II in the transgenic USP18^{C61A} mice. These mice have a mutation of the USP18 protein within the Cys at position 61 (substitution by alanine) that completely abolishes the isopeptidase activity leading to excessive ISGylation, without modifying others functions of USP18 (Ketscher et al., 2015).

Ang II infusion induced lethal aortic dissection in 11 out of 27 USP18^{C61A} mice, but only in 1 of 15 WT animals (**Figure 32**). We did not find lethal aortic dissections in untreated WT or USP18^{C61A} mice.

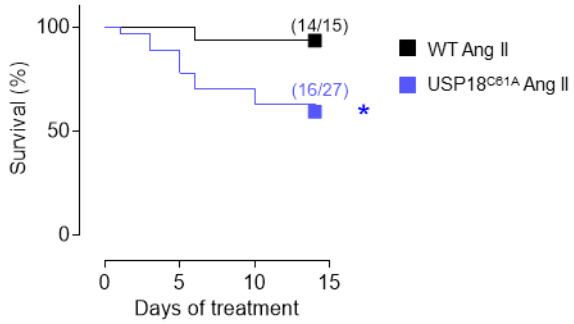


Figure 32. Ang II produces lethal aortic dissections in USP18^{C61A} mice. Survival curve of Ang II-treated WT and USP18^{C61A} mice (1.44 mg/Kg/day, 2 weeks) (n=15-27). *p<0.05 vs. WT Ang II by log-RanK (Mantel-Cox) test.

Regarding systolic blood pressure, no differences were found in untreated mice. However, Ang II-infused USP18^{C61A} mice showed a higher increase in systolic blood pressure than Ang II-infused WT mice, mainly around days 7th-10th of Ang II infusion (**Figure 33**). At the end of the treatment, systolic blood pressure was similar in both strains (**Figure 33**).

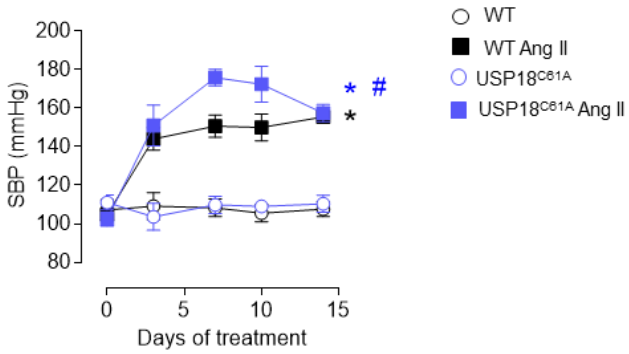


Figure 33. ISGylation increases Ang II-induced hypertension. Systolic Blood Pressure (SBP) measured by tail-cuff plethysmography in WT and USP18^{C61A} mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=8-12). *p<0.05 vs. untreated (WT or USP18^{C61A}), # p<0.05 vs. WT Ang II by two-way Anova.

In vivo ultrasound imaging showed that Ang II increased the diameter of both ascending and abdominal aorta, being this increase higher in ascending aorta from Ang II-infused USP18^{C61A} than Ang II-infused WT mice (**Figure 34A**). We did not find differences in aortic size between untreated mice (**Figure 34A**). Study of elastin fibers fragmentation by histological analysis showed that infusion of Ang II augmented elastic lamina breaks in both groups, but this effect was greater in survival USP18^{C61A} than in WT mice (**Figure 34B**).

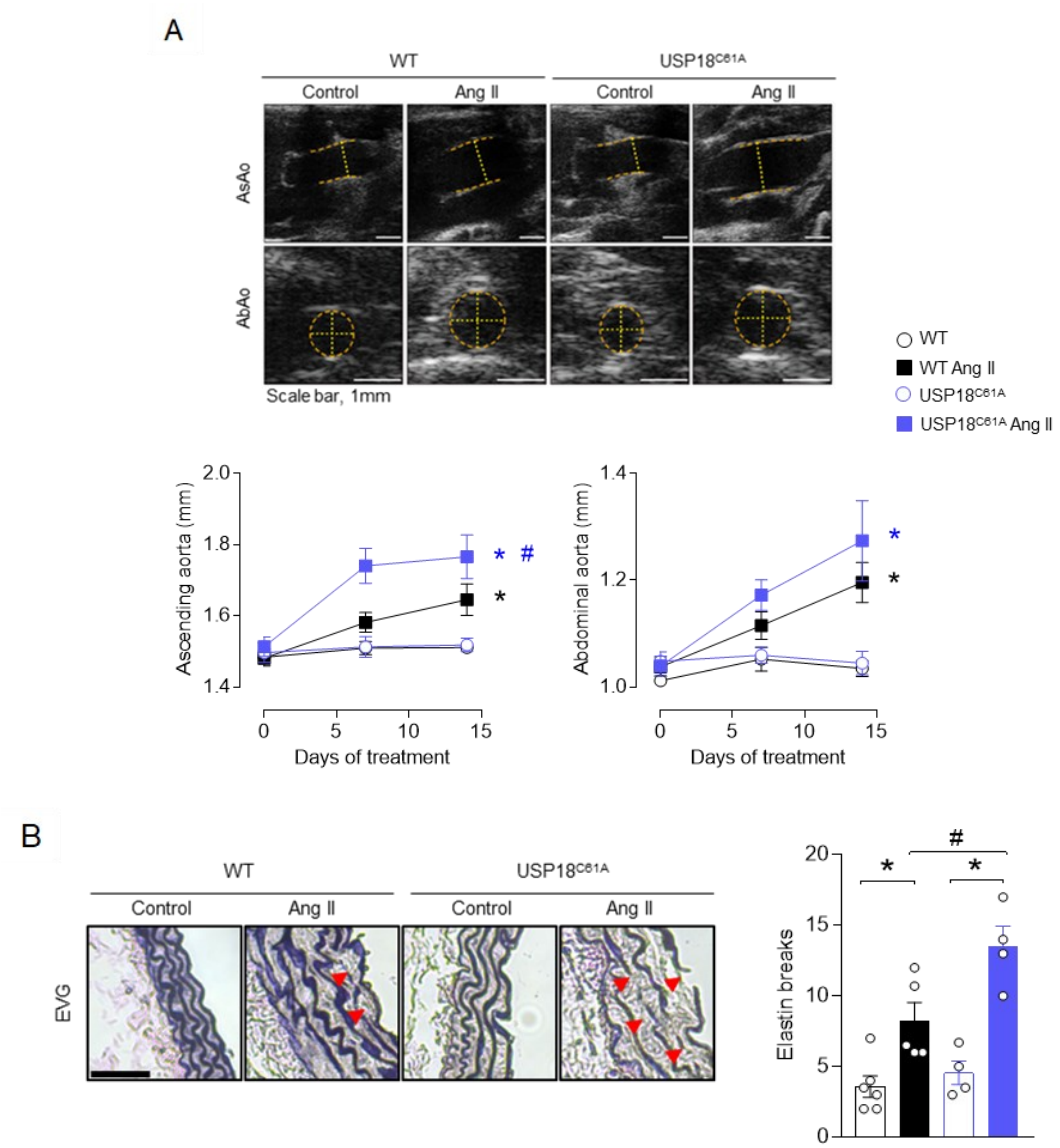


Figure 34. ISGylation exacerbates Ang II-induced vascular remodelling in aorta. (**A**), Representative ultrasound images and quantification of maximal diameter in ascending aorta (AsAo) or abdominal aorta (AbAo) from WT and USP18^{C61A} mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=8-12). (**B**), Representative aortic elastic Van Gieson (EVG) staining and quantification in the four experimental groups (dots in bars represent the number of animals). *p<0.05 vs. untreated mice (WT or USP18^{C61A}), #p<0.05 vs. WT Ang II by by two-way Anova or one-way Anova and Sidak's multiple comparisons post-test.

In vivo ultrasound imaging was carried out by Dr. Ana García Redondo and Mª Jesús Ruiz at CNIC, Madrid.

To confirm whether ISG15 might have a role in aneurysm development, we measured the expression of *ISG15* and *USP18* transcripts in murine and human AAAs. We found that the levels of *ISG15* mRNA were significantly enhanced in human aneurysms compared to aorta from healthy donors (**Figure 35A**). *Isg15* mRNA levels were also augmented in aneurysms from Ang II-infused ApoE$^{-/-}$ mice, a well-accepted animal model for aneurysms development (**Figure 35B**). Moreover, *USP18* transcript was increased in human but not in murine aneurysms (**Figure 35A, 35B**). Altogether, these results support the link between ISG15/ISGylation with hypertension and aortic remodelling.

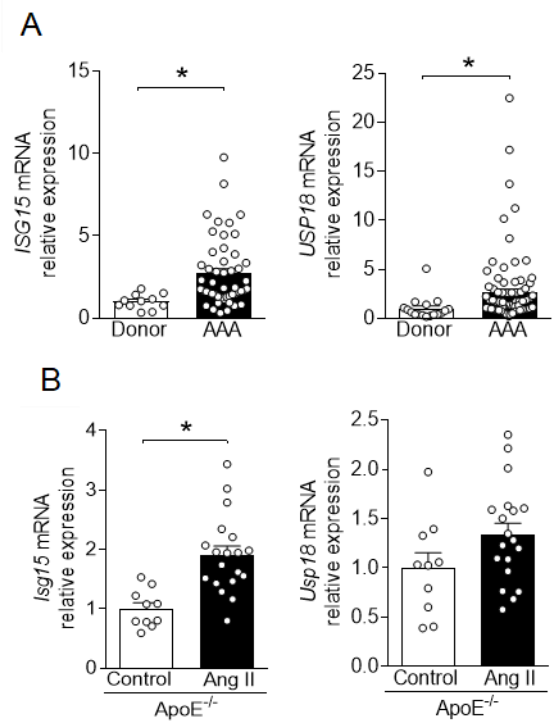


Figure 35. *ISG15* expression is increased in human and murine aortic aneurysms. *ISG15* and *USP18* mRNA levels in aortic samples from healthy donors and abdominal aortic aneurysm (AAA) patients (**A**) and in aortas from control and Ang II-infused ApoE$^{-/-}$ mice (1.44 mg/Kg/day, 4 weeks) (**B**). *p<0.05 vs. donor patients or untreated mice (Control) by unpaired Student t-test. Dots in bars represent the number of patients or animals.

Data from aneurysms (human aortic aneurysms and ApoE$^{-/-}$ mice model) were obtained by Drs. Cristina Rodríguez and José Martínez González at Institut de Recerca Hospital de la Santa Creu i Sant Pau, Barcelona.

We then evaluated the vascular phenotype of SMA. As shown in **Figure 36** no significant differences were observed in vascular structure or mechanical properties between untreated groups. Moreover, Ang II decreased lumen diameter (**Figure 36A**), increased wall thickness (**Figure 36B**), reduced the number of VSMC (**Figure 36C**) and augmented wall stiffness (**Figure 36D**) similarly in WT and USP18^{C61A} mice. Neither Ang II nor genotype affected the number of AC (**Figure 36C**).

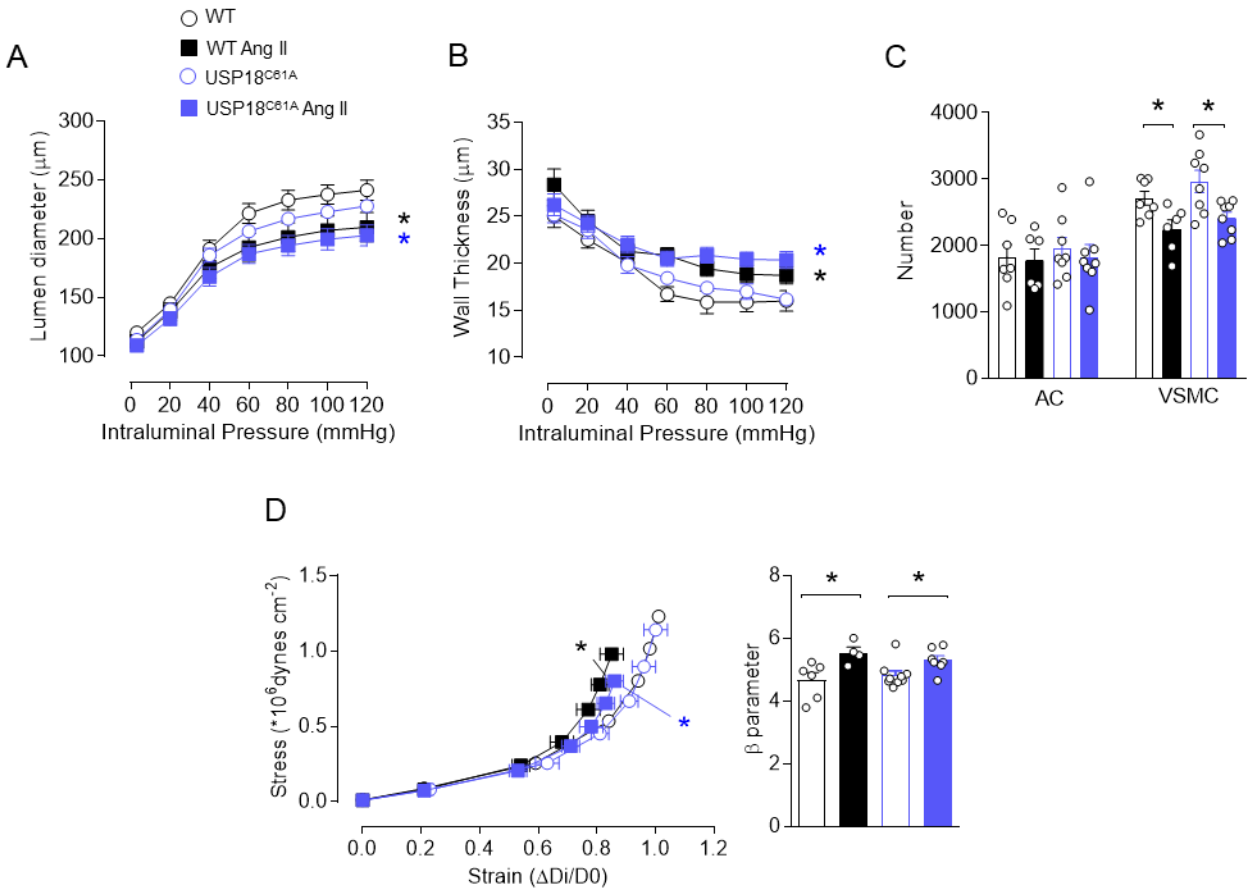


Figure 36. ISGylation does not participate in Ang II-induced structural and mechanical alterations in small mesenteric arteries. (**A**-**C**) Structural and (**D**) mechanical parameters in small mesenteric arteries (SMA) from WT and USP18^{C61A} mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=6-9). *p<0.05 vs. untreated mice (WT or USP18^{C61A}) by two-way Anova or one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

Endothelium-dependent and -independent relaxation was unchanged in arteries from untreated and Ang II-infused surviving mice from both genotypes (**Figure 37A, 37B, 37D, 37E**). Contractile responses induced by phenylephrine were slightly increased in aorta from untreated USP18^{C61A} compared to untreated WT mice (**Figure 37C**). Ang II increased phenylephrine responses to similar levels in arteries from both genotypes (**Figure 37C**). In SMA, no effect of Ang II infusion or USP18 mutation in phenylephrine response was observed (**Figure 37F**).

Together, these findings demonstrate that ISGylation is a novel determinant of Ang II-induced hypertension and the associated vascular remodelling, particularly of large arteries.

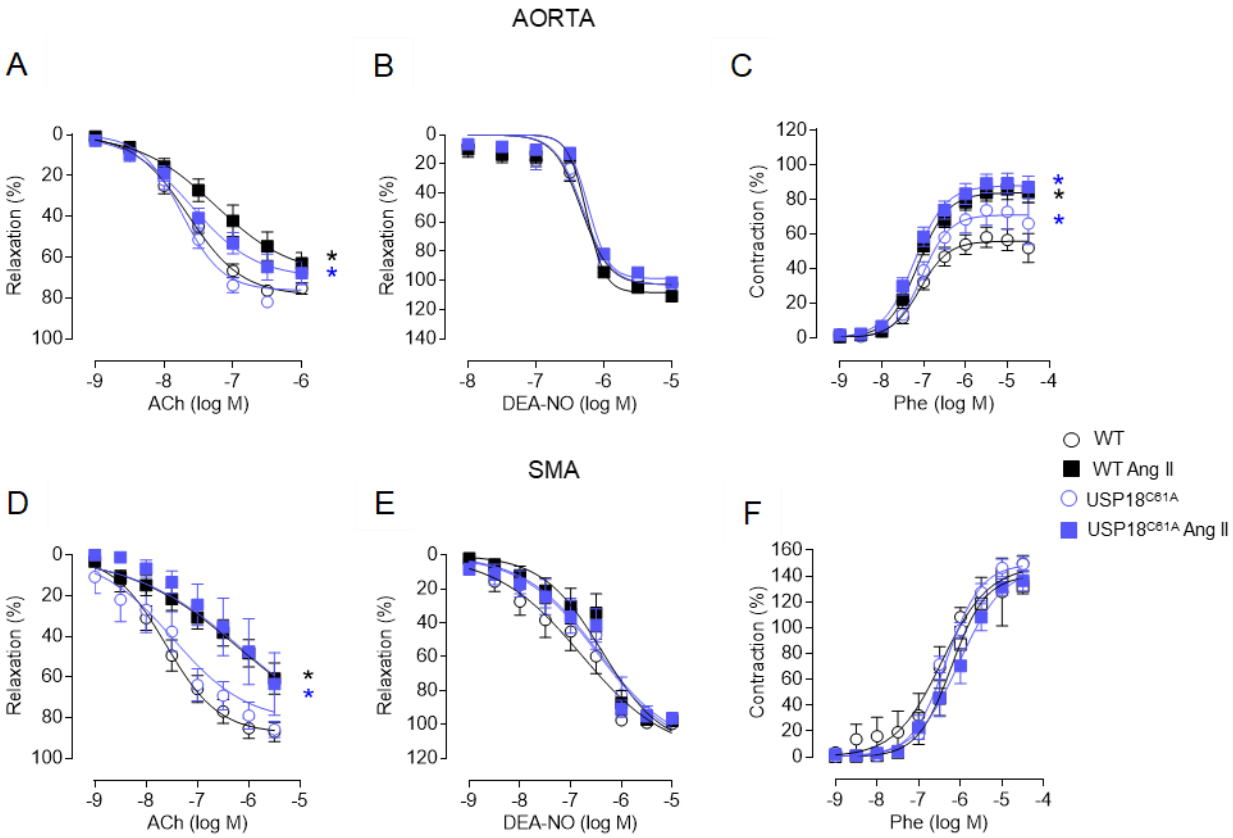


Figure 37. ISGylation does not affect vascular function. Concentration-response curves to Acetylcholine (ACh; **A**, **D**), diethylamine NONOate (DEA-NO; **B**, **E**) and phenylephrine (Phe; **C**, **F**) of aorta (**A**, **B**, **C**) or small mesenteric arteries (SMA) (**D**, **E**, **F**) from WT and USP18^{C61A} mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks) (n=6-9). *p<0.05 vs. untreated mice (WT or USP18^{C61A}) by two-way Anova.

5. Inflammation and oxidative stress are underlying mechanisms responsible for the role of ISG15 in vascular damage in hypertension.

Secreted ISG15 is an IFNγ-inducing molecule from lymphocytes (Knight and Cordova 1991; Recht et al., 1991; D'Cunha et al., 1996a, 1996b) and NK cells (Bogunovic et al., 2012; Swaim et al., 2017), being this process independent of ISGylation (Bogunovic et al., 2012). Moreover, IFNγ produces ROS that mediate the endothelial dysfunction induced by Ang II (Kossmann et al., 2013; Mikolajczyk et al., 2016), and we have previously demonstrated the participation of both oxidative stress and inflammatory mediators, such as COX-2, in endothelial dysfunction, vascular remodelling and arterial stiffness in hypertension (Martínez-Revelles et al., 2013; 2017; Avendaño et al., 2016). Then, we questioned whether inflammation and oxidative stress could be involved in the vascular damage produced by ISG15.

5.1. ISG15 deletion decreases vascular inflammation and oxidative stress in hypertension.

First, we studied the expression of some proinflammatory genes in aortas from untreated or Ang II-treated WT and ISG15$^{-/-}$ mice. No differences in transcripts levels of *Ifng* and *Ccl2* were found in aorta from untreated WT and ISG15$^{-/-}$ mice (**Figure 38A, 38C**). Surprisingly, an increase in the expression of the COX-2 gene (*Ptgs2*) and the lymphocytes marker *Cd3e* and a decrease in the expression of the macrophages marker F4/80 (*Adgre1*) were observed in aorta from untreated ISG15$^{-/-}$ compared to untreated WT mice (**Figure 38B, 38D, 38E**), suggesting that ISG15 might modulate basal inflammatory and immune status. Ang II increased the expression of the proinflammatory markers *Ifng, Ptgs2, Ccl2* and *Cd3e* in arteries from WT mice (**Figure 38A, 38B, 38C, 38E**). However, Ang II failed to increase *Ifng*, *Ptgs2* and *Cd3e* expression in arteries from ISG15$^{-/-}$ mice, suggesting that ISG15 is involved in Ang II-induced vascular inflammation. Interestingly, Ang II increased *Adgre1* expression in arteries from ISG15$^{-/-}$ but not in WT mice (**Figure 38D**).

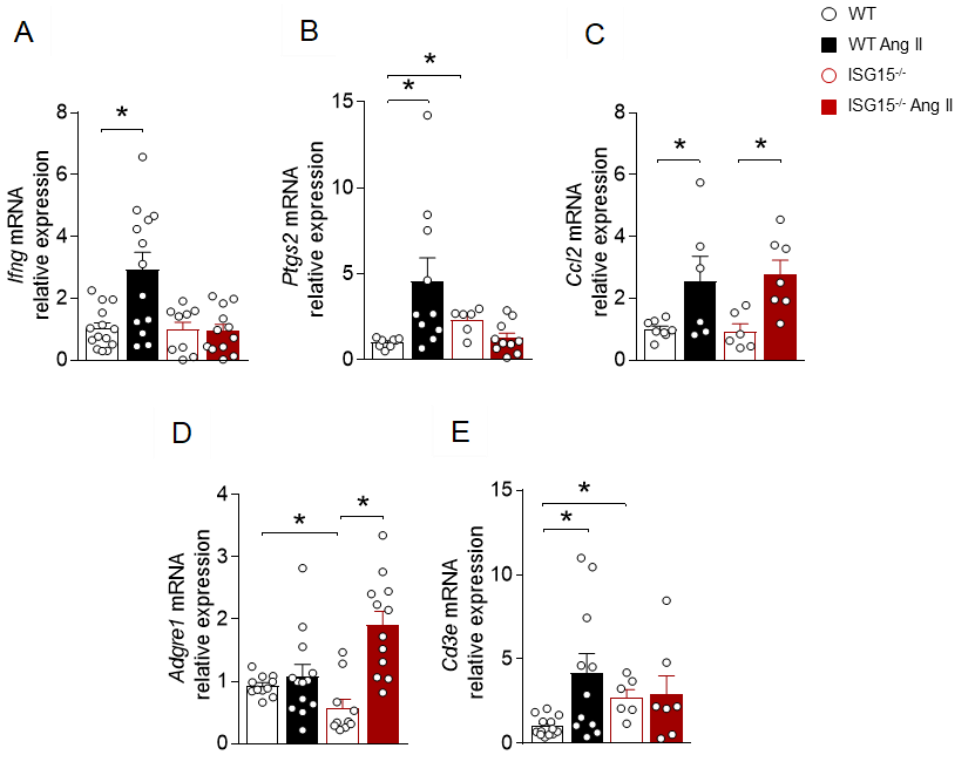


Figure 38. ISG15 participates in Ang II-induced inflammation in aorta. Aortic mRNA expression of *Ifng* (**A**), *Ptgs2* (**B**), *Ccl2* (**C**), *Adgre1* (**D**) and *Cd3e* (**E**) in WT and ISG15$^{-/-}$ mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks). *p<0.05 vs. untreated mice (WT or ISG15$^{-/-}$) by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

Regarding oxidative stress, our proteomic analysis revealed a significant coordinated decrease of proteins that belong to a cluster of 6 GO categories related to *Vascular redox state* in Ang II-infused ISG15$^{-/-}$ compared to WT mice (**Figure 39A, Annexed Table 6**). These GO include mitochondrial electron transport (cytochrome c to oxygen, NADH to ubiquinone, ubiquinol to cytochrome c), response to hypoxia, response to ischemia and thioredoxin peroxidase activity. To further explore this finding, we obtained the aortic thiol redoxome by analyzing relative changes in abundance of oxidized cysteines (Cys) in the four experimental groups using the FASILOX method (Bonzon-Kulichenko et al., 2020). Data revealed a significant increase ($p<0.05$) in the abundance of oxidized Cys-containing peptides in the aorta from Ang II-infused WT mice that was not observed in ISG15$^{-/-}$ mice (**Figure 39B**). The complete list of peptides containing oxidized Cys residues is shown in **Annexed Table 7**. We validated these results by direct measurements of $O_2^{\cdot-}$ in the aortas from the four experimental groups. Ang II increased vascular

$O_2^{\cdot-}$ in Ang II-infused WT mice, but no in ISG15$^{-/-}$ mice both in the media and the adventitial layers (**Figure 39C**). There were no differences in $O_2^{\cdot-}$ levels between untreated groups (**Figure 39C**).

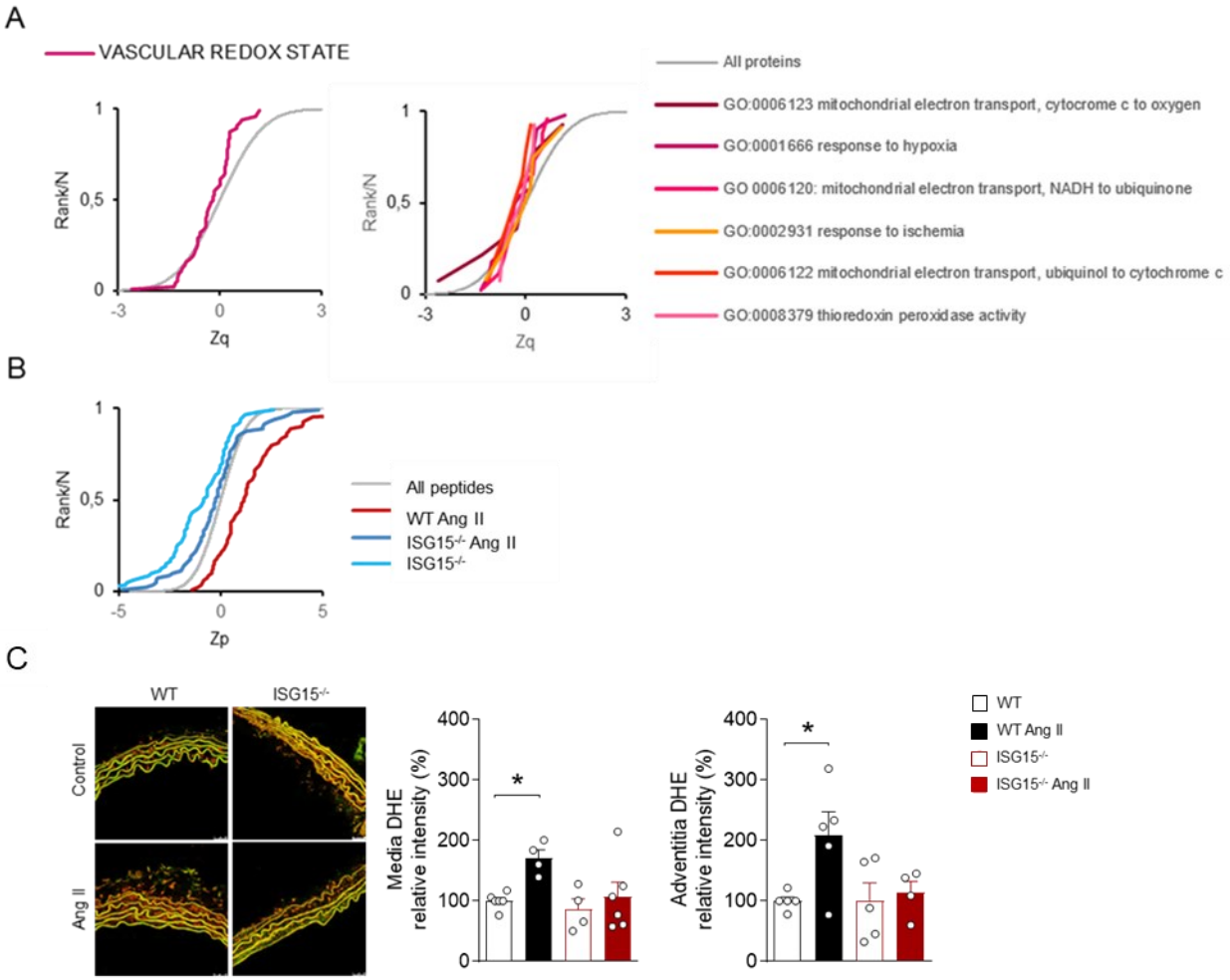
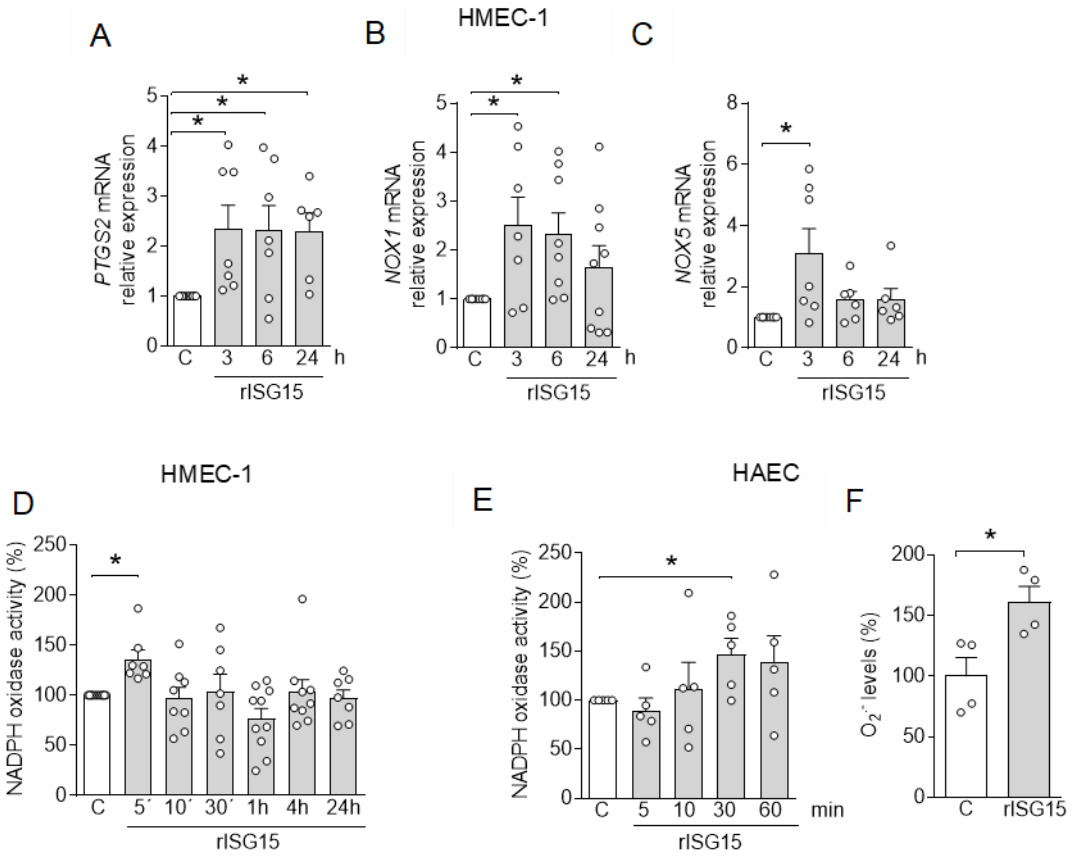


Figure 39. ISG15 participates in Ang II-induced oxidative stress in aorta. (**A**), Quantitative proteomics analysis of proteins related to the *Vascular redox state* cluster. Results were presented as in **Figure 28**. The functional category abundance change value for this cluster was Zc = -1.83 (log_2 fold change in ISG15$^{-/-}$ Ang II with respect to WT Ang II, normalized with respect to untreated samples, in units of standard deviation), which is statistically significant at FDR<0.05. The complete set of proteins belonging to this cluster is listed in **Annexed Table 6**. (**B**), Quantitative redox proteomics shows increased abundance of peptides containing reversibly oxidized Cys sites in Ang II-treated WT mice in comparison with ISG15$^{-/-}$ mice. Shown are the cumulative distributions of Zp, standardized log_2 ratio of oxidized-Cys-containing peptides in WT Ang II, ISG15$^{-/-}$ Ang II and ISG15$^{-/-}$, with respect to WT. The graph also shows the distribution of Zp for all the peptides of the experiment (in grey). The oxidized-Cys-containing peptides of the WT Ang II group is significantly increased with respect to WT; p<0.002 by Kolmogorov-Smirnov test. (**C**), Representative Dihydroethidium (DHE) fluorescence and quantification in media and adventitia layers (dots in bars represent the number of animals). Image size: 238.1x238.1 µm; *p<0.05 vs. untreated mice by one-way Anova and Sidak's multiple comparisons post-test.

5.2. Recombinant ISG15 (rISG15) induces inflammation and reactive oxygen species generation.

Because ISG15 deletion protected from Ang II-induced endothelial dysfunction, ROS generation and upregulation of *Ptgs2*, we tested the ability of ISG15 to induce ROS production and *PTGS2* expression in ECs. In HMEC-1, rISG15 enhanced *PTGS2*, *NOX1* and *NOX5* mRNA expression as early as 3h after addition (**Figure 40A-C**). NADPH oxidase activity also increased by rISG15 in HMEC-1 cells, after 5 min of exposition and then returned to basal levels (**Figure 40D**). These results were confirmed in HAEC where rISG15 increased NADPH oxidase activity (**Figure 40E**), $O_2^{\cdot-}$ generation measured by electron paramagnetic resonance (**Figure 40F**) and *NOX1/4/5* protein expression (**Figure 40G-I**).



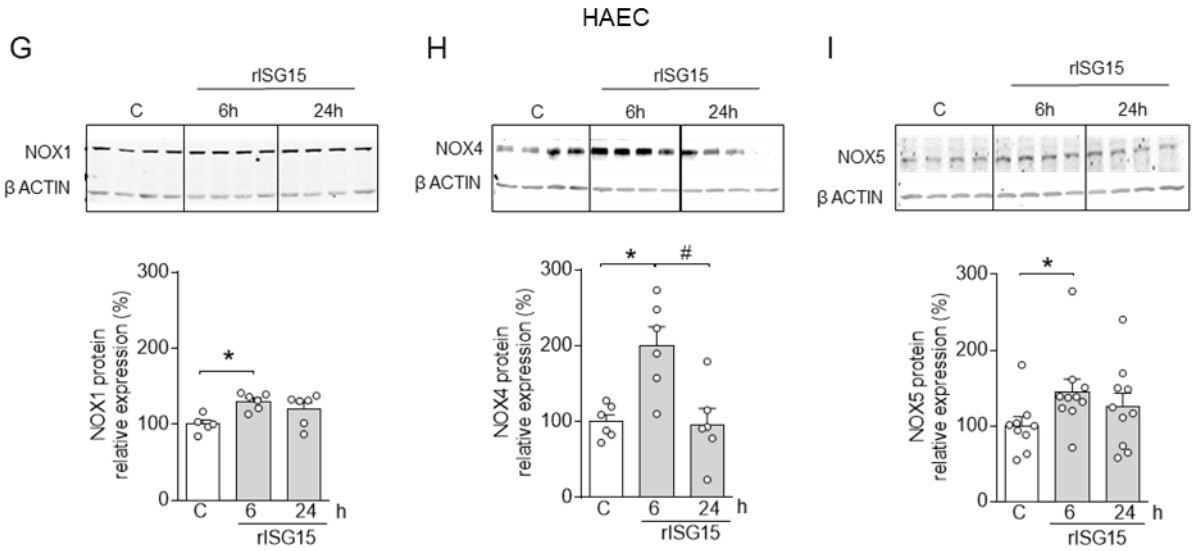


Figure 40. rISG15 increases *PTGS2* expression and oxidative stress in human endothelial cells. mRNA levels of *PTGS2* (**A**), *NOX1* (**B**) and *NOX5* (**C**) in human microvascular endothelial cells (HMEC-1) untreated or treated with rISG15 (10 ng/mL) at different times. NADPH oxidase activity in HMEC-1 (**D**) and human aortic endothelial cells (HAEC) (**E**) untreated or treated with rISG15 (10 ng/mL) at different times. (**F**), Levels of $O_2^{\cdot-}$ measured by electron paramagnetic resonance in HAEC untreated or treated with rISG15 (10 ng/mL, 30 min). Protein levels of NOX1 (**G**), NOX4 (**H**) and NOX5 (**I**) in HAEC untreated or treated with rISG15 (10 ng/mL, 6 and 24 h). *p<0.05 vs. Control (C), #p<0.05 vs. 6h rISG15 by one-way Anova and Sidak's multiple comparisons post-test or by Student t-test. Dots in bars represent the number of different cell culture experiments.

5.3. rISG15 increased ROS production in normotensive and hypertensive human fibroblasts.

Because ISG15 is expressed in fibroblasts (Giannakopoulos et al., 2005; Bogunovic et al., 2012), we tested the ability of ISG15 to induce ROS generation in human vascular fibroblasts isolated from normotensive and hypertensive patients.

Fibroblasts from hypertensive patients showed higher levels of NADPH oxidase activity compared to normotensive patients (**Figure 41A**). However, basal levels of hydrogen peroxide were similar between both groups (**Figure 41C**). rISG15 augmented NADPH oxidase activity only in human normotensive fibroblasts (**Figure 41B**), likely because of the increased levels of basal NADPH oxidase activity in hypertensive fibroblasts. In contrast, rISG15 incubation enhanced hydrogen peroxide levels only in fibroblasts from hypertensive patients (**Figure 41D**).

Interestingly, in human PBMCs, no correlation was found between ISG15 transcript and $O_2^{\cdot-}$ production (**Table 3**), suggesting that ISG15 might influence redox biology at vascular level (i.e ECs and vascular fibroblasts) with little contribution in immune cells. Altogether, these findings uncover a new role for ISG15 in vascular inflammation and ROS production.

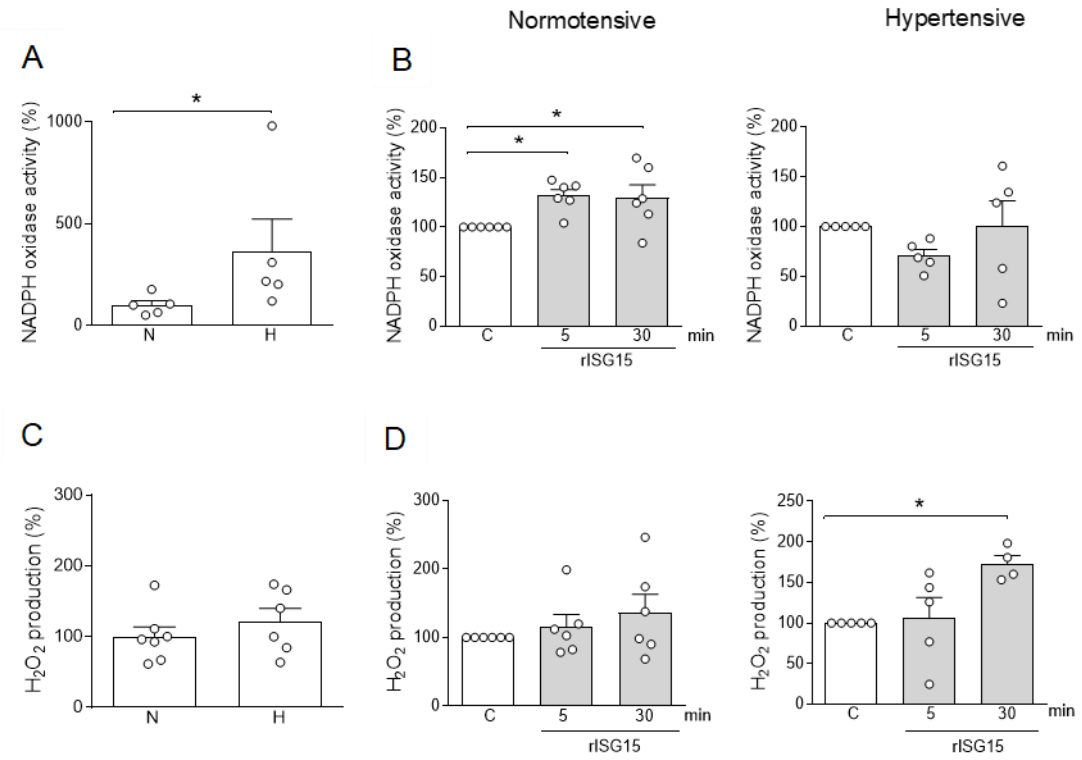


Figure 41. **rISG15 increases reactive oxygen species production in human vascular fibroblasts from normotensive and hypertensive patients.** NADPH oxidase activity (**A**) and H_2O_2 production (**C**) in basal conditions in fibroblasts from normotensive (N) and hypertensive (H) patients. Effect of rISG15 (10 ng/mL) on NADPH oxidase activity (**B**) and H_2O_2 production (**D**) in normotensive and hypertensive human fibroblasts. *p<0.05 vs. Control (C) by Student t-test or by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of different cell culture experiments.

5.4. Oxidative stress, inflammation and integrin receptors mediate ISG15-induced endothelial dysfunction.

After having observed the effect of rISG15 in human ECs and vascular fibroblasts, we evaluated the effects of rISG15 in vascular function. In aortic segments from WT animals, overnight incubation with rISG15 significantly impaired endothelium-dependent relaxation (**Figure 42A**), without modifying DEA-NO relaxation or contractile responses to phenylephrine (**Figure 42B, 42C**). The selective COX-2 inhibitor celecoxib and the selective NOX1 inhibitor NoxA1ds prevented ISG15-induced endothelial dysfunction (**Figure 42A**).

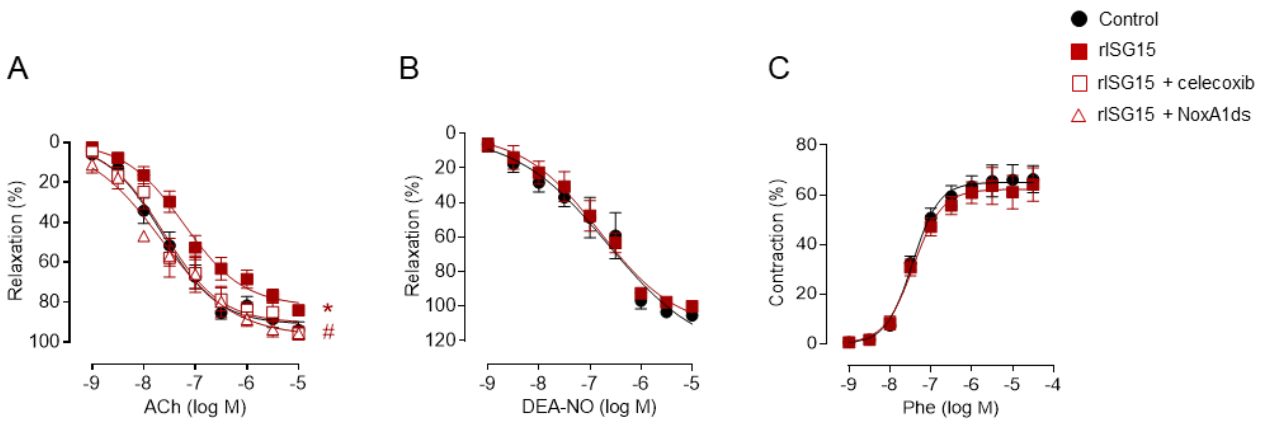


Figure 42. rISG15 induces endothelial dysfunction via oxidative stress and inflammation. Concentration-response curves to acetylcholine (ACh, **A**), diethylamine NONOate (DEA-NO, **B**) and phenylephrine (Phe, **C**) in aortic segments from C57Bl6 mice incubated or not with rISG15 (10 ng/mL, 20h) and co-incubated with celecoxib (selective COX-2 inhibitor, 1 µmol/L) or NoxA1ds (selective NOX1 inhibitor, 10 µmol/L) (**A**). Drugs were added 30 min before rISG15 stimulation. *p<0.05 vs. Control, #p<0.05 vs. rISG15 by two-way Anova (n=4-11).

In NK cells, the cellular receptor for free ISG15 is LFA-1, the classical integrin receptor for ICAM-1, and its activation produces IFNγ and IL-10 secretion (Swaim et al., 2017). We then investigated the expression of LFA-1 in the vascular wall and its involvement in ISG15-induced endothelial dysfunction. As shown in **Figure 43A** no expression of LFA-1 was found in arteries from untreated WT mice, but it was clearly detected in arteries from Ang II-infused WT mice, specifically in the perivascular adventitia. Moreover, Ang II infusion augmented *Lfa-1* mRNA expression in aorta compared to untreated mice (**Figure 43B**).

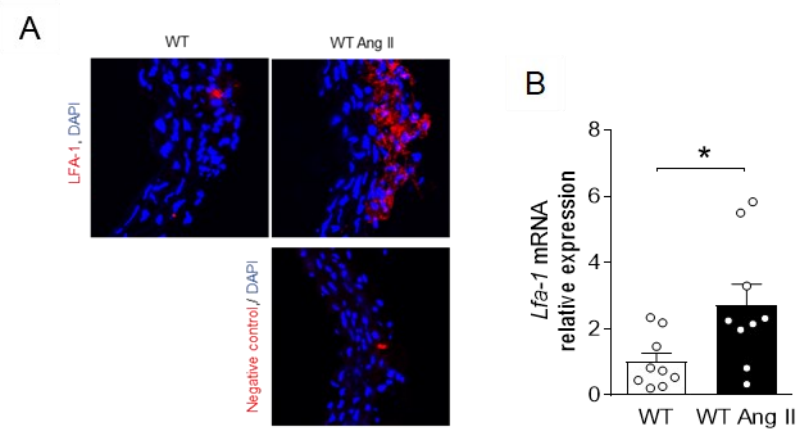


Figure 43. Ang II augments LFA-1 expression in aorta. Immunostaining images (**A**) and *Lfa-1* mRNA levels (**B**) in aorta from untreated wild type mice (WT) or Ang II-treated WT mice (1.44 mg/Kg/day, 2 weeks). Image size: 375x375µm. *p<0.05 vs. WT by Student t-test. Dots in bars represent the number of animals.

The fact that LFA-1 seems to be poorly expressed in arteries from WT untreated mice, but rISG15 induces endothelial dysfunction in these animals suggest that other receptors different to LFA-1 would be mediating ISG15 actions at the vascular level. Thus, we tested the effect of a non-specific integrin receptor blocker, RGDS peptide. As shown in **Figure 44**, the rISG15-induced endothelial dysfunction was completely prevented by RGDS peptide.

Then, we analyzed the participation of IFNγ in ISG15-induced endothelial dysfunction. As shown in **Figure 44**, a neutralizing anti-IFNγ antibody also prevented rISG15-induced endothelial dysfunction.

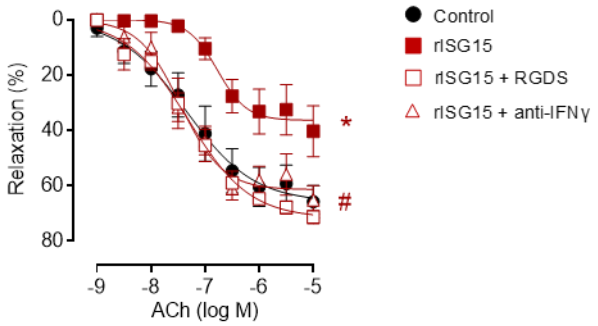


Figure 44. rISG15 induces endothelial dysfunction via integrin receptors and IFNγ. Concentration-response curve to acetylcholine (ACh) in aortic segments from C57Bl6 mice incubated or not with rISG15 (10 ng/mL, 20h) and co-incubated with RGDS (a non-specific integrin receptor blocker, 1 µmol/L) or anti-IFNγ antibody (5 µg/mL). Drugs were added 30 min before rISG15 stimulation. *p<0.05 vs. Control, #p<0.05 vs. rISG15 by two-way Anova (n=4-8).

Together, these findings suggest that, in vessels, ISG15 binds to an unknown integrin receptor, probably producing IFNγ generation, which may increase inflammation and oxidative stress provoking endothelial dysfunction.

5.5. Oxidative stress mediates ISGylation-induced vascular remodelling.

Since inflammation and oxidative stress are implicated in the vascular damage produced by ISG15, we evaluated the role of these mediators in arteries from USP18^{C61A} mice.

We found that aorta from untreated USP18^{C61A} mice displayed a clear inflammatory profile compared to WT mice, as shown by the increased *Ifng*, *Ptgs2*, *Ccl2*, *Adgre1* and *Cd3e* mRNA expression (**Figure 45**). As mentioned earlier, Ang II-infusion increased *Ifng*, *Ptgs2*, *Ccl2* and *Cd3e* mRNA expression into WT mice but it did not have any further effect in USP18^{C61A} mice (**Figure 45**).

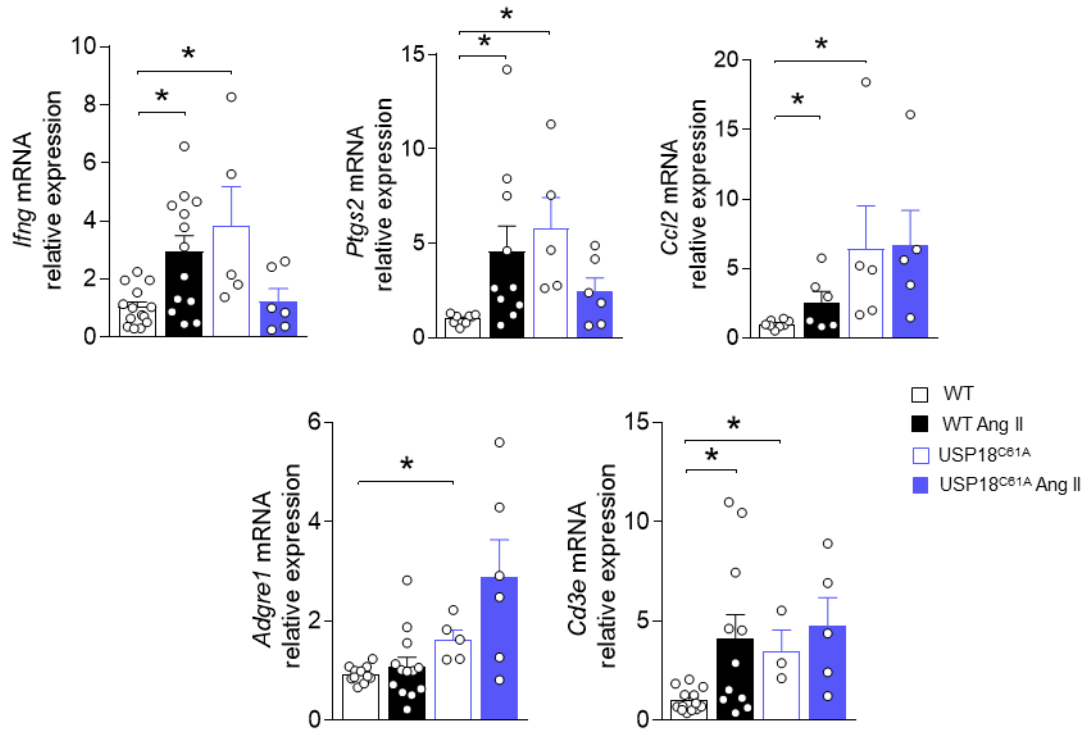


Figure 45. ISGylation increases inflammation in aorta. Aortic mRNA expression of *Ifng*, *Ptgs2*, *Ccl2*, *Adgre1* and *Cd3e* in WT and USP18^{C61A} mice treated or not with Ang II (1.44 mg/Kg/day, 2 weeks). *p<0.05 vs. untreated WT mice by one-way Anova and Sidak's multiple comparisons post-test. Because experiments were run simultaneously, data from WT and WT Ang II from this figure are the same as Figure 38. Dots in bars represent the number of animals.

Basal $O_2^{\cdot-}$ production was greater in the media of arteries from untreated USP18^{C61A} mice, but not in the adventitia (**Figure 46**) and interestingly, Ang II infusion increased $O_2^{\cdot-}$ production in the adventitia but not in the media from USP18^{C61A} mice (**Figure 46**).

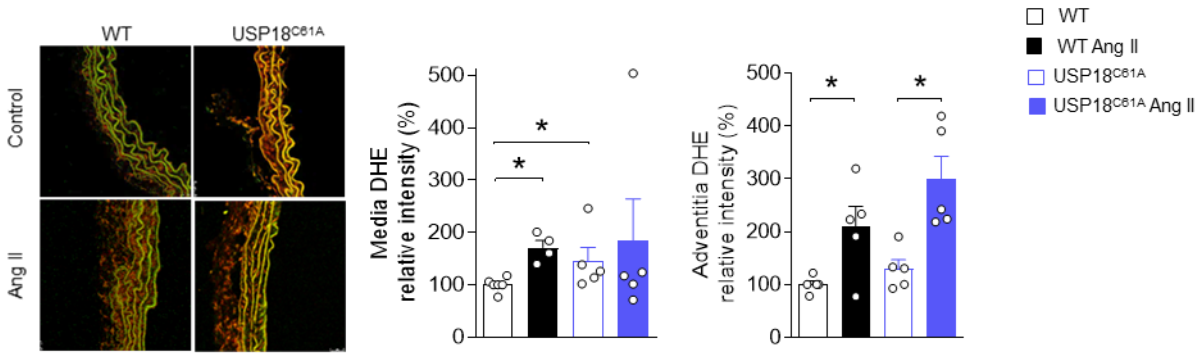


Figure 46. ISGylation increases $O_2^{\cdot-}$ production in aorta. WT and USP18^{C61A} mice were treated or not with Ang II (1.44 mg/Kg/day, 2 weeks). Representative Dihydroethidium (DHE) fluorescence and quantification in media and adventitia layers. Image size: 238.1x238.1µm. *p<0.05 vs. untreated mice (WT or USP18^{C61A}) by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

In addition, we found increased levels of *Nox1* transcript in aorta from untreated USP18^{C61A} mice compared to WT mice (**Figure 47A**). Furthermore, the vasoconstrictor response to phenylephrine was diminished after incubation with a selective NOX1 inhibitor (NoxA1ds) in aorta from USP18^{C61A}, but not in WT mice (**Figure 47B**).

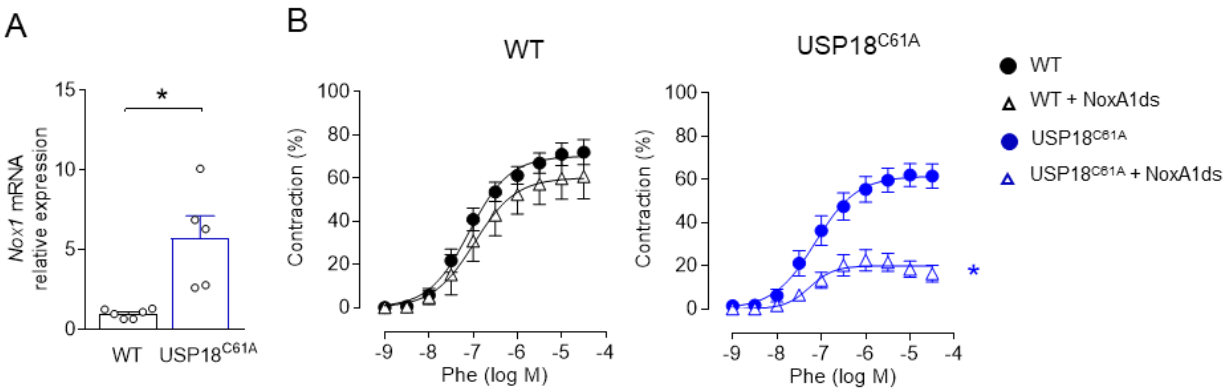


Figure 47. ISGylation increases NOX1 in aorta. A, *Nox1* mRNA levels in aorta from untreated wild type (WT) or USP18^{C61A} mice. **B**, Concentration-response curve to phenylephrine (Phe) in aortic segments from WT or USP18^{C61A} mice incubated or not with NoxA1ds (selective NOX1 inhibitor, 10 µmol/L). Drugs were added 30 min before rISG15 stimulation. *p<0.05 vs. WT or USP18^{C61A} mice by t-test or two-way Anova (n=5-10). Dots in bars represent the number of animals.

To confirm the potential role of oxidative stress in the vascular damage associated with ISGylation, Ang II-infused USP18^{C61A} mice were co-treated with the antioxidant tempol. Tempol induced a significant delay in the rise of systolic blood pressure (**Figure 48A**). More importantly, tempol treatment significantly improved survival and reduced AAs formation (**Figure 48B, 48C**).

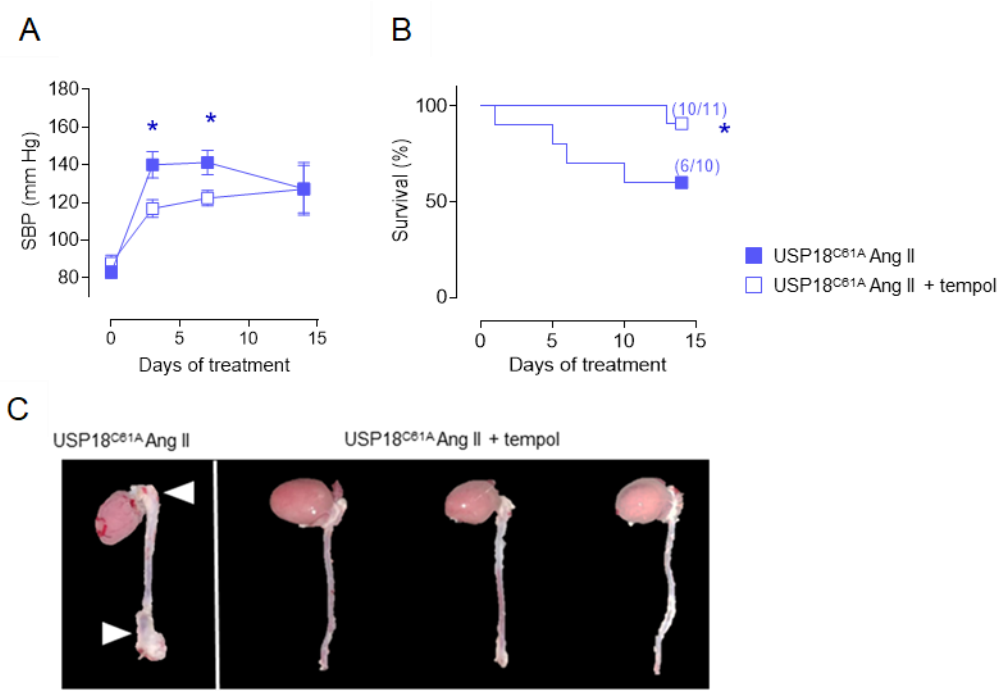


Figure 48. The antioxidant tempol improves survival and reduces aneurysms formation in Ang II-infused USP18^{C61A}. (**A**)**,** Systolic Blood Pressure (SBP; n=7-8), (**B**) survival curve (n=10-11) and (**C**) representative images of aorta from USP18^{C61A} mice treated with Ang II (1.44 mg/Kg/day, 2 weeks) and co-treated or not with the antioxidant tempol (0.288 nmol/Kg/day). *p<0.05 vs. USP18^{C61A} Ang II by two-way Anova or by log-RanK (Mantel-Cox) test.

Tempol treatment also improved vascular remodelling of SMA in Ang II-infused USP18^{C61A} mice, as shown by the increase in lumen diameter (**Figure 49A**) and the reduction in wall thickness (**Figure 49B**). However, tempol treatment did not change vascular stiffness of SMA (**Figure 49C**).

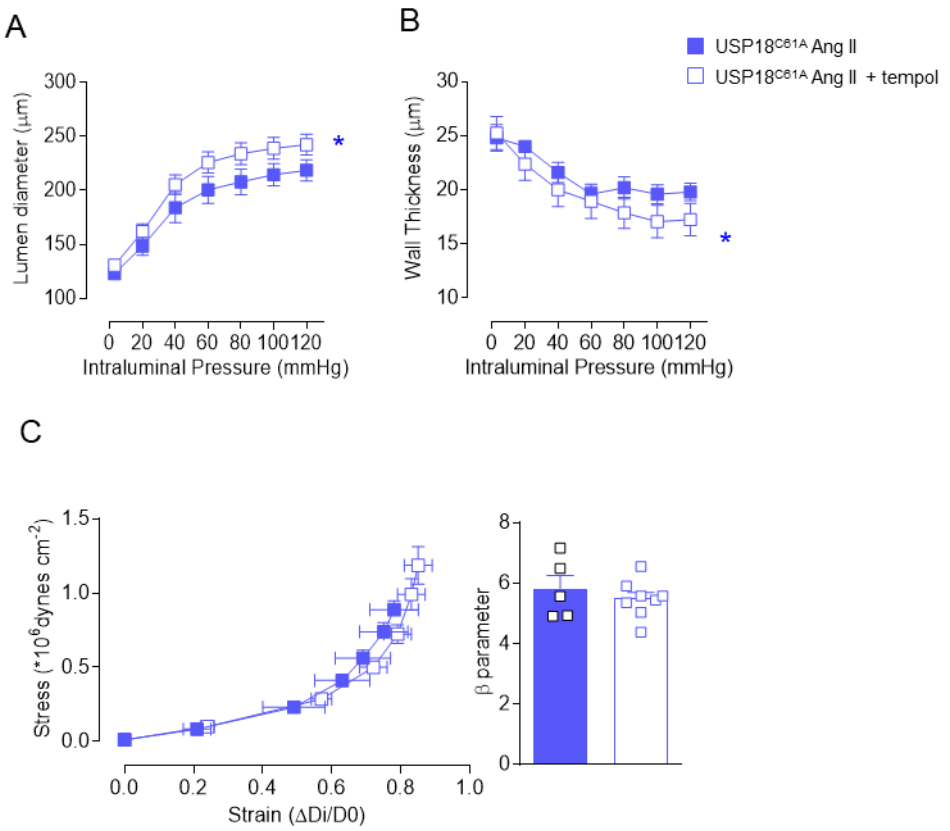


Figure 49. The antioxidant tempol changes vascular structure in Ang II-infused USP18^{C61A}. Structural (**A**, **B**) and mechanical (**C**) parameters in small mesenteric arteries from USP18^{C61A} mice treated with Ang II (1.44 mg/Kg/day, 2 weeks) and co-treated or not with the antioxidant tempol (0.288 nmol/Kg/day) (n=5-8). *p<0.05 vs. Ang II-infused USP18^{C61A} by two-way Anova. Dots in bars represent the number of animals.

Altogether these data demonstrate an essential role of oxidative stress in ISGylation-dependent vascular remodelling.

CHAPTER 2

Like hypertension, obesity is considered a low-grade inflammatory disease with increased local and circulating levels of proinflammatory cytokines like TNFα, and others, and infiltration of inflammatory cells, particularly macrophages, in the abdominal adipose tissue, in the vasculature and in the contiguous PVAT. This inflammatory milieu can modify the structure and the function of the arteries. Because of the novel role of myeloid GRK2 in insulin resistance and macrophage phenotype in obesity (Vila-Bedmar et al., 2020), in the second chapter, we investigate the role ofthis kinase expressed in myeloid cells in the vascular alterations associated with obesity.

6. GRK2 expression positively correlates with leptin, as well as with myeloid and lymphoid markers in PVAT from patients with AAA.

It has been suggested that PVAT might have a role in vascular damage in obesity, at least in part because of the infiltration of inflammatory macrophages (Fernández-Alfonso et al., 2017). Moreover, PVAT is the major site for macrophage and T cell accumulation in human AAA (Sagan et al., 2019). We used aortic PVAT from patients with AAA as a human model of vascular disease to analyze potential correlations between *GRK2* expression and obesity parameters, and between *GRK2* expression and adipokines and myeloid or lymphoid immune cell markers in this specific adipose tissue depot.

Patients from the studied population showed overweight according to their BMI and had central obesity with a mean abdominal perimeter of 109±2.01 cm (**Table 5**). Total mRNA levels for *GRK2* in PVAT did not correlate with abdominal perimeter or BMI (**Figure 50A**, **50B**). However, *GRK2* expression positively correlated with leptin but not with adiponectin mRNA (**Figure 50C**, **50D**).

Table 5. Clinical characteristics of the population included in the study of aortic perivascular adipose tissue.

Total population (n=42)	
Age, years	70.32±1.122
Gender, female/male	3/39
Body weight, Kg	85.8±2.257
Height, m	1.711±0.011
Body mass index, Kg/m^2	29.31±0.756
Abdominal perimeter, cm	109±2.01
Smoking, no/yes/ex	4/15/24
Diabetes mellitus, no/yes	32/10
Arterial hypertension, no/yes	13/29
Hyperlipidemia, no/yes	16/26
***Cardiopathies**, no/yes	23/19
Medication	
Antihypertensives, %	74%
Lipid lowering drugs, %	77%
Antidiabetic, %	23%
Antiaggregant, %	56%
Anticoagulant, %	18%
Beta blockers, %	36%

Values are expressed as mean±SEM, number of subjects or percentages. *Cardiopathies include congenital heart disease, ischemic cardiomyopathy, valvular cardiopathy, heart failure, arrhythmia, dilated cardiomyopathy, open-heart surgery and previous coronary endovascular procedure.

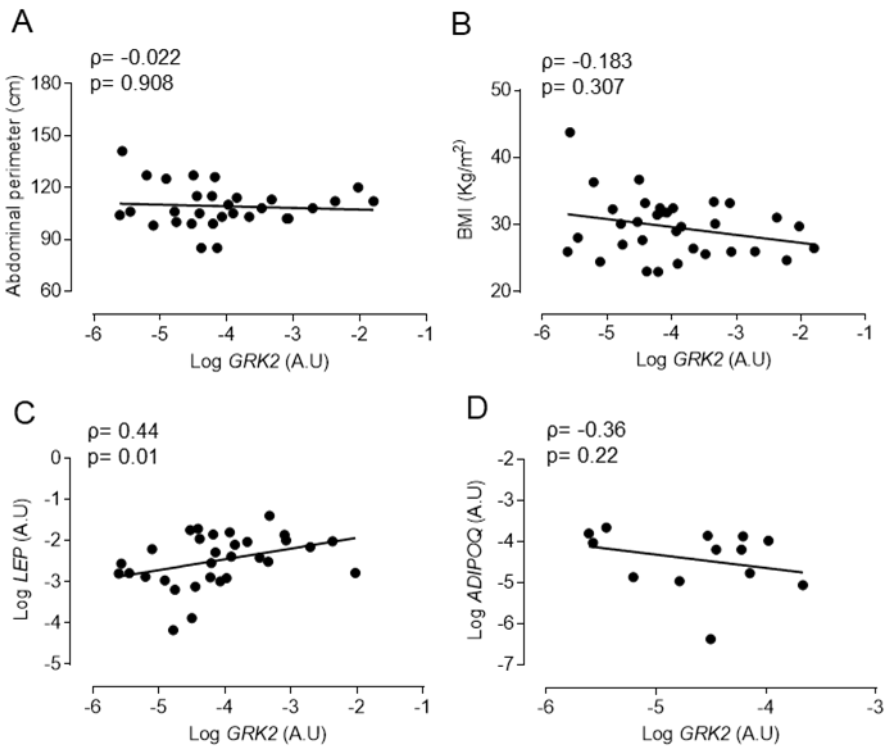


Figure 50. Correlations between abdominal perimeter (**A**), body mass index (BMI, **B**), leptin mRNA (*LEP*, **C**) and adiponectin mRNA (*ADIPOQ*, **D**), with *GRK2* mRNA, in human aortic perivascular adipose tissue from patients with abdominal aortic aneurysm. Univariate association was performed by Spearman correlation test. A.U indicates arbitrary units.

We also found a positive and highly significant correlation between *GRK2* expression in PVAT from the studied population and that of the macrophage marker *CD68* (**Figure 51A**) and specific markers of T lymphocytes such as *CD3G*, *CD4* and *CD8A* (**Figure 51B-D**).

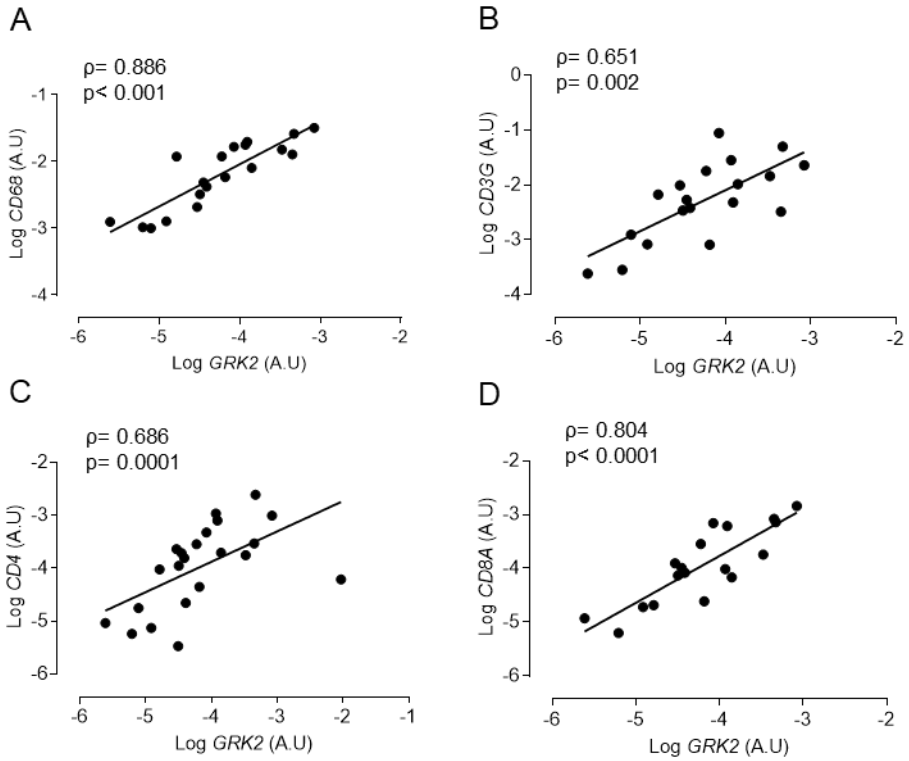


Figure 51. Correlations between mRNA expression of *CD68* (**A**), *CD3G* (**B**), *CD4* (**C**), *CD8A* (**D**) and *GRK2* mRNA in human aortic perivascular adipose tissue from patients with abdominal aortic aneurysm. Univariate association was performed by Spearman correlation test. A.U indicates arbitrary units.

These data indicate that the positive relationship between *GRK2* expression and immune cell infiltration in PVAT is not merely a consequence of enhanced/altered body weight in human patients with vascular damage and were consistent with our hypothesis that GRK2 expression in myeloid cells may modulate the inflammatory and immune landscape of PVAT and thus vascular damage.

Human PVAT samples were obtained by Dr. Rosa Moreno Carriles at Hospital Universitario La Princesa (Madrid) and processed at UAM lab.

7. Myeloid GRK2 is involved in the functional vascular alterations associated with obesity.

To directly address whether GRK2 dosage in myeloid cells might have a role in vascular functionality and damage induced by obesity, we used an HFD-induced obesity model comparing control animals with those with a selective downregulation of GRK2 in the myeloid cell lineage (LysM-GRK2$^{+/-}$). This model was characterized in a previous study reporting that compared to control mice, LysM-GRK2$^{+/-}$ animals showed better glucose tolerance and insulin sensitivity and had less inflammation in liver and in adipose tissue and smaller adipocytes than control mice, with the same degree of obesity (Vila-Bedmar et al., 2020).

We observed that in aortic rings devoid of PVAT, endothelium-dependent relaxation to acetylcholine was similar in control and LysM-GRK2$^{+/-}$ mice, both in animals fed a normal diet (ND) (**Figure 52A**) and in animals fed an HFD (**Figure 52B**). In the presence of PVAT, acetylcholine-induced relaxation was similarly rightward-shifted in arteries from both genotypes when fed a ND (**Figure 52A**), indicating a lower vasodilator capacity of vessels in the presence of PVAT. However, when fed an HFD, the presence of PVAT impaired acetylcholine-induced relaxation only in arteries from control mice and not in arteries from LysM-GRK2$^{+/-}$ mice that were protected (**Figure 52B**).

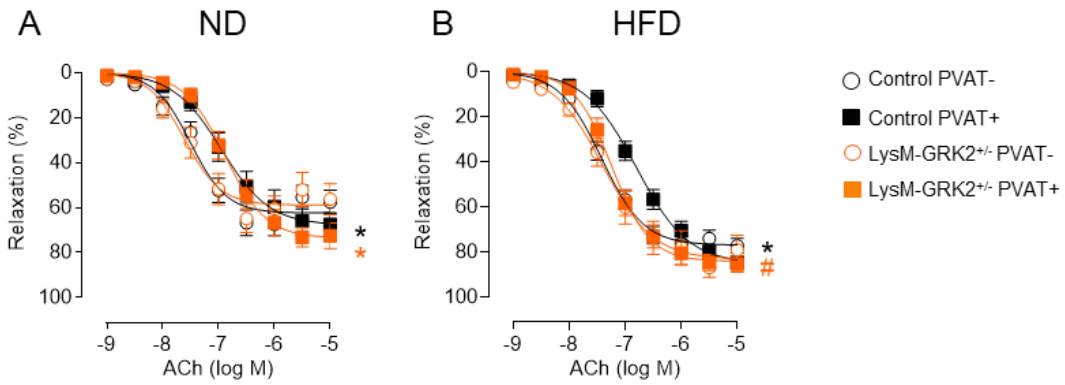


Figure 52. **GRK2 downregulation in myeloid cells preserves acetylcholine relaxation in aorta with PVAT from obese animals.** Concentration-response curves to acetylcholine (ACh) in aorta segments with perivascular adipose tissue (PVAT+) or without (PVAT-) from control and LysM-GRK2$^{+/-}$ mice fed on normal diet (ND, **A**) or high fat diet (HFD, **B**) (n=12-19). *p<0.05 vs. PVAT-, # p<0.05 vs. Control mice by two-way Anova.

We next evaluated insulin-induced vasodilator responses. Like acetylcholine, in aortic segments without PVAT, insulin-dependent relaxation was similar between control and LysM-GRK2$^{+/-}$ mice, both in animals fed a ND (**Figure 53A**) and an HFD (**Figure 53B**). In the presence of PVAT, insulin-induced relaxation was significantly impaired in arteries from control animals fed a ND

(**Figure 53A**); moreover, in control animals fed an HFD, insulin did not produce any measurable relaxant response (**Figure 53B**). Importantly, in arteries from LysM-GRK2$^{+/-}$ mice, the presence of PVAT did not impair insulin responses, neither in animals fed a ND nor in those fed an HFD (**Figure 53A, 53B**).

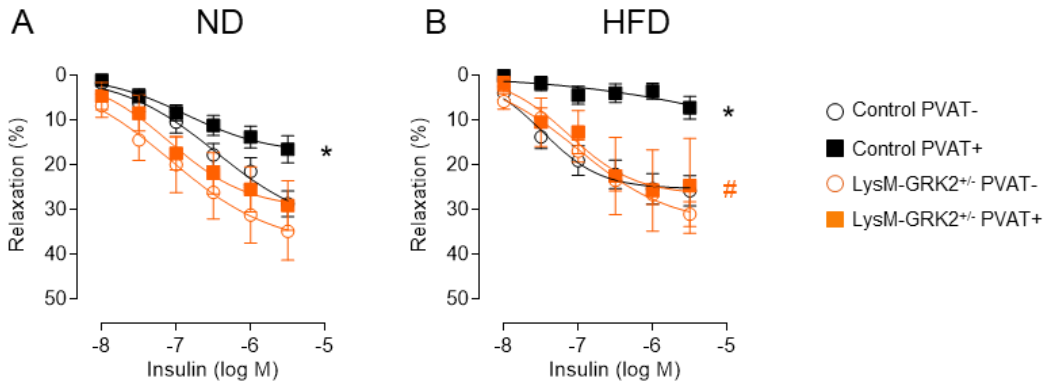


Figure 53. **GRK2 downregulation in myeloid cells preserves insulin relaxation in aorta with PVAT from lean and obese animals.** Concentration-response curves to insulin in aorta segments with perivascular adipose tissue (PVAT+) or without (PVAT-) from control and LysM-GRK2$^{+/-}$ mice fed on normal diet (ND, **A**) or high fat diet (HFD, **B**) (n=7-16). *p<0.05 vs. PVAT-, # p<0.05 vs. control mice by two-way Anova.

We then studied endothelium-independent relaxation induced by the NO-donor DEA-NO. These responses were similar in arteries without PVAT from control and LysM-GRK2$^{+/-}$ mice both in animals fed with normal (**Figure 54A**) or HFD (**Figure 54B**). The presence of PVAT very slightly impaired DEA-NO-induced relaxation in arteries from control mice fed a ND or an HFD, but not in vessels from LysM-GRK2$^{+/-}$ mice (**Figure 54A, 54B**).

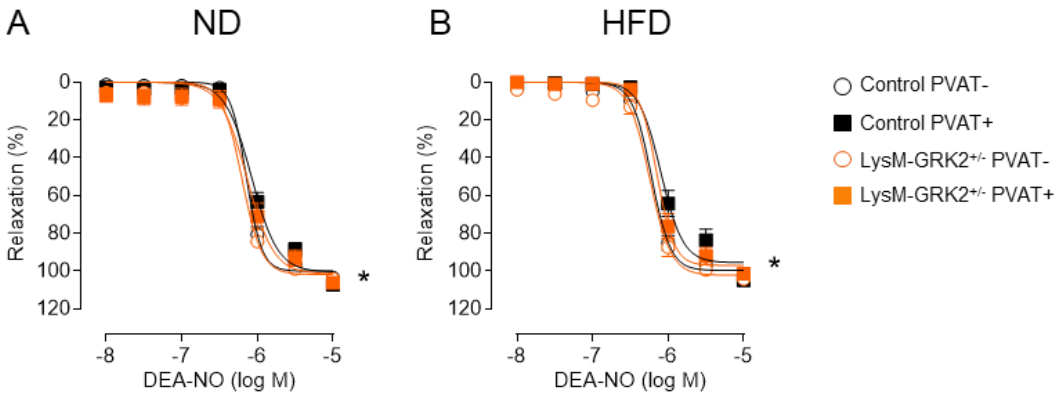


Figure 54. Concentration-response curves to the NO-donor DEA-NO in aorta segments with perivascular adipose tissue (PVAT+) or without (PVAT-) from control and LysM-GRK2$^{+/-}$ mice fed on normal diet (ND, **A**) or high fat diet (HFD, **B**) (n=10-18). *p<0.05 vs. PVAT- by two-way Anova.

We also evaluated vasoconstrictor responses. As shown in **Figure 55**, aortas with PVAT showed greater contractile responses induced by KCl independently of the genotype or type of diet (**Figure 55A, 55B**). However, no significant differences in the contractile response to phenylephrine were observed in aortas in the presence or in the absence of PVAT from ND- or HFD-fed animals (**Figure 55C, 55D**).

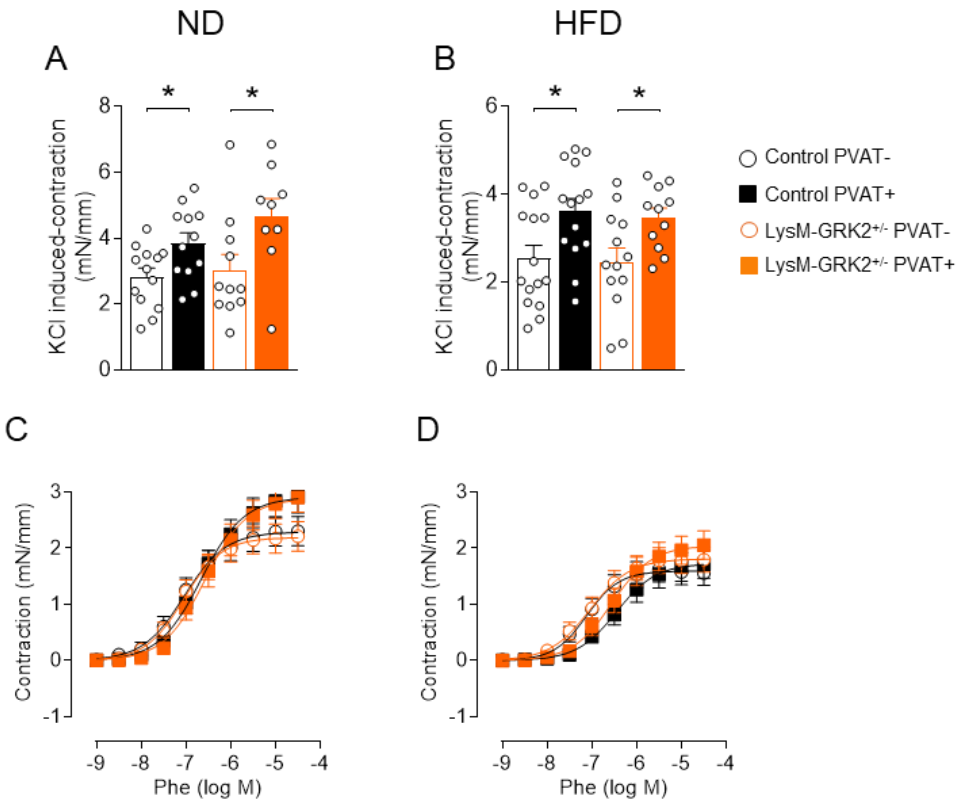


Figure 55. GRK2 downregulation in myeloid cells does not affect contractile responses. Maximum response induced by 120 mmol/L KCl solution (**A**, **B**) and concentration-response curves to phenylephrine (Phe; **C**, **D**) in aorta segments with perivascular adipose tissue (PVAT+) or without (PVAT-) from control and LysM-GRK2$^{+/-}$ from mice fed a normal diet (ND; **A**, **C**) or a high fat diet (HFD; **B**, **D**) (n=9-17). *p<0.05 vs. PVAT- by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

Together, these data suggest that GRK2 from myeloid cells modulates the phenotype of PVAT to release inter-cellular mediators that impair endothelium-dependent relaxations to acetylcholine and insulin, but not of contractility towards phenylephrine.

8. Inflammation and oxidative stress are involved in the role of myeloid GRK2 in alterations of vascular function produced by obesity.

8.1. GRK2 deficiency in myeloid cells prevents upregulation of Tnfa and Nox1 mRNA in PVAT from obese animals.

In obesity, adipose depots show an altered adipokine secretion pattern, increased infiltration of immune cells and upregulation of pro-inflammatory cytokines, such as TNFα or ROS, among many others, which can modulate vascular function (Fernández-Alfonso et al., 2017). We then analyzed possible genes differentially expressed in PVAT that might be modulating endothelium-dependent vasodilator responses. As shown in **Figure 56**, HFD increased gene expression of *Tnfa* (**Figure 56A**) and of the *Nox1* subunit of the NADPH oxidase (**Figure 56B**) in PVAT from control but not from LysM-GRK2$^{+/-}$ mice. No significant differences in the expression of other inflammatory mediators such as *Il6*, *Ptges* (microsomal prostaglandin E synthase 1, mPGES-1) and in the gene expression of adiponectin were observed between diets or genotypes (**Figure 56C-E**).

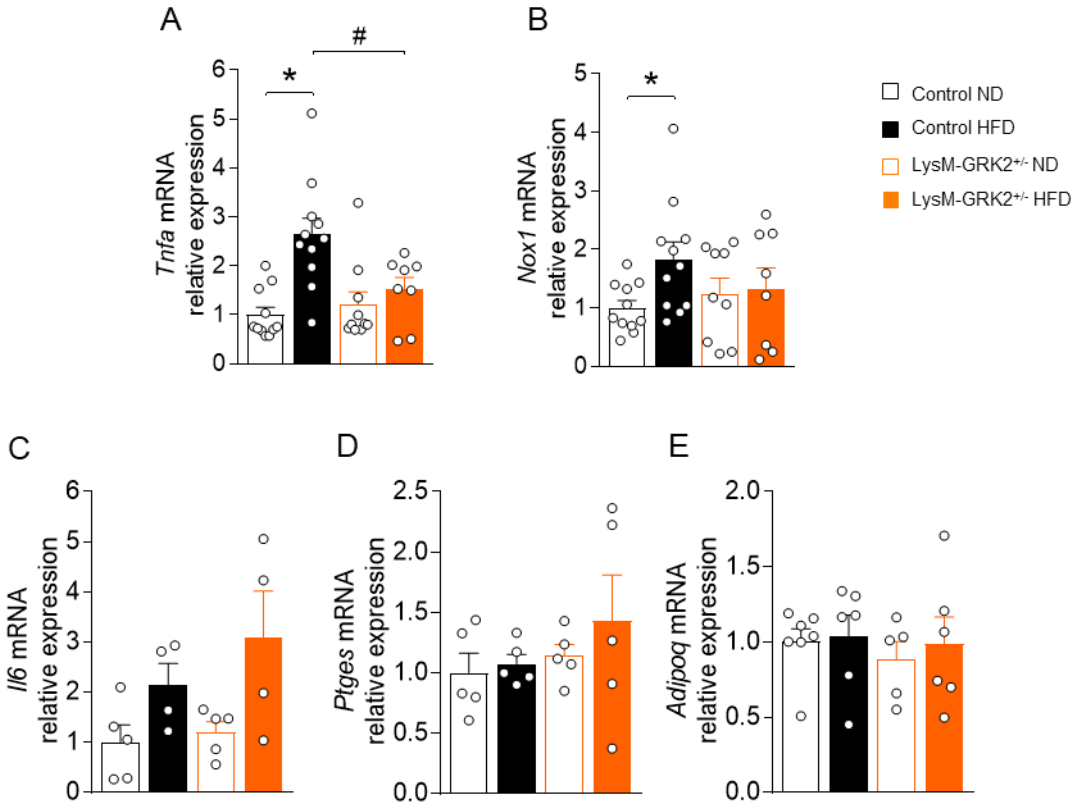


Figure 56. GRK2 deficiency in myeloid cells prevents upregulation of *Tnfa* and *Nox1* in perivascular adipose tissue (PVAT) from obese animals. mRNA expression of *Tnfa* (**A**), the NADPH Oxidase subunit *Nox1* (**B**), *Il6* (**C**), *Ptges* (mPGES-1, **D**) and *Adipoq* (adiponectin, **E**) in aortic PVAT from control and LysM-GRK2$^{+/-}$ mice fed on normal (ND) or high (HFD) fat diet. *p<0.05 vs. ND, # p<0.05 vs. Control mice by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

8.2. Pharmacological blockade of TNFα and NOX1 pathways rescues vasodilator responses to insulin in aortas with PVAT from HFD-fed control animals.

We then tested the effect of a TNFα blocking antibody and the inhibitor of NOX1, NoxA1ds, in insulin-induced vasorelaxation. Both inhibitors significantly improved the vasodilator response to insulin (**Figure 57**), indicating that both TNFα and NOX1 play a role in the negative modulation of vasorelaxation produced by PVAT from HFD-fed animals.

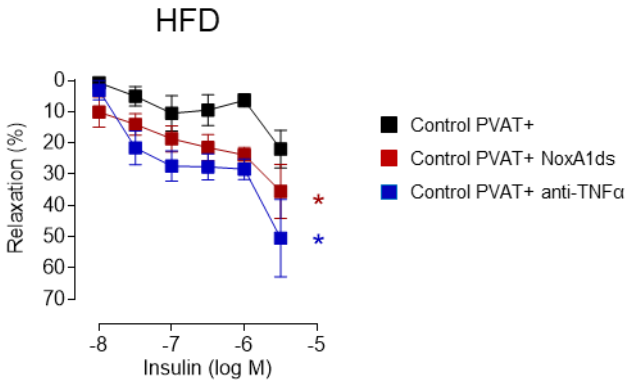


Figure 57. **TNFα and NOX1 are involved in the impairment of vasodilator responses to insulin in aorta with perivascular adipose tissue (PVAT) from high fat diet (HFD)-fed control mice.** Concentration-response curves to insulin in aorta segments with PVAT (PVAT+) in the absence or in the presence of an anti-TNFα antibody (10 µg/mL) or the specific NOX1 inhibitor NoxA1ds (10 µmol/L) from control mice fed HFD. Inhibitors were added 1h before the concentration-response curve to insulin. (n=4-5). *p<0.05 vs. arteries in the absence of inhibitors by two-way Anova.

8.3. GRK2 deficiency in myeloid cells prevents infiltration of immune cells in PVAT.

We then looked at the expression of inflammatory markers indicative of cells infiltrated in PVAT that could be involved in TNFα secretion. An HFD feeding produced a significant increase in the macrophage marker *Adgre1* (F4/80) (**Figure 58A**) and in the T lymphocyte marker *Cd3e* (**Figure 58B**) in PVAT of control but not of LysM-GRK2$^{+/-}$ mice, suggesting on the one hand, that both cell types might contribute to the inflammatory phenotype observed in PVAT from HFD-fed animals, and on the other hand, that myeloid GRK2 contributes to the infiltration of immune cells in PVAT in obesity.

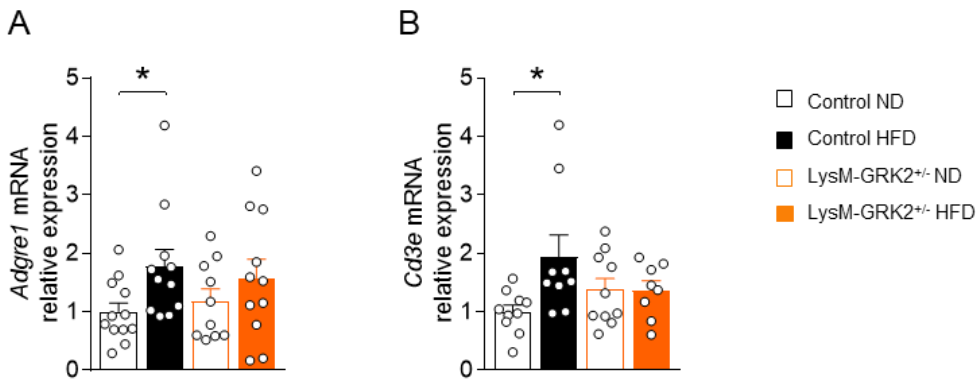


Figure 58. GRK2 deficiency in myeloid cells prevents infiltration of macrophages and T lymphocytes in perivascular adipose tissue (PVAT) from obese animals. mRNA expression of *Adgre1* (**A**) and *Cd3e* (**B**) in aortic PVAT from control and LysM-GRK2$^{+/-}$ mice fed a normal (ND) or a high (HFD) fat diet. *p<0.05 vs. ND by one-way Anova and Sidak's multiple comparisons post-test. Dots in bars represent the number of animals.

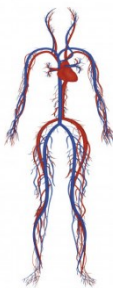
8.4. TNFα gene expression in PVAT from patients with AAA positively correlates with obesity.

Finally, we analyzed different inflammatory parameters in PVAT from patients with AAA and their correlation with BMI and abdominal perimeter. We did not find a significant correlation between macrophage or lymphocyte markers with either BMI or abdominal perimeter. However, we found a positive significant correlation between *TNFA* and BMI and a nearly significant correlation with abdominal perimeter (**Table 6**). Altogether, these results highlight the association of PVAT-derived TNFα to vascular damage in the context of human obesity.

Table 6. Correlation between body mass index (BMI) or abdominal perimeter (Ab. perimeter) with different immune cells infiltration markers and with *TNFA* in human aortic PVAT.

	BMI	Ab. Perimeter
BMI	-	p=0.001*
Ab. Perimeter	p=0.001*	-
CD68	p=0.33	p=0.57
CD3G	p=0.41	p=0.32
CD4	p=0.46	p=0.07
CD8A	p=0.53	p=0.24
TNFA	p=0.02*	p=0.06

CD68: macrophage marker, *CD3G*, *CD4* and *CD8A*: T lymphocyte markers. The correlations were analyzed by univariate association performed by Spearmann correlation test, *p<0.05.



Discussion

1. Role of ISG15 in vascular damage in hypertension.

Hypertension is the main risk factor for the development of CVD. Indeed, hypertension, the "silent killer", is the No.1 cause of mortality in humans worldwide (GBD 2019 Risk Factors Collaborators, 2020), and it is the most important determinant of CVD including stroke, heart failure, and chronic kidney disease. Among the most important features of hypertension are enhanced vasoconstrictor responses, endothelial dysfunction, vascular remodelling and increased vascular stiffness (Brandes, 2014; Laurent and Boutouyrie, 2015). Indeed, endothelial dysfunction and vascular stiffness precede the development of hypertension in different clinical conditions (DeMarco et al., 2014; Mitchell, 2014). More importantly, these vascular alterations have independent prognostic value for future adverse cardiovascular events (Perticone et al., 2001; Rizzoni et al., 2003; Laurent and Boutouyrie, 2015). Therefore, uncovering mechanisms involved in vascular damage in hypertension is a crucial need. In this sense, although with limitations, animal models of hypertension have been demonstrated to be very useful since they resemble many of the features observed in human pathology (Lin et al., 2016).

In this PhD Thesis we demonstrate the novel role of ISG15 in hypertension associated vascular disease. To date, ISG15 has been mainly studied in viral infections as a molecule to strength the antiviral response of the host (Albert et al., 2018). ISG15 seems to be synthesized mainly by immune cells, fibroblasts, epithelial-derived cell lines and several tumor cells (Knight and Cordova., 1991; Bogunovic et al., 2012; Tecalco and Mejía-Barreto, 2017; Albert et al., 2018) and some evidence suggest that cardiomyocytes are also able to express ISG15 in viral cardiomyopathy (Rahnefeld et al., 2014; Zhao G et al., 2020). ISG15 is induced by IFNs, mainly type I (α and β) but also by type II IFN (IFNγ), lipopolysaccharide, and TNFα (Levy et al., 1990; Jeon et al., 2010; Zhang and Zhang, 2011; Chairatvit et al., 2012; Albert et al., 2018). Therefore, in principle, any clinical condition associated with increased levels of these proinflammatory cytokines, might result in augmented expression of the ISG15 system at different levels. In this scenario, emerging evidence point to the alteration of the immune system and to the existence of a low chronic inflammatory status as key contributors to the development of hypertension and CVD. Indeed, it is well accepted that IFNγ has an important role in the damage associated with hypertension by inducing oxidative stress and endothelial dysfunction (Mikolajczyk et al., 2016). Thus, IFNγ deficiency resulted in blunted hypertension in response to Ang II infusion, being IFNγ KO mice protected against cardiac damage and endothelial dysfunction (Han et al., 2012; Markó et al., 2012; Kossmann et al., 2013; Saleh et al., 2015). Moreover, the role of TNFα in endothelial dysfunction in many CVD is also accepted (Zhang et al., 2009). Supporting the role of these proinflammatory cytokines in hypertension, our bioinformatics study identified that

among the more than 2200 proteins related with hypertension, TNFα and IFNγ as the first and fourth master regulators, respectively, which highlights the need of identifying their downstream mediators.

Because as mentioned, ISG15 seems to be synthesized mainly by immune cells where it promotes IFNγ release (Albert et al., 2018), we first studied a possible relationship between ISG15 from human PBMCs and hypertension and vascular damage. We found that *ISG15* mRNA in PBMCs positively correlated not only with systolic/diastolic blood pressure, but also with carotid-IMT, a surrogate marker of vascular remodelling. Importantly, these correlations remained significant after adjustment for traditional risks factors such as age, gender, smoking, body mass index, systolic blood pressure, glucose and total cholesterol, uncovering a novel role for ISG15 in human hypertension. Interestingly, *Isg15* expression was also augmented in peritoneal macrophages from our model of Ang II infusion, opening new avenues for the study of the molecular and pathophysiological implications of ISG15 in immune cells in hypertension.

At the vascular level, we found that *ISG15* is expressed in isolated mice VSMCs, human ECs and in aortic segments from mice, rats or humans. Notably, in these vascular tissues ISG15 expression was detected in basal conditions and it was upregulated by IFNγ or Ang II. Surprisingly, Ang II infusion did not modify *Isg15* mRNA expression in PVAT, the main site for vascular immune cells infiltration, despite of the increased expression of *Isg15* in peritoneal macrophages. However, we cannot discard that *in vivo* the augmented infiltration of immune inflammatory cells and IFNγ expression described in PVAT during Ang II-induced hypertension (Mikolajczyk et al., 2016), might act in the underlying vascular cells to increase ISG15 expression. It is known that free ISG15 is quickly induced after type I IFN stimulation (Farrell et al., 1979), while the conjugation with ISG15 is only appreciable after 18-24h from type I IFN stimulation (Loeb and Hass., 1992). This is probably due to the fact that an increase in conjugating enzymes is required for ISGylation and this occurs after the increase in free ISG15 (Durfee et al., 2010). In agreement, we found increased expression of ISG15 as early as 4-6 hours after Ang II-stimulation and we also observed augmented levels of free ISG15 in the aorta secretome. It has been established that ISGylation target proteins undergoing active translation because of the association of Herc5 (the major ISG15-ligating enzyme) with polyribosomes (Durfee et al., 2010). We observed an increase in the expression of ISGylation enzymes, including *Herc5,* in response to Ang II in both ECs and aorta, suggesting that the post-translational modification might be also taking place. A major limitation of our study is that we have not directly measured ISGylation in the vascular tissues in part due to the lack of specificity of the commercially available antibodies, and future dedicated studies are needed to clarify specific proteins ISGylated by Ang II. Of note,

adult and not young prehypertensive SHR, showed increased vascular *Isg15* expression, which suggests that hemodynamic alterations induced by the enhanced blood pressure might also be an ISG15 stimulus.

As mentioned earlier, it has been described that in macrophages, TLR4 seems to be an important receptor inducing protein ISGylation (Kim et al., 2005). In addition, cardiomyocyte specific IκB kinase 2 activation induces ISG15 expression and ISGylation of proteins dependent of NFκB (Maier et al., 2012). We found that underlying mechanisms responsible for the effect of Ang II in *ISG15* expression likely depend on the AT_1/NFκB pathway, probably through IFNγ release. This is because losartan, anti-IFNγ antibody and parthenolide reduced the Ang II-induced ISG15 expression in ECs or vascular tissues. This would agree with the well-known effect of Ang II/AT_1 pathway in NFκB activation and vascular inflammation (De Gasparo et al., 2000).

Out of the viral context, there is little evidence on the role of ISG15 in CVD. Maier et al. (2012) found activation of ISG15 pathway during Coxsackievirus-induced myocarditis. Using the same model of virus infection, Rahnefeld et al. (2014) demonstrated that ISG15 in cardiomyocytes contributed significantly to the suppression of viral replication. They also observed that patients with viral cardiomyopathy showed increased expression of ISG15 conjugation in the myocardium, suggesting that in this context, ISG15 conjugation seems to be a critical innate mechanism to fight against pathogens, stopping inflammatory cardiomyopathy, heart failure and death (Rahnefeld et al., 2014). Interestingly, cardiomyocyte-specific IkB kinase/NFκB activation was sufficient to enhance gene and protein expression of several inflammatory cytokines, including the ISG15 pathway leading to inflammatory cardiomyopathy and heart failure (Maier et al., 2012) although the specific consequences of ISG15 induction were not evaluated in this study. These results suggest that depending on the context, ISG15 might be protective or deleterious at the cardiac level. More recently, it has been described that lncRNA metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) is involved in cardiac innate immunity in a myocarditis model (Gast et al., 2016). Using heterozygous MALAT1-deficient $ApoE^{-/-}$ mice, the same group found that these mice displayed massive immune system dysregulation and atherosclerosis within 2 months even when kept on normal diet, and this was associated with altered transcriptomes in splenocytes with upregulation of IFN signaling including *Isg15* (Gast et al., 2019). To our knowledge, there are no studies evaluating the pathophysiological consequence of the ISG15 pathway in hypertension. Our bioinformatics approach allowed us to propose that the ISG15 pathway might have a role in the development of hypertension, endothelial dysfunction and vascular remodelling, through interaction with different proteins involved in inflammation, IFN signaling or activation of transcription factors.

This was confirmed experimentally by analyzing changes in the proteome of aorta from Ang II-infused WT and ISG15$^{-/-}$ mice that showed differential expression of proteins involved in cardiovascular function and remodelling. Notably, we did not find significant changes in proteins belonging to the immune system, likely because the limited number of proteins detected, albeit a tendency to decrease was observed in arteries from ISG15$^{-/-}$ mice.

To directly confirm the role of ISG15 system in vascular function in hypertension, we used a multidisciplinary approach including ISG15$^{-/-}$ mice, which lack free and conjugated ISG15, USP18^{C61A} mice that show excessive irreversibly ISGylation because of a mutation in the de-ISGgylating enzyme USP18, and exogenous rISG15 added to ECs or aorta segments. We found that ISG15$^{-/-}$ mice were protected against Ang II-induced vascular stiffness, elastin remodelling and endothelium dysfunction. Moreover, upon Ang II infusion, USP18^{C61A} mice develop aortic dilation, lethal dissection, and elastin degradation. More importantly, ISG15$^{-/-}$ mice showed attenuated hypertension while USP18^{C61A} mice were more sensitive to Ang II hypertensive effects. Interestingly, aorta from the classical model of aneurysm in Ang II-infused ApoE$^{-/-}$ mice and human AAs showed enhanced *ISG15* expression, suggesting that the ISG15 system is a novel mediator involved in vascular remodelling of large arteries, and that this system might have implications in human pathology. Of note, rISG15 induced endothelial dysfunction in healthy arteries pointing to the vascular endothelium as the main target for ISG15 actions. In fact, vascular contractile responses were unmodified by ISG15 deletion or rISG15 addition, although alterations in VSMCs should not be fully discarded, particularly in the model of aortic dilation by USP18 mutation. Remarkably, there were not phenotypic differences between WT and ISG15$^{-/-}$ arteries without Ang II, which suggests that protein overexpression is needed to mediate deleterious effects. Altogether, our data demonstrate for the first time, the involvement of ISG15/USP18 pathway in vascular damage in hypertension.

One intriguing finding is the fact that ISG15$^{-/-}$ mice are not protected from Ang II-induced vascular remodelling and that no differences in vascular stiffness or endothelial function were observed in surviving USP18^{C61A} mice, likely reflecting different contributions of free and conjugated ISG15. Although we cannot definitively conclude on the involvement of both ISG15 isoforms to vascular damage, the fact that upon Ang II-infusion, USP18^{C61A} mice develop aortic dilation, aneurysm formation and lethal dissection, suggest that ISGylation, rather than free ISG15, might be the mechanism involved in vascular remodelling. In fact, the development of AAs in the absence of ApoE deficiency with only 2 weeks of Ang II infusion is rare, which highlights the importance of ISGylation in vascular homeostasis. Although speculative, we believe that more aggressive strategies to induce aortic dilation and aneurysms formation

should be carried out into ISG15$^{-/-}$ mice to fully confirm (or exclude) the effects of ISG15 deletion in aortic remodelling. ISG15$^{-/-}$ mice are protected against Ang II-induced vascular stiffness, an effect not modified in USP18^{C61A} mice, pointing to free extracellular ISG15 as potential mediator. Finally, in response to Ang II, ISG15$^{-/-}$ mice showed improved endothelium function, an effect not observed in USP18^{C61A} mice, and exogenously added rISG15 induced endothelial dysfunction in healthy arteries, pointing to free extracellular ISG15 as mediator of endothelial dysfunction. A remaining question is whether the exogenously added rISG15 would be able to cross the membranes and ISGylate proteins. One additional explanation to the divergent effects observed in ISG15$^{-/-}$ and USP18^{C61A} mice might be that surviving USP18^{C61A} mice have developed protective mechanisms against the deleterious effects of Ang II. However, this clearly warrants further investigation. Of note, vascular changes induced by ISG15 might affect hypertension development since as mentioned, ISG15$^{-/-}$ mice showed an attenuated hypertensive response to Ang II and the opposite was observed in USP18^{C61A} mice. This enhanced hypertensive response in USP18^{C61A} mice might trigger aortic dissection and mortality, which was observed during the first days of Ang II infusion.

It has been recently described that LFA-1, the classical integrin receptor for ICAM-1 in immune cells, acts as a receptor of extracellular ISG15 in NK cells and lymphocytes (Swaim et al., 2017; Iglesias-Guimarais et al., 2020). In these cells, ISG15 binding to LFA-1 and provokes cytokine secretion, including but not limited to IFNγ, by intracellular mechanisms dependent on Src kinase activity (Swaim et al., 2017). LFA-1 immunostaining showed that this receptor was only expressed in aortic periadventitial cells of Ang II-treated mice, a classical location for immune cells infiltration in hypertension. Moreover, gene expression was significantly increased in aorta from hypertensive animals. It is therefore tempting to speculate a possible contribution of endocrine or paracrine ISG15 acting on LFA in local or circulating immune cells to modulate their phenotype and contribute to vascular damage in hypertension. In fact, as mentioned, peritoneal macrophages from Ang II-infused mice showed enhanced *Isg15* expression. Importantly, rISG15 is able to produce endothelial dysfunction in healthy arteries where LFA-1 positive cells are not being found, indicating that there might be additional receptors for ISG15 at the vascular level. In fact, a non-specific integrin receptor blocker produced a complete prevention of rISG15-induced endothelial dysfunction in aortic rings. More studies are needed to clearly establish the identity of this receptor.

Oxidative stress seems to play a fundamental role in the vascular damage observed in hypertension (Griendling et al., 2021). Our proteomics analysis revealed that proteins implicated in vascular redox state are decreased in Ang II-infused ISG15$^{-/-}$ mice. Moreover, the levels of

oxidized Cys-containing peptides, that were increased in aorta from Ang II-infused WT, were also decreased by ISG15 downregulation. These results were confirmed by in situ $O_2^{\cdot-}$ determination showing that aorta from ISG15$^{-/-}$ were protected against the increase in $O_2^{\cdot-}$ produced by Ang II, while aortas from USP18^{C61A} animals displayed higher levels of $O_2^{\cdot-}$. Moreover, USP18^{C61A} aorta had increased levels of *Nox1* transcript, even at basal conditions, which contributed to functional responses since NOX1 inhibition decreased contractile responses in control USP18^{C61A} mice but not in WT mice. In ECs, rISG15 increased $O_2^{\cdot-}$ generation and the activity and expression of the NADPH oxidase enzymes and, in human vascular fibroblasts, rISG15 augmented NADPH oxidase activity and H_2O_2 levels, being H_2O_2 levels higher in hypertensive than normotensive fibroblasts. More importantly, this increased oxidative stress milieu had functional consequences. Thus, endothelial dysfunction induced by rISG15 was prevented by selective inhibition of NOX1. Furthermore, in Ang II USP18^{C61A} mice, treatment with the antioxidant SOD mimetic tempol prevented hypertension, aneurysm development, mortality, and vascular remodelling. Together, these results demonstrate a novel role for ISG15 as a ROS-generating stimulus at the vascular level and point to a relationship between hypertension, ISG15 and ROS. Interestingly, ISG15 did not correlate with $O_2^{\cdot-}$ in PBMCs from patients, suggesting that ISG15 might influence redox biology in some specific cell types such as vascular cells but not in immune cells.

Earlier studies defined ISG15 as an IFNγ-inducing molecule in immune cells such as T lymphocytes or NK cells (Knight and Cordova, 1991; Recht et al., 1991; D'Cunha et al., 1996a, 1996b; Bogunovic et al., 2012) independently from ISGylation (Bogunovic et al., 2012). We did not find differences in markers of macrophage infiltration between Ang II-treated WT and ISG15$^{-/-}$ mice. However, in aorta from WT mice, Ang II increased the expression of *Ifng*, *Ptgs2* and the lymphocytes marker *Cd3e*, an effect not observed in ISG15$^{-/-}$ mice. Importantly, selective inhibition of COX-2 and IFNγ prevented the rISG15-induced endothelial dysfunction thus confirming a role of inflammation in ISG15-induced vascular damage. Of note, arteries from USP18^{C61A} mice showed a clear proinflammatory phenotype even in the absence of Ang II, as shown by the increased expression of *Ifng*, *Ptgs2* and the chemoattractant protein *Ccl2*, and enhanced infiltration of macrophages and lymphocytes, that was not further augmented by Ang II. The reasons for this vascular inflammation need to be further explored but in a pathological context, this basal proinflammatory state probably predisposes USP18^{C61A} mice to the deleterious actions of Ang II, inducing the observed vascular phenotype. In this sense, specific studies with anti-inflammatory drugs would be needed to test a potential prevention of Ang II-induced aortic dilation in USP18^{C61A} mice. In this line of evidence, previous studies have confirmed the role of inflammatory processes in AAA formation, both in mice and humans

(Thompson et al., 1995; Nordon et al., 2009; Kuivaniemi et al., 2015), although, unfortunately, anti-inflammatory therapies have not been proven successful in general in the clinical setting (Dale et al., 2015; Golledge et al., 2020b). We cannot discard that the inflammatory and oxidative environment observed in our experimental paradigm is probably interconnected, since the reciprocal relationship between both is well known. In any case, our results uncover a new mediator involved in AAA development and build on the existing information on AAA pathology. In addition, $USP18^{C61A}$ mice could be a new animal model to study aneurysms formation out of the context of ApoE deficiency or different from the classical chemical models (Trollope et al., 2011).

Insight into the molecular function of ISG15 requires identification of ISG15 substrates and/or interaction partners at the organismal level. Mass spectrometry studies have identified hundreds of proteins which can be conjugated with ISG15, including proteins induced by type I interferon or involved in IFN signaling such as Janus Kinase 1/2 (JAK1/2) and STAT1 (Jeon et al., 2010). Of note, Ang II activates the JAK-STAT pathway in the cardiovascular system mediating several of its deleterious effects (Satou and González-Villalobos, 2012). Until now, and unlike other post-translational modifications such as ubiquitination, the real relevance of ISGylation is still unknown, being more related to the stability and activity of the proteins. Because ISGylated proteins have been found in different biological processes such as metabolism, cell cycle, cell proliferation and differentiation, cell structure and motility, muscular contraction, immune response, intracellular protein traffic, protein translation, ubiquitination, autophagy, or exosome secretion (Albert et al., 2018; Villarroya-Beltri et al., 2017) and because of the paucity of information about the biological functions for these interactions, future studies are warranted to address this issue. However, our proteomic study provides a comprehensive overview of cellular protein dynamics regulated by ISG15, and this includes proteins involved in cardiovascular remodelling and function and vascular oxidative stress.

In summary, we used a multidisciplinary approach to study the role of ISG15 in vascular damage in hypertension. Our bioinformatics study pointed to a role for ISG15 pathway in hypertension development and hypertension-associated endothelial dysfunction and vascular remodelling. Using proteomics we identified biological processes and molecular pathways involved in the role of ISG15 in vascular damage in hypertension. The functional contribution of the pathway was deeply analyzed using animal models of loss and gain of function in hypertension and cell-based studies. Finally, the possible contribution of the ISG15 pathway to vascular damage was confirmed in human samples. Our results demonstrate that hypertension increases the expression of the ISG15 pathway at the vascular level. By inducing inflammation and ROS

generation, ISG15 contributes to the development of hypertension, endothelial dysfunction, vascular stiffness and remodelling and aneurysm development (**Figure 59**). Moreover, we uncover a possible role for this pathway in human pathology as *ISG15* expression correlated with vascular remodelling and aneurysms. For these reasons, we propose ISG15 as a novel mediator of vascular damage. Further studies are warranted to determine intracellular pathways by which ISG15 is affecting vascular physiopathology and to investigate the possible role of ISG15 as biomarker of vascular damage and hypertension.

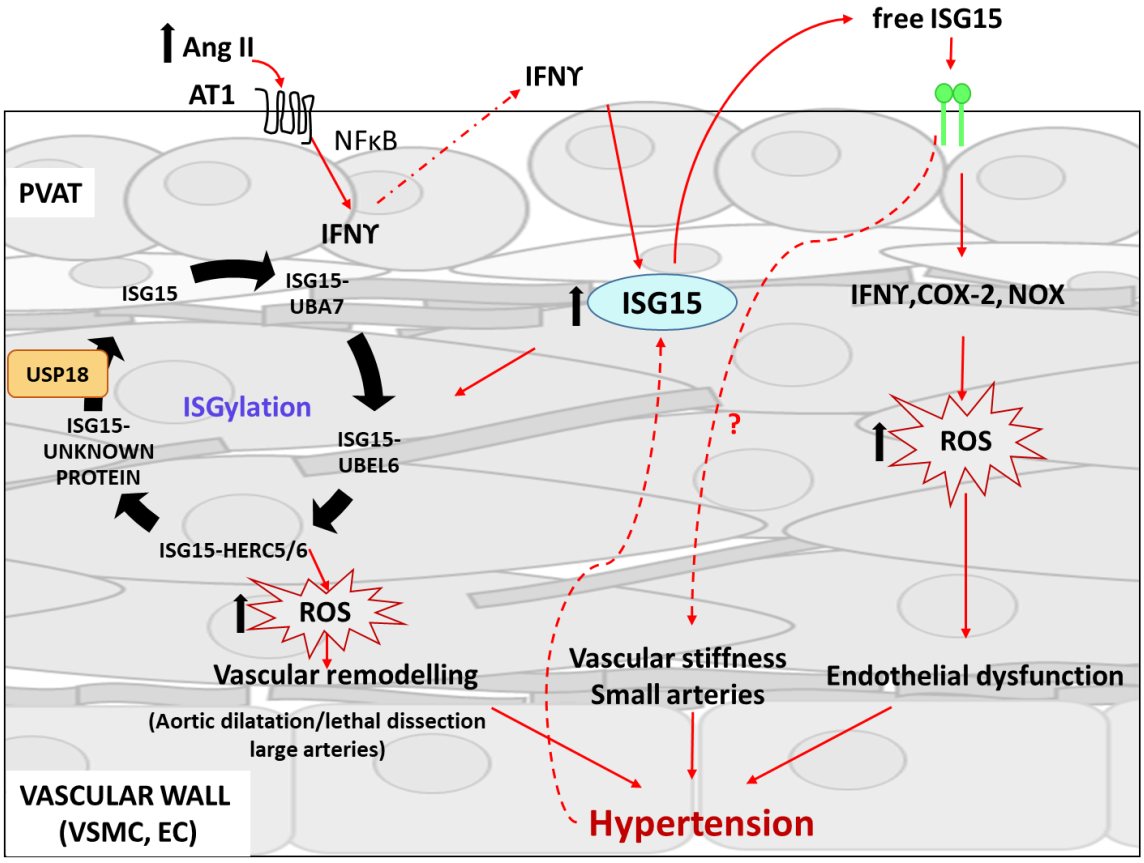


Figure 59. Proposed role of ISG15 in the regulation of Angiotensin II (Ang II)-induced hypertension and vascular injury. Ang II stimulates ISG15 expression via AT1/NFκB and IFNγ generation in vascular smooth muscle cells (VSMC), endothelial cells (EC), and/or in vascular tissue. Free ISG15 might bind an unknown integrin receptor that produce IFNγ and inflammatory mediators such as cyclooxygenase 2 (COX-2) and NADPH Oxidase (NOX)-derived reactive oxygen species (ROS) that are responsible for the ISG15-induced endothelial dysfunction. Ang II also likely induces ISGylation of unknown proteins that increases oxidative stress and induces aortic dilatation and lethal dissection. ISG15 system also participates of Ang II-induced vascular stiffness. These vascular alterations might contribute to the development of hypertension which in turn might feedback to increase ISG15 expression.

2. Role of myeloid GRK2 in vascular damage in obesity.

It is well accepted that obesity is a very prevalent condition defined by increased adiposity and metabolic dysfunction that correlates in humans and animal models of disease, with hypertension and vascular alterations such as endothelial dysfunction, vascular remodelling and altered mechanical properties. Also, extensive evidence demonstrates that in obesity, adipose tissue dysfunction is characterized by a pro-inflammatory status and secretion of proinflammatory mediators that could trigger cardiovascular alterations (Fuster et al., 2016; Vecchié et al., 2018). In this sense, PVAT might have a role in vascular damage in obesity and other pathologies such as AAA because of the infiltration of inflammatory macrophages and T cells (Fernández-Alfonso et al., 2017; Sagan et al., 2019).

PVAT-derived vasodilator and vasoconstrictor mediators are important to maintain an appropriate vascular tone (Ramirez et al., 2017; Agabiti-Rosei et al., 2018). It is well known that the volume of fat, including of PVAT, is associated with hypertension; moreover, it has been suggested that the function of PVAT, rather than the size might be more important for the control of vascular homeostasis (Huang Cao et al., 2017). In response to environmental stimuli, such as HFD, PVAT is able to change faster compared to other adipose depots, such as visceral and subcutaneous fat, promoting more readily a pro-inflammatory state. For instance, mice fed an HFD reduce the expression of anti-inflammatory and increase that of pro-inflammatory adipokines and cytokines in PVAT from the aortic arch in the first two weeks of HFD feeding, a period in which only minor changes are detected in visceral and subcutaneous fat (Chatterjee et al., 2009). As discussed earlier, increased infiltration of immune cells, including macrophages and T lymphocytes, is a hallmark of PVAT dysfunction not only in obesity but also in other CVD, such as AAA or hypertension, and both cell types play an important role in vascular alterations associated with these pathologies, in part through the modulation of vasoactive responses (Fernández-Alfonso et al., 2017; Sagan et al., 2019). An anti-contractile effect of healthy PVAT has been described by many authors over the last twenty years and this seems to be lost in obesity, likely because of the presence of contractile factors (Soltis and Cassis, 1991; Gollasch, 2012; Szasz and Webb, 2012, Fernández-Alfonso et al., 2017). However, we did not observe this effect in our experimental model. Instead, we found that PVAT impaired endothelium-dependent vasodilator effects to acetylcholine and insulin in control animals fed a normal or an HFD, thus confirming the ability of PVAT to modulate vascular responses. Notably, in animals fed an HFD, segments with PVAT were unable to achieve any observable relaxant response to insulin which is in line with findings described in previous reports for other endothelium

dependent agonists (Ketonen et al., 2010; Ma et al., 2010; Xia et al., 2016). Because NO-independent relaxation is only minimally affected by the presence of PVAT, the observed effects induced by PVAT could probably be due to a decrease in NO availability.

GRK2 is an ubiquitous member of the G protein-coupled receptor kinase family that appears to play a central integrative role in signal transduction cascades (Penela et al., 2010). Several studies have demonstrated the involvement of GRK2 in the regulation of whole organism glucose homeostasis and local insulin resistance in different tissues (Murga et al., 2019; Lucas et al., 2015). Moreover, increased expression of GRK2 has been observed in vessels from different mouse models of vascular or metabolic diseases including hypertension and diabetes, and this correlates with a decrease in NO bioavailability that may contribute to endothelial dysfunction (Avendaño et al., 2014; Lucas et al., 2015; Taguchi et al., 2015). In particular, in C57Bl6 mice infused with Ang II, lowering GRK2 increased NO bioavailability and prevented endothelial dysfunction, vascular remodelling and stiffness (Avendaño et al., 2014). GRK2 is highly expressed in various cell types of the immune system and the levels and activity of this kinase change in these cells under different pathological conditions (Vroon et al., 2006; Mayor et al., 2011; Murga et al., 2019). Moreover, it has been suggested that GRK2 may have a potential role in the onset or development of inflammatory disorders or in human pathologies with an inflammatory basis (Murga et al., 2019). In this context, it has been demonstrated that a reduction of GRK2 levels in myeloid cells prevents the development of glucose intolerance and hyperglycemia after an HFD by downregulating the pro-inflammatory macrophage profile (Vila-Bedmar et al., 2020). Here, we found that, in the absence of PVAT, endothelium-dependent or -independent vasodilator responses are unaltered by GRK2 downregulation in myeloid cells either in mice fed a ND or an HFD. However, the PVAT-induced impairment of acetylcholine or insulin responses is completely prevented by reducing GRK2 in myeloid cells in animals fed an HFD. This uncovers a new mechanism of regulation of endothelial dysfunction, and vascular insulin resistance induced by PVAT in the context of obesity. Again, because acetylcholine and insulin-induced relaxation are dependent on NO in aorta, the beneficial effects of GRK2 reduction were likely due to an increase in NO availability rather than to altered vascular smooth muscle NO sensitivity, since DEA-NO-induced responses were unaffected by the genotype. Whether this partial deficiency in GRK2 only in myeloid cells might also affect blood pressure or vascular remodelling requires further investigation. In any case, the particular effect of decreasing GRK2 in myeloid cells in vascular biology was not previously addressed in prior studies.

We found a positive correlation between GRK2 levels and macrophage- and lymphocyte-specific markers in PVAT of patients with AAA, that were not apparently dependent on adiposity. We acknowledge that for many aspects, AAA patients would not be comparable with our model of HFD-induced obesity. However, these results highlight the importance of GRK2 in immune cells in this specific adipose tissue depot. In our control mice, 12-week-long HFD increases the expression in PVAT of one of the most important PVAT-derived cytokines, TNFα. However, LysM-GRK2$^{+/-}$ mice appear to be protected from this HFD-induced TNFα upregulation. Notably, we found that, in PVAT from patients with AAA, there is a significant correlation between TNFα and BMI and nearly significant with abdominal perimeter, even when our study population is not markedly obese.

It has been suggested that, during an HFD, PVAT inflammation precedes macrophage infiltration. So, the recruitment of macrophages seems to occur in response to PVAT inflammation (Chatterjee et al., 2009). Infiltrating macrophages may, in turn, potentiate the inflammatory response of PVAT further enhancing PVAT inflammation in a positive feedback loop. Our results demonstrate that HFD increases the infiltration of both macrophages and lymphocytes in PVAT from WT mice and that lowering GRK2 in myeloid cells decreases not only macrophages but also T lymphocytes infiltration in this tissue. This might contribute to decrease TNFα expression and to deteriorate less endothelial function. In fact, we observed preserved vasodilation to insulin in arteries with PVAT from obese wild-type mice in the presence of an anti-TNFα antibody, confirming the importance of PVAT-derived TNFα in vascular relaxation in obesity. The key importance of TNFα in vascular tone is demonstrated by studies showing that a direct application of TNFα to the PVAT around healthy blood vessels decreases PVAT-induced beneficial effects on the vasculature (Greenstein et al., 2009). Importantly, high levels of free fatty acids in rat aorta have been suggested to induce TNFα upregulation and inflammation in the PVAT depot, and to attenuate its anti-contractile properties (Sun et al., 2013). A remaining question is whether this decreased recruitment of inflammatory cells is due to a reduced inflammatory response of PVAT at an early stage during the HFD feeding or rather is a consequence of the reduced levels of GRK2 within macrophages. This deserves further investigation. The results we describe here resemble the phenotype observed in other adipose depots from this same mouse strain (Vila-Bedmar et al., 2020). In particular, TNFα expression in the visceral white adipose tissue was decreased in HFD-fed LysM-GRK2$^{+/-}$ mice due to a reduced amount of the M1 type of pro-inflammatory macrophages infiltrating this adipose depot (Vila-Bedmar et al., 2020). *GRK2* mRNA levels in human PVAT also correlate with that of pro-inflammatory adipokines, such as leptin, in agreement with data obtained in visceral adipose

depots of LysM-GRK2$^{+/-}$ animals fed an HFD where leptin levels were decreased when GRK2 amount was reduced (Vila-Bedmar et al., 2020). On the contrary, *GRK2* mRNA did not correlate with adiponectin in human PVAT in agreement with the lack of differences in adiponectin levels in murine PVAT between the two genotypes. Given the described pro-inflammatory effects of leptin and its implication in the increased cardiovascular risk observed in obese patients (Landecho et al., 2019), these data support an additional mechanism associating increased GRK2 levels with enhanced inflammation and vascular dysfunction by means of increasing PVAT-derived leptin production. Altogether, these results suggest that low levels of GRK2 in myeloid cells can avoid the pro-inflammatory reprogramming taking place in different adipose depots during diet-induced obesity.

The loss of the beneficial effects of PVAT in obese humans (Greenstein et al., 2009) or in mice in inflammatory conditions (Withers et al., 2011) can be rescued not only by anti-TNFα antibodies but also by catalase and superoxide dismutase, which highlights the key importance of ROS in the PVAT-mediated control of vascular function. In fact, in obese individuals, the upregulation of $O_2^{\cdot-}$ may reduce endothelial NO production and vasodilator responses (Virdis et al., 2015; Ramirez et al., 2017). Moreover, an increased production of ROS leading to a loss of the anti-contractile effect of thoracic PVAT was demonstrated in a different murine model (Gao et al., 2006). Enhanced NADPH oxidase expression and $O_2^{\cdot-}$ production have been found in thoracic PVAT of mice after an 8-week-long HFD (60% Kcal from fat), which results in endothelial dysfunction (Ketonen et al., 2010). Consistent with all these reports, we detected an increase in the expression of the *Nox1* subunit of NADPH oxidase in the PVAT of obese control mice that does not occur in LysM-GRK2$^{+/-}$ animals. More importantly, the impaired insulin-induced vasodilation observed in arteries with PVAT from obese control animals was ameliorated by a selective NOX1 inhibitor. We do not know the precise mechanism by which GRK2 may directly or indirectly activate NADPH oxidase but, in the cardiomyocyte cell line H9c2, overexpression of GRK2 is enough to trigger ROS production in a NADPH oxidase-dependent manner, and this kinase also seems to be required for the adrenergic-mediated stimulation of ROS production (Theccanat et al., 2016). Altogether, these studies provide a novel link between GRK2 levels and NADPH activity or expression at the vascular level that deserves further investigation. One limitation of our study is that we cannot affirm whether ROS and TNFα are interrelated mechanisms, but TNFα is capable of generating an excess of ROS via NADPH oxidase activation and also induces eNOS uncoupling, which generates $O_2^{\cdot-}$, thus impairing NO bioavailability and endothelium-dependent relaxation (Virdis et al., 2015). In fact, inflammation and oxidative stress are interconnected processes associated with adipose tissue and vascular dysfunction

(Aghamohammadzadeh et al., 2015), and the relationship between both processes comes from the fact that macrophages represent a key effector of both the production of ROS and cytokines (Furukawa et al., 2004). In this sense, it is worth noting that myeloid GRK2 deletion prevented the HFD-induced TNFα and NOX1 upregulation in PVAT without affecting the expression of other proinflammatory cytokines.

Based on these findings we suggest that GRK2 in myeloid cells may play an important role in orchestrating the responses that promote both inflammation (i.e TNFα production and inflammatory cells infiltration) and excessive ROS production by NADPH oxidase in PVAT to decrease vasodilation (**Figure 60**). Lowering myeloid GRK2 protein could prevent this vicious cycle and reprogram the pro-inflammatory and pro-oxidative milieu observed in PVAT during obesity thus improving vascular function. Altogether these results uncover a potentially novel strategy for the regulation of vascular dysfunction in obesity that may have additional therapeutic implications for the treatment of vascular disorders.

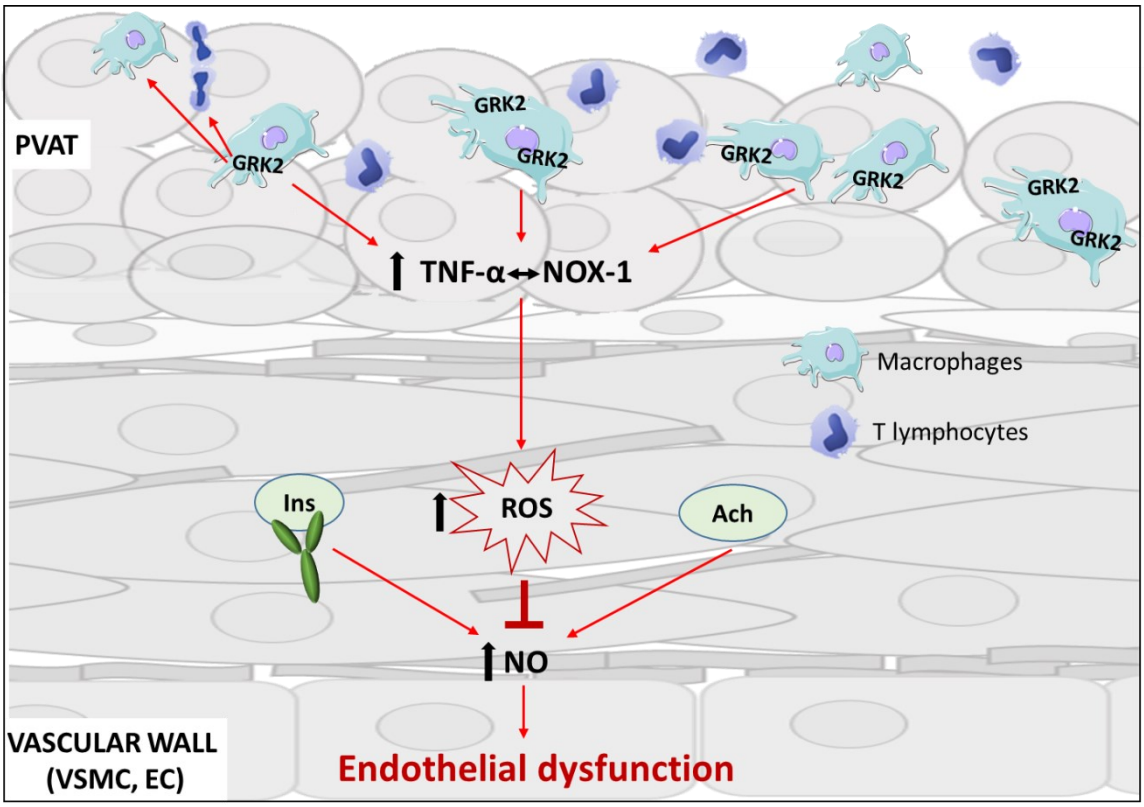


Figure 60. Schematic representation of the implication of myeloid GRK2 in vascular responses in obesity. GRK2 from myeloid cells increases macrophages and T lymphocytes infiltration and TNFα and NOX1 expression in perivascular adipose tissue (PVAT) in obesity. This enhances reactive oxygen species (ROS) generation and impairs endothelium-dependent relaxation thus provoking endothelial dysfunction. VSMC: vascular smooth muscle cells, EC: endothelial cells.

3. Novel mediators of inflammation in vascular damage in hypertension and obesity.

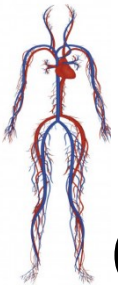
As discussed earlier, both hypertension and obesity share functional, structural and mechanical vascular alterations and are important risk factors for CVD. Moreover, obesity is a risk factor for hypertension development, at least in part because of the release of vasoactive substances from adipose tissue that impact the underlying vasculature (Martínez-Martínez et al., 2021). It is now accepted that low-grade inflammation and increased oxidative stress in both the (perivascular) adipose tissue, and the vasculature are hallmarks of hypertension and obesity. In fact, abundant evidence in preclinical animal models demonstrate that blocking either inflammation or oxidative stress have, in general, beneficial effects on vascular homeostasis in both pathologies. Another similarity between hypertension and obesity is that immune cells such as macrophages and T lymphocytes infiltrate the (perivascular) adipose tissue and the vessels and produce inflammatory mediators such as TNFα and IFNγ, which are key effectors of the increased vascular damage observed in these pathologies. In fact, TNFα and IFNγ, were identified in our bioinformatics study as the first and fourth master regulators, respectively, involved in hypertension. It is important to note that both cytokines induce the expression of ISG15 in different cells (Albert et al., 2018, results found here). Moreover, at the vascular level, ISG15 expression was induced by Ang II in an IFNγ dependent manner, it was also increased in vessels from hypertension animal models and positively correlated with systolic blood pressure in human PBMC. Interestingly, unpublished studies performed in our laboratory show that vascular ISG15 expression is enhanced in arteries from HFD-obese animals in parallel with levels of TNFα. Moreover, we found a positive correlation between PBMCs *ISG15* and body mass index and glucose, which could indicate a role of ISG15 also in obesity and diabetes. In agreement, two recent studies found positive correlations between ISG15 and obesity (Yan et al., 2021) or diabetes mellitus (Sun et al., 2019). More importantly, mice lacking ISG15 had elevated energy expenditure and were resistant to diet-induced obesity (Yan et al., 2021) and these effects were attributed to the ability of ISG15 to produce ISGylation in almost all glycolytic enzymes in adipocytes. We do not know whether $ISG15^{-/-}$ mice would be protected for the vascular alterations induced by obesity and this warrant further investigation. However, altogether these data point to a possible role of IFNγ/TNFα/ISG15 system as a common mediator of vascular damage in CVD.

One of the most characteristic features of vascular damage in the context of hypertension and obesity is endothelial dysfunction, which is influenced by IFNγ, TNFα and ROS released locally of from the underlying perivascular adipose tissue (Mikolajczyk et al., 2016; DeVallance et al., 2018). In this context, our study demonstrates that ISG15 deletion improved endothelial

dysfunction in hypertension by decreasing inflammation and oxidative stress. Moreover, we found that GRK2 downregulation specifically in myeloid cells prevented the HFD-induced endothelial dysfunction likely through downregulation of TNFα and NOX1. Because endothelial dysfunction is an early event in the development of many vascular disorders, our study contributes to clarify underlying mechanisms.

Vascular remodelling and vascular stiffness are also hallmarks of hypertension, obesity and AAA. Herein, we describe ISG15 and ISGylation as novel mediators of AAA development and hypertension-associated vascular stiffness, likely dependent of inflammation and ROS. Thus, we found that ISG15 deletion decreased Ang II-induced vascular stiffness, inflammation and ROS. Also, ISG15 expression was augmented in human and murine aortic aneurisms, and ISGylation-dependent aortic dilation was prevented by ROS inhibition. Finally, unpublished observations from our lab demonstrate that *ISG15* expression in human AAA highly positively correlates with TNFα and obesity. Although we have not specifically studied the contribution of myeloid GRK2 to vascular remodelling and stiffness, we previously described a role for GRK2 in hypertension associated vascular structural and mechanical alterations (Avendaño et al., 2014). In this sense, our study also contributes to clarify underlying mechanisms involved in vascular remodelling in CVD.

In conclusion, in this PhD Thesis we described two novel mechanisms involved in vascular damage in hypertension and obesity. This might shed some light in the search for new therapeutic targets to combat these important health problems related to CVD.



Conclusions

The general conclusion of this PhD Thesis is that ISG15 and myeloid GRK2 are novel mediators involved in the vascular damage associated with hypertension or obesity through inflammation and oxidative stress. The partial conclusions are:

1. *ISG15* mRNA expression in human peripheral blood mononuclear cells correlates with systolic blood pressure and with carotid-intima-media thickness. *ISG15* expression is also enhanced in human AAA.

2. Ang II induces ISG15 expression at the vascular level through AT_1/IFNγ/NFκB activation.

3. ISG15 deletion prevents changes in the expression of proteins implicated in cardiovascular function and remodelling and reduces Ang II-induced hypertension, vascular stiffness and endothelial dysfunction. Conversely, excessive ISGylation induced by USP18 mutation increases Ang II-induced hypertension and produces aortic dilation and rupture along with elastin breaks.

4. ISG15 deletion prevents Ang II-induced vascular inflammation and oxidative stress. Conversely, $USP18^{C61A}$ mice show enhanced expression of vascular inflammatory markers and production of ROS.

5. Recombinant ISG15 increases the expression of inflammatory markers and oxidative stress in endothelial cells, and induces endothelial dysfunction through COX-2, IFNγ, NOX1 and an integrin receptor.

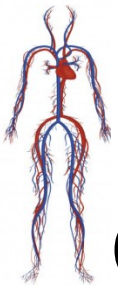
6. Ang II-induced aortic lethal dissection and vascular remodelling observed in $USP18^{C61A}$ mice is prevented by treatment with the antioxidant tempol.

7. In PVAT from patients with AAA, *GRK2* expression positively correlates with leptin, as well as with myeloid and lymphoid markers.

8. Partial GRK2 deletion in myeloid cells prevents PVAT-induced endothelial dysfunction in HFD fed animals.

8. Partial GRK2 deletion in myeloid cells prevents HFD-induced upregulation of TNFα and NOX1 as well as infiltration of macrophages and T lymphocytes in PVAT.

10. Pharmacological blockade of TNFα or NOX1 pathways restored the impaired vasodilator responses to insulin in arteries with PVAT from HFD-fed animals.



Conclusiones

La conclusión general de esta Tesis Doctoral es que ISG15 y GRK2 presente en células mieloides son nuevos mediadores implicados en el daño vascular asociado a la hipertensión u obesidad, siendo la inflamación y el estrés oxidativo los mecanismos subyacentes. Las conclusiones parciales son:

1. La expresión de ARNm de *ISG15* en células mononucleares de sangre periférica correlaciona con la presión arterial sistólica y con el grosor de la íntima media carotídeo en pacientes. La expresión de *ISG15* también está aumentada en AAA de pacientes.

2. Ang II induce la expresión de ISG15 a nivel vascular a través de la activación de AT_1/IFNγ/NFκB.

3. La eliminación de ISG15 previene los cambios en la expresión de proteínas implicadas en la función y en el remodelado cardiovascular y reduce la hipertensión inducida por Ang II, la rigidez vascular y la disfunción endotelial. Asimismo, la ISGilación excesiva inducida por la mutación de USP18 aumenta la hipertensión inducida por Ang II y produce dilatación y rotura aórtica junto con roturas en las láminas de elastina.

4. La eliminación de ISG15 previene la inflamación vascular y el estrés oxidativo inducidos por Ang II. Por el contrario, los ratones $USP18^{C61A}$ muestran una mayor expresión de marcadores inflamatorios y una incrementada producción de ROS a nivel vascular.

5. La proteína ISG15 recombinante aumenta la expresión de marcadores inflamatorios y de estrés oxidativo en células endoteliales e induce disfunción endotelial a través de COX-2, IFNγ, NOX1 y un receptor de integrinas.

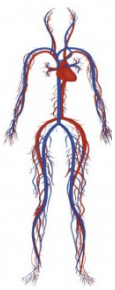
6. La disección aórtica letal y el remodelado vascular inducidos por Ang II en ratones $USP18^{C61A}$ se previene mediante el tratamiento con el antioxidante tempol.

7. En PVAT de pacientes con AAA, la expresión génica de *GRK2* se correlaciona positivamente con leptina, así como con marcadores mieloides y linfoides.

8. La deleción parcial de GRK2 en las células mieloides previene la disfunción endotelial inducida por el PVAT en animales alimentados con HFD.

9. La deleción parcial de GRK2 en las células mieloides previene la regulación positiva de TNFα y NOX1 inducida por HFD, así como la infiltración de macrófagos y linfocitos T en PVAT.

10. El bloqueo farmacológico de las rutas de TNFα o NOX1 restauró las respuestas vasodilatadoras a insulina en las arterias con PVAT de animales alimentados con HFD.



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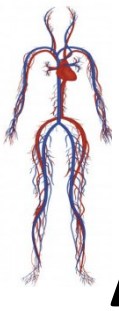

Annexes

Annexed Table 1. Proteins involved in Hypertension development by Phenopedia.

Database: Phenopedia in PHGKB.CDC.GOV

Download time: 12-17-2018

Disease: Hypertension

Number of genes: 2206

Number of Publications	Gene Symbol
668	ACE
397	AGT
314	NOS3
280	AGTR1
231	MTHFR
200	APOE
188	CYP11B2
158	GNB3
131	ADRB2
120	ADD1
87	IL6
83	F5
74	PPARG
69	REN
67	SERPINE1
66	ADRB1
64	TNF
57	F2
56	EDN1
54	TGFB1
53	ADIPOQ, LPL
52	VEGFA
50	CYBA
49	ADRB3,PON1
47	BMPR2
45	AGTR2
42	CRP,NPPA
41	IL10
40	APOB,GSTM1
38	IL1B,CETP
37	ALDH2
36	FGB,INS,BDKRB2
34	FTO
33	ITGB3,GSTT1,MMP9,CYP3A5
32	CYP17A1,ESR1,VDR
31	MMP3
30	ATP2B1

29	SLC6A4,ACE2
28	LEP
27	LIPC,APOA5
26	SELE
25	LEPR,GRK4
25	GRK4
24	NPPB,NR3C2,CYP4A11,ABCB1
23	SCNN1B,CYP2C9,DBP,LDLR,HSD11B1
22	NR3C1,STK39,ADRA2B
21	SLC12A3
20	WNK1,CYP11B1,CFH,APOA1,MMP2
19	HLA-DRB1,APOC3,IRS1,ENG,COMT
18	ADRA2A,F7,CYP2D6,NEDD4L,HMOX1,MC4R,RGS2,PPARA,APOL1
17	CAT,ACVRL1,WNK4,TCF7L2,TLR4,HFE,GSTP1,CSK,ADD2,PPARGC1A
16	EGFR,HSD11B2,ITGA2,LTA,KCNJ5,KLK1,NPR3,SOD2,CCL2
15	SCNN1G,PON2,CBS,NOS2,KCNJ11,CYP2J2,CDKN2B,COX8A
14	CCR5,ADRA1A,ABCA1,F13A1,FGF5,KDR,IL1RN,IL4,ICAM1,CYP4F2,SELENBP1,PDE4D,SCNN1A
13	BDNF,PTGIS,APLN,HTR2A,GNAS,GJA4,NPR1,FABP2,COG2,EDNRA,CYP1A1,CMA1
12	CLCNKB,CDKN2A,CYP19A1,PCSK9,LPA,GP1BA,IGF1,CACNB2,RET,SLC6A2
11	SHBG,ACSM3,PTGS2,GHRL,RNLS,UMOD,IL1A,KCNMB1,ALOX5AP,CYP3A4,APLNR,ESR2,SLCO1B1,SH2B3,ADM
10	CAPN10,EPHX2,DRD1,CYP2C19,ARMS2,HLA-DQB1,ABO,HLA-B,CD14
9	LIPG,VHL,SLC2A9,RETN,CXCL12,SDHB,SELP,GPX1,IL18,NPY,MTRR,MMP1,MPO,CYP2C8,FGA,FBN1,CDKN2B-AS1,CDH13,CCR2,ADH1B,ADRA2C
8	ADD3,IGF2BP2,ZNF652,AGER,EDNRB,ECE1,MTR,ND2,MYH9,ATP1A1,FADS1,IL4R,IL6R,IL8,INSR,HSD3B1,HIF1A,BDKRB1,SLC8A1,TNFRSF1B,HNF1A,TH,SLC4A5,PLAT,VWF,CACNA1D,CASR,CLOCK
7	CAV1,FADS2,CD36,VKORC1,UCP2,PLA2G7,PNPLA3,ADIPOR1,ENPP1,PPARD,PRKCH,TGFBR2,TLR2,SOD3,SLC12A1,SDHD,GCKR,IGF1R,ITGA2B,KCNK3,KCNQ1,NFKB1,NOS1,OLR1,TNFRSF11B,ELN,DIO2,C10orf107,CHGA,CTLA4,ADRA1B,PLEKHA7
6	CYP1A2,SERPINA3,COL4A1,NLRP3,NT5C2,SIRT1,ULK3,F12,NOTCH3,ZFHX3,MYOC,KCNA5,APOA4,IFNG,HMGCR,HP,GCK,GC,GJA5,ATXN2,CCL11,TIMP2,THBD,TBX3,PNMT,INSIG2,PCSK1,CACNA1C,ROCK2,NOS1AP
5	TBX4,NPHS2,XRCC1,UCP1,UCP3,SCGB1A1,TRPC6,ADIPOR2,ACTN4,ABCG2,KL,ERAP1,SERPINA1,CCHCR1,ULK4,PRCP,TIMP3,TP53,SOD1,TBX5,CCL5,SH2B1,GHR,GSTA1,GSTM3,HLADQA1,APOC1,IL12B,IL13,KCNJ1,ARG1,LRP5,ARNTL,MAF,MBL2,SERPINC1,MTNR1B,MTTP,MMP12,ATP2B3,OGG1,DRD2,MTCH2,FMO3,DDAH2,DDAH1,FLT1,PHACTR1,JAZF1,EMILIN1,NAT2,GNPDA2,CPB2,CYP1B1,CX3CR1,IL23R
4	CTH,HFE2,CPS1,TMEM18,CLU,CLCNKA,NAMPT,UTS2,PLCD3,NQO1,DBH,ETV5,EDN3,PAH,P2RX4,P2RX7,FURIN,NPHS1,NFKBIA,EIF2AK4,MTAP,MTHFD1,MYBPC3,NINJ2,SMAD4,CIMT,MIR146A,KIT,KNG1,KCNE1,KCNH2,IL1R1,HSPA1A,HNF4A,GSR,HLA-A,HLA-C,GUCY1A3,SLC17A5,PTPN22,SDHC,SAA1,SGK1,NOD2,THADA,SLC4A1,P2RY12,THBS2,TGFB3,PRSS8,RENBP,RAGE,CDKAL1,PITX2,GSTO1,SEC16B,CALCA,PSRC1,RGS5,STEAP4,TNFSF4,VEGF,VCAM1,XDH,GOSR2
3	HDAC9,MFN2,SLC4A7,PTGES,CELSR1,WRN,WFS1,BSND,C7orf49,TYMS,KCTD15,TRPM8,COL18A1,SLC14A2,DOCK7,LGR5,NR1I2,ABCB11,SCARB1,VNN1,PECAM1,PDGFRA,CASZ1,UGT1A1,TLR9,PMS1,PON3,POMC,POR,PTPRD,PTGS1,ZFAT,PTPN1,G6PC2,PROX1,PSMA6,ADAMTS9,CAMK1D,PTGDR,SOX6,SLC22A11,PRKG1,PRKCA,THBS1,TIMP1,TBXA2R,TFAP2B,TPM1,TSC1,TSPAN8,TNNI3,TNNT2,SREBF2,ND2,SLC22A2,SLC9A3,SPP1,MTMR9,BMP2,SHMT1,SLC4A2,SGK,SLC13A3,RYR3,SCN7A,ROS1,RXRA,SCNN1D,GCH1,GH1,NOX1,GLO1,SLCO1B3,HGF,HBB,GSS,GSTM2,GSTM4,GSTM5,HSPA1B,HSPA1L,

	APOA2,HSD3B2,IGF2,APOC4,IL6ST,JAK2,AR,IL3,IRF5,PDX1,IRAK1,KCNMA1,MIA3,KCNN3,KLC1,KRAS,CYP4F3,LTC4S,FADS3,LNPEP,MEF2A,MEF2C,ATP1A2,MYH7,MYL2,MYL3,MSRA,SMAD9,ATP1B1,NOS2A,NPPC,NPY2R,P2RY2,IL22,REG3A,EDN2,EGF,ERCC2,F8,CYP11A1,SLC30A8,DHFR,DRD4,ADRBK1,CYP21A2,CYP24A1,MS4A2,FGF1,FGG,FOXO3,FOLH1,WWC1,MTHFD1L,NEGR1,SLC22A12,CFTR,BTN2A1,CHGB,NR1H3,PROCR,TOMM40,CLCN6,CYP2R1,COL3A1,COL1A2,CSF2,MACROD2,CRY2,ADRA1D,CTGF
2	FAM78B,CTF1,SLC35F3,CTNNB1,CYBB,VCAN,CD300LG,CBLN2,ADORA2A,COL6A3,OSR1,UBR3,ADORA1,CPE,CPT1B,CPT2,GSTO2,ADH1C,CNR2,LYPLAL1,ABCC2,ATP6AP2,TSHZ1,CALCRL,TRIB1,ADA,KIR2DS2,CHI3L1,CD226,CORIN,CFHR3,STK38,CKM,OPTN,PARD3B,CHIT1,CHEK2,TIRAP,CHUK,FUT2,NCR3,COL6A5,GAA,CNTNAP2,SYNE1,PADI4,ALOX12,FOXO1,LPIN1,AKR1B1,ASTN2,CLEC16A,FAIM2,FKBP4,CARD8,FGFR2,ADRBK2,CYP2E1,KCTD7,CYP7A1,TTC39B,DHCR7,F2R,F11,FAAH,FABP1,ERBB2,EPHX1,ERCC1,CELSR2,Ppap2a,ZNF627,AHR,TRIM65,EP300,EPAS1,PAPPA,PARK2,FOXP3,PCSK6,ATP2B4,OAS3,NPY5R,NPY1R,NPR2,ROR2,NTRK1,NTRK3,NUCB2,NFKBIL1,NOTCH2,ATP2A2,NPAS2,NPC1,MME,MMP7,MOV10,TRNL1,NF1,ATM,MEFV,MET,MGP,CIITA,MIF,MITF,SMAD5,SMAD1,SMAD2,SMAD3,MAP4,LOX,LRP6,LTBP2,LGALS2,LIMK1,LLGL2,KISS1,KIR3DL1,KLKB1,KIR2DS1,KIR2DS3,IPF1,INPPL1,AQP4,ITPR2,ITGA9,AQP1,IL5,IL5RA,IL2RA,IL10RA,IL10RB,IL15,IL15RA,IL16,IL17A,ID3,SLC6A19,APOH,SLC6A18,FAS,HMGCS2,HLAG,GPX3,DROSHA,GPR39,ANG,H19,ANGPT1,CFHR1,HHEX,HLADPB1,GUCA2B,HBA1,GYS1,IL28B,ANGPTL3,GCLC,GLA,GPR77,GHSR,GIP,GIPR,TBL2,GALNT2,GATA2,BHMT,CCL18,SELPLG,RXRG,RASA1,RREB1,RYR2,ABCG8,SELL,IFIH1,ERAP2,SOX17,SLC9A1,SLC8A2,SLC6A13,SLC7A1,BMP4,SLC2A4,SLC2A1,SLC2A2,SLC26A6,AGXT2,BCL11B,SLPI,SPTA1,SPTB,SRD5A2,SLC10A1,SLC22A5,SLC19A1,SLC20A1,SLCO2A1,SLC22A1,SLC22A3,STAT4,CYTB,BMP7,ST2,ABCC8,TAP1,trnM,trnI,ND1,TNFAIP3,TSHR,CAPN5,C5,C4A,TRPC1,C3,TPH1,ACTC1,TERC,SREBF1,TCF7,THBS4,TGFBR1,PROC,SULF2,APOM,MAPK1,TMEM127,PRKCB,PTEN,PTGDS,AGTRAP,PSMD9,ATP10A,PSEN1,RNF213,USP37,TRIB3,WDR12,PTGER4,PTGFR,MIR518C,BCAT1,RBP4,BCL2A1,RARB,TRPV4,TMCO1,ATR,UGT1A8,UGT1A4,TRPM7,UGT1A9,ATG16L1,AVPR1A,PDGFRB,ZC3HC1,PCSK2,PCK1,MLXIPL,PDC,WWOX,PEE1,ATP6V1B1,PRKAG2,PGR,PIH,PKD1,PKD2,PLG,PLIN,PLTP,KYNU,KCNK17,ACVR2A,SOCS3,CD34,NRXN3,ACCN3,KALRN,MAPKAPK2,RUNX1,IRS2,SLC4A4,VAMP8,SERPINB7,PER2,CDC123,CACNA1H,TNFSF11,YEATS4,MKKS,NCOA3,CAST,BRAP,CARD14,ARMC5,OBFC1,PDGFD,CCR2,TNFRSF4,TRPM2,VCL,USF1,VEGFC,EIF4H,VIPR2,LRP8,WNT3,XPNPEP2,CACNA1A,CARTPT,GDF15,CD40,XYLB,NCOR2,RAPGEF5,ACYP2
1	GIT2,DNAJC6,GAB2,ZC3H11A,CDC5L,RHOBTB1,RABGAP1L,TOX,OXSR1,SLC23A2,NR1H4,CDC42,FGFBP1,SOX13,AKAP12,NFE2L3,SLC4A8,NCOR1,CXCL14,GABBR2,GNA14,IKBKE,CD59,WSCD2,CD69,ECE2,XPA,XPNPEP1,WNT5A,XRCC3,XRCC4,C18orf1,SF1,ZFP36,ZFP37,CA1,CA2,CA4,ZNF79,CACNA2D1,EVI5,ZNF208,CACNA1E,CACNA1S,CAD,C1orf135,ST8SIA4,PXDN,CXCR4,CACNG1,COLEC11,TRPV1,C11orf9,VIP,VIPR1,LAT2,WARS,VAV2,INS-IGF2,UCK2,UGT2B7,TXN,TXNRD1,LOC730226,TYRP1,UBE1,CPEB4,KCNIP4,EFTUD1,EFCAB1,CSRP3,THUMPD2,CYB5B,CALD1,C12orf30,NAA25,NR4A3,CTC1,ALPK1,ZMAT4,LIN28A,PALB2,BBS10,ZNF385D,ACBD4,TFPI2,GSTCD,TTC21B,AGMAT,TREML2,RIN3,ATP8B4,CALCR,NOL10,MAPKAP1,PRRC2A,GCC1,CCDC86,FZD4,SLC25A31,NUF2,NUDT12,AMAC1L2,TRAPPC9,ESYT3,TAF3,BCO2,CDCA7,STARD3NL,RAB6C,ZNRF3,KIAA1109,NBPF3,LTBP4,TCHP,STK24,NR0B2,DOT1L,MEGF11,CASQ2,MCM8,DCTN5,ACSS1,LZTR1,KDM5C,ARID1A,PICALM,TIGD6,SPACA1,LPRS1,APOL4,APOL3,MLL2,COLEC12,OR2G3,FBXO38,ECOP,ITM2C,DEFB126,FBF1,API5,FCN3,BLZF1,TSLP,RGS20,PLA2G4C,KLF7,TCAP,MADD,CAV2,CAV3,C9orf3,MAEL,TOX2,PPFIA4,ITGA8,IKBKAP,GCM1,GAS7,CNDP1,ZNF607,BUD13,C6orf105,RSPO3,ZGPAT,IL1F10,LOXL3,TIMELESS,BSN,SKAP2,CCKAR,DLK1,TNFRSF11A,ACTN2,CREG1,IL18RAP,IL18R1,INPP4B,WISP1,DLEU2,TSC22D1,CCK,CDK5R1,CBR3,TNFSF14,TNFSF13,TNFSF10,SFRS9,DNAH11,PPAP2B,STC2,OASL,AKR1C3,NCOA1,SOCS1,PDE5A,TNKS,TMEM183A,BCL7B,GPR56,NAT1,SLC25A14,MPZL1,PTER,NDST3,SLIT2,SLC22A6,ACVR2B,LY86,MED23,OPN4,CD28,SLC22A14,TGFBRAP1,SLC22A8,GRHPR,NAT8,BAZ1B,DUOXA1,PRC1,SLC13A2,IL33,PIGQ,TBX19,TRIM47,P2RX6,CD2,SLC6A5,COL23A1,IL1RL1,OSMR,CD247,TIMD4,ZNF300,GGTLC1,MAGI1,DUSP27,RCSD1,DLGAP1,CAPN13,RAB11B,C1orf156,METTL18,NAF1,GPR50,SIGLEC12,PGLYRP1,AP3D1,HPS4,ZNF259,KRIT1,PML,PKHD1,PLA2G5,PLAGL1,PLAUR,PLCB2,PLCB4,BCL11A,T

	M6SF2,UBASH3A,LRP1B,PLD2,PIK3C2B,PIK3CG,PIK3R1,PHEX,PER1,PFKP,RTEL1,SPTBN5,CRNKL1,PDE1A,TNNI3K,ATL1,POLR1D,CLEC1B,TLR7,RXFP3,KCNK9,TLR8,VTA1,SIRT6,ANGPTL4,SFMBT1,HSD17B7,TH1L,LARS,LUC7L2,PDK4,IL23A,HDAC7,GPRC5B,SLC26A4,PDYN,ETNK2,TMEM39A,THNSL2,MCOLN3,CCDC91,PPP3CA,KIR2DL5B,C10orf59,PDPR,FIGN,PRMT6,NADSYN1,DRAM1,PPP3R1,STK32B,KIR2DP1,ELOVL2,LAX1,RASIP1,UBE2R2,SDHAF2,KIR3DP1,PIGG,CNTLN,UGT1A3,Ly6g,UGT1A7,UGT1A6,UGT1A5,POU5F1,POU2F1,TOMM7,UGT1A10,CNGB3,RBFOX1,ROPN1,TET2,PPIC,CNNM2,QPCTL,TOLLIP,YIPF1,ZFAND6,GPR87,DUOX1,SLCO1C1,A4GALT,POLG,PI3,SERPINE2,KLHL12,CCND1,RARG,PTPRC,RELA,REL,RFC1,RABIF,RAC1,RAC2,RALB,ACTA2,BCHE,RARA,PTPRG,PTPRN2,PTPRO,BAX,NGB,PVR,PVRL2,BBS1,BBS2,PYGB,ZNF77,BBS4,MLL3,PTH1R,MIR499,ODZ2,SLC12A5,PLEKHG1,KIDINS220,XPO5,RPTOR,SORCS2,AADACL1,LRRC7,SEMA6A,FAM135A,KIAA1462,PTGIR,AS3MT,SLC24A3,MIR495,PTPN11,Spata5,HAMP,C1orf114,WDFY4,DENND1A,PTPN2,SPTBN4,GBA3,PTN,POGK,EPB41L5,PANX2,IFNK,PSMA4,TRPV5,HTRA1,PSMB4,ARNTL2,MRPS22,PSMB8,PYY,PRDM9,PSMB9,CHPT1,ATP10D,ERGIC1,TAS2R38,RNPEPL1,PTGER1,PTGER2,PTGER3,JPH3,SLC4A10,KIR2DL5A,CACNA2D3,AXL,ADCY10,PRKCG,VPS11,IQWD1,MFN1,C1orf112,CNDP2,OGDHL,UGCGL2,ENOSF1,PRIM2,ITLN1,OSGEP,PRELP,GPRC5D,MOSC2,MARCH1,MAPK3,GSDMB,PRKCQ,MYNN,C19orf80,MAPK8,MAP2K5,RNF17,PRL,BTNL2,CTNNBL1,RIOK2,TGFBR3,TCF1,HNF1B,TGFB2,THRA,TIE1,TBXAS1,TCF21,MLX,TCN2,TERT,TF,NR2F1,NR2F2,TFF1,TFR2,TFRC,TP53BP1,TP73,TRAF1,C2,TRPC3,TRH,TRHR,TTN,TTR,LOC727993,TNFRSF1A,TNFAIP1,TNNT3,TNNC1,TRAPPC10,TLR5,TIMP4,TKT,STAT5A,STAT5B,AURKA,STRN,SULT1A1,BTF3P11,TBCD,TBX2,TAF4,KLF5,TBX15,STAT3,SRM,BRCA2,SST,SSTR3,ND4,trnK,COX1,ND6,trnQ,SLC12A2,SLC10A2,SLC11A1,SLC14A1,SLC15A1,SLC15A2,BMPR1A,SLC18A2,BRCA1,SORL1,SP4,UAP1,SMARCA1,SMARCA2,SMARCA4,BOLL,SNAP25,SNRNP70,SNRPN,SIM1,ST3GAL4,SLC1A4,SLC1A6,SLC1A7,SLC2A3,SLC2A5,SLC3A1,SLC7A2,WNK2,SLC9A2,SLC5A1,SMTN,UBE2Z,SLC6A6,SLC6A7,SLC6A9,SLC6A11,SLC6A12,BMP6,NSD1,LMBR1,NFKBIZ,ARHGAP9,HIF3A,SFTPB,BLVRA,SGCD,HMGB3P18,DPEP3,SFRP2,ABCG5,PCIF1,PRDM16,SRSF2,SFRS3,SRSF3,SFRS5,XYLT1,XYLT2,AGXT2L1,RFX7,C12orf43,CSMD1,SHH,CFB,SORT1,S100A4,SAA@,SCN10A,BGLAP,SALL1,SBF1,MSMO1,RYR1,RGS4,RGS12,RHO,RLN2,RNASE3,BRD2,GAS5,ROCK1,RORA,SEMA3F,MCCC2,SMOC2,BLM,SLC39A8,ELTD1,SDF2,BICD1,CCL16,CCL17,CCL23,CCL25,CXCL5,XCL1,SRR,BCAN,SDC4,CCL8,OPTC,GATA4,HIBCH,VPS33B,GATM,ERAL1,CLDN17,GBA,FGF21,GCG,GCGR,GAS6,MMACHC,GDNF,GFRA1,HAVCR1,OPLAH,CHIC2,ITGB1BP2,OSTF1,MYEOV,GDF2,GJA1,GPR160,GHRH,GHRHR,RND1,GJA8,KCNMB3L,EIF2AK1,HSPB7,CRCP,ADAMDEC1,GCLM,GLDC,TOX3,BIN1,GLP1R,GLRX,GNAI2,SGSM3,GNG5,GNRH1,GNRHR,AQP11,POC1B,GP1BB,GPLD1,SLCO3A1,ACAA1,HABP2,HAS2,HAS3,TMOD4,ZDHHC1,GUCY1B3,TRPM5,ICOS,NME7,GYPA,OSGIN1,SERTAD1,PDZRN4,DMGDH,HLADPA1,HGFAC,NRG1,ANXA5,ERVW1,HBG1,HCRTR1,HTT,SLC25A42,CCDC141,GPER,COX18,XKR6,GPR37,MLNR,PRR10,PRLHR,C12orf51,UTS2R,GRK5,GRK6,SCG3,MYLIP,LGALS13,UHRF1,GSN,GPX4,GRB14,GRIA1,ANPEP,HMGB1,HMGA1,HLADRA,HLADRB5,HOXA@,HOXC13,HMOX2,HPCAL1,MMAB,HES1,HTR1B,HTR2B,HTR2C,HSPA2,HSPA4,HSPA8,HSPB2,HSPD1,HSPG2,NDST1,IKBKB,ACADS,IL1RAP,RBPJ,3.81.2,SLCO4C1,BMP8A,ACSM2B,IGF2R,IGFBP1,IGFBP3,TNC,ICAM4,ADAMTSL5,RXFP4,C1orf110,LOC347376,IFNB3,IDE,IDH2,AQP8,OR2T3,APOC2,SLC25A5P2,IL12RB1,IL12RB2,ILF3,IL12A,MRPS35P3,IL13RA2,ACADSB,AQP3,IL2RB,IL2,IL9R,IL9,CXCR2,IL7R,ITGAV,ITGB1,ITGB2,ITGB6,ITGB8,ITIH3,ITPA,ITPK1,IVD,ITGA4,JUN,K12T,GSTK1,IMPA2,INPP5B,INSIG1,IREB2,AQP9,KIR2DS4,KIR2DS5,KIF5A,ACAT1,KIR2DL1,KIR2DL2,KIR2DL3,KIR2DL4,KLRB1,KLK2,KIR3DL2,KIR3DS1,KCNN2,KCNJ14,KCNB1,SFT2D2,KCNJ4,KCNJ6,LIPE,LIPA,RHOH,LHCGR,LIG1,ABLIM1,ILDR2,FAM99A,C12orf75,C2CD4B,HES5,CD164L2,LOC388630,C21orf34,LINC00478,RHOC,ACT,HNRNPA1P4,ACAT2,OR52E4,OR4N3P,SKOR1,LAMA3,KRT18P42,KRT18P16,LBP,LCAT,LCN2,LDHA,LTF,ERVFRD1,LSS,LTA4H,LRPAP1,LSP1,MIR196A2,MIR214,MIR217,MIR224,MIR27A,MIR98,M6PR,OR2T2,OR4C45,LRP1,LRP2,LOXL2,SAMD12,PTPLAD2,LMAN1,FLJ42102,LMNA,C14orf181,LMX1A,LMX1B,MAS1,MAT1A,MAX,MC3R,MAOA,SMAD6,MIRLET7C,MIR122,MIR137,MIR143,MLLT3,MGST3,MFAP2,MGAT5,MEIS1,MELAS,MCC,CD46,MEF2D,ARVCF,NEDD4,NELL1,MYBPH,NFATC1,NFIA,NFKB2,NKTR,NNAT,NMBR,NNMT,MYLK,MYO5A,MYO6,MYO7B,MYOD1,ATF1,PPP1R12B,ATF3,NCAM1,NCF2,NDUFAB1,NDUFB3,MUT,MVK,MYB,TRNI,ATP6,COX2,CD200,ABCC1,LRRC52,FLJ16124,C8orf

	85,MIR335,MSR1,MMP14,NPHP1,NOV,NOVA2,NOTCH1,NUMA1,DDR2,NTSR1,NRAP,MIR378,NVL,OPRM1,OTC,OPA1,PAFAH1B1,PLA2G3,PAFAH1B2,DUOX2,NOX4,P200,P2RY1,FIS1,PAM,IL21R,PAX2,PAX5,F11R,HEBP1,PBX1,PDE11A,EPHA4,EPHB4,EPHB6,EMR1,AIM1,CELA1,ELANE,SERPINB1,Grhl1,AGXT,Polg,HBEGF,AHCY,RLS,EFNB1,EFNB2,EFNB3,ERBB3,EPO,LVRN,CMYA5,AKT1,ERCC6,ERVK2,MECOM,EVX1,EXT2,EYA2,FABP3,PTK2B,ALDH1B1,F2RL1,ALAD,F9,F10,DCC,TDRD5,DIO1,DIO3,AFP,ZNF596,GLIS3,Ly6c1,RHOV,NLRP6,CRPP1,MARCH10,JAG1,DRP2,DRD3,EBF1,DNASE1,DYNC1H1,TRDMT1,DOCK1,DPAGT1,DPP4,DPP6,DPT,AGRP,CYP3A,CYP2C18,CYP3A7,CYP27B1,DACH1,DGKB,CCDC63,IL28RA,Itgam,TMPRSS6,DHX15,DES,TIMM8A,OLIG3,ZFP30,COBLL1,PLEKHA6,MLXIP,MON1B,STOX1,FBLN2,FGF9,FGF10,FGFR1,FGFR3,SPATA13,FCGR2A,FCGR2B,KIF6,GDPD4,FBN2,ATOH7,SDK1,THSD7A,FDFT1,FBXL13,GPR97,ALDH9A1,FDX1,FES,ARSG,PLA2R1,FOXF1,SHANK2,FOXC1,WDR37,FKBP5,MRAS,FKBP1B,MYO16,KDM1A,MYT1L,TCF25,DIP2C,SV2C,POFUT2,CAMTA1,FLT3,NUP210,FLT4,PACS2,CUL9,CAMTA2,ZC3H3,ZBTB43,ABCA4,ALOX5,ALK,ALOX15,Nppa,SPESP1,Ret,ALPL,FSHR,FPR1,LPHN3,SGK3,BHMT2,IL17RA,FN1,UNC84A,MED13L,DICER1,SMG6,FMOD,FMR1,FOLR1,MACF1,FOLR2,FOS,SLC16A8,SEZ6L,ZFPM2,SLC7A8,GPR161,DNM3,ANKRD17,ERC2,TANC2,LDLRAP1,TIPRL,SPATS2L,GLCE,SS18L1,MCOLN2,TCERG1L,IL4I1,OLFML2B,FUT4,FUT7,FYN,CERS6,MSRB3,G6PD,Gdnf,Gfra1,NPC1,TBC1D22A,RASGRP3,RAD54B,QPCT,GCA,GALC,TPSG1,TXN2,POU2F3,USP49,PRKD2,BRP44,BTBD9,GALNT13,SORCS1,OSBPL9,OSBPL10,CIDEA,ZNF618,SLC5A11,KIR3DL3,KLK8,AKAP10,EGLN3,PADI2,PMF1,PRKCDBP,NISCH,ADCY6,SLCO2B1,ADCYAP1,Agtr1a,TADA1L,DCD,RLN3,ACOT7,ADC,CHRNA3,Nr2f2,ACSM1,IL22RA2,GRIN3A,GPR83,ADCY3,PSIP1,ADAMTS7,LDB3,ZWINT,SLC7A9,40057,CPLX2,FRS2,ALDH1L1,RUVBL2,CYP46A1,TSPAN9,USP20,OS9,LILRB5,SDS,SLC27A4,IL24,TOPBP1,DIDO1,ADAMTS8,LOC100132798,LOC100134413,LOC100128751,LOC100128922,LOC100131402,LOC100131938,CDH4,LOC100287218,MIR1265,MIR1290,HOTTIP,NPPA-AS1,MIR4301,MIR2861,DNM1L,ABCC9,ERVK9,GPA33,AP3S2,RAMP1,RGS19,NUTF2,CDK6,SCAMP2,EDIL3,SGK2,FAM13A,CDH17,ARL4C,CDH15,CDH18,MAEA,PIBF1,ADARB2,CEBPD,IPO7,PITRM1,IKZF1,COX4NB,B3GNT3,TLR6,ADARB1,IFI30,ACAA2,VAV3,ARL6IP5,SLC19A2,CXCL13,CCT2,SORBS1,TXNRD2,PDLIM5,ARID3B,TXNIP,POSTN,RGS14,CAMKK2,CES1,C6orf10,CHL1,TRAF3IP2,JARID1B,HBS1L,Cd14,CCR3,FSD2,NTAN1,CDYL2,OR14L1P,COL1A1,Ccr2,CNP,CNR1,C1orf125,GYLTL1B,LRRK2,OR10AD1,TPH2,Bmpr2,RXFP2,TDRD9,KLHDC1,JDP2,SLC24A4,CR1,SGCZ,CRHBP,CRHR1,GAB3,MTPN,ASB10,CPN1,CPN2,IRAK1BP1,TRAM1L1,UGT3A1,KLF14,ADORA2B,Cybb,C2orf65,COL13A1,COX5B,LRRC15,ADAD1,COL9A2,GOLT1A,CPT1A,MUC17,MYO3B,ZBTB46,CRY1,TRPM6,SIRPA,STK35,CRYBB3,PARP1,CRYGFP,CSE,SYT9,APCDD1,ZNF524,SIX5,CST2,CST3,NKX25,PAR1,PRICKLE1,OVOS2,BCDIN3D,WDR66,Hmox1,PNLDC1,CYP2A6,CXADR,KLB,DAB2IP,SLC36A2,CYB561,PYHIN1,CTNS,ZSWIM2,CTSH,CTSL1,FAM19A4,CTBP1,MOBKL2C

Annexed Table 3. Proteins involved in Hypertension that are related to ISG15 and its role in vascular remodelling and/or endothelial dysfunction. A protein-protein interaction network of proteins was created by introducing ISG15 into the list of proteins obtained from "Phenopedia" by STRING/Cytoscape. 30 network proteins are involved in vascular remodelling and/or endothelial dysfunction associated with hypertension.

ISG15_NETWORK	ENDOTHELIAL DYSFUNCTION	VASCULAR REMODELLING
CCL2	PMID: 25712370; PMID: 27577581	PMID: 25712370
CCL5	PMID: 30643968; PMID: 26873938	
CCL8	PMID: 23033370	
CTNNB1	PMID: 28964937	PMID: 27322082
CXCL8	PMID: 24979502	PMID: 27539364
CYP1B1	PMID: 26573711	PMID: 26573711
FOXP3	PMID: 28584011	PMID: 29688896
HLA-B	PMID: 20335527	
HLA-G		PMID: 24998350
IFIH1	PMID: 27130701	
IFNG	PMID: 31321561	PMID: 25217635
IL10	PMID: 21817097	PMID: 18818668
IL1B	PMID: 31186952	PMID: 31186952
IL6	PMID: 27167462	
IL6R	PMID: 23428306	PMID: 23428306
IRF5	PMID: 28818665; PMID: 27050551	
MAPK3	PMID: 30853343	
NEDD4	PMID: 28212825	
NEDD4L		PMID: 28212825
NFKB1	PMID: 17324119	PMID: 19837080
RNF213	PMID: 29718794	
SOCS1	PMID: 27889763	
SOCS3	PMID: 27106041	PMID: 27459385
STAT3	PMID: 27889763	PMID: 25784694
TLR2	PMID: 25029271	
TLR4	PMID: 25712370	PMID: 25712370
TLR7	PMID: 22848646	
TLR8	PMID: 22848646	
TNF	PMID: 19118493	PMID: 25015967
TNFAIP3	PMID: 25648164	PMID: 25217635

Annexed Table 4. Protein abundance changes in aorta from WT and ISG15$^{-/-}$ mice in response to Ang II. Results are reported as Zq values (log2-fold changes expressed in units of standard deviation) for each individual biological replicate and for the integration data in the comparative of ISG15$^{-/-}$ and WT samples considering the effect of Ang II and normalized with respect to the untreated samples.

-5 0 5 Zq

Protein name	WT				WT AngII				ISG15$^{-/-}$				ISG15$^{-/-}$ AngII				Zq	FDR
SAA1	-3	-1	3	1	-2	0	-1	4	-1	-1	-1	-1	19	2	-2	0	10	0
SAA2	-2		2		0		-1		0		-1		11		-2		7,5	2,4E-11
ABCB9	3	-4	-5	3	3	-1	-1	1	2	-1	-1	3	9	0	12	-1	6,8	2,5E-09
IGHG3	-10		5		-6		-2		-6		-6		-4		-4		6,7	3,0E-09
FIBA	1	-7	-1	6	2	-1	-1	2	1	-4	-5	4	9	1	11	-1	6,7	2,9E-09
Q3TGR2	2	-5	-2	4	2	-2	-1	2	0	-2	-1	4	7	1	9	-2	6,2	9,6E-08
TXNL1	-1	0	1	0	0	0	1	1	-2	1	0	0	-1	12	0	2	6,0	2,6E-07
MYL3	2		-3		0		-3		-5		-1		-2		-1		5,4	6,0E-06
KNG1		-4		3		1		2		5		-1		11		1	5,4	5,9E-06
FRIL1	-2	0	2	0	-1	4	2	1	-2	-1	-1	-2	3	-1	11	2	5,3	9,1E-06
DC1L1		-3		2		-4		0		0		0		1		0	5,2	1,3E-05
ABCG2		-2		1		-1		1		-3		-3		1		-2	4,4	6,8E-04
Q3TPL8	1	-4	-1	3	-2	-2	-1	0	-2	-1	-2	-1	-1	1	1	-2	4,3	1,1E-03
MICA2	0	1	0	-1	1	-1	0	0	-1	-1	-2	-1	2	1	0	0	3,8	7,9E-03
HYEP	3		-4		-2		-1		-2		-1		-1		0		3,6	1,2E-02
ANK3		-6		4		-3		0		-2		-2		0		-2	3,6	1,4E-02
UCP1	-5	0	7	0	-3	1	-2	1	-5	1	-4	0	-6	1	-1	4	3,5	1,5E-02
HYOU1	0		0		-1		0		-2		-2		-1		1		3,5	1,6E-02
RAB21		1		0		-1		0		0		-3		0		0	3,5	1,8E-02
DPP2	-1		1		3		0		0		-1		3		3		3,4	1,9E-02
PX11B		-1		1		0		0		-1		-1		2		0	3,3	2,5E-02
CP1B1	0		0		1		0		-1		-1		2		1		3,3	2,5E-02
ANK2		-5		4		-3		0		-2		-1		0		-1	3,2	3,2E-02
QSOX1	2	-9	-2	5	-1	-3	1	0	1	0	-1	-2	2	2	1	-2	3,2	3,3E-02
F8VPK0		0		0		-1		0		-3		-1		-1		0	3,1	5,3E-02
Q549A5	-2	0	1	1	2	2	2	2	1	-1	1	-1	6	1	9	0	2,9	7,9E-02
RACK1	0	1	1	-1	-2	1	4	1	0	0	0	-2	4	2	3	3	2,9	8,1E-02
A8DUK0	-21	-15	8	11	-8	-3	-2	4	-8	-5	-7	-3	-6	1	-10	-2	2,9	8,9E-02
|TXTP	-6	1	4	-1	1	-1	2	-2	-3	-1	-4	0	1	0	0	1	2,9	9,3E-02
SUN1	1	2	-1	-3	0	0	0	0	-1	-2	-1	0	0	1	0	0	2,7	1,6E-01
DHRS1		0		0		-1		-2		1		-2		0		0	2,7	1,6E-01
Q3TI84		2		-2		0		-1		0		-1		0		0	2,6	1,7E-01
SAE2		1		-1		-1		-1		-1		0		0		0	2,6	1,7E-01
PTMA		0		0		0		-1		0		-1		0		0	2,6	1,7E-01
RAB23		0		0		0		0		-2		1		1		0	2,6	1,9E-01
C1TC	0	1	0	-1	-1	-1	-1	0	0	-2	-1	1	-1	0	0	0	2,6	1,9E-01
LGALS	0		0		-1		-1		-1		-2		0		-1		2,6	1,9E-01
PYR1		1		-2		-1		1		-1		-1		1		1	2,5	2,0E-01
Q3UEM7	1	-9	-2	7	1	-2	-1	2	0	-5	0	4	5	1	6	-2	2,5	2,1E-01
CAPG	1		-1		2		0		-2		0		1		2		2,5	2,1E-01
VPS4A	0	0	0	0	-1	0	-1	0	-1	0	1	2	4	0	-1	0	2,5	2,1E-01

FBLN5	3		-4		0		-5		-1		-1		-2		-1		2,5	2,1E-01
HPT	1		-1		1		0		2		2		7		1		2,5	2,2E-01
PUR8		1		-1		-1		-1		-1		-2		-1		-1	2,4	2,4E-01
DAB2	0		0		0		0		-1		-1		1		1		2,4	2,4E-01
SRSF1		-2		2		-1		-1		0		1		2		0	2,4	2,4E-01
LRC40		-1		1		-1		0		0		-2		0		0	2,4	2,5E-01
FXL20		0		0		-1		0		-1		0		0		0	2,4	2,7E-01
GARS	1	1	-1	-1	0	0	0	1	-1	0	-1	-1	0	1	0	1	2,3	2,8E-01
TSP1	-1	-8	1	6	1	-1	2	2	-1	-2	-1	1	1	4	2	1	2,3	2,9E-01
CYC2		-1		1		1		-1		1		-1		2		0	2,3	3,1E-01
NHRF1	0		0		0		0		-1		-1		0		0		2,2	3,3E-01
TRIPC		1		-1		1		1		-2		0		1		1	2,2	3,7E-01
CYH1		0		0		-1		-1		1		-2		0		0	2,2	3,7E-01
RS4X	-1	1	1	-1	1	1	2	1	-2	-1	-2	-1	0	1	1	2	2,1	4,1E-01
RSMB		0		0		0		0		-1		0		1		1	2,1	4,2E-01
VWA8	-2		2		-1		1		-2		-1		-1		0		2,1	4,3E-01
ITPR2		-1		1		-1		0		-1		-1		0		-1	2,1	4,4E-01
GHC1	1		-1		0		0		-1		-2		0		0		2,1	4,5E-01
HNRPD		1		-1		0		1		0		-2		0		1	2,0	4,6E-01
TBCEL		0		0		0		0		0		-1		1		0	2,0	4,7E-01
Q544Z7	0	0	1	0	-1	0	0	0	0	-1	0	-2	1	0	1	1	2,0	4,7E-01
Q497N1		1		-1		1		0		-1		0		1		2	2,0	4,7E-01
DCXR		1		-1		-3		-1		0		-1		0		-2	2,0	4,7E-01
G3PT	-2	0	2	0	-1	-1	2	1	-1	-1	-2	-1	1	0	1	0	2,0	4,8E-01
Q3TVK3	-2		2		1		1		1		-1		0		-1		-2,0	4,8E-01
Q4FK49		1		-1		3		1		0		0		0		3	-2,0	4,6E-01
3TJ94	1	0	-1	0	1	1	0	1	0	0	6	-1	2	0	1	0	-2,1	4,5E-01
A8DUV3	-4	-9	4	6	-5	-2	-2	3	-1	-4	2	-1	-4	0	-6	-2	-2,1	4,5E-01
COPB2		-1		1		1		2		1		2		1		2	-2,1	4,5E-01
LPP		-1		1		1		0		2		2		1		1	-2,1	4,3E-01
A0A0R4J083	-3	1	2	-1	-1	2	1	0	-1	1	0	1	-3	0	-1	2	-2,1	4,3E-01
TRYP	0	-7	0	6	-2	0	-2	-2	1	1	3	7	-2	1	-1	-1	-2,1	3,9E-01
Q8BIX4	-1	1	1	-1	-1	-2	1	-2	1	1	1	1	0	-1	-2	-4	-2,2	3,9E-01
STOM		0		0		0		1		0		2		1		0	-2,2	3,7E-01
ELMO2	-2	-3	2	3	0	1	-1	0	2	1	1		1	1	0	0	-2,2	3,4E-01
H10_	1	2	-1	-2	-1	0	-2	-3	1	1	0	1	-2	-4	-1	-2	-2,2	3,4E-01
IGSF8		2		-2		0		-1		1		2		0		0	-2,3	3,2E-01
ACACA	-6	-1	4	1	-1	7	1	4	-3	-2	-3	0	-1	1	-2	3	-2,3	3,2E-01
THIO	0		0		0		0		1		0		-1		-1		-2,3	2,8E-01
ACADL	-3	-1	1	1	-2	3	2	2	0	-1	-1	0	-2	0	1	2	-2,3	2,8E-01
ECM29	0		0		1		1		2		1		1		1		-2,3	2,7E-01
NRIP1	1		-1		0		-1		2		4		1		1		-2,4	2,7E-01
FABPH	1		-1		-1		0		1		0		-2		-2		-2,4	2,4E-01
KNG1	-2	-7	2	6	-1	1	0	4	0	-1	5	0	0	-3	2	1	-2,4	2,5E-01
SNX6	1		-1		-3		-2		2		7		-1		0		-2,4	2,4E-01
ENAH	1		-1		0		0		1		1		-1		-2		-2,5	2,2E-01

PUR9		-2		2		-2		1		1		2		-1		0	-2,5	2,0E-01
|TTHY		-6		5		0		1		-1		-1		-3		-1	-2,5	2,0E-01
Q3UAI3		0		0		3		1		0		0		0		1	-2,5	2,0E-01
PNPT1		-1		1		0		-1		2		1		1		0	-2,5	2,0E-01
AN33B		0		0		1		-1		1		1		-1		0	-2,5	2,0E-01
H14		0		-1		0		-2		1		1		-3		-1	-2,6	1,9E-01
K1671		-2		2		0		1		1		1		1		0	-2,6	1,9E-01
CTL2	0	0	0	0	-1	0	1	0	2	0	5	0	1	-1	1	0	-2,6	1,9E-01
CX6B1	1	0	-1	0	0	2	1	1	1	0	0	0	-1	-1	0	1	-2,6	1,7E-01
Q3UC67		3		-3		5		2		-1		-1		0		3	-2,6	1,7E-01
FABP4	-5	3	4	-3	0	5	5	2	-3	1	-2	1	-2	0	1	5	-2,7	1,5E-01
GFAP	-1		1		-3		-1		0		-5		-7		-5		-2,7	1,3E-01
2A5E	1		-1		0		0		1		2		0		0		-2,8	1,1E-01
XPO1	-1	-6	1	4	0	-2	-1	-1	1	7	1	8	1	3	-1	-1	-2,9	9,2E-02
A0A075B5T2_		-1		1		1		2		-1		0		-1		0	-2,9	9,3E-02
MAOX	-1	2	1	-2	0	6	-1	1	-1	-1	-1	0	-1	-1	-1	1	-2,9	8,9E-02
HNRPC		1		-1		0		-1		3		1		-1		0	-3,0	6,8E-02
FETUB		-3		3		1		3		-1		-1		-2		0	-3,2	3,4E-02
NOP2	-1		1		0		4		0		2		0		2		-3,3	2,9E-02
HTRA1	3	-1	-3	1	12	8	5	6	3	2	2	-2	7	10	8	2	-3,3	2,7E-02
CO4A1		1		0		0		-1		1		3		0		0	-3,3	2,5E-02
Q545Q2		-6		4		-2		-2		3		2		-1		-1	-3,4	2,1E-02
CE290	0		0		-1		0		2		7		0		2		-3,4	2,0E-02
H15		0		0		0		2		1		1		-1		0	-3,5	1,8E-02
Q546G4	-1	-15	1	11	-4	1	-2	4	1	-5	6	-3	-4	-8	1	1	-3,5	1,6E-02
B2RXT3	-4	-1	3	1	-1	3	1	0	-1	1	-1	0	-2	-1	-1	1	-3,5	1,6E-02
CAH3	-2	0	4	0	0	8	5	5	-3	-3	-2	1	-2	-1	2	6	-3,6	1,4E-02
FETUA	1		-1		1		1		1		3		0		1		-3,7	8,6E-03
OX2G		0		0		0		-1		1		2		-1		-1	-3,7	8,6E-03
Q4FJR0		-1		1		0		0		0		1		-2		-1	-3,8	7,9E-03
SNPC4	0		0		-3		1		4		-2		-2		-4		-3,8	7,4E-03
TM201	-1		1		-1		0		4		6		1		2		-3,9	4,3E-03
PRAF3	1		-1		-1		1		2		6		1		0		-4,0	2,7E-03
SOAT1		-1		1		-2		-1		0		3		-1		-3	-4,3	1,2E-03
Q3ULU3		0		0		2		1		1		4		0		1	-4,8	9,2E-05
Q3TQW1		2		-2		6		1		-1		1		0		1	-5,1	3,0E-05
HRG		-2		2		2		4		1		-1		-1		0	-5,1	2,6E-05
PLCA	-1		1		4		-1		0		3		0		0		-5,1	2,3E-05
NCLN		-1		1		1		0		0		1		-3		-1	-6,1	1,1E-07
B2RRY4	-1		1		-4		-2		4		11		-1		0		-6,3	3,9E-08
Q8BZI2	0		0		0		4		3		4		0		1		-7,8	3,4E-12

Annexed Table 5. Functional category abundance changes in aorta from WT and ISG15$^{-/-}$ mice in response to Ang II. Results are reported as Zc values (log2-fold changes expressed in units of standard deviation) for the integration data in the comparative of ISG15$^{-/-}$ and WT samples considering the effect of Ang II, normalized with respect to the untreated samples. N prot indicates the number of quantified proteins for each category.

-5 0 5 Zq

Functional category name (GO terms)	Zc	FDR	N prot
GO:0002481 antigen processing and presentation of exogenous protein antigen via MHC class Ib	7,162	3E-10	1
GO:0002489 antigen processing and presentation of endogenous peptide antigen via MHC class Ib via ER pathway	7,162	2E-10	1
GO:0002591 positive regulation of antigen processing and presentation of peptide antigen via MHC class I	7,162	1E-10	1
GO:0000103 sulfate assimilation	6,241	5E-08	2
GO:0002024 diet induced thermogenesis	3,773	0,01	1
GO:0002930 trabecular meshwork development	3,489	0,021	1
GO:0003417 growth plate cartilage development	3,151	0,064	2
GO:0001774 microglial cell activation	3,133	0,0623	1
GO:0000105 histidine biosynthetic process	2,723	0,1863	1
GO:0000413 protein peptidyl-prolyl isomerization	2,592	0,2576	4
GO:0001947 heart looping	2,549	0,2122	2
GO:0000395 mRNA 5'-splice site recognition	2,545	0,2052	1
GO:0006167 AMP biosynthetic process	2,541	0,1989	1
GO:0002581 negative regulation of antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	2,478	0,2197	1
GO:0002605 negative regulation of dendritic cell antigen processing and presentation	2,478	0,2116	1
GO:0003096 renal sodium ion transport	2,341	0,2767	1
GO:0006166 purine ribonucleoside salvage	2,34	0,2686	3
GO:0002027 regulation of heart rate	2,337	0,2622	6
GO:0006338 chromatin remodeling	2,285	0,2919	5
GO:0006048 UDP-N-acetylglucosamine biosynthetic process	2,238	0,2948	2
GO:0006304 DNA modification	2,147	0,35213	2
GO:0005997 xylulose metabolic process	2,125	0,36242	1
GO:0001881 receptor recycling	2,102	0,36542	3
GO:0001558 regulation of cell growth	2,052	0,3773	5
GO:0001833 inner cell mass cell proliferation	1,976	0,42461	1
GO:0001834 trophectodermal cell proliferation	1,976	0,41612	1
GO:0006168 adenine salvage	1,953	0,43006	1
GO:0002329 pre-B cell differentiation	1,852	0,51245	1
GO:0001845 phagolysosome assembly	1,722	0,62305	1
GO:0002175 protein localization to paranode region of axon	1,669	0,67432	1
GO:0006336 DNA replication-independent nucleosome assembly	1,648	0,68165	2
GO:0002031 G-protein coupled receptor internalization	1,621	0,67682	2
GO:0000050 urea cycle	1,592	0,69771	1
GO:0002566 somatic diversification of immune receptors via somatic mutation	1,586	0,69622	1
GO:0000723 telomere maintenance	1,567	0,71209	4

GO:0000266 mitochondrial fission	1,553	0,72299	4
GO:0003374 dynamin polymerization involved in mitochondrial fission	1,553	0,71309	4
GO:0003300 cardiac muscle hypertrophy	1,542	0,70853	1
GO:0003104 positive regulation of glomerular filtration	1,528	0,70997	1
GO:0006221 pyrimidine nucleotide biosynthetic process	1,508	0,72877	3
GO:0000281 mitotic cytokinesis	1,495	0,72884	7
GO:0006012 galactose metabolic process	1,489	0,72757	2
GO:0006342 chromatin silencing	1,48	0,7318	5
GO:0000398 mRNA splicing	1,476	0,72794	17
GO:0006164 purine nucleotide biosynthetic process	1,476	0,71947	6
GO:0003254 regulation of membrane depolarization	1,47	0,71956	4
GO:0006042 glucosamine biosynthetic process	1,469	0,71217	1
GO:0006047 UDP-N-acetylglucosamine metabolic process	1,469	0,70398	1
GO:0002286 T cell activation involved in immune response	1,46	0,70867	1
GO:0001764 neuron migration	1,445	0,70492	11
GO:0002040 sprouting angiogenesis	1,442	0,70114	3
GO:0001921 positive regulation of receptor recycling	1,433	0,70546	2
GO:0006002 fructose 6-phosphate metabolic process	1,411	0,72786	5
GO:0000154 rRNA modification	1,395	0,73329	1
GO:0001818 negative regulation of cytokine production	1,367	0,75601	1
GO:0003197 endocardial cushion development	1,363	0,75404	2
GO:0006265 DNA topological change	1,361	0,75005	2
GO:0000187 activation of MAPK activity	1,338	0,76557	6
GO:0006091 generation of precursor metabolites and energy	1,321	0,78161	2
GO:0000920 cell separation after cytokinesis	1,307	0,76545	2
GO:0000226 microtubule cytoskeleton organization	1,297	0,75697	11
GO:0001824 blastocyst development	1,292	0,75704	3
GO:0002639 positive regulation of immunoglobulin production	1,284	0,76158	1
GO:0002925 positive regulation of humoral immune response mediated by circulating immunoglobulin	1,284	0,7549	1
GO:0002092 positive regulation of receptor internalization	1,278	0,75661	2
GO:0002317 plasma cell differentiation	1,254	0,76792	2
GO:0002544 chronic inflammatory response	1,23	0,78779	2
GO:0006006 glucose metabolic process	1,227	0,78503	18
GO:0001662 behavioral fear response	1,214	0,79527	3
GO:0001944 vasculature development	1,205	0,80198	1
GO:0001961 positive regulation of cytokine-mediated signaling pathway	1,192	0,81329	2
GO:0000463 maturation of LSU-rRNA from tricistronic rRNA transcript (SSU-rRNA	1,178	0,82533	1
GO:0000902 cell morphogenesis	1,173	0,81891	5
GO:0005981 regulation of glycogen catabolic process	1,161	0,82854	2
GO:0000082 G1/S transition of mitotic cell cycle	1,151	0,82962	6
GO:0006260 DNA replication	1,145	0,82522	5
GO:0002191 cap-dependent translational initiation	1,142	0,82288	1
GO:0003151 outflow tract morphogenesis	1,14	0,82037	4
GO:0000387 spliceosomal snRNP assembly	1,137	0,81168	4
GO:0003009 skeletal muscle contraction	1,136	0,80695	4

GO:0001708 cell fate specification	1,135	0,80259	1
GO:0002521 leukocyte differentiation	1,117	0,81418	1
GO:0002026 regulation of the force of heart contraction	1,085	0,82292	9
GO:0002502 peptide antigen assembly with MHC class I protein complex	1,074	0,82547	1
GO:0001998 angiotensin mediated vasoconstriction involved in regulation of systemic arterial blood pressure	1,055	0,82349	1
GO:0002033 vasodilation by angiotensin involved in regulation of systemic arterial blood pressure	1,055	0,81815	1
GO:0001732 formation of cytoplasmic translation initiation complex	1,013	0,8247	3
GO:0000492 box C/D snoRNP assembly	1,002	0,82274	1
GO:0002523 leukocyte migration involved in inflammatory response	0,99	0,83313	1
GO:0002021 response to dietary excess	0,967	0,85716	1
GO:0003012 muscle system process	0,967	0,84791	2
GO:0000059 protein import into nucleus	0,964	0,84603	2
GO:0002181 cytoplasmic translation	0,936	0,8617	11
GO:0006281 DNA repair	0,934	0,85986	20
GO:0000904 cell morphogenesis involved in differentiation	0,906	0,86684	3
GO:0005975 carbohydrate metabolic process	0,899	0,86071	43
GO:0001915 negative regulation of T cell mediated cytotoxicity	0,894	0,84444	1
GO:0001946 lymphangiogenesis	0,894	0,84002	1
GO:0002011 morphogenesis of an epithelial sheet	0,89	0,84017	2
GO:0006123 mitochondrial electron transport	0,886	0,84085	5
GO:0002029 desensitization of G-protein coupled receptor protein signaling pathway	0,881	0,84274	1
GO:0006147 guanine catabolic process	0,871	0,84115	1
GO:0000245 spliceosomal complex assembly	0,856	0,83454	3
GO:0002674 negative regulation of acute inflammatory response	0,835	0,85028	1
GO:0002675 positive regulation of acute inflammatory response	0,831	0,85191	2
GO:0006175 dATP biosynthetic process	0,825	0,85434	1
GO:0000045 autophagosome assembly	0,821	0,84727	2
GO:0000209 protein polyubiquitination	0,814	0,85045	3
GO:0002828 regulation of type 2 immune response	0,804	0,8502	1
GO:0003084 positive regulation of systemic arterial blood pressure	0,798	0,854	1
GO:0006225 UDP biosynthetic process	0,77	0,87085	1
GO:0006240 dCDP biosynthetic process	0,77	0,86689	1
GO:0001889 liver development	0,763	0,87089	14
GO:0001780 neutrophil homeostasis	0,758	0,86456	3
GO:0002260 lymphocyte homeostasis	0,758	0,86092	1
GO:0001829 trophectodermal cell differentiation	0,756	0,85987	1
GO:0002244 hematopoietic progenitor cell differentiation	0,743	0,86715	6
GO:0000380 alternative mRNA splicing	0,709	0,87977	5
GO:0003281 ventricular septum development	0,708	0,87653	5
GO:0006227 dUDP biosynthetic process	0,705	0,86918	2
GO:0000183 chromatin silencing at rDNA	0,694	0,87427	4
GO:0006335 DNA replication-dependent nucleosome assembly	0,694	0,87066	4
GO:0001836 release of cytochrome c from mitochondria	0,693	0,86777	3
GO:0000060 protein import into nucleus	0,688	0,86963	6

GO:0000278 mitotic cell cycle	0,684	0,87141	2
GO:0001953 negative regulation of cell-matrix adhesion	0,677	0,87496	3
GO:0006207 'de novo' pyrimidine nucleobase biosynthetic process	0,674	0,86811	3
GO:0000244 spliceosomal tri-snRNP complex assembly	0,664	0,87505	2
GO:0001701 in utero embryonic development	0,661	0,8754	30
GO:0000165 MAPK cascade	0,652	0,86764	6
GO:0006096 glycolytic process	0,649	0,86812	21
GO:0001843 neural tube closure	0,647	0,86702	12
GO:0006284 base-excision repair	0,634	0,87396	3
GO:0003420 regulation of growth plate cartilage chondrocyte proliferation	0,619	0,88058	2
GO:0006325 chromatin organization	0,599	0,89502	2
GO:0001649 osteoblast differentiation	0,597	0,88097	28
GO:0000038 very long-chain fatty acid metabolic process	0,592	0,87967	1
GO:0006086 acetyl-CoA biosynthetic process from pyruvate	0,59	0,87893	4
GO:0006121 mitochondrial electron transport	0,588	0,87785	2
GO:0003081 regulation of systemic arterial blood pressure by renin-angiotensin	0,575	0,88111	2
GO:0001937 negative regulation of endothelial cell proliferation	0,572	0,87813	5
GO:0001666 response to hypoxia	0,559	0,88911	29
GO:0001867 complement activation	0,557	0,88778	3
GO:0002931 response to ischemia	0,552	0,89032	8
GO:0006337 nucleosome disassembly	0,543	0,89578	2
GO:0000212 meiotic spindle organization	0,54	0,89573	1
GO:0001768 establishment of T cell polarity	0,54	0,89259	1
GO:0000288 nuclear-transcribed mRNA catabolic process	0,535	0,89555	2
GO:0000375 RNA splicing	0,529	0,89546	1
GO:0000042 protein targeting to Golgi	0,52	0,89887	2
GO:0003148 outflow tract septum morphogenesis	0,516	0,89915	1
GO:0001817 regulation of cytokine production	0,501	0,90863	1
GO:0002553 histamine secretion by mast cell	0,484	0,91408	1
GO:0000027 ribosomal large subunit assembly	0,48	0,9147	9
GO:0000079 regulation of cyclin-dependent protein serine/threonine kinase activity	0,477	0,91461	1
GO:0006122 mitochondrial electron transport	0,467	0,91893	8
GO:0002281 macrophage activation involved in immune response	0,45	0,93338	1
GO:0002250 adaptive immune response	0,447	0,93379	6
GO:0001675 acrosome assembly	0,446	0,92832	2
GO:0002687 positive regulation of leukocyte migration	0,418	0,95114	3
GO:0002091 negative regulation of receptor internalization	0,406	0,95723	1
GO:0006013 mannose metabolic process	0,392	0,96854	1
GO:0006139 nucleobase-containing compound metabolic process	0,389	0,96878	3
GO:0001892 embryonic placenta development	0,388	0,96687	2
GO:0001553 luteinization	0,357	0,98619	1
GO:0001570 vasculogenesis	0,341	0,99895	2
GO:0000494 box C/D snoRNA 3'-end processing	0,339	0,99844	2
GO:0002525 acute inflammatory response to non-antigenic stimulus	0,322	1,00248	1
GO:0000303 response to superoxide	0,32	1,00172	1

GO:0006163 purine nucleotide metabolic process	0,32	0,9991	3
GO:0000462 maturation of SSU-rRNA from tricistronic rRNA transcript (SSU-rRNA	0,316	0,99998	5
GO:0006189 'de novo' IMP biosynthetic process	0,309	1,001	3
GO:0006089 lactate metabolic process	0,292	1,00801	2
GO:0000132 establishment of mitotic spindle orientation	0,288	1,00295	1
GO:0003383 apical constriction	0,276	1,00943	1
GO:0001963 synaptic transmission	0,275	1,00694	2
GO:0006021 inositol biosynthetic process	0,261	1,00025	1
GO:0002262 myeloid cell homeostasis	0,257	0,9981	3
GO:0001552 ovarian follicle atresia	0,255	0,99693	1
GO:0002236 detection of misfolded protein	0,243	1,00257	1
GO:0002368 B cell cytokine production	0,243	0,99969	1
GO:0002755 MyD88-dependent toll-like receptor signaling pathway	0,243	0,99684	1
GO:0002842 positive regulation of T cell mediated immune response to tumor cell	0,243	0,994	1
GO:0001825 blastocyst formation	0,23	1,00109	1
GO:0000294 nuclear-transcribed mRNA catabolic process	0,226	1,00179	1
GO:0000956 nuclear-transcribed mRNA catabolic process	0,226	0,99897	1
GO:0001502 cartilage condensation	0,225	0,99716	2
GO:0002063 chondrocyte development	0,225	0,99437	2
GO:0000381 regulation of alternative mRNA splicing	0,22	0,99617	4
GO:0001505 regulation of neurotransmitter levels	0,215	0,99583	1
GO:0000077 DNA damage checkpoint	0,213	0,9948	1
GO:0006233 dTDP biosynthetic process	0,205	0,99964	1
GO:0006235 dTTP biosynthetic process	0,205	0,99688	1
GO:0002028 regulation of sodium ion transport	0,2	0,99823	3
GO:0001885 endothelial cell development	0,196	0,99657	1
GO:0006072 glycerol-3-phosphate metabolic process	0,196	0,99429	3
GO:0002576 platelet degranulation	0,189	0,98191	5
GO:0000729 DNA double-strand break processing	0,181	0,97649	1
GO:0006301 postreplication repair	0,181	0,97392	1
GO:0006310 DNA recombination	0,176	0,97318	6
GO:0002035 brain renin-angiotensin system	0,167	0,97597	1
GO:0002821 positive regulation of adaptive immune response	0,167	0,97343	1
GO:0002906 negative regulation of mature B cell apoptotic process	0,167	0,97091	1
GO:0001667 ameboidal-type cell migration	0,146	0,98375	3
GO:0002093 auditory receptor cell morphogenesis	0,142	0,98512	1
GO:0002551 mast cell chemotaxis	0,142	0,98259	1
GO:0001516 prostaglandin biosynthetic process	0,141	0,98122	3
GO:0002862 negative regulation of inflammatory response to antigenic stimulus	0,121	0,98086	3
GO:0001928 regulation of exocyst assembly	0,119	0,97984	1
GO:0001756 somitogenesis	0,116	0,98038	4
GO:0006090 pyruvate metabolic process	0,108	0,98008	4
GO:0001955 blood vessel maturation	0,099	0,98273	2
GO:0006177 GMP biosynthetic process	0,053	1,00641	2

GO:0000002 mitochondrial genome maintenance	0,045	1,00606	1
GO:0000712 resolution of meiotic recombination intermediates	0,034	1,01256	1
GO:0000819 sister chromatid segregation	0,034	1,01013	1
GO:0006259 DNA metabolic process	0,034	1,00771	1
GO:0006268 DNA unwinding involved in DNA replication	0,034	1,00529	1
GO:0006312 mitotic recombination	0,034	1,0029	1
GO:0002184 cytoplasmic translational termination	0,026	1,00013	1
GO:0001775 cell activation	0,02	0,99128	1
GO:0000052 citrulline metabolic process	0,014	0,99148	2
GO:0001960 negative regulation of cytokine-mediated signaling pathway	0,003	0,99787	2
GO:0002003 angiotensin maturation	-0,01	0,99346	1
GO:0001704 formation of primary germ layer	-0,02	0,99948	1
GO:0003205 cardiac chamber development	-0,02	0,99714	1
GO:0003408 optic cup formation involved in camera-type eye development	-0,02	0,9948	1
GO:0006344 maintenance of chromatin silencing	-0,02	0,99248	1
GO:0006228 UTP biosynthetic process	-0,02	1,0012	3
GO:0003382 epithelial cell morphogenesis	-0,03	1,00121	3
GO:0006011 UDP-glucose metabolic process	-0,03	1,00169	1
GO:0000338 protein deneddylation	-0,03	1,00302	1
GO:0005996 monosaccharide metabolic process	-0,05	1,00991	1
GO:0006061 sorbitol biosynthetic process	-0,05	1,00746	1
GO:0000302 response to reactive oxygen species	-0,06	1,00476	8
GO:0006172 ADP biosynthetic process	-0,07	0,99427	2
GO:0000447 endonucleolytic cleavage in ITS1 to separate SSU-rRNA from 5.8S rRNA and LSU-rRNA from tricistronic rRNA transcript (SSU-rRNA	-0,09	0,98192	2
GO:0000461 endonucleolytic cleavage to generate mature 3'-end of SSU-rRNA from (SSU-rRNA	-0,09	0,97951	2
GO:0001975 response to amphetamine	-0,1	0,98066	7
GO:0000910 cytokinesis	-0,1	0,98181	6
GO:0000961 negative regulation of mitochondrial RNA catabolic process	-0,11	0,98157	1
GO:0000189 MAPK import into nucleus	-0,11	0,98205	2
GO:0001776 leukocyte homeostasis	-0,14	0,97824	1
GO:0001782 B cell homeostasis	-0,14	0,97576	1
GO:0001783 B cell apoptotic process	-0,14	0,9733	1
GO:0002352 B cell negative selection	-0,14	0,97085	1
GO:0001765 membrane raft assembly	-0,14	0,97959	3
GO:0000184 nuclear-transcribed mRNA catabolic process	-0,14	0,98167	5
GO:0005977 glycogen metabolic process	-0,15	0,98133	7
GO:0006104 succinyl-CoA metabolic process	-0,17	0,97769	3
GO:0005979 regulation of glycogen biosynthetic process	-0,18	0,97205	4
GO:0002479 antigen processing and presentation of exogenous peptide antigen via MHC class I	-0,18	0,97819	10
GO:0002036 regulation of L-glutamate transport	-0,19	0,97635	1
GO:0002446 neutrophil mediated immunity	-0,19	0,97868	3
GO:0001654 eye development	-0,19	0,97965	1
GO:0000724 double-strand break repair via homologous recombination	-0,19	0,98264	3

GO:0001934 positive regulation of protein phosphorylation	-0,19	0,98471	27
GO:0002309 T cell proliferation involved in immune response	-0,19	0,98686	1
GO:0000448 cleavage in ITS2 between 5.8S rRNA and LSU-rRNA of tricistronic rRNA transcript (SSU-rRNA	-0,19	0,98744	1
GO:0006097 glyoxylate cycle	-0,2	0,98962	2
GO:0002376 immune system process	-0,2	0,99163	22
GO:0002062 chondrocyte differentiation	-0,2	0,99786	5
GO:0006020 inositol metabolic process	-0,22	0,99412	2
GO:0003065 positive regulation of heart rate by epinephrine	-0,24	0,99387	4
GO:0001707 mesoderm formation	-0,24	1,00432	3
GO:0006303 double-strand break repair via nonhomologous end joining	-0,26	0,99942	1
GO:0000147 actin cortical patch assembly	-0,26	0,99929	1
GO:0005980 glycogen catabolic process	-0,27	1,00153	4
GO:0003215 cardiac right ventricle morphogenesis	-0,27	1,00382	1
GO:0003350 pulmonary myocardium development	-0,27	1,00086	1
GO:0006105 succinate metabolic process	-0,27	1,00519	4
GO:0002090 regulation of receptor internalization	-0,27	1,00502	1
GO:0006116 NADH oxidation	-0,28	1,00571	4
GO:0001779 natural killer cell differentiation	-0,29	1,00874	1
GO:0003170 heart valve development	-0,29	1,0057	1
GO:0001508 action potential	-0,29	1,00979	1
GO:0003341 cilium movement	-0,3	1,00353	2
GO:0003279 cardiac septum development	-0,31	1,00222	3
GO:0006065 UDP-glucuronate biosynthetic process	-0,32	1,00506	1
GO:0006165 nucleoside diphosphate phosphorylation	-0,33	0,99934	4
GO:0006000 fructose metabolic process	-0,33	1,00004	2
GO:0002042 cell migration involved in sprouting angiogenesis	-0,37	0,97863	2
GO:0003413 chondrocyte differentiation involved in endochondral bone morphogenesis	-0,37	0,97967	1
GO:0001916 positive regulation of T cell mediated cytotoxicity	-0,38	0,96685	2
GO:0002088 lens development in camera-type eye	-0,41	0,95983	1
GO:0001819 positive regulation of cytokine production	-0,44	0,93131	4
GO:0001936 regulation of endothelial cell proliferation	-0,45	0,93074	1
GO:0006029 proteoglycan metabolic process	-0,47	0,91787	1
GO:0001541 ovarian follicle development	-0,49	0,91533	6
GO:0001954 positive regulation of cell-matrix adhesion	-0,5	0,90745	7
GO:0001702 gastrulation with mouth forming second	-0,5	0,90883	2
GO:0006120 mitochondrial electron transport	-0,5	0,90798	3
GO:0002188 translation reinitiation	-0,53	0,89523	1
GO:0006210 thymine catabolic process	-0,53	0,8984	1
GO:0001578 microtubule bundle formation	-0,58	0,87807	1
GO:0006101 citrate metabolic process	-0,59	0,87354	4
GO:0006099 tricarboxylic acid cycle	-0,59	0,8767	21
GO:0001678 cellular glucose homeostasis	-0,6	0,87789	2
GO:0006069 ethanol oxidation	-0,6	0,88259	1
GO:0001964 startle response	-0,6	0,89216	1

GO:0001976 neurological system process involved in regulation of systemic arterial blood pressure	-0,6	0,88881	1
GO:0006349 regulation of gene expression by genetic imprinting	-0,6	0,8855	1
GO:0001893 maternal placenta development	-0,61	0,88379	2
GO:0006082 organic acid metabolic process	-0,62	0,87929	3
GO:0003407 neural retina development	-0,63	0,87969	1
GO:0002536 respiratory burst involved in inflammatory response	-0,64	0,86834	1
GO:0006302 double-strand break repair	-0,66	0,86787	5
GO:0006110 regulation of glycolytic process	-0,66	0,86739	1
GO:0003091 renal water homeostasis	-0,66	0,87028	2
GO:0006024 glycosaminoglycan biosynthetic process	-0,66	0,87352	7
GO:0000028 ribosomal small subunit assembly	-0,67	0,87121	6
GO:0001731 formation of translation preinitiation complex	-0,68	0,8739	7
GO:0006114 glycerol biosynthetic process	-0,7	0,86614	1
GO:0000186 activation of MAPKK activity	-0,7	0,87276	2
GO:0002138 retinoic acid biosynthetic process	-0,71	0,87504	3
GO:0006030 chitin metabolic process	-0,71	0,87656	1
GO:0006351 transcription	-0,72	0,87708	33
GO:0006102 isocitrate metabolic process	-0,73	0,86906	6
GO:0006068 ethanol catabolic process	-0,73	0,86564	5
GO:0006094 gluconeogenesis	-0,74	0,86765	9
GO:0006183 GTP biosynthetic process	-0,74	0,86365	3
GO:0001932 regulation of protein phosphorylation	-0,75	0,8641	6
GO:0002548 monocyte chemotaxis	-0,76	0,86723	4
GO:0001935 endothelial cell proliferation	-0,77	0,87066	1
GO:0000188 inactivation of MAPK activity	-0,78	0,87154	1
GO:0003057 regulation of the force of heart contraction by chemical signal	-0,78	0,86753	1
GO:0006081 cellular aldehyde metabolic process	-0,81	0,85231	1
GO:0001656 metanephros development	-0,81	0,85592	2
GO:0001933 negative regulation of protein phosphorylation	-0,82	0,85009	14
GO:0006106 fumarate metabolic process	-0,82	0,85035	1
GO:0001957 intramembranous ossification	-0,85	0,83219	2
GO:0002438 acute inflammatory response to antigenic stimulus	-0,86	0,83683	2
GO:0002934 desmosome organization	-0,86	0,84512	1
GO:0003223 ventricular compact myocardium morphogenesis	-0,86	0,84092	1
GO:0006085 acetyl-CoA biosynthetic process	-0,86	0,8432	2
GO:0001942 hair follicle development	-0,87	0,83752	4
GO:0003007 heart morphogenesis	-0,88	0,83688	5
GO:0001886 endothelial cell morphogenesis	-0,88	0,83931	2
GO:0000086 G2/M transition of mitotic cell cycle	-0,9	0,85192	1
GO:0005513 detection of calcium ion	-0,9	0,84742	1
GO:0003006 developmental process involved in reproduction	-0,9	0,8539	1
GO:0001842 neural fold formation	-0,9	0,85744	1
GO:0006107 oxaloacetate metabolic process	-0,9	0,86067	8
GO:0006103 2-oxoglutarate metabolic process	-0,91	0,86226	10
GO:0003097 renal water transport	-0,91	0,8673	1

GO:0006182 cGMP biosynthetic process	-0,91	0,86251	1
GO:0002002 regulation of angiotensin levels in blood	-0,92	0,85931	3
GO:0001958 endochondral ossification	-0,92	0,86385	5
GO:0002685 regulation of leukocyte migration	-0,93	0,85724	2
GO:0003085 negative regulation of systemic arterial blood pressure	-0,94	0,86463	2
GO:0001525 angiogenesis	-0,95	0,8489	34
GO:0001503 ossification	-0,96	0,84733	7
GO:0002474 antigen processing and presentation of peptide antigen via MHC class I	-0,97	0,85241	4
GO:0003094 glomerular filtration	-1	0,82625	2
GO:0002230 positive regulation of defense response to virus by host	-1,01	0,82152	13
GO:0006171 cAMP biosynthetic process	-1,01	0,82704	1
GO:0001568 blood vessel development	-1,03	0,81748	8
GO:0003334 keratinocyte development	-1,03	0,81938	5
GO:0002291 T cell activation via T cell receptor contact with antigen bound to MHC molecule on antigen presenting cell	-1,03	0,83317	1
GO:0002457 T cell antigen processing and presentation	-1,03	0,82789	1
GO:0002693 positive regulation of cellular extravasation	-1,03	0,82269	1
GO:0001798 positive regulation of type IIa hypersensitivity	-1,05	0,82075	1
GO:0001970 positive regulation of activation of membrane attack complex	-1,05	0,81549	1
GO:0002227 innate immune response in mucosa	-1,06	0,82267	1
GO:0002485 antigen processing and presentation of endogenous peptide antigen via MHC class I via ER pathway	-1,06	0,82278	2
GO:0001514 selenocysteine incorporation	-1,07	0,82614	1
GO:0002072 optic cup morphogenesis involved in camera-type eye development	-1,07	0,82934	1
GO:0006098 pentose-phosphate shunt	-1,08	0,8282	10
GO:0001894 tissue homeostasis	-1,09	0,82449	4
GO:0001974 blood vessel remodeling	-1,09	0,82218	5
GO:0002762 negative regulation of myeloid leukocyte differentiation	-1,11	0,81356	2
GO:0006220 pyrimidine nucleotide metabolic process	-1,11	0,80783	2
GO:0006241 CTP biosynthetic process	-1,11	0,80218	2
GO:0001822 kidney development	-1,13	0,79789	13
GO:0006127 glycerophosphate shuttle	-1,14	0,81713	1
GO:0001778 plasma membrane repair	-1,15	0,82956	5
GO:0001542 ovulation from ovarian follicle	-1,16	0,82286	1
GO:0001837 epithelial to mesenchymal transition	-1,17	0,82297	4
GO:0003433 chondrocyte development involved in endochondral bone morphogenesis	-1,25	0,76961	1
GO:0001504 neurotransmitter uptake	-1,27	0,74863	1
GO:0003229 ventricular cardiac muscle tissue development	-1,28	0,75039	1
GO:0003073 regulation of systemic arterial blood pressure	-1,3	0,75531	3
GO:0001738 morphogenesis of a polarized epithelium	-1,31	0,7588	2
GO:0003179 heart valve morphogenesis	-1,31	0,78582	1
GO:0006109 regulation of carbohydrate metabolic process	-1,31	0,77841	1
GO:0006112 energy reserve metabolic process	-1,31	0,77113	1
GO:0002087 regulation of respiratory gaseous exchange by neurological system process	-1,31	0,79258	2

GO:0001657 ureteric bud development	-1,34	0,76922	2
GO:0001816 cytokine production	-1,38	0,74199	2
GO:0006004 fucose metabolic process	-1,41	0,72337	1
GO:0002520 immune system development	-1,45	0,70299	1
GO:0003360 brainstem development	-1,46	0,70197	2
GO:0001523 retinoid metabolic process	-1,5	0,73176	6
GO:0001755 neural crest cell migration	-1,54	0,70008	4
GO:0000422 mitophagy	-1,54	0,71785	1
GO:0001890 placenta development	-1,61	0,68845	6
GO:0001938 positive regulation of endothelial cell proliferation	-1,63	0,67014	7
GO:0000733 DNA strand renaturation	-1,64	0,66967	1
GO:0006334 nucleosome assembly	-1,64	0,67996	17
GO:0005978 glycogen biosynthetic process	-1,67	0,66594	5
GO:0001658 branching involved in ureteric bud morphogenesis	-1,67	0,68394	3
GO:0002740 negative regulation of cytokine secretion involved in immune response	-1,8	0,53079	2
GO:0000289 nuclear-transcribed mRNA poly(A) tail shortening	-1,82	0,52048	1
GO:0002215 defense response to nematode	-1,84	0,51932	1
GO:0000470 maturation of LSU-rRNA	-1,9	0,469	3
GO:0002074 extraocular skeletal muscle development	-1,95	0,42519	1
GO:0001759 organ induction	-1,98	0,42803	1
GO:0002526 acute inflammatory response	-2,05	0,37303	2
GO:0006111 regulation of gluconeogenesis	-2,07	0,36836	1
GO:0006108 malate metabolic process	-2,1	0,35817	5
GO:0001659 temperature homeostasis	-2,11	0,37116	4
GO:0000122 negative regulation of transcription from RNA polymerase II promoter	-2,18	0,336	34
GO:0000055 ribosomal large subunit export from nucleus	-2,25	0,298	2
GO:0000056 ribosomal small subunit export from nucleus	-2,25	0,2897	2
GO:0002009 morphogenesis of an epithelium	-2,28	0,2875	2
GO:0006084 acetyl-CoA metabolic process	-2,35	0,2802	6
GO:0001543 ovarian follicle rupture	-2,42	0,2415	1
GO:0001501 skeletal system development	-2,5	0,2131	7
GO:0000957 mitochondrial RNA catabolic process	-2,59	0,2461	1
GO:0000958 mitochondrial mRNA catabolic process	-2,59	0,2325	1
GO:0000962 positive regulation of mitochondrial RNA catabolic process	-2,59	0,2202	1
GO:0000964 mitochondrial RNA 5'-end processing	-2,59	0,2092	1
GO:0000965 mitochondrial RNA 3'-end processing	-2,59	0,1993	1
GO:0001676 long-chain fatty acid metabolic process	-2,73	0,1962	4
GO:0001569 patterning of blood vessels	-3,58	0,0167	2
GO:0001895 retina homeostasis	-3,73	0,0104	6
GO:0002037 negative regulation of L-glutamate transport	-4,17	0,0022	1
GO:0002839 positive regulation of immune response to tumor cell	-5,28	1E-05	1

Annexed Table 6. Protein expression changes in aorta from WT and ISG15$^{-/-}$ mice in response to Ang II in the functional categories within clusters. Results are reported as Zq and Zc values (log_2-fold changes expressed in units of standard deviation) of each protein and each cluster, respectively, for the integration data in the comparative of ISG15$^{-/-}$ and WT samples considering the effect of Ang II, normalized with respect to the untreated samples. N pept indicates the number of quantified peptides for each protein. N prot indicated the number of quantified proteins for each cluster.

	Zc	N prot	FDR
CARDIOVASCULAR REMODELING	**-2,99**	**75**	**0,0082**
Protein name	**Zq**	**N pept**	
>sp|Q9ESB3|HRG_MOUSE Histidine-rich glycoprotein	-5,09	1	
>sp|P02463|CO4A1_MOUSE Collagen alpha-1(IV) chain	-3,34	1	
>tr|Q3UAI3|Q3UAI3_MOUSE CD36 antigen, isoform CRA_a	-2,52	1	
>sp|Q5SWU9|ACACA_MOUSE Acetyl-CoA carboxylase 1	-2,25	5	
>sp|P15655|FGF2_MOUSE Fibroblast growth factor 2	-1,93	1	
>sp|Q75NR7|RECQ4_MOUSE ATP-dependent DNA helicase Q4	-1,61	1	
>sp|P27601|GNA13_MOUSE Guanine nucleotide-binding protein subunit alpha-13	-1,57	1	
>sp|Q01149|CO1A2_MOUSE Collagen alpha-2(I) chain	-1,47	6	
>sp|Q9QUP5|HPLN1_MOUSE Hyaluronan and proteoglycan link protein 1	-1,31	1	
>sp|Q9JLN9|MTOR_MOUSE Serine/threonine-protein kinase mTOR	-1,28	1	
>sp|P11087|CO1A1_MOUSE Collagen alpha-1(I) chain	-1,26	5	
>sp|Q8BTM8|FLNA_MOUSE Filamin-A	-1,17	23	
>sp|Q9Z175|LOXL3_MOUSE Lysyl oxidase homolog 3	-1,09	1	
>tr|B2RQQ8|B2RQQ8_MOUSE Collagen, type IV, alpha 2	-1,02	2	
>sp|Q62009|POSTN_MOUSE Periostin	-1,02	6	
>sp|P05622|PGFRB_MOUSE Platelet-derived growth factor receptor beta	-0,96	2	
>tr|E9QPX1|E9QPX1_MOUSE Collagen alpha-1(XVIII) chain	-0,93	1	
>sp|P31750|AKT1_MOUSE RAC-alpha serine/threonine-protein kinase	-0,91	1	
>sp|Q91X97|NCALD_MOUSE Neurocalcin-delta	-0,88	1	
>sp|P21956|MFGM_MOUSE Lactadherin	-0,85	3	
>sp|P49817|CAV1_MOUSE Caveolin-1	-0,77	3	
>tr|Q3UHH3|Q3UHH3_MOUSE Uncharacterized protein	-0,72	5	
>sp|Q61554|FBN1_MOUSE Fibrillin-1	-0,71	4	
>sp|P21981|TGM2_MOUSEProtein-glutamine gamma-glutamyltransferase 2	-0,65	4	
>sp|Q61879|MYH10_MOUSE Myosin-10	-0,63	13	
>tr|Q5EBP9|Q5EBP9_MOUSE Tripartite motif-containing 28	-0,61	1	
>sp|Q99P72|RTN4_MOUSE Reticulon-4	-0,58	1	
>sp|Q9WTR5|CAD13_MOUSE Cadherin-13	-0,52	2	
>sp|Q8R2Y2|MUC18_MOUSE Cell surface glycoprotein MUC18	-0,50	1	
>sp|Q61245|COBA1_MOUSE Collagen alpha-1(XI) chain	-0,48	1	
>sp|Q62148|AL1A2_MOUSE Retinal dehydrogenase 2	-0,46	1	
>sp|Q99JY8|PLPP3_MOUSE Phospholipid phosphatase 3	-0,39	2	

>tr|H3BJH8|H3BJH8_MOUSE Thyroid hormone receptor interactor 11 (Fragment)	-0,38	1
>sp|P43406|ITAV_MOUSE Integrin alpha-V	-0,36	2
>sp|P39061|COIA1_MOUSE Collagen alpha-1(XVIII) chain	-0,36	7
>tr|Q3TS38|Q3TS38_MOUSE UDP-glucose 6-dehydrogenase	-0,34	1
>tr|Q3UPA1|Q3UPA1_MOUSE Guanine nucleotide binding protein, alpha 11	-0,31	1
>sp|Q69ZR2|HECD1_MOUSE E3 ubiquitin-protein ligase HECTD1	-0,30	1
>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein	-0,30	27
>sp|Q62181|SEM3C_MOUSE Semaphorin-3C	-0,29	1
>sp|Q9CWS0|DDAH1_MOUSE N(G),N(G)-dimethylarginine dimethylaminohydrolase 1	-0,27	1
>tr|O08614|O08614_MOUSE Cytoskeletal protein	-0,19	4
>sp|O08734|BAK_MOUSE Bcl-2 homologous antagonist/killer	-0,16	1
>sp|P06745|G6PI_MOUSE Glucose-6-phosphate isomerase	-0,14	3
>tr|Q52KG8|Q52KG8_MOUSE Hspg2 protein (Fragment)	-0,11	1
>tr|Q3UDY1|Q3UDY1_MOUSE MCG6067, isoform CRA_b	-0,08	3
>sp|P28653|PGS1_MOUSE Biglycan	-0,05	3
>sp|Q9DBG3|AP2B1_MOUSE AP-2 complex subunit beta	-0,05	2
>tr|Q52JJ6|Q52JJ6_MOUSE Aminopeptidase	-0,04	2
>sp|Q8VHY0|CSPG4_MOUSE Chondroitin sulfate proteoglycan 4	-0,03	6
>sp|P11276|FINC_MOUSE Fibronectin	-0,02	10
>sp|Q8R3B1|PLCD1_MOUSE 1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase delta-1	0,00	2
>sp|Q8R054|SRPX2_MOUSE Sushi repeat-containing protein SRPX2	0,00	1
>sp|O54890|ITB3_MOUSE Integrin beta-3	0,03	2
>sp|Q8VE70|PDC10_MOUSE Programmed cell death protein 10	0,05	2
>sp|P16110|LEG3_MOUSE Galectin-3	0,06	1
>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1	0,09	6
>tr|Q3UG07|Q3UG07_MOUSE Matrix metallopeptidase 2	0,23	1
>sp|P11531|DMD_MOUSE Dystrophin	0,25	8
>tr|A1L353|A1L353_MOUSE Transforming growth factor, beta induced	0,26	2
>sp|P51655|GPC4_MOUSE Glypican-4	0,27	1
>sp|P09405|NUCL_MOUSE Nucleolin	0,28	4
>tr|E9PZ16|E9PZ16_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein	0,33	6
>tr|Q542G9|Q542G9_MOUSE Annexin	0,35	7
>sp|O55222|ILK_MOUSE Integrin-linked protein kinase	0,40	3
>sp|Q9EPC1|PARVA_MOUSE Alpha-parvin	0,46	3
>sp|Q8VDD5|MYH9_MOUSE Myosin-9	0,47	17
>tr|F8WIV5|F8WIV5_MOUSE Dynamin-2	0,50	2
>sp|Q8CJ53|CIP4_MOUSE Cdc42-interacting protein 4	0,54	2
>sp|P97449|AMPN_MOUSE Aminopeptidase N	0,54	2
>sp|Q61508|ECM1_MOUSE Extracellular matrix protein 1	0,73	1
>tr|Q544G5|Q544G5_MOUSE Dystroglycan 1	0,81	2
>sp|P97927|LAMA4_MOUSE Laminin subunit alpha-4	0,88	4
>sp|P09055|ITB1_MOUSE Integrin beta-1	1,04	3
>sp|P34152|FAK1_MOUSE Focal adhesion kinase 1	1,20	1

	Zc	N prot	FDR
CARDIOVASCULAR FUNCTION	**2,08**	**24**	**0,0325**
Protein name	**Zq**	**N pept**	
>sp|P09542|MYL3_MOUSE Myosin light chain 3	5,41	1	
>sp|Q8C8R3|ANK2_MOUSE Ankyrin-2	3,24	2	
>sp|P09541|MYL4_MOUSE Myosin light chain 4	1,90	2	
>sp|Q8CFI0|NED4L_MOUSE E3 ubiquitin-protein ligase NEDD4-like	1,67	1	
>tr|A2AEY2|A2AEY2_MOUSE Four and a half LIM domains 1, isoform CRA_c	1,33	1	
>tr|B2RXX9|B2RXX9_MOUSE Myosin, heavy polypeptide 7, cardiac muscle, beta	1,33	2	
>sp|P07901|HS90A_MOUSE Heat shock protein HSP 90-alpha	0,94	4	
>sp|O55143|AT2A2_MOUSE Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	0,92	3	
>sp|Q3ULJ0|GPD1L_MOUSE Glycerol-3-phosphate dehydrogenase 1-like protein	0,91	2	
>tr|G5E8R0|G5E8R0_MOUSE Tropomyosin 1, alpha, isoform CRA_i	0,62	1	
>tr|B2RQQ1|B2RQQ1_MOUSE MCG133649, isoform CRA_a	0,53	1	
>tr|Q564G1|Q564G1_MOUSE Tropomyosin 1, alpha	0,29	2	
>sp|P11531|DMD_MOUSE Dystrophin	0,25	8	
>sp|P58252|EF2_MOUSE Elongation factor 2	0,24	5	
>sp|Q6PHZ2|KCC2D_MOUSE Calcium/calmodulin-dependent protein kinase type II subunit delta	0,18	1	
>tr|Q5EBQ2|Q5EBQ2_MOUSE MCG7941, isoform CRA_f	0,17	1	
>sp|Q8VDN2|AT1A1_MOUSE Sodium/potassium-transporting ATPase subunit alpha-1	-0,08	7	
>sp|P97447|FHL1_MOUSE Four and a half LIM domains protein 1	-0,11	4	
>sp|Q6URW6|MYH14_MOUSE Myosin-14	-0,46	2	
>sp|P58771|TPM1_MOUSE Tropomyosin alpha-1 chain	-0,51	3	
>sp|P49817|CAV1_MOUSE Caveolin-1	-0,77	3	
>sp|P0DP27|CALM2_MOUSE Calmodulin-2	-0,88	1	
>tr|E9Q448|E9Q448_MOUSE Tropomyosin alpha-1 chain	-0,89	10	
>tr|Q3UHK5|Q3UHK5_MOUSE Sodium/potassium-transporting ATPase subunit alpha	-1,25	2	

	Zc	N prot	FDR
VASCULAR REDOX STATE	**-1,83**	**61**	**0,0456**
Protein name	**Zq**	**N pept**	
>sp|P56391|CX6B1_MOUSE Cytochrome c oxidase subunit 6B1	-2,61	1	
>sp|O70400|PDLI1_MOUSE PDZ and LIM domain protein 1	-1,35	2	
>sp|P19783|COX41_MOUSE Cytochrome c oxidase subunit 4 isoform 1, mitochondrial	-1,30	1	
>sp|Q9D6J6|NDUV2_MOUSE NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial	-1,26	2	
>sp|Q60994|ADIPO_MOUSE Adiponectin	-1,23	2	
>sp|P99029|PRDX5_MOUSE Peroxiredoxin-5, mitochondrial	-1,22	1	

>sp|Q9DB77|QCR2_MOUSE Cytochrome b-c1 complex subunit 2, mitochondrial	-1,14	2
>sp|P24270|CATA_MOUSE Catalase	-1,11	2
>sp|P29533|VCAM1_MOUSE Vascular cell adhesion protein 1	-1,06	1
>sp|Q62009|POSTN_MOUSE Periostin	-1,02	6
>sp|Q9CQ69|QCR8_MOUSE Cytochrome b-c1 complex subunit 8	-0,89	1
>sp|Q9CPP6|NDUA5_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 5	-0,80	1
>sp|P49817|CAV1_MOUSE Caveolin-1	-0,77	3
>sp|O08528|HXK2_MOUSE Hexokinase-2	-0,72	3
>tr|Q5FWB7|Q5FWB7_MOUSE Fructose-bisphosphate aldolase	-0,70	4
>tr|Q542X9|Q542X9_MOUSE Superoxide dismutase [Cu-Zn]	-0,67	1
>sp|Q9CQ91|NDUA3_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 3	-0,67	1
>sp|Q61171|PRDX2_MOUSE Peroxiredoxin-2	-0,64	3
>sp|Q9Z2D6|MECP2_MOUSE Methyl-CpG-binding protein 2	-0,60	2
>sp|Q7TMF3|NDUAC_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12	-0,57	1
>sp|Q9Z0X1|AIFM1_MOUSE Apoptosis-inducing factor 1, mitochondrial	-0,49	2
>sp|Q9DCS9|NDUBA_MOUSE NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10	-0,43	1
>tr|Q3ULT2|Q3ULT2_MOUSE Actinin alpha 4	-0,42	5
>sp|P23927|CRYAB_MOUSE Alpha-crystallin B chain	-0,42	1
>sp|Q9WUB3|PYGM_MOUSE Glycogen phosphorylase, muscle form	-0,40	2
>sp|Q9DC69|NDUA9_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9, mitochondrial	-0,39	2
>sp|Q9CQZ5|NDUA6_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6	-0,36	1
>sp|Q9CR68|UCRI_MOUSE Cytochrome b-c1 complex subunit Rieske, mitochondrial	-0,34	2
>tr|E9Q509|E9Q509_MOUSE Pyruvate kinase OS=Mus musculus GN=Pklr PE=1 SV=1	-0,30	1
>sp|P19536|COX5B_MOUSE Cytochrome c oxidase subunit 5B, mitochondrial	-0,28	1
>sp|Q59J78|NDUF2_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex assembly factor 2	-0,20	1
>sp|P35700|PRDX1_MOUSE Peroxiredoxin-1	-0,19	3
>sp|Q9R0E2|PLOD1_MOUSE Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1	-0,17	1
>sp|P17710|HXK1_MOUSE Hexokinase-1 OS=Mus musculus GN=Hk1 PE=1 SV=3	-0,15	6
>sp|P62897|CYC_MOUSE Cytochrome c, somatic OS=Mus musculus GN=Cycs PE=1 SV=2	-0,09	3
>sp|P00405|COX2_MOUSE Cytochrome c oxidase subunit 2 OS=Mus musculus GN=Mtco2 PE=1 SV=1	-0,01	3
>sp|Q9CZ13|QCR1_MOUSE Cytochrome b-c1 complex subunit 1, mitochondrial OS=Mus musculus GN=Uqcrc1 PE=1 SV=2	0,00	3
>sp|Q9R0P9|UCHL1_MOUSE Ubiquitin carboxyl-terminal hydrolase isozyme L1 OS=Mus musculus GN=Uchl1 PE=1 SV=1	0,00	2
>sp|Q923T9|KCC2G_MOUSE Calcium/calmodulin-dependent protein kinase type II subunit gamma OS=Mus musculus GN=Camk2g PE=1 SV=1	0,13	1
>sp|O08529|CAN2_MOUSE Calpain-2 catalytic subunit OS=Mus musculus GN=Capn2 PE=1 SV=4	0,13	3

>sp|Q9D855|QCR7_MOUSE Cytochrome b-c1 complex subunit 7 OS=Mus musculus GN=Uqcrb PE=1 SV=3	0,13	1
>tr|B1AZS9|B1AZS9_MOUSE Peroxiredoxin-4 (Fragment) OS=Mus musculus GN=Prdx4 PE=1 SV=1	0,16	2
>sp|Q6PHZ2|KCC2D_MOUSE Calcium/calmodulin-dependent protein kinase type II subunit delta OS=Mus musculus GN=Camk2d PE=1 SV=1	0,18	1
>sp|P63038|CH60_MOUSE 60 kDa heat shock protein, mitochondrial OS=Mus musculus GN=Hspd1 PE=1 SV=1	0,20	5
>sp|Q91YT0|NDUV1_MOUSE NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial OS=Mus musculus GN=Ndufv1 PE=1 SV=1	0,20	2
>sp|O08807|PRDX4_MOUSE Peroxiredoxin-4 OS=Mus musculus GN=Prdx4 PE=1 SV=1	0,22	2
>tr|Q3UG07|Q3UG07_MOUSE Matrix metallopeptidase 2 OS=Mus musculus GN=Mmp2 PE=2 SV=1	0,23	1
>sp|Q9CQ75|NDUA2_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 2 OS=Mus musculus GN=Ndufa2 PE=1 SV=3	0,23	1
>tr|Q3V2D0|Q3V2D0_MOUSE Lon protease homolog, mitochondrial OS=Mus musculus GN=Lonp1 PE=2 SV=1	0,24	1
>sp|P58252|EF2_MOUSE Elongation factor 2 OS=Mus musculus GN=Eef2 PE=1 SV=2	0,24	5
>sp|P11881|ITPR1_MOUSE Inositol 1,4,5-trisphosphate receptor type 1 OS=Mus musculus GN=Itpr1 PE=1 SV=2	0,24	5
>sp|P48771|CX7A2_MOUSE Cytochrome c oxidase subunit 7A2, mitochondrial OS=Mus musculus GN=Cox7a2 PE=1 SV=2	0,28	1
>sp|Q8BH24|TM9S4_MOUSE Transmembrane 9 superfamily member 4 OS=Mus musculus GN=Tm9sf4 PE=1 SV=1	0,30	1
>sp|O35074|PTGIS_MOUSE Prostacyclin synthase OS=Mus musculus GN=Ptgis PE=1 SV=1	0,30	3
>sp|Q99LC3|NDUAA_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial OS=Mus musculus GN=Ndufa10 PE=1 SV=1	0,50	1
>sp|Q9ERS2|NDUAD_MOUSE NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13 OS=Mus musculus GN=Ndufa13 PE=1 SV=3	0,50	1
>sp|Q8CGK3|LONM_MOUSE Lon protease homolog, mitochondrial OS=Mus musculus GN=Lonp1 PE=1 SV=2	0,61	2
>sp|Q91WD5|NDUS2_MOUSE NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial OS=Mus musculus GN=Ndufs2 PE=1 SV=1	0,65	1
>sp|O08709|PRDX6_MOUSE Peroxiredoxin-6 OS=Mus musculus GN=Prdx6 PE=1 SV=3	1,04	2
>sp|P12787|COX5A_MOUSE Cytochrome c oxidase subunit 5A, mitochondrial	1,11	3
>tr|Q3UAD6|Q3UAD6_MOUSE Heat shock protein 90kDa beta (Grp94), member 1	1,16	7

	Zc	**N prot**	**FDR**
IMMUNE SYSTEM	**-0,76**	**52**	**0,0762**
Protein name	**Zq**	**N pept**	
>sp|P54116|STOM_MOUSE Erythrocyte band 7 integral membrane protein	-2,19	1	
>tr|A0A1W2P768|A0A1W2P768_MOUSE Histone H3.2	-1,98	1	
>sp|Q60692|PSB6_MOUSE Proteasome subunit beta type-6 3	-1,92	1	
>sp|P15089|CBPA3_MOUSE Mast cell carboxypeptidase A	-1,43	3	

>tr|Q3TVW6|Q3TVW6_MOUSE LIM and cysteine-rich domains 1	-1,25	3
>tr|B7STB7|B7STB7_MOUSE Annexin	-1,20	1
>sp|P01899|HA11_MOUSE H-2 class I histocompatibility antigen, D-B alpha chain	-1,04	1
>sp|Q6PDN3|MYLK_MOUSE Myosin light chain kinase, smooth muscle	-0,90	7
>tr|Q5SUC3|Q5SUC3_MOUSE Calnexin, isoform CRA_a	-0,88	3
>tr|Q059U0|Q059U0_MOUSE 1-acyl-sn-glycerol-3-phosphate acyltransferase	-0,88	1
>sp|Q9QUM9|PSA6_MOUSE Proteasome subunit alpha type-6	-0,81	1
>tr|Q80ZI9|Q80ZI9_MOUSE WD repeat domain 1 (Fragment)	-0,77	2
>sp|Q9Z1R2|BAG6_MOUSE Large proline-rich protein BAG6	-0,77	1
>sp|Q8C4U3|SFRP1_MOUSE Secreted frizzled-related protein 1	-0,74	1
>sp|P46935|NEDD4_MOUSE E3 ubiquitin-protein ligase NEDD4	-0,59	3
>sp|P99026|PSB4_MOUSE Proteasome subunit beta type-4	-0,58	1
>sp|Q9QUM0|ITA2B_MOUSE Integrin alpha-IIb	-0,50	1
>sp|Q9CX00|IST1_MOUSE IST1 homolog	-0,49	1
>sp|O88342|WDR1_MOUSE WD repeat-containing protein 1	-0,39	5
>sp|Q9R0Q7|TEBP_MOUSE Prostaglandin E synthase 3	-0,36	1
>sp|P14152|MDHC_MOUSE Malate dehidrogenase, cytoplasmic	-0,35	3
>sp|Q9CZX8|RS19_MOUSE 40S ribosomal protein S19	-0,31	3
>tr|Q540I4|Q540I4_MOUSE Flotillin 1	-0,29	3
>tr|Q4FJV4|Q4FJV4_MOUSE Annexin	-0,19	5
>sp|Q05BC3|EMAL1_MOUSE Echinoderm microtubule-associated protein-like 1	-0,16	4
>sp|O08734|BAK_MOUSE Bcl-2 homologous antagonist/killer	-0,16	1
>sp|O54890|ITB3_MOUSE Integrin beta-3	0,03	2
>sp|P16110|LEG3_MOUSE Galectin-3	0,06	1
>sp|P34884|MIF_MOUSE Macrophage migration inhibitory factor	0,13	1
>sp|Q8BJ71|NUP93_MOUSE Nuclear pore complex protein Nup93	0,15	1
>sp|P11352|GPX1_MOUSE Glutathione peroxidase 1	0,15	3
>sp|P57716|NICA_MOUSE Nicastrin	0,17	1
>sp|O70435|PSA3_MOUSE Proteasome subunit alpha type-3	0,18	1
>sp|P48036|ANXA5_MOUSE Annexin A5	0,23	12
>sp|P58252|EF2_MOUSE Elongation factor 2	0,24	5
>sp|P08228|SODC_MOUSE Superoxide dismutase [Cu-Zn]	0,27	2
>sp|O35074|PTGIS_MOUSE Prostacyclin synthase	0,30	3
>sp|Q9R1P3|PSB2_MOUSE Proteasome subunit beta type-2	0,30	1
>sp|P26618|PGFRA_MOUSE Platelet-derived growth factor receptor alpha	0,32	1
>tr|Q3TS44|Q3TS44_MOUSE Proteasome subunit alpha type	0,38	3
>sp|Q8BP40|PPA6_MOUSE Lysophosphatidic acid phosphatase type 6	0,39	1
>sp|P70195|PSB7_MOUSE Proteasome subunit beta type-7	0,48	1
>sp|Q6ZWX6|IF2A_MOUSE Eukaryotic translation initiation factor 2 subunit 1	0,55	1
>sp|P27773|PDIA3_MOUSE Protein disulfide-isomerase A3	0,59	5
>tr|Q3TU20|Q3TU20_MOUSE Angiotensin-converting enzyme	0,72	3
>sp|Q9QYR6|MAP1A_MOUSE Microtubule-associated protein 1A	0,73	2
>sp|O55234|PSB5_MOUSE Proteasome subunit beta type-5	0,74	2
>tr|B9EI85|B9EI85_MOUSE Histone H3	0,86	6

>sp|O70423|AOC3_MOUSE Membrane primary amine oxidase	0,90	5
>tr|B2MWM9|B2MWM9_MOUSE Calreticulin	0,99	1
>sp|Q99MU3|DSRAD_MOUSE Double-stranded RNA-specific adenosine deaminase	1,50	1
>sp|P27048|RSMB_MOUSE Small nuclear ribonucleoprotein-associated protein B	2,12	1

Annexed Table 7. Oxidized Cys containing peptide abundance changes in aorta from WT and ISG15$^{-/-}$ mice in response to Ang II. Results are reported as Zp values (log2-fold changes expressed in units of standard deviation) for each individual biological replicate and for the integration data obtained as a weighted average from the four replicates. Cox stands for the oxidized Cys residues.

	Integrated Zp values				
Sequences	**WT**	**WT Ang II**	**ISG15$^{-/-}$**	**ISG15$^{-/-}$ Ang II**	**Protein name**
ILEYAPCoxR					>sp|P11688|ITA5_MOUSE Integrin alpha-5
TFYSCoxTTEGR					>sp|P11276|FINC_MOUSE Fibronectin
ISCoxTIANR					>sp|P11276|FINC_MOUSE Fibronectin
LDTRPFCoxSGR					>sp|Q80YX1|TENA_MOUSE Tenascin
LCoxAIPNLR					>tr|Q546G4|Q546G4_MOUSE Albumin 1
CoxLVTLDTQR					>sp|P21956|MFGM_MOUSE Lactadherin
CFCoxMGVSR					>tr|E9PZ16|E9PZ16_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
FFSSDICoxR					>tr|Q3UAI3|Q3UAI3_MOUSE CD36 antigen, isoform CRA_a
CoxPVGYVLR					>sp|Q61554|FBN1_MOUSE Fibrillin-1
VNSILGCoxSQ					>sp|Q91X72|HEMO_MOUSE Hemopexin
DYFVSCoxPGR					>sp|Q91X72|HEMO_MOUSE Hemopexin
ADFQCoxFQQAR					>sp|O35206|COFA1_MOUSE Collagen alpha-1(XV) chain
LGCoxPLGETR					>sp|Q61581|IBP7_MOUSE Insulin-like growth factor-binding protein 7
GSFYCoxQAR					>sp|P37889|FBLN2_MOUSE Fibulin-2
CoxLPGFLGDR					>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1
ILQEDFTCoxR					>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1
AVNEECoxPTITR					>sp|Q640N1|AEBP1_MOUSE Adipocyte enhancer-binding protein 1
CoxTVYFEGPR					>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1
GVLFQPCoxER					>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1
ECoxEEIIR					>tr|Q3TGR2|Q3TGR2_MOUSE Fibrinogen, B beta polypeptide, isoform CRA_a
IWLDNLSCoxR					>sp|Q9Z175|LOXL3_MOUSE Lysyl oxidase homolog 3
LDGLCoxIPLR					>sp|Q91ZX7|LRP1_MOUSE Prolow-density lipoprotein receptor-related protein 1
VCoxLLHEK					>tr|Q546G4|Q546G4_MOUSE Albumin 1
ISSVLAGGSCoxR					>sp|P08779|K1C16_HUMAN Keratin, type I cytoskeletal 16
AGLSSGFVGCoxVR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein

CoxLDGYIGDSIR					>sp|P97927|LAMA4_MOUSE Laminin subunit alpha-4
TCoxESLGAGGYR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
FCoxQLEIQR					>sp|Q9Z0G4|WISP2_MOUSE WNT1-inducible-signaling pathway protein 2
CoxCoxTLPEDQR					>tr|Q546G4|Q546G4_MOUSE Albumin 1 OS=Mus musculus GN=Alb PE=1 SV=1
WSPDIPACoxAR					>sp|Q01339|APOH_MOUSE Beta-2-glycoprotein 1
TYTNLCoxQLR					>sp|Q9R118|HTRA1_MOUSE Serine protease HTRA1
ALEVEECoxR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
LIDLDSCoxIDR					>sp|Q8BTJ4|ENPP4_MOUSE Bis(5'-adenosyl)-triphosphatase enpp4
VTNDNTFCoxR					>sp|P29268|CTGF_MOUSE Connective tissue growth factor
TDSFSCoxNVR					>sp|P01867|IGG2B_MOUSE Ig gamma-2B chain C region
FDVEPDTYCoxR					>tr|Q3UIP2|Q3UIP2_MOUSE Procollagen C-endopeptidase enhancer protein
CoxCoxSGSLVER					>tr|Q546G4|Q546G4_MOUSE Albumin 1
LPSWDCoxPRPR					>sp|Q9Z0G4|WISP2_MOUSE WNT1-inducible-signaling pathway protein 2
CoxRPTTQEIVR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
CoxVWDLTDDLR					>sp|P97927|LAMA4_MOUSE Laminin subunit alpha-4
GTCoxWQTVIDGR					>sp|Q61554|FBN1_MOUSE Fibrillin-1
YQCoxTEGFVQR					>sp|Q61282|PGCA_MOUSE Aggrecan core protein
AGQCoxVCoxVEGFR					>tr|O35452|O35452_MOUSE Tenascin X
EFVCoxTVTHR					>sp|P01872|IGHM_MOUSE Immunoglobulin heavy constant mu
CoxLPVTELENGR					>sp|P06909|CFAH_MOUSE Complement factor H
CoxAAEEK-					>sp|P97873|LOXL1_MOUSE Lysyl oxidase homolog 1
VCoxVDTHMR					>sp|Q61554|FBN1_MOUSE Fibrillin-1
AQCoxGGGLLGVR					>sp|Q62059|CSPG2_MOUSE Versican core protein
LSSDCoxEDQIR					>sp|Q61543|GSLG1_MOUSE Golgi apparatus protein 1
GSLGTSGETCoxR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
GCoxQPSDIENPR					>sp|P09055|ITB1_MOUSE Integrin beta-1
EYEELCoxPR					>sp|Q61554|FBN1_MOUSE Fibrillin-1
AVLCoxPPPVK					>tr|K7Q7T7|K7Q7T7_MOUSE RAS-related C3 botulinum substrate 1
WDDVVCoxESR					>sp|Q61292|LAMB2_MOUSE Laminin subunit beta-2
VDGALCoxLDK					>sp|Q91X72|HEMO_MOUSE Hemopexin
LETCoxFLK					>sp|Q61554|FBN1_MOUSE Fibrillin-1
CoxIVQTDAISR					>sp|Q8CIZ8|VWF_MOUSE von Willebrand factor
TDQVCoxINLR					>sp|Q8BPB5|FBLN3_MOUSE EGF-containing fibulin-like extracellular matrix protein 1

QFSITCoxK					>sp|Q64735|CR1L_MOUSE Complement component receptor 1-like protein
LACoxGVIGIAQ					>sp|P08228|SODC_MOUSE Superoxide dismutase [Cu-Zn]
CoxDGDFDCoxEDR					>sp|Q05793|PGBM_MOUSE Basement membrane-specific heparan sulfate proteoglycan core protein
FDAYCoxFK					>sp|Q62059-2|CSPG2_MOUSE Isoform V1 of Versican core protein
TVCoxAHEELLR					>sp|P55002|MFAP2_MOUSE Microfibrillar-associated protein 2
VVDDTACoxPLLR					>sp|Q8BY89|CTL2_MOUSE Choline transporter-like protein 2
SAPFIECoxHGR					>sp|P02463|CO4A1_MOUSE Collagen alpha-1(IV) chain
CoxIDIDECoxR					>sp|Q8K4G1-3|LTBP4_MOUSE Isoform 3 of Latent-transforming growth factor beta-binding protein 4
TICoxIETIK					>sp|Q61554|FBN1_MOUSE Fibrillin-1
CoxVCoxGTGFQAGPR					>sp|Q8K4G1|LTBP4_MOUSE Latent-transforming growth factor beta-binding protein 4
DNCoxCoxILDER					>tr|Q3UEM7|Q3UEM7_MOUSE Uncharacterized protein
VQLLCoxPGGAAPR					>sp|Q99P68|SOST_MOUSE Sclerostin
ISPDLCoxGR					>sp|Q61554|FBN1_MOUSE Fibrillin-1
RVPPPCoxDR					>sp|Q8K4G1|LTBP4_MOUSE Latent-transforming growth factor beta-binding protein 4
RVPTPCoxAPGR					>sp|Q8K4G1|LTBP4_MOUSE Latent-transforming growth factor beta-binding protein 4
DYVCoxVVK					>sp|Q9R069|BCAM_MOUSE Basal cell adhesion molecule
YVSTTNCoxK					>sp|P97873|LOXL1_MOUSE Lysyl oxidase homolog 1
GSECoxASPLPGLR					>sp|Q8K4G1|LTBP4_MOUSE Latent-transforming growth factor beta-binding protein 4

Publications directly derived from this Thesis:

González-Amor M, Vila-Bedmar R, Rodrigues-Díez R, Moreno-Carriles R, Arcones AC, Cruces-Sande M, Salaices M, Mayor F Jr, *Briones AM, *Murga C. *corresponding authors. **Myeloid GRK2 Regulates Obesity-Induced Endothelial Dysfunction by Modulating Inflammatory Responses in Perivascular Adipose Tissue**. ***Antioxidants*** *(Basel)*. 2020, 9(10):953.

Under review in ***Cardiovascular Research***: **González-Amor M,** García-Redondo AB, Jorge I, Zalba G, Bécares M, Ruiz-Rodríguez MJ, Rodríguez C, Bermeo H, Rodrigues-Díez R, Rios FJ, Montezano AC, Martínez-González J, Vázquez J, Redondo JM, Touyz RM, Guerra S, Briones AM. **Interferon stimulated gene 15 mediates angiotensin II-induced vascular dysfunction through oxidative stress**.

Communications directly derived from this Thesis:

Poster

González-Amor M, García-Redondo AB, Palacios R, Rodrigues-Díez R, Alonso MJ, Salaices M, Guerra S, Briones AM. **Role of ISG15 in hypertensive vascular and cardiac damage**. European Council for Cardiovascular Research (ECCR). 14th-16th October 2016. Poiano, Lake Garda, Italy.

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Table 2. Protein-protein interaction network between hypertension-related proteins and ISG15 by STRING/Cytoscape. The Upstream Regulator Analysis tool from Ingenuity Pathway Analysis (IPA) was applied to the 2206 hypertension-related proteins obtained from the Phenopedia.

Upstream Regulator	Molecule Type	p-value of overlap	Direct Target Molecules in Dataset	Mechanistic Network [protein in dataset(master regulators)]
TNF	cytokine	3,03E-143	A4GALT,ABCA1,ABCB11,ABCC1,ABCC2,ABCG2,ACAD9,ACE,ACTA2,ADAMTS7,ADAMTS8,ADIPOQ,ADM,ADORA1,ADORA2A,ADORA2B,ADRB1,ADRB2,ADRB3,AGER,AGT,AGTR1,AKAP12,AKR1B1,ALAD,ALDH2,ALOX5,ALOX5AP,ANGPT1,ANGPTL4,ANPEP,APLN,APOA1,APOC2,APOC4,APOE,APOL1,AQP1,AQP3,AQP9,AR,ARG1,ARL6IP5,ATF3,ATP1A1,ATP2A2,ATP2B1,ATP2B4,AVPR1A,BAX,BCL2A1,BDKRB1,BDKRB2,BDNF,BGLAP,BLVRA,BMP2,BMP4,BMPR1A,C3,C5,CA2,CALCA,CARD8,CAT,CAV1,CAVIN3,CBR3,CCK,CCL11,CCL17,CCL18,CCL2,CCL5,CCN2,CCN3,CCN4,CCND1,CCR2,CCR3,CCR5,CD14,CD200,CD247,CD28,CD36,CD40,CD59,CD69,CDC42,CDH13,CDK5R1,CDKN2A,CDKN2B-AS1,CEBPD,CERS6,CFB,CFTR,CHI3L1,CIITA,CKM,CLU,CNP,CNR2,COL1A1,COL1A2,COL3A1,CPT1A,CPT1B,CPT2,CRCP,CRHR1,CRP,CRY1,CSF2,CTLA4,CTNNB1,CX3CR1,CXCL12,CXCL13,CXCL5,CXCL8,CXCR2,CXCR4,CYBA,CYBB,CYP11A1,CYP11B1,CYP17A1,CYP19A1,CYP1A1,CYP1B1,CYP27B1,CYP2C8,CYP2E1,CYP7A1,DCD,DIO1,DPP4,EDN1,EDNRB,EFNB2,EGFR,EGLN3,ENG,EPO,ERBB2,ERCC1,ERVFRD-1,ESR1,ETV5,F11R,F2RL1,FABP1,FADS1,FAS,FCGR2B,FGF10,FGF5,FGFR1,FGFR2,FGG,FLT1,FLT4,FN1,FOS,FOXF1,FOXO1,FOXP3,FPR1,FUT4,FUT7,FYN,GAS5,GATA2,GCH1,GCLC,GCLM,GDF15,GDNF,GHR,GHRL,GJA1,GNAI2,GOSR2,GP1BA,GPRC5B,GPX1,GPX4,GRIA1,GSTA1,GSTM2,GSTP1,H19,HAS2,HAS3,HBEGF,HDAC9,HES1,HGF,HIF1A,HLA-A,HLA-B,HLA-DRA,HMGB1,HMGCR,HMOX1,HNF4A,HP,HSD11B1,HSD17B7,HSD3B2,HSPA1A/HSPA1B,HSPA4,HSPA8,HSPD1,HSPG2,ICAM1,ICOS,ID3,IDE,IDH2,IFIH1,IFNG,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IKBKE,IL10,IL10RA,IL12A,IL12B,IL12RB1,IL13,IL13RA2,IL15,IL15RA,IL16,IL17A,IL18,IL18R1,IL1A,IL1B,IL1F10,IL1R1,IL1RL1,IL1RN,IL2,IL21R,IL22,IL23A,IL24,IL2RA,IL3,IL33,IL4,IL4I1,IL4R,IL5,IL6,IL7R,IL9,INS,INSIG1,INSR,IRF5,IRS1,IRS2,ITGA2,ITGA4,ITGAM,ITGAV,ITGB1,ITGB2,ITGB3,ITGB6,ITGB8,ITPR2,JAG1,JUN,KCNH2,KCNJ1,KDR,KIT,KL,KLB,KLF5,KLF7,KLRB1,KYNU,LAMA3,LBP,LCAT,LCN2,LDHA,LDLR,LEP,LGR5,LHCGR,LIPE,LOX,LPL,LRP6,LSS,LTBP2,LTC4S,MAEA,MAGI1,MAPK1,MAPKAP1,MBL2,MECOM,MEF2C,MEFV,MET,MGP,MIF,mir-146,mir-27,MITF,MMP1,MMP12,MMP14,MMP2,MMP3,MMP7,MMP9,MOB3C,MPO,MSR1,MT-CO2,MT-CYB,MTTP,MYH7,MYH9,MYLK,MYOD1,NAMPT,NCAM1,NCF2,NCOA1,NCOR2,NFATC1,NFKB1,NFKB2,NFKBIA,NFKBIZ,NLRP3,NNMT,NOD2,NOS1,NOS2,NOS3,NOTCH1,NOX1,NOX4,NPHS1,NPPA,NPPB,NQO1,NR0B2,NR1H3,NR1H4,NR1I2,NR3C1,NR4A3,NUCB2,OAS3,OASL,OLFML2B,OLR1,OPRM1,OPTN,OSBPL10,OSMR,PAPPA,PARP1,PCK1,PCSK6,PCSK9,PDGFRA,PDX1,PECAM1,PER2,PI3,PIK3C2B,PIK3CG,PLA2G3,PLA2G4C,PLA2G5,PLAT,PLAUR,PLIN1,PML,POMC,POSTN,POU2F1,PPARA,PPARD,PPARG,PPARGC1A,PRKCA,PRL,PSEN1,PSMB8,PSMB9,PTEN,PTGES,PTGFR,PTGS1,PTGS2,PTPN11,PTPRC,RAC1,RAPGEF5,RARA,REL,RELA,RETN,RGS14,RGS2,RGS20,RGS4,RGS5,RND1,RORA,RXRA,SAA1,SCARB1,SCNN1A,SCNN1B,SCNN1G,SDC4,SELE,SELL,SELP,SELPLG,SERPINA3,SERPINB1,SERPINE1,SERPINE2,SFTPB,SGK1,SHBG,SHH,SIRT1,SIRT5,SLC10A1,SLC11A1,SLC12A1,SLC14A1,SLC16A1,SLC19A1,SLC20A1,SLC22A2,SLC22A4,SLC22A5,SLC2A1,SLC2A2,SLC2A4,SLC2A9,SLC3A1,SLC4A1,SLC5A1,SLC6A4,SL	1039 (16)
IL1B	cytokine	6,52E-118	A4GALT,ABCB11,ABCC2,ABCG2,ACTA2,ADM,ADORA2B,ADRB2,AGER,AGTR1,AKR1B1,ALOX15,ALPL,ANGPT1,ANGPTL4,APOB,APOC2,APOE,AQP4,ARG1,ARL6IP5,ASIC3,ATF3,ATP1A1,ATP2A2,AVPR1A,BAX,BCL2A1,BDKRB1,BGLAP,BMP2,BMP4,C3,CALCA,CASR,CAT,CCKAR,CCL11,CCL17,CCL2,CCL5,CCL8,CCN2,CCR2,CCR5,CD14,CD40,CD69,CDKN2B-AS1,CEBPD,CFB,CFTR,CHI3L1,CIITA,CNR2,COL1A1,CPB2,CRHR1,CRP,CSF2,CTNNB1,CX3CR1,CXCL12,CXCL13,CXCL5,CXCL8,CXCR4,CYBA,CYBB,CYP11A1,CYP11B2,CYP19A1,CYP1A1,CYP1A2,CYP27B1,CYP2C19,CYP2C9,CYP2E1,CYP3A4,CYP3A5,CYP7A1,DBP,DIO1,DPP4,EDN1,EGLN3,ELN,ENG,ENPP1,EP300,EPAS1,EPO,ERBB2,ESR1,F13A1,F2RL1,FABP1,FAS,FCGR2B,FGB,FGFR2,FGFR3,FGG,FKBP5,FLT1,FMR1,FN1,FOS,FOXO1,FURIN,FUT7,G6PD,GAS5,GAS6,GCH1,GCK,GCLC,GDF15,GHR,GJA1,GLA,GNAS,GNRH1,GRIA1,GSTA1,GYS1,H19,HAMP,HAS2,HBEGF,HES1,HGF,HIF1A,HLA-A,HLA-DRA,HMGA1,HMGB1,HMOX1,HNF1B,HNF4A,HP,HSD11B1,HSPA1A/HSPA1B,HSPA1L,HSPG2,ICAM1,ID3,IFNG,IGF1,IGFBP1,IGFBP3,IKBKE,IL10,IL10RA,IL12A,IL12B,IL15,IL15RA,IL16,IL17A,IL18,IL18R1,IL18RAP,IL1A,IL1B,IL1R1,IL1RAP,IL1RL1,IL1RN,IL2,IL22,IL23A,IL23R,IL24,IL2RA,IL33,IL4I1,IL6,IL6R,IL9,INS,INSR,IRAK1,IRS1,IRS2,ITGAM,ITGAV,ITGB1,ITGB3,ITGB8,JUN,KCNH2,KCNJ1,KDR,KLK2,KLRB1,LAMA3,LBP,LCN2,LDHA,LDLR,LEP,LOX,LTA,MEF2C,MEFV,MFAP2,MIF,mir-146,MMP1,MMP12,MMP14,MMP2,MMP3,MMP7,MMP9,MT-CO2,MYLK,MYOD1,NAMPT,NFKB1,NFKB2,NFKBIA,NFKBIZ,NOS1,NOS2,NOS3,NOTCH1,NOX1,NPPA,NPY,NQO1,NR0B2,NR1H3,NR1H4,NR4A3,NTRK1,OLR1,OSMR,PAPPA,PCSK1,PCSK2,PCSK6,PDGFRA,PDX1,PFKP,PI3,PLA2G3,PLA2G5,PLAT,POMC,POSTN,PPARA,PPARG,PPARGC1A,PSEN1,PSMB8,PSMB9,PTGDS,PTGES,PTGFR,PTGIS,PTGS1,PTGS2,RAC2,RARA,RARB,REL,RELA,REN,RORA,RXRA,SAA1,SCARB1,SCNN1A,SCNN1B,SCNN1G,SDC4,SELE,SERPINA3,SERPINE1,SHH,SIRT1,SLC10A1,SLC10A2,SLC12A1,SLC14A1,SLC14A2,SLC20A1,SLC2A1,SLC2A2,SLC2A4,SLC2A9,SLC3A1,SLC6A4,SLC9A3,SLCO1B1,SNAP25,SOCS1,SOCS3,SOD2,SPP1,SREBF1,STAT3,STAT4,STAT5A,TERC,TFF1,TFPI2,TGFB1,TGFB3,TGFBR2,THBD,THBS1,TIMP1,TIMP2,TIMP3,TIMP4,TLR2,TLR4,TLR7,TLR8,TNF,TNFAIP3,TNFRSF11A,TNFRSF11B,TNFRSF1B,TNFSF10,TNFSF11,TRAF1,TRH,TSLP,TXNIP,UAP1,UCP3,UGT1A1,VCAM1,VCAN,VDR,VEGFA,VEGFC,WNT5A,XDH,XYLT1,ZFP36	925 (16)
TGFB1	growth factor	2,86E-117	ABCA1,ABCC2,ABCG2,ACAA2,ACE,ACSM5,ACSS1,ACTA2,ACTC1,ACVRL1,ADIPOQ,ADM,ADORA1,ADORA2B,ADRA1D,ADRA2A,AFP,AGTR2,AHR,AKT1,ALDH2,ALOX12,ALOX15,ALOX5,ALOX5AP,ANGPT1,ANGPTL4,ANPEP,AOPEP,APLN,APLNR,APOB,APOC2,APOE,AQP1,AQP11,AQP8,AQP9,ARG1,ATM,AXL,BAX,BDKRB2,BDNF,BGLAP,BIN1,BMP2,BMP4,BMP6,BMP7,C2,C3,C5,CALCA,CALCR,CALD1,CAT,CAV1,CAV2,CBR3,CCL11,CCL18,CCL2,CCL23,CCL5,CCL8,CCN2,CCN3,CCN4,CCND1,CCR2,CCR3,CCR5,CCT2,CD14,CD28,CD34,CD36,CD40,CD46,CD59,CD69,CDH4,CDK5R1,CDKN2A,CDKN2B,CELSR2,CFB,CFH,CHI3L1,CIITA,CKM,CLU,COL18A1,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,CORIN,CPT1B,CRP,CSF2,CST3,CTLA4,CTNNB1,CTSH,CX3CR1,CXADR,CXCL12,CXCL13,CXCL8,CXCR2,CXCR4,CYB561,CYBA,CYBB,CYP11A1,CYP11B1,CYP11B2,CYP17A1,CYP19A1,CYP21A2,CYP27B1,CYP3A7,CYP7A1,DACH1,DBP,DDR2,DES,ECE1,EDN1,EDNRA,EDNRB,EGF,EIF4H,ELN,EMILIN1,ENG,ENPP1,ESR2,EXT2,F12,F13A1,F2,F2R,F2RL1,F5,FAS,FBLN2,FBN1,FGA,FGB,FGF10,FGF21,FGF5,FGF9,FGFBP1,FGFR1,FGFR2,FGG,FLT1,FN1,FOS,FOXC1,FOXO1,FOXO3,FOXP3,FURIN,FUT7,FYN,GAS7,GATM,GCLC,GDF15,GDNF,GJA1,GLCE,GNA14,GNAI2,GNAS,GNRH1,GPER1,GPR83,GPRC5B,GRHL1,GRIA1,GSN,HABP2,HAMP,HAS2,HAS3,HBEGF,HDAC9,HEBP1,HES1,HGF,HIF1A,HLA-DQA1,HLA-DQB1,HLA-DRB5,HMGA1,HMGB1,HMOX1,HMOX2,HNF1A,HNF4A,HSD3B2,HSPA1A/HSPA1B,HSPB2,HSPG2,HTR2B,HTRA1,ICAM1,ID3,IFI30,IFIH1,IFNG,IGF1,IGF2,IGFBP3,IL10,IL10RA,IL12A,IL12B,IL13,IL13RA2,IL15,IL17A,IL18,IL1A,IL1B,IL1R1,IL1RL1,IL1RN,IL2,IL22,IL23A,IL23R,IL2RA,IL2RB,IL33,IL4,IL4R,IL5,IL6,IL6R,IL9,IRS1,ITGA2,ITGA4,ITGAM,ITGAV,ITGB1,ITGB2,ITGB3,ITGB6,ITIH3,ITPK1,ITPR2,JAG1,JUN,KCNMB1,KDM5B,KDR,KIT,KLRB1,KNG1,KRAS,LCAT,LCN2,LDHA,LDLR,LEP,let-7,LHCGR,LOX,LOXL2,LPL,LTA,LTA4H,LTBP2,LTC4S,Ly6a (includes others),MAF,MAOA,MAP4,MAPK1,MAPK3,MAPKAPK2,MEF2C,MEFV,MET,MFAP2,MGAT5,MGP,MIA3,mir-143,mir-146,mir-196,mir-217,mir-224,mir-27,MITF,MLXIP,MLXIPL,MMP1,MMP12,MMP14,MMP2,MMP3,MMP7,MMP9,MS4A2,MSMO1,MSR1,MTRR,MYB,MYH7,MYH9,MYL3,MYLK,MYOD1,NAMPT,NCAM1,NCF2,NCOA3,NCR3,NDST1,NEGR1,NFATC1,NFKBIA,NLRP3,NNMT,NOS2,NOS3,NOTCH1,NOTCH3,NOX4,NPAS2,NPPA,NPPB,NPR1,NR1H3,NR4A3,NUCB2,OLR1,OSTF1,P2RX6,P2RY1,PAPPA,PBX1,PDE4D,PDGFRA,PDGFRB,PDLIM5,PECAM1,PFKP,PHACTR1,PLAGL1,PLAT,PLAUR,PML,PNMT,POMC,POSTN,PPARD,PPARG,PPARGC1A,PRC1,PRKCA,PRKCG,PRL,PTEN,PTGDS,PTGER2,PTGER4,PTGES,PTGS1,PTGS2,PTH1R,PTK2B,PTPRC,RAC1,RALB,RARA,RARG,RASA1,RASGRP3,RETN,RHOC,RND1,RORA,RUNX1,RXRA,S100A4,SCARB1,SDC4,SELE,SELENBP1,SELP,SELPLG,SERPINA1,SERPINA3,SERPINB1,SERPINE1,SERPINE2,SERTAD1,SFTPB,SGK1,SHMT1,SLC13A3,SLC20A1,SLC23A2,SLC25A14,SLC2A1,SLC2A3,SLC39A8,SLC4A1,SLC4A2,SLC7A1,SMAD2,SMAD3,SMAD4,SMAD6,SMOC2,SMTN,SNRNP70,SOCS1,SOCS3,SOD2,SOD3,SPP1,SRM,SRR,SRSF2,SRSF3,SRSF5,ST3GAL4,STAT3,STAT5A,STAT5B,STC2,TBX2,TBX3,TCN2,TERT,TFPI,TGFA,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,TGFBR3,THBD,THBS1,THBS2,THBS4,TIMP1,TIMP	1035 (18)

IFNG	cytokine	1,80E-103	ABCA1,ABCB1,ABCC1,ACE,ACSS1,ACTA2,ADAMTS8,ADAMTS9,ADGRG1,ADIPOQ,ADM,ADORA1,ADORA2A,ADORA2B,ADRA2A,AGER,AGT,AGTR1,AHCY,AHR,ALDH1L1,ALOX12,ALOX15,ALOX5AP,ALPL,ANGPTL4,APOL1,AQP1,AQP11,AQP9,ARG1,ARL6IP5,ATF3,ATP1A1,ATP1B1,ATP2A2,AVPR1A,BAX,BCAN,BCL2A1,BDNF,BMP6,BRCA2,C2,C3,C4A/C4B,CALCA,CAT,CAV1,CCKAR,CCL11,CCL17,CCL18,CCL2,CCL23,CCL25,CCL5,CCL8,CCN2,CCND1,CCR2,CCR3,CCR5,CD14,CD2,CD200,CD36,CD40,CDH13,CDK5R1,CDKN2A,CDKN2B,CDKN2B-AS1,CEBPD,CELSR1,CELSR2,CERS6,CFB,CFTR,CIITA,CNR1,COL1A1,COL1A2,CSF2,CSK,CTNNB1,CTSH,CX3CR1,CXADR,CXCL12,CXCL5,CXCL8,CXCR4,CYB561,CYBA,CYBB,CYP11A1,CYP1A2,CYP24A1,CYP2C9,CYP2E1,CYP3A4,DBP,DDR2,DIO1,DPP4,DUOX2,ECE1,EDN1,EDNRA,EDNRB,EFNB2,EGF,EGLN3,ELN,ERAP1,ERAP2,ERBB2,F11R,F2R,F2RL1,FAAH,FAS,FCGR2A,FCGR2B,FGF1,FGG,FKBP5,FLT1,FLT4,FN1,FOS,FOXO1,FOXP3,FURIN,GAS5,GAS6,GCH1,GCK,GDF15,GDNF,GJA1,GJA5,GLA,GNA14,GNAI2,GNAS,GPER1,GPR83,GPRC5B,GRIA1,GRK2,GSTP1,HAS2,HBEGF,HDAC9,HIF1A,HLA-A,HLA-B,HLA-C,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,HLA-G,HMGA1,HMGB1,HMGCR,HMOX1,HSPA1A/HSPA1B,HSPA1L,HSPA8,HSPD1,HSPG2,HTRA1,ICAM1,IDE,IFI30,IFIH1,IFNG,IFNK,IGF1,IGF1R,IKBKE,IL10,IL10RA,IL12A,IL12B,IL12RB1,IL12RB2,IL13,IL13RA2,IL15,IL15RA,IL17A,IL17RA,IL18,IL18R1,IL18RAP,IL1A,IL1B,IL1R1,IL1RL1,IL1RN,IL2,IL23A,IL23R,IL2RA,IL4,IL4I1,IL4R,IL5,IL6,IL6R,IL7R,IL9,INS,INSR,IRAK1,IREB2,IRF5,IRS1,IRS2,ITGA4,ITGAM,ITGAV,ITGB1,ITGB2,ITGB3,ITPK1,JAG1,JAK2,JUN,KCNJ1,KCNMA1,KCTD7,KDR,KRAS,KYNU,LAT2,LCN2,LDHA,LEP,LIMK1,LOX,LPL,LTA,Ly6a (includes others),MAX,MEFV,MIF,mir-146,MITF,MMP1,MMP12,MMP2,MMP3,MMP9,MRAS,MSR1,MYB,MYH9,MYOD1,NAMPT,NCAM1,NCF2,NCR3,NF1,NFE2L3,NFKB1,NFKB2,NFKBIA,NFKBIZ,NLRP3,NOD2,NOS1,NOS2,NOS3,NOTCH1,NOTCH3,NOX1,NOX4,NPY2R,NQO1,NTRK1,OAS3,OASL,OPTN,P2RY1,PAM,PAPPA,PCK1,PCSK1,PCSK2,PDX1,PECAM1,PHACTR1,PLA2G5,PLA2G7,PLAUR,PML,POMC,PPARA,PPARD,PPARG,PPARGC1A,PRKCA,PRKCQ,PRL,PRSS8,PSMA4,PSMA6,PSMB8,PSMB9,PTGES,PTGS2,PTN,PTPN1,PTPN11,RAC2,RELA,SBF1,SCARB1,SCNN1A,SCNN1B,SCNN1G,SDC4,SELE,SELL,SELP,SERPINA1,SERPINE1,SHH,SLC11A1,SLC12A1,SLC12A2,SLC14A1,SLC14A2,SLC2A1,SLC2A2,SLC2A4,SLC3A1,SLC4A2,SLC4A4,SLC6A6,SLC8A1,SLC9A3,SLPI,SMAD1,SMAD3,SMAD4,SMTN,SNAP25,SOCS1,SOCS3,SOD2,SOD3,SORT1,SPP1,SREBF1,SREBF2,STAT3,STAT4,TAP1,TBXAS1,TCF7L2,TERC,TERT,TFRC,TGFB1,TGFB2,TGFBR1,TGFBR2,TGFBR3,THBS1,TIMP1,TIMP3,TIMP4,TLR2,TLR4,TLR5,TLR6,TLR7,TLR8,TLR9,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFSF10,TNFSF11,TNFSF13,TP53,TP73,TRH,TSHR,TXNIP,TYRP1,VCAM1,VDR,VEGFA,VEGFC,VIPR1,WARS,WNT5A,XCL1,ZFP36,ZPR1	932 (15)
SP1	transcription reg	9,20E-102	ABCA1,ABCB1,ABCC8,ACSS1,ACTA2,ACVRL1,ADA,ADD3,ADRA1B,ADRA1D,AGER,AGTR1,AKAP12,ALOX12,ALOX5,ALPL,APOA1,APOC3,APOE,AR,ATF3,ATM,ATP2A2,BAX,BDNF,BGLAP,BMP4,BMP7,CAD,CAT,CAV1,CBS/CBSL,CCL2,CCL5,CCN2,CCND1,CD28,CD40,CD59,CDK6,CDKN2A,CDKN2B,CEBPD,CES1,CETP,CHGA,CHI3L1,CHRNA3,CIITA,COL1A1,COL1A2,CRYBB3,CTH,CXCL12,CXCL5,CXCL8,CXCR4,CYP11A1,CYP17A1,CYP19A1,CYP1B1,CYP21A2,DBH,DHFR,DRD1,DRD2,EGFR,ELANE,ENG,ESR1,F10,F2R,F7,FAS,FDX1,FES,FGF10,FGFR1,FLT1,FN1,FOLR2,FOS,FOXP3,FYN,GDF15,GHR,GJA1,GNAI2,GNAS,GPX4,GRIA1,GSS,HAS2,HBB,HBEGF,HGF,HIF1A,HMGA1,HMGCR,HMOX1,HNF4A,HSD11B2,HSD17B7,HSD3B1,ICAM1,IFNG,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IL10,IL12A,IL12RB2,IL15,IL1A,IL1B,IL21R,IL2RB,IL4R,INSR,ITGA2,ITGAM,ITGAV,ITGB3,JUN,KDR,KISS1,KIT,LCAT,LDLR,LHCGR,LIPA,LPL,MAOA,MET,MFN2,mir-146,mir-27,MMP1,MMP14,MMP2,MMP9,MYH7,MYLK,NCF2,NCOA3,NF1,NFKB1,NFKBIA,NOS1,NOS3,NOX4,NPPA,NPR1,NTRK1,OGG1,P2RX7,PADI4,PARP1,PCK1,PDGFRA,PDGFRB,PGR,PLAUR,PNMT,POU5F1,PPARD,PRKCA,PRKCB,PRKG1,PROCR,PSIP1,PTGER4,PTGS1,PTGS2,PTH1R,PTN,PTPN1,PYY,RARA,RELA,RNLS,SCARB1,SELL,SERPINE1,SERPINE2,SF1,SGK1,SIRT1,SLC11A1,SLC19A1,SLC2A1,SLC2A3,SLC39A8,SLC4A2,SLC4A7,SLC5A1,SLC6A2,SLC7A1,SLC9A3,SMAD3,SNAP25,SNRPN,SOCS1,SOD1,SOD2,SPP1,SPTB,SREBF1,SREBF2,STAT3,TBXA2R,TCF7,TERT,TFF1,TFPI2,TGFB1,TGFB2,TGFBR1,TGFBR2,TGFBR3,THBD,TIMP1,TIMP2,TIMP3,TIMP4,TLR2,TNC,TNF,TNFAIP3,TNFRSF4,TNFSF10,TNFSF11,TNFSF14,TNNC1,TP53,TP73,TRH,TRIB1,TXNRD1,TYMS,UGT1A7 (includes others),VDR,VEGFA,VWF	1163 (24)
LEP	growth factor	1,23E-94	ABCB11,ABCG5,ABCG8,ACAT1,ACTA2,ADGRE1,ADIPOQ,ADRB3,AGRP,ANGPTL4,APOA1,APOA2,APOA4,APOH,APOM,AQP3,AQP9,AR,ATP2A2,BAX,BCL2A1,BDNF,BGLAP,CARTPT,CAV1,CCK,CCL2,CCL5,CCND1,CD14,CD36,CD40,CIDEA,COL1A1,COL3A1,COL4A1,CPS1,CPT1A,CPT1B,CRP,CSF2,CTSL,CYBA,CYBB,CYP11A1,CYP17A1,CYP19A1,CYP24A1,CYP27B1,CYP2C18,CYP2C8,CYP2E1,CYP3A5,CYP4A11,CYP7A1,DLK1,DRD2,EDN1,EPHX2,ERBB2,ESR1,ESR2,FAAH,FABP3,FADS2,FAS,FDX1,FGF21,FGFR1,FGFR2,FLT1,FOS,FOXO3,FOXP3,FTO,GCG,GCK,GCLC,GDNF,GHRL,GHSR,GNAS,GNRH1,GPX1,GRIA1,HES1,HMGCR,ICAM1,IFNG,IGF1,IGFBP3,IL10,IL12A,IL12B,IL13,IL1B,IL1R1,IL1RN,IL2,IL4,IL5,IL6,INS,IRS1,IRS2,ITGAM,JAK2,JUN,KCNB1,KISS1,KLB,LDLR,LEP,LEPR,LIPA,LIPC,LIPE,LPL,LTC4S,mir-143,MLX,MLXIPL,MMP1,MMP12,MMP14,MMP2,MMP3,MMP7,MSMO1,MT-CYB,MT-ND1,MT-ND4,MYH7,MYOD1,NAMPT,NCF2,NOS1,NOS2,NOS3,NOTCH1,NPPA,NPPC,NPR1,NPR2,NPY,NPY1R,NR3C1,OPLAH,P2RX4,PCK1,PCSK1,PCSK2,PECAM1,PER2,PGR,PLAT,PLIN1,POMC,PPARA,PPARG,PPARGC1A,PRDM16,PRL,PTGS2,PTPN1,RAC1,RETN,SCARB1,SELE,SELP,SERPINE1,SIM1,SLC13A2,SLC15A1,SLC27A4,SLC2A2,SLC2A4,SNAP25,SOCS3,SOD1,SOD2,SPP1,SREBF1,SREBF2,SST,STAT3,STEAP4,TERT,TFF1,TGFB1,TH,THBS1,TIMP1,TIMP3,TNF,TNFRSF11B,TNFRSF1A,TNFSF10,TNFSF11,TP53,TRH,TRPV1,UCP1,UCP2,UCP3,UTS2,UTS2R,VCAM1,VEGFA,WNT5A,ZFP36	1031 (21)
AGT	growth factor	1,75E-85	ACAT2,ACE,ACE2,ACTA2,ADD3,ADGRE1,ADH1C,ADIPOQ,ADIPOR1,ADM,ADORA2B,AGER,AGT,AGTR1,AGTR2,ALOX12,ALOX15,ANGPT1,APLN,ATF3,ATP1A1,ATP1B1,ATP2B1,BAX,BDKRB2,BDNF,BMP6,BRCA1,CACNA1C,CAT,CAV1,CAV3,CCL2,CCL5,CCL8,CCN2,CCND1,CD36,CDH13,CDKN2A,COL1A1,COL1A2,COL3A1,COL4A1,CR1,CRP,CTF1,CXCL8,CYBA,CYBB,CYP11B1,CYP11B2,CYP17A1,CYP19A1,CYP2C9,CYP2E1,CYP2J2,CYP4A11,DDAH2,DHFR,EDN1,EDNRA,EDNRB,EFNB2,EGFR,ENG,FDFT1,FDX1,FLT1,FN1,FOS,FOXO3,GALNT13,GCH1,GJA1,GRK5,GSS,GSTM5,GSTP1,HAS2,HBEGF,HES1,HGF,HIF1A,HMGCR,HMOX1,HSD3B1,HSD3B2,HSPA1A/HSPA1B,HSPG2,ICAM1,ID3,IFNG,IGF1,IGF1R,IGFBP3,IL13,IL15,IL18,IL18R1,IL1B,IL6,IL6ST,INSR,ITGA2,ITGAV,ITGB1,ITGB3,ITPR2,JAG1,JUN,KL,KLF5,KRAS,LDLR,LEP,LEPR,LSS,LTA,MAS1,MIF,MMP1,MMP2,MMP9,MSMO1,MSR1,MYB,MYH7,NAMPT,NCF2,NFKB2,NOS1,NOS2,NOS3,NOTCH3,NOX1,NOX4,NPHS1,NPPA,NPPB,NPR1,NPR3,NPY,NRG1,OLR1,PARP1,PECAM1,PIK3R1,POSTN,PPARG,PPARGC1A,PSMB8,PTEN,PTGFR,PTGS1,PTGS2,RAC1,RELA,REN,RGS2,SCARB1,SCNN1A,SELE,SELL,SEMA6A,SERPINE1,SGCD,SGK1,SLC12A1,SLC14A2,SLC2A1,SLC6A2,SLC8A1,SLC9A1,SOCS1,SOCS3,SOD2,SOD3,SOX6,SPP1,TBX2,TBX5,TFRC,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,TH,THBD,TIMP1,TNF,TNFRSF1B,TNFSF11,TP53,TRPM7,TTN,TXNIP,UCP2,VCAM1,VEGFA,VEGFC,WNK4,ZFP36	1040 (17)
[Nle4, D-Phe7] -	biologic drug	3,31E-03	PPARD,PPARG,UCP1	370 (7)
IL6	cytokine	1,67E-83	ABCA1,ABCB11,ABCC1,ABCC2,ABCG2,ACVR2A,ACVRL1,ADGRE1,ADM,ADORA2B,AFP,AGRP,AGT,AHR,AKT1,ANG,ANGPT1,ANPEP,APOA1,APOB,APOE,AQP4,ARG1,ARL4C,ATF3,ATP2A2,BAX,BDNF,BMP2,BMP6,C3,CALCA,CALCR,CCK,CCL11,CCL2,CCL5,CCN2,CCND1,CCR2,CCR3,CCR5,CD14,CD36,CD40,CD46,CDKN2A,CDKN2B,CEBPD,CES1,CFH,CIITA,CLU,COL1A1,COL3A1,CPB2,CRP,CSF2,CST3,CTNNB1,CX3CR1,CXCL13,CXCL5,CXCL8,CXCR4,CYBB,CYP19A1,CYP1A1,CYP1A2,CYP1B1,CYP2C8,CYP2C9,CYP2E1,CYP3A4,CYP3A5,DHFR,DIO1,EGFR,EGLN3,ELANE,EPHA4,EPO,ESR2,F12,FAS,FGA,FGB,FGG,FN1,FOS,FOXP3,GCG,GCH1,GHRH,GLRX,GP1BA,GRK2,GSTA1,HAMP,HFE,HGF,HIF1A,HJV,HLA-A,HLA-DQA1,HLA-DRB5,HMOX1,HP,ICAM1,ICOS,IFNG,IGF1,IGF2,IGFBP1,IGFBP3,IKBKE,IL10,IL12A,IL12B,IL13,IL15,IL17A,IL1R1,IL1RL1,IL1RN,IL2,IL22,IL23A,IL23R,IL4,IL4R,IL5,IL6,IL6R,IL6ST,IL7R,IL9,IRS1,ITGAM,ITGAV,ITGB1,ITGB3,ITLN1,JAK2,JUN,KDR,KISS1,KIT,KLRB1,LBP,LCAT,LCN2,LDLR,LEP,let-7,LHCGR,LIG1,LIN28A,LPA,LPL,LRP6,LTF,LY86,MAF,MEF2D,MET,MMP1,MMP12,MMP2,MMP3,MMP7,MMP9,MPO,MRAS,MSR1,MTTP,MYB,MYOD1,NAMPT,NCF2,NFKB1,NFKBIA,NOS2,NOS3,NOTCH1,NPHP1,NPY,NR1H4,NR1I2,NR3C1,NUCB2,OPRM1,PCSK1,PECAM1,PLAT,PLG,POMC,PON1,POU2F1,POU5F1,PPARG,PSMB8,PSMB9,PTGER4,PTGES,PTGFR,PTGS2,PTPRC,RASA1,RET,RORA,SAA1,SCNN1A,SERPINA1,SERPINA3,SERPINE1,SFTPB,SGK1,SHH,SLC10A1,SLC12A2,SLC14A1,SLC14A2,SLC2A2,SLC2A4,SOCS1,SOCS3,SOD2,SPP1,SST,STAT3,STAT4,STEAP4,TAP1,TBXAS1,TERT,TF,TFR2,TFRC,TGFB1,TH,THBS1,TIMP1,TLR2,TLR4,TLR5,TLR6,TLR7,TLR8,TLR9,TNC,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFSF10,TNFSF11,TP53,TRH,TTR,UCP1,VCAM1,VEGFA,VIP,WARS,WNT5A,XPNPEP2	926 (15)

STAT3	transcription reg	3,62E-75	ACTA2,ADIPOQ,ADM,AGRP,AGT,AHR,AKT1,ALOX15,ANGPTL4,APOA4,ARG1,C5,CAT,CCL11,CCL17,CCL2,CCL5,CCN2,CCND1,CCR5,CD226,CD40,CD46,CDKN2A,CDKN2B,CEBPD,CFB,CHI3L1,CIITA,COL1A1,COL1A2,COL3A1,CRP,CSF2,CTF1,CTLA4,CTSL,CXCL13,CXCL8,CXCR2,CXCR4,DPP4,EDN1,EPAS1,ESR1,ESR2,FAS,FGA,FGB,FGG,FLT1,FN1,FOS,FOXP3,FUT4,GJA1,HAMP,HAS2,HAVCR1,HBB,HBG1,HES5,HGF,HIF1A,HLA-A,HLA-DQA1,HLA-DRB5,HMOX1,HNF4A,HP,HTR2A,ICAM1,ICOS,IFI30,IFIH1,IFNG,IGF1R,IGFBP1,IKBKE,IL10,IL12B,IL12RB1,IL13,IL13RA2,IL17A,IL18R1,IL1B,IL1R1,IL1RN,IL2,IL22,IL23A,IL23R,IL2RA,IL2RB,IL4,IL4R,IL5,IL6,IL6R,IL6ST,IL9,IL9R,IRF5,ITGAM,ITGAV,ITGB1,ITGB2,ITGB6,JAG1,JAK2,KDR,LBP,LCAT,LDHA,LEP,LEPR,LOX,LRP2,LTA,LTF,MAF,MAP2K5,MGAT5,MITF,MMP12,MMP2,MMP3,MMP7,MMP9,MRAS,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6,MYB,MYH7,MYOD1,NAMPT,NFKB1,NFKBIZ,NOS2,NOS3,NOTCH1,NOTCH3,NOX1,NPPA,NPY,OAS3,OASL,PAX5,PCK1,PCSK1,PCSK9,PECAM1,PGR,PLAUR,PML,POMC,POU2F1,POU5F1,PPARGC1A,PROCR,PSIP1,PSMB8,PSMB9,PTGS2,PTN,PTPN2,RBPJ,REG3A,REN,RET,RNLS,RORA,RUNX1,SAA1,SERPINA1,SERPINA3,SERPINB1,SERPINE1,SERPINE2,SFTPB,SGK1,SHH,SLC2A1,SLC9A3,SMAD6,SMAD9,SOCS1,SOCS3,SOD2,SOX6,SREBF1,STAT3,STC2,TAP1,TERT,TFPI2,TGFB1,THBD,THBS1,TIMP1,TNF,TNFRSF1B,TNFSF10,TNFSF11,TP53,TRH,VCAN,VEGFA,VIP,WARS,WNT5A,ZFP36	950 (15)
abatacept	biologic drug	5,14E-05	ICOS,IFNG,IL17A,IL2,SELL,TNFRSF4	348 (10)
NFkB (complex)	complex	1,88E-74	ABCB1,ADAMTS9,ADGRE1,ADM,ADORA2B,ADRA2A,ADRA2C,AGER,AGT,AHR,ALDH1B1,APOE,AQP1,ATF3,ATP2A2,ATP6AP2,BAX,BCL11A,BCL2A1,BDNF,BLVRA,BMP2,C3,CARD8,CAV3,CBR3,CCK,CCKAR,CCL11,CCL17,CCL2,CCL5,CCL8,CCN2,CCND1,CCR2,CD36,CD40,CD69,CEBPD,CETP,CFB,CFTR,CIITA,CLU,COL18A1,COL1A2,CRHR1,CRP,CSF2,CTNNB1,CXCL12,CXCL5,CXCL8,CXCR4,CYBB,CYP3A4,CYP3A5,DBP,DIO1,DRD2,EDN1,EDNRB,EGFR,ENPP1,EPAS1,ERAP1,ERAP2,ERBB2,F2RL1,FAS,FGF1,FGF5,FGG,FN1,FOS,FOXF1,FOXP3,GAS6,GCH1,GCLC,GDF15,GDNF,GLA,GNAS,GRK5,HAMP,HAS2,HDAC9,HES5,HGFAC,HIF1A,HIF3A,HLA-A,HMOX1,HNF4A,HSPA1L,ICAM1,ICOS,IFNG,IFNK,IKBKE,IL10,IL10RA,IL12A,IL12B,IL13,IL13RA2,IL15,IL15RA,IL17A,IL18,IL1A,IL1B,IL1RN,IL2,IL22,IL23A,IL24,IL2RA,IL4,IL5,IL6,IL7R,ITGAM,ITGAV,ITGB1,ITGB8,JAG1,JUN,KDR,KIT,KYNU,LCN2,LHCGR,LSP1,LTA,LTC4S,MBL2,mir-146,MMP1,MMP2,MMP3,MMP9,MT-CO2,MYLK,NAMPT,NCAM1,NCF2,NFKB1,NFKB2,NFKBIA,NFKBIZ,NOS1,NOS2,NOTCH1,NPPA,NPPB,OLR1,OPRM1,P2RY2,PDX1,PECAM1,PPARA,PPARG,PSMB9,PTGES,PTGS2,RBPJ,REL,RELA,RUNX1,SAA1,SDC4,SELE,SELPLG,SERPINA3,SERPINE1,SFRP2,SHH,SLC2A1,SLC2A2,SLC2A4,SLC2A5,SLC3A1,SLC7A1,SLIT2,SLPI,SMAD3,SOCS1,SOCS3,SOD2,SOD3,SPP1,STAT4,STAT5A,TAP1,TERT,TFPI2,TFRC,TGFB1,TGFB3,TIMP1,TIMP2,TLR2,TLR4,TNF,TNFAIP3,TNFRSF11B,TNFRSF1A,TNFRSF4,TNFSF10,TNFSF11,TNFSF14,TNFSF4,TOLLIP,TP53,TRAF1,TRH,TRIB3,TRPC3,TRPC6,TSLP,VCAM1,VEGFA,VEGFC,WNT5A,ZFP36	981 (15)
JUN	transcription reg	1,49E-71	ABCB1,ACAT2,ACTA2,AFP,AKAP12,AKT1,ALOX12,APOC3,APOE,APOM,AR,ARG1,ATF3,AXL,BAX,BCL2A1,BDNF,BGLAP,BRCA1,C3,C5,CAV1,CCL2,CCL8,CCN2,CCN3,CCND1,CD14,CD247,CDK5R1,CDKN2A,CHGA,CHL1,CLU,COL1A1,COL1A2,COMT,CSF2,CTSL,CXCL5,CXCL8,CYP11A1,CYP11B1,CYP17A1,CYP19A1,CYP1B1,CYP2J2,CYP7A1,DBH,DICER1,DIO2,DROSHA,EDN1,EGFR,EPHX2,ERCC1,EVX1,FAS,FN1,FOLR2,FOS,FOXC1,FOXO3,GAS6,GCLC,GDNF,GIP,GJA1,GNRH1,GNRHR,GSTP1,HES1,HLA-B,HLA-G,HMGA1,HMOX1,HSPB2,ICAM1,IFNG,IGF1R,IGF2R,IGFBP1,IGFBP3,IL10,IL12B,IL1A,IL1B,IL1RL1,IL2,IL23A,IL24,IL2RA,IL6,IL7R,IRS2,ITGAM,ITGAV,ITGB1,ITGB8,JUN,KDR,LBP,LGR5,LHCGR,LMNA,MAF,MAPK3,MET,mir-146,MMP1,MMP12,MMP2,MMP3,MMP7,MMP9,MSR1,MTHFR,MYB,MYOD1,NCAM1,NCF2,NFATC1,NFKBIA,NFKBIZ,NKX2-5,NOS2,NPPA,NQO1,NR0B2,NRAP,PADI4,PCSK1,PGR,PLAGL1,PLAUR,POU5F1,PRL,PTEN,PTGDS,PTGES,PTGS2,PTPRD,PTPRO,PXDN,RARA,RARG,RASA1,RXRA,SAA1,SDK1,SERPINE1,SGK1,SHH,SLC10A2,SLC19A1,SLC6A6,SLC7A1,SLC8A1,SNRNP70,SNRPN,SOCS3,SOD2,SPP1,SRSF2,SST,SULF2,TCF7L2,TF,TFF1,TGFB1,TH,THBS1,TIMP1,TIMP3,TNC,TNF,TNNC1,TP53,TP73,TXN,UCP1,UGT1A3,VAV3,VCAM1,VDR,VEGFA,WNT5A,XPO5,XYLT1,ZFP36	983 (17)
PPARG	ligand-depende	4,13E-67	ABCA1,ABCG2,ACAA1,ACAA2,ACADS,ACTA2,ADIPOQ,ADIPOR2,ADRB2,ADRB3,AGT,ALDH9A1,ALOX12,ANGPTL4,APOA1,APOA2,APOE,AQP3,ARG1,ATP2A2,BAX,BGLAP,BIN1,BRCA1,C3,CA2,CAT,CAV1,CAV2,CCL11,CCL17,CCL2,CCL5,CCN2,CCND1,CD36,CD40,CDK6,CES1,CIDEA,COL1A1,COL1A2,CORIN,CPLX2,CPT1A,CPT1B,CPT2,CTNNB1,CTSL,CXCL14,CXCL5,CXCL8,CYBA,CYP19A1,CYP4A11,DLK1,EDN1,EDN2,EGFR,EGLN3,EPAS1,EPHX1,F11R,FABP1,FABP2,FABP3,FGF1,FGF21,FN1,GATA2,GCK,GDF15,GIPR,GSTA1,HEBP1,HES1,HGF,HMGCR,HMGCS2,HMOX1,HP,ICAM1,IFNG,IGF1,IGFBP1,IGFBP3,IL10,IL12A,IL13,IL17A,IL1B,IL23A,IL2RA,IL33,IL4,IL6,IL9,INS,INSIG1,INSIG2,INSR,IRS1,IRS2,IVD,JUN,KLB,LDLR,LEP,LIPE,LNPEP,LPL,MMP14,MMP9,MPO,MTTP,MYH7,MYOD1,NOS2,NOS3,NOX4,NPPA,NPPB,NR1H3,NR2F2,OLR1,PCK1,PDK4,PDX1,PECAM1,PLA2G3,PLIN1,POU2F1,PPARA,PPARD,PPARG,PPARGC1A,PPIC,PTEN,PTGES,PTGS2,RARB,RBP4,RELA,REN,RETN,SAA1,SCARB1,SCNN1G,SELE,SERPINA1,SERPINE1,SFTPB,SGK1,SHBG,SIRT1,SLC27A4,SLC2A1,SLC2A2,SLC2A4,SLC9A1,SOCS1,SOCS3,SOD1,SORBS1,SPP1,SREBF1,STAT5B,TBXA2R,TBXAS1,TGFBR1,TGFBR2,TKT,TLR4,TNF,TNFSF10,TP53,TRIB3,TSLP,UCP1,UCP2,UCP3,UGT1A7 (includes others),VAMP8,VCAM1,VDR,VEGFA,VNN1,XYLT1	1069 (21)
P38 MAPK	group	6,96E-66	ABCA1,ADIPOQ,AGER,ANGPT1,ANXA5,AQP4,ATF3,BAX,BCL2A1,BDNF,BMP2,CAV1,CAV3,CCK,CCL11,CCL2,CCL5,CCL8,CCN2,CCND1,CD36,CD40,CD46,CD69,CDKN2A,CEBPD,COL3A1,CRHR1,CSF2,CTNNB1,CXCL12,CXCL8,CXCR4,CYBB,CYP19A1,CYP1A1,CYP4F3,DES,DIO2,DIO3,DUOX2,EDN1,EDNRB,FAS,FGF10,FGF21,FN1,FOS,GCG,GCLC,GJA1,HAS2,HIF1A,HMOX1,HP,HTRA1,ICAM1,ID3,IFNG,IL10,IL12A,IL12B,IL13,IL17A,IL1A,IL1B,IL1RL1,IL1RN,IL2,IL23A,IL2RA,IL5,IL6,ITGA4,ITGAM,ITGAV,ITGB2,ITGB3,ITGB8,JUN,KCNB1,KLF5,LAMA3,LDB3,LEP,MAP4,MEF2C,MIF,mir-143,MITF,MMP1,MMP12,MMP2,MMP3,MMP9,MT-CO2,MYBPH,NFATC1,NFKB1,NKX2-5,NOS2,NOS3,NOTCH3,NOX1,NPPA,NPPB,NPR1,NR1H4,NR4A3,PCK1,PDX1,PLA2G7,PLAUR,PML,POSTN,POU5F1,PPARG,PPARGC1A,PTEN,PTGS2,RARA,RASA1,RGS4,RUNX1,RYR1,SCNN1A,SELE,SERPINE1,SGK1,SLC6A12,SLC6A2,SLC8A1,SMAD2,SMAD3,SOCS3,TERT,TGFB1,TH,THBS1,TIMP1,TIMP2,TIMP3,TLR2,TNF,TNFRSF1A,TNFSF10,TNFSF11,TNNC1,TNNT3,TP53,TRIB1,TRPC3,TSLP,UCP1,VCAM1,VDR,VEGFA,VEGFC,VIP,WNT5A,ZFP36	888 (17)
RXRA	ligand-depende	9,06E-63	ABCA1,ABCB1,ABCB11,ABCC2,ABCG2,ADH1B,ADH1C,AHCY,ANGPTL3,APOA1,APOA2,APOA5,APOC3,APOE,APOM,ARL4C,BGLAP,BRCA1,C3,CAT,CCL17,CCND1,CD36,CDKN2A,CEBPD,CETP,CIDEA,CLOCK,COL1A1,COLEC12,CPT1A,CPT1B,CPT2,CTSH,CYP1A2,CYP24A1,CYP27B1,CYP2C9,CYP3A4,CYP3A5,CYP4A11,CYP7A1,DLK1,DRD2,ENG,EPHX1,EPO,FABP1,FABP2,FABP3,FADS2,FGF21,FGG,FOS,GAS6,GCK,GCLC,GHRHR,GPX1,HAS2,HBEGF,HIF1A,HMGCS2,HMOX1,HNF1B,HNF4A,IFNG,IGF1,IGFBP1,IL10,IL12B,IL13,IL1A,IL1B,IL2,IL4,IL5,IL6,INSIG1,KNG1,LCN2,LPL,LTF,MGP,MLXIPL,MMP12,MMP2,MPO,NPPA,NPPB,NPY,NR0B2,NR1H3,NTRK1,OLR1,PCK1,PCSK2,PLIN1,PLTP,PNMT,POU5F1,PPARA,PPARD,PPARG,PRL,PTGDS,RARA,RARB,RARG,REN,RET,RORA,RXRA,RXRG,S100A4,SFTPB,SLC10A1,SLC10A2,SLC2A2,SLC2A4,SORBS1,SPP1,SREBF1,SREBF2,TBXA2R,TCF7,TGFB1,TGFB2,TH,THBD,TNF,TRH,TSLP,TXN,UCP1,UCP3,UGT1A7 (includes others),VCAN,VDR,VEGFA	971 (22)
RELA	transcription reg	3,16E-61	ABCB1,ABCG2,ACTA2,ACTN4,AFP,AGT,AHR,ALOX5AP,APOE,AR,ATP6AP2,BAX,BCL2A1,BLVRA,BMP2,BRCA2,C3,CARD8,CASR,CAV1,CBS/CBSL,CCL11,CCL2,CCL5,CCN2,CCND1,CD14,CD40,CD59,CD69,CDKN2A,CFB,CFTR,CHI3L1,CIITA,COL1A1,COL1A2,CRP,CSF2,CXCL5,CXCL8,CXCR4,CYBB,CYP17A1,CYP19A1,CYP1A1,CYP2C9,CYP3A4,DIO2,EDN1,ELN,EPAS1,ERAP1,ERAP2,ERBB2,FAS,FGF10,FN1,FOS,FOXP3,GCH1,GDF15,GP1BB,GRK5,GSTA1,HAS2,HES1,HIF1A,HLA-B,HMOX1,HNF4A,ICAM1,IFNG,IGF1,IGF1R,IKBKE,IL10,IL12A,IL12B,IL13,IL15RA,IL1A,IL1B,IL1RN,IL2,IL22,IL23A,IL2RA,IL4,IL6,IL7R,IL9,JUN,KIT,LGR5,LTA,LTC4S,MIF,mir-146,MMP1,MMP3,MMP7,MMP9,MT-CYB,MYB,MYOD1,NAMPT,NFATC1,NFKB1,NFKB2,NFKBIA,NOD2,NOS2,NOTCH1,NOX1,NPPB,NR4A3,OLR1,P2RY2,PARP1,PAX2,PCK1,PECAM1,PI3,POU5F1,PPARG,PSMB9,PTEN,PTGDS,PTGES,PTGS2,REG3A,RELA,SAA1,SBF1,SDC4,SELE,SELP,SERPINE2,SHBG,SHH,SLC2A4,SLC2A5,SLCO1B1,SMAD4,SMOC2,SOD2,SREBF1,SREBF2,STAT5A,TAP1,TERT,TFPI2,TGFB1,TLR2,TLR9,TNF,TNFAIP3,TNFRSF11B,TNFRSF4,TP53,TP73,TRAF1,TRPC6,TSLP,UGT1A1,VCAM1,VEGFA,VHL	981 (15)

TP53	transcription reg	3,17E-60	ABCB1,ABCC1,ABCC2,ABCG2,ACAA2,ACADS,ACAT1,ACE,ACSS1,ACTA2,ACTN4,ADA,ADD3,ADORA2B,ADRA1A,ADRB2,ADRB3,AFP,AGTR1,AHCY,AKAP12,AKR1B1,AKT1,ALDH1B1,ALDH9A1,ALOX15,ALOX5,ANGPT1,API5,APOA1,APOE,APOL1,AQP3,AR,ASTN2,ATF3,ATP1A1,AURKA,BAX,BCAT1,BCL2A1,BDKRB2,BDNF,BLZF1,BRCA1,BRCA2,C2,CALCRL,CAT,CAV1,CAV2,CCL2,CCL5,CCN2,CCND1,CD247,CD36,CD59,CDKN2A,CEBPD,CELSR1,CERS6,CHEK2,CHUK,CKM,CLU,COL13A1,COL18A1,COL1A1,COL1A2,COL3A1,COL4A1,COMT,CPT1A,CPT1B,CPT2,CSF2,CSK,CTF1,CTNNB1,CTSH,CXCL12,CXCL8,CXCR2,CYP19A1,CYP1A1,CYP24A1,DBP,DHCR7,DHFR,DICER1,DLGAP1,DNASE1,DNM1L,DPP4,DRAM1,EDIL3,EDN1,EDNRA,EGF,EGFR,EMILIN1,ENG,EPAS1,EPHX1,ERBB2,ERCC1,ESR1,F11R,F2R,F5,FABP3,FAS,FBLN2,FDFT1,FGFBP1,FGFR1,FKBP1B,FKBP4,FKBP5,FN1,FOS,FOXO1,FOXO3,FOXP3,FYN,G6PD,GAS6,GAS7,GATA4,GATM,GC,GDF15,GJA1,GLRX,GNA14,GNAI2,GPR160,GPR83,GPR87,GPX1,GPX3,GRK3,GSN,GSR,GSTM1,GSTM5,GSTP1,H19,HAS2,HBEGF,HDAC9,HGF,HIF1A,HLA-B,HLA-DQA1,HMGA1,HMGB1,HMGCR,HMOX1,HSPA1A/HSPA1B,HSPA1L,HSPA8,HSPB7,HSPD1,HSPG2,HTT,ICAM1,ID3,IDH2,IFI30,IFNG,IGF1,IGF1R,IGF2,IGF2BP2,IGFBP3,IL10,IL10RA,IL12A,IL12RB1,IL16,IL17RA,IL1A,IL1B,IL1RN,IL2,IL21R,IL2RA,IL4,IL4I1,IL4R,IL5,IL5RA,IL6,IL9,INSR,IPO7,IREB2,IRF5,IRS1,ITGA2,ITGA2B,ITGAV,ITGB1BP2,JUN,KCNB1,KCNH2,KCNJ4,KCNK3,KCNMA1,KDR,KIT,KMT2D,LDHA,LDLR,let-7,LGR5,LIMK1,LOX,LPIN1,LSP1,LSS,Ly6a (includes others),MAP4,MAPK1,MAPK3,MED13L,MEF2A,MEF2D,MET,MFAP2,mir-143,mir-224,mir-27,mir-378,mir-515,MMP1,MMP2,MMP3,MMP9,MT-CO2,MT-CYB,MVK,MYH9,MYL2,MYL3,MYO5A,MYO6,NAMPT,NCOR2,NFKB1,NFKB2,NFKBIA,NKX2-5,NOS1,NOS2,NOS3,NOTCH1,NOX4,NR0B2,NR2F1,NRAP,OPA1,OSGIN1,P2RX4,PADI2,PADI4,PAFAH1B2,PAPPA,PARP1,PCK1,PDGFRA,PDGFRB,PDLIM5,PDYN,PECAM1,PFKP,PGR,PIK3CG,PIK3R1,PLAUR,PLTP,PML,POSTN,POU5F1,PPARA,PPARD,PPARG,PPARGC1A,PPIC,PPP3CA,PRC1,PRKAG2,PRKCA,PRKCB,PRKCG,PRKG1,PRKN,PRL,PSEN1,PSMB9,PSRC1,PTEN,PTGDS,PTGER1,PTGS1,PTGS2,PTK2B,PTN,PTPN1,PTPN11,PTPRO,RAC2,RAD54B,RBPJ,RELA,RFC1,RGS12,RUNX1,RUVBL2,RYR2,S100A4,SCNN1A,SDHB,SDHC,SDHD,SELE,SELP,SEMA6A,SERPINA3,SERPINC1,SERPINE1,SERPINE2,SFRP2,SGK1,SIRT1,SIRT6,SLC19A1,SLC19A2,SLC2A1,SLC2A4,SLC2A9,SLC6A6,SLPI,SMAD6,SOD1,SOD2,SORBS1,SPP1,SREBF1,SRSF3,STAT3,SULF2,TAP1,TBX3,TBX5,TBXAS1,TCAP,TCF7L2,TCN2,TERT,TET2,TFPI2,TFRC,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,THBD,THBS1,THBS2,THBS4,THRA,TIMP1,TIMP2,TIMP3,TKT,TLR6,TMEM127,TMOD4,TNC,TNF,TNFRSF1A,TNFRSF1B,TNFSF10,TOMM40,TP53,TP73,TRAF1,TRIB3,TRPV1,TTN,TXN2,TYMS,UBA1,UCP3,UHRF1,VCAN,VCL,VDR,VEGFA,WNT3,XPNPEP1,XPO5,XRCC3,ZFP36,ZNF79	1235 (24)
IGF1	growth factor	6,15E-60	ABCA1,ACTA2,ADA,ADIPOQ,ADM,ADORA2B,AGTR2,AKR1B1,AKT1,ANPEP,AQP4,ATM,BAX,BCL2A1,BDNF,BGLAP,BMP2,BMP4,BRCA1,C4A/C4B,CACNA1S,CCL11,CCL5,CCN2,CCND1,CDKN2A,CEBPD,CHGA,CLU,CNP,COL1A1,COL3A1,CTNNB1,CXCL8,CYBA,CYBB,CYP11A1,CYP17A1,CYP19A1,CYP27B1,EDN1,EDN2,EFNB2,EGF,ELN,EPAS1,ESR1,ESR2,FGFR1,FN1,FOS,FOXO1,FSHR,GATA2,GCK,GDNF,GH1,GHR,GHRH,GHRHR,GHSR,GNRH1,GPER1,HBB,HGF,HIF1A,HMGA1,HMGCR,HMOX1,HSD11B1,HSD11B2,HSD3B1,HSPA4,ICAM1,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IL10,IL16,IL18,IL1B,IL1R1,Il4,IL4R,IL6,INSR,IRS1,IRS2,ITGAV,JUN,KISS1,LCN2,LDHA,LEP,LEPR,LHCGR,LPL,Ly6a (includes others),MAPK1,MAPK3,MIF,mir-378,MMP1,MMP14,MMP2,MMP3,MYB,MYOD1,NCAM1,NCF2,NFKBIA,NOS2,NOX1,NOX4,NPPA,NR3C1,NTRK1,OSMR,PARP1,PDGFRA,PDGFRB,PDYN,PGR,PLAUR,PPARG,PPP3CA,PRL,PSMB8,PSMB9,PTEN,PTGER4,PTGS2,PTH1R,PTPRC,PYY,RARB,RELA,SELE,SERPINE1,SGK1,SHBG,SIRT1,SLC1A6,SLC20A1,SLC23A2,SLC2A1,SLC2A4,SLPI,SOCS3,SPP1,SREBF1,SRM,SRSF3,SST,TAP1,TBX2,TF,TFF1,TGFB1,TH,THBS1,TLR4,TNF,TNFRSF11B,TNNI3,TOMM40,TP53,TRPV1,TSHR,TXNIP,UCP1,VCAM1,VEGFA,VEGFC,ZFP36	1211 (22)
Insulin	group	1,66E-59	ABCA1,ACAT1,ACTC1,ACVR2A,ADIPOQ,ADIPOR1,ADIPOR2,ADRB3,AGRP,AGT,AGTR1,AKT1,ANGPTL4,APLN,APLNR,APOA1,APOE,APOM,AQP9,ATF3,BMPR1A,BMPR2,CARTPT,CCL2,CCN2,CCND1,CCT2,CD36,CDKN2B,CIDEA,COL1A1,COL1A2,COL3A1,COL4A1,CTH,CTNNB1,CYBB,CYP11A1,CYP11B1,CYP17A1,CYP19A1,CYP1A1,CYP1A2,CYP2C9,CYP7A1,DUOX1,EDN1,EGFR,EPAS1,EPO,FADS1,FADS2,FGB,FGF21,FN1,FOS,FOXO1,G6PD,GCG,GCK,GCLC,GHRH,GHRL,GHSR,GNRH1,GRB14,GRK2,GSTP1,HES1,HIF1A,HIF3A,HMGCR,HMOX1,HNF1A,HSD11B1,HSD3B2,HSPA4,HSPA8,ICAM1,IDE,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IL6,INSIG1,INSIG2,INSR,IRS1,IRS2,ITGB3,JAK2,JUN,LDHA,LEP,LEPR,LIPE,LPIN1,LPL,MAOA,MAT1A,mir-27,MLXIPL,MMP2,MMP3,MMP9,MT-ND1,MTCH2,MTTP,NFKBIA,NOS2,NOS3,NPR1,NPY,NR1H3,NR1H4,NR3C1,NR4A3,NUCB2,PCK1,PCSK9,PDGFRA,PDGFRB,PDK4,PER2,PIK3R1,PLIN1,POMC,PPARA,PPARD,PPARG,PPARGC1A,PPIC,PRKCA,PRL,PTEN,PTPN11,RAC1,RBP4,RETN,ROCK2,SCARB1,SDHB,SERPINE1,SGK1,SIRT1,SLC10A2,SLC15A1,SLC2A1,SLC2A2,SLC2A3,SLC2A4,SLC2A5,SLC3A1,SLC6A4,SLC7A1,SOD1,SORBS1,SORT1,SREBF1,SREBF2,SRSF3,STAT3,TGFB1,THBS1,THBS2,TLR2,TNC,TNF,TRPV1,TSHR,UCP1,UCP2,VEGFA	972 (21)
IL1	group	1,88E-59	ABCG2,ADRB2,AHR,APOC3,APOE,AR,BAX,BDNF,BMP2,C2,C3,CBR3,CCL2,CCL23,CCL5,CD34,CD40,CD59,CEBPD,CFB,CHI3L1,COL1A1,CPT1A,CRP,CSF2,CTSL,CXCL5,CXCL8,CYP17A1,CYP1A1,CYP1A2,CYP7A1,EDN1,EGFR,EPO,FAS,FN1,FOS,FPR1,GCK,GDNF,GJA1,GNRHR,H19,HGF,HIF1A,HMGB1,HMGCR,HMOX1,HP,HSD11B1,ICAM1,IFNG,IGF1,IGF1R,IGFBP1,IL10,IL17A,IL1B,IL1R1,IL1RL1,IL1RN,IL2,IL22,IL2RA,IL2RB,IL3,IL33,IL4,IL4R,IL5,IL5RA,IL6,IL9,ITGAM,ITGB2,JUN,KIT,KYNU,LDLR,LEP,LIPC,LOX,LRP1,MAPK1,MMP1,MMP2,MMP3,MMP7,MMP9,MTTP,NCOA1,NOS2,NOX1,NR1H3,NR1H4,NR1I2,NRG1,NTRK1,PDGFRA,PDGFRB,POMC,PPARA,PPARG,PPARGC1A,PTGS1,PTGS2,RBP4,RELA,RORA,RXRA,SAA1,SDC4,SELE,SELL,SELP,SERPINE1,SFTPB,SHBG,SLC2A1,SLC2A3,SOCS3,SOD2,SREBF1,TGFB1,TGFB3,TGFBR1,THBD,TIMP1,TLR2,TLR4,TLR7,TNC,TNF,TNFAIP3,TNFRSF11B,TNFRSF1B,TNFRSF4,TNFSF10,TNFSF11,TP53,TRAF3IP2,VCAM1,VCAN,VEGFA,WNT5A,XDH	1039 (16)
Akt	group	4,94E-58	ACTA2,ADIPOQ,ADM,ANGPT1,AQP3,AR,BAX,BCL2A1,BMP2,BRCA1,CAV3,CCL2,CCN2,CCND1,CD36,CIDEA,COL3A1,CPT1A,CSF2,CTNNB1,CXCL12,CXCL8,CXCR4,CYP19A1,EGFR,EPAS1,EPO,ERBB3,ESR1,FAS,FKBP5,FN1,FOS,FOXO1,FOXO3,FOXP3,GATA2,GCK,GSR,GSS,GSTK1,HES1,HIF1A,HIF3A,HMOX1,IFNG,IGF1,IGF1R,IGF2,IL10,IL12A,IL12B,IL13,IL17A,IL1B,IL1R1,IL22,IL2RB,IL4,IL5,IL6,IL7R,INSR,JUN,KCNA5,KISS1,KL,LCN2,LEP,LHCGR,LMNA,LPL,MFN2,MMP12,MMP14,MMP2,MMP9,MT-CO1,MT-CO2,MYB,NFATC1,NFKB1,NFKBIA,NOS1,NOS2,NOTCH1,NOTCH2,NOX4,NPPA,NR0B2,OSTF1,PCK1,PDK4,PDX1,PGR,PLG,POU5F1,PPARD,PPARG,PPARGC1A,PRDM16,PTGER2,PTGER4,PTGS1,PTGS2,PTN,RELA,SCARB1,SDHB,SERPINE1,SGK1,SHH,SLC2A4,SLC4A7,SLC8A1,SOCS3,SOD2,SPP1,TERT,THBS1,THBS2,TLR2,TNC,TNF,TNFRSF11A,TNFSF10,TNFSF14,TP53,UCP1,VCAM1,VCAN,VEGFA	1087 (21)
ESR1	ligand-depende	1,24E-57	ABCA4,ABCB1,ABCB11,ABCG2,ABCG5,ABCG8,ABLIM1,ACE,ACTC1,ADA,ADD3,ADH1C,ADORA1,AGT,AKT1,ALK,ALOX5,APOA1,APOE,AQP1,AQP3,AQP9,AR,ARNTL,ARSG,ATF3,ATP1B1,ATP2B1,AURKA,BAX,BCAT1,BIN1,BMP2,BMP4,BMPR2,BRAP,BRCA1,BRCA2,C3,C5,CA2,CACNA1D,CALD1,CARD14,CASQ2,CAV1,CAV2,CCL2,CCN3,CCND1,CD59,CD69,CDC42,CDC5L,CDK5R1,CDK6,CDKN2A,CDKN2B,CEBPD,CELSR2,CHEK2,CLEC1B,COG2,COL13A1,COMT,CPE,CSF2,CTNNB1,CTNS,CXADR,CXCL12,CXCL8,CYP11A1,CYP17A1,CYP19A1,CYP1A1,CYP1B1,CYP2E1,CYP4A11,CYP7A1,DHCR7,EDN1,EFNB2,EGF,EGFR,EP300,ERBB2,ERBB3,ESR1,ESR2,F12,F2RL1,FABP1,FAS,FGF10,FGFR1,FGFR2,FIS1,FKBP4,FMR1,FOLR1,FOS,FOXC1,FOXO1,FOXP3,FSHR,G6PD,GABBR2,GAS7,GDF15,GHR,GIT2,GJA1,GLRX,GNAS,GNRH1,GNRHR,GPER1,GPR37,GSN,GUCY1A1,GUCY1B1,H19,HAMP,HBEGF,HEBP1,HFE,HIF1A,HLA-B,HLA-C,HLA-G,HMGCR,HMGCS2,HSD17B7,HSD3B2,HSPA2,HSPD1,HTRA1,ICAM1,IFNG,IGF1,IGF1R,IGF2,IGFBP3,IKBKE,IL12A,IL17RA,IL1A,IL1B,IL2,IL2RA,IL5,IL6,IL6ST,INSR,IPO7,IRF5,IRS1,IRS2,ITGA2B,JAK2,JUN,KCNMA1,KISS1,KL,KRAS,LBP,LCN2,LDLR,LEP,LEPR,LHCGR,LILRB5,LIPC,LPL,LTBP4,LTF,M6PR,MADD,MAGI1,MAP2K5,MAPK1,MAPK8,MEF2D,mir-515,MME,MMP1,MMP9,MYB,MYO6,NCF2,NCOA1,NCOA3,NEDD4,NF1,NFATC1,NFE2L3,NFKB1,NFKB2,NFKBIA,NOS2,NOS3,NOTCH1,NOTCH3,NPR3,NPY,NQO1,NR0B2,NR1H3,NSD1,NTRK1,NUP210,OLR1,OPA1,OS9,OSTF1,P2RY2,PADI4,PDGFD,PDK4,PDLIM5,PGR,PIBF1,PITX2,PLA2G4C,PLAUR,PON3,POR,PPARD,PPARGC1A,PRKCH,PRL,PSIP1,PTEN,PTGER3,PTGS2,PVR,RARA,RBP4,RELA,REN,RENBP,RET,RGS19,RND1,ROCK1,SCARB1,SCNN1B,SELE,SELL,SEMA3F,SERPINE1,SGK1,SGSM3,SH2B1,SHANK2,SIRT1,SLC10A1,SLC1A4,SLC2A4,SLC39A8,SLC4A5,SLC6A4,SLC6A6,SLC7A1,SLC7A2,SLC7A8,SLC9A2,SLC9A3,SLCO1B1,SLCO1C1,SMAD2,SMAD3,SMAD5,SMAD6,SP4,SPP1,SRM,STAT3,STAT5A,STAT5B,STC2,TBCD,TCF25,TCF7L2,TERT,TFF1,TFRC,TGFB1,TGFB2,TGFB3,TGFBR1,TH,THBS4,TIMP2,TIRAP,TNF,TNFAIP3,TNFRSF11B,TNFSF10,TNFSF11,TNNI3,TP53,TP53BP1,TPM1,TRIB1,TRIB3,TRPC1,TRPM2,TSPAN9,TTR,TXNIP,UCK2,UGT2B7,VAV3,VEGFA,VEGFC,VPS11,WARS,WNK1	1082 (20)
abciximab	biologic drug	9,27E-03	CRP,TNF	

CEBPB	transcription reg	1,06E-56	ABCB1,ACTA2,ADH1C,ADIPOQ,ADM,ADRB3,AGT,AKR1C3,ALOX5AP,APCDD1,APLN,APLNR,APOB,APOC3,ARG1,ATM,ATR,BCL2A1,BDNF,BGLAP,BHMT,C3,CCL2,CCL5,CCND1,CCR5,CD14,CDKN2B,CEBPD,CFTR,CHIT1,COL1A1,COL1A2,CPB2,CPT1A,CRP,CTNNB1,CXCL5,CXCL8,CXCR4,CYP11A1,CYP17A1,CYP19A1,CYP1A1,CYP24A1,CYP27B1,CYP2A6 (includes others),CYP2E1,CYP3A4,DHCR7,DHFR,EFNB2,ELANE,F7,F8,FAS,FGFR2,FOS,FOXO3,GNAS,GSTA1,HAMP,HAS2,HBB,HGF,HLA-A,HMGA1,HP,HSD11B1,HSD3B2,HSPA8,HSPD1,ICAM1,IFNG,IGF1,IGFBP1,IGFBP3,IKBKE,IL10,IL12A,IL12B,IL1A,IL1B,IL1RN,IL2,IL24,IL4,IL5,IL6,INS,INSR,IRS1,IRS2,JUN,LBP,LCN2,LDLR,LEP,LEPR,LHCGR,MBL2,MGP,mir-143,mir-146,MMP1,MMP3,MSR1,NFKBIZ,NOS2,NR1H3,PCK1,PDGFRA,PDK4,PI3,PLAUR,PLG,POMC,PPARA,PPARD,PPARG,PPARGC1A,PRL,PRSS8,PSMA6,PTGES,PTGFR,PTGS1,PTGS2,RAC2,RGS4,RORA,SAA1,SCARB1,SERPINA1,SERPINE1,SGK1,SIRT1,SLC10A1,SLC12A2,SLC7A1,SMAD2,SOCS3,SPP1,SREBF1,SST,STAT3,TF,TGFB1,TIMP4,TLR8,TLR9,TNF,TNFRSF1A,TNFSF11,TP53,TRIB3,UCP1,UGT1A6,VCAN,VDR,XDH	1053 (24)
EGF	growth factor	3,98E-53	ABCG2,ADA,AFP,AKT1,ALOX12,ALOX15,ANGPT1,ANPEP,APOA1,AQP3,AR,ATF3,ATM,ATP2A2,AURKA,BRCA1,CAV1,CCL17,CCN2,CCND1,CDH4,CDKN2A,CEBPD,CHGB,CLU,COL1A1,COL1A2,COL3A1,CPB2,CXCL13,CXCL14,CXCL5,CXCL8,CXCR4,CYP11A1,CYP11B1,CYP1A1,CYP21A2,DIO2,DIO3,DPP4,EDN1,EFNB2,EGFR,EPAS1,ERBB2,ERCC1,ESR1,ESR2,FGFR1,FLT1,FN1,FOS,FSHR,FUT2,GAB2,GATA2,GDF2,GJA1,GPER1,GSTP1,HAS2,HAS3,HBEGF,HES1,HGF,HIF1A,HMOX1,HNF4A,HSD3B2,ICAM1,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IL10,IL17A,IL1B,IL1R1,IL6,IL7R,IL9R,IRS1,ITGA2,ITGAM,ITGB1,ITGB3,JUN,KRAS,LCN2,LDHA,let-7,LHCGR,LTF,MAPK1,MAPK3,MEF2D,MET,mir-27,MMP1,MMP12,MMP2,MMP3,MMP9,MT-CO2,NCAM1,NOS2,NOTCH1,NPPA,NPR2,NR4A3,PDGFRB,PDK4,PER1,PGR,PLAGL1,PLAT,PLAUR,PLPP3,POU5F1,PPARD,PPARG,PRKCH,PRL,PSMB4,PTGES,PTGS1,PTGS2,RAC1,REN,RUNX1,RXRA,S100A4,SCGB1A1,SERPINA1,SERPINA3,SERPINE1,SH2B3,SLC2A4,SLC4A7,SLC9A2,SMAD1,SMAD3,SNAP25,SOCS3,SP4,SPP1,SREBF1,ST3GAL4,TERT,TF,TFF1,TFPI2,TGFB1,TGFB3,TGFBR2,TH,THBS1,TIMP1,TIMP3,TNC,TNFAIP1,TNFRSF4,TP53,TRH,TRPM7,VCAM1,VCAN,VCL,VDR,VEGFA,VEGFC,VIP,ZFP36	1238 (20)
NR3C1	ligand-depende	5,07E-53	ABCA1,ACAT1,ACTN2,ADH1C,ADM,ADRA1D,AGT,AKT1,ALOX5AP,ANGPTL4,APOA2,APOE,APOL3,AQP1,AS3MT,ATP1B1,BAX,BDNF,BGLAP,BIN1,BMP2,BRCA1,BRD2,C4A/C4B,CACNA2D3,CARD14,CAT,CAV1,CCL2,CCL5,CCND1,CD69,CHIC2,CIDEA,COMT,CPB2,CPEB4,CPS1,CSF2,CTNNBL1,CXCL8,CXCR4,CYP11A1,CYP11B1,CYP11B2,CYP19A1,CYP2A6 (includes others),CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,CYP7A1,EDN1,EDN2,EPO,ETNK2,F2R,F2RL1,FGF21,FKBP4,FKBP5,FN1,FOS,FOXO1,FOXO3,G6PD,GCLM,GHRHR,GNRH1,GPR83,GPX1,GPX3,GRIA1,GSTA1,GSTP1,HMGCS2,HSD11B1,HSD11B2,ICAM1,IFIH1,IGF1,IGF1R,IGFBP1,IKBKB,IL10,IL12A,IL12B,IL13,IL15,IL15RA,IL18,IL1A,IL1B,IL1RAP,IL2,IL24,IL33,IL5,IL6,IL7R,INSR,ITGAV,ITGB2,ITGB6,JUN,LEP,LIPC,MAEA,MAOA,MAPK1,MAPK3,MAT1A,MAX,MMP1,MMP9,MTCH2,MTHFD1,MYOC,NAMPT,NFATC1,NFKB1,NFKB2,NFKBIA,NLRP3,NOD2,NOS2,NOS3,NPPA,NPY,NQO1,NR0B2,NR3C1,NTRK1,OASL,OLR1,PCK1,PER1,PIK3R1,PLAGL1,PNMT,POGK,POMC,POU5F1,PPARA,PPARG,PPP3CA,PPP3R1,PRKCB,PRL,PSEN1,PSMA6,PTEN,PTGS2,PTK2B,RELA,RGS2,ROCK1,SCARB1,SCNN1A,SDS,SELE,SERPINA1,SERPINE1,SGK1,SLC10A2,SLC19A2,SLC1A6,SLC1A7,SLC2A5,SMAD1,SPP1,SRD5A2,STAT3,STAT5A,STK39,TGFB1,THBD,THBS1,TIMP3,TLR2,TLR5,TNF,TNFAIP1,TNFAIP3,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFSF11,TNFSF14,TNFSF4,TP53,TPH2,TRAF1,TRAF3IP2,TRIB3,TSLP,TXN,VCAM1,VDR,VIPR1,WDR12,WDR37,WNT5A	1245 (18)
PPARA	ligand-depende	7,78E-52	ABCA1,ACAA1,ACAA2,ACADS,ACAT1,ACAT2,ADIPOQ,ADRB3,ADTRP,AGXT,AHCY,ALDH2,ALDH9A1,ANGPTL4,APOA1,APOA2,APOA4,APOA5,APOC2,APOC3,APOE,APOM,AQP3,AQP8,AQP9,ARG1,AURKA,BAX,BDNF,C2,C3,C5,CAT,CCND1,CD36,CDKN2A,CEBPD,CFH,CIDEA,CPS1,CPT1A,CPT1B,CPT2,CTH,CTSL,CXCL12,CYB5B,CYBA,CYBB,CYP1A1,CYP2C8,CYP2C9,CYP4A11,CYP7A1,DHCR7,DIO1,DIO2,EDN1,F11R,FABP1,FABP2,FABP3,FADS1,FADS2,FDFT1,FGA,FGB,FGF21,FGG,FOS,G6PD,GCK,GSTK1,GSTM3,GSTP1,HGF,HIF1A,HLA-DQA1,HMGCR,HMGCS2,HMOX1,HNF4A,HSD3B1,IFNG,IGFBP1,IGFBP3,IL10,IL12B,IL17A,IL1B,IL1RN,IL2,IL22,IL4,IL6,INSIG1,INSIG2,let-7,LIPG,LPL,LSS,MBL2,MGST3,mir-143,mir-146,mir-378,MMP9,MSMO1,MT-CO2,MTTP,MVK,NCF2,NFKB1,NFKBIA,NOS2,NPPA,NPPB,NR1H3,NR1I2,OGG1,OTC,PAH,PCK1,PDK4,PLA2G7,PLIN1,PLTP,PON1,POR,PPARA,PPARD,PPARG,PPARGC1A,PRC1,PRDM16,PRL,PTGS2,QPCT,RBP4,REG3A,RETN,SAA1,SCARB1,SELENBP1,SLC10A2,SLC27A4,SLC2A4,SREBF1,SREBF2,SRM,TERT,TLR2,TLR5,TNF,TXN,UCP1,UCP2,UCP3,UGT1A7 (includes others),VCAM1,VEGFA,VNN1	812 (21)
CEBPA	transcription reg	1,09E-51	ABCB1,ADH1B,ADH1C,ADIPOQ,ADRB3,AGT,AKAP12,AKR1B1,AKR1C3,ALOX5AP,ANPEP,APCDD1,APLN,APLNR,APOA4,APOB,APOC3,APOC4,ARG1,ARL4C,ARL6IP5,BCL2A1,BHMT,BIN1,C3,CA2,CCND1,CD14,CEBPD,CETP,CHI3L1,CIITA,COL1A1,COL1A2,CPB2,CPS1,CPT1A,CREG1,CXCL8,CXCR4,CYP11A1,CYP19A1,CYP2A6 (includes others),CYP2C9,CYP3A4,CYP3A5,CYP3A7,CYP7A1,DHCR7,DHFR,EBF1,EFNB2,ELANE,EPHX1,F8,F9,FLT1,FOS,FOXO1,FOXO3,FTO,GATA2,GCH1,GJA1,GLRX,GSTP1,HAMP,HAS2,HGF,HLA-B,HMGA1,HMGCR,HMOX1,HNF1A,HNF1B,HP,HSD11B1,ICAM1,IGF1,IGFBP3,IL10,IL12B,IL1RN,IL2,IL4,IL6,IL6R,INSR,IRS1,IRS2,ITGAM,JUN,KCNMB1,KDM1A,KLF5,KLK8,LCN2,LEP,LEPR,LHCGR,LIN28A,LPL,LTF,Ly6a (includes others),MAPKAPK2,MPO,MT-CO1,MYOD1,NFATC1,NR1H4,NR1I2,OLR1,OTC,PAX2,PAX5,PCK1,PCSK6,PLIN1,PPARA,PPARD,PPARG,PPARGC1A,PRL,PTGFR,PTGS1,PTGS2,PTPRC,RETN,RGS2,RORA,SAA1,SCGB1A1,SERPINB1,SERPINE1,SFTPB,SLC10A1,SLC2A4,SOCS3,SOD1,SOD2,SPP1,SREBF1,STEAP4,TBXAS1,TET2,TFR2,TGFB2,THBD,THBS1,THRA,TIMP4,TLR9,TNFRSF11A,TNFRSF1A,TNFSF10,TRIB1,UCP1,VCAN,VCL,VDR	993 (22)
CG	complex	2,86E-51	ABCB1,ACTA2,ADCYAP1,ADM,AKR1C3,APCDD1,APLN,APLNR,AR,BAX,BCAT1,BDNF,BHMT,BLM,BMP2,CCDC86,CCL2,CEBPD,CLU,CXCL8,CXCR4,CYP11A1,CYP17A1,CYP19A1,DHCR7,DNAH11,DPT,EDN2,EDN3,EFNB2,EPAS1,EPHB6,ESR2,F2RL1,FAS,FGF9,FOS,FYN,FZD4,GATA4,GHRL,GJA1,GNRH1,GNRHR,HAS2,HIF1A,HLA-A,HLA-DQA1,HMGA1,HMGCR,HSD11B1,HSD11B2,HSD17B7,HSD3B1,HSD3B2,ICAM1,IFNG,IGF1,IGF1R,IGFBP3,IL10,IL13RA2,IL1B,IL33,IL4R,IL6,IRS2,ITGA4,ITGAV,ITGB1,ITGB3,JUN,KISS1,LDLR,LEPR,let-7,LHCGR,LRP1B,MAF,MAP2K5,MAPK3,MAPKAPK2,mir-143,MMP1,MMP2,MMP9,MTPN,MVK,NOS2,NOS3,NPR1,NPR3,NR2F1,NR3C2,NUCB2,PAPPA,PDE4D,PDYN,PECAM1,PGR,PLAT,PLAUR,PLPP3,PPARA,PPARG,PTGER2,PTGFR,PTGS1,PTGS2,RETN,RGS2,RGS20,RGS4,RORA,RUNX1,SCARB1,SDC4,SLC20A1,SLC4A4,SMAD2,SMAD4,SMAD6,SMARCA1,SNAP25,SPP1,SRD5A2,SREBF1,ST8SIA4,TDRD5,TFPI2,TGFB2,TGFBR1,TGFBR3,TIMP1,TIMP4,TNF,TP53,TSHR,VCAN,VEGFA,VEGFC	1091 (20)
ERK1/2	group	1,56E-50	ABCA1,ADIPOQ,AKR1C3,ALOX5,APLN,BAX,BCL2A1,BDNF,BHMT,BMP2,BRCA1,C3,CACNA1C,CAT,CAV1,CAV3,CCK,CCL11,CCL2,CCL5,CCL8,CCN2,CCN4,CCND1,CD40,CMA1,COL1A1,COL3A1,CRHR1,CSF2,CXCL12,CXCL5,CXCL8,CXCR4,CYBB,CYP17A1,CYP19A1,CYP46A1,CYP7A1,ECE1,EDN1,EFNB2,ESR1,ESR2,FGFR2,FKBP5,FLT1,FN1,FOS,FOXO1,GJA1,GNRH1,GRK5,H19,HAMP,HAS2,HBEGF,HIF1A,HLA-A,HMGA1,ICAM1,ID3,IFNG,IGF1R,IGFBP3,IL10,IL12A,IL12B,IL1A,IL1B,IL2,IL2RA,IL4,IL6,INS,IRS2,ITGA2,ITGB3,JUN,KCNH2,LDLR,LEPR,MAPK1,MAPK3,MMP1,MMP12,MMP2,MMP3,MMP9,NAMPT,NKX2-5,NOS2,NOX1,NOX4,NPPA,NR4A3,PDGFRA,PLAUR,POMC,POSTN,PRL,PSMB8,PSMB9,PTGER2,PTGER4,PTGES,PTGS2,PTN,PTPN11,RAC1,RHOC,SERPINE1,SGK1,SOCS3,SOD1,SPP1,SSTR3,TAP1,TERT,TH,TIMP1,TIMP2,TNF,TSLP,VCAM1,VCAN,VEGFA,VNN1	967 (17)
IL4	cytokine	2,82E-50	ABCA1,ABLIM1,ACTA2,ADGRE1,ADORA2B,AHR,ALDH2,ALOX12,ALOX15,ALOX5,ALOX5AP,APOE,ARG1,ARNTL2,BAX,BCL11A,BDNF,BIN1,C3,CA2,CAD,CALCR,CAMK1D,CAT,CCDC86,CCL11,CCL17,CCL18,CCL2,CCL23,CCL25,CCL5,CCL8,CCN2,CCND1,CCR3,CCR5,CD14,CD2,CD200,CD36,CD40,CD69,CDK6,CIITA,CNR2,COBLL1,COL18A1,COL1A1,COL1A2,COL6A3,CSF2,CTNS,CXCL8,CXCR4,CYBB,CYP2E1,DDAH1,DPP4,DUOX1,DYNC1H1,EFL1,EPAS1,EPHB4,EPHX1,EVI5,F13A1,F2R,F2RL1,FAAH,FADS1,FAS,FCGR2A,FCGR2B,FKBP5,FLT1,FN1,FOS,FOXP3,FUT7,GATM,GJA1,GNA14,GPX4,HBEGF,HGF,HMGCR,HSD11B1,HSD3B1,HSD3B2,HSPA1A/HSPA1B,ICAM1,ICOS,ID3,IDE,IFI30,IFIH1,IFNG,IFNLR1,IGF1,IGF1R,IGF2R,IL10,IL10RA,IL12A,IL12B,IL12RB1,IL12RB2,IL13,IL13RA2,IL15,IL15RA,IL16,IL17A,IL18,IL18R1,IL18RAP,IL1A,IL1B,IL1R1,IL1RL1,IL1RN,IL2,IL24,IL2RA,IL2RB,IL3,IL33,IL4,IL4I1,IL4R,IL5,IL5RA,IL6,IL6ST,IL7R,IL9,IRF5,ITGA2,ITGA4,ITGAV,ITGB1,ITGB2,ITGB3,ITPA,ITPK1,JAG1,JAK2,JUN,KIDINS220,KIT,KLRB1,LGALS2,LIPG,LPL,LRP1,LSP1,LTA,LTA4H,LTC4S,Ly6a (includes others),MAF,MAOA,MAP4,MAPK1,MAPK3,MEFV,MMP1,MMP12,MMP2,MMP3,MMP9,MOV10,MS4A2,MSR1,MVK,MYH9,MYOD1,NCOA3,NFATC1,NFKB1,NFKB2,NFKBIA,NOS2,NR3C1,NR4A3,NUMA1,OAS3,OASL,OPRM1,PAX5,PFKP,PLA2G4C,PMS1,POLG,POSTN,PPARG,PPARGC1A,PRKCA,PRSS8,PSMA6,PSMB8,PTGS2,PTPN1,RASGRP3,RELA,RNF213,SELE,SELL,SELP,SELPLG,SERPINE1,SIRPA,SLC2A1,SLC4A7,SLC7A2,SOCS1,SOCS3,SOX13,SPP1,SRM,STAT4,STAT5A,STAT5B,STK39,TCF7,TFRC,TGFB1,TGFB3,TGFBR1,TGFBR2,THBD,TIMP1,TIMP2,TIMP3,TLR2,TLR4,TNC,TNF,TNFRSF11A,TNFRSF11B,TNFRSF4,TNFSF11,TNFSF4,TP53,TSLP,UCP1,VCAM1,VDR,VEGFA,VIPR1,VIPR2,XCL1,ZFP36	836 (17)

APOE	transporter	8,88E-50	ABCA1,ABCG8,ACAT1,ACTA2,ADGRE1,ADGRG1,ADIPOQ,AGER,ALOX12,APOA1,APOB,APOE,ATF3,BAX,BMP4,C2,C5AR2,CAT,CAV1,CCKAR,CCL5,CCN2,CCND1,CCR5,CD36,CD40,CETP,CLU,COL18A1,COL1A1,CPT1A,CTNNB1,CYBB,CYP3A5,CYP7A1,EDN1,EMILIN1,ESR1,F2R,F2RL1,FCGR2B,FKBP4,FKBP5,FOS,GAS7,GPX3,GPX4,GRIA1,HABP2,HMGCR,HMOX1,HPCAL1,HSD11B1,HSPA1A/HSPA1B,HSPD1,HSPG2,ICAM1,IFNG,IGF1,IGF1R,IL10,IL10RA,IL10RB,IL12A,IL12B,IL17A,IL1A,IL1B,IL1RN,IL2,IL4,IL5,IL6,INSR,ITGAM,JUN,LCN2,LDLR,LEP,LIPA,LIPG,LPL,LRP1,LRP8,LTBP2,M6PR,MADD,MGP,MMP2,MMP3,MMP9,MSR1,MYLIP,NCF2,NOS2,NOS3,NOX4,NR1H3,OLIG3,PCSK2,PCSK9,PLPP3,PPARD,PPARG,PRKCB,PRKCQ,PTGES,PTGS2,RELA,SCARB1,SDC4,SELE,SERPINA3,SERPINE1,SIRT1,SLC27A4,SMAD1,SOCS3,SOD1,SOD2,SORBS1,SPP1,SREBF2,STAT4,TGFB1,TIMP1,TNF,TNFRSF1A,TNFSF14,TXNIP,UCP2,VCAM1	1099 (20)
LDL	complex	8,97E-50	ABCA1,APOE,ATF3,ATP2A2,AXL,BCL2A1,BMP2,C3,CBS/CBSL,CCL2,CCL5,CCL8,CCN2,CCND1,CCR2,CD36,CD40,CDKN2A,CETP,CSF2,CTNNB1,CX3CR1,CXCL13,CXCL8,CYBB,CYP11B2,CYP2C8,CYP2C9,CYP2J2,ECE1,EDNRB,ERBB2,FAS,FCGR2B,FOS,GAS6,GCLC,GCLM,GJA5,GPX1,HAS2,HAS3,HIF1A,HMGCR,HMOX1,ICAM1,IFNG,IGF1,IGF1R,IGFBP3,IL10RA,IL12B,IL17RA,IL1A,IL1B,IL1RN,IL6,INSIG1,ITGAV,ITGB3,ITPR2,JAK2,JUN,LDLR,LRP1,LTA,mir-146,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,MSR1,NAMPT,NFKB1,NLRP3,NOS2,NOS3,NOX1,NPC1,NR0B2,NR1H3,NR4A3,OLR1,PARP1,PECAM1,PLAT,PPARG,PTEN,PTGS2,RARA,RYR2,SCARB1,SELE,SELP,SERPINE1,SMAD3,SOCS1,SOCS3,SOD2,SREBF1,SREBF2,STAT3,TGFB1,TGFBR1,TGFBR2,TGFBR3,TLR4,TNF,TNFAIP3,TNFSF10,TP53,VCAM1,VEGFA,VNN1	929 (16)
Ins1	other	1,46E-48	ADH1C,ADIPOQ,ADIPOR1,ADIPOR2,AGT,AGTR2,AKT1,ALAD,ANGPTL4,APLN,APOA1,APOA5,APOC3,ATP1A1,ATP1A2,BDNF,CARTPT,CCK,CCL5,CCND1,CEBPD,CETP,CKM,COL18A1,COL1A1,CYP1A1,CYP2E1,CYP7A1,DHFR,DLK1,EDN1,EPO,ERCC1,FABP3,FADS1,FADS2,FDFT1,FOS,G6PD,GCG,GCK,GH1,GNRH1,GPLD1,GSTP1,HMGCR,HP,HSD11B2,IDE,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,IL10,IL1B,IL4,IL6,IL6ST,INS,INSR,IRS1,IRS2,IVD,JUN,LDHA,LDLR,LEP,LIPE,LPL,LRP1,MAPK1,MAPK3,MIF,MLXIPL,MMP1,MMP2,MMP3,MTTP,MYOD1,NOS1,NOS2,NOS3,NPPA,NPY,NR1H3,PCK1,PER1,PGR,PIK3R1,PLAT,PLIN1,POMC,PPARA,PPARD,PPARG,PRKCA,PRKCB,PRKCQ,PRL,PTEN,PTGS2,REN,RETN,RXRA,SDHB,SERPINE1,SFTPB,SIRT1,SLC2A1,SLC2A2,SLC2A4,SLC6A2,SNAP25,SOCS3,SOD2,SREBF1,STAT3,STAT5A,TF,TIMP1,TIMP2,TIMP3,TNF,TSHR,UCP1,VEGFA	939 (21)
IL10	cytokine	2,79E-47	ABCA1,ACTA2,ADM,AGER,ALOX5AP,ARG1,BAX,BCL2A1,BDKRB1,BMP2,BMP6,BMPR1A,CCL11,CCL16,CCL17,CCL18,CCL2,CCL23,CCL5,CCR2,CCR5,CD14,CD2,CD28,CD40,CDH13,CDK6,CHUK,CIITA,COL1A1,CR1,CSF2,CTLA4,CX3CR1,CXCL12,CXCL13,CXCL5,CXCL8,CXCR4,FAAH,FAS,FCGR2A,FCGR2B,FKBP5,FOS,FOXP3,FPR1,GPRC5B,HDAC9,HLA-G,HMOX1,ICAM1,IFNG,IKBKB,IL10,IL10RA,IL12A,IL12B,IL12RB2,IL13,IL13RA2,IL17A,IL17RA,IL18,IL1A,IL1B,IL1R1,IL1RN,IL2,IL22,IL23A,IL24,IL3,IL33,IL4,IL4R,IL5,IL6,IL6ST,IL7R,IL9,IRAK1,ITGA4,ITGAM,JUN,MAF,MEFV,MMP1,MMP2,MMP9,MS4A2,MSR1,NFATC1,NOD2,NOS2,NOS3,NPHS1,NR4A3,PAM,PIK3CG,POMC,PSMB9,PTGS2,PTPN1,PTPN2,REG3A,SCARB1,SELE,SELL,SELPLG,SLC6A4,SOCS1,SOCS3,STAT3,STAT4,TAP1,TERT,TFRC,TGFB1,TIMP1,TLR2,TLR4,TLR5,TLR7,TLR8,TLR9,TNF,TNFRSF11A,TNFRSF1A,TNFRSF1B,TNFSF10,TNFSF11,VCAM1,VCAN,VEGFA,XCL1,ZFP36	809 (18)
SP3	transcription reg	1,64E-46	ABCA1,ABCB1,ACTA2,ADD3,AKAP12,ALOX12,ATF3,BGLAP,CBS/CBSL,CCND1,CD40,CDK5R1,CES1,CETP,CHI3L1,CHRNA3,COL1A1,COL1A2,CYP17A1,CYP46A1,DHFR,DRD1,DRD2,EGFR,ESR1,F10,F2R,FAS,FDX1,FGF10,FLT1,FOS,FOXP3,GDF15,GHR,GNAI2,HAS2,HGF,HSD11B2,IGF1,IGF1R,IGF2,IGFBP3,IL10,IL12RB2,IL1A,IL2RB,ITGA2,ITGB8,JUN,KDR,KISS1,LCAT,LDLR,LHCGR,LPL,MET,mir-27,MMP2,MYH7,MYLK,NCF2,NFKB1,NOS1,NOS3,PADI4,PGR,PLAUR,PRKG1,PROCR,PTGS1,PTGS2,PTPN1,PYY,RELA,SCARB1,SERPINE1,SGK1,SLC19A1,SLC2A3,SLC39A8,SLC4A7,SLC9A3,SOD2,SREBF1,STAT3,TERT,TFF1,TGFBR1,TGFBR2,TGFBR3,TIMP1,TIMP2,TLR2,TNC,TNFRSF4,TNFSF14,TNNC1,TP53,TXNRD1,VEGFA,XYLT1	1103 (20)
APP	other	2,72E-46	ABCA1,ABCG2,ACTA2,ACTN2,ADCYAP1,AGER,AKT1,ANXA5,APOE,ARG1,ARL6IP5,ARNTL,ATF1,ATM,ATP1A2,ATP1B1,AXL,BAX,BDNF,BIN1,BMP4,BMP6,BRD2,C3,C4A/C4B,CAST,CAT,CCL2,CCL5,CCN2,CCND1,CCR5,CD40,CD59,CD69,CDC42,CDK5R1,CDK6,CLU,COL13A1,COL18A1,CPLX2,CSF2,CTNNB1,CXCL12,CXCL5,CXCL8,CXCR2,CXCR4,CYBB,DDAH1,DNM1L,DRD2,ECE2,EDN1,EGFR,ELN,ENG,EPAS1,ERBB2,ESR1,F2RL1,FABP3,FCGR2A,FCGR2B,FGFR1,FN1,FOLR1,FOS,FOXO3,FYN,GABBR2,GDF15,GDNF,GHR,GLIS3,GRIA1,GSTM3,GSTP1,H19,HBA1/HBA2,HES1,HGF,HMGA1,HMGB1,HMGCR,HMOX1,HSPA1A/HSPA1B,HSPA8,HSPD1,HSPG2,ICAM1,IDE,IFIH1,IFNG,IGF1,IGF1R,IGF2,IGF2BP2,IGF2R,IL10,IL12B,IL13RA2,IL18,IL1A,IL1B,IL4,IL4I1,IL6,IL6ST,INSR,IRF5,IRS2,ITGA2,ITGA4,ITGAM,ITGB3,JUN,KCNB1,KL,KYNU,LBP,LCAT,LDHA,LDLR,let-7,LIMK1,LRP1,LRP1B,LRP5,LRP6,Ly6a (includes others),MADD,MAF,MAGI1,MAPK1,MAPKAPK2,MEF2C,MME,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,MPO,MSR1,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6,MTHFD1L,NAMPT,NCOA1,NCOA3,NF1,NFKB1,NNAT,NOS1,NOS2,NOS3,NPY,NRG1,OLR1,PACS2,PAFAH1B2,PAX5,PDGFRA,PDGFRB,PFKP,PIK3R1,PLAT,PPARD,PPARG,PRKCA,PRKCB,PRKCG,PSEN1,PTGDS,PTGS2,PTPRC,RAMP1,RBPJ,RELA,RNF213,ROCK1,RYR3,SCARB1,SDC4,SERPINE1,SHH,SIRPA,SIRT1,SIRT6,SLC13A3,SLIT2,SMARCA2,SMARCA4,SNAP25,SOCS1,SOCS3,SOD1,SOD2,SREBF2,ST8SIA4,STAT3,TCF21,TERT,TGFB1,TGFBR2,TH,TLR2,TLR4,TLR5,TLR7,TLR8,TLR9,TNF,TNFSF10,TP53,TP73,TPM1,TRIB3,TTR,TXN,VCAM1,VCAN,VEGFA,WNK1,WNT3,ZFHX3	1084 (19)
Tgf beta	group	3,72E-46	ABCA1,ACTA2,ADH1C,ANGPTL4,BGLAP,CALCR,CCL11,CCL2,CCL5,CCN2,CCND1,CCR2,CD69,CDK6,CDKN2A,CDKN2B,CIITA,CLU,COL1A1,COL1A2,COL4A1,CSF2,CTF1,CTLA4,CTNNB1,CX3CR1,CXCL8,CXCR4,EDN1,ENG,F10,FBLN2,FGF10,FGG,FN1,FOS,FOXP3,FURIN,GCLC,HMOX1,HSPG2,ID3,IFNG,IGF1,IGFBP3,IL10,IL12B,IL13,IL16,IL1A,IL1B,IL1RN,IL2,IL4,IL5,IL6,IL9,ITGA2,ITGAV,ITGB1,ITGB3,JAG1,JUN,LAMA3,LCAT,let-7,LOX,Ly6a (includes others),MAF,MET,MIF,MMP1,MMP14,MMP2,MMP3,MMP7,MMP9,NCOR2,NCR3,NOS2,NOS3,NOX4,PLAT,PLPP3,POSTN,PPARGC1A,PTEN,PTGER2,PTGS2,RORA,RUNX1,RYR2,RYR3,SELE,SERPINE1,SGK1,SMAD2,SMAD4,SMAD6,SMTN,SOCS3,SPP1,TERT,TFRC,TGFB1,THBS1,TIMP1,TIMP2,TIMP3,TLR2,TNF,TNFRSF11A,TNFRSF11B,TNFSF10,TNFSF11,TSLP,UCP1,VCAM1,VEGFA	1127 (20)
FOXO1	transcription reg	7,67E-46	ADIPOQ,ADIPOR1,AGRP,AGXT,ANGPT1,ANGPTL4,APLN,APOA5,APOC3,APOM,AQP9,AR,BAX,BCL2A1,BGLAP,CA2,CAT,CAV1,CCN2,CCN3,CCND1,CD36,CD40,CDKN2A,CDKN2B,CIDEA,CNR1,COL4A1,COX18,CPT1B,CPT2,CXCL8,CYP7A1,DIO2,EBF1,EDN1,EDNRB,FABP2,FAS,FGF21,FLT4,FMOD,FN1,FOLR1,FOS,FOXC1,FOXO1,FOXP3,FYN,GATA2,GCK,GRHPR,GSTK1,HIF1A,HMGCR,HMOX1,HSPD1,ICAM1,IFNG,IGF1,IGF1R,IGFBP1,IKZF1,IL10RB,IL15,IL17A,IL17RA,IL18,IL1B,IL1R1,IL22,IL23R,IL6,IL7R,INS,INSR,IRF5,IRS1,IRS2,ITGAM,ITGAV,ITGB2,ITGB6,JAG1,JUN,KLF7,KLK2,LEP,LHCGR,LPL,MFN1,MLXIPL,MMP1,MMP3,MMP9,MRPS22,MTTP,MYL3,NAMPT,NFATC1,NOS3,NPC1,NPY,PAX5,PCK1,PDK4,PDX1,POMC,POU5F1,PPARG,PPARGC1A,PRC1,PRCP,PRL,PSMB8,PTEN,PTGS1,PTPRC,RELA,SCARB1,SELL,SERPINE1,SGK1,SIRT1,SLC25A14,SLC25A31,SLC2A2,SLC2A4,SMAD4,SOD2,SREBF1,SREBF2,STAT5B,TGFB1,THBS1,TIE1,TIMM8A,TKT,TNF,TNFRSF11A,TNFSF10,TNNC1,TOMM40,TP53,TRAF1,TRIB3,TXNIP,UCP1,VCAM1	926 (21)
HIF1A	transcription reg	4,24E-45	ABCB1,ABCC8,ACTA2,ADIPOQ,ADM,ADORA2B,AFP,AGT,AKAP12,AKT1,ALOX5AP,ANGPTL4,APLN,APOE,AQP4,AQP9,ATP2A2,AURKA,AXL,BAX,BMP2,BRCA1,CAV1,CCL5,CCN2,CCN3,CCND1,CCR2,CCR5,CD36,CDKN2A,CXCL12,CXCL8,CXCR4,CYP19A1,CYP46A1,CYP4F3,DNASE1,EDN1,EDNRB,EGFR,EGLN3,ENG,EPAS1,EPO,ERBB2,ERGIC1,FAM13A,FLT1,FN1,FOS,FURIN,FUT7,FYN,GCK,GHR,GJA1,GPER1,HAMP,HIF1A,HIF3A,HMOX1,HP,HSPA4,IFNG,IGF1,IGF2,IGFBP3,IL10,IL12B,IL15,IL17A,IL17RA,IL1A,IL1B,IL22,IL23R,IL4,IL6,INSIG2,IRS2,ITGA2B,ITGAV,ITGB2,ITGB3,JUN,LDHA,LEP,LOX,LOXL2,MEF2C,MET,MIF,MITF,MMP1,MMP2,MMP7,MMP9,MT-ND1,MYH7,NOS2,NOS3,NOTCH1,NOX4,NPPA,NR4A3,PLAUR,POLG,POU5F1,PPARA,PPFIA4,PRKCA,PTEN,PTGIS,PTGS2,RELA,RET,SDC4,SERPINE1,SHH,SLC2A1,SLC2A3,SLC2A4,SOCS3,SOD2,STAT3,STC2,TBX5,TERC,TERT,TFRC,TGFB1,TGFB2,TGFB3,THBS1,TLR2,TLR6,TMPRSS6,TNF,TNFRSF11B,TP53,TTN,TXN,VCAM1,VEGFA,VEGFC	958 (16)
ESR2	ligand-depende	4,68E-45	A4GALT,ABCA1,ABLIM1,ACTC1,ADORA1,AGT,AKAP12,ANPEP,APOE,AQP3,AR,ATF3,ATP2B1,BCAT1,BIN1,BMP2,BMP4,BMPR2,BSND,C3,CA2,CACNA1D,CAV1,CBS/CBSL,CCL2,CCN2,CCN3,CCND1,CD34,CDK5R1,CDK6,CEBPD,CES1,CHUK,CLEC1B,COL13A1,COL1A1,COL1A2,CSF2,CST2,CTNNB1,CXCL12,CXCL8,CYP11A1,CYP17A1,CYP19A1,CYP2A6 (includes others),DDAH1,DHCR7,DNAH11,EDN1,EGFR,EP300,ERBB2,ESR1,ESR2,F2RL1,FGFR1,FMR1,FN1,FOS,FOXO1,FOXO3,GABBR2,GCLC,GLRX,GSTP1,HEBP1,HSD17B7,HSPA2,IGF1,IGF1R,IGFBP3,IKBKB,IL1A,IL1B,IL23A,IL23R,IL6,ITGA2,ITGB1,JAG1,KDR,LEP,LHCGR,LILRB5,LMNA,LOX,LPL,LRP1B,MAOA,MAPK1,MAPK3,MBL2,MME,MMP1,MMP14,MMP2,MMP3,MYH7,MYOD1,NFE2L3,NFKB1,NFKB2,NFKBIA,NOS2,NOTCH1,NPY,NTRK1,PDK4,PGR,PIBF1,PLAT,PLAUR,POU5F1,PRKCH,PRL,PTEN,PTGDS,PTGFR,PTGIS,PTGS2,PTH1R,RARA,RBP4,REL,RELA,RETN,ROCK1,SCARB1,SELE,SEMA3F,SERPINE1,SGK1,SMAD2,SMAD3,SMAD4,SOCS3,SPP1,ST8SIA4,TDRD5,TERT,TFF1,TGFB1,TGFBR1,TGFBR2,THBS4,TIMP1,TIMP2,TNF,TNFRSF11B,TNFSF11,TPM1,TRIB1,TSC22D1,UCK2,VAV3,VEGFA,VWF	1074 (19)

FGF2	growth factor	8,57E-45	ACE,ACTA2,ADM,AFP,AGTR2,AKR1B1,AKT1,ANG,ANGPT1,ANGPTL4,ANPEP,AQP3,AR,BAX,BDNF,BGLAP,BMP4,CAV1,CCK,CCL2,CCN3,CCN4,CCND1,CNP,COL1A1,COL1A2,COL3A1,CTNNB1,CTSL,CXCL12,CXCR4,CYP11A1,DIO3,EDNRB,EFNB2,EGFR,EGLN3,ELN,ENPP1,EPAS1,EPHA4,ETV5,FAS,FBN1,FDX1,FGFR1,FGFR2,FGFR3,FLT1,FN1,FOS,FOXO1,FOXO3,FSHR,FUT2,GCH1,GDNF,GJA1,GNRH1,GRIA1,HAS2,HBEGF,HES1,HGF,HIF1A,ICAM1,ID3,IGF1,IGF1R,IGF2,IGFBP3,IL1B,IL6,IRS1,ITGA4,ITGB1,JUN,KDR,KL,KRAS,LMNA,LOX,LRP5,LRP6,MEF2D,MET,MGP,MIF,MITF,MMP1,MMP2,MMP3,MMP9,MYOD1,NF1,NKX2-5,NOS2,NOS3,NOTCH1,NPY,NR3C1,NR3C2,PCSK2,PDGFRA,PDGFRB,PDX1,PITX2,PLAT,PLAUR,POU5F1,PPARG,PRL,PTGS2,PTPN1,RET,RUNX1,S100A4,SELE,SERPINE1,SHBG,SHH,SLC20A1,SLC2A1,SOCS3,SOX17,SPP1,ST3GAL4,TF,TGFB1,TGFB2,TGFBR3,THBS1,TIMP1,TIMP3,TNF,TNFSF10,TNFSF11,TP53,TSHR,VCAM1,VEGFA,VEGFC,VWF,WNT5A	1107 (19)
EDN1	cytokine	1,28E-44	ACTA2,ADIPOQ,ANXA5,APLN,ATP2A2,BCL2A1,CALCRL,CCL2,CCN2,CCND1,CDC42,COL1A2,COL4A1,CST3,CTNNB1,CXCL8,CXCR4,CYBB,CYP11A1,CYP11B2,EDN1,EDN3,EDNRA,EDNRB,EGFR,FLT4,FN1,FOS,GATA4,GJA1,HBEGF,HIF1A,HSPA8,ICAM1,IL18,IL6,INSR,ITGA2,ITGAM,ITGAV,ITGB1,ITGB1BP2,ITGB3,ITPR2,JUN,LEP,LEPR,MAS1,MITF,MMP1,MMP2,MMP3,MMP7,MMP9,MYH7,MYL2,NPPA,NPPB,NRG1,OLR1,PLAUR,PLCB4,POMC,PPARA,PRKCA,PRKCB,PRL,PTGER2,PTGER4,PTGS1,PTGS2,REN,RHO,SELE,SELL,SERPINE1,SLC2A1,SLC8A1,SOCS1,SOCS3,SOD1,TBX5,THBS1,TIMP1,TIMP3,TNC,TP53,TRPC6,TTN,TYRP1,VCAM1,VCAN,VCL,VEGFA,VEGFC,VWF	883 (15)
AHR	ligand-depende	1,47E-44	ABCG2,ACTA2,ADGRE1,ADIPOR2,ADM,ALDH1B1,ALDH2,ALOX5,ATP2B1,BAX,CBR3,CCL5,CCND1,CD14,CD36,CDKN2A,CDKN2B,CELA1,COL13A1,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,COX8A,CRP,CTNNB1,CYP17A1,CYP19A1,CYP1A1,CYP1A2,CYP1B1,CYP2A6 (includes others),CYP2C8,CYP3A4,DHFR,DIO1,EBF1,EDN1,EGLN3,EMILIN1,EPB41L5,EPO,ESR1,FAS,FBLN2,FBN2,FGF21,FGF9,FGFR2,FMO3,FN1,FOS,FOXP3,GAS6,GSTA1,GSTM5,HDAC9,HES1,HIF1A,HMGCR,HP,IFNG,IGFBP1,IL10,IL17A,IL1B,IL22,IL6,IL9R,INSIG2,ITGAM,JAG1,JUN,KIT,LBP,LDHA,LTBP2,LTC4S,MMP2,MT-CO1,MT-CYB,MT-ND4,MYH7,MYL2,NNMT,NOS2,NOTCH1,NOTCH3,NQO1,OPA1,PCK1,PDGFRA,PDGFRB,PLAT,POU5F1,PPARG,PRL,PTGS2,SAA1,SEMA3F,SERPINE1,SIM1,SIRT1,SLC1A4,SLC2A1,SOCS3,SOD1,SOD2,SPP1,SREBF1,STAT3,STEAP4,TFF1,TGFB1,TGFB2,TGFB3,TGFBR2,TH,THBS1,TIMP2,TIMP3,TNF,TP53,TP73,TXN,UGT1A1,UGT1A6,UGT1A7 (includes others),VCL,VEGFA,VEGFC	853 (16)
CTNNB1	transcription reg	6,79E-44	ABCB1,ABCC1,ACAT1,ACAT2,ACTA2,ACTC1,ACTN4,ACVR2A,ADIPOQ,ADRA2C,AFP,AHR,APCDD1,AQP4,AR,ATM,AURKA,BMP2,BMP4,BMP7,CCN2,CCN4,CCND1,CD34,CD36,CDKN2A,CDKN2B,CELSR1,CHEK2,CHGA,CLU,CNR1,COL1A1,COL4A1,CPT1A,CPT2,CREG1,CRYBG1,CTNNB1,CXCL12,CXCL8,CYP11A1,CYP19A1,CYP1A1,CYP1A2,CYP1B1,CYP24A1,CYP2A6 (includes others),CYP2E1,DBH,DES,DIO1,DIO2,DLK1,DNAJC6,EDIL3,EDN1,EDN3,EGFR,ENPP1,EPHB4,ERBB3,ESR2,EVX1,EYA2,F13A1,F2R,FAS,FBLN2,FGF5,FGF9,FGFBP1,FN1,FOS,FOXC1,FSHR,FUT2,GALC,GATA2,GCH1,GDNF,GHR,GJA1,GPA33,HES1,HHEX,HMGCR,HMGCS2,HNF1A,HNF4A,HTRA1,ID3,IFNG,IGF2,IL10,IL13,IL17A,IL1B,IL1R1,IL2,IL22,IL23A,IL2RA,IL4,IL6,IL9,ILF3,IRS1,ITGA4,ITGB1,ITGB2,JUN,KDR,KIT,KLF5,KLK2,LGR5,LHCGR,LIPA,LMNA,LMX1B,LPL,LRP6,LSP1,Ly6a (includes others),MAP4,MECOM,MEF2D,MITF,MME,MMP1,MMP14,MMP2,MMP3,MMP7,MMP9,MYLK,MYOD1,NAT8,NCAM1,NFATC1,NKX2-5,NOS2,NOTCH1,NOTCH3,NOX1,NPHS2,NRG1,OGG1,P2RX7,PCSK6,PDYN,PECAM1,PIK3R1,PITX2,PKD1,PLAUR,PML,POU5F1,PPARG,PPP3CA,PRRC2A,PTEN,PTGS2,QPCT,RBP4,REG3A,RETN,S100A4,SAA1,SALL1,SERPINA1,SERPINA3,SERPINE1,SERPINE2,SGK1,SHH,SLC12A2,SLC6A2,SMAD6,SNRNP70,SOX17,SPP1,STAT3,STAT5A,STAT5B,TBX5,TCF7,TCF7L2,TERT,TFF1,TGFB1,TGFB3,TIMP1,TIMP3,TNC,TNF,TNFRSF11B,TNFRSF1A,TNFSF10,TNFSF11,TNNC1,TP53,TP73,TRAF1,TRH,TSC22D1,TSPAN8,UBA1,VCAM1,VCAN,VEGFA,WNT3	1068 (21)
actinomycin D	biologic drug	1,24E-39	ABCA1,ABCC2,ADM,AFP,AGT,APOA1,AR,ATP1A1,AVPR1A,BAX,BCL2A1,BDNF,BRCA1,CAV1,CCK,CCL11,CCL2,CCN2,CCND1,CD28,CERS6,COL1A2,CTNNB1,CXCL8,CYP1A1,CYP24A1,DIO3,EDN1,EGLN3,EPAS1,FAS,FGB,FGFR1,FN1,FOS,FPR1,GCH1,GNRHR,GSTA1,GSTM5,GSTP1,GUCY1A1,GUCY1B1,HBEGF,HIF1A,HMOX1,IFNG,IGF1R,IL6,IL7R,IRS1,IRS2,ITPR2,JUN,LPL,LTA,MADD,MAOA,MAT1A,MMP12,MMP2,MMP3,MTTP,NOS2,NPPB,NPY,PAPPA,PLAUR,PPARG,PRL,PSRC1,PTGIS,PTGS2,PTH1R,RELA,RGS2,RGS4,ROCK2,SCNN1B,SCNN1G,SELE,SERPINE1,SLC20A1,SLC2A1,SOCS3,SPP1,TAP1,TF,TGFB1,THRA,TLR2,TNF,TNFRSF1B,TP53,TRAF1,TRAF3IP2,VDR,VEGFA,VEGFC,VIP	1031 (18)
PI3K (complex)	complex	1,36E-43	ABCA1,ADIPOR1,ADRB2,AKT1,ALOX5AP,APLN,APOA5,ATF3,CCL2,CCN2,CCND1,CD2,CDK5R1,CDKN2B,CHGA,CNR2,COL1A1,CXCL8,CXCR4,CYBB,CYP7A1,FN1,FOS,FOXO1,FUT7,G6PD,GATA2,GCG,GCLC,GCLM,GJA1,GSTA1,GSTM5,GSTP1,H19,HAS3,HBEGF,HIF1A,HMGCR,HMOX1,ICAM1,IFNG,IGF1,IGF1R,IGF2,IGFBP1,IL10,IL12B,IL17A,IL1B,IL1RN,IL2,IL22,IL23A,IL33,IL4,IL6,IL7R,INS,ITGAM,ITGB1,ITGB2,JUN,KDR,KRAS,LCN2,LEP,LHCGR,LSP1,LTBP2,MEF2C,MITF,MMP1,MMP12,MMP14,MMP2,MMP9,MT-CO1,MYOD1,NFATC1,NFKB2,NFKBIA,NOS2,NOS3,NOTCH1,NOX1,NOX4,NPPA,NQO1,OSTF1,PDX1,PIK3CG,PLA2G5,POSTN,PTGS2,RELA,RGS2,SELL,SERPINE1,SGK1,SLC9A1,SOCS3,SPP1,SREBF1,SST,THBS1,TLR4,TNF,TNFAIP3,TNFRSF11A,TNFSF10,TP53,TXNIP,UCP1,VCAM1,VEGFA,VIP	939 (17)
AKT1	kinase	1,72E-43	ABCB1,ACAT2,ACTA2,ACTC1,ADIPOQ,AKT1,APOC3,AR,BAX,BCL2A1,BMP2,CCL11,CCL2,CCL5,CCND1,CD40,CD69,CEBPD,CIDEA,CLU,COL4A1,CST3,CTNNB1,CXCL8,CXCR4,CYP7A1,DHCR7,EP300,EPO,ESR1,FAS,FN1,FOS,FOXO1,FOXP3,GATM,GCK,GCLC,GCLM,GDF15,GOSR2,GSR,GSS,GSTM5,HIF1A,HMGCR,HMOX1,IFNG,IGF1R,IGF2,IGFBP1,IL10,IL12B,IL2,IL2RA,IL4,IL6,IRS1,IRS2,ITGB1,KDR,LCN2,LEP,LIPA,LSS,MMP14,MMP2,MMP9,MMUT,MSMO1,MSR1,MYB,NFATC1,NFKB1,NFKB2,NOS2,NOTCH1,NOX4,NPPA,NQO1,PCK1,PDGFRA,PDGFRB,PGR,PIK3R1,PLG,PPARA,PPARG,PPARGC1A,PRL,PTGS1,PTGS2,RAMP1,REN,SERPINE1,SIRT6,SLC2A1,SLC4A7,SORT1,SPP1,SREBF1,SREBF2,TFF1,TGFB2,TGFBR3,THBS1,THBS2,TIMP1,TNF,TNFSF10,TNFSF11,TP53,TYMS,VCAN,VEGFA,ZWINT	938 (19)
IL1A	cytokine	3,16E-43	ABCC2,ADORA2A,ADORA2B,ASIC3,ATF3,BAX,CA2,CCL11,CCL2,CCL5,CCL8,CCR2,CD40,CSF2,CXCL12,CXCL5,CXCL8,CYP11A1,CYP17A1,CYP1A1,CYP1A2,CYP2E1,CYP3A4,CYP3A5,DPP4,EPO,F2RL1,FAS,FGFR1,FOS,GCH1,GNRHR,HMOX1,HSD11B1,HSD11B2,HSD3B1,HSPG2,ICAM1,IFNG,IGF1,IL10,IL12B,IL13,IL17A,IL18,IL1A,IL1B,IL1RN,IL2,IL2RA,IL4,IL5,IL6,IL9,IRAK1,ITGAV,ITGB1,ITGB3,JUN,KIT,LCN2,LDHA,LEP,LOX,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,NFKB1,NFKBIA,NFKBIZ,NOS2,NPY,NR2F2,NR3C1,PI3,POMC,PPARG,PTGES,PTGS2,RELA,SAA1,SELE,SERPINA1,SERPINA3,SERPINE1,SOD2,SPP1,TGFB1,TLR2,TNF,TNFAIP3,TNFRSF11B,TNFSF11,TOX3,TRH,TSLP,VCAM1,VEGFC,VIP,WNT5A	906 (16)
IL13	cytokine	9,72E-43	ABCA1,ADA,ADAMDEC1,ADORA1,ADORA2A,ADORA2B,ALOX15,ALOX5AP,ARG1,ARNTL2,ATF3,BAX,BCL2A1,BDNF,BLVRA,C3,CA2,CALCR,CCL11,CCL17,CCL18,CCL2,CCL23,CCL25,CCL5,CCN2,CCR5,CD14,CD247,CD36,CD40,CHI3L1,CIDEA,COL18A1,COL1A1,COL1A2,COL3A1,CTSH,CXCL5,CXCL8,CXCR2,CXCR4,CYBB,DUOX1,EGFR,EPAS1,F13A1,FADS1,FADS2,FAS,FCGR2A,FCGR2B,G6PD,GAS6,GAS7,GNAI2,GPX3,GPX4,GSN,HMOX1,HSD11B1,HSD3B1,HTRA1,ICAM1,IFNG,IGF1,IL10,IL12A,IL12B,IL13,IL13RA2,IL17A,IL18,IL1B,IL1R1,IL1RL1,IL1RN,IL23A,IL4,IL6,JAG1,JUN,LIPA,LTA4H,MAF,MAOA,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,MSMO1,MYOD1,NFATC1,NOS2,OPRM1,PFKP,PITRM1,POSTN,PPARG,PPARGC1A,PRSS8,PTGES,PTGS2,SELP,SERPINA1,SERPINE1,SLC26A4,SLC26A6,SLC7A2,SLC8A1,SLPI,SOCS1,SOCS3,SORT1,SPP1,ST8SIA4,TFRC,TGFB1,THBS1,TIMP1,TIMP2,TIMP4,TLR4,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFSF11,TRPV1,TSLP,UCP1,VCAM1,VNN1,WNT5A	915 (16)
PPARGC1A	transcription reg	1,21E-42	ABCB11,ACAT1,ADGRG1,ADIPOQ,AGT,ANG,APOA4,APOC2,APOC3,BAX,BMP4,C2,C3,CAT,CAV3,CCN2,CCN4,CD36,CD40,CEBPD,CIDEA,COL1A2,COL6A3,COX5B,CPN1,CPT1A,CPT1B,CXCL14,CYP11A1,CYP1A1,CYP1A2,CYP2A6 (includes others),CYP2C9,CYP2D6,CYP3A4,CYP3A5,CYP7A1,DIO1,DIO2,DPT,EDN1,EGFR,EPAS1,ERBB2,FABP3,FBLN2,FGF21,GAS6,GDF15,GPX1,HAMP,HMGCS2,HSD3B2,IGFBP3,IL10,IL18,IL1RAP,IL1RN,IL4R,IL6,INSIG1,INSIG2,IRS2,LDHA,LDLR,LIPA,LIPC,LPIN1,LPL,MFN2,MITF,MMP2,MSMO1,MT-CO1,MT-CO2,MYH7,MYL2,NCEH1,NPPA,NR1H3,NR1H4,OLR1,PCK1,PDK4,PIK3R1,PLA2G7,PLA2R1,POSTN,PPARA,PPARGC1A,PTGS2,PTN,RBP4,RXRA,SCARB1,SDHB,SDHD,SEMA6A,SERPINA3,SERPINE2,SLC2A4,SOCS1,SOCS3,SOD1,SOD2,SREBF1,TCHP,TGFBR3,THRA,TIMP1,TIMP2,TIMP3,TNF,TNFRSF11B,TNFSF10,TNFSF11,TP53,TRIB3,TXN2,TXNRD2,UCP1,UCP2,UCP3,UGT1A1,VCAN,VEGFA,XDH	902 (17)
CSF2	cytokine	1,87E-42	ABCA1,ACE,ADA,ADORA2B,ALOX5,ALOX5AP,ARG1,ATM,AURKA,BAX,BCL2A1,BMPR1A,C3,C4A/C4B,CCL17,CCL18,CCL2,CCL23,CCL25,CCND1,CCR2,CCR5,CD14,CD28,CD40,CD69,CDC123,CDKN2B,CFH,CIITA,CSF2,CTLA4,CXCL8,CXCR4,CYBB,EDN1,ELN,F2R,F2RL1,FAS,FCGR2B,FLT1,FOLR2,FOS,FOXP3,GCH1,GCLM,GDF15,GHRL,GRK3,HAS2,HBEGF,HGF,HIF1A,HLA-DQB1,HMGB1,HMGCR,HSPD1,ICAM1,ICOS,ID3,IFNG,IFNLR1,IGF1,IL10,IL12B,IL13,IL15,IL16,IL1A,IL1B,IL1R1,IL1RL1,IL1RN,IL23A,IL24,IL2RA,IL4,IL5,IL5RA,IL6,ILF3,IRAK1,IRF5,ITGA4,ITGAM,ITGB3,JAK2,JUN,LDHA,LEP,let-7,MAEA,MET,MME,MMP1,MMP14,MMP2,MMP9,MPO,MYB,NDST1,NFATC1,NFKB1,NFKB2,NFKBIA,NLRP3,NOS2,NOX1,NR1H3,OSMR,PIK3CG,PPARG,PRC1,PSEN1,PTGER2,PTGER4,PTGS2,PTK2B,RARA,REG3A,RELA,RHOH,SF1,SGK1,SLC2A1,SLC2A3,SLC2A4,SOCS1,SOCS3,SOD2,SPP1,SREBF1,SREBF2,TERT,TF,TGFB1,TGFBR1,THBS1,TLR2,TLR4,TLR5,TLR9,TNF,TNFAIP3,TNFRSF11A,TNFRSF1A,TNFRSF1B,TNFRSF4,TNFSF14,TP53,UHRF1,VDR,ZFP36	1055 (19)

KLF2	transcription reg	2,81E-42	ACE,ADM,APLN,APLNR,BMP4,CAV1,CCL2,CCL5,CCN2,CCR2,CCR3,CCR5,CD36,CD40,CDKN2B,CNP,COL4A1,CRP,CX3CR1,CXCL8,CXCR4,CYP1B1,EDN1,ELN,EPAS1,F2RL1,FGF5,FLT1,FOXP3,FUT4,GATA4,HBB,HIF1A,ID3,IFNG,IGF2,IL17A,IL1B,IL1RL1,IL2,IL22,IL4,IL6,IL6R,IL7R,ITGA4,ITGB1,ITGB2,ITGB3,KDR,LBP,LEPR,LTC4S,MMP14,NFKBIA,NOS3,NOTCH1,NOTCH2,NOTCH3,NQO1,PECAM1,PLPP3,PPARG,PTGDS,PTGIS,PTGS2,RELA,SELL,SELPLG,SEMA3F,SERPINE1,SLC2A1,SLCO2A1,SREBF1,STAT3,TBX5,TERT,TFPI2,TFRC,TGFB1,TGFB2,TGFBR1,THBD,THBS1,TIMP1,TNF,TNFRSF4,VCAM1,VWF	709 (16)
adalimumab	biologic drug	2,60E-02	FCGR2B,TNF	
KLF11	transcription reg	1,09E-41	ACTA2,ADAMTS8,AGT,AKT1,BMP7,CAT,CAV1,CCL11,CCL2,CCN2,CCR2,CHRNA3,COL1A2,COL3A1,CPT1B,CPT2,CXCR4,DIO2,DRD2,DRD4,EDN1,EGF,ENG,FABP3,HGF,IFNG,IL10,IL12B,IL13,IL13RA2,IL1B,IL4,IL5,INS,ITGA2,ITGAV,ITGB3,ITGB6,ITGB8,LOX,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,NFKB1,PDK4,PDX1,PLAT,PLG,PPARGC1A,SERPINA1,SERPINE1,SMAD2,SMAD3,SMAD4,SMAD6,SOD2,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,THBS1,THBS2,TIMP1,TIMP2,TIMP3,TIMP4,TNF,TSHR,UCP1,VEGFA	948 (20)
Growth hormon	group	1,29E-41	ACAA1,ADIPOQ,ADRB2,AGT,AKR1B1,ANGPTL4,APOE,BGLAP,BMP2,BMP4,BMP7,C3,CAT,CCND1,CD36,CEBPD,CLU,COL18A1,COL1A1,COL3A1,COMT,CRHR1,CTH,CYB5B,CYP27B1,CYP2C19,CYP2C8,CYP2C9,CYP2E1,CYP3A4,CYP7A1,DLK1,EGFR,EPO,FGF21,FGFR3,FGG,FKBP5,FN1,FOS,G6PD,GCLC,GDF15,GHR,GHRHR,GHRL,GSTA1,GSTM1,GSTM5,GSTP1,HBB,IGF1,IGF1R,IGF2,IGFBP1,IGFBP3,INSR,JUN,LDLR,LEPR,LIPE,LPL,MMP9,MT-CO2,MT-CYB,MYOD1,NAMPT,NFKBIA,NOX4,NPPA,PCK1,PDK4,PIK3C2B,PON1,PPARA,PPARG,PRKAG2,PRL,SCARB1,SCNN1A,SGK1,SIRT1,SLC2A1,SLC7A9,SOCS1,SOCS3,SOD1,SPP1,SST,STAT5A,TCF21,TF,TFF1,TGFB3,TGFBR2,TKT,TNFSF10,TSC22D1,TXNIP,XDH	948 (17)
SMAD3	transcription reg	8,32E-41	ACTA2,ADORA1,APOA1,APOA2,APOA4,APOB,APOC3,BGLAP,BMP2,BMP6,C3,CCL2,CCN2,CCND1,CD59,CDKN2A,CDKN2B,CES1,CIITA,CKM,COL1A1,COL1A2,COL3A1,COL6A3,CPT1B,CRP,CTNNB1,CYP11A1,CYP19A1,CYP21A2,CYP7A1,DES,EDN1,ELN,ENG,ESR1,ESR2,F12,FDFT1,FN1,FOS,FOXO3,FOXP3,GNRHR,HAS2,HBEGF,HMOX1,HNF4A,HP,ID3,IFNG,IL12B,IL13,IL15,IL1B,IL2,IL23A,IL2RA,IL4,IL5,IL6,IL9,ITGB1,JAG1,JUN,let-7,Ly6a (includes others),MAX,MEF2D,MMP1,MMP12,MMP9,MYOD1,NOS2,PNMT,POR,POU5F1,PPARD,PPARGC1A,PTGS2,RAC1,SERPINE1,SFTPB,SMAD1,SMAD3,SMAD5,SPP1,STAT3,TBX3,TERT,TF,TGFB1,TGFB2,TGFB3,TGFBR1,THBS1,TIMP1,TIMP3,TNC,TNF,TPM1,VEGFA,VEGFC,VIP,ZFP36	1040 (20)
OSM	cytokine	9,01E-41	ABCA1,ABCC1,ABCC8,ACAA1,ACE,ACTA2,AFP,AHR,AKR1C3,AQP9,ARG1,ARL4C,ATF3,ATP2B4,CAT,CCL11,CCL2,CCL5,CCND1,CEBPD,CHI3L1,CKM,COL1A1,COL1A2,COL3A1,CRP,CRY1,CSF2,CTSH,CTSL,CXADR,CXCL12,CXCL13,CXCL5,CXCL8,CYP19A1,CYP1B1,CYP3A5,CYP4F3,DNM1L,EPHB6,ERBB3,FGA,FGB,FN1,FOS,FOXC1,FSHR,GAS7,GCA,GHRH,GNRH1,GRHPR,HAMP,HBEGF,HGF,HIF1A,HLA-A,HLA-B,HLA-C,HMOX1,HP,HSD11B1,HSD11B2,HSPA2,ICAM1,IFNG,IGFBP3,IL10,IL13,IL15,IL15RA,IL17A,IL18,IL1B,IL33,IL4,IL4R,IL5,IL6,IL6R,IL6ST,IRAK1,IRS1,JAG1,JUN,KLK1,LBP,LCN2,LDLR,LDLRAD4,MAOA,MMP1,MMP2,MMP3,MMP9,NAMPT,NEDD4,NEDD4L,NOS2,NOTCH3,OSMR,PDLIM5,PI3,PITX2,PLCB4,POMC,POU5F1,PPARG,PSMB8,PSMB9,PTEN,PTGES,PTPN11,RARG,REG3A,RELA,RORA,RUNX1,SAA1,SBF1,SCNN1B,SELE,SELP,SERPINA1,SERPINA3,SERPINB1,SERPINE1,SLC15A1,SLC4A8,SLC7A8,SLPI,SMAD4,SMAD5,SOCS1,SOCS3,SPP1,STAT3,SYNE1,TAP1,TERT,TIMP1,TIMP3,TLR2,TNC,TNF,TNFRSF11A,TNFRSF11B,TNFSF11,TNNC1,TP53,TPM1,UAP1,UGT1A1,VCAM1,VDR,VEGFA,VIP,VPS11,WNT5A,XDH,ZBTB43,ZFP36	966 (18)
EP300	transcription reg	1,08E-40	ADIPOQ,ADORA2A,AGT,AKAP12,ANGPT1,AQP11,AR,BAX,BDKRB2,BRCA1,CA2,CAD,CAV3,CCL2,CCND1,CD36,CD59,CDKN2A,CDKN2B,CHPT1,CKM,CLOCK,COL1A2,COMT,CPT1A,CPT2,CXCL8,CXCR4,CYP11A1,CYP19A1,CYP1A1,CYP7A1,DHFR,DIO1,DRD2,EDN1,EP300,ERBB2,EYA2,FDX1,FN1,FOS,FOXO1,GCG,GFRA1,HBB,HLA-B,HLA-G,HMGCR,HMGCS2,HMOX1,HSD11B1,HSD11B2,ID3,IGF1,IGF1R,IL10RA,IL12B,IL12RB1,IL15RA,IL17A,IL17RA,IL18R1,IL18RAP,IL1R1,IL2,IL23R,IL2RA,IL6,IL7R,IL9,INS,ITGA9,ITGB2,JUN,KDR,KLK2,LAMA3,LDHA,LEP,LMNA,LTA,MAF,MEF2C,MME,MMP1,MMP7,NFKBIA,NOS2,NOTCH1,NPAS2,NPPA,NPR1,NR3C1,NTRK3,OAS3,OLR1,PARP1,PCK1,PDGFRB,PDK4,PDX1,PGR,PLA2G7,POU5F1,PPARA,PPARGC1A,PRL,PSEN1,PTEN,PTGS2,RARB,RCSD1,REN,RETN,SDC4,SELE,SIRT1,SLC6A19,SMAD6,SOCS3,SOD2,STAT4,TANC2,TBX19,TBXAS1,TERT,TFF1,TGFB2,TGFBR1,TGFBR2,TLR2,TNC,TNF,TNFAIP1,TNFAIP3,TP53,TRAF1,TRHR,TXNIP,VEGFA,WFS1	963 (20)
PDGF BB	complex	3,75E-40	ACAT2,ACTA2,ADARB1,ADD3,ADM,ADRA1D,ADRB2,AKAP12,ATF3,ATP2A2,ATP2B1,AVPR1A,BDKRB1,BDKRB2,BMP4,BMP6,BRAP,BRCA1,C3,CALD1,CAV2,CCL2,CCL8,CCN2,CCND1,CEBPD,COL18A1,COL3A1,CSF2,CTH,CXCL8,EDN1,EDNRB,EGFR,ELOVL2,ENPP1,EPO,FGFR1,FLT1,FN1,FOS,GDF15,GDNF,GHR,GJA1,GJA5,GSS,GUCY1B1,H19,HBEGF,HES1,HMGCR,HMOX1,ID3,IGF1,IGF1R,IGF2,IL1B,IL1RL1,IL2,IL6,ITGB1,JUN,KRAS,LBP,LDLR,LMNA,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,NAMPT,NOS1,NOS2,NOX4,NPR3,NR4A3,OLR1,PDGFRA,PDGFRB,PLAT,POSTN,PPARD,PPARG,PSMB4,PTGS2,RGS2,RXRG,RYR3,SERPINA3,SERPINE1,SGK1,SHH,SLC2A3,SLC6A4,SLC6A6,SLC7A1,SOCS3,SOD2,SREBF1,STAT3,SYNE1,TGFB1,TGFB3,TH,THBD,THBS1,TIMP1,TNC,TNFAIP3,TP53,TRIB1,TRIB3,VCAM1,VCAN,VEGFA,XDH,ZFP36	1054 (20)
LEPR	transmembrane	1,16E-39	ABCG5,ABCG8,ACTA2,ADCYAP1,ADGRE1,ADIPOQ,ADRB3,AGRP,ALOX15,ANGPTL4,ANXA5,APOA1,APOA2,APOA4,APOB,APOE,ATP2A2,CARTPT,CNR1,CNR2,COL1A1,COL4A1,CYP2E1,FN1,FOS,GATA4,GCK,GCKR,GNRH1,HIF1A,HMGCR,IGF1,IGFBP3,IL17A,IL1RN,IL24,IL6,INPPL1,IRS2,ITGAM,KISS1,LCN2,LDLR,LEP,LEPR,LIPC,LPL,MMP12,MMP14,MMP2,MMP3,MMP7,MTTP,NOS2,NPY,NR3C2,PDX1,POMC,PPARA,PPARD,PPARG,PPARGC1A,PSMB8,RETN,SCARB1,SERPINE1,SLC2A2,SLC2A4,SNAP25,SOCS3,SREBF1,SREBF2,STAT3,TCF7L2,TGFB1,TGFBR2,TIMP1,TIMP3,TNF,TNFRSF4,TRH,TRPV1,UCP1,UCP2	922 (21)
ERBB2	kinase	1,17E-39	ABCG2,ACAA2,ACTA2,ADIPOR2,ADRB3,AKT1,ALAD,ALOX15,ANG,ANGPTL4,AR,ATP6AP2,AURKA,BMP7,CAVIN3,CCL11,CCL2,CCL5,CCN2,CCND1,CD34,CD36,CD59,CDC42,CDCA7,CDK6,CDKN2A,CDKN2B,CES1,CHUK,CLU,COL18A1,COL1A1,COL3A1,COL4A1,COL6A3,CPS1,CPT2,CRYBG1,CSF2,CTNNB1,CXCL12,CXCL8,CYB561,CYP2J2,DHFR,DPT,EDN1,EDN2,EGFR,EPHX2,ERBB2,ERBB3,ESR1,ESR2,ETV5,F2R,FBLN2,FGF9,FLT1,FN1,FOLR1,FOS,FOXO1,FZD4,GAS6,GHR,GJA1,GLO1,GPX3,H19,HAS2,HBEGF,HES1,HIF1A,HMGCR,HP,HSPA1A/HSPA1B,HTRA1,IFNG,IGF1R,IGF2,IGF2R,IGFBP3,IKBKB,IL1A,IL1B,IL2,IL6,IL6R,IL6ST,ITGA2,ITGB1,ITGB3,ITPR2,JAG1,JUN,KDM5B,KDR,KIT,LCN2,LDHA,LIG1,LSS,LTBP2,MACF1,MAF,MAOA,MAP4,MCM8,MFAP2,MGAT5,MIF,MITF,MLXIP,MME,MMP1,MMP12,MMP14,MMP3,MMP7,MMP9,NDST1,NDUFAB1,NFKB1,NFKB2,NNMT,NOS2,NOTCH1,NOTCH3,NOX4,NR1H3,NRG1,NUCB2,PBX1,PDGFD,PDK4,PLAT,PLAUR,POLR1D,PPARG,PRC1,PRIM2,PRL,PSEN1,PSMB9,PTEN,PTGES,PTGS1,PTGS2,PTPN1,RALB,RARB,RARG,S100A4,SCARB1,SERPINA3,SERPINE1,SHMT1,SIRPA,SLC1A6,SLC2A1,SLC4A7,SLPI,SMAD2,SMAD3,SMTN,SORBS1,ST3GAL4,STAT3,TAP1,TERT,TGFBR1,THBD,THBS1,THBS4,TIMP3,TNC,TNF,TNNT3,TOPBP1,TP53,TPM1,TRAF1,TSC22D1,TYMS,UGT1A6,VCAN,VCL,VDR,VEGFA,VEGFC,VWF,WFS1,WNT5A,WWC1,ZWINT	1056 (22)
HRAS	enzyme	3,35E-39	ADARB1,ADM,ADRA2A,ADRA2C,AFP,AKT1,ATP2A2,AURKA,BAX,BMP4,BMP7,CALCRL,CALD1,CAV1,CAV3,CCL5,CCN2,CCND1,CD69,CDKN2A,CDKN2B,CEBPD,CFB,CFH,CHGA,CLU,COL18A1,COL1A1,COL1A2,COL3A1,COL4A1,CPT1A,CRP,CSF2,CTNNB1,CXCL12,CXCL8,CYP1A1,CYP24A1,DPP4,EGFR,ELN,ENPP1,EPHX1,ERCC1,ETV5,F2R,FABP3,FAS,FBLN2,FDFT1,FGFBP1,FN1,FOS,FOXO1,FURIN,FUT7,GAS6,GJA1,GNA14,GPX3,GSN,HAS2,HES1,HES5,HGF,HIF1A,HLA-B,HMGB1,HMOX1,HSPA8,HTRA1,ICAM1,IFI30,IFNG,IGF1R,IGF2,IL1A,IL1B,IL1RL1,IL2,IL24,IL6,IL7R,ITGA4,ITGAM,ITGAV,ITGB1,JAZF1,JUN,KLF5,KRAS,let-7,LIPG,LSP1,MAPK1,MAPK3,MET,mir-335,MMP1,MMP14,MMP2,MMP3,MMP9,MSMO1,MTHFD1L,MYL3,MYOD1,NCOR2,NFKBIA,NNAT,NOS2,NOTCH1,NPPA,NPPB,NQO1,NRAP,PCK1,PDGFRA,PDGFRB,PDLIM5,PER2,PLAUR,PLTP,PML,POSTN,PPIC,PRKCA,PRKCB,PRL,PSEN1,PSMB9,PTEN,PTGS1,PTGS2,RARB,RELA,RGS12,S100A4,SCNN1A,SELPLG,SERPINA3,SERPINE1,SERPINE2,SIRPA,SLC1A7,SLC2A2,SMAD3,SMAD4,SMARCA2,SOCS3,SOD1,SORBS1,SPP1,SREBF1,TAP1,TBX3,TERT,TGFB1,TGFB2,TGFB3,THBS1,THRA,TIMP3,TNF,TNFSF11,TOX2,TP53,TP73,TPH1,TRPC6,TRPV1,TSC22D1,TSLP,TYMS,VCAN,VCL,VEGFA	1000 (20)
PTEN	phosphatase	4,19E-39	ACAA1,ACAA2,ADAMDEC1,ADIPOQ,ADM,AKR1C3,AKT1,ALOX5AP,ANGPT1,AR,ARG1,ATF3,ATL1,AURKA,BAX,BDKRB1,C3,CA2,CAD,CALCRL,CCL5,CCND1,CD40,CDK6,CDKN2A,CDKN2B,CELSR1,COX8A,CRCP,CTNNB1,CTNNBL1,CX3CR1,CXCL13,CXCL8,CXCR4,CYB561,DHFR,EDN1,EFNB2,EGF,EGFR,EPAS1,EPO,ERBB2,ERBB3,ESR1,FAS,FDFT1,FES,FGF1,FGF10,FGF21,FGF5,FGF9,FGFR1,FGFR2,FGFR3,FLT1,FOS,FOXO1,FOXO3,GJA5,GPR160,GPR83,GPX3,GSR,GSS,GYS1,HAVCR1,HGFAC,HIF1A,HMGCR,HSPA1A/HSPA1B,HSPB2,IDH2,IFI30,IFNG,IGF1,IGF1R,IGF2,IGFBP3,IL10,IL12A,IL12B,IL17A,IL1B,IL2,IL22,IL23A,IL4R,IL6,INPPL1,IRS2,ITGB1,JAG1,KDR,KLF5,LGR5,LMX1B,LSS,LZTR1,MAPK8,MEF2D,MET,mir-146,MME,MMP14,MMP2,MMP3,MMP9,MT-ATP6,MT-CO2,MT-CYB,MT-ND1,MYO6,NCAM1,NDUFB3,NFATC1,NFKB1,NKX2-5,NOS2,NPPA,NQO1,NR2F2,NTRK1,PARP1,PDGFRB,PECAM1,PIK3R1,PPARG,PPARGC1A,PRKCB,PRL,PTEN,PTGS1,PTGS2,PTN,PTPRC,RUNX1,SBF1,SDC4,SDHB,SDHD,SELL,SERPINE1,SFTPB,SHH,SLC20A1,SLC7A8,SLCO2B1,SMAD1,SMAD2,SMAD4,SMAD6,SMARCA4,SOCS3,SP4,SPP1,SREBF1,STAT3,STAT5A,STAT5B,SULF2,TGFB1,TGFBR2,TH,THBS1,TNF,TNFAIP1,TNFRSF11B,TNFSF10,TP53,VAV3,VCAM1,VEGFA,VEGFC,VHL,VNN1	1052 (18)

VEGFA	growth factor	4,42E-39	ABCC1,ACE,ACTA2,ADRB3,AKT1,ALDH2,ANGPT1,ANPEP,BAX,BCL2A1,BMP2,BMP4,CAV1,CCL2,CCN2,CCND1,CD34,CD36,CD40,CDKN2A,COL1A1,COX5B,COX8A,CSF2,CST2,CST3,CTLA4,CTNNB1,CXCL12,CXCL8,CXCR4,CYB5B,EDN1,EFNB2,EPHB4,ERAP1,ETV5,FGFR1,FLT1,FLT4,FN1,FOS,GJA1,HBEGF,HES1,HIF1A,HLA-DQB1,HMOX1,ICAM1,ID3,IFNG,IKBKE,IL10,IL17A,IL1B,IL6,ITGA2,ITGA4,ITGAV,ITGB1,ITGB3,KDR,LIPE,LMNA,MEF2C,MMP1,MMP12,MMP2,MMP9,MYLK,NFATC1,NOS2,NOS3,NOTCH1,NPHS1,NR2F2,PARP1,PDGFRB,PECAM1,PIK3CG,PLAT,PLPP3,PPARGC1A,PRKCA,PSEN1,PTGS1,PTGS2,RASGRP3,RGS5,RHO,RUNX1,SDHB,SDHD,SELE,SERPINE1,SFTPB,SMTN,SOD2,TERT,TFPI2,TGFB1,THBD,THBS1,TIMP1,TNC,TNF,TP53,TRPC6,TXN2,UCP1,VCAM1,VEGFA,XCL1	891 (18)
CSF3	cytokine	6,17E-39	ADGRE1,AGTR1,ARG1,BAX,CCL5,CD14,CD34,CDK6,CST3,CTLA4,CX3CR1,CXCL12,CXCL5,CXCL8,CXCR2,CXCR4,CYBB,DES,EDN1,ELANE,ERAP2,FGB,FOS,FPR1,GATA4,GDNF,GJA1,HGF,HLA-DPA1,HLA-DQA1,HLA-DRA,HLA-DRB1,HMOX1,HSPD1,ICAM1,IFNG,IGF1,IL10,IL12A,IL12B,IL1RN,IL2,IL4,IL6,ITGAM,ITGB2,JUN,KIT,LBP,LCN2,LTA,LTF,Ly6a (includes others),MET,MMP2,MMP9,MPO,NFATC1,NOS3,PLCB2,PPARG,PRKCA,PRKCB,PYHIN1,RARA,SELL,SOCS1,SOCS3,STAT3,TFRC,TGFB1,TLR2,TLR4,TLR5,TLR8,TNF,TNFAIP3,TNFRSF1A,TNFRSF1B,TNFSF10,TNNI3,TP53,VCAM1,VEGFA	897 (16)
MAPK14	kinase	1,66E-38	ABCA1,ACTA2,ALOX5AP,BAX,BGLAP,BMP2,CAT,CCL2,CCL25,CCL5,CCND1,CD40,CDKN2A,CEBPD,CKM,COL1A1,CRP,CXCL8,CYP7A1,EGFR,EPO,FAS,FGFBP1,FLT1,FN1,FOS,GJA1,GNAS,HAS2,HMGCR,HMOX1,ICAM1,IFNG,IGF2,IL10,IL12A,IL12B,IL13,IL18,IL1B,IL2,IL22,IL4,IL5,IL6,ITGB8,JUN,KDR,LDLR,LRP6,MEF2C,MMP1,MMP3,MMP9,NFATC1,NOS2,NPPA,NPY,PCK1,PECAM1,PLA2G5,PLAUR,PPARGC1A,PRL,PSEN1,PTEN,PTGES,PTGS2,SGK1,SOCS3,SOD1,SOD2,SREBF1,SREBF2,TGFB1,TIMP1,TIMP2,TNF,TP53,TRPV1,UCP1,VCAM1,VDR,VEGFA,VEGFC,VIP,ZFP36	833 (14)
SIRT1	transcription reg	2,79E-38	ABCA1,ABCB1,ABCC2,ADIPOQ,AFP,AGT,AGTRAP,APLN,AQP11,BAX,BDNF,CAT,CAV1,CCL5,CCND1,CD36,CDKN2A,CDKN2B,CELA1,CNR1,CPT1A,CPT1B,CTBP1,CTNNB1,CYP19A1,CYP1A1,DBP,DDAH2,EP300,EPAS1,ESR1,FAS,FGF10,FGF21,FGF5,FGFR1,FGFR3,FN1,FOXO1,FOXO3,FOXP3,GATA4,GCK,GSTM1,GSTM3,HES5,HGF,HIF1A,HLA-A,HLA-DQA1,HLA-DQB1,HLA-DRB5,HMGCR,HMOX1,ICAM1,IDH2,IFNG,IGF1,IGF1R,IL10,IL12B,IL13,IL17A,IL1B,IL2,IL4,IL6,KALRN,KDM5B,LDLR,LEP,LTBP2,MADD,MAOA,MEF2C,MMP1,MMP2,MMP3,MMP9,MT-CO1,MTHFD1L,MVK,NAT1,NEDD4L,NEGR1,NF1,NOS3,NPY,NR1H4,PARP1,PCK1,PCSK2,PDGFRA,PDK4,PER1,PLEKHA6,PML,PNPLA3,POU5F1,PPARGC1A,PRDM16,PSMB9,PTN,RAC1,RNF213,ROCK1,SCNN1A,SDS,SERPINE1,SFRP2,SHANK2,SIRT1,SIRT6,SLC36A2,SNRNP70,SOCS3,SOD2,SOD3,SREBF1,STAT3,STRN,TAP1,TERT,THBD,TIMP2,TIMP3,TNF,TNFSF11,TP53,TP73,UCP2,ZNF618	1002 (18)
NR1H4	ligand-depende	3,04E-38	ABCB11,ABCC2,ABCG5,ABCG8,ACSS1,ACTA2,ADH1B,ADRB2,APOA1,APOA5,APOC2,APOC3,APOM,C3,CDKN2A,CETP,CPT2,CYP19A1,CYP3A4,CYP3A5,CYP7A1,DDAH1,EDN1,FABP1,FABP2,FAS,FGB,GCLM,GPX1,HNF1A,HNF4A,IFNG,IL1B,IL2,IL6,INSR,ITGAM,KNG1,LCAT,LCN2,LDHA,LIPC,LIPE,MMP2,MMP3,MTTP,NOS2,NR0B2,NR1H4,NR1I2,NR3C1,PCK1,PDX1,PLTP,PNMT,PNPLA3,PON1,PPARA,PPARG,PPARGC1A,PTGS1,PTGS2,RARA,RARB,RXRA,SCARB1,SLC10A1,SLC10A2,SLCO1B1,SLCO1B3,SPP1,SREBF1,TGFB1,THBD,TIMP1,TIMP2,TNF,TXNIP,UCP1,UCP3,UGT1A1	845 (21)
EGR1	transcription reg	4,91E-38	ABCB1,ACE,ACTA2,ALOX5AP,APOA1,AR,ATF3,ATP2A2,BAX,CACNA1H,CARTPT,CAV1,CCL2,CCND1,CCR2,CDK5R1,CHGA,CHGB,CLU,COL1A1,COL1A2,CXCL8,CYP17A1,EGFR,FAS,FLT1,FN1,FOXP3,FYN,GDF15,GDNF,GNAS,GRIA1,HBEGF,HIF1A,HMGCR,HMOX1,ICAM1,IGF1R,IGF2,IL13,IL1B,IL4,IL6R,ITGAM,JUN,LDLR,LHCGR,MMP14,MMP9,MYB,NFKB1,PCSK2,PDX1,PNMT,PPARG,PRL,PTEN,PTGES,PTGS2,PTPN1,SERPINE1,SF1,SGK1,SHH,SLC12A2,SLC12A5,SLC4A2,SOCS1,SOD1,SOD2,SPP1,SV2C,TGFB1,TGFBR2,TH,THBS1,TIMP1,TLR4,TNF,TNFSF10,TNFSF11,TP53,TP73,VCAM1,VEGFA	1114 (19)
Immunoglobuli	complex	6,61E-38	ACTA2,ADIPOR1,ADM,AGER,AKT1,ANPEP,AQP9,BCL2A1,BDNF,CBS/CBSL,CCL17,CCL18,CCL2,CCL5,CCL8,CCR2,CD14,CD28,CD40,CD69,CDK6,CEBPD,CIDEA,CIITA,CMA1,CSF2,CTH,CTNNB1,CXCL12,CXCL13,CXCL5,CXCL8,CXCR2,CXCR4,CYP1B1,CYP27B1,CYP2E1,ETV5,FAS,FCGR2A,FN1,FOS,FOXO3,FOXP3,FPR1,FTO,G6PD,GAS7,GCK,GPR83,GPX1,GYS1,HLA-DQB1,HMOX1,HSD11B2,ICAM1,ICOS,IDH2,IFI30,IFNG,IL10,IL10RA,IL10RB,IL12A,IL12B,IL13,IL17A,IL18,IL18R1,IL1A,IL1B,IL1RN,IL2,IL22,IL23A,IL24,IL2RA,IL2RB,IL33,IL4,IL4R,IL5,IL6,IL7R,IL9,IRAK1,IRF5,ITGA4,ITGB8,KDR,LCN2,LTA,Ly6a (includes others),MAF,MEF2C,MMP1,MMP2,MMP9,MPO,MTHFD1,NAMPT,NCF2,NDUFB3,NFATC1,NFKB2,NFKBIA,NKTR,NLRP3,NOS1,NOS2,NOS3,P2RY12,PAX5,PCK1,PDK4,PDPR,POMC,POSTN,PTGER2,PTGS2,RELA,RGS2,SDHC,SDHD,SELL,SIRPA,SLC11A1,SLC2A1,SOCS3,SOD1,SOD2,SPP1,STAT3,TCF7L2,TFRC,TGFB1,TGFBR3,TIMP1,TLR2,TLR7,TLR8,TNF,TNFRSF11A,TNFRSF1B,TNFRSF4,TNFSF13,TRAF1,TSLP,TTN,TXN,TXNRD1,UCP1,VCAM1,VCAN,VEGFA	879 (16)
Ap1	complex	8,59E-38	ACE,ATF3,ATP6AP2,BCL2A1,BDNF,BGLAP,CCL2,CCL5,CCN2,CCND1,CD40,CDKN2A,CLU,CSF2,CXCL12,CXCL8,EDN1,ERCC1,F2RL1,FN1,FOS,GNRHR,GSS,GSTP1,HBB,HMOX1,IFNG,IGF1,IGFBP3,IL10,IL12B,IL13,IL1A,IL1B,IL2,IL23A,IL2RA,IL3,IL4,IL5,IL6,ITGA2,JUN,LHCGR,LPL,MET,MMP1,MMP12,MMP2,MMP3,MMP7,MMP9,MSR1,MT-CO2,MYOD1,NOS2,NQO1,NR3C1,OPRM1,PADI4,PCK1,PRL,PTGS2,RSPO3,S100A4,SELE,SERPINE1,SLC8A1,TGFB1,TH,TIMP1,TLR4,TNF,TSLP,VCAM1,VDR,VEGFA,VIP,XYLT1	781 (18)
NFKBIA	transcription reg	9,06E-38	AGTR1,APOA1,ATP6V1B1,AXL,BAX,BCL11A,BCL2A1,BMP2,C3,CCL11,CCL2,CCL5,CCND1,CCR3,CD40,CD69,CDH13,CEBPD,CFTR,CHI3L1,CLU,COL1A2,COL3A1,CSF2,CSK,CTNNB1,CXCL12,CXCL8,CXCR4,CYBA,CYP1B1,EPO,ERAP1,ERAP2,ERBB2,FAS,FN1,FOS,GAS5,GCH1,GNRH1,GPX3,GRK5,GSTM5,HES1,HIF1A,HLA-A,HMGA1,HMOX1,HSPA8,ICAM1,IFNG,IGF2,IGF2R,IL10,IL12A,IL13,IL15,IL15RA,IL1A,IL1B,IL1RN,IL2,IL2RA,IL33,IL5,IL6,IL7R,IRAK1,ITGA2,ITGAV,ITGB1,JDP2,JUN,KCNH2,KLF5,LCN2,MGP,MMP1,MMP14,MMP3,MMP9,MT-CYB,MYOD1,NFKB1,NFKB2,NFKBIA,NOD2,NOS2,NOS3,NPPA,PICALM,PIK3R1,PLAT,PRL,PTEN,PTGES,PTGS2,RAC1,RELA,RGS4,ROCK1,SDC4,SELE,SEMA3F,SERPINE2,SGK1,SHH,SLC12A2,SMAD4,SOCS3,SOD1,SOD2,SOD3,SORL1,TFRC,TGFB1,TGFB2,TIMP1,TIMP2,TIMP3,TLR2,TLR4,TNC,TNF,TNFAIP3,TNFRSF11B,TNFRSF1B,TNFSF10,TNFSF14,TOLLIP,TP53,TRAF1,TRPC1,UBA1,VCAM1,VEGFA,VEGFC	891 (17)
Pkc(s)	group	9,50E-38	ABCA1,ACAT1,ACTA2,ADM,AHR,APLN,APOA1,AQP3,AQP4,ATF3,BCL11B,BDNF,CACNA1C,CARTPT,CCL2,CCN2,CCR2,CCR5,CD36,COL3A1,CPT1A,CRHR1,CTNNB1,CXCL8,CXCR4,CYBB,CYP19A1,CYP1A1,CYP2A6 (includes others),CYP2E1,DBP,DES,EDN1,EGFR,EP300,FAS,FGFBP1,FN1,FOS,GNRH1,GNRHR,GPER1,HIF1A,HMGCR,HMOX1,IGF2,IL10,IL12B,IL1B,IL2,IL6,IRS1,ITGB1,JUN,LIPA,MAPK1,MAPK3,MMP1,MMP2,MMP9,MSR1,NFKB1,NOS1,NOS2,NOX4,NQO1,NR4A3,PER1,PER2,PON1,PPARA,PPARG,PRKCA,PRL,PTGS2,RARA,RARB,RGS2,SCARB1,SERPINE1,SLC6A2,SLC6A4,SLC6A9,SPP1,STC2,TGFB1,TH,TNF,TNFRSF11A,TP73,VCAM1,VDR,VEGFA	945 (19)
ERK	group	1,11E-37	ABCA1,ACTA2,AGER,AGT,AXL,BAX,BGLAP,CAV1,CCK,CCL2,CCN2,CCND1,CDK5R1,CEBPD,CLU,COL1A1,COL3A1,CSF2,CTNNB1,CXCL8,CYP1A1,DIO2,DIO3,EDN1,EGFR,EPAS1,ESR1,FAS,FN1,FOS,FOXO1,FOXO3,FOXP3,GCLC,GDF15,HAS3,HBEGF,HMGA1,HMOX1,ICAM1,IFNG,IGFBP1,IL10,IL12A,IL12B,IL17A,IL1B,IL2,IL22,IL23A,IL23R,IL6,IRS1,ITGA2B,ITGAM,ITGAV,ITGB2,ITGB3,JAG1,JUN,KLF5,KYNU,LCN2,LDLR,MMP1,MMP14,MMP2,MMP3,MMP9,MYLK,NFKBIZ,NOTCH3,OSBPL10,PDK4,PECAM1,POSTN,POU5F1,PPARD,PTGES,PTGS2,RARB,RGS4,ROCK1,SELL,SERPINE1,SFTPB,SIRT6,SLC2A1,SLC4A7,SORT1,TERT,THBS1,TIMP1,TNF,TP53,TRPC3,VCAN,VEGFA,ZFP36	966 (18)
Jnk	group	1,75E-37	ABCA1,ACTA2,ADARB1,AGER,AGRP,AGT,ANXA5,APLN,BAX,BRCA1,CCL11,CCL2,CCL5,CCN2,CCND1,CD40,CD69,COL1A1,COL3A1,CXCL12,CXCL8,CXCR4,EDN1,F12,F2RL1,FAS,FN1,FOS,GCM1,GDF15,GDNF,GJA1,GRIA1,HES1,HMOX1,HNF4A,ICAM1,IFNG,IGF1,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL2,IL23A,IL2RA,IL5,IL6,INS,ITGA4,JUN,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,MT-CO2,NOS2,NOX4,NQO1,PLAT,PLAUR,PLG,PON2,POSTN,POU5F1,PPARD,PRL,PTEN,PTGES,PTGS2,RARA,RARG,RXRA,SELE,SERPINE1,SHH,SOCS3,SOD2,TERT,TGFB1,TGFBR2,TIMP1,TNF,TP53,TRPC3,VCAM1,VCAN,ZFP36	961 (17)
LIF	cytokine	2,77E-37	ACAA2,ACTA2,AFP,ARID1A,BGLAP,BMP2,BMP7,CALCA,CCND1,CD34,CEBPD,CRP,CXCL8,CYP11A1,CYP11B2,CYP17A1,CYP19A1,CYP21A2,DBH,ERAP1,EVX1,FGB,FGF5,FGG,FN1,FOS,FOXF1,FOXP3,GATA4,GHRH,HBEGF,HES1,HES5,HGF,HIF1A,HLA-G,IFNG,IGF1,IL17A,IL1B,IL2RA,IL6,IL6ST,JUN,KDR,KLRB1,KNG1,LBP,LEP,LPL,MEF2C,MMP1,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6,MYH7,NKX2-5,NPPA,NPY,PECAM1,PGR,POMC,POU5F1,PPARG,PTGS2,PTPN1,REG3A,RET,RGS4,RHO,SERPINA3,SOCS1,SOCS3,SOD2,SPP1,STAT3,TH,TIMP1,TNC,TNF,TNFRSF11B,TNFSF11,TP53,VEGFA,VIP,VWF,WNT5A	924 (19)
NOTCH1	transcription reg	9,02E-37	ACTA2,ANGPT1,AQP3,BGLAP,BMP2,CAD,CCN2,CCND1,CD14,CDCA7,CEBPD,CHGA,CKM,COL1A1,COL1A2,CTNNB1,CXCL8,DES,DLK1,EFNB2,EGFR,ELANE,EPAS1,EPHA4,ERBB2,ERBB3,FCGR2A,FCGR2B,FLT1,FOS,GAA,GATA2,GYPA,HBA1/HBA2,HES1,HES5,HIF1A,HMOX1,HSPA8,ICAM1,IFNG,IGF1R,IGFBP3,IL10,IL17A,IL18,IL1A,IL2,IL22,IL2RA,IL6,IL7R,IL9,ITGA2B,ITGAM,ITGB1,JAG1,LOX,Ly6a (includes others),mir-143,MMP1,MMP2,MMP3,MPO,MYH7,MYLK,NFKB1,NFKB2,NOS2,NOTCH1,NOTCH3,NR2F2,NRG1,PDGFRB,PPARG,PROX1,PTEN,PTGDS,PTGS2,REL,RELA,REN,RGS5,SELE,SERPINE1,SOCS1,SPP1,TFF1,TGFB1,TGFB2,TGFB3,TGFBR2,TGFBR3,TH,TIE1,TNF,TNFSF11,TP53,TSLP,VEGFA,WNT3,WNT5A	1010 (16)

FAS	transmembrane	1,34E-36	ACTA2,AGER,API5,BAX,BCL11A,BCL2A1,CAST,CCL2,CCL5,CCN2,CD200,CD59,CDK5R1,CEBPD,COL18A1,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,CRYBG1,CTSL,CXCL8,CXCR2,ERCC1,F2RL1,F5,FAIM2,FAS,FBN1,FCGR2B,FES,FLT1,FOS,FOXO1,FOXO3,FPR1,GIT2,GNAI2,GPLD1,GRK5,HLA-DQB1,ICAM1,IFNG,IL10,IL10RA,IL15RA,IL16,IL17RA,IL18,IL18R1,IL1A,IL1B,IL1RAP,IL2,IL6,IL9R,IMPA2,ITGAV,ITGB8,JUN,LDLR,MAP2K5,MEF2C,MET,MGP,MIF,mir-143,MME,MMP1,MMP9,MPZL1,MYO5A,NFKBIA,NOS2,NR3C1,NUMA1,OPTN,P2RX4,P2RY2,PDX1,PECAM1,PGLYRP1,PIK3C2B,PIK3CG,PLD2,PRKCB,PTGER2,PTGER4,PTPN1,PTPRN2,RAPGEF5,RARA,RASA1,RELA,RGS14,RND1,SELP,SELPLG,SERPINE1,SLPI,SOD2,SORL1,SPP1,STK38,TFRC,TGFB1,THBD,TLR2,TLR8,TNC,TNF,TNFAIP3,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFSF10,TP53BP1,TPM1,TRIB1,VCAM1,VEGFA,WNK1,ZFP36	838 (15)
TLR4	transmembrane	1,69E-36	ADM,ATF3,ATM,BAX,BMP2,C3,CAST,CCL2,CCL5,CCL8,CCR5,CD14,CD200,CD40,CDC42,CDK6,CEBPD,CERS6,CFB,CMA1,CSF2,CXCL8,CXCR2,CYP27B1,CYP3A5,DLK1,DUOX2,EDN1,EGF,FAS,FCGR2B,GDNF,GJA1,GRK2,HBEGF,HHEX,HLA-DQA1,HMGB1,HMOX1,HTRA1,ICAM1,IDH2,IFNG,IFNK,IL10,IL12A,IL12B,IL13,IL15,IL15RA,IL17A,IL18,IL1A,IL1B,IL2,IL23A,IL2RA,IL2RB,IL4,IL5,IL6,ITGAM,JAG1,LCN2,LRRK2,LTA,LTC4S,MCOLN2,MET,MIF,mir-146,MMP1,MMP9,MT-ND6,NFKB1,NFKB2,NFKBIA,NFKBIZ,NOD2,NOS1,NOS2,NOS3,NR1H4,NR4A3,OASL,PGR,PLAGL1,PLAT,PML,PPARG,PTGES,PTGFR,PTGS2,RAC1,REL,RELA,RGS14,RUNX1,RXRA,SCARB1,SELE,SELP,SLC6A12,SLCO3A1,SOCS1,SOCS3,SOD2,SPP1,STAT3,STAT5A,TFRC,TGFB1,TIMELESS,TLR2,TLR4,TNF,TNFAIP3,TNFSF10,TNFSF11,TPM1,TRAF1,TSC22D1,TSLP,UGT1A1,VCAM1	808 (16)
IKBKB	kinase	5,44E-36	ABCA1,AFP,AGER,ATF3,BAX,BMP2,BRCA1,BRCA2,C3,CALCR,CCL11,CCL17,CCL2,CCL25,CCL5,CCN2,CCND1,CCR3,CDH13,CEBPD,CLU,CSF2,CTNNB1,CXCL12,CXCL5,CXCL8,CXCR4,CYBA,CYP1B1,EDN1,FAS,FGF10,FOS,FOXO1,FOXO3,FYN,GCH1,GNRH1,GRK5,HGF,HIF1A,HLA-A,HMOX1,ICAM1,IFNG,IKBKB,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL1RN,IL2,IL4,IL5,IL6,ITGB3,KLF5,LCN2,LIPE,MGP,MMP1,MMP2,MMP3,MMP9,NFKB1,NFKB2,NFKBIA,NOS2,NOS3,NPPA,PLIN1,POSTN,PTEN,PTGS2,PTK2B,REL,RELA,S100A4,SELE,SERPINE2,SGK1,SOCS1,SOCS3,SOD2,SOD3,STAT3,TGFB1,TGFBR1,TGFBR2,TIMP2,TIMP3,TNC,TNF,TNFAIP3,TNFRSF11B,TNFRSF1B,TNFRSF4,TP53,TRPC1,TSLP,VCAM1,VCAN,VEGFA	952 (15)
MAPK8	kinase	2,04E-35	ABCA1,ABCB1,ADARB1,AGRP,AKT1,APOA1,APOE,AQP1,BMP2,BMP4,CAT,CCL5,CCN2,CCND1,CDKN2A,COL1A1,CRP,CXCL8,CYBB,CYP11A1,CYP19A1,CYP1A1,CYP7A1,DIO2,EGF,FOS,FOXO1,GCK,GSTM1,HMOX1,IFNG,IL10,IL12B,IL13,IL1B,IL2,IL2RA,IL4,IL5,IL6,JUN,KLB,LEP,MIF,MMP1,MMP2,MMP3,MMP7,MMP9,MSR1,MTHFR,MTTP,NOS2,NOX4,NPPA,NPPB,PLAUR,PPARD,PPARGC1A,PTEN,PTGES,PTGS2,RARA,RELA,RGS4,SELE,SHH,SLC10A1,SOD2,TLR2,TNF,TNFAIP3,TP53,TRH,TRHR,VDR,VEGFC,WNT5A,ZFP36	814 (13)
FOXA2	transcription reg	5,07E-35	ABCB1,ABCC8,ACTA2,ACTC1,ADH1C,AFP,ALOX15,ALOX5,APOA1,APOB,APOC3,APOM,C3,C5,CCL11,CCL17,CCND1,CCR5,CHI3L1,CPN1,CPT1A,CXCR4,CYB561,CYP2A6 (includes others),CYP2C9,DLK1,EPHX1,FGB,FOXO1,G6PC2,GATA4,GCG,GCK,GRIN3A,GSTM3,HMGCS2,HNF1A,HNF1B,HNF4A,IGF1,IGFBP1,IL13,IL13RA2,IL33,IL4,IL5,IL6,KCNJ11,LIPE,LPL,LTC4S,mir-122,MLXIPL,MTTP,NFKB2,NR1H4,NR1I2,PCK1,PDX1,PON1,PPARA,PPARG,PTGDS,PYY,RARA,RARB,RARG,RORA,SAA1,SCGB1A1,SERPINA1,SFTPB,SHH,SLC10A1,SLC2A2,SLC2A4,SLCO1B3,SOD3,SOX17,SST,TBXAS1,TCF7,TF,TGFB1,TH,TRH,TTR,UCP2,UCP3,WNT5A	1047 (22)
CREBBP	transcription reg	5,76E-35	ADCYAP1,ADORA2A,AGT,AKAP12,ANGPT1,AQP11,AR,BDKRB2,BMP7,CA2,CCL5,CCND1,CCR5,CD59,CKM,CLOCK,COL1A2,CXCL12,CXCL8,CXCR4,CYBB,CYP11A1,CYP24A1,CYP7A1,DHFR,ELANE,EPO,ERCC1,EYA2,FDX1,FGFR3,FOS,FUT7,GFRA1,GH1,GHRH,GNAS,GNRHR,HAMP,HAS2,HBB,HLA-B,HLA-DRA,HLA-G,HMGCS2,HSD11B1,HSD3B2,IFNG,IGF1R,IL10,IL10RA,IL12RB1,IL17A,IL18R1,IL18RAP,IL2,IL23R,IL2RA,IL2RB,IL6,IL7R,ITGA9,JUN,LDLR,LPL,LTA,MAF,MEF2C,MMP9,MPO,MYH7,MYOD1,NFKBIA,NOS2,NOTCH1,NPAS2,NPPA,NR3C1,NR4A3,NTRK3,OAS3,OPRM1,PCK1,PDGFRB,PGR,PKHD1,PPARGC1A,PRL,PSMB9,PTGS2,RARB,RCSD1,REN,RETN,RGS2,SDC4,SDHC,SELE,SELP,SERPINA3,SERPINE2,SFTPB,SLC18A2,SLC6A19,SOCS3,SREBF1,SST,STAT4,TANC2,TBX15,TBX19,TBX4,TFF1,TH,TLR2,TNC,TNF,TNFAIP1,TNFAIP3,TNFSF10,TRAF1,UCP1,VCAM1,VEGFA,WFS1	995 (23)
MYC	transcription reg	7,60E-35	ABCA1,ABCC1,ACAT1,ACSS1,ACTN4,ACVR2A,ADARB1,ADD1,ADIPOR1,ADM,AFP,AHCY,AHR,AKAP12,AKT1,ALOX5,ANGPT1,ANKRD17,ANXA5,AOPEP,APCDD1,APOC3,AQP1,AR,ARG1,AXL,BAX,BCAT1,BCL2A1,BDNF,BIN1,BMPR1A,BRCA1,BRD2,CAD,CAST,CAV1,CCN4,CCND1,CD69,CDCA7,CDK6,CDKN2A,CDKN2B,CEBPD,CLU,CNP,CNTNAP2,COBLL1,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,COX5B,CPT1A,CPT2,CTNNB1,CXCL8,CYP2C9,DHFR,DLEU2,DROSHA,EBF1,EDN1,ELANE,ERAP1,ERBB2,EVX1,EXT2,F2,F2R,FABP1,FABP2,FADS2,FAS,FBLN2,FBN1,FBN2,FGF5,FGFR1,FKBP5,FMOD,FN1,FOS,FOXF1,G6PD,GAA,GATA4,GCK,GCLC,GCLM,GGTLC1,GH1,GJA1,GP1BA,GRK4,GSR,H19,HAMP,HAS2,HES1,HIF1A,HLA-A,HLA-B,HMGA1,HMOX1,HMOX2,HSD11B2,HSPD1,ICAM1,ID3,IDH2,IFIH1,IKZF1,IL10,IL12B,IL1RAP,IL5RA,IMPA2,INS,IPO7,IREB2,IRS1,ITGAM,ITGB1,JUN,KDR,KLK1,KRAS,LDHA,LEP,let-7,LGR5,LOX,Ly6a (includes others),MAP4,MAPK3,MAX,MGP,MGST3,MIF,mir-27,mir-378,mir-515,MITF,MMP7,MMP9,MTHFD1,MTHFR,MYBPH,MYH7,NCAM1,NFKBIA,NPPA,NPY,NQO1,OASL,PAM,PARP1,PAX2,PAX5,PCK1,PDGFRA,PDGFRB,PECAM1,PFKP,PITX2,PLAUR,PML,POU5F1,PPARA,PPARD,PSMB8,PTEN,PTGS2,PTN,PTPRC,RARA,RARB,RARG,REN,RIN3,ROCK1,ROCK2,RUVBL2,SCARB1,SERPINA1,SERPINE1,SERPINE2,SGK1,SHMT1,SIRT1,SLC11A1,SLC2A1,SLC2A2,SLC2A3,SMAD1,SMAD4,SNRPN,SOD2,SOX17,SOX6,SPP1,SRM,SRSF2,ST3GAL4,STAT3,TERT,TF,TFF1,TFRC,TGFB1,TGFB2,TGFBR2,THBS1,THBS2,TIMP1,TIMP2,TKT,TLR7,TNC,TNF,TNFSF10,TNFSF11,TNNI3,TNNT3,TP53,TP73,TXN,TXNIP,TXNRD1,TYMS,UGT1A1,UGT1A3,UGT1A6,VCAM1,VEGFA,VEGFC,VHL,WNT3,WNT5A,WRN,XRCC3,ZFP36	1152 (18)
F2	peptidase	1,01E-34	ACTA2,ADAMTS9,ADIPOQ,AKR1B1,ALDH1B1,ANGPT1,ANGPTL4,BAX,CAD,CALD1,CBR3,CCL2,CCL8,CCN2,CCND1,CLU,COL1A1,COL4A1,CXCL13,CXCL8,CXCR4,CYBB,DIO3,ECE1,EDN1,EDNRB,EPO,F2R,F2RL1,F7,FLT1,FN1,FOS,HAS2,HBEGF,HDAC9,HIF1A,HMGA1,HMOX1,ICAM1,IGF1,IGF1R,IL13,IL15RA,IL1B,IL2,IL6,ITGB1,JUN,KDR,LOXL2,MAPK3,MIF,MMP1,MMP2,MMP9,MYH9,NCF2,NFKBIA,NOS2,NOS3,NR4A3,PDGFRA,PGR,PLAT,PLAUR,PROCR,PTGS2,RAC1,RAC2,SDC4,SELE,SELP,SERPINC1,SERPINE1,SLC2A3,SLC7A1,SLIT2,SMTN,SOD2,SRM,TFPI2,TGFB2,TGFB3,THBD,THBS1,TIMP2,TNF,TNFAIP3,TNFSF10,TNNT2,TOMM40,TRAF1,TRPC1,TRPC3,TXNRD2,UCK2,VCAM1,VEGFA,VWF	1004 (19)
FOXO3	transcription reg	1,33E-34	ACTA2,AHR,ANGPT1,APLN,AQP4,AR,AURKA,BAX,BMP2,CAD,CAT,CAV1,CCN2,CCND1,CDKN2B,COL4A1,CPT1A,CXCL8,CXCR4,DNM1L,EDNRB,ESR1,FGFR2,FLT4,FMOD,FN1,FOS,FOXC1,FOXO1,FOXO3,FOXP3,FYN,GATA2,GCLC,GPX1,GRB14,GSTM5,GYPA,HIF1A,HMGCR,HMGCS2,ICAM1,IFIH1,IFNG,IGF1,IGF1R,IGFBP1,IL10,IL10RB,IL12A,IL13,IL17A,IL1R1,IL2,IL4,IL5,IL6,IRS2,ITGAM,ITGB2,JAG1,LARS,LCN2,MAX,MEF2C,MET,MMP9,MYO6,MYOD1,NAMPT,NFKBIA,NOS2,NOS3,OPTN,PECAM1,POMC,PPARGC1A,PRCP,PTEN,PTGS1,PTPRC,RASA1,RELA,SELL,SERPINE1,SGK1,SH2B3,SIRT1,SLC1A4,SLC7A1,SLIT2,SMAD4,SOD1,SOD2,SREBF2,TFF1,TGFB1,TGFB2,TIE1,TNF,TNFRSF1A,TNFRSF1B,TNFSF10,TP53,TSC1,TXN2,TXNIP,TXNRD2,UCP2,VCAM1,VEGFA,ZWINT	1085 (20)
NR1I2	ligand-depende	1,84E-34	ABCA1,ABCB1,ABCC2,ADH1C,AHCY,AHR,ANG,APOA4,APOC2,APOC4,BHMT,CAT,CD36,CES1,CPT1A,CTH,CYP1A1,CYP1A2,CYP24A1,CYP2A6 (includes others),CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,CYP4A11,CYP7A1,DHCR7,FABP1,GSTA1,GSTM1,GSTM3,GSTM5,GSTP1,HMGCS2,HNF4A,HSD3B2,HTT,IFNG,IGF1,IL10,IL2,IL2RA,IL6,INSIG1,INSIG2,JUN,LCN2,MGP,MT-CO2,MTTP,MYB,NAT8,NR0B2,NR1H4,NR1I2,POR,PPARA,PPARG,RELA,SCARB1,SLCO1B1,SLCO1B3,SLCO1C1,SOCS1,SREBF1,STAT3,TCN2,TF,TNF,TNFRSF11B,UGT1A1,UGT1A3,UGT1A4,UGT1A6	1177 (25)
FOS	transcription reg	1,96E-34	ABCB1,ABCC1,ABCG5,ABCG8,ADD2,AGT,AGTR1,AKR1C3,AP3D1,APLN,AQP3,ATF3,ATXN2,BDNF,BGLAP,C3,C5,CA2,CAST,CASZ1,CAT,CCL2,CCL5,CCN2,CCND1,CD14,CHGA,CHI3L1,CLU,COBLL1,COL18A1,COL1A1,CTH,CTSH,CXCL8,CYP17A1,CYP2J2,CYP7A1,DBH,DIO2,DOCK1,EDN1,ELP1,EPHX2,ERCC1,EVX1,FBN1,FGA,FN1,FOLR2,FOS,FOXC1,FOXO3,GAS5,GATA4,GBA,GIT2,GJA1,GNRHR,GPER1,GSR,GSTP1,HAMP,HAS2,HBA1/HBA2,HLA-B,HMOX1,HSD3B1,HSD3B2,ICAM1,IFNG,IGFBP1,IL10,IL12B,IL1A,IL1RL1,IL2,IL23A,IL6,IRS2,ITGB1,JUN,LAMA3,LOX,LPL,LRP8,LTBP2,MAOA,MET,MMP1,MMP2,MMP3,MMP7,MMP9,MYH9,NCF2,NFATC1,NPPA,NPPB,NPY,NQO1,NR1H3,NR3C1,NR3C2,PGR,PLAGL1,PLAT,PLAUR,POMC,PRL,PTGDS,PTGS2,PTH1R,PTPRD,PTPRO,RALB,RARA,RARG,RGS4,RUNX1,RXRA,SDK1,SELENBP1,SERPINB7,SERPINE1,SERPINE2,SFRP2,SIRPA,SIRT6,SLC10A2,SLC19A1,SLPI,SMAD5,SOCS3,SPP1,SULF2,TFF1,TGFB1,TH,TIMP1,TNF,TNFRSF11A,TNFRSF11B,TNFSF11,TP53,TSC1,TSLP,TXN,VAV3,VCAM1,VEGFA,WNT5A,XDH,XYLT1	897 (18)

HGF	growth factor	3,88E-34	ABCG2,ACTA2,ADGRG1,ADORA2A,AFP,AHR,AKAP12,AKT1,ANGPTL4,ARNTL,ATF3,ATM,AURKA,BCL2A1,BMP2,CALCR,CALCRL,CAV1,CCL2,CCL5,CCN2,CCND1,CD28,CD40,CD46,CDKN2A,CDKN2B,CELSR1,COL1A1,COL1A2,COL3A1,COL4A1,CRY1,CSF2,CTNNB1,CXCL8,CXCR4,CYP17A1,DES,DRD3,EDN1,EFNB2,EPHA4,FAIM2,FKBP5,FLT1,FN1,FOS,GBA,GH1,GRB14,GRK5,GUCY1B1,HBEGF,HES1,HGF,HMOX1,ICAM1,IFNG,IGF1,IGFBP3,IL10,IL12B,IL13,IL15RA,IL1B,IL4,IL5,IL5RA,IL6,IL6ST,INPPL1,INSIG1,ITGA2,ITGB1,ITGB8,KIR2DL4,LCN2,LDHA,LDLR,LRP8,LTA,MAPKAPK2,MAS1,MET,MMP1,MMP14,MMP2,MMP9,NAMPT,NFATC1,NFKB1,NOS2,NOS3,NPC1,NR0B2,NR4A3,NRG1,NUMA1,OSMR,PCK1,PKD1,PLA2R1,PLAUR,PLPP3,PPARD,PRC1,PTGS1,PTGS2,PTPN2,PVR,RAC1,RGS2,RGS20,SERPINE1,SGK1,SLC19A2,SLC20A1,SLC2A2,SLC7A1,SMAD5,SNRNP70,SOCS3,SOD2,SPP1,TBXA2R,TGFB1,TGFB2,TGFBR2,THBD,THBS1,TIMP1,TIMP3,TNF,TNFAIP3,TNFRSF1A,TOPBP1,TP53,TRIB1,VCAM1,VDR,VEGFA,VEGFC	843 (15)
Vegf	group	5,24E-34	ABCB1,ACE,ACTA2,ADGRG1,ADORA2A,AHR,AKAP12,ALOX5AP,ANGPTL4,ANPEP,APLN,APLNR,APOM,AQP4,ARNTL,ATF3,AURKA,BAX,BCL2A1,BMP2,BMP7,CA2,CALCRL,CD40,CD46,CDC42,CDKN2A,CELSR1,CHI3L1,CRY1,CSF2,CTNNB1,CXCL12,CXCL8,CXCR2,CXCR4,CYP4A11,DRD3,EDN1,EFNB2,ELN,EPHA4,EPO,ERBB3,ETV5,FAIM2,FAS,FKBP5,FLT1,FLT4,FN1,GH1,GPRC5B,GRB14,GRK5,GUCY1B1,HBEGF,HES1,HIF1A,HMGCS2,HMOX1,ICAM1,IFNG,IGFBP3,IL12B,IL15RA,IL18,IL1A,IL1R1,IL4,IL5RA,IL6,IL6ST,INSIG1,ITGA2,ITGB1,ITGB8,JUN,KDR,KIR2DL4,LCN2,LDLR,LRP2,LRP8,MAGI1,MAPKAPK2,MEF2C,MET,MGP,MIF,MMP14,MMP2,MMP9,NAMPT,NFATC1,NFKB1,NGB,NOS3,NOTCH1,NPC1,NR2F2,NR4A3,NRG1,OSBPL10,OSMR,PIK3CG,PLAUR,PLPP3,PPARD,PRC1,PRKCB,PTGS2,PVR,RAC1,RGS2,RGS20,SELE,SGK1,SLC19A2,SLC20A1,SLC7A1,SLC7A2,SLCO2B1,SMAD5,SOCS3,ST8SIA4,STAT3,TBXA2R,TGFB1,TGFBR2,THBD,TIMP1,TNC,TNF,TNFRSF11A,TNFRSF11B,TRIB1,TSHZ1,VAV3,VCAM1,VEGFA,VEGFC,VWF,XDH	939 (16)
ADIPOQ	other	8,26E-34	ADIPOQ,ADIPOR1,ADIPOR2,ARG1,BMP2,CCL2,CCL5,CCN2,CCND1,CD36,CDKN2A,COL3A1,CXCL8,CYBA,CYBB,CYP11A1,CYP19A1,CYP7A1,DLK1,ESR2,FABP3,FN1,FOS,FOXP3,GCK,HBEGF,HMGCS2,HMOX1,ICAM1,IFNG,IL10,IL12B,IL17A,IL4,IL4R,IL6,LDLR,LEP,LEPR,LHCGR,LPL,MMP1,MMP2,MMP3,MSR1,NCF2,NFKBIA,NOS2,NOX4,NPPA,NR1H3,PCK1,PPARA,PPARD,PPARG,PPARGC1A,PTEN,PTGS2,PTK2B,ROCK1,SLC2A3,SLC2A4,SOCS3,SOD2,SREBF1,STAT3,TGFB1,TIMP1,TNF,TNFAIP3,TP53,TRAF1,UCP1,UCP2,UCP3,VCAM1,VEGFC	878 (19)
HMOX1	enzyme	9,64E-34	ABCA1,ACTA2,ADIPOQ,ADORA2A,ANGPT1,ANGPTL3,AQP1,BDNF,CCL17,CCL2,CCND1,CD14,CDK6,COL1A1,CXCL12,CXCL5,CXCL8,CYP1A1,CYP2E1,ENG,FGF1,FLT1,FOS,FOXP3,G6PD,GCLC,GDNF,GPX3,HGF,HMOX1,ICAM1,ID3,IFNG,IGF1,IL10,IL12B,IL17A,IL1B,IL1RN,IL23A,IL6,ITGAM,ITGB3,KDR,LIN28A,MMP9,MSR1,NOS2,NPPA,NQO1,PECAM1,PROCR,PTGS2,SELE,TGFB1,TGFB2,TH,THBD,THBS1,THBS2,TNF,TNFSF14,TP53,VCAM1,VEGFA,ZFP36	880 (15)
SMARCA4	transcription reg	1,12E-33	ABCA1,ABCB1,ACE,ACE2,ACTA2,ACTN4,ADGRG1,ADIPOQ,AFP,AGMAT,AGT,AHR,ALDH2,APOA1,APOL3,ARL4C,ATP2B4,ATP6V1B1,BCL2A1,BGLAP,BIN1,BMP4,CCL2,CCN2,CCND1,CCR2,CDKN2A,CDKN2B,CHEK2,CIITA,CKM,CNP,COL1A1,CPS1,CRYBG1,CTSH,CXCR4,CYP1A1,CYP3A4,DES,DHFR,DYNC1H1,EBF1,EDNRA,EFNB1,EPHA4,EPO,FADS3,FAS,FCGR2A,FGF9,FGFR2,FGG,FKBP5,FN1,FOLR1,FOS,GCLC,GPR83,GPX1,GSTO1,GSTP1,GYS1,HBB,HBG1,HFE,HLA-B,HLA-C,HLADRA,HNF4A,ICAM1,ID3,IFI30,IFNG,IGF1,IL13,IL15RA,IL1B,IL23A,IL4,IL5,IL6,IL7R,ITGAV,ITGB1,JUN,KDR,KIR2DL1/KIR2DL3,KIT,LAMA3,LMNA,LOX,LOXL2,MAPK1,MARCH1,MC3R,MC4R,MEF2C,MEIS1,MGP,mir-143,MMP1,MMP2,MMP7,MT-ND2,MYB,MYBPH,MYLK,MYRF,MYT1L,NADSYN1,NFKB2,NFKBIZ,NOS3,NR2F2,PCSK9,PHEX,PITX2,PLAT,PLAUR,PLPP3,PON3,POU5F1,PPARG,PSMB9,RAC2,RAMP1,RETN,RGS2,ROCK1,SERPINB7,SERPINE1,SERPINE2,SERTAD1,SFTPB,SHH,SKAP2,SLC11A1,SLC23A2,SLC2A4,SMAD6,SMARCA2,SMARCA4,SOD3,SOX17,SPP1,TAP1,TBX15,TBX2,TFF1,TGFB2,TIMP2,TLR2,TNFSF10,TNFSF13,TNNT2,TNNT3,TP53,TPM1,TSPAN8,TTR,TXNRD1,TYMS,TYRP1	1042 (21)
IL17A	cytokine	1,66E-33	ACTA2,BCL2A1,C3,CCL11,CCL17,CCL2,CCL5,CCN2,CCND1,CD14,CD40,CEBPD,COL1A1,CRP,CSF2,CXCL12,CXCL13,CXCL5,CXCL8,CXCR4,EDIL3,FAS,FOS,HBEGF,ICAM1,IFNG,IL10,IL12A,IL13,IL16,IL17A,IL17RA,IL1A,IL1B,IL1RN,IL22,IL23A,IL24,IL33,IL4,IL5,IL6,IL9,ITPR2,JAG1,JUN,LCN2,LEP,LOX,LPL,LRRK2,MLXIPL,MMP1,MMP2,MMP3,MMP9,MPO,NFKBIZ,NOS2,NOS3,OSMR,PECAM1,PPARA,PPARG,PTGFR,PTGS2,REG3A,SELE,SELP,SLC2A1,SOCS3,SREBF1,STAT3,STEAP4,TGFBR2,THBD,TIMP1,TIMP2,TIMP4,TLR2,TLR4,TNC,TNF,TNFAIP3,TNFRSF11A,TNFRSF11B,TNFRSF1B,TNFSF11,TNNC1,TSLP,VCAM1,VEGFA,VEGFC,VWF	882 (15)
Rxr	group	2,74E-33	ABCA1,ABCB11,ABCC2,ANGPTL4,APOE,AQP3,BCL11B,BGLAP,BMP7,CD36,CPT1A,CPT1B,CYP24A1,CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP4F2,CYP7A1,DIO1,DLK1,EFNB3,FURIN,GSTA1,HBEGF,HNF1B,IFNG,IGF1,IL1A,IL1B,IL2,IL6,INSIG1,INSR,ITGB2,KNG1,LEP,LTF,MGP,MMP1,MMP2,NOS2,NR0B2,NR1H3,PCK1,PDK4,PDX1,PLTP,POR,PPARG,PTGS2,PTPRO,RARB,RXRA,SLC10A1,SLCO1B3,SPP1,SREBF1,TERT,TPH1,TPH2	964 (24)
NFE2L2	transcription reg	3,18E-33	ABCB11,ABCC1,ABCC2,ABCG2,ACE,ACE2,ADCYAP1,AGT,AHR,ANG,APOA4,ATF3,ATP1A1,BDNF,BGLAP,BHMT,BRCA1,C5,CAT,CCL5,CCN2,CD36,CELA1,CHGB,COL1A1,COL3A1,CREG1,CXCL8,CYBB,DHCR7,ELN,EPAS1,EPHB4,EPHX1,F10,FABP1,FKBP5,FN1,FOXO3,G6PD,GCLC,GCLM,GHR,GNA14,GNAI2,GPX1,GPX3,GSR,GSS,GSTA1,GSTM1,GSTM4,GSTM5,GSTO1,GSTP1,HBG1,HMOX1,HNF1A,HSD3B1,ICAM1,IDE,IFNG,IL10,IL13,IL1A,IL1B,IL1RN,IL4,IL5,IL6,LMNA,LPL,M6PR,MAS1,MEF2C,MGST3,MMP9,MSMO1,NCF2,NFE2L3,NOS2,NQO1,NR0B2,NUCB2,OSGIN1,P2RX4,PAFAH1B1,PITX2,PPARG,PPARGC1A,PRKCB,PSMA4,PSMA6,PSMB4,PTGS2,PTPN1,PTPRO,RELA,RYR3,SAA1,SCARB1,SERPINA3,SERPINE1,SLC10A1,SLC1A4,SLC2A1,SLC3A1,SLC6A9,SLC7A8,SLCO1B3,SOCS3,SOD1,SOD2,SOD3,SREBF1,TBXAS1,TCN2,TGFB1,TKT,TNF,TP53,TTR,TXN,TXNRD1,UCP1,UGT1A1,UGT1A6,UGT1A7 (includes others),VCAM1,VEGFA	938 (19)
VDR	transcription reg	4,53E-33	ABCB11,ACE,ACTA2,ADIPOQ,AGT,AGTR1,AKT1,ATM,BGLAP,BRCA1,CCND1,CD14,COL1A1,CPT2,CSF2,CXCL8,CYP19A1,CYP24A1,CYP27B1,CYP2C9,CYP3A4,FGG,ICAM1,IFNG,IGFBP3,IL12B,IL18,IL1A,IL1RN,IL2,IL4,IL6,JUN,KL,LDLR,LEP,LIPE,NOD2,NPHS1,NPPA,NR0B2,NR1H4,PHEX,PRL,PTGS2,PYY,RARB,REN,SELE,SERPINC1,SLC10A2,SLCO1B3,SOCS1,SPP1,SREBF1,STAT4,TERT,TGFB1,TGFB2,THBD,TNFSF11,TPH1,TPH2,TRPV5,TSLP,UCP1,UCP2,UCP3,VDR	1028 (22)
Nr1h	group	4,85E-33	ABCA1,ABCG5,ABCG8,ACE,AGT,ANGPTL3,APOC1,APOC2,APOC4,APOE,AQP3,ATP1B1,BMP6,C2,C3,CAV1,CCL2,CCL5,CCR2,CCR5,CD40,CETP,CPT2,CSF2,CXCL8,CYP7A1,ECE1,EDN1,EDNRA,F2R,FGF1,FLT1,FLT4,GCK,IFIH1,IL10,IL12B,IL15,IL1B,IL6,INSIG2,LAT2,LIPE,LPL,MLXIPL,MYLIP,NFKB2,NFKBIZ,NLRP3,NOS2,NOS3,NPC1,PDX1,PLIN1,PLTP,PML,PPARGC1A,PRKCQ,PTGES,PTGS2,REN,SCARB1,SELP,SLC2A4,SLC8A1,SREBF1,TAP1,THBS1,TIMP3,TLR4,TNF,TP53	854 (20)
EGFR	kinase	8,31E-33	ABCG2,ACOT7,ACTA2,AKT1,AR,ARG1,BAX,CAD,CAV1,CCL2,CCL5,CCN2,CCND1,CDK6,CDKN2A,CHI3L1,CMA1,COL1A1,COL3A1,CSF2,CST3,CTNNB1,CXCL12,CXCL14,CXCL5,CXCL8,CXCR4,CYP19A1,EFNB2,EGF,EGFR,ERBB2,ERBB3,ESR1,ESR2,F2R,F2RL1,F7,FBLN2,FBN1,FOS,FOXP3,GAS5,GHR,GJA1,HAMP,HAS2,HBEGF,HIF1A,HMGA1,HP,HSD11B2,ICAM1,IFNG,IGF1,IGF2,IGFBP3,IL10,IL13RA2,IL1B,IL33,IL6,ITGA2,JAG1,JUN,LCN2,LRP8,MACF1,MET,MME,MMP1,MMP14,MMP2,MMP3,MMP9,MT-CO2,MTHFD1,MTHFR,NFKBIA,NOS2,NOTCH1,NOX1,NPPA,NUTF2,OSMR,PBX1,PLAT,PLAUR,POMC,POSTN,POU5F1,PSEN1,PSMB4,PTEN,PTGER2,PTGER4,PTGES,PTGIS,PTGS1,PTGS2,RELA,RUNX1,SDHB,SERPINA3,SERPINE1,SERPINE2,SLC2A1,SLC2A3,SLC4A7,SLPI,SOCS3,STAT3,TBXAS1,THBS1,TNC,TNF,TNFRSF11B,TNFSF11,TNNT3,TXNIP,UBA1,VCAN,VCL,VDR,VEGFA	1078 (23)
STAT1	transcription reg	1,78E-32	ABCA1,AGT,ALOX15,ALPK1,APOC2,APOE,APOL4,ARG1,AXL,BAX,C3,C4A/C4B,CCL2,CCL5,CCND1,CD14,CD40,CEBPD,CFB,CIITA,CSF2,CX3CR1,CXCL8,CYP1A2,CYP2C8,CYP2E1,CYP3A5,CYP4A11,DPP4,DUOX2,EDN1,EGLN3,FAS,FCGR2B,FOS,FOXO1,FOXP3,FURIN,GCK,HBG1,HES1,HIF1A,HLA-DQA1,HLA-DRB5,HTRA1,ICAM1,IFI30,IFIH1,IFNG,IFNL3,IGF1,IGF1R,IL10,IL12A,IL12B,IL12RB2,IL15,IL15RA,IL17A,IL18,IL1B,IL1R1,IL2,IL4,IL6,INS,IRF5,JAK2,JUN,LCN2,Ly6a (includes others),mir-27,MMP9,NOS2,NOX1,NOX4,NPPA,OAS3,OASL,PDGFRB,PDX1,PECAM1,PHACTR1,POMC,PPARG,PRL,PSMB8,PSMB9,PTGS2,PTN,RARB,RNF213,RUNX1,SERPINA3,SHH,SLC2A2,SLC8A1,SMAD2,SMAD3,SOCS1,SOCS3,SORT1,SREBF1,STAT3,TAP1,TFF1,TIGD6,TLR4,TLR8,TLR9,TNF,TNFSF10,TNFSF11,TP53,WARS,ZNF652	830 (14)
FSH	complex	2,41E-32	ACTA2,ACVR2A,ADCYAP1,ADGRG1,ADM,AHR,AKAP12,ALPL,APLN,AQP3,AR,ARL4C,ARL6IP5,ATP2A2,ATP2B1,AXL,BCL11A,BDNF,BMPR1A,BMPR2,CCN2,CCND1,CDK6,CHUK,COL18A1,CPE,CTNNB1,CXCR4,CYP11A1,CYP17A1,CYP19A1,DHCR7,DHX15,EGFR,ESR1,ESR2,FDX1,FGFR1,FKBP5,FOS,FOXO1,FSHR,GATA4,GCLC,GNAS,GNRHR,GPER1,GPRC5B,GRK5,HCRTR1,HSD11B1,HSD3B1,HSD3B2,IGF1R,IGFBP3,IL1RN,IL6,IL6R,JUN,KIDINS220,LDLR,let-7,LHCGR,LOX,LZTR1,MEF2D,mir-335,MMP2,MMP9,MSMO1,MYRF,NPPC,NPY,NPY1R,PCK1,PCSK6,PDYN,PGR,PLAT,PPARA,PPFIA4,PPP3R1,PSIP1,PTEN,PTGER2,PTGS1,PTGS2,PTPN1,RARA,RGS12,RGS4,RGS5,SCARB1,SERPINE1,SGK1,SHBG,SLC2A1,SMAD1,SMAD2,SMAD4,SMAD5,SMAD6,SMARCA4,SNAP25,STK24,TF,TFPI2,TFRC,TGFB2,TGFBR1,TGFBR2,TGFBR3,THBS1,TIMP1,TIMP2,TNFAIP3,TNFRSF11B,TP53,TPM1,TRIB1,VCL,VEGFA,VEGFC	1150 (21)
estrogen recept	group	2,51E-32	ABCA1,ABCG2,ADIPOQ,AXL,BAX,BDNF,BMP7,C3,CALD1,CAV1,CAV2,CCN2,CCND1,CD59,CDH13,CDH15,CDH4,COL13A1,COL4A1,COL9A2,CXCL12,CXCL8,CXCR4,CYP1A1,DICER1,DRD1,EDN1,EGFR,ERBB2,ERBB3,F11R,F12,FGF1,FGF5,FGFR1,FGFR2,FGFR3,FN1,FOS,HBEGF,HSPA1A/HSPA1B,ICAM1,IGF1,IL1A,IL6,IRS1,ITGB1,JAG1,JPH3,JUN,LDLR,LOXL2,LTF,mir-27,MMP1,MMP14,MMP9,MT-CO2,NOTCH3,PDGFD,PDYN,PGR,PLAUR,POR,RGS2,SELL,SERPINE1,SHH,SMAD1,SMAD3,SMAD4,SMAD6,TERT,TFF1,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,TGFBR3,TIMP1,TIMP2,TIMP3,TIMP4,TLR4,TNC,TP53,VEGFA,VEGFC,WNT3,WNT5A	1131 (18)

SMAD4	transcription reg	2,51E-32	AFP,ANGPT1,ANGPTL4,APOA1,APOA2,APOA4,APOB,APOC3,BGLAP,BMP2,BMP4,BMP7,CCL2,CCN2,CCND1,CDKN2A,CDKN2B,COL1A2,CTNNB1,CYB561,CYP17A1,CYP19A1,EDN1,EGFR,ENG,ERBB2,FGFR3,FN1,FOS,FOXP3,FUT7,GJA1,GNRHR,HAMP,HAS2,HEBP1,HHEX,HMOX1,HNF4A,HP,HSD3B1,ICAM1,IFNG,IL10,IL12B,IL17A,IL1B,IL9,ITGB1,JAG1,MET,mir-143,MMP1,NAMPT,NFKBIA,NKX2-5,NOTCH3,NPPC,NPR2,PDGFRB,POR,PTEN,PTGS2,PTK2B,PTPRC,RAC1,RUNX1,SELE,SELPLG,SERPINE1,SERTAD1,SFTPB,SGK1,SHH,SLC23A2,SMAD2,SMAD3,SMAD4,SMAD6,TBX3,TGFB1,TGFB2,THBS1,TIMP1,TIMP3,TNC,TNF,TPM1,VEGFA,VIP,ZFP36	1045 (23)
TGFBR2	kinase	2,77E-32	ACTA2,ADORA2B,ALOX12,ALOX15,ALOX5,ALOX5AP,ANGPTL4,AR,ATP1A2,BDNF,BMP6,CCN2,CCND1,CD14,CDKN2A,CDKN2B,CLU,COL1A1,COL1A2,CTNNB1,EXT2,FGF5,FGF9,FMOD,FN1,GATM,GJA1,GNRH1,HGF,HSD11B1,ICAM1,IFNG,IL10,IL17A,IL1A,IL1B,IL1RAP,IL5,IL6,JUN,KDR,KLRB1,KRAS,MMP12,MMP14,MMP2,MMP3,MMP9,NOS2,NOS3,OSTF1,PITX2,PLAGL1,PTGDS,PTGES,PTGIS,PTGS2,PTH1R,SCN7A,SELP,SERPINE1,SLC2A3,SMAD1,SMAD3,SMAD4,SOCS3,SPP1,STAT3,TBXAS1,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,THBD,THBS1,TIMP1,TNF,TNFRSF11B,TXNIP,VCL,VEGFA	1025 (20)
NFKB1	transcription reg	3,89E-32	ABCB1,ADORA1,AKR1B1,APOE,AR,ARG1,ATP6AP2,BAX,BCL2A1,BMP2,BRCA2,CASR,CCL11,CCL17,CCL2,CCL5,CCN2,CCND1,CD40,CD59,CFB,CFTR,CHI3L1,CIITA,COL1A1,COL1A2,CRP,CSF2,CXCL8,CYBB,DICER1,DROSHA,EGFR,FAS,FGG,FOS,FOXP3,GFRA1,GJA1,GRK5,HAS2,HES5,HMOX1,ICAM1,IFNG,IGFBP3,IKBKB,IKBKE,IL10,IL12A,IL12B,IL13,IL18,IL1B,IL1RN,IL2,IL23A,IL2RA,IL5,IL6,JAG1,let-7,LTA,LTC4S,mir-146,MMP3,MMP7,MMP9,MSR1,MYB,NFATC1,NFKB1,NFKB2,NFKBIA,NOD2,NOS2,NPPB,NR4A3,PI3,PTGS2,RELA,SDC4,SELE,SELP,SOD2,TERT,TGFB1,TLR2,TLR9,TNF,TNFAIP3,TNFRSF4,TNFSF10,TP53,TRAF1,TSLP,VCAM1,VEGFA	990 (15)
ETS1	transcription reg	4,11E-32	ABCB1,ANPEP,APOC2,ARL4C,BAX,BCL11A,BMP4,BRCA1,CAV1,CCL2,CCL5,CCN2,CCND1,CD14,CD69,CDK6,CDKN2A,CHUK,COL1A2,CSF2,CST2,CYP24A1,ERBB2,FCGR2A,FLT1,FN1,FOXP3,HGF,HMOX1,HSPA1A/HSPA1B,HSPA1L,HSPA8,ICAM1,IFNG,IL10,IL12A,IL12B,IL13,IL17A,IL2,IL24,IL2RA,IL2RB,IL3,IL4,IL5,IL7R,INSIG1,ITGA2B,ITGB2,ITGB3,ITGB6,MET,MGAT5,mir-146,MMP1,MMP2,MMP3,MMP7,MMP9,MSR1,MYB,NOS3,NPR1,NQO1,PARP1,PML,PRIM2,PRL,PSEN1,PTPRN2,PVR,REN,RUNX1,SELL,SERPINE1,SPP1,TBXAS1,TGFB2,TGFBR2,TNF,TNFSF14,TP53,TRPC1,TYMS,VEGFA	1065 (21)
NR1H3	ligand-depende	7,15E-32	ABCA1,ABCG5,ABCG8,ACTA2,ADRB2,ADRB3,ANGPTL3,APOA1,APOC2,APOC3,APOC4,APOE,APOM,ARL4C,ATF3,AURKA,CAT,CCL17,CCL2,CCL5,CCR2,CCR3,CCR5,CD40,CETP,CFB,CHEK2,CIDEA,CRP,CX3CR1,CYP7A1,DIO2,FDFT1,FPR1,GAS6,GCK,GPX1,GPX3,GSTM5,GSTP1,HMGCR,HSD11B1,IL10,IL12RB1,IL1B,IL1RN,IL6,INSIG2,ITGB3,LDLR,LPL,LSP1,LY86,MIF,MLXIPL,MMP9,MYLIP,NFKBIA,NOS2,NR0B2,NR1H3,PLTP,PPARG,PPARGC1A,PRC1,PRDM16,PTGS2,RARA,REN,SCARB1,SLC2A4,SLCO1B1,SOCS1,SREBF1,SREBF2,TAP1,THRA,TNF,TRH,TRIB1,TSHR,UCP1,UHRF1,VCAN,VEGFA,VEGFC,VIPR1	839 (23)
SREBF1	transcription reg	9,00E-32	ABCA1,ACADS,ADGRG1,ADH1C,ADIPOQ,AGMAT,ALOX12,APOA2,APOA5,APOC3,AR,BAX,BGLAP,CAMK1D,CCL17,CD14,CEBPD,CIDEA,CXADR,CYP27B1,CYP4F2,CYP7A1,DHCR7,DLK1,FABP3,FADS1,FADS2,FAS,FDFT1,FN1,FOXO1,G6PD,GCK,GPX3,GSR,HFE,HMGCR,HMOX1,HNF4A,HSPA1A/HSPA1B,IFI30,IL10,IL12A,IL1A,IL1B,IL6,INS,INSIG1,IRS2,KCNJ11,LDLR,LEP,LPIN1,LPL,LSS,MAT1A,MEF2C,MSMO1,MTTP,MYOD1,NCF2,NOS2,NPC1,NR0B2,NR1H3,PCK1,PCSK9,PDX1,PLA2G3,PLTP,PNPLA3,PPARG,PTGDS,PTGS2,RETN,SCARB1,SERPINA1,SERPINA3,SERPINE1,SLC20A1,SLC22A5,SLC2A2,SREBF1,TF,TGFB1,TNF,TNFRSF1B,TP53,TTN,UCP1,UCP2,UCP3,VEGFA	802 (18)
THRB	ligand-depende	1,74E-31	AKT1,ANGPTL3,APOA1,APOA2,APOA5,APOC3,APOM,ATP2A2,CCL17,CCL2,CCN4,CCND1,CDK6,CPT1A,CSF2,CTBP1,CTNNB1,CTSH,CXCR4,CYP27B1,CYP7A1,DIO1,EGF,EGFR,ENG,ERBB3,F12,FGF21,FGFR1,FGFR3,FOS,FZD4,GCH1,GHRHR,GJA5,GSN,HIF1A,IGF1R,IGFBP3,IL4,IL6,JUN,KCNMA1,LDLR,LPL,MAPK3,MAPK8,MC4R,MET,MLXIPL,MMP1,MMP2,MMP7,MMP9,MYH7,NCOR2,NPPA,NPPB,NR1H3,PAM,PCK1,PCSK2,PDK4,PER1,PITX2,PLIN1,POR,PPARG,PRL,PTGDS,PTGS2,SERPINE1,SFRP2,SLC2A4,SREBF1,SREBF2,STAT5B,TGFB1,TNF,TNFSF11,TP53,TRH,TSHR,UCP1,UCP3	771 (16)
CXCL12	cytokine	1,88E-31	ACTA2,AFP,AKR1C3,AXL,BAX,BMP2,BMP6,C5,CA2,CCL2,CCL5,CCND1,CD14,CD36,CD69,COL1A1,CTNNB1,CXCL12,CXCL8,CXCR4,CYP2A6 (includes others),CYP2C18,CYP2C9,CYP2D6,CYP3A5,DPP4,EGFR,ERBB2,ERCC1,FAS,FN1,FOS,FYN,GSR,ICAM1,IFNG,IL1A,IL1B,IL24,IL2RA,IL6,ITGB1,ITGB3,JUN,KIT,let-7,LOXL2,Ly6a (includes others),MMP14,MMP2,MMP3,MMP9,NPHS1,NUMA1,PDX1,PGR,PKD1,PTGS2,RHOC,ROCK1,RYR1,RYR2,RYR3,SELE,SELPLG,SHH,SOCS1,SOCS3,TF,TFF1,THBS1,TIMP1,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1B,TNFSF10,TNFSF11,TNNC1,TP53,XRCC3	941 (16)
AR	ligand-depende	4,14E-31	ABCA1,ADCYAP1,ADM,AKR1C3,AKT1,AQP3,AQP8,AR,ATP2A2,AVPR1A,BMP4,BMPR2,C3,C4A/C4B,CA4,CACNA1A,CACNA1C,CAMKK2,CASQ2,CAST,CAV1,CAV2,CCND1,CDKN2A,COL3A1,CORIN,CSRP3,CTNNB1,CXCL12,CYP11A1,CYP17A1,DES,DHCR7,DNM1L,DRD4,EDN1,EDN2,EDNRA,EDNRB,EGFR,ELOVL2,EPAS1,EPHX1,ERBB2,ERBB3,F9,FGF10,FGFR2,FKBP4,FKBP5,FSHR,GAS6,GDF15,GDNF,GJA1,GSN,GSTM1,GSTP1,GUCY1A1,HGF,HMGCR,HSD3B1,HSD3B2,HSPB7,IGF1,IGF1R,IGF2,IGFBP3,IL1R1,IL6,INPP4B,ITGA2,KCNH2,KCNQ1,KLK2,KLKB1,LHCGR,LMAN1,Ly6a (includes others),MAOA,MECOM,MEF2C,mir-27,MME,MRAS,MSMO1,MYB,MYL3,MYOD1,NOTCH1,NPC1,NR3C1,OVOS2,PDGFRA,PDYN,PER1,PGR,PLAT,PNMT,POMC,PRKCA,PTEN,PTGDS,PTGS1,REN,SERPINA3,SERPINE1,SGK1,SHBG,SLC2A3,SLC39A8,SLCO3A1,SMAD3,SMTN,SPP1,SRD5A2,STK39,TBXAS1,TERT,TF,TFF1,TGFB1,TGFB2,TGFBR2,THBS1,TIMP2,TIMP3,TNF,TNFSF10,TNFSF11,TNNT2,TSPAN8,VCAN,VCL,VEGFA,VIP,ZWINT	1129 (20)
WNT3A	cytokine	5,49E-31	ACTA2,AHR,ALPL,ANGPT1,ATP1B1,BDNF,BGLAP,BMP2,BMP4,CCN2,CCN4,CCND1,COL1A1,CPT2,CTNNB1,CXCL12,DLK1,DNAJC6,DPAGT1,EDN1,EFNB1,ENG,EPAS1,ERBB3,ETV5,FGF5,FMOD,FN1,GATA4,GDNF,GPA33,HAS2,HAS3,IL10,IL12B,IL6,IRS1,IRS2,JAG1,JUN,KCNK17,KDR,KIT,LCN2,LGR5,LRP6,MEF2C,MITF,MMP14,MPO,NCAM1,NKX2-5,NOS2,NRG1,PDGFRA,PITX2,PLIN1,PNPLA3,POU5F1,PPARG,PRICKLE1,PTGS2,PTH1R,ROCK2,RUNX1,SDC4,SERPINB1,SFRP2,SHH,SIM1,SLC7A1,SLC7A2,SLPI,SOX17,TBX3,TBX5,TCF7,TCF7L2,TERT,TGFB1,TGFB2,TGFB3,THBS1,TIMP3,TNC,TNF,TNFRSF11B,TNFSF11,TRIB3,TXNIP,TYRP1,VCAM1,VEGFA,WNT5A	974 (18)
KRAS	enzyme	1,34E-30	ABCA1,AGER,AHR,ANPEP,ARG1,ATF3,ATP1B1,AXL,BCL2A1,BMP4,CAD,CAV1,CCN2,CCND1,CDKN2A,CDKN2B,CHI3L1,CLU,COL1A1,COL3A1,COL4A1,CPT1B,CTNNB1,CXADR,CXCL14,CXCL8,CYBB,DDAH1,DHFR,EGFR,ELN,EPHB4,ETV5,F2RL1,FAS,FBLN2,FBN1,FCGR2A,FCGR2B,FES,FGF10,FGFR1,FN1,FOS,FOXP3,G6PD,GBA,GCLC,GCLM,GJA1,GSN,GSTM1,GSTM3,HAMP,HBEGF,HES1,HIF1A,HLA-DRB1,HMGA1,HMOX1,IFNG,IGF1R,IGF2,IGF2BP2,IKBKB,IL17A,IL1A,IL1B,IL24,IL33,IL6,ITGAM,ITGB2,ITGB3,JUN,KRAS,LCN2,LDHA,LIPG,LOX,LRP8,LTBP4,Ly6a (includes others),MADD,MAPK8,MET,MMP2,MMP3,MMP7,MMP9,MSR1,MT-CO1,MT-ND4,MTHFD1,MTRR,MYLK,NCAM1,NCF2,NF1,NFKB1,NFKB2,NFKBIA,NOS2,NOX1,NPC1,NQO1,NR3C1,NUTF2,PDGFRA,PECAM1,PLAGL1,PLAT,PPARD,PPARG,PRC1,PSEN1,PTEN,PTGS1,PTGS2,PTK2B,PTPRC,RELA,RHOC,ROCK1,S100A4,SCARB1,SDC4,SERPINA3,SERPINE2,SFTPB,SIRPA,SIRT1,SLC20A1,SLC36A2,SOD3,SORT1,SOX17,SPP1,SREBF1,SREBF2,STAT3,STAT5A,TAP1,TGFB1,TGFBR2,THBS1,TIMP2,TIMP3,TNC,TNF,TNFRSF11B,TP53,TRIB1,UBA1,VCAN,VEGFA	1068 (20)
TGFB2	growth factor	1,54E-30	ABCA1,ACTA2,AHR,ANGPTL4,BGLAP,BMP4,CCN2,CD36,CD40,CD46,CD59,CDKN2A,CIITA,COL1A1,COL1A2,COL3A1,CYP24A1,DES,EDN1,FAS,FMOD,FN1,FOS,FURIN,HAS2,HBEGF,HMOX1,HSPG2,IFNG,JAG1,KDR,LIPG,LTC4S,MLLT3,MMP9,NOS2,NOTCH1,OSR1,PDGFRB,PDK4,PECAM1,PTEN,RUNX1,SELL,SERPINE1,SMAD2,SMAD3,SMAD4,SPP1,TGFB1,TGFB2,TGFBR3,THBS1,TIMP1,TNFRSF11B,VCAN,VDR,VEGFA	917 (19)
Histone h4	group	1,77E-30	ABCB1,ADA,ADIPOQ,AGT,AKAP12,BGLAP,CCL5,CCND1,CD247,CD40,CD69,CDKN2A,CHRNA3,CIITA,CXCL8,CYP19A1,CYP24A1,DHFR,DIO1,ESR1,FLT1,FMR1,FOS,G6PD,GSTP1,HAS2,HES1,ICAM1,IGFBP1,IL1A,IL1B,IL2RA,IL6,IL9,INS,KALRN,KDM5B,KIR3DL1,MEF2C,MMP9,NEDD4L,NEGR1,NF1,OAS3,PPARG,PTGS2,RARB,SELE,SHANK2,SOCS3,SPP1,SREBF1,STAT3,STRN,TBX15,TBX2,TBX4,TBX5,TERT,TFF1,TGFBR1,TGFBR2,TNF,TNFRSF4,TNFSF10,TNFSF11,TYMS,VCAM1	1046 (22)
IL2	cytokine	2,70E-30	ABCA1,ABCC1,ACVR2A,ADCY3,AHR,ATM,BAX,BCL2A1,BMP2,C3,CACNA1E,CALCA,CAPN5,CCL11,CCL17,CCL2,CCL5,CCND1,CCR2,CCR3,CCR5,CD2,CD247,CD28,CD40,CD46,CD59,CD69,CDK5R1,CDK6,CSF2,CTLA4,CX3CR1,CXCL12,CXCL8,CXCR4,CYP1A1,CYP1A2,CYP2C9,DPP4,EDN1,EPAS1,EPHA4,FAS,FGFR1,FGFR2,FOS,FOXO1,FOXO3,FOXP3,FYN,GDF15,GPLD1,GPR83,HSPA1A/HSPA1B,HSPD1,ICAM1,ICOS,IFNG,IL10,IL10RA,IL12B,IL12RB1,IL12RB2,IL13,IL17A,IL18,IL18R1,IL18RAP,IL1A,IL1B,IL1R1,IL1RL1,IL2,IL22,IL23R,IL24,IL2RA,IL2RB,IL3,IL4,IL4R,IL5,IL6,IL7R,IL9,ITGA2,ITGA4,ITGB1,ITGB8,JAK2,JUN,KIR2DL1/KIR2DL3,KIR2DL2,KIR2DL4,KIR3DL1,KIT,KLK8,KLRB1,LDLR,LTA,Ly6a (includes others),MAF,MAPKAPK2,MLLT3,MME,MMP2,MMP9,MYB,NCR3,NFKB1,NOS2,PAX5,PECAM1,PPARG,PRKD2,PTGER2,PTGIR,PTGS2,PTPRC,RGS2,RHOC,RREB1,RXRA,S100A4,SELL,SELP,SELPLG,SLC2A3,SOCS1,SOCS3,SPP1,STAT3,STAT4,STAT5B,STC2,TFRC,TGFB1,TGFBR1,TGFBR3,TIMP1,TLR2,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1A,TNFRSF1B,TNFRSF4,TNFSF10,TNFSF11,TNFSF14,TP53,TRAF1,TRIB3,TTN,UCK2,VEGFA,XCL1	795 (17)

RNA polymeras	complex	4,18E-30	ACTC1,ADIPOQ,ALPL,APOC3,APOM,ARG1,BGLAP,BRCA1,CCL5,CD14,CD40,CDKN2A,CHEK2,CIITA,CKM,COL1A2,CXCL8,CXCR4,CYP1A1,CYP1B1,CYP24A1,CYP7A1,DHFR,DIO1,ERBB2,ESR1,FGG,FLT1,FOS,FOXC1,GATA4,GDF15,GHR,HAS2,HBB,HLA-DQA1,HNF1A,HNF4A,HSD11B2,HSPA1A/HSPA1B,ICAM1,IGF1,IGFBP1,IGFBP3,IL12B,IL17A,IL1B,IL1RN,IL2RA,IL4,IL5,IL6,INS,JUN,KISS1,LDLR,MAPK1,MAPK8,MEF2A,MEF2C,MEIS1,MMP2,MMP9,NCOA3,NFKBIA,NOS2,NOS3,NR1H4,OASL,OSGIN1,PBX1,PCK1,POMC,PPARG,PSMB9,PTGS2,RARB,SCGB1A1,SDHC,SLC6A2,SOCS3,SOD2,SORBS1,SPP1,SPTA1,TAP1,TERC,TERT,TFF1,TGFB1,THBS2,TNF,TNFSF11,TNNT2,TXN	973 (16)
Histone h3	group	7,52E-30	ABCB1,ABCB11,ADD2,ADD3,ADIPOQ,ADRA1A,ADRA1B,ADRB1,AFP,AKAP12,ARSG,BDNF,BGLAP,BMP4,CA4,CAV1,CCL2,CCL5,CCND1,CCR3,CD40,CD69,CDKN2A,CDKN2B,CIITA,COL1A2,CTNNB1,CXCL8,CYP19A1,CYP3A5,DAB2IP,DIO1,ESR1,EVX1,FGF5,FGFR1,FGFR2,FKBP5,FLT1,FMR1,FOS,G6PD,GATA2,GATA4,GHR,HES1,HNF4A,ICAM1,IFNG,IGF1,IGF1R,IGF2R,IGFBP3,IL10,IL13,IL17A,IL1A,IL1B,IL2RA,IL4,IL5,IL6,IL6R,IL9,INS,JUN,KDR,KIR3DL1,KLK2,KMT2C,let-7,MEIS1,MET,MITF,MMP9,NFKBIA,NOS2,NOS3,OPA1,OSGIN1,PAX5,PDX1,PGR,PITX2,POU2F3,POU5F1,PPARG,PPARGC1A,PTEN,PTGES,PTGS2,RARA,RARB,RETN,RGS4,RHO,SBF1,SCARB1,SCNN1A,SFTPB,SGK1,SHH,SLC12A5,SLC2A2,SLC6A2,SOCS3,SOD2,SOX17,SPATS2L,SPP1,SPTA1,SREBF1,TBX15,TBX2,TBX3,TBX5,TERT,TFF1,TGFBR1,TGFBR2,TLR2,TNFAIP3,TNFSF10,TNFSF11,TRIB1,VAMP8,VEGFA,VKORC1,ZMAT4	1069 (21)
STAT6	transcription reg	9,97E-30	ABLIM1,ALDH2,ALOX15,APOE,ARG1,ARNTL2,BAX,CA2,CAMK1D,CCDC86,CCL11,CCL17,CCL2,CCL23,CCL5,CCL8,CCR5,CD2,CD40,CD69,CNR2,COBLL1,COL1A1,COL1A2,CPT1A,CTNS,CYBB,CYP4A11,DDAH1,EFL1,EPHX1,FABP1,FADS1,FCGR2A,FGF21,FKBP5,FOXP3,GATM,GNA14,HAMP,HMGCR,HMGCS2,HSD3B1,ICOS,IFIH1,IFNG,IGF1,IGF2R,IL10,IL10RA,IL12B,IL13,IL13RA2,IL15,IL17A,IL18R1,IL1A,IL1RN,IL2,IL24,IL2RA,IL33,IL4,IL4I1,IL4R,IL5,IL5RA,IL6,IL6ST,IL9,IRS2,ITPK1,JAG1,JAK2,KIDINS220,LIPE,LTA,Ly6a (includes others),MAF,MMP12,MMP14,MMP2,MMP9,MOV10,MVK,MYB,MYO6,NCOA3,NFATC1,NFKBIA,OAS3,OASL,OPRM1,PDK4,PMS1,PPARA,PPARGC1A,PRKCA,PTGS2,RASGRP3,RNF213,SELE,SELENBP1,SELP,SERPINA1,SERPINE1,SLC4A7,SOCS1,SOX13,STAT4,STAT5A,STAT5B,STK39,TCF7,TIMP1,TNF,TNFRSF11A,TNFSF11,TSLP,UCP1,VCAM1,ZFP36	839 (17)
Creb	group	1,36E-29	ACVR2B,ADCYAP1,ADIPOQ,ADM,AKT1,ALOX5,ARG1,ATF3,ATP2A2,BDNF,BMP6,CACNA1C,CACNA1S,CALCA,CARTPT,CCK,CCN4,CCND1,CD14,CD59,CEBPD,CHGA,COMT,CPT1A,CTH,CXCL8,CYP11B2,CYP17A1,CYP19A1,DBH,EPHB4,ETV5,FAS,FOS,GJA1,GJA5,GNAS,GPR50,GRK3,GSTM3,GSTM4,HAS2,HES1,HLA-G,HTT,IFNG,IGF1,IL10,IL1B,IL2,IL22,IL6,ITGAM,JUN,KLRB1,LDLR,LEP,MAPK8,MIF,MITF,MMP1,MMP2,MYB,NF1,NOS3,NR3C1,NR4A3,OPRM1,PCK1,PDYN,PER1,PER2,PLAT,PPARG,PPARGC1A,PRKCA,PRL,PRLHR,PTGS2,RBFOX1,RET,RGS2,RYR2,SLC8A1,SLIT2,SMAD4,SOD1,SOX17,SST,SYT9,TF,TFF1,TH,TMOD4,TNF,TNFRSF11B,TNFSF11,TRH,TSHR,UCP1,USF1,VEGFA,WNT3	1066 (25)
C5	cytokine	1,50E-29	ACTA2,AKT1,ATF3,C5,C5AR2,CCL11,CCL2,CCL5,CCND1,CD46,CD59,CRP,CSF2,CXCL8,CYBB,CYP3A4,EFNB2,FCGR2A,FCGR2B,FLT1,FN1,GDF15,HGF,ICAM1,IFNG,IL10,IL12A,IL12B,IL13,IL17A,IL18R1,IL1A,IL1B,IL2,IL23A,IL4,IL5,IL6,IL9,ITGAM,ITGB2,MBL2,MET,MMP1,MMP3,MMP9,MPO,NFKB1,NFKBIA,PLAT,RNASE3,SELE,SERPINE1,SF1,TGFB1,TNF,TNFAIP3,VCAM1,VEGFA,VEGFC,ZFP36	657 (15)
RETN	other	1,76E-29	AGRP,APOA1,CARTPT,CCL2,CCN2,CX3CR1,EDN1,FABP3,FOS,FURIN,GHSR,HMOX1,ICAM1,IL6,INSR,LDLR,LPL,mir-143,MMP14,NOS3,NPY,PLAT,PTEN,PTGS2,RELA,RETN,SELE,SELP,SERPINE1,SIRT1,SLC2A4,SOCS3,SPP1,SREBF1,STAT3,TNF,UCP1,VCAM1	953 (23)
MYD88	other	2,19E-29	ARG1,ATM,ATR,BLM,C3,CCL17,CCL2,CCL5,CCN4,CD14,CD200,CD40,CEBPD,CSF2,CXCL12,CXCL13,CXCL8,EDNRB,FGF10,FOS,FPR1,GDF15,HIF1A,HLA-A,HMOX1,HP,ICAM1,IFNG,IFNK,IFNL3,IGF1,IKBKE,IL10,IL12A,IL12B,IL13,IL15,IL17A,IL18,IL1A,IL1B,IL1RN,IL22,IL23A,IL4,IL5,IL6,ITGA4,ITPR2,JAG1,JUN,let-7,MEFV,MET,mir-27,MMP14,MMP2,MMP7,MMP9,MSR1,NFKB1,NFKB2,NFKBIA,NFKBIZ,NOD2,NOS2,NOS3,NOX1,OASL,OLR1,PARP1,PTGES,PTGS2,REG3A,RELA,SAA1,SCARB1,SELE,SERPINE1,SLC7A2,SLCO3A1,SOCS1,SOCS3,SPP1,TGFB1,TIMP1,TLR2,TNF,TNFAIP3,TNFSF11,TSC22D1,VCAM1,XPA	799 (14)
MIF	cytokine	2,25E-29	ACTA2,ADGRE1,ARG1,CCL2,CCND1,CCR5,COL1A1,CRP,CXCL8,CXCR4,F2R,F2RL1,FOS,HGF,HIF1A,ICAM1,IFNG,IL10,IL12A,IL12B,IL13,IL15,IL15RA,IL16,IL17A,IL17RA,IL1B,IL2,IL23A,IL23R,IL2RA,IL4,IL4R,IL5,IL6,IL6ST,IL7R,IL9R,ITGA4,JUN,MAPK8,MET,MMP1,MMP2,MMP3,MMP9,NOS2,NR1H3,PTGS2,RETN,SOX6,SREBF1,TGFB1,TIMP1,TLR4,TNF,TP53,TPH2,VCAM1	706 (16)
Ige	complex	2,70E-29	ALOX5,AQP3,ARG1,ATP2A2,BCAT1,BCL2A1,C3,CAV1,CCL11,CCL17,CCL2,CCL5,CCR5,CD34,CD40,COBLL1,COL18A1,CSF2,CXADR,CXCL8,EDN1,EMILIN1,ETV5,F2R,FAS,FCGR2B,FLT1,FYN,GDF15,GSN,HBA1/HBA2,HBEGF,HFE,HMOX1,HSPD1,ICAM1,IFNG,IKBKE,IL10,IL12B,IL13,IL15,IL17A,IL1A,IL1B,IL2,IL2RA,IL33,IL4,IL5,IL6,IL7R,IL9,ITGAV,JAK2,KLC1,KRAS,LTA,MAPKAPK2,MIF,NFATC1,NFKB1,NFKB2,NFKBIA,NOX1,NPHS2,NPY,PECAM1,PPARG,PRKCA,PTGS2,PTPN2,PTPN22,PTPRG,RNASE3,ROCK2,RUNX1,SCARB1,SERPINB1,SLC11A1,SLC6A19,SOCS1,SOCS3,SPP1,SRM,STAT5A,TFRC,TGFB1,TLR2,TLR7,TLR9,TNC,TNF,TNFRSF11B,TNFRSF1B,TNFSF10,TNFSF14,TNFSF4,TRAF1,TSLP,VAV2,VCAM1,VDR,VEGFC,XCL1	795 (16)
VCAN	other	4,44E-29	ADAMTS9,ADM,ANG,ANGPTL4,APOE,BDNF,C3,C4A/C4B,CASQ2,CCL2,CD247,CD34,CD59,CDH13,CDKN2A,CIDEA,CLU,CPE,CXCL12,CXCL8,CYBA,EGFR,ELN,FAS,FN1,GLIS3,GUCY1B1,HAS2,HAS3,ICAM1,IFNG,IL10,IL12B,IL1B,IL1RN,IL6,ITGB1,LBP,LCN2,MEF2C,MIF,MMP9,NFKB1,NFKBIA,NOTCH3,OAS3,OLFML2B,PAM,PRELP,PTGIS,RBPJ,RGS2,ROCK1,RXRA,SMAD3,SOD2,SORT1,SPATS2L,TCF7L2,TGFB1,TGFB3,THBD,TIMP1,TNF,TP53,VCAM1,VCAN,VCL,VEGFA,ZNF618	701 (14)
ANGPT2	growth factor	4,61E-29	ABCC1,ACTA2,ADA,AGTR1,ARL4C,CAT,CCL5,CFB,COL18A1,COL1A1,COL1A2,COL3A1,COMT,CRYBB3,CYBA,CYBB,CYP11B2,DNASE1,EDN1,EGFR,EPHX2,EXT2,FAS,FKBP4,FLT4,FN1,GATA4,GSTT1,HIF1A,HMOX1,HSPA1A/HSPA1B,HSPA2,HSPA4,HSPB2,HSPD1,ICAM1,IL17A,IL18,IL1B,IL6,KLF5,LEP,LEPR,MIF,MMP1,MMP2,MMP7,MMP9,MYH7,MYOD1,NOS3,NOX1,NOX4,NPHS1,NPPA,NR3C2,OLR1,PDGFRB,PLG,POSTN,PPARA,PTGES,PTGS2,RFC1,SERPINE1,SOD1,SOD2,SOD3,TCN2,TGFBR2,THBS1,THBS2,TLR4,TNFSF11,TP53,TRAF3IP2,TXNIP,VCAM1,WNT3,XRCC1	978 (20)
INS	other	5,73E-29	ADIPOQ,ADIPOR1,ADM,APOA1,AQP3,AQP9,CAT,CBS/CBSL,CCN2,CCND1,CD36,CIDEA,CPT1A,CRP,CYP17A1,EDN1,ERBB3,F7,FADS3,FAS,FOS,FOXO1,GCG,GCK,GHRL,HGF,HIF1A,HMGCR,ICAM1,IGF1,IGF1R,IGFBP1,IGFBP3,IL6,INSR,IRS1,IRS2,JUN,LEP,LPL,MT-ND4,NOS1,NOS3,NOX4,NPY,NR1H3,PCK1,PPARG,PPARGC1A,PRDM16,PTGS1,PTGS2,PTPN1,RARB,SDHC,SELP,SLC2A1,SLC2A2,SLC2A4,SOD1,SREBF1,SREBF2,TGFB1,TNF,TP53,TRIB3,UCP1,VEGFA	973 (21)
CREB1	transcription reg	1,85E-28	ABCA1,ACVR2A,ADM,ADORA2A,ADRA1A,APOE,AQP11,ARG1,ATF1,ATF3,ATP1A1,ATP2B4,AURKA,BDNF,CACNA1C,CACNA2D1,CAMK1D,CAMKK2,CAPN5,CARTPT,CCK,CCND1,CDH13,CEBPD,CHGA,CHGB,CIITA,COX8A,CPT1A,CRHBP,CXCL8,CXCR4,CYP11A1,CYP19A1,CYP46A1,DBH,DIO2,EDIL3,EDN1,ERC2,FABP2,FGFR2,FLT1,FN1,FOS,FOXO3,FOXP3,FUT7,GAA,GFRA1,GHSR,GLA,GPR83,GRIA1,HAS2,HIF1A,HLA-A,HLA-DQB1,HLA-DRA,HLA-G,HMGCR,HMOX1,HPCAL1,HSD11B1,HSPA4,HTR2A,HTR2C,IFNG,IL10,IL1B,IL2,IL2RA,IL4,IL6,IRS2,JUN,KLF5,KLF7,LCN2,LDLR,LEP,LPL,LSS,mir-329,MMP1,MSMO1,MVK,NF1,NNAT,NOS1,NOS2,NOTCH1,NPY,NR4A3,NTSR1,OPRM1,OSTF1,PAM,PCK1,PCSK1,PDGFRA,PDYN,PER1,PER2,PLAT,PNMT,PPARG,PPARGC1A,PRCP,PRL,PSEN1,PTGS2,RBP4,REN,RGS2,SERTAD1,SFTPB,SGK1,SLC18A2,SLC19A1,SLC2A3,SLC2A4,SLC6A11,SLC8A2,SMAD6,SOD2,SST,STAT3,SV2C,TF,TFF1,TFRC,TGFBR1,TH,TLR9,TNF,TNFSF11,TRH,TRPC6,TSHR,TXN,UCP1,VEGFA,ZFP36,ZFPM2	989 (20)
MAP2K1	kinase	2,75E-28	ABCB1,ABCC1,ACTA2,ADGRG1,AHR,ALDH1L1,APOE,ATF3,BCL2A1,BRCA1,CCL2,CCL5,CCN2,CCND1,CDKN2A,CDKN2B,CKM,COL1A1,COL1A2,COL3A1,CRP,CSF2,CXCL8,CYP11A1,CYP17A1,CYP46A1,DPP4,ETV5,F2R,FOS,FURIN,GPRC5B,HIF1A,IGF1R,IL13RA2,IL1A,IL2,IL6,INS,IRS1,ITGA2B,ITGB1,ITGB3,JUN,LDLR,LEP,LHCGR,MITF,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,NFKBIA,NOS1,NOS2,PDGFRA,PECAM1,PLAUR,PTGS2,SCARB1,SERPINA1,SERPINE2,SIRPA,SMAD2,SMAD3,TFPI2,THBS1,TNC,TNF,TNFRSF11A,TNFSF10,UCP1,VEGFA,ZWINT	1109 (22)
aldesleukin	biologic drug	1,59E-03	FCGR2A,FCGR2B,HLA-B,HLA-C,HLA-DRA,HLA-DRB1,HLA-G,IFI30,JAK2,KIR2DL2,PSMB9,TAP1	
PARP1	enzyme	4,09E-28	ABCA1,BAX,BRCA2,CCL5,CCND1,COL3A1,CSF2,CTLA4,CXCL12,CXCR2,ECE1,ERBB2,FAS,FKBP5,FOS,FOXP3,GDF15,H19,HAS2,HES1,HMOX1,ICAM1,IFNG,IGF1,IL10,IL12B,IL17A,IL1B,IL2,IL2RA,IL4,IL5,IL6,JUN,KRAS,MITF,MMP2,MMP9,MT-CO1,NAT1,NOS2,NVL,OPRM1,PARP1,POU2F1,PRIM2,PTGS2,RELA,SDK1,SELP,SFTPB,SOCS1,TIMP2,TLR4,TLR9,TNF,TP53,VCAM1,VEGFC	736 (15)
KLF4	transcription reg	4,13E-28	ACTA2,ACTC1,ACVR2A,ADGRE1,ADRB2,ALPL,ANGPT1,ANKRD17,APCDD1,ARG1,ATP2A2,BAX,BCL11B,BMPR1A,CCL2,CCN3,CCND1,CD14,CD34,CDKN2B,COBLL1,COL1A1,CTNNB1,CXCL8,CYP1A1,EVX1,EXT2,FABP1,FABP2,FGF5,FLT1,FN1,FOXF1,GATA4,GPA33,HES1,ID3,IL10,IL17A,IL6,IRS1,ITGAM,KDR,KLF5,LGR5,LIN28A,MEF2C,MYH7,NF1,NOS2,NOS3,NOTCH1,NPPA,PAX2,PDGFRA,PECAM1,PFKP,PITX2,PLAT,PLAUR,POU5F1,PPARA,PRKG1,SEMA3F,SERPINA1,SERPINE1,SLC4A7,SLPI,SMAD1,SMAD4,SOCS1,SOD2,SOD3,SOX17,TBX3,TERT,TF,TGFB1,TGFB2,TGFB3,TGFBR1,THBD,THBS1,TNC,TNFSF11,TP53,TXNRD1,VCAM1,VEGFA,WNT3,WNT5A	1047 (22)

IL33	cytokine	4,26E-28	ABCA1,ACAT1,ADORA2B,APOE,ARG1,ATP10A,AXL,BCL2A1,CAMKK2,CCL11,CCL17,CCL18,CCL2,CCL5,CCND1,CCR2,CD36,CD40,CD69,CDK5R1,COL3A1,CSF2,CXCL8,CXCR2,EPAS1,EPHX2,FAS,FLT1,GOSR2,GRK2,HIF1A,HMOX1,ICAM1,IFNG,IKBKE,IL10,IL13,IL15,IL17A,IL1A,IL1B,IL1RL1,IL2,IL2RA,IL4,IL5,IL6,IL9,IRF5,ITGAM,JAG1,JAK2,KLC1,LEPR,MSR1,MYLK,NFATC1,NFKB1,NFKB2,NFKBIA,NFKBIZ,NLRP3,NOS2,NPHS2,PLAT,REL,RELA,SCARB1,SLC11A1,SOCS3,SOD2,STAT5A,TGFB1,TIMP1,TLR2,TNF,TNFAIP3,TNFRSF1B,TNFSF10,TNFSF11,TPH1,TRAF1,TSLP,UCP1,VEGFC,ZFHX3	880 (15)
COL18A1	other	5,37E-28	CCL2,CCND1,CD34,CHGA,CTNNB1,EDN1,EDNRB,EFNB2,EGFR,EPHB4,F10,F11,F12,F2R,F2RL1,F7,FGFR1,FN1,FOS,HGF,HIF1A,ICAM1,ID3,IL18,IL6,ITGAV,ITGB2,ITGB3,JUN,KDR,KNG1,LDHA,MAPK1,MAPK8,MAX,MMP1,MMP2,NOS2,PECAM1,PTGS2,RELA,RHO,SELP,SERPINE1,STAT3,THBS1,TNF,TNFRSF1A,VEGFA,VWF	846 (19)
TLR2	transmembrane	8,32E-28	ARG1,ATF3,BMP2,CAST,CCL2,CCL5,CCR2,CCR5,CD40,CD69,CEBPD,CRP,CSF2,CXCL8,CYBB,CYP27B1,FN1,FOXP3,GDNF,GJA1,GP1BA,HLA-DQA1,HLA-DRB5,HMOX1,ICAM1,IFNG,IL10,IL12B,IL13,IL15,IL15RA,IL17A,IL18,IL1A,IL1B,IL1RN,IL2,IL23A,IL2RA,IL33,IL4,IL5,IL6,IRAK1,ITGA2B,ITGA4,LEP,let-7,MCOLN2,mir-27,MMP1,MMP3,MMP9,MPO,NFKB1,NOS2,NR1H4,POMC,PTGFR,PTGS2,RELA,SELE,SELP,SOCS1,SOCS3,TGFB1,TLR2,TLR4,TNF,VDR,VWF	609 (15)
RAC1	enzyme	1,90E-27	ABCB1,ACTA2,AGT,AKT1,ATF3,CCN2,CCND1,CIITA,CKM,COL1A2,CRP,CTNNB1,CXCL8,ESR1,FAS,FN1,FOS,GSN,HIF1A,HMOX1,HSD11B2,ICAM1,IFNG,IL10,IL13,IL1B,IL2,IL23A,IL33,IL4,IL5,IL6,IL6R,ITGB1,JUN,KIR3DL2,MAPK8,MMP1,MMP14,MMP2,MMP9,MYH7,NPPA,NPPB,PLAUR,PRKG1,PRL,PTGS2,RAC1,SOD2,SOX6,STAT3,TGFB1,VCAM1,VEGFA,WNT5A	701 (15)
alefacept	biologic drug	4,58E-11	ABCB1,ADGRG1,AKR1C3,CCL5,CD2,CD69,CXCL8,CYBA,IFNG,IL12B,IL18RAP,IL23A,IL2RA,IL2RB,IL7R,KLRB1,NCAM1,NFKB2,NOS2,SOCS1,SOCS3,STAT4,TGFB1,TGFBR3	
CSF1	cytokine	1,92E-27	APOE,ARG1,BAX,CALCR,CCL2,CCL5,CCND1,CCR5,COL23A1,CTNNB1,CYBB,CYP11A1,CYP17A1,DHCR7,F2R,F2RL1,FAS,FCGR2A,FDFT1,FN1,FOLR2,FOS,GAB3,GDF15,HMGCR,HSD17B7,IFNG,IGF1,IGF1R,IKBKE,IL10,IL10RA,IL12A,IL12B,IL18,IL1A,IL1B,IL1RL1,IL23A,IL6,IL6ST,IRF5,ITGA4,ITGAM,ITGAV,ITGB1,ITGB3,JDP2,JUN,LDHA,let-7,LSS,MMP12,MMP9,MPO,MSMO1,MSR1,MVK,NCF2,NFATC1,NFKB2,PGR,PPARG,PTPRC,RUNX1,SLC2A1,SREBF2,THBS1,TLR2,TLR5,TLR6,TLR9,TNF,TNFAIP3,TNFRSF11A,TNFRSF1A,TNFRSF1B,TP53,VCAM1,VEGFA	953 (16)
CD3	complex	3,47E-27	ACADS,ACTN4,AHR,ANG,AQP3,ATM,BCL2A1,C2,CCL17,CCL18,CCL5,CCND1,CCR2,CCR5,CD2,CD226,CD247,CD28,CD69,CDK6,CSF2,CTLA4,CXCL8,CXCR4,CYBA,DPP4,EDIL3,FAS,FMO3,FOS,FOXP3,FUT7,FYN,G6PD,GLDC,GNAS,GPR37,GUCY1B1,GYS1,H19,HBG1,HIF1A,HLA-DQB1,HSPA1A/HSPA1B,HSPA8,ICAM1,ICOS,ID3,IFNG,IGF1,IL10,IL10RB,IL12B,IL12RB1,IL12RB2,IL13,IL15RA,IL16,IL17A,IL18R1,IL1A,IL1B,IL1R1,IL1RAP,IL2,IL21R,IL22,IL23R,IL2RA,IL2RB,IL3,IL4,IL4I1,IL4R,IL5,IL6,IL7R,IL9,ITGA4,JAK2,JUN,KCNA5,KCNK3,LNPEP,LRP1,LSP1,LTA,Ly6a (includes others),MAF,MAPK1,MMP2,MSR1,MT-CO1,NAMPT,NFATC1,NFKB1,NFKBIA,NKTR,NOS1,NOS2,NOS3,NR3C2,P2RY2,PDE4D,PLA2R1,PPARG,PSMA6,PTEN,PTGER4,PTGS2,PTPN22,PTPRC,RAC2,RBPJ,REL,RHOC,RHOH,RORA,RXRA,SDF2,SELPLG,SF1,SHH,SLC23A2,SLC7A1,SLPI,SNRPN,SOCS1,SOCS3,SORL1,TCF7,TFPI2,TFRC,TGFB1,TGFBRAP1,THBS1,TLR2,TNF,TNFAIP3,TNFRSF11A,TNFRSF4,TNFSF10,TNFSF11,TNFSF4,TP73,TRAF1,TSPAN9,TXNRD1,VEGFA,VIPR1,VIPR2,XCL1,ZFP36	748 (20)
IL15	cytokine	4,14E-27	ACADS,ACTN4,AHR,AKT1,AQP3,CCL11,CCL17,CCL18,CCL2,CCL5,CCN2,CCND1,CCR2,CD2,CD226,CD28,CD40,CD46,CD59,CD69,CDK6,CDKN2B,CPT1A,CSF2,CX3CR1,CXCL12,CXCL8,CXCR4,DPP4,EDN1,ERBB2,FAS,FMO3,FOXP3,FYN,G6PD,GLDC,GNAS,HMOX1,HSPA8,ICOS,IFNG,IGF1R,IL10,IL12B,IL12RB1,IL12RB2,IL13,IL15,IL15RA,IL17A,IL18R1,IL18RAP,IL1R1,IL1RAP,IL2,IL21R,IL22,IL24,IL2RA,IL2RB,IL4,IL5,IL6,IL7R,IL9,ITGB1,JUN,KIR2DL1/KIR2DL3,KIR3DL1,KIT,KLRB1,LDHA,LEP,LSP1,LTA,MAF,MAPK1,MAPK3,MIF,MLLT3,NCAM1,NCR3,NFKB1,NFKBIA,NOS2,NOTCH1,NR3C2,PFKP,PIK3R1,PPARD,PPARGC1A,PSMB8,PSMB9,PTPRC,RAC2,RBPJ,SELL,SELPLG,SF1,SIRT1,SMAD2,SMAD3,SOCS1,SORL1,TCF7,TFRC,TGFBR2,TIMP1,TKT,TLR2,TNF,TNFRSF1A,TNFSF10,TNFSF11,TNFSF4,TXNRD1,VCAM1,VDR,VEGFA,ZFP36	811 (17)
NFAT5	transcription reg	4,39E-27	AKR1B1,AQP1,AR,ATP2A2,BCL2A1,C2,CCL2,CCN4,CHEK2,COL1A1,COL1A2,CSF2,CYBB,EDN1,HSPA2,IL18R1,IL1B,IL1RN,IL2,IL23A,IL23R,IL4,IL6,IL6R,IRAK1,LCN2,NFKB1,NFKBIA,NOS2,NOX4,NRG1,PFKP,PLAT,PTGES,PTGIS,PTGS1,S100A4,SGK1,SLC14A2,SLC6A12,SLC6A6,SLC7A2,SPP1,TLR2,TNF,TNFAIP3,TNFRSF11B,TRAF1,VEGFA,VWF	1011 (18)
MTOR	kinase	4,62E-27	ADM,AKR1B1,AR,ARL4C,ATP2A2,ATP2B1,CAV3,CCL2,CCND1,CD40,CEBPD,CNP,CPT1B,CPT2,CTNNB1,CXCL8,CXCR4,CYP11A1,CYP17A1,DDAH2,DHFR,EGFR,EPAS1,ERCC1,FGB,FGFR3,FN1,FOXP3,GSTM5,HAMP,HBA1/HBA2,HIF1A,HMGCS2,HSD11B1,IFNG,IGF1,IGF2,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL1R1,IL22,IL23A,IL2RB,IL4,IL4R,IL5,IL6,IRAK1,IRS1,IRS2,JAK2,LDHA,LEP,LHCGR,MADD,MEFV,MFN2,MLXIPL,MMP9,MT-CO1,NCAM1,NFKBIL1,NOS2,NOX4,PDK4,PECAM1,PFKP,PGR,PLD2,PPARA,PPARD,PPARG,PPARGC1A,PTEN,PTH1R,PYGB,RAB11B,RELA,SELL,SERPINA1,SERPINB1,SLC12A2,SLC2A1,SLC2A4,SLC8A2,SOCS3,SOD1,SREBF1,SREBF2,STAT3,TLR4,TLR5,TNF,TNFRSF11B,TNFRSF1A,TNFSF10,TNFSF13,TP53,TXNIP,VCAM1,VEGFA	1098 (19)
Mapk	group	5,08E-27	ABCB1,ADA,APLN,APOA1,APOC3,BDNF,CAT,CCL2,CCND1,COL1A1,CXCL8,CYBB,DBP,EP300,ESR1,FOS,FURIN,GJA1,HGF,HMOX1,IFNG,IGF1,IL17A,IL1B,IL6,IRS1,ITGA4,JUN,LEP,MMP3,MMP7,MMP9,NOS1,NOS2,NOX1,NPPB,NR3C1,NR4A3,PER1,PER2,PPARD,PRL,PTEN,PTGS2,RELA,SLC6A2,SOD1,SPP1,TH,TNF,UCP1,UGT1A1,VCAM1,VEGFA	998 (19)
CD40	transmembrane	7,91E-27	A4GALT,AGTR1,ANPEP,BAX,BCL2A1,CCL17,CCL18,CCL2,CCL5,CCND1,CD40,CD69,CDK6,CNR2,CTLA4,CXCL12,CXCL8,FAS,FCGR2B,FOS,HLA-DQB1,ICAM1,IFNG,IL10,IL10RA,IL12A,IL12B,IL15,IL15RA,IL18,IL1A,IL1B,IL1RN,IL2,IL24,IL2RA,IL2RB,IL4,IL4I1,IL4R,IL5RA,IL6,IL6R,ITGAM,ITGB1,ITGB2,JUN,LTA,Ly6a (includes others),MET,MMP14,MMP3,MMP9,NFATC1,NFKB1,NFKB2,NFKBIA,NOS2,PSMB9,PTGER2,PTGS2,REL,RELA,SELE,SELL,SERPINE1,SLC2A1,TAP1,THBD,TLR2,TLR9,TNF,TNFAIP3,TNFRSF11B,TNFSF10,TNFSF4,TP53,TRAF1,VCAM1,VEGFA	677 (14)
cytokine	group	9,06E-27	ADORA2A,AGTR2,ALOX5,ANG,AQP4,BAX,CCL2,CCL5,CCN3,CCND1,CD40,CD69,CLU,CRP,CSF2,CXCL8,DICER1,EDN1,FAS,FOS,FOXP3,HIF1A,HMOX1,ICAM1,IFNG,IGFBP1,IL24,IL2RA,IL6,JUN,LEP,LIPG,Ly6a (includes others),MAPK8,MMP1,MMP12,MMP2,MMP3,MMP9,NOS1,NOS2,PLAT,PLAUR,PON1,PTGS2,RETN,S100A4,SAA1,SELE,SELP,SERPINE1,SGK1,SOCS1,SOCS3,SOD2,STAT3,STAT5A,TGFB2,TIMP1,TLR2,TLR4,TNFRSF1B,TNFSF11,VCAM1,VWF	844 (15)
HTT	transcription reg	1,92E-26	ABCA1,ACAT2,ACTA2,ACTN2,ADORA2A,ADRA2B,AGT,AKAP12,AKT1,APOA1,APOE,AQP1,ARNTL,ATF3,ATP1A1,ATP2A2,ATP2B3,BCL11B,BDNF,CA4,CACNA2D3,CARTPT,CAST,CAVIN3,CCK,CCL5,CCN2,CCN4,CCND1,CHUK,CKM,CLOCK,CNR1,CNR2,COL18A1,COL4A1,COL6A3,CPLX2,CTNNB1,DBP,DHCR7,DIO2,DRD1,DRD2,DRD3,DRD4,EBF1,EDNRB,EMC8,EP300,ETNPPL,FDFT1,FGF1,FGFR1,FKBP4,FN1,FOLR1,FOS,FOXO3,GAS7,GCLC,GHRH,GLO1,GNRH1,GPX3,GRIA1,GRK2,GRK5,GSN,GSR,GSS,HBA1/HBA2,HBEGF,HIF1A,HMGA1,HMGCR,HPCAL1,HSPA8,HSPD1,HTT,IGF2,IL15,ITGB1,JUN,KCNB1,KCNJ1,KCNJ4,KCNK3,KL,KLF5,LDHA,LDLR,LOX,LTBP2,LTF,MGP,MMP14,MMP2,MMP3,MT-CYB,MYL2,MYOD1,MYT1L,NOS1,NOS2,NPY,NR2F1,NTRK1,P2RX7,PDX1,PER1,PER2,PLAUR,POR,PPARA,PPARD,PPARG,PPARGC1A,PPP3CA,PRELP,PRKCB,PRKCG,PSMB4,PSMB8,PSMB9,PTPN22,RABIF,RARA,RARB,RBP4,RELA,RGS14,RGS4,RXRG,SDHB,SERPINA1,SERPINA3,SGK1,SIRPA,SLC12A2,SLC2A1,SNAP25,SOD1,SOD2,SORT1,SPP1,SRM,SRSF2,SST,STRN,TFRC,TH,THBS2,THRA,TIMP3,TNFSF13,TNNT3,TP53,TRH,UCP1,VCAM1,VIP,VIPR2	1153 (24)
NR1H2	ligand-depende	2,42E-26	ABCA1,ABCG5,ABCG8,ACE,AGT,APOE,AQP1,C3,CCL5,CETP,CIDEA,CRP,CYP7A1,DIO2,FDFT1,GCK,HMGCR,HSD11B1,HSD3B2,IFNG,IL1B,IL1RN,IL6,INS,LDLR,LIPE,LPL,LRP8,MMP9,NFKBIA,NOS2,NR1H3,PDX1,PLTP,PRDM16,PTGS2,RARB,REN,SCARB1,SLC2A2,SLC2A4,SMAD2,SMAD4,SREBF1,SREBF2,THRA,TNF,TRH,TSHR,UCP1,VEGFA,VEGFC	774 (21)
SMAD7	transcription reg	2,62E-26	ACTA2,ACVR2A,ACVR2B,ADH1C,APOC3,BMP2,BMP7,BMPR1A,BMPR2,CCL2,CCL5,CCN2,CDKN2B,CKM,COL1A1,COL1A2,COL3A1,COL6A3,CRP,CXCL12,CYP1A2,FAS,FGF5,FN1,FOXO1,FURIN,GAS6,GATA4,HAMP,HBEGF,HDAC9,HMOX1,ICAM1,ID3,IFNG,IL12B,IL1B,LTBP2,MET,MMP1,MMP12,MMP2,MMP9,NFKBIA,NOS2,PITX2,PLAT,POU5F1,RAC1,SEMA3F,SERPINE1,SMAD3,SOX17,TERT,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,TIMP1,TIMP3,TNF,TXN,VEGFA	804 (17)
TNFSF11	cytokine	2,66E-26	ADGRE1,ADORA2B,ADRA1A,AHR,AQP9,AURKA,BCL2A1,BMP4,CA2,CALCR,CAV1,CCL2,CCL5,CCND1,CD14,CD40,CLOCK,CTNNB1,CXCL8,CYP1A1,CYP1A2,ESR1,FAS,FOS,FOXO1,FPR1,GCH1,GCLC,GLRX,HMOX1,ICAM1,IFNG,IGF1,IKBKE,IL10,IL12B,IL13,IL15,IL15RA,IL1A,IL1B,IL1RN,IL6,IL9,IL9R,ILF3,ITGAM,ITGAV,ITGB3,JDP2,JUN,LIMK1,MMP1,MMP9,MT-CO1,MT-CYB,MT-ND4,NFATC1,NFKB1,NFKB2,NFKBIA,NFKBIZ,NOS2,NR1H3,PLAUR,POR,PTGER2,PTGER4,PTGS2,SAA1,SDC4,SERPINE1,SLC20A1,SLC2A1,SOCS1,SOCS3,SOD2,SPP1,TGFB1,TLR2,TLR4,TNF,TNFRSF11A,TNFRSF11B,TNFRSF1B,TNFSF11,TRAF1,VCAM1	905 (14)

HNF1A	transcription reg	2,96E-26	ABCC2,ABCC9,ACAT2,ACE2,ADCY10,ADH1B,ADH1C,AFP,AGT,AKR1C3,ANGPTL3,ANPEP,APOA2,APOB,APOC3,APOH,APOM,AQP3,AQP9,BTN2A1,C2,C5,CBS/CBSL,CCND1,COL3A1,CPB2,CPN1,CRP,CYB5B,CYP1A2,CYP2C9,CYP2E1,CYP7A1,DPP4,EBF1,ELOVL2,ETV5,F11,F8,FABP1,FAS,FGA,FGB,FGF10,FOLR1,FUT7,G6PC2,GATM,GC,GCK,GCKR,GLA,GLP1R,GOLT1A,GPR39,GRHPR,GSTA1,GSTCD,HABP2,HAVCR1,HGFAC,HMGCR,HNF1A,HNF1B,HNF4A,HSD11B1,IGF1,IGF1R,IGFBP1,IL17A,INS,INSR,KIR3DL1,KNG1,LBP,LCAT,LDLR,LIPA,mir-122,MLXIPL,MON1B,MTHFD1,MTTP,NPY2R,NR0B2,NR1H4,NUF2,PAH,PAX5,PCK1,PCSK1,PCSK9,PDX1,PFKP,PKHD1,PLG,PROC,RARB,SERPINA1,SERPINE1,SGK2,SLC10A1,SLC10A2,SLC22A11,SLC22A12,SLC2A2,SLC4A2,SLC5A1,SLC7A2,SLCO1B1,SLCO1B3,SLCO3A1,SLPI,SOCS3,STN1,TFRC,TNFRSF1A,TRPM2,TRPM5,TTR,UCP2,UGT1A1,UGT1A7 (includes others),UGT2B7,WDR12,WNK4,ZNF300	1027 (21)
Pka	complex	3,48E-26	APOE,BAX,CAV1,CCK,CCN2,CD14,CD40,CETP,CYP11A1,CYP19A1,DUOX1,EDN1,FGF21,FOS,GHRL,GJA1,HAS2,HMGCR,HMOX1,HNF4A,IFNG,IGF1,IGF1R,IL23A,IL4,IL5,IL6,IL9,JUN,KCNB1,LDLR,LEP,LHCGR,LIPE,mir-214,MMP3,NOS2,NOS3,NOX1,NR4A3,PCK1,PCSK1,PDE4D,PNMT,POMC,PPARGC1A,PTGS2,REN,RGS2,RUNX1,SFTPB,SGK1,SHH,SIRT6,SREBF1,SST,TNF,TNFRSF11B,TNFSF11,TSLP,TYRP1,UCP1	841 (18)
USF1	transcription reg	3,84E-26	ABCA1,AGT,AGTRAP,AKAP12,APLN,APOA2,APOA5,BAX,BRCA2,CAD,CAT,CBS/CBSL,CD2,CHI3L1,CIITA,CPT1A,CPT1B,CYP19A1,FMR1,FSHR,GHRL,HAMP,HGF,IGF2R,IGFBP1,IGFBP3,LDLR,MYH9,PCK1,PDX1,POMC,PRKG1,PTGS2,REN,SERPINE1,SHBG,SLC19A1,SLC22A2,SPP1,TBX2,TERT,TGFB1,TNFAIP3,TP53,TXNIP,UCP2	472 (7)
Pdgf (complex)	complex	3,85E-26	AKT1,BAX,CAV1,CCL2,CCN3,CCND1,CDK6,CDKN2B,COL4A1,CYBA,DIO3,EDN1,EGFR,F10,FN1,FOS,FOXO1,FOXO3,GJA1,GRIA1,HIF1A,HMOX1,ICAM1,IL13,IRS2,ITGB3,JAG1,JUN,LDLR,mir-143,MMP1,MMP2,NCAM1,NOTCH1,NOTCH3,NOX1,NOX4,PLAUR,PPARG,PTGS2,PTPN1,SERPINE1,TERT,TGFB1,TGFB3,THBD,TIMP1,TIMP3,TP53,VCAM1,VEGFA	769 (16)
anakinra	biologic drug	2,02E-09	ABCC2,CCL2,EDN1,HBA1/HBA2,HMOX1,ICAM1,IL1A,IL1B,IL6,INS,NOS2,PTGS2,SELE,SLC10A1,TNF,VCAM1	767 (19)
SPP1	cytokine	4,87E-26	ABCG2,ADIPOQ,AKT1,ANGPT1,ARG1,ATM,AURKA,BAX,BRCA1,CA2,CCL18,CCL2,CCL5,CCR2,COL1A1,CXCL12,CXCL5,CXCL8,CYP7A1,DHCR7,EGF,EGFR,ERBB2,FGFR2,FN1,FOS,GPX4,HAS2,HMGCR,HMOX1,HMOX2,ICAM1,IFNG,IGF1,IL10,IL12B,IL17A,IL1A,IL1B,IL6,INSIG1,ITGA2,ITGAV,ITGB3,JAG1,LOX,MMP1,MMP14,MMP2,MMP7,MMP9,NOS2,NOS3,NOTCH1,PIK3R1,POR,PPARG,PTGS2,S100A4,SERPINE1,SPP1,TERT,TGFB1,TGFBR1,TGFBR2,TIMP1,TNF,TNFSF11,TP53,TXNRD2,VEGFA	1007 (17)
EZH2	transcription reg	4,92E-26	ADRB1,ADRB2,ALOX5AP,ALPL,ATF3,BGLAP,BMP4,BMP7,BRCA1,C3,CACNA1E,CCL5,CCND1,CCR5,CDK6,CDKN2A,CDKN2B,CNR1,COL4A1,CSF2,CTNNB1,CXCL8,CYP1B1,DAB2IP,EGFR,EP300,EPAS1,ERBB2,EVX1,FBN1,FGF5,FKBP5,FLT1,FLT3,FOXO3,FOXP3,GATA4,GDF15,GSTM4,HOXC13,HSD11B2,ICAM1,IFNG,IGFBP1,IGFBP3,IKZF1,IL10,IL10RA,IL12B,IL12RB2,IL13,IL17A,IL18R1,IL18RAP,IL23A,IL24,IL4,IL5,IL6,JPH3,KMT2C,KRAS,LCN2,MCM8,MMP2,MMP7,MMP9,MYOD1,NFKBIA,NOTCH2,PDGFRA,PER1,PER2,PGR,PITX2,PLEKHA6,POU2F3,PPARG,PRICKLE1,PRL,PTEN,PTGES,PTGS2,PTN,RUNX1,S100A4,SAA1,SCAMP2,SERPINA1,SFRP2,SHH,SIRT1,SMAD3,SOCS1,SOCS3,SOX17,TBX3,TGFB1,TGFB2,TGFBR1,TIMP2,TIMP3,TNF,TP53,VEGFA,WNT3	1058 (24)
CD28	transmembrane	6,76E-26	AHR,ATM,BCL2A1,BIN1,C2,CCND1,CCR5,CD226,CD247,CD28,CD69,CDK6,CSF2,CTLA4,CXCL13,CXCL8,CXCR4,FOS,FOXP3,FYN,GPR37,GUCY1B1,GYS1,H19,HAMP,HBG1,HLA-DQB1,HSPA1A/HSPA1B,HSPA8,ICOS,IFNG,IGF1R,IL10,IL10RA,IL10RB,IL12A,IL12RB1,IL12RB2,IL13,IL15RA,IL17A,IL18R1,IL1B,IL1R1,IL1RAP,IL2,IL21R,IL22,IL23R,IL2RA,IL3,IL4,IL4I1,IL5,IL6,IL7R,IL9,ITGA4,JUN,LDHA,LNPEP,LSP1,LTA,MAF,mir-146,MMP2,MSR1,MT-CO1,NAMPT,NFATC1,NFKB1,NFKB2,NFKBIA,NOS1,NOS3,NR1I2,PDE4D,PLA2R1,PSMA6,PTEN,PTGER4,PTGS2,REL,RELA,RHOC,RORA,SHH,SLC7A1,SOCS1,SOCS3,STAT3,TCF7,TFPI2,TFRC,THBS1,TNF,TNFAIP3,TNFRSF11A,TNFRSF1B,TNFSF10,TNFSF11,TSC22D1,VIPR1,XCL1	668 (18)
Tnf (family)	group	7,56E-26	ADIPOQ,ATF3,BCL2A1,CAVIN3,CCL2,CCL23,CCL5,CCL8,CCND1,CCR5,CD40,CXCL12,CXCL8,CYP1A1,CYP1A2,CYP3A4,CYP3A5,DUOX1,GHR,GJA1,GJA5,HIF1A,HSD11B1,HTR2A,ICAM1,IFNG,IGF1,IKBKE,IL12A,IL12B,IL12RB2,IL1A,IL1B,IL1R1,IL33,IL6,JAG1,JUN,KDR,KL,LCN2,MMP9,NFKBIA,NOS2,NOS3,NOX4,PHEX,POMC,PTGER3,PTGS2,SAA1,SELE,SELL,SERPINE1,SHBG,SOCS3,TLR2,TNFAIP3,TNFRSF1B,TNFRSF4,TNFSF11,TRAF1,VCAM1	691 (14)
NFATC1	transcription reg	8,05E-26	AHR,BMP7,CALCR,CCND1,CD40,COL1A1,CSF2,CX3CR1,CYBB,CYP1A1,CYP1B1,EDN1,FAS,FOXP3,GCK,HNF1A,HNF1B,HNF4A,ICAM1,ICOS,IFNG,IL12B,IL17A,IL1B,IL2,IL22,IL2RA,IL33,IL4,IL5,IL6,INS,ITGAV,ITGB3,ITPR2,MYH7,NFATC1,NOX4,NQO1,PDX1,PPARG,PPP3R1,PTEN,PTGS2,SELL,SELPLG,SLC2A2,SPP1,TNF,TNFSF10,TNFSF11,VCAM1	745 (18)
PTGS2	enzyme	8,38E-26	ANG,ANGPT1,AQP1,BAX,BRCA1,CCL2,CCL5,CCND1,CHGA,CLU,CXCL12,CXCL14,CXCL5,CXCL8,CXCR2,CXCR4,CYP19A1,CYP1B1,DLK1,EDNRA,ERBB2,ERBB3,FLT1,FN1,FOS,GATA4,GRIA1,ICAM1,IGF1,IGFBP3,IL10,IL12A,IL1B,IL2,IL23A,IL6,ITGAV,KDR,LEP,LPL,MMP1,MMP14,MMP2,MMP7,MMP9,MSR1,NOS2,NOS3,PIK3CG,PPARG,PTGER1,PTGER2,PTGER3,PTGER4,PTGS1,PTGS2,RAC1,RETN,SELL,TNF,TNFSF10,TNFSF11,TP53,TRAF1,VEGFA,VEGFC,VNN1	986 (20)
CCN1	other	1,11E-25	BAX,C3,CCL2,CCND1,COL1A1,COL1A2,CTNNB1,CXCL8,ESR1,FN1,HIF1A,IFNG,IL10RB,IL12B,IL18,IL1A,IL1B,IL6,IL6ST,ITGA2,ITGAV,ITGB1,ITGB3,KDR,MIF,MMP1,MMP2,MMP3,MMP9,NOS2,NOX1,PECAM1,PTGS2,SERPINE1,TGFB1,TIE1,TIMP1,TIMP2,TLR4,TLR7,TNF,TNFSF10,TOLLIP,TP53,VEGFA,VEGFC,WNT5A	978 (20)
NR3C2	ligand-depende	1,27E-25	ABCC9,AGT,APOE,AQP4,ARG1,ATP1B1,BAX,BCL2A1,BMP4,CACNA1H,CACNA2D3,CAT,CCL2,CCN2,COL1A1,COL3A1,CXCL8,CXCR2,CXCR4,CYP1B1,DES,EDN1,FKBP1B,FKBP4,FKBP5,FN1,GHR,GPR83,GPX1,GPX3,GUCY1A1,HLA-DQB1,HMOX2,ICAM1,IGF1,IGF1R,IL1B,IL6,KDR,LCN2,MMP1,NFIA,NOS3,NOX4,NPPA,NR3C1,PLAT,PROCR,PTGS2,RGS2,SCNN1A,SERPINA3,SERPINE1,SGK1,TGFB1,TNF,TNNT3,TP53,VEGFA	756 (17)
Interferon alpha	group	1,32E-25	A4GALT,AFP,ANXA5,APOL1,APOL3,AQP3,ATF3,AXL,BCL2A1,BMP4,C3,CCL2,CCL5,CCND1,CCR3,CCR5,CD40,CD69,CELSR1,CIITA,CSF2,CTH,CXCL5,CXCL8,CYB561,CYP1A2,CYP2C9,CYP2E1,CYP3A4,EGFR,FAS,FCGR2B,FOS,HLA-A,HLA-B,HLAC,HLA-G,HSPA1A/HSPA1B,ICAM1,IFIH1,IFNG,IFNLR1,IKBKE,IL10,IL10RA,IL12B,IL12RB1,IL12RB2,IL13,IL15,IL15RA,IL17RA,IL18R1,IL18RAP,IL1B,IL1R1,IL1RN,IL2,IL21R,IL2RA,IL4R,IL5,IL6,IL6R,IL6ST,IL7R,IL9,INSR,IRF5,ITGA4,ITGAM,ITGB1,MEFV,mir-27,MMP3,MOB3C,MYLIP,NCR3,NFE2L3,NFKBIA,NOS2,OAS3,PLAT,PML,POMC,PRL,PSMB8,PSMB9,PTGES,PTGS2,PYHIN1,RABGAP1L,RELA,RNF213,SERPINB1,SGSM3,SHH,SLC2A3,SLC5A1,SLC6A4,SOCS1,SOCS3,SREBF2,STAT3,STAT4,TAP1,TERT,TGFB1,TLR2,TLR4,TLR7,TLR8,TNF,TNFSF10,TOPBP1,TYMS,VCAM1,WARS,ZNRF3	706 (14)
CRH	cytokine	1,38E-25	AQP4,AR,BAX,BDKRB2,BDNF,CRHR1,CXCL8,CYP11A1,CYP17A1,DIO2,EDN1,FOS,GNRH1,HSD3B1,IL10,IL18,IL1B,IL1RN,IL2RA,IL4,IL6,KCNMA1,KCNMB1,LEP,NOS1,NOS3,NPPA,NTSR1,OPRM1,PNMT,POMC,SCARB1,SGK1,SLC2A1,SLC2A3,SOCS3,TLR4,TNF,TPH1,VDR,VEGFA	808 (19)
BMP7	growth factor	1,39E-25	ACTA2,ADIPOQ,ADORA1,AKT1,BGLAP,BMP4,BMP7,BMPR1A,BMPR2,CCL2,CCR2,CD34,CEBPD,CIDEA,COL1A1,COL1A2,CRHR1,CXCL8,CYP19A1,DLK1,EDN1,EDN2,FN1,GJA1,GRB14,HAMP,ICAM1,IGF1,IGF1R,IGF2,IGFBP3,IL1B,IL6,IRS1,MAPK3,MMP2,NCAM1,NPHS1,PAX2,PCSK6,PIK3R1,POMC,PPARG,PPARGC1A,PRDM16,S100A4,SERPINE1,SLC2A4,SMAD1,SMAD2,SMAD5,SMAD6,SOCS3,SPP1,TCF21,TGFBR1,UCP1,VEGFA	973 (25)
APOA1	transporter	1,45E-25	ABCA1,APOA1,APOA2,APOC3,APOE,ATF3,CAV1,CCR2,CDC42,CYBB,HMGCR,ICAM1,IL1B,IL6,INSIG1,ITGAM,LCAT,MLXIPL,MPO,NOS2,NOS3,PON1,PTGIS,PTGS2,RAC1,SCARB1,SLC2A1,SOD2,SREBF1,TGFB1,TLR2,TLR4,TNF,TSLP,VCAM1,XDH	833 (19)
CCR2	G-protein coupl	1,59E-25	ADIPOQ,ARG1,CCL11,CCL17,CCL2,CCL5,CCR2,CCR5,CD40,COL1A1,COL1A2,COL4A1,COL6A3,CSF2,CXCL12,CXCL13,CXCR4,DPT,F13A1,FBLN2,FBN1,FN1,HSPG2,HTR2B,IFNG,IGF1,IL10,IL12B,IL13,IL17A,IL18,IL1A,IL1B,IL2,IL22,IL23A,IL4,IL5,IL6,ITIH3,MMP2,MMP9,PRELP,SLPI,TGFB1,TGFB2,THBS1,TIMP1,TIMP2,TIMP4,TNC,TNF,TSLP,VCAN	897 (18)
CCL2	cytokine	2,18E-25	ABCA1,ACTA2,ADIPOQ,CCL11,CCL2,CCL5,CCND1,CCR2,CD40,CEBPD,CXCL8,EGLN3,FOLR2,FOS,HTR2B,ICAM1,IFNG,IGF1,IL10,IL12A,IL12B,IL13,IL15,IL18,IL1A,IL1B,IL2,IL23A,IL4,IL6,LCN2,LPL,MMP1,MMP2,MMP9,NOTCH1,NPHS1,PPARG,PTGDS,PTGS2,SCARB1,SERPINE1,SLC11A1,TGFB1,TIMP1,TNF,VCAM1	786 (16)
RAF1	kinase	2,26E-25	ACAT2,ACOT7,AKAP12,ATP6V1B1,CA2,CALCA,CCND1,CDKN2A,CDKN2B,CRP,CSF2,CTNNB1,CTSH,CTSL,DIO2,ERBB2,ESR1,FAM13A,FAS,FGFBP1,FOS,GNRHR,HBEGF,HIF1A,HPCAL1,HSD11B2,ID3,IGF1R,IGFBP3,IL10,IL12A,IL12B,IL1B,IL1R1,IL2,IL23A,IL6,INS,ITGA2,ITGAM,ITGB1,ITGB3,JUN,LAMA3,LDHA,MCM8,MET,MGAT5,MMP1,MMP3,MMP9,NFKB1,NPPA,NPY,NQO1,OSMR,PCK1,PCSK6,PLAT,PLAUR,PRL,PTGS2,RAC1,RET,SCNN1A,SELENBP1,SERPINB7,ST3GAL4,TERT,TFPI2,TIMP1,TNF,TOMM40,TRAF1,TSC22D1,TXNIP,VEGFA	885 (18)
ZBTB16	transcription reg	2,55E-25	BGLAP,BMP2,BMP7,CCR2,CD14,CD2,CD34,COL1A1,CSF2,EYA2,F13A1,F2R,F2RL1,FGFR3,GP1BA,ICOS,ID3,IL10RA,IL12B,IL12RB1,IL13,IL17A,IL18R1,IL18RAP,IL1A,IL21R,IL22,IL23R,IL2RA,IL4,IL4R,IL6,IL6ST,IL7R,IL9R,ITGAV,ITGB3,KIT,KLRB1,Ly6a (includes others),LY86,MAF,MMP9,NFKBIZ,PBX1,PIK3R1,PTGS2,RARG,RORA,SELL,SELP,SHH,SLC2A1,SOX13,SPP1,TLR6,TNF,TNFRSF4,TNFSF11,TSC22D1,TYRP1	967 (20)

IL10RA	transmembrane	3,14E-25	ABCB1,ACSM3,ADD3,ADH1C,ALDH2,ALOX5,APOC2,BAX,BMP2,BMP4,C3,CA2,CBS/CBSL,CCL5,CCN3,CD34,CD36,CD40,CD69,CELA1,CFB,CFTR,CTH,CTLA4,CYP2C18,DPT,DRAM1,EDN1,EDNRB,EGF,F10,F13A1,FADS3,FAS,FBN1,FN1,FOLR2,FOXF1,FOXP3,GAS6,GHR,GSTM1,GSTM2,GSTM5,HGF,HGFAC,HLA-A,HSPA8,IFNG,IKBKE,IL12B,IL12RB1,IL15RA,IL17A,IL1A,IL1B,IL1RN,IL2,IL23A,IL6,ITGAM,LCN2,LTC4S,Ly6a (includes others),MECOM,MYB,NAMPT,NOS2,NR1H3,OLR1,PAM,PCK1,PDGFRA,POMC,POSTN,PPARGC1A,PROCR,PSMB8,PSMB9,REG3A,RNF213,SELENBP1,SELL,SLC2A1,SLCO2B1,SOCS3,STAT3,TAP1,TGFB1,THBS4,TLR2,TNF,TNNI3,TRPM2,TTR	600 (15)
MEF2C	transcription reg	6,01E-25	ACE2,ACTC1,ACTN2,ATF3,ATP2A2,BDNF,BGLAP,CACNA1C,CASQ2,CCL11,CCL2,CCR2,CCR5,CKM,COL1A1,COL1A2,COL3A1,CPT1B,CXCR4,DES,FOS,GATA4,GJA1,GJA5,GNRH1,HDAC9,HSPB7,IKZF1,IL6,ITGB1BP2,JUN,KCNA5,MEF2A,MEF2C,MEF2D,MMP12,MYH7,MYL2,MYOD1,NPPA,NPPB,PLAGL1,POSTN,PPARA,PPARGC1A,PTGS1,PTGS2,PTH1R,RYR2,S100A4,SFRP2,SLC2A4,SLC8A1,TNNC1,TNNT2,TPM1,TTN,ZFP36	794 (24)
IL27	cytokine	9,79E-25	ADGRE1,AHR,APOL1,CCL16,CCL2,CCL5,CD14,CD69,CEBPD,CIITA,CR1,CSF2,CTLA4,CXCL8,FOS,FOXP3,HLA-A,HLA-B,HLA-C,HLA-DPA1,HLA-DQA1,HLA-DQB1,HLA-DRA,ICAM1,ICOS,IFNG,IFNLR1,IL10,IL10RB,IL12A,IL12B,IL12RB2,IL13,IL15RA,IL17A,IL18,IL1A,IL1B,IL1RN,IL2,IL22,IL2RA,IL4,IL5,IL6,IL9,ITGAM,MAF,NFATC1,NOS2,PTGS2,SOCS1,SOCS3,TAP1,TNF,TNFRSF4,TNFSF10,TNFSF11,TNFSF13,TNFSF14,VCAM1	715 (17)
TNFRSF1A	transmembrane	1,27E-24	ABCC1,BDNF,CCL2,CCL5,CCN2,CD36,CSF2,CXCL13,CXCL8,CYP3A5,DIO2,FLT1,GCLM,GHR,GSTA1,ICAM1,IFNG,IGF1,IL10,IL12A,IL12B,IL15,IL17A,IL1A,IL1B,IL22,IL23A,IL24,IL4,IL6,ITGAM,JUN,KDR,LBP,LCN2,MMP1,MMP14,MMP2,MMP7,MMP9,MPO,MYOD1,NOS2,NQO1,P2RX7,RELA,SAA1,SELE,SELL,SELP,SERPINE1,SOCS3,SOD2,SOX6,TFRC,TGFB1,TH,THBD,TLR4,TNF,TNFRSF1A,TRAF1,VCAM1,VEGFA	983 (18)
GATA4	transcription reg	1,57E-24	ABCG5,ABCG8,ACE2,ACTC1,ACTN2,ADORA1,AGTR1,ATP2A2,CACNA1C,CASQ2,CCK,CCL11,CCL2,CCN2,CDKN2B,COL1A1,COL1A2,COL3A1,CORIN,CXCR4,CYP11A1,CYP17A1,CYP19A1,DES,DIO2,EDN1,EPHX1,EPO,F10,FABP1,FOS,FSHR,GATA4,GJA1,GJA5,HES1,HSD3B2,HSPB7,IL5,IL6,ITGB1BP2,JUN,KCNA5,LHCGR,LTBP2,MEF2C,MYH7,MYH9,MYL2,NKX2-5,NPPA,NPPB,PAX2,PML,POSTN,PTGS1,PTGS2,PYY,RARB,RYR2,S100A4,SLC10A2,SLC8A1,SLC9A3,SPP1,THBS4,TIMP1,TNNC1,TNNI3,TNNT2,TPM1,TTN,VCAM1	536 (11)
IL12 (complex)	complex	1,63E-24	ADGRE1,AHR,CCL17,CCL2,CCL5,CCR2,CCR5,CD226,CD28,CD69,CSF2,CXCL8,FAAH,FAS,FLT4,FOS,FOXP3,FURIN,FUT7,GAS5,GJA1,ICAM1,ICOS,IFIH1,IFNG,IL10,IL12A,IL12B,IL12RB1,IL12RB2,IL13,IL15,IL17A,IL18,IL18R1,IL18RAP,IL1B,IL2,IL2RA,IL3,IL4,IL5,IL6,IL7R,ITGA4,ITGB2,JUN,KIT,KLRB1,LTA,Ly6a (includes others),MIF,MMP2,MMP9,NOS2,PTGS2,SELL,SELP,SELPLG,SMAD2,SMAD3,SOCS1,SOCS3,STAT4,TFRC,TGFB1,TGFBR2,TIMP1,TLR2,TLR4,TNF,TNFRSF1A,VEGFA,XCL1	792 (18)
Mek	group	1,64E-24	ABCG2,ACAT1,ANPEP,APOE,AXL,CCN2,CCND1,CD200,CD36,CDCA7,CDK5R1,CDKN2A,CLU,COL1A2,CTNNB1,CXCL8,DDR2,EPAS1,ERBB2,ERBB3,ESR1,ETV5,FGFBP1,FGFR1,FOS,FOXP3,GDF15,GPER1,HAS2,HIF1A,IFNG,IL10,IL12B,IL15,IL1B,IL2,IL4,IL6,ITGA2B,ITGB1,ITGB3,JUN,KDR,LEP,LRP8,MAF,MMP14,MMP2,MMP9,NOX1,NOX4,NPPB,NQO1,NR1H3,PDGFRA,PDGFRB,PLPP3,POU5F1,PPARGC1A,PRL,PSEN1,PTEN,PTGS2,ROCK1,ROCK2,RUNX1,SEMA6A,SERPINE1,SH2B3,SLC20A1,SORL1,THBS1,TNF,TNFAIP3,TP53,TSHR,TYRP1,VEGFC	969 (20)
CD40LG	cytokine	1,91E-24	A4GALT,AHR,ATF3,AXL,BAX,BCL2A1,CA2,CAST,CCL17,CCL18,CCL2,CCL5,CCN2,CCR2,CCR5,CD40,CD69,CDK6,CIITA,CLU,CXCL5,CXCL8,CXCR4,CYP1B1,EGFR,FAS,FCGR2B,FLT1,FOS,FURIN,GCH1,HIF1A,HLA-DQA1,HLA-DQB1,HSPA1A/HSPA1B,ICAM1,ID3,IFNG,IL10,IL10RA,IL12A,IL12B,IL12RB1,IL15,IL1A,IL1B,IL1RAP,IL2,IL21R,IL24,IL2RA,IL2RB,IL4,IL4R,IL6,IL7R,ITGA4,ITGAM,ITPA,JAK2,JUN,LTA,MIF,MMP14,NAMPT,NCOA3,NFKB1,NFKB2,NFKBIA,NOS2,NR4A3,PLA2G4C,PLAUR,PML,PSMB8,PSMB9,PTGS2,PTPN1,PTPRG,PVR,RASA1,REL,RELA,RGS2,RNASE3,SELE,SELL,SELP,SELPLG,SERPINE1,SOCS1,SOD2,STAT3,STAT4,STAT5A,TAP1,TFRC,TNF,TNFAIP3,TNFRSF11A,TNFRSF11B,TNFSF10,TNFSF11,TNFSF4,TP53,TRAF1,VCAM1,VEGFA,WNT5A	843 (15)
DICER1	enzyme	2,56E-24	AFP,AGRP,AKT1,ANGPTL4,ANPEP,ARID3B,BDNF,CACNA1C,CCND1,CCR2,CD226,CDKN2A,CDKN2B,COL18A1,CXCL8,CXCR4,ELOVL2,ENG,ERBB2,FCGR2A,FGF10,FOS,FOXP3,GHSR,H19,HES1,HMGCR,HSD17B7,ICAM1,ID3,IFNG,IGF2,IGF2BP2,IGF2R,IL10,IL18R1,IL1B,IL2RA,IL7R,ITGA2,ITGA4,ITGAV,ITGB1,JUN,KDR,KRAS,let-7,LGR5,LIPG,LRP5,LRP6,MAF,mir-122,mir-137,mir-143,mir-146,mir-196,mir-27,mir-335,mir-515,MITF,MMP9,MYH7,NFATC1,NOS3,NOTCH1,NPHS1,NPHS2,OPTN,PIK3CG,PITX2,PRKCA,PRKCQ,PROCR,PTPRN2,RBFOX1,RET,RGS5,RUNX1,SCN10A,SERPINA1,SERPINE1,SLC4A4,SOCS3,THBS1,TNF,TP53,TRPC3,TRPC6,UCP1,WNT5A	1101 (21)
IRS1	enzyme	2,81E-24	ACTC1,ADIPOQ,BMP6,CCN4,CCND1,CDKN2B,CEBPD,CIDEA,COL3A1,COL4A1,COL6A3,DLK1,EFNB2,FOS,GAS5,GCK,GJA1,HMGCR,HMOX1,IGF1,IGFBP1,IL6,INS,INSR,IRS1,IRS2,LDLR,LEP,LPL,MEF2C,MMP14,MPO,NFKBIA,NR2F1,PCK1,PIK3R1,PLPP3,PPARG,PPARGC1A,PRDM16,RELA,SFRP2,SLC2A4,SPP1,SREBF1,SREBF2,TFF1,THRA,TNNC1,TNNT2,TNNT3,TRIB3,UCP1,UCP2,UCP3,VEGFA,WNT5A	1043 (24)
LPL	enzyme	3,31E-24	ADIPOQ,APOA1,APOA4,APOB,CCL2,CD36,CPT1A,CXCL8,FABP3,FOXO3,ICAM1,IL1B,IL6,IRS1,IRS2,LDLR,LIPE,LPL,MSR1,MYL2,NPPA,PDK4,PPARA,PPARG,PPARGC1A,SCARB1,SELE,SLC2A1,SLC2A4,TGFB1,THBS1,TNF,UCP2,UCP3,VCAM1,VEGFA	872 (21)
IL18	cytokine	3,32E-24	ADIPOQ,AQP3,ATF3,CCL11,CCL2,CCL5,CCR5,CD226,CD40,CD69,CSF2,CTH,CXCL12,CXCL8,CYP11B2,FAS,GJA1,ICAM1,IFNG,IL10,IL12A,IL12RB1,IL12RB2,IL13,IL17A,IL18,IL18R1,IL18RAP,IL1A,IL1B,IL2,IL22,IL22RA2,IL2RA,IL4,IL5,IL6,IL9,ITGAM,JUN,KIT,MMP1,MMP3,MMP9,MPO,NCR3,NFKBIZ,NOS2,NPPA,NPY,PTEN,PTGS2,SELL,SERPINB1,SLC2A3,SMAD2,SMAD3,SPP1,TF,TGFBR2,TIMP1,TLR4,TNF,TNFRSF11B,TNFSF11,VCAM1,VEGFA,XCL1	756 (16)
PGR	ligand-depende	5,33E-24	ABCG2,ADARB1,AKR1C3,ALOX15,AR,ATP1B1,CALD1,CCL8,CCND1,CD36,CD59,CEBPD,COMT,CPT1B,CPT2,CYP19A1,EDN1,EDNRA,EGFR,EPAS1,ERBB2,ESR1,F2RL1,FKBP5,FN1,FOS,FOXC1,FOXO1,GAS6,GNRHR,GPER1,GPR160,GRK4,GSTM3,H19,HBA1/HBA2,HBEGF,HES1,HIF1A,HPCAL1,HSD11B2,HSPA2,ICAM1,IGFBP1,IL12B,IL1R1,IRS1,IRS2,ITGB1,KLF5,LDLRAD4,LIG1,NFKBIA,NPC1,NT5C2,OGG1,P2RX4,P2RY2,PFKP,PGR,PNMT,POSTN,PPARG,PRKCH,PRL,PTGES,PTGS2,RHOC,RUNX1,SERPINA1,SGK1,SLC39A8,SLC9A1,SNAP25,ST3GAL4,STAT3,STAT5A,STAT5B,TFF1,TGFB3,TNC,TNF,TNFSF11,UCK2,VCAN,VCL,VDR	1168 (21)
aplidine	biologic drug	3,45E-02	FOS,JUN,RELA	
NR4A1	ligand-depende	6,52E-24	ABCG5,ABCG8,ACTA2,ADIPOQ,ADIPOR2,ADM,APOB,APOE,ATF3,CAV3,CCL5,CCND1,CD36,CD69,CIDEA,COL1A1,COL1A2,CSF2,CTNNB1,CXCL12,CYP17A1,EP300,FOXP3,G6PD,GCK,GNRHR,GSTM5,GYS1,HIF1A,HMOX1,HSD3B2,ICAM1,IDH2,IFNG,IL10,IL12B,IL13,IL16,IL17A,IL1B,IL2RA,IL4,IL5,IL6,INS,LDLR,LEP,LIPC,LPIN1,LPL,Ly6a (includes others),MAPK8,MMP7,MMP9,MTNR1B,NDUFB3,NFKBIA,NOS3,NPY,NR1H4,NR4A3,NUCB2,PCK1,PDK4,PDPR,PDX1,POMC,PPARG,PRL,PTGDS,RARB,RXRA,SDHC,SDHD,SERPINE1,SLC2A4,SMAD3,SREBF1,TGFB3,TNF,TNFSF10,UCP1,UCP2,UCP3,VCAM1	901 (20)
PROC	peptidase	6,61E-24	ACE,ACE2,AGT,ANGPT1,BCL2A1,CCL2,CLU,CXCL5,CXCL8,F2,F5,ICAM1,IL12B,IL1B,IL6,MMP2,MMP9,MOK,MPO,NFKB2,NOS2,NOS3,PROCR,SELE,SERPINE1,THBD,THBS1,TLR2,TLR4,TNF,TNFAIP3,TP53,VCAM1	859 (17)
NR5A2	ligand-depende	6,92E-24	ABCB11,ABCG5,ABCG8,AFP,APOA1,APOM,C3,C5,CCND1,CEBPD,CELA1,CETP,CRP,CYP11A1,CYP11B1,CYP11B2,CYP17A1,CYP19A1,CYP21A2,CYP7A1,FGB,FOS,GATM,HMGCR,HNF1A,HNF4A,HP,HSD3B2,ICAM1,IGFBP1,IL1B,IL1RN,IL24,IL6,JUN,KISS1,LDLR,MMP7,MMP9,NR0B2,NR1H4,NR1I2,POU5F1,PTGDS,RGS4,SAA1,SCARB1,SLC10A2,TNF,TNFRSF1B	1035 (24)
SOD1	enzyme	8,45E-24	ADORA2B,APOE,ATF1,ATP1A1,ATP1A2,BAX,BGLAP,BMP4,C5AR2,CARTPT,CAST,CCND1,CD14,CD36,CLU,CNR1,COL1A1,COMT,CTNNB1,CYB561,DCC,ERVW-1,FAS,FGF10,FGFR1,FOS,GCLC,GCLM,GDNF,GNAS,GNG5,GPX3,GSTM1,GSTM3,GSTM5,GSTP1,HMOX1,HPCAL1,HSPA4,HSPA8,HSPB2,ICAM1,IFNG,IGF1,IL10,IL15,IL1B,IL6,JUN,LIMK1,LPL,MET,MMP9,MT-CO1,MT-ND1,MT-ND4,NOS1,NOS2,NPY,P2RX4,P2RX7,PLCB4,PSMB8,PTGS2,PTK2B,RAC1,SHANK2,SIRT1,SOD1,SOD2,SPP1,STAT4,TFRC,TGFB1,TGFBR2,TNF,TNFAIP3,TNFSF11,TP53,UTS2,VCAM1,VIP	947 (20)
RORA	ligand-depende	1,12E-23	ABCA1,ABCG5,ADIPOR1,ADIPOR2,APOA4,APOA5,APOC3,APOE,AQP8,ARNTL,ARSG,ATP1B1,BHMT,CAV3,CCL5,CD36,CDKN2A,CXCL8,CXCR2,CYP19A1,CYP2A6 (includes others),CYP2C8,CYP2E1,CYP3A5,CYP46A1,CYP4A11,EPO,FABP3,FDFT1,GPX1,GSTM2,GSTM4,GSTP1,HMGCR,HSD17B7,HSD3B1,IFNG,IGF1,IGFBP1,IL10,IL17A,IL18,IL1B,IL22,IL23R,IL6,LCN2,MGST3,NAT2,NAT8,NFKBIA,NNMT,PCK1,POR,PPARGC1A,PTGS2,RBFOX1,RORA,SELENBP1,SEMA3F,SLC13A2,SLC2A3,SLC2A4,SOCS3,SREBF1,SULF2,TNF,UCP2,UCP3,UGGT2	882 (17)
DNMT3A	enzyme	1,27E-23	ACE,ACTC1,ADAMTS9,ADORA1,AGTR2,AKAP12,APLN,ATP2B4,CACNA1C,CASQ2,CKM,CNR1,CPLX2,CXCR4,CYBB,EDNRA,ETV5,FOXO1,FOXP3,FURIN,GPER1,GRK3,GSS,GUCY1A1,IFNG,IL17A,IL18R1,IL2,IRF5,IRS1,ITGAV,LRP2,MYH7,MYL2,MYL3,P2RX7,P2RY1,PAX5,PDE1A,PIK3C2B,PLA2G7,PLCB4,POU5F1,PPP3R1,PRKCB,PTGS1,PTGS2,PTPRC,RYR2,SDC4,SLC8A1,SLC8A2,SLIT2,SNRPN,SOCS3,SPP1,TGFB1,TNNC1,TNNI3,TNNT2,TSC22D1	764 (16)
IL11	cytokine	1,97E-23	ACTA2,BCL2A1,CD40,CEBPD,CRP,CXCL8,DLK1,F8,FOS,GP1BA,ICAM1,IGF1,IL10,IL13,IL15,IL18,IL1B,IL4,IL5,IL6,IL6ST,LBP,MMP1,POMC,POSTN,PPARG,SERPINA3,SFTPB,SMAD6,SOCS3,SPP1,TIMP1,TNFSF11,VCAM1,VIP,VWF,WNT5A	626 (15)

WNT5A	cytokine	2,36E-23	BMP6,CCK,CCL2,CCND1,CD14,CD40,COL1A1,CTNNB1,CXCL12,CXCL8,CXCR4,CYP11A1,CYP19A1,EGFR,ERBB2,ESR1,ESR2,FLT1,FN1,FSHR,ID3,IFNG,IKBKB,IL10,IL12B,IL15,IL1A,IL1B,IL2,IL6,KISS1,KIT,LAMA3,LHCGR,Ly6a (includes others),MMP1,MMP7,MYOD1,NFKB1,NOS2,NR0B2,PTEN,PTGS2,RET,ROR2,SOCS3,SPP1,STAT3,TLR4,TLR5,TNF,TNFRSF11A,TNFSF10,TNFSF11,VEGFA	982 (18)
IL6R	transmembrane	2,37E-23	ABCC1,CCK,CCL2,CCL5,CD36,COL1A1,COL1A2,CXCL5,CXCL8,EPO,FN1,HP,ICAM1,IGF1,IGF2,IGFBP1,IL10,IL1B,IL6,IL6R,IL6ST,MMP2,MMP3,MMP9,NAMPT,NPY,PTGS2,SAA1,SERPINA3,SOCS3,SST,STAT3,TGFB1,TH,TIMP1,TNF,TNFRSF11A,TNFRSF11B,TNFSF11,TRH,VCAM1,VEGFA	797 (17)
KITLG	growth factor	2,84E-23	ALOX5,ALOX5AP,AXL,CA2,CCL2,CCN2,CD14,CD247,CDKN2B,CMA1,CREG1,CSF2,CXCL12,CXCL8,CXCR4,EDNRB,EFNB2,ELANE,EPHB4,EPO,FGFR1,FOS,GAS6,GJA1,HMOX1,IFNG,IGF1R,IGFBP3,IL10,IL13,IL16,IL18,IL1A,IL1B,IL1RL1,IL1RN,IL3,IL4,IL5,IL6,IL9,ITGAV,ITGB3,KDR,KIR2DL1/KIR2DL3,KIT,LDLR,LTC4S,LTF,MEF2C,MME,MMP2,MPO,MS4A2,MYB,NFKBIA,NOS3,NPPA,NR3C1,OGG1,PRKCA,PRKCB,PRKCQ,PTGS2,SDHC,SLC4A1,SOCS1,ST3GAL4,STAT3,TERT,TNF,TNFRSF1A,TNFSF4,TPH1,TXNIP,UCP2,XRCC4	828 (21)
INSIG1	other	3,53E-23	ABCA1,ALOX5AP,APOE,CCL17,CCL5,CCR5,CXCL13,CXCR4,CYP4F2,DHCR7,DLK1,FADS1,FADS2,FDFT1,G6PD,HLA-DQA1,HMGCR,HMGCS2,IFNG,IL12B,IL6,IRS2,LCN2,LDLR,LHCGR,LIPA,LIPG,LPIN1,LPL,LSS,MLXIPL,MVK,NFKBIZ,OLR1,PDX1,PLA2G7,PPARG,PTGES,PTGS1,SCARB1,SELPLG,SLC2A2,SREBF1,SREBF2,STAT4,STAT5A,TGFB1,UCP2,VNN1	724 (16)
PDGFB	growth factor	3,80E-23	ACTA2,ADAMTS7,AKT1,BGLAP,CCN3,COL1A1,COL1A2,CXCL8,EPO,FGF1,FGF10,FN1,FOS,FOXO1,FOXO3,HDAC7,ICAM1,IL1RN,IL6,KCNA5,mir-143,MMP2,MMP3,MMP9,NOTCH2,NOTCH3,PDGFRB,PTEN,PTGS2,RGS5,SF1,SMAD1,SPP1,STAT3,THBS1,TIMP1,TNC,VEGFA	987 (21)
MAPK9	kinase	3,92E-23	AQP1,BAX,BMP4,CAV1,CCL2,CCL5,CCN2,CDKN2A,CXCL8,CYP1A1,DIO2,DLK1,EDN1,EGF,EPAS1,FAS,FOS,FOXP3,GSTM1,HIF1A,HMGA1,HSPB2,IFNG,IL12A,IL12B,IL12RB2,IL15RA,IL18,IL1B,IL2,IL4,IL5,IL6,JUN,LMNA,LPL,LTA,MIF,MMP12,MMP3,MMP9,NOS2,NOS3,NR1H3,NR3C2,PLAT,PPARA,PPARG,PTEN,PTGES,RAC1,SELPLG,SERPINA1,SHH,SOD2,SOD3,SREBF1,THRA,TNF,TNFAIP3,TP53,VDR,ZFP36	613 (12)
HDAC1	transcription reg	4,27E-23	ABCB1,ADIPOQ,AKAP12,APOA1,AR,ATF3,BAX,BDNF,BRCA2,CARTPT,CCL5,CCND1,CD34,CDKN2A,COL1A1,COL1A2,CXCL8,DAB2IP,DHFR,EGFR,ESR1,FABP1,FABP2,FAS,FLT1,FOS,FOXP3,GNAS,GSTP1,HBG1,HES1,IL10,IL13,IL17A,IL2,IL24,IL4,IL5,IL6,IL9,KDR,KLK2,LCN2,LGR5,LHCGR,LIG1,MEF2C,mir-146,MME,MMP9,MYH7,NFATC1,NFKBIA,NKX2-5,NOS2,PAX2,PCK1,POU5F1,PPARG,PPARGC1A,PRIM2,PTEN,PTGS2,SERPINE1,SGK1,SIRT1,SLC12A5,SLC8A1,SPP1,SREBF1,STAT3,TBX2,TBX5,TERT,TGFBR2,TNF,TP53,TP73,TYMS,UCP3,UHRF1,VDR,VHL	1103 (24)
INSR	kinase	7,34E-23	ACAA2,ACADS,ACTN4,ALAD,ALDH2,AQP1,ATF3,BCL2A1,C2,CCL2,CCN2,CCND1,CD36,CDC5L,COL6A3,CPT1B,CPT2,CRY1,CXCR4,CYP1B1,DDR2,DES,DHCR7,DIO3,DLK1,EDN1,FDFT1,FOS,FURIN,GCH1,GCK,H19,HBEGF,HMGCR,HSPD1,IFNG,IGF1,IGF1R,IGF2,IGF2R,IGFBP1,IL10,IL1B,IL4,IL6,INS,INSR,IRS1,KIT,LAT2,LEP,LEPR,let-7,LSS,LTC4S,MAOA,mir-196,mir-329,mir-335,MMP12,MMP2,MMP9,MSMO1,MT-CO1,MVK,MYH7,NAMPT,NFKB2,NOS3,NPPA,NR1H3,OLR1,PDK4,PDX1,PLAGL1,PMS1,PPARA,PPARGC1A,PRKCQ,RUVBL2,SCARB1,SERPINE1,SIRT1,SKAP2,SLC20A1,SLC2A1,SLC2A3,SLC2A4,SMAD4,SOCS3,SREBF1,SREBF2,TGFB1,TGFB3,THBS2,THRA,TNF,TNFRSF1A,TOMM40,TSC22D1,UCP1,UCP2,UCP3,UHRF1,VCAM1,YEATS4	1070 (23)
AMPK	complex	7,75E-23	ACE,ADIPOQ,AR,BAX,BMP2,CAT,CCL2,CIITA,CTNNB1,CXCL12,CXCL8,CYBB,CYP3A4,CYP4F2,FOXO3,GJA1,GSTK1,HAMP,HIF1A,HMOX1,IFNG,IL17A,IL1RN,IL22,IL6,KCNB1,LPIN1,MMP9,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,NOS2,NOX4,NR0B2,PCK1,PLIN1,PPARG,PPARGC1A,PTGS2,SERPINE1,SIRT1,SLC2A1,SLC2A4,SOD1,SREBF1,TNF,TP53,UCP1,UCP2,UCP3,VCAM1	1006 (21)
APC	enzyme	7,94E-23	APCDD1,APOB,CCK,CCND1,CHGA,CHGB,CLU,CTNNB1,CXCL12,CXCR2,DPP4,EDN1,FABP2,FGF10,GHRL,GIP,HAMP,HES1,HIF1A,HNF1A,ID3,IGF1,IL10,IL17A,IL6,JAG1,let-7,LGR5,LPL,mir-196,mir-335,mir-515,MMP3,MMP7,NOS2,NOTCH1,PDK4,PPARA,PPARD,PRKCA,PRKCB,PTEN,PTGS1,PTGS2,PYY,REG3A,SDHB,SGK1,SPP1,SST,TIMP1,TNF,TNFRSF11B,TNFSF11,TP53,VEGFA	993 (23)
IgG	complex	8,61E-23	ADGRG1,ADM,APOE,ATP1B1,C3,C5,CCL11,CCL2,CCL5,CCR2,CD40,CD69,CDKN2B,CEBPD,COL3A1,CSF2,CXCL8,DHCR7,EDN1,EGLN3,FCGR2A,FCGR2B,FGFBP1,FLT1,FN1,FOLR2,FOXP3,GNAS,GPX1,HAMP,HTR2B,IFNG,IL10,IL12B,IL12RB2,IL13,IL16,IL17A,IL1B,IL1RN,IL2,IL2RA,IL4,IL5,IL6,ITGAM,ITGB8,KLK8,LCN2,LDLR,Ly6a (includes others),MAF,MMP12,MMP9,PLAUR,PRSS8,PTGS2,SERPINB7,SERPINE1,SLC2A3,STK24,TGFB1,THBS1,TLR4,TLR7,TNC,TNF,TNFAIP3,TSLP,VCAM1,VEGFA,ZFP36	708 (16)
ITGB1	transmembrane	1,02E-22	ABCC1,ACTA2,APOE,BCAN,BMPR1A,CCL2,CCN4,CDKN2A,COL1A1,COL1A2,CXCL8,ERBB2,FBN2,FGF1,FGFR3,FN1,FOS,FOXO3,HAS3,HSPG2,ICAM1,IFNG,IGF2,IL12A,IL12B,IL17A,IL1B,IL1RN,IL2,IL6,ITGA9,ITGAV,ITGB3,JUN,LOX,LRP6,MMP1,MMP2,MMP9,NOS2,NPPB,PAPPA,PLAUR,PTGS2,RAC1,RAC2,SERPINE1,SHH,TGFB1,THBS1,TIMP2,TNF,TNFAIP3,TNFSF11,TP53,VEGFA,WNT5A	710 (15)
PPARD	ligand-depende	1,12E-22	ACAA1,ACAA2,ACTA2,ADORA1,ADORA2A,ALDH2,ALDH9A1,ANGPTL3,ANGPTL4,APOA1,APOA2,APOA4,APOB,APOE,AQP3,CCND1,CD36,CPT1A,CPT1B,CPT2,FABP1,FABP3,FLT1,FN1,GAS6,GCK,HMGCS2,HSD11B2,ICAM1,IFNG,IGFBP1,IKBKE,IL10,IL12A,IL12B,IL17A,IL1B,IL2,IL23A,IL6,LDHA,LIPE,LIPG,LPL,LRP5,MAPK1,MAPK3,MMP9,NOS2,NPPA,NPY,PCSK6,PCSK9,PDK4,PPARD,PPARG,PPARGC1A,PTEN,PTGS2,SIRT1,SLC10A2,SLC22A3,SLC2A2,SLC2A4,SREBF1,THBS1,TLR5,TNF,TNFRSF11B,TP53,UCP1,UCP2,UCP3,VEGFA	874 (20)
LDLR	transporter	1,58E-22	ABCA1,APOB,APOE,AURKA,BMP2,CCL2,CCL5,CCND1,CCR2,CCR3,CCR5,CD36,CD40,CFB,CX3CR1,CYP7A1,FADS2,FOXP3,FPR1,G6PD,GAS6,GATM,GJA1,GJA4,GJA5,HMGCR,HSPG2,ICAM1,IFNG,IL10,IL12B,IL12RB1,IL1A,IL1B,IL1RN,IL2,IL6,ITGB3,LCN2,LDLR,LPL,LRP1,LSP1,LY86,MIF,MMP14,MMP2,MMP9,MPO,MSR1,NOS3,NR1H3,PLTP,PPARA,PPARG,PPARGC1A,PRC1,PSMB9,SCARB1,SELE,SOCS1,SPP1,SREBF1,TAP1,TNF,TNFSF14,TRIB1,UCP1,UCP3,UHRF1,VCAM1,VCAN,VIPR1	1024 (20)
CEBPD	transcription reg	1,77E-22	AGT,ALOX5AP,APOC3,BCL2A1,BRCA1,BRCA2,C3,CCND1,CD14,CEBPD,CLU,CPB2,CXCL8,CXCR4,CYP19A1,CYP1A1,CYP2A6 (includes others),CYP2E1,FOS,HAMP,HGF,HIF1A,HP,IGF1,IKBKE,IL10,IL1B,IL23A,IL5,IL6,ITGAM,LEP,MITF,MMP3,NOS2,NOX1,PDGFRA,PPARG,PRL,PTGS2,TLR8,TLR9,TNF,TNFSF11,TP53,UCP1,VEGFC	1073 (25)
TWIST1	transcription reg	2,34E-22	ACTA2,AOPEP,AR,AXL,BAX,BGLAP,C3,CCK,CCL2,CCN4,CD40,CDKN2A,CELSR1,CHI3L1,CLU,COL1A1,CXCL12,CXCL8,DDR2,EFNB2,EMILIN1,ESR1,FAS,FBN2,FGF10,FGFR2,FGFR3,FMOD,FN1,FOS,FOXO1,GSN,IGFBP1,IL1B,IL6,ITGA8,ITGB3,KIT,LMNA,MET,MGST3,MME,MMP1,MMP2,NCAM1,OSGIN1,PAM,PDGFRA,PRL,PXDN,RHOC,SHH,SPP1,TF,TGFB1,TGFBR2,THBS2,TIMP3,TNF,TP53,VCAN,VEGFA	1034 (24)
TCR	complex	2,51E-22	ABLIM1,ADM,ADORA2A,ALOX12,APOA4,APOC3,APOE,BCAT1,BCL2A1,BIN1,CARD8,CCL17,CCL5,CCND1,CCR2,CCR3,CCR5,CD200,CD28,CD69,CSF2,CTLA4,CXCL13,CXCL8,CXCR4,ETV5,F5,FAS,FOS,FOXP3,FYN,HIF1A,HSPD1,ICOS,ID3,IDH2,IFIH1,IFNG,IL10,IL12RB1,IL12RB2,IL13,IL16,IL17A,IL18R1,IL1RL1,IL2,IL24,IL2RA,IL4,IL4R,IL5,IL6,IL7R,IL9,JUN,KIR3DL1,LIPA,LTA,MAF,MAPK1,MAPK8,NFATC1,NFE2L3,NFKB1,NFKB2,NFKBIA,NR3C1,OASL,P2RX7,PIK3R1,POMC,PTEN,PTK2B,PTPRC,REL,RELA,RUNX1,SELL,SERPINA3,SLC2A1,SLC2A3,SOCS1,SOCS3,SPP1,STAT3,STAT4,STAT5A,TGFB1,TLR4,TLR7,TLR9,TNF,TNFAIP3,TNFRSF1A,TNFRSF1B,TNFRSF4,TNFSF11,TSC22D1,VDR,XCL1	706 (19)
THRA	ligand-depende	3,53E-22	ANGPTL4,APOA1,APOA5,ATP2A2,BMP4,CCL17,CCL2,CCND1,CPT1A,CSF2,CTBP1,CTSH,CYP27B1,CYP7A1,DES,DIO1,DIO3,ENG,FGFR1,FGFR3,FOS,FURIN,GHRHR,HAMP,HMOX1,IGF1,IL4,IL6,JUN,LDLR,LPL,MC4R,MMP7,MYH7,NPPA,NTRK1,PCK1,PCSK2,PDX1,PGR,POR,PPARG,PRL,RARB,SERPINE1,SFRP2,SLC2A4,SLC6A12,SLC9A1,SREBF1,SREBF2,TGFB1,TNF,TP53,TRH	846 (18)
DCN	other	4,11E-22	BAX,CCN2,CKM,COL1A2,ENG,ERBB2,FBN1,HIF1A,HLA-DQA1,HLA-DQB1,ICAM1,IFNG,IGF1R,IL1B,IL6,IRS1,ITGAV,ITGB1,KIT,MET,MMP1,MMP2,MMP9,NOS2,SERPINE1,SMAD3,TCHP,TGFB1,THBS1,TIMP3,TNF,TP53,VCAM1,VEGFA	1000 (20)
NOS2	enzyme	4,47E-22	ACTC1,ADIPOQ,API5,AR,ATP2A2,BAX,BCL2A1,CAV3,CCL2,CD14,CHI3L1,COL4A1,CXCL8,CYP2E1,EDN1,FAS,FOXO1,FOXP3,G6PD,GDNF,GJA1,H19,HIF1A,HMOX1,IFNG,IL10,IL12B,IL17A,IL1B,IL1RN,IL2,IL6,IRAK1,IRS1,IRS2,KDR,LCN2,LEP,MAPK8,MMP9,MYH7,MYL2,MYL3,NFKBIA,NKX2-5,NOS2,NOS3,NPPA,PPARGC1A,PRL,PTGS1,PTGS2,RELA,SERPINA3,SLC2A4,TCAP,TGFB1,TIMP1,TKT,TLR4,TNF,TNFSF10,TNNC1,TNNI3,TNNT2,TNNT3,VEGFA	925 (22)
JUNB	transcription reg	5,43E-22	ACAT2,AGTR1,APOC3,APOM,ATF3,BDNF,C3,C5,CAV1,CCND1,CDKN2A,CLU,COL1A1,COL1A2,COMT,CSF2,CYP19A1,CYP1B1,FBLN2,FN1,FOXP3,GCM1,HES1,HMOX1,IL10,IL12B,IL1RL1,IL2,IL4,IL5,IL6,ITGAV,ITGB3,LCN2,LIPE,MMP1,MMP2,MMP3,MMP9,NCF2,PLAUR,PLIN1,POMC,ROCK1,SERPINE1,SGK1,SLC7A1,SLC8A1,SST,TBX3,TIMP1,TIMP3,TNF,UGT1A3,VAMP8	1060 (22)

MAPK1	kinase	6,87E-22	ADH1C,ANPEP,APOE,AR,ATF3,ATP1A2,ATP1B1,AURKA,BCL11A,BDNF,BGLAP,BLZF1,CAV1,CAV3,CCL2,CCL5,CCN2,CCND1,CD69,CDK5R1,CFB,CRYBG1,CTNNB1,CXCL8,EGLN3,ERAP1,ERCC1,ESR1,EVI5,F9,FES,FN1,FOS,FOXP3,GNRHR,GPR83,HBA1/HBA2,HBB,HLA-B,HLA-C,HMOX1,IFIH1,IFNG,IL12RB1,IL13,IL1B,IL1RN,IL2,IL2RA,IL5,IL6,ITGA2B,ITGAV,ITGB3,ITPR2,JUN,LIG1,LMNA,MAPK3,MITF,MMP1,MMP2,MMP9,MYH7,MYRF,NFATC1,NOS2,NPPA,OAS3,OASL,PITX2,PLA2G5,PML,POU5F1,PRKG1,PRL,PSMB8,PSMB9,PTGER2,PTGS2,RGS2,SCNN1A,SFRP2,SHANK2,SIRT1,SIRT6,SLC4A7,SPP1,TAP1,TFF1,TNF,TNFRSF1B,TNFSF10,TNFSF11,TP53,TRPC1,VDR	881 (18)
Hdac	group	7,12E-22	ACVR2B,ADGRL3,AGTR1,AGTR2,AHR,ATF3,BDNF,BMP2,CCND1,CTNNB1,CXCL8,CXCR4,CYP24A1,EDN1,EDN3,EDNRA,EDNRB,EGFR,ERBB2,FOS,GDNF,HIF1A,HLA-DRA,HNF1B,HTRA1,IGF1,IGFBP3,IL1B,IL2,IL6,IL6R,IL9,ITGA8,JUN,KCNH2,let-7,LHCGR,LRP2,mir-146,mir-27,MMP14,MYOD1,NTRK1,OSR1,PBX1,PKHD1,PPARGC1A,RARB,SFRP2,SLC8A1,SPP1,TBX3,TCF21,TFAP2B,TGFBR2,THBS4,TIMELESS,TNF,TNFSF10,TNFSF4,TRPC6,TXNIP	1160 (20)
ATF2	transcription reg	8,81E-22	APOC3,ATF3,BCL2A1,CCND1,CDKN2A,CTNNB1,CXCL8,CYP11B2,FGF21,FN1,FOS,GIP,IFNG,IL10,IL13,IL1RL1,IL2,IL23A,IL6,ITGB8,JUN,MMP1,MYH7,MYLK,NOS2,NOTCH1,NPPA,NPPB,PCK1,PDGFRA,PPARG,PPARGC1A,PSEN1,PTEN,PTGS2,RELA,SOD2,SST,TF,TGFB2,TH,TNF,TSHR,UCP1,VCAM1	936 (16)
NRG1	growth factor	9,24E-22	ABCA1,ACAT1,ANGPT1,AR,ATF1,BIN1,BRCA1,CAV1,CCN2,CCND1,CDH4,COL1A1,COL6A3,CXCL8,CXCR4,CYP11B1,EDN1,ERBB2,ERBB3,ESR2,FGF1,FN1,FOS,GATA2,GATA4,GPER1,GPX3,HES1,HIF1A,HMGA1,HMGCR,HMOX1,IGF2,IL10,ITGAM,ITGAV,ITGB3,JUN,MAF,MMP9,MSR1,MYBPC3,MYL2,NCOR2,NKX2-5,NOTCH1,NPPA,NR4A3,NRG1,NTRK1,PAFAH1B1,PGR,PLAUR,PLG,POU5F1,PRL,PTGS2,RUNX1,SELE,SHBG,SLC2A1,SLC2A3,SLC2A4,SLC4A7,TF,TFF1,TGFBR1,TNFAIP1,TNNI3,VCL,VEGFA,VEGFC,VIP,ZFP36	927 (17)
RUNX1	transcription reg	1,18E-21	ADGRG1,ALOX12,BAX,BGLAP,CD34,CDKN2A,CDKN2B,CHI3L1,CSF2,CTLA4,CYB561,CYP11A1,ENG,EP300,EPAS1,EVI5,FAS,FOXP3,GATA2,HBA1/HBA2,IFNG,IGF2R,IGFBP3,IL10,IL17A,IL1B,IL2,IL2RA,IL3,IL4,IL6R,IL7R,ITGA2,ITGA2B,ITGA4,ITGA9,ITGAV,ITGB1,ITGB3,KLRB1,Ly6a (includes others),MECOM,MET,mir-143,mir-27,MPO,MYH9,NCAM1,NR2F2,NR4A3,NTRK1,PRKCB,PRKCQ,ROCK1,RUNX1,SERPINE1,SHANK2,SLC24A3,SOX17,SOX6,SPP1,STAT3,TIMP1,TP53,VEGFA	944 (25)
Pro-inflammato	group	1,71E-21	ABCC2,ADIPOR2,ADM,AKR1B1,APOE,CALCA,CCN3,CLU,CSF2,CXCL13,ENPP1,EPO,GCLC,GSTA1,HAMP,HMOX1,HP,ICAM1,IL6,LCN2,LIPG,mir-146,MMP3,MMP9,NOS2,NR1H4,OLR1,PI3,SDC4,SELE,SELP,SIRT1,SLC6A4,SOCS3,TIMP1,TLR2,TSLP,VCAM1	948 (19)
PIK3R1	kinase	1,91E-21	AR,ATP1A1,CCND1,CD36,COL1A2,CXCL8,ENG,FOS,FOXO1,GCH1,HIF1A,HMOX1,ICAM1,IFNG,IL12A,IL12B,IL1B,IL2,IL6,LDHA,MITF,MMP2,NOS2,PCK1,PDGFRA,PDGFRB,PDX1,PIK3R1,PPARG,PTEN,PTGS2,SELP,SERPINE1,SLC2A1,SOD2,TNF,TRIB3,TXNIP,VCAM1,VEGFA,VEGFC	1076 (18)
CNR1	G-protein coupl	2,31E-21	ADIPOQ,ADORA1,ADRB3,ALPL,APCDD1,APOE,BCL11B,BDNF,BMP2,BMP4,BMP7,CARTPT,CNR1,DRD2,EGF,ERBB2,FGF10,FOS,GDNF,GLO1,HSPA4,IFNG,IGF1,IGF1R,IL10,IL6,LEP,LIPC,MAEL,NOD2,NPHS1,NPHS2,NR3C1,PAFAH1B1,PAX5,PDGFRA,PDGFRB,PDYN,PECAM1,POMC,PTGS2,PTK2B,RAC1,RXRG,SCARB1,SHH,SLC2A4,SLIT2,SOX6,SREBF1,STAT3,TGFB1,TIMP1,TNF,UCP1,VEGFC	896 (19)
GSK3B	kinase	2,62E-21	AR,ATP2A2,BAX,BCL2A1,CCL2,CCND1,CKM,CSF2,CTNNB1,CXCL8,ESR1,FOS,FTO,GATA4,HIF1A,IFNG,IGF1R,IL10,IL12B,IL13,IL1B,IL6,IRS2,KDR,LCN2,MAP4,MMP9,MYB,NCOA1,NFATC1,NFE2L3,NFKBIZ,NKX2-5,NOS2,NPPA,NTSR1,PDX1,PTGS2,RAC1,SELP,SERPINE1,SIRT1,SPP1,SREBF1,TCF7L2,TNF,TNFSF10,TNNC1,TNNI3,TP53,TRAF1	849 (19)
BMP2	growth factor	3,02E-21	ACTA2,ADAMTS7,ALPL,BGLAP,BMP2,BMP4,BMPR1A,BMPR2,CALCA,CCND1,COL1A1,COL1A2,CXCL12,CYP17A1,CYP19A1,DBH,EGF,EPHX2,FGF21,FGFR1,FGFR2,FN1,FOS,FOXO1,FOXP3,GFRA1,HAMP,HAS2,HES5,ID3,IL2,JUN,let-7,LHCGR,LRP5,MEF2C,mir-2861,MMP9,MRAS,NFATC1,NKX2-5,NOS3,NOTCH1,NPPA,NTRK3,PCSK6,PITX2,POMC,POSTN,POU5F1,PPARG,PTGS2,PTH1R,RET,SMAD1,SMAD4,SMAD6,SOX6,SPP1,TBX2,TH,TIMP1,TIMP3,TNFRSF11B,TNFSF11,TNNI3,VCAN,VDR,VEGFA	968 (19)
PI3K (family)	group	3,43E-21	ABCA1,ACTA2,ADM,CAT,CCL2,CDKN2B,CXCL12,CXCL8,CXCR4,EGLN3,ESR1,FOS,FOXO1,FOXO3,GCLC,GCLM,HAMP,HIF1A,HMOX1,IL10,IL12B,IL17A,IL1B,IL6,ITGB1,LEP,MMP12,MMP2,MMP3,MMP9,NOS2,NQO1,PTEN,PTGS1,PTGS2,SCARB1,SERPINE1,SHH,SIRT1,SLC2A1,SLC4A7,SREBF1,THBS1,TNC,TNF,TNFSF10,TP73,TXNIP,VEGFA	1043 (19)
FGF1	growth factor	3,47E-21	ADGRE1,AFP,AHR,AKR1B1,APOE,CCN2,CCN4,CCND1,CTNNB1,DIO3,EDN1,FGFR1,FOS,GCLC,GCLM,GDNF,GPX1,GSTM1,GSTM5,GSTP1,HAS2,HMOX1,ICAM1,IL1B,IL4,IL6,IRS1,ITGAM,JUN,NOS3,NOTCH1,NOTCH3,NQO1,NR1H3,POSTN,PRICKLE1,PTGS2,SELE,SERPINB1,SLC7A2,SPP1,TGFB1,TGFB2,TGFB3,TH,THBS1,TIMP3,TNF,TTR,VCAM1,VEGFA,VEGFC	1011 (19)
RAS	group	3,60E-21	ANPEP,AURKA,CAV1,CCK,CCL2,CCN2,CCND1,CDK6,CDKN2A,CDKN2B,CSF2,CXCL8,CYP24A1,EDN1,FN1,FOS,GSTP1,HMGA1,HMOX1,IFNG,IGF1,IL1A,IL1B,IL2,IL24,IL4,IL6,JUN,LDLR,MET,MITF,MMP1,MMP2,MMP9,NFKB1,NOS2,NOX1,NPY,PLAUR,PML,PPARD,PRL,PTEN,PTGES,PTGS2,PVR,SERPINE1,SERPINE2,SOD2,SREBF1,TFPI2,TNF,TP53,VEGFA	775 (15)
VIP	other	3,81E-21	BAX,CCL2,CCL5,CCND1,CD40,CEBPD,CFTR,CHGB,CHUK,CTLA4,CXCL8,EGF,FOS,FOXP3,FSHR,GCG,HAMP,IFNG,IGF1,IL10,IL12B,IL17A,IL1B,IL1RL1,IL2,IL2RA,IL4,IL6,IRAK1,NFKBIA,NOS2,POMC,PRL,PTGS2,RELA,SORT1,TH,TLR4,TLR6,TLR8,TLR9,TNF,TNFRSF11A,TNFRSF1A,TRH,TRHR,VIP,VIPR1	841 (18)
STAT5A	transcription reg	4,21E-21	ABCB1,ADIPOQ,AKR1C3,APOE,AR,ATM,BAX,BCL11A,BCL2A1,CCND1,CCR5,CDH17,CDK6,CXCL5,CYP1B1,CYP27B1,CYP2J2,EGLN3,EPAS1,ERAP2,ESR1,ESR2,FAS,FGFBP1,FOS,GALC,GSTT1,HAMP,HSD3B2,ICAM1,IFNG,IGF1,IL12RB2,IL24,IL2RA,IL2RB,IL4,IL5,IL6,IL6R,IL6ST,IL7R,IL9,KIT,KLRB1,LCN2,LTA,MAF,MMP7,MYH7,MYL2,NR1H3,OLR1,PPARG,PRL,PSMB8,QPCT,RORA,SELENBP1,SERPINA3,SLC10A1,SLC2A1,SLC2A3,SLC7A8,SOCS1,SOCS3,SREBF1,STAT5A,STAT5B,TGFBR2,TIMP4,TNF,TNFRSF11A,TNFRSF1A,TNFRSF4,TNFSF11,TNFSF4,TNNC1,TP53,TRAF1,TSPAN8,TXNIP,WARS,ZFP36	892 (17)
FOXC2	transcription reg	4,36E-21	ACTA2,ADD1,ADIPOQ,ADRB1,ADRB2,ADRB3,BAX,CTNNB1,CXCR4,EFNB2,FN1,HES5,INSR,IRS1,IRS2,ITGB3,KDR,LEP,LIPE,LPL,MET,MMP2,MMP9,NOTCH1,PDGFRB,PLIN1,PPARA,PPARG,PPARGC1A,PRDM16,PTGS2,SLC2A4,TP53,UCP1,WNT5A	900 (20)
EPAS1	transcription reg	4,63E-21	ABCG2,ADIPOQ,ADM,AKAP12,ANGPTL4,APLN,ARG1,AXL,CACNA1A,CAT,CAV1,CCN2,CCND1,CCR2,CCR5,CKM,CXCR4,EDN1,EGFR,EGLN3,EPO,FABP2,FAM13A,FBLN2,FLT1,FN1,FOS,GJA1,GPX1,HAMP,HIF1A,HSPA4,IGFBP3,IL6,IRS2,ITGA2B,ITGAV,ITGB3,KDR,LDHA,LDLR,LEP,LOX,LOXL2,LPL,MIF,MMP14,NAMPT,NOS3,NOTCH1,P2RY1,POU5F1,PPARG,PRKCA,RET,SERPINE1,SFTPB,SLC2A1,SLC2A3,SLC2A4,SOD1,SOD2,SREBF1,STC2,TERT,TGFB3,TGFBR2,TMPRSS6,TNFAIP3,TNFRSF11B,TP53,VEGFA	1006 (20)
RORC	ligand-depende	4,98E-21	ABCG5,APOA4,APOA5,AQP8,ARNTL,ARSG,ATP1B1,BHMT,CCL5,CD28,CD36,CSF2,CYP2A6 (includes others),CYP2C8,CYP2E1,CYP3A5,CYP4A11,FDFT1,FOXP3,GSTM2,GSTM4,GSTP1,HIF1A,HMGCR,HSD17B7,HSD3B1,IFNG,IGFBP1,IL12RB1,IL17A,IL17RA,IL1A,IL1B,IL1R1,IL2,IL22,IL23R,IL2RA,IL4I1,IL6,KLRB1,LCN2,MGST3,NAT2,NAT8,NNMT,PCK1,POR,PROCR,REL,RORA,SELENBP1,SLC13A2,SLC2A3,SLC7A2,SULF2,TNF,UGGT2,VEGFA	888 (20)
CD44	other	5,58E-21	ABCB1,ABCG2,ACTA2,ADGRE1,ADRB2,CCL5,CCND1,CCR2,CCR5,CD36,CD69,CELA1,CIDEA,CLU,COL18A1,COL1A1,COL3A1,CSF2,CX3CR1,CXADR,EMILIN1,EP300,ERBB2,FAS,FKBP4,FKBP5,FN1,HAS3,IFNG,IL10,IL1A,IL1B,IL1RN,IL2,IL2RA,IL6,ITGA4,ITGAV,JUN,KDM1A,LTBP2,Ly6a (includes others),MAPK8,MET,MMP12,MMP14,MMP2,MMP3,MMP7,MMP9,NFKB2,NOX4,PECAM1,PLPP3,POU5F1,SDC4,SELL,SERPINA1,SFRP2,SMAD1,SPP1,THBS1,THBS2,TLR8,TNF,TNFRSF11A,VCAM1,WNT5A,XCL1	1073 (18)
MAPK3	kinase	7,23E-21	BMP4,CCND1,CD69,CDKN2B,CTNNB1,CXCL8,CYP24A1,ESR1,FN1,FOS,FOXP3,FURIN,GNRHR,HLA-DQB1,IFNG,IL10,IL13,IL2,IL2RA,IL4,IL5,IL6,ITGB1,JUN,MMP1,MMP9,MYRF,PLAUR,PPARGC1A,PTGES,PTGS2,RET,RGS2,SIRT6,SLC4A7,SMAD3,SOD1,SPP1,THBS1,TIMP1,TNF,TNFSF11	1036 (21)
OLR1	transmembrane	8,11E-21	ACE,CCL2,CXCR2,CYBA,CYBB,FN1,HAMP,HAS2,HAS3,ICAM1,IL10,IL6,ITGAM,MMP1,MMP3,NCF2,NOS3,NOX4,OLR1,RARA,RARG,RXRA,RXRG,SELP,SPP1,TGFB1,TGFBR1,TGFBR2,TGFBR3,TNF,VCAM1	712 (16)
FN1	enzyme	1,02E-20	ACE,ACTA2,ACTN4,ADD1,AHCY,APOE,BCAT1,BCL7B,CALCR,CCL2,CCL5,CCN2,CCND1,CDK6,COL1A1,CRP,CSF2,CTBP1,CXCL5,CXCL8,EGFR,FN1,FOS,GPX1,HLA-B,IFNG,IL1B,IL1R1,IL6,IRS1,ITGA4,ITGAM,ITGAV,ITGB1,ITGB3,KCNH2,MAPK8,MAX,MGP,MMP1,MMP14,MMP2,MMP3,MMP9,NFKBIA,NOS2,NPPB,PDGFRA,PGR,PLAUR,POU5F1,RALB,SDC4,SDHC,SERPINE1,SLC2A1,SLC9A1,SMAD2,SMARCA4,SOCS3,SPP1,TFF1,TGFB1,TGFBR2,THBS1,TIMP2,TLR2,TNF,VAV2	866 (21)
SRC	kinase	1,38E-20	ACAT1,CA2,CAV1,CCL2,CCND1,CKM,COL1A2,CSF2,CTNNB1,CXCL8,CYP1A1,EGFR,ERBB2,F2R,FN1,FOS,GJA1,HAS2,HIF1A,ICAM1,IGF1R,IL2,IL6,INS,JUN,LDLR,MMP1,MMP2,MMP9,MYOD1,NFKB1,NPPA,PLAUR,POSTN,POU5F1,PRKCA,PRL,PTGS2,PTH1R,SIRPA,SLC2A1,SLC4A7,SPP1,STAT3,TFPI2,TNFRSF11A,VCAM1,VEGFA,VEGFC	952 (18)
CAV1	transmembrane	1,44E-20	ACVRL1,ADIPOQ,AFP,AKT1,ARG1,ATM,CAV1,CAV2,CCND1,CD14,CD36,CDKN2A,CRNKL1,CTNNB1,ESR1,FAS,FGB,FOLR1,FOS,HGF,HMOX1,HSPA8,ICAM1,IFNG,IL10,IL6,INSR,KDR,LEP,LRP6,MMP1,NEDD4L,NFATC1,NOS2,NOS3,NOTCH1,NPPA,NQO1,NR3C2,POU5F1,PTEN,RAC1,SERPINE1,SLC12A2,SLC14A1,SLC20A1,SLC2A3,SLC7A2,SMAD4,TGFBR1,THBS1,TNF,TNFRSF1A,TP53,VCAM1	1003 (19)

ATF4	transcription reg	1,48E-20	ABCA1,ABCG2,ABCG5,ABCG8,ANGPTL3,ATF3,BCAT1,BGLAP,CCL2,CDKN2A,CPT1A,CSRP3,CTH,CTNNB1,CYP7A1,DDR2,EDN1,FGF21,FN1,FUT7,FYN,GCH1,GDF15,GYS1,HNF4A,IL6,JAG1,JUN,LARS,MED13L,MITF,NOX4,NR1H3,OSMR,PCK1,PPARG,PRKN,PSEN1,PTGS2,RBPJ,SLC1A4,SLC6A9,SLC7A1,SOD2,SREBF1,SST,STAT3,STC2,TGFB2,TKT,TNFRSF11A,TNFRSF11B,TNFSF11,TRIB3,VEGFA,WARS,WFS1,XDH,XRCC1	935 (22)
EPO	cytokine	1,81E-20	BAX,BDNF,BLM,BMP4,CA1,CA2,CD36,CHIT1,CREG1,CXCL12,CXCR4,DES,EDN1,EDN3,EPO,FABP1,FAS,FOS,FPR1,GATA2,GATA4,GBA,GDF15,GYPA,HBA1/HBA2,HBB,HLA-DRB1,HMGB1,IGF2,IL18,IL1RL1,IL2,IL6,ITGA4,ITGB1,JUN,KIT,LDLR,mir-146,MMP2,MPO,MYB,MYOD1,NFATC1,NFKBIA,NOS3,NR3C1,PLCB2,PRKCA,PRKCB,PRKCQ,PTGS2,RELA,REN,ROCK1,ROCK2,SDHC,SELE,SELP,SHH,SIRT1,SLC4A1,SOCS1,SOCS3,SOD1,SPP1,ST3GAL4,STAT3,TF,TFRC,TIE1,TLR4,TNF,TNFRSF11B,TNFSF10,TNNI3,TP53,TPH1,TPH2,TXNIP,UCP2,VEGFA,VEGFC,VWF	1044 (18)
CHUK	kinase	1,86E-20	ARL6IP5,ATF3,BMP2,C3,CCL11,CCL2,CCL5,CCN3,CCND1,CDH13,CEBPD,CHUK,CLU,COL18A1,CSF2,CXCL12,CXCL13,CXCL8,CYBA,EGF,FAS,FOS,GCH1,HAMP,HLA-A,HMOX1,ICAM1,IFNG,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL1RN,IL2,IL22,IL4,IL5,IL6,ITGB3,KCNH2,KLF5,LCN2,MGP,MMP2,MMP3,MMP9,NFKB2,NFKBIA,NOTCH1,PTGS2,RELA,SELE,SERPINE2,SGK1,SMOC2,SOCS3,SOD3,SPP1,TIMP3,TNF,TNFAIP3,TNFRSF11B,TNFRSF1B,TP53,VCAM1,VEGFA,VEGFC	924 (15)
TP73	transcription reg	1,87E-20	ABCB1,ABCC1,ACTA2,ADA,ADORA2B,AFP,ANGPTL4,ARNTL,ATF3,ATM,AURKA,BAX,BDKRB2,BLZF1,BMP7,C3,CCL2,COL18A1,COL1A1,CTH,CTNNB1,CYP21A2,DBP,DHFR,DRAM1,EDN1,EGFR,ENG,ERCC2,FAM78B,FAS,FGFR2,FGFR3,FKBP1B,FLT1,FN1,FOXF1,FOXO3,G6PD,GAB2,GATA2,GRK5,HBEGF,HES1,HIF1A,HSPA1A/HSPA1B,IDH2,IGFBP3,IL1B,IL4R,IL6,IRF5,JAG1,KCNJ4,KCNQ1,KIT,KLF5,LDHA,LIG1,MMP14,MMP2,MTHFD1,NCAM1,NFKB1,NOTCH1,NTRK1,P2RX4,P2RY2,PDGFRB,PLCD3,PML,PRKAG2,PRL,PROCR,PSRC1,PTEN,PTGES,RUNX1,SERPINA1,SERPINA3,SERPINE1,SERPINE2,SPP1,TAP1,TBX5,TERT,TGFB1,TGFB2,TH,THBS1,THBS2,TIMP1,TIMP3,TIMP4,TNFRSF1A,TNFRSF1B,TP53,TP73,TTR,VDR,VEGFA,VEGFC,XRCC1	965 (19)
astressin 2B	biologic drug	1,18E-04	FOS,KCNMA1,KCNMB1,SLC2A1,SLC2A3,VEGFA	776 (13)
POMC	other	2,14E-20	APOB,CXCR4,CYP11A1,CYP11B1,CYP17A1,CYP1B1,CYP21A2,DBH,FOS,GCG,GCLC,GSTM5,GSTP1,H19,HMOX1,HSD11B2,ICAM1,IFNG,IGF2,IL10,IL18,IL6,JUN,LDLR,LEP,MITF,NOS1,NOS2,NOS3,NR4A3,OPRM1,PDYN,POMC,PPARGC1A,REN,SCARB1,SELE,SMAD3,SOD2,TH,TIMP2,TNF,TRH,TYRP1,VCAM1	920 (23)
IL3	cytokine	2,54E-20	ADA,ADGRE1,ALDH2,ALOX5AP,ARG1,BMP2,CAMKK2,CAT,CCL11,CCL17,CCL2,CCN3,CCND1,CCR3,CD14,CD247,CD40,CD69,CPT1A,CSF2,CTLA4,CXCL8,CXCR4,F2R,FAS,FCGR2A,FCGR2B,FGFR1,FOS,GATA2,GNAS,GP1BA,GPX1,HBA1/HBA2,HBEGF,HGF,HLA-A,HNF1A,HNF4A,HSPA2,ICAM1,IL12B,IL13,IL1B,IL1RL1,IL2RA,IL33,IL4,IL5RA,IL6,ITGAM,ITGAV,ITGB3,JUN,LCN2,LTA,MMP1,MMP3,MPO,MS4A2,NFATC1,NOTCH1,PLA2G7,PLCB2,PROX1,PTPN11,PTPN22,RBPJ,SELE,SELL,SERPINA3,SLC2A1,SLC2A3,SMAD4,SMAD5,SOCS1,SOCS3,SOD1,STAT4,TERT,TLR2,TLR4,TNF,TNFRSF11A,TNFRSF4,TNFSF10,TNFSF4,UCP2,VAV2,VCAM1,VEGFA,WNK1	819 (16)
MAP2K6	kinase	3,10E-20	ACTA2,ATP2A2,BAX,CCL2,CCL8,CCND1,CD40,CHGA,CKM,CXCL8,ESR1,ESR2,IFNG,IL13RA2,IL2,IL4,IL6,IRS1,IRS2,JUN,LDLR,MEF2A,MMP1,MMP2,MMP3,MMP9,MYH7,MYOD1,NOS2,NPPA,NPPB,NPR1,PPARGC1A,PTGS2,PTH1R,RELA,SLC2A4,TNFSF10,VDR	909 (17)
PML	transcription reg	4,06E-20	ACADS,ACSM1,ADIPOQ,APOA1,APOE,BAX,BRCA1,CAT,CCND1,CDKN2A,CDKN2B,CIITA,CPE,CPT1A,CPT1B,CXCR4,EGFR,FABP1,FAS,GCLM,HBB,HLA-DRA,HMGCR,HMOX1,IFIH1,IL1A,IL1B,LDLR,LEP,LIPC,LIPE,LPL,MAF,MAPK1,NQO1,NR3C1,OAS3,PDK4,PML,PPARGC1A,PRKCA,PRKCH,PSMB8,PSMB9,RXRA,SREBF1,SREBF2,TAP1,TBX2,TNFAIP3,TOPBP1,TP53,TXN,TXN2,TXNRD1,UCP1,UCP2,UCP3	1092 (25)
PRKCA	kinase	4,37E-20	APOM,ARL4C,BCL11A,CAV1,CCL2,CCN2,CCND1,CIITA,COL1A1,CSF2,CST2,CYBB,ERBB2,FN1,FOS,GBA,GDF15,HES1,HSPA1A/HSPA1B,ICAM1,ID3,IFNG,IGFBP3,IL17A,INSIG1,JUN,LPL,MMP1,MMP3,MMP9,NFKB1,NFKBIA,NOS2,NPPA,NQO1,OASL,PML,PTEN,PTGS2,PTPRN2,PVR,RUNX1,SELP,SERPINE1,TGFB2,TNF,TP53,TRPC1,VCAM1,VEGFA	798 (14)
HDL	complex	5,14E-20	ADIPOQ,AGTR1,ATF3,CCL2,CCL5,CCR2,CD40,CX3CR1,CXCL8,EGLN3,HIF1A,ICAM1,IL1B,IL6,INSIG1,ITGAM,ITGAV,ITGB1,ITGB2,ITGB3,LDLR,NOS3,PON1,PTGIS,PTGS2,RAC1,SELP,SIRT1,SREBF1,TNF,VCAM1	847 (18)
PLG	peptidase	5,69E-20	ADIPOQ,AGER,APOH,ARG1,BAX,BDNF,CAV1,CCL2,CD40,COL1A1,COLEC12,DOCK1,EDN1,EDNRB,FCGR2B,FYN,IFNG,IL1A,IL1B,IL1RL1,IL6,MCOLN3,MIF,MMP1,MMP12,MMP9,NOS2,PECAM1,PLA2G5,PLG,PTGS2,RAC1,RAC2,RALB,RHO,SERPINE1,TNF,TNFRSF11B,TNFSF11	718 (16)
NR4A2	ligand-depende	6,29E-20	ACVR2B,ADCYAP1,ADM,BGLAP,CD40,COL1A1,CPT1B,CXCL8,CYP11B2,CYP19A1,FABP2,FOXP3,HMOX1,HSD3B2,IL10,IL13,IL17A,IL23A,IL23R,IL2RA,IL4,IL5,KCNMA1,LMX1B,MMP1,MMP3,MMP9,NOS2,PRL,PTGS2,RARB,RET,SLC18A2,SLC2A4,SLC39A8,SMAD3,SOD1,TGFB3,TH,TNF	906 (20)
S100A8	other	8,60E-20	ACSS1,AKAP12,ALPL,APLN,ATF3,BCHE,CCL11,CCL2,CCND1,CD69,CTLA4,CXCL14,CXCL8,ELN,ETV5,FAS,FCGR2A,FURIN,H19,HMOX1,ICAM1,IGF1,IL10,IL1A,IL1B,IL1RL1,IL22,IL23A,IL24,IL33,IL6,ITGAM,KCNMA1,MMP1,MMP14,MMP2,MMP3,MMP9,NFKB1,NFKBIA,NOS2,NR1H4,NR4A3,NRG1,NTRK3,OLR1,PER1,POSTN,PTGES,PTPRO,RBFOX1,RXRG,SGK1,SHH,SLC6A12,SOCS3,TNF,TXNIP,TYRP1,UGT1A6,VCAM1,VCAN	893 (17)
USF2	transcription reg	8,62E-20	ABCA1,AGT,AGTRAP,APLN,APOA2,APOA5,APOC3,BRCA2,CD2,CFTR,CHI3L1,CPT1A,CPT1B,CYP19A1,FMR1,FSHR,GCK,GHRL,HAMP,HGF,HMOX1,IGF2R,IGFBP1,IGFBP3,MYH9,PRKG1,REN,SERPINE1,SHBG,SPP1,TERT,TGFB1,THBS1,UCP2,USF1	432 (7)
PTH	other	8,64E-20	ADD3,ALOX15,ALPL,ANGPT1,ATP2A2,BGLAP,BMP2,CARD14,CCL2,CCN2,CCND1,COL1A1,COL1A2,CTNNB1,CXCL12,CXCR4,CYBA,CYP24A1,CYP27B1,CYP3A4,EFNB2,EGFR,FN1,FOS,GJA1,IGF1,IGFBP3,IL33,IL6,IL6R,ITGAV,JUN,KL,LMNA,MGP,MME,MMP1,MMP2,POSTN,PTGS2,PTH1R,RGS2,RUNX1,SDC4,SFRP2,SLC12A1,SLC2A4,SLC8A1,SLC9A3,SMAD3,SOCS3,SORT1,SPP1,TFPI2,TGFB1,THBS4,TNFRSF11B,TNFSF11,TRPV5,VDR	980 (22)
LIPE	enzyme	1,02E-19	ABCA1,ADH1C,ADIPOQ,AGRP,ANGPT1,AQP1,AQP4,ARNTL,ATF3,CA2,CD36,COL1A1,COL1A2,CSRP3,EDN1,FKBP5,FMOD,FOS,GJA1,HLA-DQA1,HSPA1A/HSPA1B,IL1RL1,MAPKAPK2,MEF2C,MSR1,NPY,PAM,PCK1,PDK4,PER1,POSTN,PPARG,PPARGC1A,PTGS2,RAMP1,RARA,RARB,RBP4,RGS5,RXRA,RXRG,SCARB1,SDC4,SLC22A2,SLC2A4,SREBF1,ST8SIA4,TKT,TNF,UCP1	987 (23)
TBX5	transcription reg	1,11E-19	ACE2,ACTC1,ACTN2,ATP2A2,CACNA1C,CASQ2,CCL11,CCL2,COL1A1,COL1A2,COL3A1,CXCL8,CXCR4,DES,FGF10,GATA4,GJA1,GJA5,HSPB7,IL2,IL6,ITGB1BP2,KCNA5,MEF2C,MYL2,NKX2-5,NPPA,NPPB,OXSR1,POSTN,PTGS1,PTGS2,RYR2,S100A4,SLC8A1,TCF7,TNNC1,TNNT2,TPM1,TTN	857 (17)
SOCS3	phosphatase	1,14E-19	ABCA1,APOB,ARG1,ATF3,CCND1,CD40,CTLA4,FOS,FOXP3,HAMP,ICAM1,IFNG,IL10,IL12B,IL17A,IL1B,IL1RN,IL2,IL23A,IL4,IL4R,IL6,IRS1,IRS2,JAK2,JUN,LEP,NOS2,NPPA,PCK1,PCSK9,POMC,PPARGC1A,SOCS1,SOCS3,SREBF1,STAT3,STAT5A,TGFB1,TNF,TNFRSF1B,TP53	749 (15)
Lh	complex	1,18E-19	ACTA2,ADGRG1,AKAP12,ALPL,AR,ARL4C,ARL6IP5,ARNTL,ATP2A2,ATP2B1,AXL,BDNF,CHUK,COL18A1,CTNNB1,CXCL8,CXCR4,CYP11A1,CYP11B2,CYP17A1,CYP19A1,DHCR7,EGFR,FDX1,FKBP5,FOS,GJA1,GNAS,GNRH1,GNRHR,GPRC5B,GRK5,HAS2,HSD11B1,HSD3B1,HSD3B2,IL6,KIDINS220,LHCGR,MMP2,MMP9,MSMO1,PDE4D,PER1,PGR,PLAT,PPFIA4,PPP3R1,PSIP1,PTGS1,PTGS2,PTPN1,RGS12,RGS4,RGS5,RUNX1,SGK1,SLIT2,SMARCA4,SNAP25,SOD2,SRD5A2,STK24,TFPI2,TGFB2,THBS1,THBS2,TNFAIP3,TNFRSF11B,TP53,TPM1,TRIB1,VCL,VEGFA,VEGFC	1080 (20)
BMP4	growth factor	1,24E-19	ABCG2,ACTA2,ACVR2A,ACVR2B,ADGRG1,BGLAP,BMP2,BMP4,CCL11,CCND1,CDKN2A,COBLL1,CYP11A1,CYP17A1,CYP19A1,DIO2,DIO3,EGFR,ERVFRD-1,ERVW-1,FGFR2,FOXF1,FOXP3,GATA2,GCM1,GJA1,HAMP,HES1,HSD3B1,ID3,IFNG,IL6,ITGA4,ITGB6,JUN,KDR,KIT,MITF,MMP14,MMP3,NCAM1,NOS2,PAX2,PITX2,POMC,POSTN,POU5F1,PPARD,PPARG,PRKCH,RET,SCARB1,SHH,SIRT1,SMAD1,SMAD5,SMAD6,SMAD9,SOX17,TBX15,TBX3,TBX5,TNFRSF11B,TNFSF11,TP53,VEGFA,WNT5A	904 (20)
NR2F2	ligand-depende	1,29E-19	ALDH2,ANGPT1,APOA1,APOA4,APOC3,CYP11B2,CYP7A1,EFNB2,HNF1A,HNF1B,HNF4A,KDR,LIPC,LPL,LTF,NPPA,NR1H4,NR1I2,NR2F2,PCK1,POU5F1,PPARA,PROX1,RARB,SHBG,SLC9A1,VEGFA	871 (18)
AGTR1	G-protein coupl	1,48E-19	ACE2,AGT,CCND1,COL3A1,CYBA,CYP11B1,EDN1,EGFR,FN1,FOS,GSTM5,GSTP1,HGF,HMOX1,IL6,JUN,MAPK1,NOS3,NPPA,OLR1,PTGS2,REN,SERPINE1,SGK1,TGFB1,TGFB3,TXNIP,XDH	841 (22)
F2R	G-protein coupl	1,51E-19	ANGPT1,CCL2,CCN2,CCND1,COL13A1,CXCL12,CXCL8,ECE1,ESR1,F11,F2R,FGFR2,FLT1,FN1,FOS,GJA1,HAMP,HMOX1,ICAM1,IGFBP1,IL17A,IL1B,IL6,KDR,MIF,MMP2,MMP9,PGR,PLAT,PLAUR,PTGS2,S100A4,SELE,SELP,TFF1,TFPI2,TGFB2,THBS1,TNFAIP3,TP53,TRPC3,VCAM1,VEGFA,VEGFC,VWF	934 (19)
TXN	enzyme	1,52E-19	APOA1,C5,CD40,CDKN2A,CPT1B,CXCL8,CYP1A1,CYP1B1,ESR1,FOS,HIF1A,HMOX1,ICAM1,IL1A,IL1B,IL2,IL6,MIF,MMP9,NFKB1,NFKBIA,NOS2,RELA,SELL,SOD2,TNF,TP53,TXN,VEGFA	962 (17)
IRF4	transcription reg	1,57E-19	ADA,ALPL,ARG1,CCL17,CDK6,CDKN2A,CIITA,CSF2,CTLA4,CX3CR1,CXCR4,ERBB3,FLT1,FOXP3,GALNT2,HSPA8,IFNG,IL10,IL12A,IL12B,IL12RB1,IL13,IL15RA,IL17A,IL17RA,IL18RAP,IL1B,IL1R1,IL1RN,IL2,IL22,IL23R,IL33,IL4,IL6,IL7R,IL9,IRF5,ITGB1,JAK2,MAP2K5,PAX5,PLAUR,PRKCA,PRKCQ,PROCR,RAC1,RORA,SLC2A1,SMARCA4,SPP1,TCF7,TNF,TNFSF10,TRIM65,XCL1,XRCC1	703 (19)

STAT5B	transcription reg	1,58E-19	ABCB1,ACTC1,AKR1C3,AR,ATM,ATP2A2,BAX,CA2,CCDC141,CCND1,CDK6,CIDEA,CORIN,CSRP3,CYP17A1,CYP2A6 (includes others),CYP2C8,CYP2C9,CYP3A5,CYP4A11,EBF1,EGFR,ESR1,ESR2,FAS,FOS,FOXP3,GAB3,GCK,GSTP1,HAMP,HSD3B2,IFNG,IGF1,IL24,IL2RA,IL2RB,IL4,IL5,IL6,IL9,LAMA3,LEP,LTA,MAF,MPC2,MYH7,MYL2,NAT8,NNMT,NOX4,NPPA,NQO1,PAX5,PDK4,PLTP,RABIF,RELA,RUVBL2,SOCS1,SOCS3,ST8SIA4,STAT5A,STAT5B,TCAP,TF,THADA,TLR2,TNF,TNFRSF11A,TNFRSF1A,TNFRSF4,TNFSF11,TNFSF4,TNNC1,TOX,TRAF1,UCP1,VNN1,WARS,ZFP36	985 (22)
ADCYAP1	other	1,74E-19	ACAT1,ADCYAP1,ADD3,AGER,AGTR2,AKT1,ANGPT1,BDNF,BMP6,CACNA2D3,CARTPT,CCL5,CD40,CEBPD,CHGA,CHGB,CNTNAP2,COL3A1,CYP11B1,EDIL3,FGFR2,FOS,GCG,GCLM,GNRH1,GNRHR,GRK5,ID3,IDH2,IL10,IL12B,IL23A,IL6,ITGAM,LRPAP1,MME,NFKBIA,NOS1,NOS2,NPR3,NPY1R,NPY5R,NQO1,P2RY2,PHEX,PLAGL1,PNMT,POMC,POR,POSTN,PRL,RELA,SCARB1,SERPINA3,SERPINB1,SERPINE2,SEZ6L,SLC18A2,SLC2A1,SMAD1,SNAP25,SOCS3,SST,TENM2,TGFB2,TNF,TSC22D1,TSHZ1,TXNRD1,UCP2,UGT1A6,VIP	912 (23)
SMAD2	transcription reg	1,83E-19	ACTA2,AFP,BGLAP,CCN2,CDKN2A,CDKN2B,CES1,COL1A2,CYP21A2,FDFT1,FLT1,FN1,FOXP3,FURIN,GNRHR,HABP2,HAS2,HES1,HHEX,HMOX1,IFNG,IL2,IL4,IL6,IL6R,IL9,ITGB1,MET,MMP2,MMP9,NOS3,POU5F1,RAC1,SELE,SERPINE1,SFTPB,SMAD2,SMAD3,SMAD4,THBS1,TIMP3,TPM1,VEGFC	896 (17)
POU2F1	transcription reg	1,90E-19	ATM,CCND1,CRP,CXCL8,CYP1A1,CYP2A6 (includes others),CYP2C8,CYP2C9,CYP2J2,ESR1,GAS5,GAS6,GCLM,GNRH1,GNRHR,GPX3,GSTK1,GSTM1,GSTM3,GSTM4,GSTM5,HBG1,HLA-DRA,HNF1B,ICAM1,IL17A,IL2,IL5,IL6,LPL,NFKB1,NOS2,OLR1,POU2F1,PTGDS,PTGES,REL,RELA,SAA1,SELE,SOD1,SPP1,TIMP3,TLR4,TNFAIP3,TNNC1,VCAM1,VIP,VWF	1036 (19)
RUNX3	transcription reg	2,32E-19	ABCC1,ABCC2,AGTRAP,AKT1,BAX,BGLAP,CCN2,CCND1,CIITA,COL4A1,CXCL8,DIP2C,FBN1,FGF9,FOXP3,GRK5,IFNG,IL13,IL18,IL1B,IL4,IL5,IL6ST,ITGAM,JAG1,KCTD15,KIR2DL1/KIR2DL3,KIR2DL4,KIR3DL3,LOX,MACF1,MMP2,MMP9,MSRB3,NEGR1,PAPPA,PXDN,RHOBTB1,RUNX1,SCGB1A1,SGCD,SLIT2,SPP1,STC2,TGFB1,TGFB2,TIMP2,TNF,TNFSF4,VWF	815 (20)
RARA	ligand-depende	2,54E-19	ABCA1,ABCC2,ABLIM1,ADH1C,ALOX5,APOA1,APOC3,APOM,AR,BMP8A,C5,CCND1,CD14,CLOCK,CXCL5,CXCL8,CYP19A1,CYP7A1,DRD2,EPO,F12,FGF21,FGFR1,FOLR2,FOS,FOXC1,FOXP3,FUT4,GATA4,GCK,GDF15,GDF2,GHR,HLA-B,HLA-C,HLA-G,HNF1B,IDE,IFNG,IL12RB1,IL12RB2,IL13,IL16,IL1A,IL1R1,IL22,IL23R,IL3,IL4,IL5,IL5RA,IL6,IL6R,IL9,ITGA4,JUN,LTF,MAPK1,MGP,NCOA3,NR2F1,NTRK1,PCK1,PIK3CG,PITX2,POU5F1,PTGS2,PVR,RARA,RARB,RARG,RET,RUNX1,SELL,SFTPB,SGSM3,SHANK2,SLC10A1,SLC2A2,SMAD3,SOX17,SPP1,TERT,TFF1,TGFB1,TH,THBD,TNF,TNFRSF11B,TRH,UCP1,UCP3,ZMAT4	920 (24)
RET	kinase	2,79E-19	CCL2,CCN3,CCND1,CLU,COL1A1,COL1A2,CSF2,CXCL12,CXCL8,CXCR4,EDNRB,FKBP4,FOS,GJA1,HSPA1A/HSPA1B,HSPA1L,HSPA8,HSPD1,IFNG,IL10,IL13,IL1B,IL22,IL5,IL6,LOX,MAF,MAPKAPK2,MET,MMP1,MMP14,MMP3,MMP7,MMP9,NOS1,PHEX,PLAUR,PTN,RET,SDK1,SELL,SST,TH,TIMP3,TNF,TP53,VIP	925 (17)
SIRT3	enzyme	2,85E-19	ACTA2,BAX,CAT,CYP11A1,DIO2,IFNG,IL10,IL1B,IL6,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6,MYH7,NPPA,PDX1,PECAM1,PPARA,PPARGC1A,SLC2A1,SLC2A2,SOD2,TFRC,TNF,TP53,UCP1,VEGFA	969 (21)
JUND	transcription reg	3,28E-19	AGT,AGTR1,APOC3,BDNF,BGLAP,C3,C5,CCL5,CCND1,CDKN2A,CLU,CTLA4,CYBB,CYP19A1,DBH,GNRHR,HMOX1,IFNG,IL10,IL21R,IL5,IL6,LHCGR,MMP1,MMP3,MMP7,MMP9,NCF2,NOS2,NOX4,PLAUR,PRL,SOCS1,SPP1,SST,TH,TIMP1,TNF,VEGFA	846 (17)
NR0B2	ligand-depende	3,36E-19	ABCA1,ABCB11,AGT,APOA1,APOM,ARG1,CCN2,CD36,CETP,COL1A1,COL1A2,CPT1A,CYP11A1,CYP11B2,CYP7A1,GCK,HMGCR,HNF1A,HNF4A,IL6,LPIN1,mir-329,MTTP,NOS2,NR0B2,NR1H4,PCK1,PDK4,PPARG,PPARGC1A,SCARB1,SERPINE1,SLC10A1,SLC10A2,SLCO1B1,SPP1,SREBF1,TFF1,TGFB1,TIMP1,TNF	789 (22)
POR	enzyme	4,29E-19	ABCA1,ACAT2,AHR,ANXA5,APCDD1,APOA4,AQP8,CD36,CIITA,CPT1A,CPT2,CYB5B,CYP17A1,CYP1A1,CYP1A2,CYP2A6 (includes others),CYP2C18,CYP2C8,CYP4A11,CYP7A1,DHCR7,ELOVL2,EPO,FABP2,FADS2,FDFT1,FGF1,FOXC1,GCK,GSTM1,GSTM5,HIF1A,HLA-A,HLA-DQA1,HLA-DQB1,HLA-DRB5,HMGCR,HMOX1,HSD3B1,INSIG1,JDP2,KDR,LDLR,LPL,LSS,MSMO1,MVK,NR0B2,PDK4,PLA2G7,POR,PPARG,SDC4,SDS,SERPINA3,SLC22A5,SLC23A2,SREBF2,VEGFA,VNN1,ZMAT4	389 (7)
MOG	other	4,87E-19	ARG1,BDNF,C5,CCL5,CCR2,CCR5,CD40,CIITA,CSF2,CTLA4,FOXP3,GDNF,ICAM1,IFNG,IGF1,IL10,IL13,IL17A,IL2,IL22,IL23A,IL4,IL5,IL6,LEP,MMP3,MMP9,NOS2,PECAM1,TGFB1,TNF,VCAM1	712 (14)
N-cor	group	7,00E-19	ABCA1,ADIPOQ,ADIPOR2,ARNTL,BIN1,CCL5,CCND1,CD36,CDK6,CRP,CXCL14,ESR1,FADS2,FOLR1,G6PD,GSTP1,HBEGF,HEBP1,HES1,IGF1,IGFBP3,IL1A,IL1B,INPP4B,MMP12,MMP2,MMP9,NFATC1,OLR1,PCK1,PLA2G3,PLIN1,PTGS2,RARB,SGK1,SLC2A4,SOCS1,SREBF1,TBX15,TBX2,TBX4,TBX5,TNFSF11,XYLT1	1029 (25)
INHBA	growth factor	7,16E-19	ACTA2,ACVR2A,ACVR2B,ADRB2,AKR1C3,BAX,BMP2,CCL17,CCL2,CCN2,CCR2,CDKN2B,CXCL8,CXCR4,CYP11A1,CYP11B1,CYP17A1,CYP19A1,DACH1,EFNB2,EGLN3,ESR1,F13A1,FIGN,FN1,FOLR2,FRS2,FSHR,FURIN,GNRHR,HLA-G,HMGB1,HNF1A,HSD3B2,IFNG,IGF1,IL10,IL12A,IL6,ILF3,KRAS,let-7,LHCGR,LOX,MAF,MGP,mir-217,MMP2,NRG1,PCSK6,POMC,POU5F1,PRL,PSMD9,PTEN,SERPINE1,SLC2A2,SMAD6,SOCS1,SOX17,TIMP1,VAV3,VEGFA	1100 (22)
IL1RN	cytokine	7,65E-19	ACTA2,ATF3,BDKRB1,CCL2,CIITA,CXCL5,CXCL8,CYP1A2,CYP2E1,CYP3A5,CYP7A1,ERAP2,GRIA1,HDAC9,HLA-DQB1,HSD11B1,ICAM1,IFIH1,IFNG,IGF1,IL10,IL17A,IL1A,IL1B,IL2,IL23A,IL6,INS,KCTD7,MMP1,MMP9,NOS2,NPY2R,NR0B2,NTRK1,OAS3,OASL,PML,PTGS2,RELA,SELE,SERPINE1,SLC6A4,SPP1,TCF7L2,TIMP1,TNF,TNFSF10,VEGFA,VEGFC	786 (16)
NCOA1	transcription reg	7,83E-19	ABCA1,ABCB11,ADIPOQ,AHR,APOA4,BGLAP,C3,CCND1,CYP11A1,CYP1A1,CYP2C9,CYP7A1,DBP,DIO1,ERBB3,ERVFRD-1,FGFR2,FOS,GCM1,HAS2,HIF1A,HNF1A,HSD3B2,IGF1,IL12B,IL1RN,IL6,KDR,LEP,LPIN1,MAPK3,NELFCD,NFKBIA,NFKBIZ,NR0B2,OLR1,PCK1,PGR,POU2F1,PPARD,PPARG,PRL,RARB,SERPINE1,SFTPB,SLC2A1,SLC2A2,SMG6,SORBS1,SREBF1,STRN,TFF1,UCP1,UCP3	856 (20)
NCOA2	transcription reg	7,99E-19	ABCB11,ADIPOQ,AHR,ALDH1B1,APOA4,APOC2,APOM,AR,BMP2,CCL5,CCND1,CTNNB1,CYP17A1,CYP1A1,CYP7A1,FGB,GCK,GLO1,HMGCR,HNF1A,IFNG,IL1A,IL1B,IL6,LDLR,LIPC,LIPG,LPIN1,LPL,MYB,NFKBIA,OASL,PCK1,PGR,PLIN1,PLTP,PPARG,PTGS2,RET,SFTPB,SLC2A2,SLC3A1,SREBF1,TFF1,TNF,UCP3	841 (22)
FOXM1	transcription reg	8,71E-19	ACE,ACE2,AR,BRCA2,CAT,CAV1,CCL11,CCND1,CDKN2A,CRP,CTNNB1,CXCL12,CYP7A1,ESR1,FLT1,FOS,FOXF1,FUT4,GCG,HSD11B2,IGF1,IKBKB,IL1RN,IL6,IPO7,JUN,KDR,LDHA,LOX,MAPK8,MCM8,MET,MMP2,MMP7,MMP9,NEDD4,NFKB1,NFKB2,PECAM1,PLAUR,POU5F1,PRC1,RELA,SFTPB,SOD2,STAT3,TGFBR2,TP53,VCAN,VEGFA,XRCC1	1035 (20)
TLR3	transmembrane	8,75E-19	ABCA1,ATF3,C3,CAST,CCL17,CCL2,CCL5,CD40,CD69,CFB,CLU,CSF2,CSRP3,CTH,CXCL8,EDN1,FAS,FOS,FURIN,GCH1,GDNF,HAMP,HMOX1,ICAM1,IFIH1,IFNG,IFNK,IFNL3,IL10,IL12A,IL12B,IL13,IL15,IL1A,IL1B,IL1RN,IL23A,IL33,IL4,IL5,IL6,LCN2,LIPA,LIPG,MBL2,MMP1,NFE2L3,NFKB1,NFKBIZ,NOS2,NPY,OASL,PECAM1,PIK3R1,PROCR,PTGER2,PTGES,PTGS2,RARB,SELE,SERPINE1,SLPI,SOCS1,SOCS3,TIMP1,TLR4,TLR7,TNC,TNF,TNFRSF1A,TNFRSF1B,TNFSF10,TREML2,TSLP,VAV2	622 (15)
ID3	transcription reg	8,95E-19	ADGRG1,ADIPOQ,ADM,BMP7,CCL11,CCL5,CCR5,CDKN2A,CXCL8,CXCR4,FOXO1,FOXO3,FOXP3,HES5,HIF1A,ICAM1,ID3,IFNG,IL10,IL10RA,IL2,IL2RB,IL4,IL4R,IL6,IL6R,IL7R,IL9R,IRF5,ITGB3,JAK2,JDP2,KLF7,LEPR,LTA,MAF,MMP2,MMP9,MYB,NFATC1,NOTCH1,NPPA,NR4A3,PIK3C2B,PIK3R1,PKD2,PTPN22,REL,RORA,SELE,SELL,SOCS3,SOX13,STAT4,TGFBR3,TNFRSF1A,TNFRSF4,TNFSF10,TNFSF11,TNFSF14,TOX2,TP53,TRAF1,VCAM1	988 (21)
HMGA1	transcription reg	1,11E-18	ACTA2,ALPL,ATM,BRCA1,CAV1,CAV2,CCND1,CLCN6,COL1A1,COL1A2,COL4A1,CPE,CSK,CTSH,CYP7A1,DHCR7,ESR1,FOS,GHR,GSN,H19,HMGCR,ID3,IGF1,IGFBP1,IGFBP3,IL15,IL2,IL2RA,IL4,IL6,INSIG1,INSR,KCNJ11,KIT,LIPE,LTA,Ly6a (includes others),MAPKAPK2,mir-196,MMP9,MVK,NKX2-5,NOS2,PPARG,PTGS2,PTH1R,RARA,SDC4,SOD3,SOX17,STAT3,TRH,XPA	1111 (24)
PRKCD	kinase	1,38E-18	ABCA1,ARID3B,BCL2A1,CCL2,CCL5,CCND1,CDKN2A,CIITA,COL1A1,COL1A2,CSF2,CTNNB1,CXCL12,CXCL8,FBN1,FOS,GDF15,GPR87,ICAM1,IL10,IL12B,IL13,IL1B,IL1RN,IL23A,IL4,IL6,ITGAM,JCAD,JUN,KLF5,LDLR,LIPG,MMP12,MMP2,MMP9,NEDD4,NFKB2,NFKBIA,NOS2,NOTCH1,NOTCH2,NOX1,NR0B2,PRL,PTGS2,SERPINE1,SLC15A1,SLC22A1,SMAD6,SOCS1,STAT3,TFF1,TLR2,TNF,TNFRSF11B,TP53,TRAF1,TRPC1,VCAM1,VEGFA,ZFP36	778 (14)
bacitracin	biologic drug	8,91E-04	ANXA5,IL23A,TNF	
NFATC2	transcription reg	1,59E-18	ABCA1,ATM,CCL17,CCL5,CCR5,CD40,CSF2,CTLA4,CX3CR1,EDN1,FAS,FOXP3,GCG,ICOS,IFNG,IKZF1,IL10,IL12A,IL12B,IL12RB2,IL13,IL15,IL17A,IL18,IL1A,IL1B,IL2,IL22,IL2RA,IL4,IL5,IL6,IL9,JUN,LDHA,MAF,MAPK3,MITF,NFATC1,NFKB1,NFKBIA,NFKBIZ,NOX4,OASL,PLAT,PML,PPARG,PPARGC1A,PPP3R1,PTGS2,PTPN1,REL,RGS2,SELE,SLCO3A1,SOCS1,SOCS3,STAT5A,TERT,TGFB1,TLR2,TNF,TRAF1,TSC22D1	716 (19)
GATA3	transcription reg	1,77E-18	ACBD4,ADM,ANGPTL4,BCL11A,BCL11B,CCL5,CCND1,CCR2,CCR3,CCR5,CTLA4,CXCR4,CYP11A1,CYP19A1,EBF1,EPO,ESR1,FN1,FOS,FOXP3,HIF1A,ICAM1,ICOS,IFNG,IL10,IL12RB2,IL13,IL17A,IL18RAP,IL1RL1,IL2,IL22,IL24,IL2RA,IL2RB,IL3,IL4,IL5,IL6,IL7R,IL9,IL9R,KIT,LOX,LTA,MAF,NCOA3,NFKB1,NOTCH1,NOTCH2,NPPA,OPRM1,PALB2,PAX5,PPARA,PPARD,PPARG,PTGER4,PTGS1,RET,RUNX1,SELPLG,SLC2A1,SLPI,STAT4,TBX3,TFF1,TGFB1,TNF,VCAM1,VEGFA,WDR37	865 (21)

FOSL2	transcription reg	2,13E-18	ABCA1,BDNF,BGLAP,BRCA1,CCR2,COL1A2,CSF2,CXCL8,CYP2J2,DBH,DIO2,FAS,FOLR2,GCM1,HAMP,IL17A,IL1B,IL5,IL6,LEP,MMP1,MMP2,MMP3,MYOD1,NOS2,PRL,SPP1,TFF1,TH,TIMP1,TNF,TP53	806 (15)
NCOR2	transcription reg	2,13E-18	ABCB11,ADIPOQ,AR,C3,CCND1,CD69,CXCL8,CYP3A4,DIO1,FOLR1,FOS,HBEGF,IGF1,IL12B,IL1A,IL1B,IL6,JUN,LEP,LPL,MMP12,MMP2,NFATC1,PGR,PLIN1,POMC,PTGS2,RARA,RARB,TFF1,TRH,TSLP	804 (21)
PLAU	peptidase	2,34E-18	ACTA2,ANG,ARG1,CCL2,CCL5,CCND1,CCR5,EGFR,FLT1,FN1,GDF15,GJA1,HGF,ICAM1,IGF1,IL1B,IL6,ITGAV,KDR,MMP1,MMP12,MMP9,NPY,OAS3,PIK3CG,PLAUR,PLG,PON1,PTN,SERPINB1,SERPINE1,SLC2A1,SLPI,TNF,TP53	1002 (20)
IL21	cytokine	2,97E-18	ARG1,CCL11,CCL17,CCL5,CD2,CD28,CD69,CSF2,CXCL13,CXCL8,DPP4,FCGR2B,FOXP3,HIF1A,HLA-DRB5,IFNG,IL10,IL12RB2,IL13,IL17A,IL18R1,IL18RAP,IL2,IL21R,IL23A,IL23R,IL2RA,IL2RB,IL4,IL4I1,IL5,IL6,IL7R,IL9,IRF5,KLRB1,MMP12,MMP2,MMP9,NCR3,NOS2,OASL,PAX5,PSMB9,PTPRC,RORA,RUNX1,SELL,SGK1,SOCS1,SOCS3,STAT3,STAT4,TAP1,TGFB1,TIRAP,TLR4,TNF,TNFSF11	754 (16)
MAP3K1	kinase	2,98E-18	ATF3,CCN3,CCND1,COL3A1,COL4A1,CSF2,CXCL8,CYP7A1,FAS,FOS,HMOX1,IKBKB,IL2,JUN,LDLR,LOXL3,MMP3,NPPA,PGR,PLAUR,PPARD,PTGS2,RGS4,SERPINE1,TGFB1,THBS1,TIMP1,TNC,TNF,TP53,TPH1	761 (16)
JAK2	kinase	3,03E-18	ACE,AKAP12,AKR1C3,AKT1,BAX,BMP7,CCL2,CCL5,CCND1,CD36,CDKN2A,CPLX2,CSF2,CXCL8,CYBB,ESR1,F10,F5,FCGR2B,FOS,FOXO1,GNRH1,HTR2A,ICAM1,IGF1R,IL17A,IL1B,IL6,JAK2,KLK8,LAT2,LCN2,MPO,NOS2,OSMR,PAX5,PECAM1,PSMB9,PTGS2,RARA,SDC4,SELP,SLC11A1,SOCS1,SOCS3,SPTB,STAT3,TAP1,TF,THBS1,TNF,TP53,TSC22D1	712 (19)
IL22	cytokine	3,15E-18	ACTA2,AKT1,C3,CCL17,CCL5,CCND1,CXCL12,CXCL13,CXCL5,CXCL8,CYBA,CYP1A2,CYP2E1,FGA,HBEGF,HLA-B,HMOX1,HNF1A,HP,IFNG,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL22,IL23A,IL24,IL33,IL4,IL5,IL6,LBP,LCN2,MMP1,MMP3,MMP9,NOS2,PTGS1,PTGS2,REG3A,SAA1,SERPINA3,SOCS3,SOD2,TNF,TNFSF11,TSLP	734 (15)
SRF	transcription reg	3,70E-18	ABCA4,ACTA2,ACTC1,AKAP12,AVPR1A,BMP2,CALD1,CCL5,CCN2,CDKN2B,CEBPD,CKM,CMA1,CORIN,CTNNB1,CTNNBL1,CXCR4,DES,ELANE,EYA2,FGF1,FLT1,FLT4,FOS,GATA4,GCH1,GCKR,GP1BA,GSN,GSTM5,HAMP,HIF3A,HMOX1,HSPG2,IGF1,IL15,IL2,IL4,ITGA2B,ITGA9,ITGAM,ITGB1,JUN,KDR,KRIT1,LAMA3,LCN2,LDB3,LDLR,LEPR,LPL,LRP1,LTF,MAT1A,MEIS1,mir-143,MMP9,MYB,MYH7,MYH9,MYL2,MYL3,MYLK,MYOD1,NKX2-5,NPPA,PAFAH1B1,PDX1,PGLYRP1,PLA2R1,PTGS2,RAMP1,SELP,SHH,SLC2A1,SLC6A4,SLC8A1,SLPI,SMTN,SREBF2,TBXAS1,TCAP,TCF7,TNC,TNNC1,TNNT2,TTN,VCAN,VCL	901 (18)
PRL	cytokine	4,29E-18	ABCG2,AKR1C3,ANXA5,ATP2A2,CAV1,CCL2,CCND1,CD40,CD69,CEBPD,CLU,COL1A1,COL1A2,COL3A1,CST3,CTSH,CYP11A1,DES,EGF,EGFR,ERBB2,ERBB3,ESR1,ESR2,FLT4,FN1,FOS,GNRH1,GNRHR,GSTM1,HSD11B2,HSD17B7,HSPD1,ID3,IDE,IFIH1,IGF2,IGFBP3,IL2,IL2RA,IL6,JAK2,JUN,LHCGR,MGP,MME,MMP14,NFKB1,NOS2,NOS3,NPY,OAS3,PDGFRA,PDK4,PLAT,PRL,PROX1,PTGFR,RALB,SCARB1,SERPINA3,SFRP2,SLC10A1,SOCS1,SOCS3,SOD1,SPP1,STAT5A,TGFB1,TIMP1,TIMP2,TNF,TNFSF11,TP53,TPH1,UCP1,VDR,XDH	1165 (20)
RBPJ	transcription reg	4,29E-18	BMP2,BMP7,CCND1,CDCA7,CDKN2A,CELA1,CRP,CSF2,CXCL12,CYP11A1,CYP19A1,EGF,ELANE,EPHA4,FGF1,FGF10,FGF5,FGF9,FOS,GDNF,HAS2,HES1,HES5,HGF,IGF1,IGF2,IKBKB,IL12A,IL17A,IL17RA,IL18,IL1B,IL22,IL4,IL6,IL7R,IL9,JAG1,JUN,mir-143,MMP3,NFATC1,NFKB1,PIK3CG,REN,SLC2A1,TFF1,TGFB2,TGFB3,TNC,VEGFA,VEGFC,WNT5A	875 (19)
CCL11	cytokine	4,32E-18	BMP6,CCL11,CCL16,CCL18,CCL2,CCL8,CCR2,CCR3,CXCL12,CXCL5,CXCL8,DPP4,FAS,FGF1,FGF10,FGF5,ICAM1,IL1B,IL22,IL4,IL6,IL9,ITGA2,ITGAM,ITGB1,LEP,MMP3,NOS2,TNF,TNFSF14,TNFSF4,VEGFC	792 (16)
DUSP1	phosphatase	4,34E-18	BMP2,CCL2,CD40,CFB,CIDEA,COL3A1,CSF2,CXCL8,CYBB,CYP17A1,EGFR,GDF15,ICAM1,IL10,IL12RB2,IL1A,IL1B,IL1RN,IL23R,IL6,JUN,LTF,MEFV,MMP1,MYH7,NOS2,OLR1,PARP1,PIK3R1,PLAT,PLAUR,PTEN,PTGS2,SELE,SERPINE1,SOCS1,SOD2,STAT5A,TGFB2,THBD,TLR2,TNF,VCAM1,VEGFC,VNN1,ZFP36	630 (14)
ATG7	enzyme	4,75E-18	ACAT1,ACTA2,ARG1,CCN2,CXCL8,CYP2A6 (includes others),FGF21,GSTM5,HIF1A,IFIH1,IFNG,IKBKE,IL10,IL13,IL1B,IL4,IL6,ITLN1,LIPE,MSR1,NFKBIA,NQO1,PECAM1,S100A4,SCARB1,SLC2A1,SOCS3,SREBF1,SREBF2,TGFB1,TGFBR1,TGFBR2,TLR4,TNF,TNFRSF1A,TP53	890 (15)
SHH	peptidase	5,47E-18	ABCG2,ALAD,ANGPT1,BAX,BMP2,BMP4,BRCA1,CAV1,CCND1,CD69,DHFR,EBF1,EGFR,EPHB4,FGF10,FN1,FOXF1,GATA2,GATA4,GDNF,HES5,HMGA1,IFNG,IGF1,IGF2,IL10,IL2,IL2RA,IL4,IL6,LMX1A,MAGI1,MEF2C,MYOD1,NKX2-5,NOS3,NPY,NR2F2,PAX2,PAX5,PDGFRA,PDX1,PITX2,PLAT,PPARG,PVR,SALL1,SERPINE1,SFRP2,SHH,SMAD1,SPP1,SREBF1,SRM,TGFB2,TGFB3,TH,THBD,TYMS	893 (22)
BCG vaccine	biologic drug	6,01E-08	CCL2,CYP2C8,CYP3A5,IFNG,IL10,IL17A,IL4,PTGS2	499 (7)
UBE2I	enzyme	5,82E-18	ABCB11,CCND1,CEBPD,CIDEA,CPT1A,CYP11A1,CYP11B1,CYP11B2,CYP17A1,HBB,NOS2,NR0B2,PDK4,PML,PPARG,PPARGC1A,PRDM16,SCNN1A,SGK1,SLC2A1,SLC2A4,SMAD4,TAP1,UCP1	916 (26)
SPI1	transcription reg	5,88E-18	ACTA2,ADGRE1,ARID1A,BAX,BCL11A,CCL17,CCND1,CD14,CDK6,CHI3L1,CHIT1,CIITA,CYBB,EBF1,ELANE,EVI5,FCGR2B,FES,FOS,FOXO1,FUT7,GATA2,GPX1,HDAC7,HES1,HSPA8,ID3,IKZF1,IL10,IL12A,IL12B,IL13,IL18,IL1B,IL1RN,IL2,IL24,IL2RA,IL4,IL5,IL7R,IL9,ITGA4,ITGAM,ITGB2,JDP2,JUN,KIT,KLK1,LTF,MEF2C,mir-27,MME,MMP1,MMP2,MYB,NCF2,NKX2-5,NOS2,OASL,OPRM1,PIK3CG,PML,POLR1D,PSMB8,PSMB9,PTEN,PTGS2,PTPRC,RELA,SPP1,TLR2,TLR4,TNF,TNFSF10	916 (19)
CREM	transcription reg	6,16E-18	ABCA1,ACE,ACTC1,ADRB1,ADRB2,APOE,ATF3,ATP2A2,CCND1,CD247,COL3A1,CSF2,CXCL8,CYP11B2,CYP19A1,CYP46A1,DBH,DIO2,FOS,FSHR,FUT7,HLA-DRA,HMGCR,HSPA4,IFNG,IL17A,IL2,IL4,INS,IRAK1,IRS2,KLF5,LDLR,LSS,MSMO1,MVK,NFATC1,NOS1,NOS2,NOTCH1,PCSK1,PDYN,PER1,PRL,RARB,REN,RYR2,SERTAD1,SST,TH,THBS1,TNF,TSHR,VEGFA	1053 (20)
YAP1	transcription reg	6,16E-18	ACAT1,ACAT2,ACTA2,AKT1,BAX,BMP2,CCN2,CCND1,CD36,CDC42,CDK6,CDKN2B,CPT1A,CPT2,CXCL8,DDAH1,DICER1,EDN1,EGFR,FGF1,FN1,FOS,HMGCR,HMGCS2,ICAM1,IGF1R,IGF2,IL1A,IL1B,IL6,ITGB2,LDHA,let-7,LMNA,LPL,mir-196,MYH7,MYH9,NDUFB3,NEGR1,NPPA,PTEN,PTGS2,SERPINE1,SLC2A3,SMAD2,SORBS1,THBS1,TP73,TYMS,UHRF1,VCAM1,VCL,WWC1	911 (20)
MED1	transcription reg	6,18E-18	ACAA1,ADIPOQ,APOB,ARID1A,AURKA,BAX,BCL11A,CCND1,CIDEA,CYP11A1,CYP17A1,CYP1A1,CYP1A2,CYP24A1,CYP3A5,CYP4A11,CYP7A1,DIO1,EBF1,ERBB2,FADS2,FOXO1,GCK,GHR,GSTP1,HAS2,HDAC7,IGF1,IGFBP1,IGFBP3,IKZF1,IL2RB,MET,MYH7,MYOD1,NF1,NFKBIA,NR3C1,OLR1,PDK4,POU5F1,PPARG,RARB,SLC2A4,SMARCA4,STC2,TBX3,TERT,TET2,TFF1,THBS1,TNNC1,TP53,UCP1,VDR	904 (21)
CAT	enzyme	6,21E-18	ADM,AGT,BAX,BCL2A1,CAV1,CCL2,CD36,CD69,COL1A1,CXCL8,CYP1B1,FN1,GCLC,HIF1A,HLA-DRA,HMOX1,HSPA4,IGF1R,IL2RA,IL6,MMP1,MMP9,NOS2,PAX2,PTGS2,SERPINE1,THBS1,TIMP1,TNC,TP53,VCAM1	936 (17)
Nfat (family)	group	7,82E-18	ATF3,CALCR,CALD1,CCL2,CCND1,CD40,CSF2,CTLA4,CXCL8,CYBB,F2RL1,FAS,FOXP3,GRIA1,HBEGF,ICAM1,IFNG,IL10,IL13,IL17A,IL2,IL3,IL4,IL5,ITPR2,LTA,NOX4,NPPB,PTGS2,SDC4,SELE,SERPINE1,SLC7A1,SMAD2,SOD2,TCF7,TGFB2,TNF,TNFSF14,TNNI3,TNNT2,TRAF1,VCAM1	834 (20)
RIPK2	kinase	7,82E-18	ABCA1,ABCG5,CCL5,CD36,CD40,CD69,CYP7A1,FABP1,HAMP,HMGCR,ICAM1,IFNG,IL17A,IL2,IL33,IL6,LDLR,MCOLN2,MEFV,MTTP,NFKB2,NOS2,NR1H3,PPARA,PPARD,PPARGC1A,PTGES,RASGRP3,SELE,SOD2,SREBF1,TNF,TRAF1,TSLP,VCAM1	908 (17)
OGA	enzyme	7,96E-18	ABCC9,ABLIM1,ACSS1,ACTN4,ADIPOQ,AGTR2,ALOX5AP,APOC2,APOE,BAX,CACNA2D3,CALCRL,CAMK1D,CASQ2,CAV1,CCL2,CCND1,CCR5,CD14,CD36,CD40,CDCA7,CDH15,CDK6,CDKAL1,CDKN2B,CELSR1,COLEC11,CPE,CTNNB1,CX3CR1,CXCL8,DHCR7,EFNB1,EFNB2,EPHA4,EPHB6,ERBB3,FABP3,FAS,FDFT1,FGF21,FGF5,FGF9,FGFBP1,FGFR1,FN1,G6PD,GAA,GAS6,GPER1,GRIN3A,GSN,HMGCR,IGF1,IGF2,IGFBP3,IL18,IL1RL1,IL21R,IL23A,IL6R,IL6ST,INS-IGF2,ITGA2,JDP2,JUN,LEP,LIPC,LSS,MMP14,MSMO1,NOTCH2,NPHS1,PIK3R1,PLPP3,PRKG1,PTGDS,RBP4,SERPINE2,SLC2A9,SOCS1,SOCS3,SORBS1,SREBF2,TCF25,TGFB1,TGFBR2,TGFBR3,THBS1,THRA,TIMP1,TIMP2,TIMP3,TNC,TNFRSF11B,TP53,TP53BP1,TP73,TRH	1174 (25)
SCARB1	transporter	1,15E-17	ABCA1,ABCG5,ABCG8,APOA1,APOB,APOE,CCL2,CCL5,FABP3,FOXO1,HMGCR,ICAM1,IFNG,IL10,IL1B,IL1RN,IL6,LDLR,LTA,NLRP3,NOS2,PTGS2,SELE,SELP,SPP1,SREBF1,SREBF2,TNF,VCAM1	817 (18)
GNA15	enzyme	1,23E-17	ACTA2,ADARB1,ADD3,ADM,AKAP12,ARG1,AVPR1A,BMP4,C3,CAV2,CD69,CEBPD,CTH,CXCL8,ELOVL2,ENPP1,GUCY1B1,HES1,HMOX1,IL10,IL1RN,IL6,LBP,NFKB1,NOX1,NOX4,NPR3,OLR1,PLAT,PTGS2,RGS2,SELENBP1,SERPINA3,SLC6A4,SLC6A6,SLC7A1,SOD2,SYNE1,TGFB3,THBD,TIMP1,TRIB3,VCAN,XCL1,XDH	770 (16)
Collagen type I	complex	1,27E-17	ACTA2,APOE,BAX,CCL5,CCND1,CDKN2A,COL1A1,CPB2,CSF2,CTNNB1,F11,F13A1,FN1,FOXO3,ITGA2,ITGAV,ITGB1,KDR,MMP1,MMP12,MMP14,MMP2,MMP3,MMP9,NOS3,PGR,PTEN,PTGS2,RAC1,TGFB1,TIMP2,TNC,TNF,TP53	942 (20)
GHRL	growth factor	1,27E-17	AGRP,BAX,BDNF,CARTPT,CPT1A,CPT1B,CYP11A1,EDN1,FOS,FOXO1,IL1B,IL1R1,IL6,LEP,LPL,MYOD1,NPPA,NPY,OPRM1,PCK1,PCSK2,POMC,PPARG,PPARGC1A,PTGS2,PTPRN2,SIRT1,SPP1,SREBF1,SST,TNF,UCP1,UCP2,UCP3	902 (22)
TP63	transcription reg	1,36E-17	ABCB1,ADA,ADM,AHR,AKT1,ALOX12,ARG1,ATM,AXL,BAX,BLM,BMP7,BRCA1,CA4,CAD,CAST,CCND1,CDC42,CDK6,CDKN2A,CDKN2B,COL4A1,CPT2,CTNNB1,CXCL8,CXCR4,CYP2A6 (includes others),DICER1,EGFR,ENG,F2R,FAS,FBN1,FGF21,FGFR2,FGFR3,FN1,FOS,FOXO3,G6PD,HAS3,HBEGF,HES1,HES5,HSPA4,HSPA8,ID3,IGFBP3,IKBKE,IL1B,IL1RAP,IL6,INSR,IRF5,ITGA2,ITGA4,ITGB1,ITGB8,JAG1,let-7,LIN28A,MAPK8,mir-515,MYB,MYNN,NOTCH1,NOTCH3,PI3,POSTN,PPARA,PRKAG2,PTEN,RAC2,REL,RELA,RUNX1,S100A4,SERPINE1,SH2B3,SMAD2,SMAD3,SMAD4,TERT,TGFB1,TGFB2,TGFB3,TGFBR2,THBS1,TIMP3,TNC,TNFRSF1A,TNFSF10,TP53,TP73,TPM1,TRAF1,UGT1A1,UGT1A7 (includes others),UHRF1,VDR,VEGFA,WNT5A	991 (17)

TREM1	transmembrane	1,37E-17	ADORA2B,ADRB2,ATF3,ATP1B1,CCL17,CCL18,CCL23,CCL5,CD14,CDKN2B,CFB,CSF2,CXCL5,CXCL8,CXCR4,EDN1,FABP3,GCLM,GIPR,GLA,HBEGF,HES1,IFNG,IL10,IL12B,IL15RA,IL17A,IL1B,IL1R1,IL1RL1,IL2,IL23A,IL4,IL5,IL6,IL6R,LPL,MCOLN2,MFN1,MFN2,MMP1,NEDD4L,NFKB2,NFKBIA,NME7,NOD2,NPC1,OASL,OSGIN1,PGLYRP1,PLPP3,PPARG,PTGS2,SPP1,TFPI2,THBD,THBS1,TLR2,TLR4,TNF,TNFSF14,WNT5A	873 (18)
KNG1	other	1,38E-17	ASIC3,BDKRB1,BDKRB2,CCN2,CCND1,COL1A1,COL1A2,CXCL8,EGFR,F11,F12,FOS,IDE,IGF1,IL1B,IL6,KDR,KLKB1,NOS3,PTGS1,PTGS2,TGFB1,TNFSF11	919 (20)
ABCA1	transporter	1,47E-17	ABCA1,ADIPOQ,APOA1,APOA2,APOB,APOE,APOM,CPT1A,FDFT1,HMGCR,IL12B,IL1B,IL6,LDLR,LEP,MMP9,NAMPT,NOS2,PPARG,PTGS2,SCARB1,SELP,SLC2A1,SLC2A4,SREBF1,SREBF2,TLR4,TNF	882 (22)
SPHK1	kinase	1,47E-17	ACTA2,CCL17,CCL5,CCN2,CCND1,CDKN2A,COL1A2,CXCL8,FN1,GCH1,HIF1A,IFNG,IL10,IL1B,IL2,IL33,IL6,JUN,PTGES,PTGS2,SELP,SERPINE1,SLC2A1,SOCS3,TIMP1,TNF,TP53,TRAF1	849 (16)
NRAS	enzyme	1,81E-17	AKAP12,BAX,CALCA,CALCRL,CCL5,CCND1,CD34,CDKN2A,CDKN2B,CFH,CKM,COL1A2,CRYBG1,CTNNB1,CX3CR1,CYBB,EPAS1,EPHX1,ETV5,FBLN2,FN1,GJA1,HIF1A,HLA-A,HTRA1,IFIH1,IFNG,IL1A,IL1B,IL1RN,IL6,ITGA2,KDR,KRAS,LBP,LCN2,LIMK1,LSP1,LY86,MGP,mir-146,MITF,MSR1,NCAM1,NCF2,NPPA,NPR3,NQO1,PLTP,PON3,PSMB8,PTGS2,PTPRC,SERPINE2,SLC2A1,SLC2A4,STAT3,TAP1,UGT1A6,VEGFA,VNN1,XPNPEP2	905 (18)
ERBB3	kinase	2,16E-17	ACTA2,BAX,CCND1,CLU,CMA1,COL1A1,CXCL12,CXCR4,EGFR,ERBB2,ERBB3,FBLN2,FBN1,FN1,GAS5,GHR,HAS2,HBA1/HBA2,HBEGF,HIF1A,HMGB1,HMOX1,HP,IGF1R,IGF2,MMP3,PRL,PTEN,PTGS1,PTGS2,SERPINA3,SLC4A7,SLPI,SOCS3,THBS1,TIMP3,TNC,TNNT3,VEGFA	1017 (19)
MAP3K14	kinase	2,31E-17	CCL5,CXCL8,CYP19A1,EGFR,FAS,ICAM1,IKBKB,IL10,IL13,IL15,IL1A,IL2,IL22,IL4,IL5,IL6,IL7R,IL9,LTA,MMP9,NFKB1,NFKB2,NFKBIA,NOS2,PON2,PTEN,PTGS2,REL,RELA,TNF,TNFAIP3,TNFSF10,TNFSF4,VCAM1	667 (14)
S100A9	other	2,90E-17	ACSS1,AKAP12,ALPL,APLN,ATF3,BCHE,C3,CCL11,CCND1,CD69,CTLA4,CXCL14,CXCL8,ELN,ETV5,FAS,FCGR2A,FURIN,H19,ICAM1,IFNG,IGF1,IL1B,IL1RL1,IL22,IL33,IL6,ITGAM,KCNMA1,MMP1,MMP14,MMP2,MMP3,MMP9,NOS2,NR1H4,NR4A3,NRG1,NTRK3,OLR1,PER1,POSTN,PTGES,PTPRO,RBFOX1,RXRG,SGK1,SLC6A12,SOCS3,TNF,TNFRSF4,TXNIP,TYRP1,UGT1A6,VCAM1,VCAN	694 (19)
WT1	transcription reg	3,85E-17	AHCY,ANPEP,BCL2A1,CBS/CBSL,CCL2,CCN2,CCND1,CKM,COL4A1,CTNNB1,CYP19A1,EGFR,EPO,ERBB2,ESR1,EXT2,FDFT1,FGF1,FGFR1,GSN,GSR,HAMP,HBEGF,HSPG2,IGF1,IGF1R,IGF2,IL10,IL1B,IL1RAP,IL2RB,INSR,ITGAM,KRAS,LMAN1,LRP1,LSS,MAPK8,MMP14,MMP2,MMP3,MMP9,NOTCH3,NPHS1,NRAP,OS9,PAX2,PECAM1,PLAUR,RARA,RBPJ,ROCK1,SERPINE1,SLC15A2,SLC20A1,SLC2A3,SLC6A6,SMAD3,SREBF2,TERT,TGFB1,TGFB3,THBS1,TIMP3,TSC22D1,VDR,VEGFA,WARS	1045 (22)
bevacizumab	biologic drug	3,97E-04	ANGPT1,CXCL12,CXCR4,EGFR,FN1,KDR,VEGFA	795 (14)
IGF2	growth factor	3,93E-17	AKT1,ALAD,APOA2,BMP2,CAV3,CCN2,CCND1,CD36,CKM,CRY1,CXCR4,CYP1B1,DHCR7,FN1,GCH1,GHR,GNAI2,H19,HBEGF,HIF1A,IGF1,IGF1R,IGF2,IGF2R,IGFBP3,IL10,IL6,LEP,MEF2D,MMP1,MMP12,MMP3,MYOD1,NFKBIA,NOS2,PIK3R1,PMS1,PRDM16,PRKCQ,PTEN,PTGS2,SERPINE1,SFTPB,SKAP2,SLC20A1,SLC2A4,SOCS3,SPP1,SREBF1,THBS2,THRA,TOMM40,TP53,UCP1,UHRF1,VEGFA	925 (23)
CXCL8	cytokine	4,15E-17	ABCB1,ABCG2,AR,BAX,CD69,COL18A1,CPE,CR1,CXCL8,CXCR2,CYP19A1,FAS,HABP2,HSPG2,ICAM1,IL1B,IL2RA,ITGAM,ITGB2,MMP2,MMP9,MTPN,NFKBIA,NOX1,NR3C1,PLD2,POU5F1,PTGS2,RAC1,SELL,SOCS1,SREBF1,TGFBR1,TNF,TPM1,VCAM1,ZFP36	702 (14)
AGER	transmembrane	4,31E-17	AGER,ARG1,CALCR,CCL2,CCND1,CHGA,CHGB,CKM,COL4A1,CTNNB1,CXCL8,FAS,FLT1,ICAM1,IL10,IL1B,IL22,IL4R,IL6,LPL,MMP12,MMP2,MMP3,MMP9,NPHS1,PTGS2,SELE,SERPINE1,TGFB1,TNC,TNF,TP53,TXNIP,VCAM1,VEGFA	933 (18)
NOSTRIN	transcription reg	4,44E-17	ACE,ANXA5,CAV1,CCL5,COL18A1,FGF1,FLT1,FN1,IL6,ITGB3,KDR,KIT,MMP1,MMP2,MMP9,NFKB1,NOS3,NPR1,PECAM1,SELE,SELP,SOD1,THBS1	895 (16)
NPY	other	4,44E-17	BDNF,CBS/CBSL,CYP21A2,DIO2,DPP4,FOS,GHRH,GPX4,HSD3B2,IL10,IL6,KISS1,LEP,NOS2,NPY,NPY5R,POMC,SST,TH,TNF,TRH,UCP1,UCP3	897 (21)
CD14	transmembrane	4,91E-17	BCL2A1,CCL2,CCL5,CXCL12,CXCL8,CXCR2,CYP27B1,ICAM1,IFNG,IL10,IL10RA,IL12B,IL1B,IL1R1,IL2RA,IL4,IL6,ITGB1,MSR1,NFKB1,NOS2,PTGS2,SELE,SELP,SOCS1,SOCS3,TGFB1,TLR2,TNF,TNFAIP3,VCAM1	623 (15)
PRKCB	kinase	4,91E-17	ADRB1,ADRB3,BAX,CCL11,CCND1,CD40,CTNNB1,CYP7A1,FN1,FOS,ICAM1,IL10,IL2,IL6,INS,IRS2,JUN,MMP2,MMP9,MYH7,NOS2,NPPA,PPARGC1A,PRKCB,PTGS2,SERPINE1,SOD2,SREBF1,TGFB1,TGFBR2,UCP1	712 (15)
ID2	transcription reg	5,09E-17	ACTA2,ADM,BMP7,CCL11,CCL5,CCND1,CCR5,CDKN2A,CTNNB1,CXCR4,FGFR3,FOXO1,FOXO3,HES5,HIF1A,ICAM1,IFNG,IL10,IL10RA,IL2,IL2RB,IL4,IL4R,IL6R,IL7R,IL9R,IRF5,ITGB3,JAK2,JDP2,KLF7,LEPR,LTA,MAF,MMP2,MYB,NFATC1,NOTCH1,NR4A3,PIK3C2B,PIK3R1,PKD2,PTPN22,REL,RORA,SELL,SEMA3F,SOCS3,SOX13,STAT4,TF,TGFBR3,TNFRSF1A,TNFRSF4,TNFSF10,TNFSF11,TNFSF14,TOX2,TRAF1,VCAM1	934 (22)
EGLN1	enzyme	5,98E-17	ADM,AGER,AURKA,CDKN2B,CXCR4,EDN1,EGLN3,EPAS1,EPO,HIF1A,ICAM1,IFNG,IL1A,IL1B,IL4,IL6,LEP,MMP3,NOS3,PTGS2,SDC4,SELL,SLC2A1,TGFB1,TGFB2,TGFB3,TGFBR1,TGFBR2,TNF,TNFRSF11B,VCAM1,VEGFA	875 (23)
PRKD1	kinase	7,18E-17	ADIPOQ,CCL11,CCL5,CCND1,CD2,CYP11B2,GATA4,IFNG,IL10,IL12B,IL13,IL1B,IL23A,IL2RA,IL6,KIDINS220,LOXL3,LPL,MEF2D,MMP1,MMP2,MMP3,MMP9,NKX2-5,PTGS2,TNF,TNFAIP3,VCAM1	681 (15)
blinatumomab	biologic drug	4,55E-05	CCL2,CXCL8,IFNG,IL10,IL6	138 (6)
CCL5	cytokine	7,27E-17	AHR,BDNF,CCL2,CCL5,CCR3,CCR5,CD40,CXCL8,CYP1B1,DDAH1,EGF,F2R,F2RL1,FOS,HMGA1,IFNG,IL12A,IL1B,IL6,ITGAM,MAPK1,MAPK3,MMP9,NAMPT,NCOR2,NOS2,OLR1,PLAUR,PTGDS,SGK1,SOD1,STAT3,THBS1,TLR4,TNF,ZFP36	833 (20)
NOD2	other	7,43E-17	BCL2A1,BMP2,C5,CCL2,CCL5,CD40,CXCL8,ICAM1,IFNG,IL10,IL12B,IL17A,IL18,IL1A,IL1B,IL2,IL23A,IL6,ITGAM,MCOLN2,MEFV,NFKB1,NFKB2,NFKBIA,NOS2,NPHS1,NR1H3,PTGES,RASGRP3,SOCS3,SOD2,TNF,TNFAIP3,TNFSF11,TRAF1	727 (16)
GDF2	growth factor	8,88E-17	ABCG2,ATP1A1,BMPR2,CAV1,COL1A1,CXCL12,CXCL8,CXCR4,DLK1,EDN1,EFNB2,EGFR,ENG,FGFR3,FMOD,FOS,GATA2,GJA4,HAMP,HIF1A,HTRA1,ICAM1,ID3,IGF1,MMP9,NFKBIA,NPY,NTRK1,POSTN,PROX1,RAMP1,SELE,SERPINE2,SLC6A6,SMAD1,SMAD6,SPP1,TLR4,VCAM1	698 (19)
NOS3	enzyme	9,39E-17	ACE2,ADGRE1,ADIPOQ,ATF3,BMP2,CCL2,CCN2,CXCL12,GSTP1,ICAM1,IFNG,IL12B,IL2,IL6,MMP14,MMP2,NOS2,NOS3,NPR1,PDE5A,PTGS2,SOD3,TERT,TGFB1,TLR4,TNF,VCAM1	684 (14)
RHOA	enzyme	1,01E-16	ACTA2,AGT,BAX,CCN2,CCND1,CDKN2A,CDKN2B,COL1A1,COL3A1,CTNNB1,CXCL8,ERBB2,ESR1,FN1,FOS,GDF15,ICAM1,IL1B,IL6,ITGB1,JUN,MMP1,MMP14,MMP9,MYOD1,NFKB1,NOS2,NOS3,NPPA,PIK3CG,PPARA,PRKG1,RHOC,ROCK2,SCARB1,STAT3,TGFB1,VCAM1	895 (18)
TGFB3	growth factor	1,14E-16	ACTA2,CCN2,CCN3,CD46,CD59,CDKN2A,CDKN2B,COL1A1,COL1A2,COL3A1,CYP19A1,ELN,ENG,F2RL1,FN1,FOS,GJA1,HTRA1,ITGAV,ITGB3,JUN,LTBP2,LTC4S,MGP,MMP1,MMP2,MMP3,MMP9,PLAUR,PPARGC1A,PTEN,SERPINE1,SERPINE2,SMAD2,STAT4,TGFB1,TGFB3,TGFBR3,THBS1,TIMP3,TNC,TNFRSF11B,TPM1,VEGFA	973 (20)
HNF4A	transcription reg	1,34E-16	ABCB11,ABCC2,ABCG5,ABCG8,ACAA2,ACAT1,ACTA2,ADCY10,ADH1B,ADIPOR1,ADRB2,AFP,AGT,AGXT2,AKR1B1,AKR1C3,ALDH1L1,ALDH2,ANG,ANPEP,ANXA5,APOA1,APOA2,APOA4,APOB,APOC1,APOC2,APOC3,APOE,APOH,APOM,AQP1,AQP3,AQP8,AQP9,ARG1,ARL4C,AS3MT,ATP10A,BAZ1B,BHMT,BLZF1,BMP7,BRAP,BTN2A1,C2,C3,C4A/C4B,CAT,CAV1,CBR3,CBS/CBSL,CCL16,CCND1,CD46,CDC123,CDC5L,CDKAL1,CEBPD,CHEK2,CHI3L1,CHIC2,CLCN6,CLCNKA,COX8A,CPB2,CPT1A,CPT1B,CPT2,CRP,CRY1,CSK,CTNNB1,CTNNBL1,CXADR,CXCL8,CYP11A1,CYP1A1,CYP1A2,CYP1B1,CYP2A6 (includes others),CYP2C8,CYP2C9,CYP2E1,CYP2J2,CYP3A4,CYP3A5,CYP3A7,CYP4F2,CYP4F3,CYP7A1,DACH1,DBP,DCTN5,DPAGT1,EFCAB1,EPHX1,EPO,ERCC6,ETNK2,ETNPPL,F11,F11R,F12,F7,F9,FABP1,FABP2,FAIM2,FAS,FDX1,FGA,FGB,FMO3,FOXO1,FURIN,G6PD,GCKR,GDF15,GLA,GLCE,GNG5,GPLD1,GPR160,GPR37,GPR39,GPX1,GRB14,GRHL1,GRHPR,GSN,GSS,GSTA1,GSTCD,GSTK1,GSTM4,GSTO1,HBEGF,HBS1L,HIF1A,HLA-A,HLA-B,HLA-C,HLA-G,HMGB1,HMOX2,HNF1A,HNF1B,HNF4A,HSD11B1,HSPA8,IFI30,IGF1,IGF1R,IGFBP1,IL10RA,IL15,IL1RAP,IL2RB,IL6,IL6ST,ITGA9,ITIH3,JUN,KCNJ11,KCNN2,KDM5C,KNG1,LBP,LCN2,LDHA,LDLR,LEPR,LGR5,LIPA,LIPC,LPA,LRP5,LTA4H,LTF,LUC7L2,LZTR1,MAOA,MAP2K5,MBL2,MCM8,MED23,METTL18,MGST3,mir-122,mir-335,MLXIPL,MMUT,MON1B,MOV10,MTHFD1,MTR,MTTP,NAMPT,NAT8,NBPF3,NCOA3,NCOR1,NDUFB3,NFE2L3,NFKBIL1,NME7,NOD2,NOX4,NR0B2,NR1H3,NR1H4,NR1I2,NR2F1,NR2F2,NUF2,NUTF2,NVL,OAS3,OPA1,OR52E4,OSMR,OTC,P2RY2,PANX2,PARD3B,PAX2,PCK1,PDE11A,PDK4,PLD2,PLG,PMS1,PNPLA3,PON1,POR,POU5F1,PPARA,PPARD,PPARG,PPARGC1A,PPP1R12B,PRCP,PRRC2A,PTGDS,PTGFR,PTPN11,PTPRG,RAC1,RARA,RARB,RARG,RASA1,RASGRP3,RIOK2,RNASE3,RNPEPL1,ROCK1,RORA,RUVBL2,RXRA,SAA1,SCARB1,SDF2,SELP,SERPINA1,SERPINA3,SERPINE1,SGK1,SGK2,SHBG,SHH,SLC10A1,SLC17A5,SLC22A3,SLC2A2,SLPI,SMAD4,SOD1,SOX17,SPATS2L,SPP1,SREBF1,SREBF2,SRR,SRSF2,SRSF3,STK24,SULT1A1,TADA1,TCF21,TCF7,TCF7L2,TF,TFR2,TFRC,TIGD6,TIMP3,TNC,TNFAIP1,TNFRSF11B,TNFSF13,TOX,TTR,TXN,TXNIP,TXNRD1,TYMS,UCP2,UGT1A1,UGT1A6,UGT1A7 (includes others),USF1,VEGFC,VKORC1,WDR12,XPA,XPNPEP2,XRCC4,ZFP36,ZFP37,ZNF300	1046 (23)
NR2F1	ligand-depende	1,34E-16	AGT,ALDH2,APOA1,APOA4,APOC3,CPT2,CYP11B2,CYP19A1,CYP2D6,CYP7A1,EPO,GDF15,HES5,HGF,HNF1B,JAG1,LHCGR,LPL,LTF,PCK1,POMC,POU5F1,RARB,SLC9A1,TH	420 (8)
CD36	transmembrane	1,40E-16	ADIPOQ,APOA1,APOA4,APOB,ARG1,ATP2A2,AXL,CCL5,COL1A1,COL4A1,CSF2,CXCL5,CXCL8,FABP1,FAS,ICAM1,IFNG,IGF1R,IL10,IL13,IL15,IL1A,IL1B,IL6,LEP,LPL,LRP1,MMP1,MMP14,MMP3,MTTP,PLAUR,PPARG,PPARGC1A,SERPINE1,SLC2A4,TNF,TNFRSF11B,UCP1	1112 (21)

TNFRSF1B	transmembrane	1,51E-16	CCR5,CD69,CSF2,CXCL12,CXCL13,CXCL8,CYP3A5,FAS,ICAM1,IFNG,IL12B,IL2,IL2RA,IL6,JUN,LBP,LEP,let-7,MMP1,MMP14,MMP2,MMP3,MMP9,MSR1,MYOD1,NFKB1,NOS2,OPRM1,P2RX7,PTEN,SAA1,SELL,SERPINE1,SOCS3,SOD2,TH,TIMP1,TNF,TNFAIP3,TNFRSF11A,TRAF1	948 (16)
PRKAA1	kinase	1,63E-16	ACOT7,ACTA2,ATF3,BAX,CA2,CARTPT,CAT,CHGB,CLU,CXCL12,CXCL8,CYP3A5,DDAH1,EGF,EGLN3,ELOVL2,FGFR2,FKBP5,FN1,FOXO3,GHR,GPX1,GSTA1,HSD3B2,IFNG,IGF1,IGF1R,IL12B,IL17A,IL6,LDHA,Ly6a (includes others),MMP9,MT-CO1,MYLK,NCF2,NFKBIA,PDGFRA,PDYN,PPARGC1A,PSMB8,RGS2,SIRT1,SIRT6,SMAD3,SOCS3,SOD2,SORL1,TNF,TP53,VCAM1	929 (18)
GATA1	transcription reg	1,64E-16	ALOX12,ALOX5,ALOX5AP,AQP1,BMP6,CA1,CA2,CCL5,CCND1,CCR3,CCR5,CD36,CDK6,CDKN2A,CIITA,CMA1,CREG1,CYBB,DICER1,ENPP1,EPO,F10,GATA2,GNAS,GP1BA,GP1BB,GUCY1B1,GYPA,HBA1/HBA2,HBB,HBG1,HHEX,IFNG,IKZF1,IL13,IL1RL1,IL4,IL5,IL6R,IL6ST,IL7R,ITGA2B,ITGB3,JAZF1,JDP2,KDR,KIT,LEPR,MECOM,mir-146,MITF,MS4A2,MTHFD1,MYB,NFKB1,NPPA,PECAM1,PIGQ,PRKG1,REL,SELP,SLC19A1,SLC4A1,SOX6,SPTA1,SPTB,SRM,SRSF2,STAT4,STAT5A,TANC2,TFR2,TFRC,UAP1,UHRF1,VDR,VWF	968 (23)
HMGB1	transcription reg	1,82E-16	AGER,BAX,BRCA1,CCL2,CD40,CDKN2A,CKM,CXCL5,CXCL8,HIF1A,HLA-DRB1,HLA-G,HMGB1,ICAM1,IFNG,IL10,IL17A,IL1A,IL1B,IL1R1,IL6,INSR,MMP1,MMP3,MMP9,MOK,PTGES,PTGS2,SELE,SIRT1,SREBF1,TH,TLR2,TLR4,TNF,TNFSF11,VCAM1	675 (14)
IGF1R	transmembrane	1,97E-16	ACADS,ACTA2,ACTN4,AQP4,ATM,BAX,CAVIN3,CCL5,CD36,CDC42,CLU,COL18A1,COL1A1,COL3A1,COL4A1,CPT2,CTNNB1,CYP11A1,DES,DIO3,DLK1,EDN1,ESR1,FOS,GCK,GHRH,GPER1,H19,HIF1A,HTRA1,IGF1,IGF1R,IGF2,IGF2R,IGFBP3,IL16,IL1B,IL6,IRS1,IRS2,ITGAM,let-7,LHCGR,mir-196,mir-329,mir-335,MT-ATP6,MT-CO1,MT-ND4,MYH7,MYOD1,NOS3,PLAT,POU5F1,PTGS2,RAC1,RELA,S100A4,SDC4,SLC2A2,SREBF1,SST,STAT3,TGFB1,TIMP3,TNF,TNFSF10,TP53,TXN,TYMS,UCP1,VEGFA,VEGFC	1133 (25)
F2RL1	G-protein coupl	2,01E-16	ACTA2,BDNF,CAV1,CCL2,CCN2,CSF2,CXCL8,F2RL1,FAS,FGF5,FOS,HBEGF,IFNG,IL10,IL13,IL1A,IL1B,IL4,IL6,let-7,MMP9,NOS2,PSEN1,PTGS2,RARG,TGFBR1,TNF,TSLP,TXNIP,VEGFA,VEGFC,WWOX	677 (16)
IL12A	cytokine	2,06E-16	CCL5,FAS,FUT7,ICAM1,ICOS,IFNG,IL10,IL12A,IL12B,IL12RB1,IL12RB2,IL17A,IL1A,IL1B,IL2,IL22,IL4,IL6,LTA,NOS2,SELPLG,SOCS1,SOCS3,STAT3,STAT4,TNF,VCAM1	795 (18)
C3	peptidase	2,15E-16	ACTA2,C3,C5,CCL2,CCL5,CD46,CRP,CXCL8,FN1,IFNG,IL10,IL12B,IL13,IL17A,IL1A,IL1B,IL4,IL6,ITGAM,LCN2,LEP,NOS2,PTPRC,RNASE3,SELL,SELP,TGFB1,THBD,TNF,TNFRSF1A,UCP2,UCP3,VEGFA	755 (20)
FABP4	transporter	2,50E-16	ABCA1,ACAT1,CCK,CD36,IFNG,IL12B,IL1A,IL1B,IL2,IL6,LIPE,MSR1,NOS2,NOS3,NR1H3,PPARA,PPARD,PPARG,PTGS2,SOCS3,TNF	944 (20)
BQ 123	biologic drug	5,14E-05	CCL2,CCN2,GJA1,IL6,TNF,VEGFA	959 (22)
BQ-788	biologic drug	1,12E-02	AQP9,CTNNB1,EDN1,TNF	
ZFP36	transcription reg	2,56E-16	CD36,COL3A1,CSF2,CYBB,FOS,HIF1A,ICAM1,IFNG,IL10,IL12A,IL12B,IL17A,IL1A,IL1B,IL23A,IL6,JUN,LCN2,LTF,MEFV,MMP1,MPO,NFKBIA,NUF2,PLAUR,PRC1,PTGS2,SOCS1,SOX6,SPP1,TFF1,TFRC,THBD,TLR4,TNF,TRAF1,VCAM1,ZFP36	913 (15)
FGF19	growth factor	2,93E-16	AFP,APOE,AQP4,AQP8,CCND1,CD36,CTNNB1,CYP17A1,CYP7A1,FABP3,FOS,GCK,HLA-DQB1,HMGCR,HSD3B2,IGFBP1,IL1RN,KL,LCN2,LEP,LEPR,MME,MMP12,NNAT,NR0B2,PON1,PRL,PTGDS,RGS2,SERPINA1,SERPINA3,SGK1,SLC10A2,SLC2A2,SLC2A5,SLPI,SREBF1	753 (18)
SMARCB1	transcription reg	3,30E-16	ABCB1,ACAT1,ADD3,APOA5,APOC4,ATP1B1,AURKA,BGLAP,BICD1,C4A/C4B,CCND1,CDKN2A,COL18A1,COL1A1,COL1A2,CRP,CXCR4,CYP2C8,CYP2E1,CYP3A7,CYP4A11,DACH1,DHFR,ERBB2,F10,F11,F11R,FAS,FCGR2A,FOS,GJA1,GSN,HBEGF,HBG1,HES1,HES5,HP,IFNG,IL12B,IL15RA,IL1A,LBP,MMP1,OAS3,PCK1,PGLYRP1,POSTN,POU5F1,PPARG,PTN,RAD54B,SMAD5,TCF21,TFF1,TP53	992 (20)
EHF	transcription reg	3,39E-16	ALOX5,ANGPTL4,ANPEP,BMP4,CDKN2A,CYP1A1,ERBB2,FOLH1,GATA2,HMOX1,IL13,IL1RN,IL6,JAG1,KDR,KIT,KLF5,KLK8,MET,MMP1,MMP3,MS4A2,NOTCH2,NOTCH3,PLAT,PLAUR,PPARD,RARB,RBPJ,SAA1,SERPINA3,SERPINE1,STAT5B,THBD,TIMP1,TNC,VEGFA,VEGFC,VNN1	733 (11)
Notch	group	3,54E-16	ACTA2,ADM,AFP,AGT,CCN4,CDCA7,CDKN2B,FGF5,FLT4,GUCY1A1,GUCY1B1,HES1,HES5,ID3,IFNG,IL10,IL4,IL6,JAG1,mir-143,MMP2,MYLK,NFATC1,NOTCH1,NOTCH3,POU5F1,PROX1,RELA,SMAD1,SMAD2,SMAD3,SMAD6,TNF,TRPC6,VEGFA	859 (20)
XDH	enzyme	3,66E-16	ABCA1,ACTA2,AVPR1A,CCN2,CCR5,CD69,CXCL8,CXCR4,CYBB,HIF1A,ID3,IL1B,IL2RA,INSR,MMP14,MMP2,PLAUR,PPARA,PPARG,SERPINE1,SLC2A1,SPP1,TIMP2,TNF	802 (15)
TRAF3IP2	other	3,71E-16	ACE,AGER,AGT,CCL11,CCL5,CCN2,CCR2,CCR3,CEBPD,COL1A1,COL3A1,CSF2,ICAM1,IFNG,IL13,IL17A,IL18,IL1B,IL33,IL4,IL5,IL6,LCN2,MMP2,MMP3,MMP9,NFKBIZ,NOS2,POSTN,SELP,STEAP4,TGFB1,TNF,VCAM1	805 (14)
mir-21	microRNA	3,77E-16	ACSM2B,ACTA2,ALOX15,ARNTL,BMPR2,C8orf44-SGK3/SGK3,CCL17,CCL2,CCND1,CD226,CDK6,CDKN2A,CDKN2B,CLU,COL1A1,COL3A1,CRY2,DBP,DDAH1,DDAH2,ELN,FAS,FCGR2A,FGF1,FN1,FOXP3,GAS5,ICAM1,IFNG,IL12A,IL12RB2,IL18,IL1B,IL23R,IL4,IL6,IL6R,IRAK1,JAG1,JAK2,LEPR,MMP2,MMP9,NLRP3,NOS2,NPAS2,OAS3,PECAM1,PER2,PLAT,POU5F1,PPARA,PRC1,PTEN,SLPI,SMAD2,SMAD5,SMARCA4,SOD2,SOD3,SRSF3,STAT3,TAP1,TCF21,TERT,TGFB1,TIMP3,TLR2,TLR4,TNF,TP53,TPM1,TRAF1,VCAM1	856 (17)
brodalumab	biologic drug	7,85E-03	IL12A,IL17A,IL22,IL23A,IL4R	
ARNT	transcription reg	3,88E-16	ADM,AHR,ANGPTL4,CAV1,CCR5,CXCR4,CYP1A1,CYP1A2,CYP1B1,CYP2A6 (includes others),EDN1,ENG,EPAS1,EPO,FGF21,FLT1,FURIN,G6PD,GSTA1,HGF,HIF1A,HNF1A,HNF4A,IL10,INSR,IRS2,ITGAV,ITGB3,LDHA,LEP,LOXL2,NOS3,NQO1,RGS5,SELL,SERPINE1,SHH,SIM1,SLC2A1,SLC2A3,SOCS3,TFRC,TP53,UGT1A6,VEGFA	1250 (23)
BCL2	transporter	4,07E-16	ABCC1,ATP2A2,BAX,CCND1,CHGB,CKM,CSF2,CTSH,CXCL8,FAS,FOS,GCLC,HAMP,HIF1A,ICAM1,IFNG,IL10,IL12B,IL15,IL17A,IL1B,IL2,IL23A,IL3,IL4,IL6,ITGB1,MMP2,MMP9,NFKBIA,NNAT,NTRK1,PLAUR,PTEN,SCG3,SNAP25,TGFB2,TIMP1,TIMP2,TNF,TP53,VEGFA	704 (16)
PDX1	transcription reg	4,26E-16	ACE2,AKR1B1,ATF3,ATP2A2,CAT,CCND1,CHGB,COL1A1,COL3A1,CPT2,CXCR4,DLK1,FGF1,FGF5,FGFR1,G6PC2,GCH1,GCK,GCLM,GIP,GLP1R,GNAS,HNF4A,ID3,IGF1R,IGFBP3,IL1B,IL6,INS,INSIG1,IRS2,JUN,LTA4H,MITF,MT-ND1,NFKB1,NNAT,NQO1,PCSK1,PDX1,PTGER3,RABGAP1L,RHOBTB1,SEZ6L,SLC2A1,SLC2A2,SLC6A6,SPP1,SST,TCF7L2,TGFBR3,TIPRL,TRIB3,TRPC3,TRPC6,TSPAN8,TXNIP,WFS1	1027 (22)
mir-155	microRNA	5,15E-16	AGTR1,CCL18,CCL2,CCL5,CCND1,CD69,CXCL8,DOCK1,EDN1,EGFR,FOXO3,HIF1A,HMOX1,IFNG,IKBKE,IL10,IL12B,IL13,IL17A,IL1B,IL5,IL6,MAF,mir-143,MME,MMP3,MYB,NOS2,NOS3,PPARG,PSIP1,PTEN,PTGS2,RELA,RORA,SERPINE1,SMAD2,SMAD5,SOCS1,SOCS3,STAT3,TNF,TP53,ZNF652	792 (19)
MTPN	transcription reg	5,29E-16	BAX,BCL2A1,CCND1,COL1A1,COL1A2,DBH,EDN1,ENG,FAS,FN1,FOS,GAS5,GAS6,IFNG,IGF1,IL6,JUN,MIF,MMP3,MTPN,MYH7,NFKB1,NPPA,PLAT,RELA,SERPINE1,SPP1,TCF21,TGFB1,TGFB2,TGFB3,TH,TNF,TNFRSF1A,TNFSF10,VCAM1	799 (12)
Collagen type II	complex	5,93E-16	BMP2,BMP4,BMP6,BMP7,CCL18,CCL23,CCL8,CCR2,CRP,CX3CR1,CXCL5,CXCR2,IFNG,IL1A,IL1B,IL1R1,IL1RN,IL22,IL6,JAK2,MMP7,TLR7,TLR8,TNF,TNFSF10,TNFSF14	862 (18)
IKBKG	kinase	6,09E-16	ATP2A2,BAX,BMP2,C3,CCL5,CD247,CDH13,CEBPD,CLU,CSF2,CXCL12,CXCL8,EPAS1,FOS,GCH1,HIF1A,HLA-A,ICAM1,IFNL3,IKBKE,IL1A,IL1B,IL1RN,IL2,IL6,KCNH2,KLF5,LCN2,MGP,MYH7,NFKB2,NFKBIA,NPPA,PPARA,PPARG,PTEN,RYR2,SERPINE2,SGK1,SOCS3,SOD3,TNF,TNFAIP3,TNFRSF1B,TNFSF10,TRPC1,TSHR,VEGFA	910 (14)
TIMP3	other	6,32E-16	BMP4,CTNNB1,ENG,FAS,FOS,IL6,ITGB6,JUN,KIT,LRP8,MAPK3,MET,MMP2,MMP9,NFKB1,SERPINE1,SMAD1,SMAD2,SMAD4,SMAD5,SMAD6,STAT3,TGFB1,TGFBR1,TGFBR2,TGFBR3,THBS1,TNF	846 (19)
STAT5a/b	group	6,48E-16	AHR,AKT1,ARG1,BCL2A1,BMP6,CCND1,CD36,CD69,CDKN2A,EBF1,EPHA4,FOS,FOXP3,GATA2,GYPA,IFNG,IGF1,IL13,IL17A,IL2,IL2RA,IL4,IL4R,IL5,IL9,LEPR,MAF,OPRM1,PAX5,PCK1,PROX1,PTGS2,RARA,RARB,SLC10A1,SLC2A3,SOCS1,SOCS3,TLR2,TSLP	787 (17)
FOXP3	transcription reg	7,70E-16	BRCA1,CCR2,CTLA4,CXCL13,ERBB2,FOXP3,GPR83,HLA-A,ICOS,IFNG,IL10,IL17A,IL17RA,IL1RL1,IL2,IL2RA,IL4,IL5,IL6,IL7R,IL9,IRAK1,LIG1,MAF,MAPK8,mir-146,MMP2,MMP9,NFKB1,NPR1,NTRK3,PLAGL1,PTPN22,RAD54B,RUNX1,SELL,TGFB1,TNF,TNFAIP3,TTR,VEGFA	810 (17)
FGFR2	kinase	8,24E-16	AFP,AQP8,BAX,BGLAP,BMP4,CA2,CA4,CCN4,CCND1,COL1A1,COL3A1,COL4A1,CPE,CTSH,CYP7A1,DRAM1,FAS,FGF10,FGFR2,FN1,GJA1,HES1,ICAM1,IGF1,IGF2,IL10,IL1A,IL1B,IL2,KLB,LGALS2,LGR5,MAEL,MRAS,NNAT,NOTCH1,PDGFRA,PITX2,PLAUR,PTH1R,SOX17,SPP1,TSPAN8,TTR,VCAM1,VEGFC	1057 (20)
TICAM1	other	8,33E-16	CCL2,CCL5,CD40,CEBPD,CFB,CXCL13,CXCL8,EDNRB,FAS,FPR1,GDF15,ICAM1,IFNG,IFNL3,IKBKE,IL10,IL12A,IL12B,IL15,IL15RA,IL17A,IL18,IL1A,IL1B,IL23A,IL4,IL6,ITPR2,JAG1,MEFV,MET,NFKB1,NFKB2,NFKBIA,NFKBIZ,OASL,PTGS2,SELE,SERPINE1,SLC7A2,SOCS1,SOCS3,TLR2,TNF,TNFAIP3,TNFSF10,TNFSF11,TSC22D1,VCAM1	810 (16)
AVP	other	9,15E-16	ACTA2,ADM,APLN,ATF3,ATP1A1,BGLAP,CCL2,CCND1,CKM,COL3A1,CRHR1,EDNRB,FOS,GATA2,IL6,KCNJ1,NOS1,NOS2,NOS3,NPPA,POMC,PRKCA,SCNN1B,SCNN1G,SLC12A1,SST,TGFB1	1099 (25)
MAP2K1/2	group	9,52E-16	ATF3,BDNF,C3,CCN2,CCND1,CHI3L1,CYP7A1,ELN,FOS,FOXP3,FURIN,GCLC,GJA1,HMOX1,IL10,IL13,IL1B,IL2,IL2RA,IL4,IL5,JAG1,JUN,KLF5,let-7,MMP9,NFKB1,NOS2,NOX1,PGR,PIK3CG,PPARA,SCARB1,TNF,VEGFA	854 (18)

MAP3K7	kinase	9,52E-16	CCL5,CD14,CFB,CXCL8,GATA4,GCH1,HMOX1,IFIH1,IL12B,IL1B,IL2,IL6,IL9,ITGB1,JUN,MMP1,MMP3,MYH7,MYOD1,NFKB1,NKX2-5,NPPA,OASL,PTGS2,RELA,RGS2,SAA1,SELE,SERPINE1,SLPI,TERT,TNF,TNFSF10,VHL,WNT5A	851 (19)
buserelin	biologic drug	3,59E-04	ANXA5,FOS,GNRH1,GNRHR,PRL	949 (20)
MMP9	peptidase	9,52E-16	ACTA2,CALCR,CCL11,CCND1,COL18A1,CTNNB1,CXCL12,CXCR4,EGFR,FOS,GJA1,HTR1B,ICAM1,IFNG,IL10,IL13,IL1A,IL23A,IL4,IL6,ITGB1,JAG1,MMP12,MMP14,MMP2,MMP3,MMP9,NFATC1,SDC4,SERPINA1,SERPINE2,TGFB1,TIMP1,TNF,VEGFA	724 (17)
TLR9	transmembrane	9,60E-16	ABCA1,AKT1,ATF3,CAST,CCL17,CCL5,CCND1,CD40,CD69,CERS6,CSF2,CTH,CXCL8,EDN1,FAS,FURIN,GCH1,GDNF,HMOX1,IFNG,IFNK,IFNL3,IL10,IL10RA,IL12A,IL12B,IL17A,IL18,IL1A,IL1B,IL2,IL21R,IL23A,IL2RA,IL33,IL4,IL4I1,IL6,LCN2,LIPG,LTA,NAMPT,NFKBIZ,NOS2,NPY,NR0B2,NR1H4,OAS3,PROCR,PTGER2,PTGS2,RELA,SERPINE1,SOCS1,SOCS3,TGFB1,TIMP1,TLR4,TLR7,TNC,TNF,TNFRSF1B,TNFSF10,TP53,TSLP,UAP1,VAV2	730 (18)
PRKCQ	kinase	9,92E-16	CAV3,CD69,FOXP3,IFNG,IL10,IL13,IL17A,IL2,IL24,IL2RA,IL4,IL5,IL6,ITGB1,MMP1,MMP2,MMP9,NFKB2,PRKCB,PRKCH,STAT3,TNF,TNFRSF4	696 (16)
LGALS1	other	1,09E-15	ACTA2,AHR,ANG,CD69,CLCNKB,CTLA4,DHCR7,FIS1,FN1,HBEGF,HLA-G,IFNG,IL10,IL17A,IL1A,IL1B,IL2,IL2RA,IL6,INSIG1,KRAS,LEP,MAF,MMP1,MMP12,MMP2,MMP3,MMP9,ROCK1,SERPINE1,TFRC,TNF,TOX	740 (15)
CCN2	growth factor	1,14E-15	AFP,AKT1,BCL2A1,CCN2,CCN3,CCND1,COL1A1,CTNNB1,CYP17A1,EGLN3,EMILIN1,ESR1,FN1,HAMP,HES1,HIF1A,HSD17B7,IGF1,IGF2,IL17A,IL6,JUN,LHCGR,LOX,MIA3,MMP1,MMP14,MMP2,MMP3,MMP9,POU5F1,PTGFR,PTH1R,SDC4,SERPINE1,TGFB1,TIMP1,TIMP3,TP53,VEGFA,WNK1	924 (16)
ITGA1	other	1,20E-15	CAV1,CD36,COL9A2,EGFR,IFNG,IL10,IL1B,IL2,MMP2,MMP3,MMP7,MMP9,NOS2,PPARG,PTGS1,PTGS2,RAC1,TNF,TNFSF11	764 (16)
GATA2	transcription reg	1,43E-15	ADGRG1,ALOX5,ANGPT1,AQP9,AR,CCL5,CCN3,CCND1,CCR3,CD226,CD34,CD36,CD69,CDC42,CDK6,CES1,CHGA,CHI3L1,CMA1,CYBB,CYP11A1,DIO2,DLK1,EDN1,EDNRA,ELANE,EPO,EVI5,F13A1,FUT7,GATA2,GFRA1,GNRHR,GP1BB,GPX3,HBA1/HBA2,HHEX,HNF4A,ICAM4,ICOS,IKZF1,IL13,IL1RL1,IL2RB,IL4,IL4R,IL5,IL6,ITGA2,ITGA2B,ITGAM,KDR,KIT,KLK2,LAX1,LCN2,LTF,Ly6a (includes others),MAT1A,MEF2C,MMP2,MPO,MS4A2,MYB,NOS3,NPPA,PBX1,PECAM1,PGR,PPARG,ROCK1,RUNX1,RXRG,SELP,SLC18A2,SLC4A1,TBX19,TFR2,TFRC,TGFBR3,THBS1,TNFSF4,TP53,TPH1,TPSG1,UBASH3A,UGT1A6,UGT2B7,VCAM1,VEGFA	1101 (19)
Gsk3	group	1,54E-15	CCND1,CD40,CTNNB1,CXCL8,EGFR,ESR1,FOS,GDF15,HIF1A,HMGCR,ICAM1,IFNG,IGF1R,IL10,IL12B,IL1B,IL6,IRS1,JUN,KDR,LDLR,MYB,NKX2-5,NOS2,NPPA,PPARG,PTGS2,SPP1,SREBF1,SREBF2,TNF,TNFAIP3,TNNC1,TNNI3,TP53	782 (18)
NGF	growth factor	1,65E-15	ADM,ASIC3,ATF3,BAX,BDNF,CAV1,CCND1,CD40,CDK5R1,CDKN2A,CHGB,DRD2,EGFR,EGLN3,EPAS1,EPHA4,ETV5,FAS,FOS,FSHR,GCH1,GUCY1A1,GUCY1B1,HAMP,HMOX1,HTT,IGF2,ITGA2,JUN,LDLR,LRP1,MMP2,MMP3,MMP9,MT-CO1,NOS1,NPY,NTRK1,PLAUR,PLG,PNMT,PPARG,PTEN,RAC1,RELA,REN,RET,RGS4,RHO,SNAP25,SOD1,SORT1,STAT3,TGFB1,TH,TNF,TP73,TRPV1,TRPV4,TXN,VEGFA,VIP,WNT5A,ZWINT	1203 (21)
CCR5	G-protein coupl	1,70E-15	BAX,CCL5,CCR5,CXCL12,FAS,FOS,IFNG,IL10,IL12A,IL12B,IL17A,IL1B,IL2,IL22,IL23A,IL4,IL5,IL6,MMP9,NOS2,SERPINA1,SLPI,TNF,TNFRSF1A,TNFRSF1B	723 (16)
IFI16	transcription reg	1,70E-15	BAX,CCL2,CCL5,CCND1,CD28,CDKN2A,CXCL8,CYP1A1,DHFR,EDN1,ESR1,FSHR,GATA4,GPX1,HSD3B1,ICAM1,IL1B,IL1RN,IL2RB,IL6,IL7R,LDLR,LPL,MIF,MPO,NFKBIA,NKX2-5,NPPA,SELE,SOD1,TNF,UCP3,VCAM1,XRCC1	1021 (18)
ETS2	transcription reg	1,83E-15	ANPEP,BMP4,BRCA1,CD34,CDKN2A,ERBB2,FGF1,FLT1,FOS,HMOX1,ICAM1,IL12B,IL2,IL2RA,ITGA2B,JUN,MGAT5,MMP1,MMP3,MMP9,MSR1,NOS2,PCSK6,PRIM2,PRL,PSEN1,SPP1,TERT,TGFBR2,TIE1,TLR9,TNF,TNFSF14	1078 (26)
LGALS3	other	1,83E-15	ABCB1,ABCC1,ADIPOQ,AGER,BAX,CCND1,CCR2,COL3A1,COL4A1,CTNNB1,CTSH,FGF21,FN1,GFRA1,ICAM1,IFNG,IGF1,IL10,IL12A,IL13,IL1B,IL5,IL6,ITGAM,ITGAV,ITGB1,KRAS,MSR1,NOS2,PPARG,PPARGC1A,PTEN,RAC1,SAA1,SELE,SOCS3,TGFB1,TNF,VCAM1	976 (17)
MAPK7	kinase	1,85E-15	ADRB2,BCL2A1,BDNF,CCN3,CCND1,CXCL8,EDN1,HMOX1,IL1A,IL1B,IL6,JUN,MEF2A,MEF2C,MEF2D,NOS3,NQO1,PLAT,PTGER2,PTGS2,SEMA3F,STEAP4,TH,THBD,TNF,TP53,VEGFA	989 (23)
NPR1	enzyme	1,97E-15	ABCC8,ACE,AGT,COL1A1,COL3A1,FN1,GBA,GUCY1A1,GUCY1B1,KCNJ11,MMP2,MMP9,MYH7,NPPA,PPP3R1,RGS4,SLC9A1,TGFB1,TGFB3,TNF	720 (20)
GFI1	transcription reg	2,16E-15	AKT1,ATF1,BAX,CD40,CXCL8,CXCR4,ELANE,F2R,GJA1,ICAM1,IFNG,IKBKB,IL10,IL1A,IL1B,IL1R1,IL2,IL5,IL6,IL6R,IL7R,JUN,LTA,MAPK3,mir-196,MMP7,NFKB1,NFKB2,NFKBIA,PTEN,REL,RELA,SERPINA1,SERPINA3,SMAD3,TNF,TNFRSF1A,TNFSF14,TOLLIP,VDR	612 (13)
ADRB	group	2,20E-15	ACAT2,ACSS1,ADGRL4,ANGPTL4,ANXA5,ARG1,ATF3,AXL,BAX,BDNF,BRCA2,CCND1,CD40,CDK6,CDKN2A,DIO2,FAS,FGF21,FOS,GATA4,GCLM,GDF15,HMOX1,HSD17B7,HSPD1,ICAM1,INSIG1,JUN,LPIN1,LSS,MMP9,MSMO1,NFKBIA,NOS2,NOTCH2,NPPA,NQO1,NR4A3,OASL,PKD1,PPARGC1A,PTGS2,SLC6A9,SLC8A1,SMAD6,SRM,TRAF1,UCP1	1030 (19)
PTPN1	phosphatase	2,40E-15	ADRA1A,ADRA1B,ADRA1D,ATM,CIDEA,CYP11B1,HHEX,IFNG,IL23A,INSR,IRS1,IRS2,LEP,MET,NFKBIA,NOS2,NOX1,NOX4,PGR,PIK3R1,PLAGL1,PPARGC1A,PRDM16,RASA1,SOCS1,SREBF1,TNF,UCP1	1072 (22)
ALOX15	enzyme	2,66E-15	ABCA1,ALOX15,BAX,CD36,CTNNB1,FN1,HAMP,HMOX1,ICAM1,ID3,IL12B,IL1B,IL6,JUN,MMP2,NOS2,NOTCH3,PPARD,PPARG,RGS2,TNF,VCAM1	819 (17)
GJA1	transporter	2,66E-15	BGLAP,BMP2,BMP4,CCL2,CCN3,CCND1,CD40,CD69,CDKN2A,FGFR3,FOXO1,GJA1,ICAM1,IL10,IL1B,IL2RA,NOS2,SPP1,THBS1,TNF,TNFRSF11B,VEGFA	965 (19)
IL23	complex	2,67E-15	AHR,CCR2,CSF2,CXCL8,ICOS,IFNG,IL10,IL12A,IL12B,IL17A,IL2,IL22,IL23R,IL2RA,IL4,IL4I1,IL6,IL9,REG3A,RORA,STAT3,TLR2,TLR4,TNF,TNFSF11,TSLP	679 (15)
MYOCD	transcription reg	2,77E-15	ACE2,ACTA2,ACTC1,ACTN2,ATP2A2,CACNA1C,CACNA1D,CALD1,CASQ2,COL1A1,COL1A2,COL3A1,DES,FN1,FOS,GATA4,GJA1,GJA5,HSPB7,ITGB1BP2,KCNMB1,MEF2C,mir-143,MYH7,MYL2,MYLK,NPPA,NPPB,S100A4,SREBF2,TNNC1,TNNT2,TP53,TPM1,TTN,VCAN,VEGFA	387 (11)
SERPINF1	other	2,84E-15	ACTA2,ADIPOQ,AGER,BAX,BCL2A1,BDNF,CCN2,CCND1,CD34,CXCL8,CYBA,CYBB,GDNF,IL10,LOXL2,LRP6,NFKB1,NFKBIA,NOS2,PDGFRA,PPARG,PPARGC1A,RHO,SELP,SOD2,TGFB1,THBS1,TNFRSF11B,TNFSF10	1003 (17)
BDNF	growth factor	2,92E-15	ACOT7,ADCYAP1,ADRB2,ANXA5,AP3D1,AR,ARVCF,BDNF,BMP2,BMP7,CAV2,CD36,CHGA,CNR1,CPLX2,CXCR4,DRD2,DRD3,EPO,FOS,GRB14,GRIA1,HMGCR,HSPA2,IL6,ITIH3,JUN,KIF5A,KLC1,LCN2,LEP,LIMK1,MAPK1,mir-214,mir-329,MMP1,MYO5A,MYO6,MYOD1,NCAM1,NOS1,NOS2,NPR1,NPY,NPY5R,NR4A3,NTRK1,PAFAH1B1,PDE1A,PDLIM5,PER2,PLG,PLTP,POMC,PSEN1,PTEN,RGS4,RYR2,RYR3,SCARB1,SFRP2,SHH,SLC12A5,SNAP25,SOD2,SORL1,SPP1,SST,TFRC,TH,THBS1,THRA,TNFRSF11B,TP53BP1,TPH1,TRH,TRPC3,TSC1,TXNIP	836 (18)
C5AR1	G-protein coupl	3,12E-15	ATP2A2,C3,C5,CD28,CD40,CD46,COL1A1,COL1A2,CXCL8,FCGR2A,FCGR2B,IFNG,IGF1,IL10,IL12B,IL13,IL17A,IL1B,IL23A,IL4,IL6,LTBP2,MMP1,MMP9,SELP,SERPINE1,TGFB2,TGFBR1,TGFBR2,TNF	820 (15)
LCN2	transporter	3,32E-15	ADIPOQ,ARG1,BAX,BMP2,CCL17,CCL5,CCR5,COL1A1,CXCL13,CYP19A1,ESR1,HIF1A,HMOX1,IL10,IL15,IL1A,IL1B,IL1RN,IL2,IL23A,IL6,LDLR,MIF,MMP2,NOS2,PPARGC1A,PTEN,RARA,RARB,RBP4,RXRA,SPP1,TGFB1,TNF,TNFRSF11B,UCP1	791 (17)
TAC1	other	3,32E-15	BAX,CCL2,CRHR1,CSF2,CXCL8,CXCR4,EGFR,FOS,HIF1A,HMOX1,IFNG,IL17A,IL1A,IL1B,IL1RN,IL2,IL3,IL4,IL5,IL6,MME,NFKB1,NOS2,PDYN,PLAT,PTGS2,SELE,SELP,SERPINE1,SLC6A2,SOX13,TGFB1,TH,TNF,TNFRSF11B,TNFSF11	730 (16)
PAX3	transcription reg	3,40E-15	ATP2B4,BMP4,CLU,CNR1,COL1A2,CPN2,CRY1,CST3,CXCR4,CYP1B1,EYA2,F2RL1,FGF9,FLT3,FMR1,G6PD,GLDC,GPX4,GSTM5,GUCY1A1,HLA-DRB1,HSPG2,ID3,IL6,IL6R,IL7R,IRS1,LIPE,LNPEP,M6PR,MAP2K5,MCC,MET,MGP,MITF,MMP9,MYL2,MYOD1,NFKB2,NNMT,PCSK2,PTGER3,PXDN,RAB11B,RET,SHMT1,SREBF1,SRSF3,TCN2,TFPI2,TGFB2,TIMP3,TNC,TP53,TRPC1,TSC22D1,TYRP1,VCAN	786 (7)
TNFSF10	cytokine	4,08E-15	AKT1,ANGPT1,BAX,CD14,CD69,CTNNB1,CXCL8,CXCR4,EGFR,FOS,HLA-A,HLA-C,IFNG,IGF1R,IL13,IL1B,IL1RN,IL2,IL2RA,IL5,IL6,ITGAM,JUN,mir-146,MMP2,MMP3,MMP9,NFKBIA,PTGS2,RELA,SELE,TFRC,TIMP1,TNF,TNFAIP3,TNFSF10,TP53,TRAF1,VEGFA	812 (15)
YY1	transcription reg	4,44E-15	ACTA2,ACTC1,API5,ARID3B,AURKA,BDNF,BGLAP,BMP4,BMP6,BRCA1,CCR5,CDKN2A,CFTR,CIITA,CLU,COL1A1,CXCL12,CXCR4,CYBB,CYP24A1,DBH,DROSHA,EGFR,ERBB2,FAS,FOS,HAMP,HAS2,HLA-DRA,HMGCR,HMOX1,ID3,IFNG,IL1B,IL4,KCNB1,KDR,KISS1,LDLR,let-7,LMAN1,LRP2,LUC7L2,MMP2,MYOD1,NFKBIZ,NKX2-5,NNAT,NOTCH2,NR3C1,PDGFRA,PLAGL1,PRC1,PROX1,PSRC1,RELA,SCARB1,SIM1,SLC23A2,SNRPN,SRSF5,TGFB2,TGFBR1,TNFRSF4,TNNC1,TP53,TPH1,TSLP,UHRF1,VEGFA,VEGFC,VWF	1059 (23)
GCG	other	4,45E-15	ACADS,ADIPOQ,ADRB3,AGER,AQP8,BMP4,CBS/CBSL,CCL2,CCN2,CPT1A,CYP2C9,ETNPPL,FN1,FOS,GCGR,GSTP1,HMGCR,IGF1R,IGFBP1,INS,IVD,LPIN1,NR3C1,PCK1,PDX1,PPARGC1A,SCARB1,SDS,SLC2A1,SLC2A4,SREBF1,SREBF2,TGFB1,VCAM1	806 (17)
MAP2K4	kinase	5,15E-15	ATF3,CCL5,CCND1,CRP,CXCL8,EGFR,FAS,FOS,GNRHR,IL12B,IL2,IL6,JUN,MAPK8,MEF2C,MMP1,MYH7,NOS2,NPPA,PPARD,PPARG,PTGS2,ROCK1,ROCK2,STAT3,TGFB1,TNF,TP53,VDR	667 (15)

SOX2	transcription reg	5,18E-15	ABCG2,ACVR2A,ADRA2B,AHR,ALOX5,ANGPT1,ANKRD17,APCDD1,AQP4,ATF3,BCAN,BGLAP,BMP4,BMPR1A,CASR,CCN2,CCN4,CCND1,CDKN2A,CNP,COBLL1,COL1A1,CTNNB1,CXCL14,CXCR4,CYP2J2,EGFR,ETV5,EVX1,EXT2,FABP1,FABP2,FGF5,FLT1,FOS,FOXF1,FUT4,FYN,GAB2,GATA2,GATA4,GCK,GJA1,GSN,H19,HES5,ID3,IGF1,IL23A,INPPL1,IRS1,ITPR2,JAG1,JUN,KDR,LIN28A,LLGL2,MAX,MEF2C,MEIS1,mir-217,MPZL1,MYRF,NFKB2,NOTCH1,NOTCH3,PAX2,PDGFRA,PDX1,PECAM1,PIK3R1,PITX2,POU5F1,PPARA,PPARG,PRKCH,PRKCQ,RBPJ,SEMA6A,SERPINA1,SERPINE1,SGK2,SLC12A2,SMAD1,SMAD4,SOX13,SOX17,SOX6,TBX3,TET2,TF,TGFB1,TGFB2,TGFB3,TIMP3,TXNRD1,VCAN,VEGFA,VEGFC,WNT3,WNT5A,ZFHX3	964 (23)
LRP6	transmembrane	5,42E-15	ACTA2,CAV1,CCND1,CTNNB1,FOS,IFNG,IL10,IL17A,IL1B,IL22,IL6,LEPR,LRP6,MMP14,MMP2,MMP3,MMP7,MMP9,MPO,PNPLA3,PPARGC1A,ROCK2,SLC2A3,TGFB1,TNF,UCP1	971 (20)
CD3E	transmembrane	5,54E-15	CCL17,CD69,CSF2,CTLA4,FAS,FOS,ICOS,IFNG,IL10,IL13,IL2,IL2RA,IL4,IL5,IL6,JUN,KRAS,LTA,MMP9,MYB,NFATC1,NFKB1,NFKBIA,PIK3CG,PIK3R1,PTGS2,SOCS1,TNF,TNFRSF1A,TNFRSF1B,TNFSF11	737 (19)
CTF1	cytokine	6,00E-15	AGT,CEBPD,CRP,FOS,GATA4,IL6ST,IRS1,LBP,LEP,MMP1,MYH7,MYLK,NKX2-5,NPPA,POMC,PPARG,REG3A,SERPINA3,SOCS1,SOCS3,TIMP1,TNF,VIP	956 (19)
CAMP	other	6,03E-15	BAX,BMP8A,CCL2,CCL5,CSF2,CXCL13,CXCL5,CXCL8,CXCR2,CXCR4,HBEGF,ICAM1,IL10,IL12A,IL12B,IL18,IL1A,IL1B,IL1F10,IL1RAP,IL1RN,IL23A,IL4,IL6,ITGAM,ITGB2,NFKB1,NOS2,PDGFRB,PTGS2,TGFB1,TLR2,TLR4,TNF,TNFAIP3,TP53,VEGFC,XPA,XRCC1	714 (16)
CNTF	cytokine	6,11E-15	CALCA,CEBPD,CNR1,CRP,CXCL8,DBH,DRD2,EDN2,FGFR1,FOS,GJA1,IL1A,IL6ST,IRS1,LBP,LEP,MMP1,MYOD1,NOTCH1,NPY,NTRK1,POMC,REG3A,RHO,SERPINA3,SOCS1,SOCS3,SREBF1,SST,STAT3,TGFB1,TIMP1,VIP,WNT5A,ZFP36	766 (19)
ADA	enzyme	6,27E-15	ADA,ADORA1,ADORA2B,CCL11,CCL17,COL1A2,HIF1A,IL13,IL4,IL6,MMP12,MMP9,PDE5A,PLAT,SERPINE1,SPP1,TGFB1,TIMP1,TNF,VEGFA	759 (20)
mir-29	microRNA	7,10E-15	ACTA2,ADAMTS9,ANGPTL4,AR,BDKRB2,CCL8,CCND1,CDC42,CDK6,COL1A1,COL3A1,ELN,FKBP5,FLT3,FN1,GLDC,IGF1,IL12B,IL23A,IL2RA,KIT,LPL,MMP2,OLR1,PDGFRB,PIK3R1,PTEN,SCARB1,SFRP2,THBS1,TIMP3,TNFAIP3,TP53,VEGFA	1077 (19)
GH1	growth factor	7,92E-15	ABCC1,ADRB3,ATF3,CEBPD,CLU,CTNNB1,CXCR4,CYP2C9,CYP3A4,ERBB3,FN1,FOS,GATA2,GHR,GHRH,GHRHR,ID3,IGF1,IGF1R,IGFBP1,IGFBP3,IL4R,IL6,JUN,LDLR,MYB,NOS2,PTEN,RETN,RFC1,SIRT1,SLCO1B3,SMARCA4,SOCS1,SOCS3,SOD1,SPP1,SREBF1,TKT,TNFRSF1A,XRCC1,ZFP36	968 (22)
RELB	transcription reg	8,04E-15	ABCB1,ANXA5,CCL11,CCND1,CCR3,CD40,CHI3L1,CIITA,CSF2,CXCL12,CXCL13,CXCL8,ESR1,IFNG,IL10,IL1B,IL2,IL4,IL5,IL6,LTA,MPO,MYB,NFKB2,NFKBIA,NOS2,PTGS2,RELA,SOD2,STAT4,TNF,TNFRSF1A,TNFSF14	731 (18)
RUNX2	transcription reg	8,23E-15	ABCB1,ACTA2,AKT1,ALPL,BAX,BGLAP,BMP2,C4A/C4B,CCND1,CCR2,CCR5,CEBPD,CIITA,COL1A1,COL1A2,CXCL8,CYP19A1,FGFR2,FN1,GNAS,HIF1A,HTRA1,IGF1R,LEP,mir-2861,MMP14,MMP2,MYOD1,NUDT12,PTGDS,RUNX1,SELPLG,SERPINE1,SHH,SMAD6,SOX6,SPP1,TCF7,TIMP1,TNFRSF11B,TNFSF11,TPM1,VEGFA	946 (21)
IRF1	transcription reg	8,58E-15	AGTR2,BAX,CCL2,CCL5,CCND1,CD40,CFB,CFTR,CIITA,CXCL8,CYBB,ERAP1,FOXP3,HLA-G,IFIH1,IFNG,IFNL3,IL10,IL12A,IL12B,IL12RB1,IL12RB2,IL13,IL15,IL17RA,IL18,IL1B,IL2,IL4,IL5,IL6,IRF5,JAK2,MMP9,MYB,NOS2,OASL,PML,PSMB8,PSMB9,PTGS2,SELL,SLPI,SOCS1,STAT3,TAP1,TBX3,TERT,TGFB1,TLR6,TLR9,TNF,TNFSF10,TP53,VCAM1	719 (15)
MAP2K3	kinase	8,83E-15	ATP2A2,BAX,CCL8,COL1A1,COL1A2,COL3A1,CXCL8,GSTP1,ICAM1,IFNG,IL10,IL12A,IL12B,IL1B,IL4,IL6,MMP1,MMP3,MMP9,MYH7,NFATC1,NOS2,NPPA,PPARGC1A,PTGS2,RELA,SERPINE1,SGK1,SLC2A4,TNF,TNFSF10,VEGFA	855 (15)
CDH1	other	9,51E-15	APOA4,BMP4,BMP7,CCL17,CCND1,CDC42,CTNNB1,EGFR,ERBB2,ERBB3,FABP2,FN1,GRIA1,IFNG,IGFBP3,IL13,IL5,ITGB3,JUN,LCN2,MMP1,MMP14,MMP3,MMP9,NCAM1,PIK3R1,PLAUR,PTEN,RPTOR,S100A4,TGFB1,TNF,TSLP,VEGFA,VHL	1059 (21)
ITK	kinase	9,51E-15	AHR,BAX,CCL5,CX3CR1,F2R,FAS,FOS,FOXP3,HIF1A,HLA-A,IFNG,IL10,IL10RA,IL13,IL17A,IL18RAP,IL2,IL2RB,IL4,IL5,KLRB1,LAT2,Ly6a (includes others),MAF,PRKCB,PTEN,SLC2A1,STAT4,SULF2,TF,TIRAP,TNF,TNFSF10,TP53,XCL1	814 (19)
MET	kinase	9,87E-15	AKT1,AQP3,ATM,AURKA,CCND1,CXCL8,EDN1,FN1,FOS,GCLC,HBEGF,HGF,HMOX1,IL15,IL15RA,IL18,IL1B,IL6,ITGB1,JUN,LTA,mir-27,MMP2,MYOD1,NFKBIZ,NOX4,NPHS1,POU5F1,PTGS2,PTPN1,RUNX1,SLCO3A1,SOCS3,SOD1,SOD2,SPP1,TCHP,TGFB1,TSC22D1,VEGFA	949 (18)
Ifn gamma	complex	1,14E-14	AGT,BGLAP,CCL2,CCL5,CDKN2A,CHI3L1,COL1A1,CXCL8,CYBB,EDN1,ESR1,FAS,FLT1,FN1,HLA-DRA,ICAM1,IL10,IL17RA,IL1B,IL33,JAK2,Ly6a (includes others),MAPK1,MMP9,MYH7,NOS2,NR3C1,NR4A3,PCK1,PML,PPARG,SOCS1,SOCS3,TERT,TGFB2,TLR4,TNF,TNFSF10	849 (14)
SRC (family)	group	1,33E-14	ATP1A1,BMP2,CCL2,CD36,CYP1A1,FLT1,FN1,GRK6,HIF1A,ICAM1,IGFBP1,IL10,IL12B,IL6,ITGAV,ITGB3,KCNB1,MAOA,NOX1,PTGS2,S100A4,SLC4A7,SLC6A4,SMAD2,TNF,VCAM1,VEGFC	862 (19)
RXRB	ligand-depende	1,44E-14	ABCA1,BGLAP,CCL17,COLEC12,CYP24A1,DRD2,EPO,FABP1,FGFR1,GAS6,HBEGF,IFNG,IGF1,IL10,IL13,IL1A,IL1B,IL4,IL5,LCN2,MMP12,MMP2,NPY,POU5F1,S100A4,SPP1,SREBF1,TERT,TFF1,TNF,TSLP,VCAN	1015 (26)
FOXO4	transcription reg	1,45E-14	ANGPT1,APLN,CAV1,CCN2,CCND1,CDKN2B,COL4A1,EDNRB,EPO,FDFT1,FLT4,FMOD,FOXC1,FYN,HIF1A,HMGCR,IGFBP1,IL10RB,IL1R1,ITGAM,ITGB2,JAG1,MMP9,NAMPT,PRCP,PTGS1,PTPRC,SELL,SERPINE1,SGK1,SLC2A1,SOD2,SREBF2,TGFB1,TIE1,VCAM1,VEGFA	937 (18)
TGM2	enzyme	1,46E-14	ALPL,AQP9,BCL2A1,C3,CA2,CAD,CCL2,CCND1,CD36,CDCA7,CDK6,CX3CR1,CXCL8,CYP2R1,CYP4F3,EPO,FN1,GCA,GJA1,HIF1A,HLA-B,HTT,IFNG,IGF1R,IL10RA,IL1B,IL6,ITGAM,ITGB3,LRRK2,LSP1,MGP,MMP2,MMP9,MYH7,NCF2,OAS3,OASL,PADI4,PDGFRB,POR,PTGES,PTGS1,RARA,RNF213,SELL,SELP,SIGLEC12,SIRPA,SLC20A1,SLC7A2,SLPI,SPP1,TAP1,TGFB1,THBS1,TIMM8A,TNF,TNFRSF11B,TP53,VHL,VIP	786 (17)
REL	transcription reg	1,54E-14	AHR,BCL2A1,BRCA1,CACNA1E,CCL2,CCND1,CD200,CD40,CD59,CIITA,CSF2,CXCL8,DHFR,ESR1,ETV5,EVI5,FADS2,FAS,FN1,FOS,FOXO3,FOXP3,HBEGF,HLA-A,ICAM1,IFNG,IL12A,IL12B,IL13,IL18,IL2,IL22,IL23A,IL2RA,IL4,IL5,IL6,IL9,IRF5,JUN,KDR,MLLT3,MMP9,MYH7,NFATC1,NFKB1,NFKB2,NFKBIA,NOS2,NR4A3,PIBF1,PTGDS,REL,RELA,SH2B3,SOD2,SORBS1,STAT3,STAT5B,TNF,TNFAIP3,TNFRSF4,TNFSF10,UBE2Z	870 (19)
F3	transmembrane	1,56E-14	ANGPT1,ARG1,CCL2,CCN2,CDC42,CXCL8,F2,FOS,GJA1,HAMP,ICAM1,IFNG,IL10,IL1B,IL6,ITGA2,ITGAM,KRAS,MMP2,MMP7,MMP9,PLPP3,RAC1,SELE,SERPINC1,SERPINE1,TGFBR2,TNF,TNFRSF11A,VCAM1,VEGFA	727 (16)
NR4A3	ligand-depende	1,63E-14	BAX,CAV3,CCND1,COL1A1,CYP21A2,FOXO1,FOXP3,HIF1A,HSD3B2,IL10,IL13,IL2RA,IL4,IL5,LPIN1,MEF2C,MFN2,MT-CO1,NQO1,PDPR,POMC,PPARGC1A,PRL,SDHB,SLC39A8,SMAD3,TGFB3,UCP1,UCP2,UCP3	1039 (20)
GAST	other	1,75E-14	ABCC2,CCND1,CHGA,COX5B,CTNNB1,FOS,HBEGF,HES1,IFNG,JAG1,JAK2,JUN,MAPK1,MMP7,MMP9,MYLK,NFKBIA,PDX1,PIK3R1,PLA2G7,POMC,POR,PPARG,PTGS2,RAC1,RELA,SELP,SLC18A2,SLC4A2,SLC9A3,SRSF2,STAT3,TNC,VCAM1	779 (17)
KLF6	transcription reg	1,75E-14	ALOX5,ARG1,ATF3,CCL2,CHI3L1,COL1A1,CXCL8,CYP1A1,DLK1,ENG,HNF4A,IGF1R,IL12A,IL1A,IL1B,IL6,MMP9,NCOA1,NFKBIA,NOS2,NR2F1,PPARA,PPARG,PTGS2,RARB,RARG,SHH,TFPI2,TGFB1,TGFBR1,TNF,TNFAIP3,VAV3,VEGFA	831 (18)
TGFA	growth factor	1,75E-14	AKT1,CCL2,CCL5,CCN2,CCND1,CSF2,CTNNB1,CXCL8,EGFR,ESR1,FOS,GSTP1,HGF,ICAM1,IL6,ITGAM,LCN2,MMP9,PECAM1,PLA2G5,PLAGL1,PLAT,PTGS1,PTGS2,PYY,SERPINA1,SERPINE1,SLPI,TGFB1,TLR5,TLR9,TP53,VEGFA,WNT5A	1037 (19)
PRKCZ	kinase	1,86E-14	ABCA1,BAX,CCL11,CCND1,COL1A2,CXCL8,HMOX1,IL2,IL4,JUN,KRAS,LHCGR,MAPK1,MAPK3,MMP2,MMP9,NFKBIA,NOS3,NPPA,VCAM1,VEGFA	801 (15)
BSG	transporter	2,08E-14	ABCC2,ABCG2,APOC3,CCND1,CRP,CXCL12,CXCL8,CYP1A2,EPAS1,HIF1A,IL18,IL1A,IL1B,IL2,IL2RA,KDR,MMP1,MMP2,MMP3,MMP9,PLAUR,SELP,SERPINE1,TGFB1,TNF,VEGFA	875 (16)
HDAC3	transcription reg	2,16E-14	ALOX5,BMP2,CCND1,CD34,CD36,CDKN2A,COL1A2,CXCL8,DIO1,FOS,G6PD,GUCY1B1,HMOX1,HP,ICAM1,IL12B,IL6,KLK2,mir-217,mir-335,MMP12,MMP9,NFATC1,NFKBIA,NOS3,PTEN,PTGS2,RARB,SERPINE1,SMARCA2,SPP1,TBX2,TBX4,TBX5,TFF1,TLR9,TNF	952 (25)
NAMPT	cytokine	2,25E-14	AXL,BDNF,CCR3,CXCL8,FN1,IL16,IL6,ITGB1,JUN,MITF,MMP1,MMP3,MMP9,NAMPT,NAT1,NPY1R,PDGFRB,PECAM1,PPARGC1A,TGFB1,TGFB2,TNF,TP53,WNT5A	934 (16)
NPC1	transporter	2,25E-14	ABCA1,ABCG8,ALPL,APOB,ARNTL,CAV1,CAV2,CCND1,CCR2,CCR3,CCR5,CDYL2,CYP27B1,CYP7A1,HLA-DQB1,HLA-DRB5,HMGCR,LDLR,LIPA,LIPG,LPL,LSS,MMP14,MVK,MYLIP,NPC1,PCSK9,PNPLA3,PTGS2,SREBF1,SREBF2,STAT3,STAT4,TLR4,TNF	694 (17)
RNF31	enzyme	2,33E-14	ACE,ADORA1,APOA1,AURKA,C8orf44-SGK3/SGK3,CCL11,CCL17,CCL2,CCL5,CCND1,CXCL13,CXCR4,CYP19A1,ESR1,IL10RA,IL15RA,IL18,IL18RAP,IL1A,IL1B,IL1RL1,IL1RN,IL24,IL33,IL4R,IL6,IL6R,KCNMA1,SCARB1,TFF1,TGFB3,TNF	923 (15)

ADM	other	2,47E-14	ACE,ADM,AGT,BAX,CALCA,CALCR,EDN1,FN1,FOS,HIF1A,ICAM1,IL1B,IL6,MAX,NOS1,NOS2,PPARG,PRKG1,PTGS2,RAMP1,REN,SPP1,TGFB1,TNF,TNFRSF11B,TNFSF11,VCAM1	898 (19)
MMP1	peptidase	2,47E-14	ANGPT1,BAX,BRCA1,CDKN2A,CXCL12,CXCL8,ERBB2,FGFR2,FN1,FOS,HIF1A,IGF1,JUN,KDR,MMP1,MMP9,MYOD1,NFKB1,NFKBIA,PLTP,PTGES,PTGS2,S100A4,SERPINE1,TGFB1,TGFBR1,TNF	815 (16)
MAP2K7	kinase	2,71E-14	ATF3,CCL5,CCND1,CDKN2A,CXCL8,EFNB2,ERCC1,FAS,FN1,GJA1,HSPA1L,IL1R1,IL2,IL4,ITGB1,KLC1,LSP1,MAPK8,MMP3,MTTP,MYH7,NPPA,P2RX4,PTPN11,SERPINC1,TFPI2,TNF,VDR	824 (19)
TNFSF12	cytokine	2,72E-14	CCL11,CCL2,CCL5,CCND1,CCR5,CSF2,CXCL8,ICAM1,IL17A,IL1B,IL6,ITGAM,let-7,MEF2A,MEF2C,MEF2D,mir-146,mir-27,MMP1,MMP12,MMP3,MMP9,MT-CO2,MYOD1,NFKB2,NFKBIA,NOS1,NOTCH1,NOTCH3,NPHS1,PPARGC1A,SELE,SLC2A4,TCAP,TIMP1,TNF,TNFSF4,TSLP,VCAM1	801 (18)
IL1R1	transmembrane	2,80E-14	ABCC1,ACTA2,CCL5,CXCL12,CXCL8,FOS,ICAM1,IFNG,IGF1,IL10,IL17A,IL18,IL1A,IL1B,IL1RAP,IL6,LBP,LEP,MMP2,MMP9,NOS2,PTGS2,REG3A,SAA1,SELE,TGFB1,TIMP1,TNF,TRAF1	835 (16)
IKZF1	transcription reg	2,93E-14	AQP1,AXL,CAV1,CAV2,CD34,CDK6,CNR2,CYP2J2,DNAJC6,DNM3,DOCK1,EBF1,FGFR1,FLT3,FN1,FOXO1,G6PD,GAS6,GHRH,GP1BA,HES1,IFNG,IGF1,IL10,IL13,IL18R1,IL2RB,IL4,IL5,IL6,IL6ST,IL7R,INSR,ITGA2B,KIT,LRP1,MLXIP,MMP14,NCAM1,NFKBIZ,NOTCH1,NOTCH3,NR1H4,NR3C1,P2RX4,PAX5,POMC,PRKCQ,PTH1R,RALB,RNF213,RUNX1,RYR1,SLC19A1,SLC2A1,SLC2A3,SLPI,SMAD3,SULF2,TLR4,TNF,TNNT2,TSHZ1,TXNIP,VIPR1,VWF	959 (19)
BCL6	transcription reg	3,16E-14	BAX,BCL2A1,CCL2,CCND1,CD2,CD69,CDKN2A,CIITA,COL1A1,CTLA4,FAS,FMOD,FOXP3,FUT7,GIT2,GPX4,HDAC9,IFNG,IL10,IL12A,IL13,IL17A,IL18,IL1A,IL1B,IL21R,IL23A,IL24,IL2RA,IL2RB,IL4,IL4R,IL5,IL6,IL6R,IL7R,IL9,KLK1,LDLR,LPIN1,Ly6a (includes others),MAF,MGP,MITF,MYB,NFATC1,NFKB1,NOS2,PIK3CG,PTEN,PTPRO,RGS4,SERPINE1,SLC39A8,SOCS3,SOX6,TGFB1,TNF,TP53	712 (14)
ATF3	transcription reg	3,19E-14	ADIPOQ,ADIPOR1,ATF3,AURKA,CCL5,CCND1,CD69,CTNNB1,EPO,GCG,GSN,HSPB2,ICAM1,IFNG,IL12B,IL1B,IL4,IL6,JUN,LDLR,MMP1,MMP2,MMP3,NFKB2,NFKBIZ,NOS2,PCK1,PTGES,SELE,SERPINE1,SLC11A1,STAT3,TLR2,TNF,TP53,TP73,TSLP	659 (13)
ADRB3	G-protein coupl	3,78E-14	ADRB1,ADRB2,CCL2,CXCL12,FOS,IL1B,IL6,JUN,LEP,mir-196,PPARGC1A,PTGS2,TNF,UCP1,UCP2,UCP3	847 (20)
Ap2	group	3,92E-14	ADM,AFP,APOB,C3,ERBB2,ERBB3,F2R,ICAM1,IGF2,IL3,KIT,LHCGR,LIPA,MMP2,MT-CO2,PCK1,PTGDS,SAA1,TERT,TGFB1,TGFB3,VEGFA	931 (13)
catumaxomab	biologic drug	2,32E-02	CD40,CD69,TNFSF10	
mir-27	microRNA	4,49E-14	ABCA1,ABCB1,ACSM2B,BMP2,BMPR1A,CAD,EDN1,EGFR,ESR1,FLT1,IGF1,IKZF1,IL10,IL1B,IL6,KRAS,MET,MYH7,NF1,PPARA,PPARG,PTGS2,RUNX1,SEMA6A,SMAD9,SP4,TNF	1014 (21)
RGS10	other	4,49E-14	ARG1,CCL11,CCL2,CCR3,CRP,FAS,IFNG,IL10,IL10RA,IL10RB,IL13,IL18,IL1A,IL1B,IL2RB,IL4,IL5RA,IL6,IL6ST,ITGAM,ITGB2,LTA,TGFB1,TNF,TNFRSF1A,TNFRSF1B,TOLLIP	855 (15)
CYBB	enzyme	4,66E-14	AKT1,CCL5,CCN2,COL3A1,CSF2,CYBA,CYBB,DUOX1,DUOX2,ICAM1,IFNG,IL1B,IL2,IL4,IL5,IL6,KIT,PPARG,TGFB3,TNF,TNFRSF11A	699 (17)
HSD11B1	enzyme	4,66E-14	ADIPOQ,AGT,ANGPTL4,APOA1,CCL2,CPT1A,CPT1B,CYP11B2,FGA,IL12B,IL6,LEP,LIPE,NOS2,NR1H3,PDK4,PPARA,PPARGC1A,SREBF1,TNF,UCP2	1003 (24)
NPPB	other	4,66E-14	ACAT2,BAX,CCN2,COL1A1,COL3A1,CYP11B1,CYP11B2,CYP19A1,FDFT1,FDX1,FN1,HMGCR,HSD3B1,IL1B,LDLR,LSS,MSMO1,PPARGC1A,SCARB1,TGFB1,UCP1	1063 (21)
PTX3	other	5,01E-14	CCL2,CCL5,CCN2,CCR2,CCR5,CX3CR1,CXCL8,FOS,GATA4,IGF1,IL1B,IL4,IL6,IRAK1,JUN,MMP9,NFKB1,TLR2,TLR4,TNF	889 (16)
SFTPA1	transporter	5,03E-14	ADRB2,ANGPTL4,ANPEP,CCN2,CLEC1B,COL1A1,CXCL5,CYP1B1,FOS,FOXP3,GSTO2,GUCY1A1,HBA1/HBA2,HBEGF,HBG1,IL10,IL1A,IL1B,IL1RL1,IL2,IL2RA,IL6,LOX,NAMPT,NOS2,PDK4,RELA,SERPINE1,SFRP2,SLC22A3,TGFB1,TH,TNF	824 (14)
POU5F1	transcription reg	5,90E-14	ACVR2A,AFP,AHR,AKT1,ANGPT1,ANKRD17,APCDD1,BAX,BCL2A1,BMP4,BMPR1A,BRCA1,CCND1,CD40,CIDEA,COBLL1,CTNNB1,EVX1,EXT2,FABP1,FABP2,FAS,FGF5,FOXF1,FUT4,GATA2,GATA4,GCK,H19,HIF1A,ID3,IGF1R,IL6,IRS1,LIN28A,LTA,MAX,MEF2A,MEF2C,MEIS1,mir-217,MMP2,MMP9,NCAM1,NR2F2,PARP1,PCSK6,PDGFRA,PDX1,PECAM1,PITX2,POU5F1,PPARA,RARA,SERPINA1,SIRPA,SIRT1,SLC27A4,SMAD1,SMAD4,SOX17,SPP1,TBX3,TET2,TF,TGFB1,TGFB2,TGFB3,TNF,TNFRSF11B,TNFRSF1A,TNFSF10,TP53,TP73,TXNRD1,VEGFA,WNT3,WNT5A,ZFHX3	1145 (20)
FGF21	growth factor	6,13E-14	ADIPOQ,CIDEA,CPT1A,CPT1B,DIO2,FGFR1,FGFR2,FOS,GHR,HMGCS2,IGF1,IGFBP1,IRS2,KISS1,KLB,LDLR,LEP,MYLIP,PCK1,PPARGC1A,SERPINE1,SLC2A1,SREBF1,TGFB1,UCP1	1022 (22)
CFTR	ion channel	6,39E-14	ABCA1,ACAA1,ACAA2,AQP1,CA4,CCL5,CFH,CFTR,CXCL8,CYP3A5,CYP4A11,EPHX2,FAAH,FABP2,FADS1,FADS2,FAS,FDFT1,GSR,KCNJ1,NFKB1,NFKBIA,NFKBIZ,NOS2,PGLYRP1,PLA2G5,POR,PTGS2,SAA1,SLC7A8,SLC9A3,SOCS3,TNF,TNFAIP3	885 (18)
TSLP	cytokine	6,54E-14	ABCA1,ACTA2,CCL11,CCL17,CD40,COL1A2,CXCL8,ICAM1,IL10,IL12B,IL13,IL2RA,IL4,IL5,IL6,IL9,SELE,SELL,SELP,SLPI,TGFB1,TIMP1,TNFSF4	720 (17)
ADRB2	G-protein coupl	7,29E-14	ADIPOQ,ADRA2B,ATP1A1,ATP1B1,CCR2,COL1A1,CYP1B1,GNAS,GRK3,IDE,IFNG,IL10,IL12A,IL12B,IL17A,IL2,IL6,LEP,MME,RETN,SCNN1A,SPP1,TNF,TNFRSF11B,TNFSF11,UCP1	1051 (25)
TFAP2A	transcription reg	7,47E-14	ABCA1,ADRA1D,APOE,BAX,CHRNA3,CYP11A1,DRD1,EGFR,ERBB2,ESR1,F2R,FOXP3,GLO1,GNRH1,GPR37,IGF2,KISS1,LHCGR,LIPA,Ly6a (includes others),MMP14,MMP2,MMP9,NOS1,NPY,PITX2,PLAUR,POR,PPARD,PPARG,SERPINE1,SLC19A1,SOD2,TERT,TIMP1,TPM1,UTS2,VEGFA	1021 (22)
RETNLB	other	7,78E-14	ACTA2,AKT1,CCL2,CCL5,CCN2,CCN4,CCR2,CCR5,COL1A1,COL1A2,ELN,FABP1,FGFR1,FN1,IGF1,IL13,IL1B,IL4,IL4R,IL6,IRS1,IRS2,MMP12,MMP2,PTEN,SMAD1,TERT,TGFB1,THBS4,TIMP1,TLR2,TNNC1,WNT5A	965 (18)
Ccl2	cytokine	8,01E-14	ADIPOQ,ADRB3,CCL11,CCL5,CCR2,CD14,HGF,IFNG,IGF1,IL10,IL1B,IL2,IL4,IL5,IL6,ITGB3,KDR,LEP,LPL,PPARG,SDC4,SLC2A4,TBX3,TIE1,TLR4,TNF,VCAM1	904 (16)
IL25	cytokine	8,04E-14	CCL11,CCL17,CCL2,CCL5,CIDEA,CSF2,CXCL8,F11R,FLT1,IFNG,IL10,IL12A,IL12B,IL13,IL17A,IL1B,IL1RL1,IL22,IL23A,IL2RA,IL33,IL4,IL5,IL6,IL9,JAG1,KDR,TNF,TSLP	610 (15)
ALOX5	enzyme	8,79E-14	ALOX5,CALCR,CCND1,CD36,FABP1,IFNG,IL17A,ITGAV,ITGB3,LEP,MMP12,MMP9,MSR1,NFATC1,NOS2,PPARA,PTGS2,RELA,SCARB1,SOCS1,TGFB1,TNF	1099 (25)
let-7	microRNA	8,95E-14	ACTA2,ALDH1B1,AR,AURKA,BCAT1,BCL11A,BDNF,BMPR1A,BRCA1,BRCA2,CCND1,CDCA7,CDK6,CEBPD,COL1A1,COL1A2,COL3A1,DICER1,FN1,GAB2,HBA1/HBA2,HMGA1,IGF1R,IGF2BP2,IL10,IL17A,IL6,IL6R,IRS2,ITGA4,ITGB3,KRAS,LIN28A,MCM8,NFKB1,NR1H4,NUF2,PLAGL1,PLAUR,POU5F1,PPP1R12B,PTGS2,RELA,S100A4,SERPINE1,SMAD2,SMAD4,STAT3,TGFBR1,THBS1,TLR4,TNF,TRIB1,XPO5,XRCC3,ZC3H3,ZFP36	875 (20)
FOXA1	transcription reg	9,84E-14	ACTA2,ACTC1,ADH1C,AFP,AQP3,BMP2,CDKN2A,CFTR,COL18A1,CPS1,EPHX1,ERBB3,ESR1,FABP2,FKBP4,FOXC1,GRIN3A,HNF1A,HNF1B,HNF4A,IGFBP1,IL6,JAG1,KLK2,MGP,mir-122,MLXIPL,NPY,PAM,PCK1,PGR,PPARA,PYY,RARA,RORA,SCGB1A1,SHH,SLC12A1,SLC12A2,SLPI,SOD1,SST,TCF7,TF,TFF1,TH,TTR,UCP1	1096 (23)
SOD2	enzyme	9,91E-14	ADCY10,ANGPT1,ATP1A1,CAT,COLEC12,GCH1,GSN,HMOX1,ICOS,IL1B,IL6,JDP2,KCNN2,KLKB1,KNG1,LIPC,MLXIP,MMP1,MMP2,MMP3,MMP7,MMP9,MYO3B,NOS3,PLAGL1,PTGS2,PTPRO,SERPINE1,SLC19A2,SOD2,SORT1,TGFB1,TNF,TP53,TRPM8,UCP1,UCP2	944 (20)
IFNA2	cytokine	1,01E-13	ADGRE1,ALOX5,BAX,CAV1,CCL2,CCL5,CCL8,CD28,CD69,CDKN2A,CDKN2B,CNP,CXCL13,DPP4,EFNB3,EGLN3,ENPP1,FAS,GAB3,GNAS,HBEGF,HIF1A,HLA-A,HLA-B,HLA-C,IFIH1,IFNG,IL10,IL10RB,IL12RB2,IL1B,IL2,IL2RA,IL2RB,IL4,IL5,IL6,IRF5,KCNJ1,KCNJ6,KCNK17,MET,MMP9,MT-ATP6,MT-CO2,MYRF,NOS3,OAS3,PLAT,PML,SLC18A2,SOCS1,SOCS3,STAT4,TAP1,TNF,TNFRSF1A,TNFSF10,TP53,UGT1A6,VCAM1,VEGFA,VEGFC	661 (16)
Calcineurin A	group	1,11E-13	AKT1,ATP2A2,ATP2B4,CCN2,CCND1,COL1A1,COL1A2,COL3A1,FOS,GCG,GJA1,IL2,INSR,ITPR2,JUN,NPPA,PPARGC1A,SLC2A1,SLC2A4,TGFB1,TIMP1	853 (19)
NCOR-LXR-Oxys	complex	1,17E-13	ABCA1,ABCG5,ABCG8,APOA4,APOA5,APOC1,APOC2,APOC4,APOE,CD36,CETP,CYP7A1,FDFT1,LPL,MLXIPL,PLTP,SREBF1,UGT1A3	
PRNP	other	1,19E-13	ABCB1,AHR,APOE,BAX,CCL2,CCL5,CCND1,CDKN2A,FGF9,GJA1,HSPA1A/HSPA1B,HSPA8,IFNG,IGF1R,IGF2,IL17A,IL1B,IL2,IL6,IRS1,LRP1,MMP2,NFKBIA,NOS2,NOTCH1,PLAUR,PLPP3,RELA,SNAP25,TCF7,TH,TNF,TP53	881 (19)
CBL	transcription reg	1,33E-13	BGLAP,CDKN2B,CFTR,COL1A1,EGFR,EPHA4,ERBB2,FGFR2,FLT3,FN1,FOS,GBA,IFNG,IL12B,IL17RA,IL1B,IL2,IL4,IL6,INSR,JAK2,LEP,MMP2,PDGFRA,TNF,UCP3	816 (22)
REN	peptidase	1,33E-13	ACE,ADD3,AGT,APLN,CCN2,COL3A1,CYP2C9,CYP2E1,CYP2J2,FOS,ICAM1,IL6,MYH7,NOX1,NOX4,NPPA,RELA,REN,TNF	979 (21)
KL	enzyme	1,35E-13	ACTA2,AXL,BAX,CAST,CCND1,CTNNB1,CYBB,CYP27B1,CYP46A1,ICAM1,IL6,KDR,KL,MITF,MMP7,MMP9,SELP,SOD2,TGFB1,TNF,TNFRSF11B,VDR,VEGFA	989 (24)

HDAC4	transcription reg	1,40E-13	ANGPTL4,ATF3,BDNF,CACNA1C,CACNA2D1,CAMTA2,CDKN2A,CKM,CSRP3,DGKB,DRP2,ETNPPL,FOS,HDAC9,HIF1A,HLA-DRA,HMGCR,IGFBP1,IL2,IL6,JUN,LDHA,MAPK1,MAPK8,MEF2C,MMP9,NOS2,PPP3CA,PRKCA,PRKCB,PTGS2,RGS2,RGS4,SLC2A1,SLC2A4,SLC8A1,SMAD4,SNAP25,TERT,TNF,TP53BP1,TRPV1,VCAM1,VEGFA	889 (24)
ERG	transcription reg	1,41E-13	ADD1,ADGRG1,ADRB2,ALOX12,APOC1,AR,BDKRB1,CAMK1D,CD59,CHRNA3,CNR1,CTNNB1,CXCL8,CXCR4,DOCK1,EVI5,FKBP5,FLT1,FOLH1,FYN,GDF2,GUCY1A1,GUCY1B1,HMGB1,HPCAL1,ICAM1,IGF1R,KLK2,MAGI1,MET,MMP1,MMP3,MMP9,MYO5A,NOS3,NPHP1,NRG1,PECAM1,PLAT,PLAUR,PLPP3,POU2F1,PTPN11,PTPN22,RAPGEF5,RASIP1,RHOBTB1,ROCK2,RYR3,SLIT2,SPP1,SPTBN5,SREBF2,TDRD5,TGFBR2,THBS1,VWF	799 (17)
SYK	kinase	1,58E-13	AKAP12,CCL2,CCL5,CCND1,CD247,CD69,CFTR,CSF2,CXCL8,CXCR4,EDN1,GPLD1,ICAM1,IL10,IL1B,IL2,IL23A,IL3,IL4,IL6,ITGAM,ITGB3,NOTCH1,PLEKHG1,PRKCQ,RCSD1,RELA,ROCK1,SHH,SREBF1,TFPI2,TGFB1,TIMELESS,TNF,TNFSF10,TNFSF4,TSC22D1,UCP1,VEGFA	752 (20)
IFNB1	cytokine	1,69E-13	ANXA5,APOL1,APOL3,AXL,CALCR,CCL2,CCL5,CCR5,CD14,CD40,CSF2,CXCL8,CYP1A1,CYP1A2,CYP2E1,DICER1,F2R,FBLN2,FBN1,FOS,HLA-A,HMGCR,IFIH1,IFNG,IFNK,IL10,IL12A,IL12B,IL13,IL17A,IL18,IL1B,IL1R1,IL2,IL24,IL4,IL5,IL6,ITGAV,ITGB3,mir-196,MMP2,MMP9,NFATC1,NNMT,NOD2,NOS2,NOTCH1,PDK4,PML,PRL,PTGS2,REL,SHH,SOCS1,SPP1,SREBF2,STAT4,THBS1,THBS2,TIMP1,TIMP2,TLR7,TLR8,TLR9,TNF,TNFRSF4,TNFSF10,TNFSF4,VCL,VDR	622 (16)
TXNIP	other	1,80E-13	AGER,CCND1,CD36,COL1A2,DES,DHCR7,FABP2,FGF21,ICAM1,IL1B,IL2RB,IL6,KISS1,LPL,MTTP,NFKB1,NOX4,NPHS2,PPARA,PPARGC1A,PTGS2,RELA,TXNIP,VEGFA	841 (21)
ADORA2B	G-protein coupl	1,90E-13	ARG1,CCL11,CCL17,COL1A2,CXCL8,HIF1A,IL10,IL13,IL1B,IL4,IL5,IL6,MMP12,MMP9,NOS2,PDE5A,SERPINE1,SPP1,TGFB1,TIMP1,TNF,VEGFA	855 (15)
MRTFA	transcription reg	1,94E-13	ACTA2,ACTC1,CCL5,CDKN2A,CMA1,COMT,CXCL12,CXCR4,CYBA,EDN1,ELANE,EYA2,F11R,F2R,FABP3,FADS2,FOS,GP1BA,GSTM5,HAMP,HLA-A,ICAM1,ITGB1,LCN2,LIMK1,LTF,MMP9,MYH9,MYLK,NPPA,NPPB,P2RY1,PDGFRA,PGLYRP1,PGR,RAC1,RAMP1,RHOBTB1,RUNX1,SCARB1,SELP,SLC20A1,SLC6A4,SLPI,TBXAS1,TFF1,TNC,UCP1,VCL	740 (13)
FASN	enzyme	1,96E-13	ACTA2,ADIPOQ,ALOX5,CAV1,CD36,CIDEA,CXCL8,EDNRB,ERBB2,FGF1,FOXO1,GRK2,IL10,IL12B,IL1B,IL6,LPL,LRRK2,MET,MRAS,PCK1,PON1,PTGS2,RBP4,RELA,RETN,SFRP2,TBXA2R,TNF,UCP1	1007 (22)
ITGB3	transmembrane	1,96E-13	CD36,CD40,COL1A1,COL1A2,FN1,FOS,HAS2,IL10,IL1B,ITGA2B,ITGAV,ITGB3,KDR,LDLR,MMP1,MMP14,MMP2,MMP9,NPPB,PLAUR,PTGS2,RUNX1,SDHC,SELP,SERPINE1,SMAD3,TGFB1,TGFBR1,TGFBR2,TIMP1	869 (21)
C/EBP	group	2,15E-13	ADH1B,ADH1C,CYP1A1,DIO2,F8,FOXO1,GSTA1,HAMP,HGF,HIF1A,HNF1A,HSD11B1,IGF1,IL12A,IL12B,IL6,LCN2,LEP,MMP1,NOS2,PCK1,PTGES,PTGS2,SST,TGFB1	922 (23)
Ifn	group	2,18E-13	CD40,CD69,CFH,CYP4A11,EDN1,FAS,FOS,HGF,HIF1A,HLA-A,ICAM1,IFIH1,IGF1,IL10,IL10RA,IL12B,IL15,IL15RA,IL17A,IL1R1,IL23A,IL33,IL9,ITGA4,LCN2,MMP9,NOS2,OAS3,OASL,PECAM1,PML,SERPINE1,SOCS1,SPP1,TAP1,TFRC,TLR2,TLR5,TLR7,TP53,XDH	623 (16)
LMNA	other	2,24E-13	ABCC8,ACTA2,AFP,CAMK1D,CCL8,CCN2,CD28,CDH15,CERS6,COL1A1,COL3A1,DES,EDN1,EFNB3,ELN,FLT1,FN1,FUT4,GATA4,GCLC,GJA1,GLIS3,HAS3,HNF1B,ID3,IFIH1,IGF2R,JAZF1,JUN,KLF5,KLF7,LEP,LMNA,MAPKAP1,mir-335,MMP14,MMP3,MMP9,MYH7,MYL2,MYOD1,NOS3,NPC1,NPPA,NPR2,PKD1,PLD2,PMF1/PMF1-BGLAP,PPARA,PPARG,PTEN,SKAP2,SLC25A42,SMARCA2,SOX13,SPP1,STK35,SUN1,TGFB1,TH,TIMP2,TIMP3,TMEM183A,ZFP36	1102 (19)
MSTN	growth factor	2,36E-13	ACTA2,AKT1,CAV3,CKM,DES,FN1,HAMP,HIF1A,IGF1,IGF1R,IGF2,IGFBP3,IL6,LEP,MEF2A,MEF2C,MYH7,MYO5A,MYOD1,NFATC1,PPARGC1A,SLC2A1,SMAD3,TGFB1,TNC,VEGFA	991 (23)
SNCA	enzyme	2,37E-13	ADRA1A,AGT,ALK,BAX,BCL11B,BDNF,BGLAP,BRCA1,CACNA1D,CALCA,CCK,CCL2,CCN3,CDH13,CDH15,CHGB,CHL1,CIITA,CRHBP,CYBB,DLK1,DNM1L,EGF,EGFR,EP300,ERC2,GDNF,GLDC,GLO1,GSN,HES1,HES5,HLA-DQA1,HLA-DRA,HLA-DRB5,IFNG,IGF1,IL1B,IL6,ITPA,KCNIP4,KCNJ11,KCNN3,LRRC7,LRRK2,MEF2D,MEGF11,MMP1,MMP3,MMP9,NCF2,NOS2,NOTCH1,NPY5R,PBX1,PRKCG,PSMB9,PTK2B,PYGB,RBP4,RET,RGS14,SCN7A,SERPINB1,SERPINE1,SLC18A2,SLC2A3,SLC6A11,SORCS1,SV2C,TH,TNF,TP53,TRIB3	926 (19)
DNMT3B	enzyme	2,42E-13	ACTC1,ADORA1,ADRB1,AGTR1,ATM,ATP2A2,CACNA1C,CASQ2,CCL5,CD36,CDKN2A,CKM,CNR1,CYP1B1,EDNRA,ESR1,FOXP3,GATA4,GRK3,GUCY1A1,HDAC9,HLA-DQB1,HTR2A,IRF5,ITPR2,KDR,KIT,MFN2,MYH7,MYL2,MYL3,NOS2,PECAM1,PIK3C2B,PLEKHA6,PNPLA3,POU5F1,PRKCB,PTEN,PTN,RGS4,RYR2,SFRP2,SLC8A1,SLC8A2,TIMP3,TNNC1,TNNI3,TNNT2,TNNT3,TRPC3	631 (14)
CLEC4G	other	2,43E-13	ARG1,BMP2,CCN2,CDK6,EBF1,FGF1,FGF10,FLT3,FZD4,HBEGF,IFNG,IGF2,IL12A,IL17A,IL1B,IL23A,IL6,NOS2,NOTCH3,PDGFD,RSPO3,TGFB1,TGFB3,THBS4,TNF,VEGFA,VEGFC	329 (3)
CYP27B1	enzyme	2,52E-13	ALPL,ATP2B1,CCL11,CCL17,CCR3,CD14,CTLA4,CYP27B1,CYP3A4,CYP3A5,IFNG,IL10,IL15,IL18,IL4,IL6,SLC8A1,SPP1,TLR2,TRPV5,VDR	871 (19)
PKD1	ion channel	2,54E-13	ABCG2,ACSS1,ADCY6,APOM,ATP1A1,ATP1B1,AXL,BCAT1,BGLAP,BHMT2,CALCR,CCN2,CPN2,CTNNB1,EDIL3,EGFR,EMILIN1,FGF10,FGFR1,FGFR3,FOXO1,GATM,HBEGF,HDAC9,IFNLR1,IL1RL1,IL4I1,KLKB1,KNG1,LOX,NNMT,P2RX7,PAH,PCK1,PICALM,PITX2,PML,POU2F1,PRKCB,PSEN1,QPCT,SLC13A2,SLC2A2,SLC2A9,SLC4A1,SLC8A1,SOX6,SYNE1,TENM2,TGFBR1,TNFRSF11B,TNFSF11,TTR,UMOD,VWF	
CSF1R	kinase	2,72E-13	ADGRE1,ARG1,CCND1,FMOD,FOS,GAB3,HAMP,HMOX1,IDE,IL1A,IL22RA2,IL4R,IL6,JUN,LGR5,MMP9,MSR1,MYB,NOS2,NR1H3,PGR,STAT3,VCAM1	863 (20)
IRS2	enzyme	2,72E-13	CCND1,FOS,GCK,GCKR,HMGCR,HMOX1,IGFBP1,INS,IRS1,LEP,LPL,PCK1,PDX1,PPARG,PPARGC1A,PRL,RELA,SLC2A1,SLC2A2,SREBF1,SREBF2,TNF,VEGFA	1077 (24)
IL7	cytokine	2,76E-13	AHR,BAX,CCL2,CD2,CD247,CD69,CDK6,COL1A1,CSF2,CXCR4,DPP4,EBF1,FAS,FN1,FOXO1,FOXP3,GSR,ICOS,IFNG,IL13,IL17A,IL18R1,IL18RAP,IL1R1,IL2,IL22,IL24,IL2RA,IL4,IL5,IL6,IL7R,LTA,Ly6a (includes others),MAF,MLLT3,MMP9,PAX5,SELL,SELPLG,SLC2A1,SOCS1,SOCS3,TNF,TNFSF10,TNFSF11	712 (18)
NADPH oxidase	complex	2,84E-13	CCL2,CYBB,EDN1,EGFR,FOS,HMOX1,IL6,JUN,MMP12,MMP9,NOX1,NPHS1,NPHS2,PTGS2,SERPINE1,TBXA2R,VCAM1	784 (17)
NfkB-RelA	complex	2,84E-13	AGT,CCL11,CCL2,CCL5,CSF2,CXCL8,ICAM1,IL10,IL1B,IL2,IL6,NFKBIA,NOS2,PTGS2,SELE,TNF,VCAM1	
Tlr	group	3,05E-13	ARG1,C5AR2,CCL2,CCL5,CD40,CSF2,CXCL8,CXCR2,HBEGF,HLA-A,ICAM1,IFNG,IFNK,IFNL3,IL10,IL12A,IL12B,IL1B,IL2,IL33,IL6,JAG1,LCN2,mir-146,NFKBIA,NOS2,NOTCH1,NOTCH2,P2RX4,PAX5,PTGS2,RGS14,RGS20,SOCS1,SOCS3,TNF,TNFAIP3,TNFSF13,WNT5A,ZBTB46	571 (16)
PRKG1	kinase	3,11E-13	ACTA2,ALOX15,CCN2,CCND1,COL1A1,COL3A1,CTNNB1,FN1,FOS,GUCY1A1,GUCY1B1,IL17A,IL4,MPO,NOS2,PPARG,SERPINE1,TGFB1,THBS1,VCAM1	894 (20)
Stat3-Stat3	complex	3,11E-13	CRP,FGA,FGB,FGG,HIF1A,ICAM1,IL17A,IL22,IL23R,JUN,LBP,LTA,POMC,RORA,SERPINA3,SOCS3,SOD2,TNFSF11,VEGFA,WNT5A	776 (7)
NLRP3	other	3,20E-13	ACTA2,ATF1,ATM,BRCA1,CCL11,CCL5,CCR5,CD69,FN1,FOXP3,HMOX1,IFNG,IL10,IL13,IL17A,IL18,IL1B,IL22RA2,IL4,IL5,IL6,LIG1,MMP9,MSR1,NFKB2,OGG1,PARP1,PRIM2,STAT3,TGFB1,TNF,TP53,TYMS,XRCC1	590 (16)
SOCS1	other	3,34E-13	ARG1,BAX,BCL2A1,CCL2,CCND1,CD40,CD69,CIITA,CXCL8,FAS,FKBP5,FOS,HAMP,ICAM1,IFIH1,IFNG,IFNL3,IL12RB1,IL15,IL17A,IL1B,IL2RB,IL4,IL4R,IL5,IL6,INS,IRS1,IRS2,JAK2,JUN,MMP1,MMP12,NOS2,PTGS2,RELA,SELE,SOCS1,SOCS3,STAT3,STAT5A,TNF,TXN,VCAM1	615 (15)
NfkB1-RelA	complex	3,46E-13	CCL2,CCL5,CCND1,CRP,CSF2,CXCL8,ICAM1,IL12B,IL15,IL6,MMP1,MMP3,NOS2,PTGS2,SELE,TNF,TNFSF11,VCAM1	534 (4)
LTB4R	G-protein coupl	3,50E-13	ALOX5,CXCL8,EGF,FLT1,HAMP,IL10,IL13,IL4,IL5,LDLR,mir-146,MMP2,MMP9,NR1H3,PTGS2,PTPN1,SREBF1,TNF,VEGFA	929 (21)
GNAQ	enzyme	4,05E-13	ABCB1,ADM,AGTR1,ARG1,ATF3,ATP2A2,AVPR1A,BMP2,BMP4,CCN2,CCND1,CXCL12,CXCL8,EDN1,EDN2,F2RL1,FOS,GAS6,GJA4,GRB14,HAS2,IL1RN,IL2,IL6,INSIG1,MYH7,NFIA,NPPA,NPR3,NR4A3,OLR1,PGR,PLAT,PLAUR,PTGS2,SELENBP1,SERPINE1,SGK1,SLC8A1,TGFB2,VEGFA	976 (24)
SCD	enzyme	4,12E-13	ABCA1,ADRB3,ANGPTL4,ATF3,CD36,CPT1A,CPT1B,CXCL8,DIO2,IFNG,IL1B,IL6,LEP,LIPE,LPL,NOS2,PCK1,PPARD,PPARGC1A,PTPN1,SLC25A14,SLC2A1,SREBF1,TNF,UCP1,UCP2,UCP3	1060 (24)
FOSL1	transcription reg	4,13E-13	ADM,AXL,BDNF,CCL2,CCND1,CDKN2A,CXCL8,CYP2J2,ELN,FOS,GCLC,GCM1,HAMP,IL10,IL1B,IL2,IL4,IL6,JUN,LHCGR,MET,MMP1,MMP2,MMP3,MMP9,PLAUR,SERPINE1,SERPINE2,TF,THBD,TNF	882 (20)
EBF1	transcription reg	4,82E-13	ADCY3,ADIPOQ,CCL5,CHUK,COL1A1,CXCL12,EBF1,ESR1,FOXO1,GYS1,IKBKB,IL12RB1,IL6,INPPL1,INS,INSR,IRS1,KLRB1,KRAS,LIPE,LNPEP,Ly6a (includes others),MAPK1,MAPK8,PAX5,PFKP,PIK3R1,POSTN,PPARG,PPARGC1A,PRKAG2,PTPN1,PYGB,RPTOR,SFRP2,SLC2A4,SOCS1,SOCS3,SREBF1,TLR2,TLR4,TNFSF11,UCP3	991 (24)
CALR	transcription reg	5,32E-13	ATP2A2,CASQ2,COL1A1,COL1A2,COL3A1,FN1,GJA1,GJA5,ICAM1,IFNG,IL17A,INSR,LPL,MEF2C,MYL2,PTGS2,RYR2,SCNN1A,SCNN1G,SREBF1,TGFB1,TNF,VCL	1026 (24)
FASLG	cytokine	5,49E-13	CCL2,CSF2,CXCL8,FAS,FOS,IFNG,IL10,IL17A,IL1B,IL4,IL6,NFKB1,PTPN2,RELA,STAT4,TGFB1,TGFB2,TGFB3,TNF,TNFRSF11B,VEGFA	698 (16)

NLRP12	other	5,49E-13	AKT1,CXCL12,CXCL13,CXCL8,CXCR4,HLA-A,HLA-B,HLA-C,HLA-G,ICAM1,IFNG,IL1B,IL1RN,IL6,JUN,NOS2,NR3C1,PSMB8,TIRAP,TLR4,TNF	959 (20)
PELP1	other	5,49E-13	ADA,ADRB2,BMP2,CCND1,CES1,CTSH,CXCL8,CYP19A1,EGF,EGFR,F12,FBN2,FGFR3,FOS,FYN,GCA,IKBKE,IL13RA2,IL1A,IL1B,KYNU,LEP,MMP2,MMP9,MRAS,NCOR2,PI3,PPARG,PPARGC1A,PRKCQ,PRMT6,PTEN,PTGES,PTGS2,SAA1,SLPI,TCF7L2,TCN2,TFF1,TOX2,ZGPAT	969 (23)
NR5A1	ligand-depende	5,69E-13	AFP,AGRP,C4A/C4B,CYP11A1,CYP11B1,CYP11B2,CYP17A1,CYP19A1,CYP21A2,CYP7A1,FSHR,FUT4,GNRHR,GSTA1,HSD3B2,KIT,LEP,LEPR,LHCGR,NOS1,NR0B2,NR2F1,PNMT,POMC,POU5F1,SCARB1,SGCZ,TH,VNN1	1023 (12)
NR1I3	ligand-depende	5,92E-13	ABCB1,ABCC2,AHR,APOA1,CCN4,CYP1A2,CYP2A6 (includes others),CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,CYP7A1,DIO1,EPHX1,GSTM1,GSTM4,GSTM5,GSTP1,HNF4A,ICAM1,IGF2R,IL1R1,INSIG1,INSIG2,NR1I2,PCK1,POR,PTPN11,RARB,SLCO1B3,SLCO1C1,SREBF1,STEAP4,TNFRSF1A,UGT1A1,UGT1A3	997 (22)
C3AR1	G-protein coupl	6,37E-13	C3,C5,CCL5,CD28,CD40,CD46,COL1A1,COL1A2,CXCL8,IFNG,IGF1,IL10,IL17A,IL1B,IL23A,IL6,LTBP2,MEFV,SERPINE1,SREBF1,TGFB2,TGFBR1,TGFBR2,TNF	969 (20)
ICAM1	transmembrane	6,37E-13	ACTA2,CCL5,CD69,COL4A1,FOS,HES1,ICAM1,IFNG,IL12RB2,IL17A,IL1A,IL1B,IL2,IL2RA,IL6,ITGA4,MMP9,MPO,NOTCH1,SREBF1,TGFB1,TNF,VCAM1,VEGFA	629 (17)
Fcer1	complex	6,39E-13	ATP2A2,BCL2A1,CCL18,CCL2,CCL5,CSF2,CXCL8,FCGR2B,FOS,FYN,IFNG,IL10,IL13,IL16,IL1B,IL1RN,IL2,IL3,IL33,IL4,IL5,IL6,JUN,NFATC1,NFKB1,RELA,TNF,TNFSF4	817 (21)
IL12B	cytokine	6,91E-13	CCL5,CCR5,CEBPD,CXCL8,ICAM1,IFNG,IL10,IL12A,IL12B,IL12RB1,IL17A,IL1A,IL1B,IL22,IL23A,IL4,IL6,LTA,NOS2,SELPLG,SOCS1,SOCS3,STAT3,STAT4,TGFB1,TNF,VCAM1	608 (14)
NCOA3	transcription reg	7,70E-13	AHR,CCND1,CYP1A1,ERBB2,ERVFRD-1,FGFR2,GCM1,HES1,HES5,HMOX1,IGF1,IGF1R,IGFBP1,IGFBP3,IRS1,KDR,LDHA,MAPK1,MMP9,NCOA3,NFKBIA,PGR,PPARD,PPARG,PTGS2,RARB,SFTPB,SLC2A1,SREBF1,TFF1,TKT,XDH	1087 (21)
BRCA1	transcription reg	8,08E-13	ANGPT1,AR,ATM,BAX,BRCA1,BRCA2,CASR,CCL5,CCND1,COL18A1,CTNNB1,CYP19A1,CYP1A1,CYP1B1,CYP3A4,EGFR,EP300,ESR1,FAS,FKBP5,FOXO1,FOXO3,GDF15,HBB,HMOX1,HSD11B2,IGF1R,KIT,LAMA3,LPIN1,Ly6a (includes others),NOS3,NOTCH1,NQO1,NR3C1,PLTP,POU2F1,PTEN,RUVBL2,SERPINE2,SIRT1,SMAD3,STAT5A,STAT5B,TAP1,TERT,TFF1,TNF,TP53,VCAN,VEGFA	1121 (22)
MAP3K3	kinase	8,84E-13	BMP2,CXCL8,FOS,HAS2,IFNG,IL10,IL2,IL6,JUN,MYH7,POSTN,STEAP4,TGFB1,TGFB2,TGFB3,TGFBR3,TNFAIP3	801 (19)
CRP	other	1,01E-12	AGER,CCL2,CCL5,CD40,CXCL8,F8,IFNG,IL10,IL1RN,IL6,IL6R,ITGAM,LPL,NOS2,NOS3,PRKCA,PRKCB,PRKCG,PSMB9,SELL,SERPINE1,TNF,TNFSF10	1024 (19)
ILK	kinase	1,01E-12	CCND1,CHUK,CTNNB1,DHFR,ERBB2,FN1,HAMP,HSPA8,IKBKB,IL1B,IL6,ITGB1,KRAS,MAPK1,MAPK3,MMP2,MMP9,MYH7,NOS2,NOTCH1,SLC4A1,TGFB1,TNF	959 (19)
SST	other	1,01E-12	ABCB1,CCND1,FOS,GCG,GCGR,GHR,GHRH,GHRHR,GHSR,IFNG,IGF1,IGF1R,IL10,IL1B,IL6,INS,ITPR2,NR3C1,PRL,RXFP3,SST,SSTR3,TOX	934 (22)
PRKAA2	kinase	1,13E-12	ACOT7,ACTA2,BAX,CA2,CARTPT,CHGB,CIDEA,CXCL12,CYBB,CYP3A5,DDAH1,ELOVL2,FGFR2,FN1,FOXO3,IL6,INS,LDHA,LEP,Ly6a (includes others),MMP9,MT-CO1,MYLK,NCF2,NFKBIA,NOS1,NOX4,PDGFRA,PDYN,PPARG,PPARGC1A,PRDM16,SMAD3,SORL1,SREBF1,TNF,TP53,UCP1	1001 (22)
FST	other	1,22E-12	ADIPOQ,APOA2,ATP1A2,BMP7,CD36,CIDEA,CPS1,FABP3,FN1,FSHR,GNRH1,GNRHR,HP,IL6,INS,MMP2,PAX2,PLG,POU5F1,PPARG,PPARGC1A,PRDM16,SAA1,SERPINA1,UCP1	1044 (23)
TBX21	transcription reg	1,41E-12	CCR5,CDK6,CX3CR1,ICOS,IFNG,IL12RB1,IL12RB2,IL13,IL17A,IL18RAP,IL1RL1,IL2,IL22,IL23R,IL2RB,IL4,IL5,IL6R,IL6ST,IL7R,PTGER4,RUNX1,SELL,SELPLG,SPP1,STAT4,TGFBR2,TNFSF11,TP53	780 (21)
TRAF6	enzyme	1,41E-12	CCL17,CCL2,CRP,CSF2,CTNNB1,CXCL13,CXCL5,CXCL8,CYBB,EGFR,HIF1A,ICAM1,IL10,IL12B,IL15,IL1B,IL2,IL6,IRF5,NCF2,NFKB1,NOS2,RELA,SELE,SERPINA3,SOD2,TGFB1,TNF,TNFAIP3	567 (13)
F7	peptidase	1,57E-12	AR,CCN2,CCND1,CXCL8,FGF5,FOS,HBEGF,ICAM1,IL1B,IL6,JAG1,KLF5,MMP14,MMP7,PLAUR,PTGER2,PTGS2,RELA,TNF,VCAM1,VEGFA,ZFP36	766 (18)
Esrra	transcription reg	1,58E-12	ACAT1,ACE2,AGT,APOA4,ATP1A1,BGLAP,BSND,COX8A,CPT1A,CPT2,EPAS1,ERBB2,FABP1,FABP2,GCGR,GYS1,HGF,HSD3B1,IFNG,IL1A,IL2,IL6,KCNQ1,LEPR,PCK1,PDK4,PPARGC1A,PTGS2,RARA,REN,SCNN1A,SDHB,SLC2A1,SPP1,TFF1,THRA,TNF	962 (22)
ARRB2	other	1,59E-12	ADRA2A,ADRB2,ATP2A2,CCR2,CTNNB1,GRK5,HIF1A,IL10,IL13,IL1B,IL4,IL6,MMP2,NFKBIZ,OPRM1,PTGS2,SERPINE1,TGFB1,TNF,VEGFA	828 (17)
PLAT	peptidase	1,59E-12	AGER,BDNF,CCND1,FN1,FOS,IFNG,IL1B,IL6,JUN,MMP1,MMP2,MMP3,MMP9,NOS2,PLAT,PLG,SERPINE1,TGFB1,TLR4,TNF	951 (18)
MYB	transcription reg	1,67E-12	ADM,ANPEP,ATP2B1,BAX,BRCA1,C3,CCND1,CD14,CD34,CDKN2B,COL1A2,COL4A1,CXCL12,CXCR4,EGFR,ELANE,FN1,GSTM1,HSPA8,ICAM1,IGF1,IGF1R,IGF2,IGFBP3,IKBKE,IL13,IL18R1,IL1A,IL4,IL5,IL7R,ITGA2B,JUN,KDR,KIT,LCN2,MMP1,MMP3,MYB,NOD2,NOTCH1,PPP3CA,PTGS2,PTPN22,SDC4,SHH,SPP1,TRHR	1025 (21)
IFN Beta	group	1,75E-12	ATF3,CCL5,CD247,CD40,CD69,CXCL8,CYP1A2,CYP2C9,CYP2E1,CYP3A4,DPP4,FN1,HLA-A,HLA-B,HLA-G,IFIH1,IFNG,IL10,IL12A,IL15,IL15RA,IL17A,IL1B,IL1RN,IL24,IL6,IL9,INSIG1,MMP9,MT-CO2,MT-ND2,NOS2,OAS3,OASL,PRKCA,SOCS1,TGFB1,TGFBR1,TNF,TNFSF10,TP53,TRAF3IP2,TSLP,TXNRD1	688 (15)
GPX1	enzyme	1,88E-12	ACTA2,ADGRE1,AGER,CAT,CCN2,CD14,CYBB,FAS,GLRX,GPX3,GPX4,ICAM1,IL6,MMP9,RELA,SOD1,SOD2,TNF,TNFRSF1A,TNFSF10,TXN,TXN2,VCAM1	959 (17)
IL32	cytokine	2,02E-12	BAX,CCL2,CD36,CTNNB1,CXCL8,FAS,ICAM1,IL10,IL12B,IL1A,IL1B,IL23A,IL6,ITGAM,ITGB2,MMP2,MMP3,MMP9,NFATC1,NOS2,PTGS2,THBD,TNF,TNFRSF11B,TNFSF11,TP53	711 (14)
MAPKAPK2	kinase	2,02E-12	ARG1,CCL11,CCL2,CEBPD,CXCL8,ICAM1,IL10,IL13,IL18,IL1B,IL23A,IL4,IL5,IL6,LTA,MMP2,MMP9,MSR1,NFKBIA,NOS2,PLAT,STAT5A,TNF,TP53,TSC22D1,VCAM1	804 (15)
AKT2	kinase	2,10E-12	ACTA2,CIDEA,CTNNB1,ESR1,FOXP3,GCLC,GCLM,GSR,GSS,IFNG,IGF1R,IGF2,IL13,ITGB1,LEP,MMP9,NFKB2,NQO1,PPARG,PRL,PTEN,RAC1,TGFB1,TIMP1,TNF	980 (20)
NOG	growth factor	2,10E-12	BGLAP,BMP2,BMP4,BMP7,CCN2,CD2,FAS,HAS2,ID3,IL2,KDR,MITF,MMP3,NCAM1,POMC,PTGS2,SHH,SMAD1,SMAD5,SPP1,TNFRSF1A,TNFSF11,VCAN,VEGFA,WNT5A	890 (20)
SATB1	transcription reg	2,13E-12	ADCY3,BCL2A1,CCND1,CD40,CD69,CSF2,CYBB,ENOSF1,EPAS1,F5,GDF15,GLRX,HBB,HBG1,HSPA8,ID3,IKZF1,IL10RA,IL13,IL16,IL18RAP,IL2,IL2RA,IL3,IL4,IL4R,IL5,IL7R,ILF3,ITGB1,LAX1,MAF,MEF2A,NCOR1,PGR,PRKCB,PTGS2,RUNX1,SELL,SGK1,SMAD3,SP4,SS18L1,TNF,TSLP,UHRF1,VTA1,WARS	743 (15)
PTPN11	phosphatase	2,17E-12	ATP2A2,BAX,CCND1,CD14,CXCL8,CYBB,ELANE,FOS,GATA2,GP1BA,IFNG,IL6,JUN,KDR,KIT,LTF,MEF2C,MMP12,MPO,NCF2,NF1,NFATC1,PDGFRB,PLAUR,PTPN11,SFTPB,SOCS3,TNF,TP53,TP73,VIP	856 (22)
TEAD4	transcription reg	2,17E-12	ADM,BMP4,CALD1,CCN2,CCND1,CDK6,CKM,COL3A1,DES,EDN1,EDNRA,FGFR1,FGFR2,FLT1,GPR37,HIF1A,JUN,MYH7,NFKBIZ,NOTCH2,POSTN,PTPRO,RHOBTB1,SLC2A3,SLC2A4,SMAD1,THBS1,TNNC1,TNNT2,TPM1,VEGFA	498 (7)
NFATC3	transcription reg	2,19E-12	ACTA2,ATF3,BMP2,CD69,COL1A1,EDN1,FOS,GJA1,IFNG,IL10,IL12B,IL13,IL2,IL2RA,IL4,IL5,IL6,JUN,MMP3,MYH7,NFATC1,NPPA,PPARG,PPP3R1,PTGS2,SFTPB,TNF,TNFSF11,TNNI3	908 (23)
TLR6	transmembrane	2,20E-12	ATF3,CCL5,CSF2,CXCL8,HAMP,IFNG,IL12B,IL13,IL15,IL17A,IL1B,IL23A,IL4,IL6,NR1H4,TNF	670 (20)
NCF1	enzyme	2,41E-12	ACTA2,ALOX5AP,CCL5,CD14,EDN1,FN1,HAS2,HMOX1,ICAM1,IFNG,IGF1,IL12RB2,IL17A,IL2,SERPINE1,TGFB1,THBD,TNF	943 (17)
MAP3K8	kinase	2,59E-12	APOE,ARG1,CCR2,CCR5,CDK5R1,CEBPD,CIITA,COBLL1,COLEC12,CSF2,CXCL8,FOS,GCA,GPR160,HP,IFNG,IGF1R,IL10,IL12A,IL12B,IL18,IL1A,IL1B,IL2,IL23A,IL4,IL4I1,IL5,IL6,JUN,MMP3,MMP9,P2RY1,PGR,PLAT,PTGER2,PTGER4,PTGS2,RCSD1,SOCS3,SPATS2L,STAT4,TIMELESS,TNF,TXNIP	690 (18)
PTGER4	G-protein coupl	2,59E-12	APOA5,APOC2,BRCA1,CCL2,CD40,CD69,CDK6,CXCL8,CXCR4,CYBB,CYP19A1,EDN1,FOXP3,GDNF,GLIS3,HAMP,HAS2,HGF,ICAM1,IFIH1,IGF2BP2,IL10,IL12B,IL13RA2,IL18,IL1B,IL23A,IL4I1,IL6,let-7,MMP2,MMP9,NCF2,NOS2,OLR1,PGR,PTGER3,PTGS2,RNF213,SLC13A3,SPP1,ST8SIA4,TLR8,TNF,TNFSF10	861 (17)
miR-146a-5p (a	mature microRN	2,92E-12	BRCA1,CAT,CCL2,CCL8,CCR3,CD40,CFH,CHUK,COL13A1,CRP,CXCL8,CXCR4,EGFR,IL10,IL12RB2,IL1F10,IL1R1,IL1RAP,IL2,IL6,IRAK1,IRF5,LBP,LTF,NFKBIA,NOS2,PDGFRA,PGLYRP1,RELA,TIMELESS,TLR4,TLR9,TNF,UHRF1	879 (16)
ATF1	transcription reg	2,99E-12	ATP1A1,CALCA,CCK,CIITA,CYP11B2,FOS,FUT7,HLA-B,HLA-G,HMOX1,IFNG,JUN,NOS2,NOX1,PCSK1,PTGS2,REN,SOD2,SST,TGFBR2,THBS1,UCP3	591 (10)
MEF2D	transcription reg	2,99E-12	BDNF,CCN2,CCND1,CKM,COL1A2,COL3A1,FN1,FOS,HDAC9,IKZF1,IL10,IL2,JUN,MEF2A,MT-ND6,MYH7,MYOD1,NPPA,PPARA,PPARGC1A,PTEN,SLC2A4,TGFB1,TGFB2,TGFB3,TNNC1,ZFP36	949 (19)
ABCG1	transporter	3,36E-12	CCR5,CXCL13,IFNG,IL10,IL10RA,IL10RB,IL12A,IL12B,IL12RB2,IL13,IL17A,IL1B,IL4,IL5,IL5RA,IL6,SLC2A1,TGFB1,TLR4,TNF	898 (20)
VitaminD3-VDR	complex	3,42E-12	BGLAP,CASR,CCL5,CD14,COL13A1,CSF2,CYP24A1,CYP27B1,FOXO1,IFNG,IGFBP1,IGFBP3,IL12A,IL1RL1,IL2,LRP5,PPARD,SERPINB1,SPP1,TGFB2,THBD,TNFSF11,TRPV5	
CDK9	kinase	3,56E-12	BGLAP,CAD,CCL5,COL1A1,CXCL8,CXCR4,FGG,FOS,G6PD,GATA2,HLA-DQA1,HLA-DRA,IL6,MAGI1,MMP9,NFKBIA,PDK4,PPARG,PPARGC1A,RUNX1,SELE,STC2,TERT,TNFAIP3,WNT5A	1000 (20)

NFKBIB	transcription reg	3,56E-12	BCL2A1,CASR,CCL2,CCL5,CD40,CXCL8,FGF10,GNAI2,ICAM1,IFNG,IGF1R,IL1B,IL2,IL6,MMP9,NFKBIA,NOS2,NOS3,RYR1,SELE,TNF,TNFSF10,TP73,VCAM1,VEGFA	648 (16)
SQSTM1	transcription reg	3,60E-12	ATM,CYP2A6 (includes others),EDN1,EGLN3,GCLC,GSTM5,HBEGF,HMOX1,IL12B,IL15,IL15RA,IL18,IL1B,IL6,JUN,LEP,LTA,NFKBIA,NOS2,NQO1,PLAT,RELA,TNF,TSC22D1	803 (17)
HAND2	transcription reg	4,05E-12	ACE2,ACTC1,ACTN2,ATP2A2,CASQ2,CCL11,CCL2,COL1A1,COL1A2,COL3A1,CXCR4,DBH,DES,GJA1,GJA5,HSPB7,IL6,ITGB1BP2,NPPA,NPPB,PTGS1,PTGS2,S100A4,SHH,TNNC1,TNNT2,TPM1,TTN	
WNT1	cytokine	4,17E-12	ACTA2,APCDD1,BMP4,CCN4,CCND1,CDKN2A,COL3A1,CTNNB1,DHFR,EDN1,EFNB1,FN1,FOS,HES1,HES5,HNF1A,HNF4A,IGF1,IGF1R,IGF2,JUN,KIT,KLF5,LMX1A,MMP3,MRAS,NOTCH3,PITX2,PPARG,PTGS2,RARB,RARG,SERPINE1,SERPINE2,SIM1,SPP1,STAT5A,TERC,TGFBR1,TP53,VEGFC	995 (18)
CORT	other	4,57E-12	BDNF,CCL5,CCR2,CCR3,CCR5,IFNG,IL10,IL12A,IL15,IL17A,IL18,IL1A,IL1B,IL6,MIF,POMC,PRL,SLC20A1,TNF	278 (5)
PRDM1	transcription reg	4,84E-12	ADA,ADGRG1,AFP,ALPL,ANGPTL4,APOM,AQP3,BCL2A1,CDK6,CFH,CHI3L1,CIITA,CRP,CXCR4,ERAP1,ESR1,F5,F9,FGA,FGB,FGG,FOS,GALNT2,HLA-DQA1,HLA-DRA,ID3,IFNG,IGF1R,IL10,IL17A,IL18RAP,IL1A,IL1B,IL2,IL24,IL6,IL7R,ITGA4,JAG1,NFATC1,NLRP3,NOS2,PAX5,PCSK6,PROX1,PSMB8,SELL,SERPINA3,SLC2A5,SLC6A12,SLCO2B1,SMAD3,TNF,TNFSF10,TRIB1,TRIM65,TRPM8,TTR	909 (20)
PIN1	enzyme	5,11E-12	BAX,BCL2A1,CCND1,CDK5R1,COL3A1,CTNNB1,CXCL8,ESR1,FN1,HES1,IFNL3,IL1B,IL6,MAPK8,MMP2,MMP3,MMP9,NCOR2,NOS2,NOTCH3,PGR,PML,PPARD,PPARGC1A,PTGS2,TGFB1,TIMP1,TIMP4,TNF	962 (21)
EDNRA	transmembrane	5,15E-12	COL1A1,COL3A1,ECE1,FOS,ICAM1,ITGAM,MMP2,PTGS1,PTGS2,SELL,TGFB1,TIMP1,TIMP2	963 (19)
TNFRSF25	transmembrane	5,15E-12	CCL2,CXCL8,IFNG,IL10,IL13,IL17A,IL2,IL5,IL6,IL9,SELE,STAT3,TNF	670 (19)
LYN	kinase	5,24E-12	ATP2A2,BCL2A1,BDNF,C5,CCL5,CD40,CDKN2A,CSF2,FCGR2B,FYN,IFNG,IL13,IL17A,IL1A,IL1B,IL4,IL5RA,IL6,KLRB1,MITF,NFKB1,NFKB2,NFKBIA,NFKBIZ,SOCS1,SOCS3,STAT3,STAT5A,STAT5B,TGFB3,TNF,TRAF1	640 (17)
BTK	kinase	5,31E-12	BCL2A1,CD2,CD40,CD69,CDK6,CDKN2A,CXCL8,CXCR4,ELANE,FOXO1,HMOX1,ICOS,IFNG,IL10,IL10RA,IL12B,IL13,IL18,IL1A,IL1B,IL21R,IL2RA,IL4I1,IL5,IL6,ITGAV,ITGB3,JUN,MPO,NFATC1,NFKB2,OAS3,RELA,SELP,SLC2A3,TLR9,TNF,TP53	734 (15)
HDAC6	transcription reg	5,57E-12	AR,BAX,COL1A1,CYP1A1,CYP1B1,ESR1,HIF1A,IFNG,IGF1,IL10,IL2,IL6,JUN,LTBP2,NOS2,NR3C1,SERPINE1,SRSF2,TGFB1,TGFBR1,TNF,TPH2	978 (20)
CLEC7A	transmembrane	5,78E-12	CCL17,CCL2,IL10,IL12A,IL12B,IL13,IL17A,IL1B,IL2,IL23A,IL33,IL5,IL6,PTGS2,SOCS1,TLR4,TNF,TNFSF4	675 (17)
FGF10	growth factor	5,92E-12	AGER,BMP4,BMPR1A,CTSH,CYP19A1,CYP1B1,FGFR2,FOXF1,HSD3B1,IL10RB,LDLR,LIPE,LRPAP1,LSS,MMP14,MMP9,MYH7,PDX1,PTEN,PTGS2,SHH,TGFB1,TIMP3,TSPAN8,VNN1	750 (18)
IRF2	transcription reg	6,07E-12	ANG,ARG1,CCND1,CD14,CES1,CFB,CFTR,CIITA,CXCL5,ERAP1,FGA,FGB,FGG,IFNG,IGFBP1,IL12A,IL12B,IL12RB2,IL1B,IL6,IL6ST,LBP,LCN2,MMP7,MYH9,NAMPT,NOS2,PSMB8,PSMB9,PTGS2,SLC7A1,SLCO2B1,SOCS1,TAP1,TLR4,TLR5,TNFSF10,TPM1,TXNRD1,VCAM1	677 (17)
TNFAIP3	enzyme	6,09E-12	BAX,CHUK,CSF2,CXCL8,FAS,ICAM1,IL10,IL1A,IL1B,IL2,IL23A,IL6,MMP9,NFKBIA,NLRP3,NOS2,NPPA,SELE,SOCS3,TGFB1,TNF,TNFAIP3,VCAM1	788 (15)
ARNTL	transcription reg	6,19E-12	AGRP,ARNTL,CARTPT,CLOCK,CRY1,DBP,EGLN3,GCK,GNRH1,GSR,HIF1A,HMGCS2,HMOX1,IL1B,MLXIPL,NPY,NQO1,PER1,PER2,PPARA,PRL,RYR2,SREBF1,TP53	673 (16)
FHL2	transcription reg	6,19E-12	ACTA2,ADGRE1,ARG1,BGLAP,CCND1,CXCL12,CXCL8,CYP11A1,IFNG,IL10,IL12B,IL13,IL17A,IL23A,IL4,IL5,MITF,MPO,NOS2,NPPA,PDGFRB,SPP1,TNF,WNT5A	753 (20)
TERT	enzyme	6,42E-12	AR,ATF3,BAX,CALD1,CAV1,CCN2,CCND1,CDKN2A,CXCL8,EGFR,F2R,FUT4,GSN,HLA-B,HMGB1,HTRA1,ICAM1,IL1B,IL6,ITGAV,KDM5C,LIPG,MMP1,MMP14,MMP2,MMP3,MMP9,MTHFD1L,NFKBIA,NOS3,PLTP,POU5F1,PTGS1,PTGS2,SMAD3,SOD2,SPP1,TBX3,TERC,TERT,TOX2,TP53	926 (18)
CYP7A1	enzyme	6,57E-12	ABCA1,ABCG5,ABCG8,CYP7A1,FDFT1,HMGCR,IL1B,IL6,LDLR,MTTP,NOS2,PTGS2,SREBF1,SREBF2,TIMP1,TNF	650 (20)
SEMA7A	transmembrane	6,57E-12	BAX,CCN2,CCN3,CCN4,COL1A1,COL1A2,COL3A1,ELN,FN1,IL13RA2,IL18,IL4R,SMAD6,TGFB1,TIMP1,TNF	731 (12)
MST1	growth factor	6,61E-12	CCN2,CCND1,FAS,FOS,FOXP3,IL12B,IL15,IL18,IL1RN,IL6,MSR1,NR0B2,PAX2,PCK1,PTGS2,SPP1,TNF	979 (21)
MIR17HG	other	6,63E-12	ACTA2,ALPL,APCDD1,ATM,BMP4,BMPR2,CCND1,CELSR1,CPE,DAB2IP,ECE1,FBN2,FZD4,HIF1A,HNF1B,HSPG2,IFNG,IL6ST,IL7R,JAG1,KIT,LRP1,LRP6,NCOR2,NOTCH2,PDGFRA,PITX2,PKD1,PKD2,PTEN,RGS5,SMAD6,SORT1,TBX3,TGFBR2,TNFAIP3,TNKS,WNT5A,ZNRF3	
CASP1	peptidase	6,88E-12	ACTA2,CCL11,COL1A1,CSF2,IFNG,IL18,IL1A,IL1B,IL22RA2,IL4,IL5,IL6,KDR,NOS2,PPARA,PPARG,PTGS2,SREBF1,SREBF2,TNF	755 (18)
ERBB4	kinase	7,53E-12	ACTA2,BDNF,BRCA1,CCL2,CCND1,COL3A1,CTNNB1,CXCL12,EFNB2,EGFR,FBLN2,GHR,GJA1,HBA1/HBA2,HBEGF,HIF1A,HMOX1,IGF2,JUN,PGR,PTGIS,PTGS2,SERPINA3,SERPINE2,SLC2A1,SLPI,SOCS3,TBXAS1,THBS1,TIMP3,TNC,TP53	1056 (21)
NFYA	transcription reg	7,53E-12	ABCB1,CAT,CBS/CBSL,CDC42,CHEK2,COL1A2,CYP1A1,ELANE,EPHX1,F12,F8,FGFR2,GUCY1B1,HLA-DQB1,HLA-DRA,HSD17B7,ICAM1,IGF1,JUN,LMAN1,LPIN1,NOTCH1,NPR1,OGG1,PADI4,PCK1,PDGFRB,POU2F1,RGS4,TGFBR2,TXNIP,VWF	890 (13)
HDAC5	transcription reg	7,71E-12	ACTA2,CKM,CPT1A,CPT1B,CPT2,CTNNB1,DRP2,ETNPPL,FGF21,HES1,HLA-DRA,HMGCR,HMGCS2,IGFBP1,JUN,LPL,MEF2C,MYH7,NOS2,NPPA,PPARA,PPARG,PPARGC1A,PRKN,PTEN,SLC2A4,SLC8A1,TNF,TNFRSF1A	940 (23)
PTGES	enzyme	8,68E-12	CCN2,CXCL14,CYBA,CYBB,ERBB3,FLT1,GATA4,IFNG,IL17A,IL1B,IL6,MMP9,MYH7,NOS1,NOS2,NOS3,NOX1,NOX4,NPPA,PPARG,PTGES,PTGS2,SDS,SERPINE1,TNF,TRAF1	1027 (23)
PLAUR	transmembrane	8,84E-12	ACTA2,ANG,CCL2,CCL5,CCND1,CYBB,ITGAM,ITGAV,ITGB1,ITGB3,JUN,KDR,MMP2,MMP3,MMP9,MT-CO1,PLAUR,PLG,RAC1,SOCS1,TNF	820 (20)
E2F1	transcription reg	9,57E-12	ABCB1,ABCG2,ADIPOQ,ADIPOR2,AKT1,ALPL,AR,ATM,AURKA,BAX,BGLAP,BMP4,BRCA1,CA2,CALD1,CAV1,CCND1,CCT2,CDKN2A,CHEK2,CTNNB1,CYP27B1,DCC,DDAH2,DHFR,DLEU2,EYA2,FAS,FGFR1,FGFR2,FGFR3,FLT1,FOS,FOXO1,FOXO3,H19,HES1,HMGA1,HMGB1,HSD11B2,HSPA8,HSPD1,ICAM1,ID3,IFNG,IGF1,IGF2,IRS1,IRS2,KCNJ11,KDR,KIT,KRAS,LEP,let-7,LTA4H,MAF,MEIS1,mir-143,mir-27,MMP1,MMP3,MTHFD1,MYB,MYH7,NCOA3,NFKBIA,PDK4,PDX1,PIK3R1,PPARG,PPARGC1A,PRIM2,PSMB9,SELE,SERPINE1,SOD2,SRSF2,TAP1,TERT,TGFB1,THBS1,TNF,TOPBP1,TP53,TP73,TXNRD1,TYMS,UCK2,UCP1,UCP2,UHRF1,VCAM1,VEGFA,WWOX,XRCC1,ZFP36	838 (17)
CR1L	other	9,80E-12	C3,CCN2,COL18A1,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,FBN1,IFNG,IL10,IL1B,MGP,PTGER4,SERPINE1,TGFB1,TNC,TNF,TNFRSF1A	828 (17)
LRP5	transmembrane	9,80E-12	ADRB2,AHR,GCK,HNF1A,HNF1B,HNF4A,IFNG,IGF1R,IGF2,IL10,IL17A,IL1B,IL22,IL6,INSR,IRS1,IRS2,SLC2A2,TNF	1053 (25)
ZBTB20	transcription reg	1,04E-11	AFP,AKT1,CYP1A2,CYP2C8,CYP3A5,GAS6,GCGR,GCK,GHR,GSTM4,GSTM5,IGF1,IGFBP1,IL6,IRS1,LEP,LEPR,NFKBIA,NR3C1,PCK1,PDK4,PPARGC1A,SOCS3,TNF	746 (12)
APLN	other	1,06E-11	ACE2,ADIPOQ,BAX,CAT,CCN2,CD34,FOS,GATA2,GYPA,HBA1/HBA2,HBG1,IFNG,IL2,IL4,IRS1,ITGA2B,KDR,MYB,MYH7,NKX2-5,NPPA,PECAM1,SOD1	930 (21)
ITGB2	transmembrane	1,06E-11	ACTA2,BAX,BCL2A1,BDKRB1,CD69,CSF2,FN1,HES1,IFNG,IL12A,IL12B,IL4,IL6,ITGA4,MMP9,PTGS2,RAC1,RAC2,TGFB1,TGFBR2,TNF,VCAM1,VEGFA	694 (19)
IRF8	transcription reg	1,08E-11	ACVRL1,ADGRE1,ATF3,BAX,CCL5,CCR2,CD14,CD40,CFB,CIITA,CYBB,FAS,FOS,ICAM1,ID3,IFNG,IFNK,IL12A,IL12B,IL15,IL17RA,IL18,IL1B,IL4,IL5,IL6,IRF5,ITGAM,LSP1,MAF,MMP9,MSR1,NF1,NFATC1,NOS2,PML,TERT,TLR4,TLR9,TNF,TP53,ZFHX3	640 (14)
KIT	transmembrane	1,12E-11	CCL2,CCR2,CDKN2B,CMA1,CSF2,CXCR4,HMGB1,HMOX1,ICAM1,IFNG,IL10,IL12RB1,IL13,IL15,IL15RA,IL17A,IL17RA,IL2RA,IL4,IL4R,IL5,IL6,ITGA2B,ITGAM,ITGB2,KIT,MITF,NF1,PRKCQ,SOCS1,SOCS3,SPP1,SPTA1,STAT3,TNF	721 (19)
VHL	transcription reg	1,23E-11	ADGRG1,AKT1,CAV1,CCN2,CCND1,CPT2,CXCL12,CXCR4,DUOX2,EGFR,EGLN3,EPAS1,EPO,FN1,GLCE,GLO1,GPX1,HIF1A,HMOX1,HNF1A,INSIG2,LMNA,LOX,LOXL2,MAF,MIF,MMP14,NOX4,RUNX1,SLC2A1,SOD2,TFRC,TH,TNF,TNFSF10,TP53,TRAF1,TYMS,VCAM1,VEGFA,VEGFC	838 (18)
ARRB1	other	1,31E-11	ABCG2,ADRB2,CXCL8,EGFR,IL17A,IL22,IL6,IRS2,LPL,MMP3,NOS2,PTGS2,SCARB1,SERPINE1,SPP1,TNF,TNFSF11,VCAM1	901 (22)
mir-17	microRNA	1,32E-11	ABCA1,AKT1,AR,ATM,CCN2,CCND1,CXCL8,EP300,ESR1,FAS,FGF9,FN1,GCLC,IL6,MAPK8,MMP1,MYLIP,NCOA3,PKD1,PKD2,POU5F1,PTEN,RUNX1,SMAD2,STAT3,TGFBR1,THBS1,TNFAIP3,TXNIP,UCP1	1015 (21)
SNAI1	transcription reg	1,34E-11	ADD2,ADIPOQ,AXL,BGLAP,BMP4,CCL2,CCN2,CCND1,CD46,CDC42,CDH4,COL1A1,COL1A2,CXADR,CXCL8,CYP19A1,ERCC1,FN1,FOS,GDF15,GSN,HNF4A,ITGA2,ITGB1,MLXIPL,MMP14,MMP9,MYO5A,PFKP,POU5F1,PTEN,PTGS2,SERPINE1,SMAD3,SMAD6,TF,TGFB1,TGFBR1,TGFBR2,TGFBR3,THBD,TMOD4,TPM1,VDR	1112 (20)
ELANE	peptidase	1,36E-11	CD14,CSF2,CXCL5,CXCL8,EGFR,ELANE,ELN,F2RL1,FOS,HMOX1,IL1B,IL6,MMP2,MMP7,MMP9,SERPINA1,SIRT1,SLPI,TLR4,TNF	796 (17)
SAA	group	1,36E-11	ARG1,CCL17,CCL2,CXCL8,ICAM1,IL10,IL12B,IL17A,IL1B,IL1RN,IL23A,IL33,IL6,MMP1,NOS2,PLIN1,PTGS2,RELA,TLR2,VCAM1	660 (14)
miR-21-5p (and	mature microRN	1,37E-11	ACTA2,BMPR2,C8orf44-SGK3/SGK3,CD69,CDK6,FAS,IFNG,IL6R,IRAK1,JAG1,KDR,MMP2,MTAP,PECAM1,PIK3R1,PTEN,SLC12A1,SOD3,STAT3,TCF21,TGFB2,TGFBR2,TIMP3,TNF,TNFRSF11B,TPM1	875 (19)

CCNC	other	1,62E-11	ADIPOQ,CD36,CIDEA,CPT2,FAS,FGF21,LIPE,LPL,NOTCH1,PLIN1,PPARG,PPARGC1A,SLC2A4,SREBF1,TYMS,UCP1,VCAM1	498 (9)
CX3CL1	cytokine	1,62E-11	EGFR,HIF1A,HMOX1,ICAM1,IL1A,IL1B,IL6,MMP2,MMP9,MSR1,PDX1,PPARG,SELP,SLC2A2,TGFB1,TIMP1,TNF	846 (14)
LIPG	enzyme	1,67E-11	ABCA1,CCL2,CD36,IL10,IL12A,IL1B,IL6,LCAT,LDLR,LIPC,LPL,MSR1,PLTP,TNF,VEGFA	999 (22)
GATA6	transcription reg	1,78E-11	ABCB1,ACTA2,ACTC1,AFP,ALOX15,ARG1,BMP4,BMPR1A,BMPR2,C4A/C4B,CAV1,COL4A1,CXCL13,CYP11A1,CYP17A1,CYP19A1,DLK1,DPP4,EDN1,EPO,GATA4,HBA1/HBA2,HES1,HNF1B,HNF4A,HSD3B2,KDM5B,LGR5,LHCGR,MEF2C,MYH7,MYH9,MYLK,NFIA,NOS3,NPPA,PAX2,PDGFRA,PECAM1,POU5F1,PTGES,RARB,SCGB1A1,SHH,SLC9A3,SLPI,SOX17,TGFB1,TGFB2,TNFSF10,TNNC1	996 (18)
UCN	other	1,79E-11	CCL5,CYP11A1,CYP17A1,FOS,GNAS,ICAM1,IFNG,IL1B,IL6,LEP,MAPK3,NPY,TLR4,TNF,UCP1,UCP3	814 (20)
CITED2	transcription reg	1,80E-11	ADM,ANGPTL4,ARG1,CCL2,CDKN2A,CDKN2B,CXCL8,EGLN3,FGF5,HIF1A,IL12B,IL1A,IL1B,IL2,IL6,LPL,MMP1,NOS2,PITX2,POU5F1,TNFAIP3,VEGFA	779 (18)
PRKACA	kinase	1,80E-11	ADIPOQ,BDNF,CCK,CCND1,CYP17A1,CYP19A1,DBH,DIO2,FSHR,GNRHR,HSPA1A/HSPA1B,IGF1,IL2,IL4,IL5,LEP,PCK1,PRL,RARB,SOCS3,UCP1,VCAM1	1068 (21)
OSCAR	other	2,02E-11	CCR2,CD40,CX3CR1,CXCL5,CXCL8,ICAM1,IL12B,IL1A,IL1R1,IL1RN,IL2,ITGAM,JAK2,MMP7,TLR7,TLR8,TNF,TNFSF10,TNFSF14	868 (17)
Hsp90	group	2,06E-11	ABCC1,AHR,AKT1,AR,ATR,AXL,CD2,CD28,CD69,CIITA,CLU,CYP19A1,EGFR,EPAS1,ERBB2,ERBB3,ESR1,FN1,GJA1,GRK6,HIF1A,HSPA1A/HSPA1B,IFNG,IL6,KCNJ11,KIR2DS4 (includes others),NCR3,NOS1,SLC6A4,TNF,TP53	1141 (23)
TAZ	enzyme	2,15E-11	ADRB2,AXL,BDNF,CAV1,CAV2,CCL2,CCN2,CDC42,COL1A1,CYP1B1,DICER1,EDN1,F2RL1,FLT1,FN1,HIF1A,HMOX1,IRS1,KIT,LDHA,LDLR,LOX,LOXL2,LRP2,MET,NOS2,PTGS2,RGS4,SERPINB7,SERPINE1,SLC2A1,TFPI2,TGFB1,VEGFA	809 (17)
NKX2-1	transcription reg	2,16E-11	ADCYAP1,AGER,AGT,AGTR2,AQP1,BCL2A1,BMP4,C5,CA4,CCKAR,CD14,CDKN2B,CLU,CTNNB1,DIO2,DPP4,EDIL3,FSHR,GNRH1,HLA-A,KISS1,LCN2,LRP2,LSP1,MMP2,MYB,MYBPH,PDGFRA,PGLYRP1,POLG,PON1,RAC2,RET,ROS1,SCGB1A1,SCN7A,SCNN1G,SERPINE1,SFTPB,SHH,SLCO1B3,SOX17,SREBF2,TGFB1,TGFB2,THBS1,TOX,TSHR,VEGFA	260 (3)
PTK2	kinase	2,51E-11	ACTA2,CCND1,COL1A1,COL1A2,FN1,FOS,GATA4,IL6,IRS1,LDLR,MMP2,MMP7,MMP9,MYH7,NPPA,PDGFRB,PTK2B,SERPINB1,SPP1,THBS1,TIMP1,TIMP3,TNC,TP53,VCAM1	937 (19)
ceruletide	biologic drug	1,76E-03	HMOX1,IFNG,MME,MPO,PTGS2,REG3A,SELP,TNF	827 (16)
CYLD	transcription reg	2,62E-11	CD40,CTLA4,CXCL8,ICOS,IFNG,IL10,IL12B,IL17A,IL1B,IL2,IL2RA,IL6,IL7R,JUN,NFKB2,NTRK3,REL,SERPINE1,TGFB1,TNFSF4	752 (21)
DLL4	other	2,62E-11	ACTA2,DES,EFNB2,EPHB4,FLT1,HES1,IL10,IL13,IL2,IL4,IL5,KDR,MAF,NFKB1,NFKB2,NOS2,NR2F2,PECAM1,RELA,RGS5	590 (15)
cetrorelix	biologic drug	1,42E-04	ANXA5,BAX,CYP19A1,GNRH1,GNRHR,TP53,VEGFC	890 (17)
cetuximab	biologic drug	1,84E-03	EGFR,FN1,HIF1A,NRG1,PLAUR,STAT3	1018 (23)
cetuximab/radi	biologic drug	8,91E-04	FLT1,KDR,TYMS	
TLR5	transmembrane	2,62E-11	ATF3,CCL11,CCL5,CD40,CSF2,CXCL8,ICAM1,IL10,IL12B,IL15,IL17A,IL1A,IL1B,IL33,IL6,MMP1,NR1H4,TLR7,TNF,TSLP	733 (17)
MAF	transcription reg	2,72E-11	ANPEP,CRYBB3,FDFT1,G6PC2,GCG,GCLM,HMGCR,IFNG,IL10,IL12A,IL12B,IL12RB1,IL13,IL17A,IL1R1,IL23R,IL2RA,IL4,IL5,INS,LSS,MAF,NQO1,PCSK2,TP53,TXN,VCAM1	655 (13)
DRD2	G-protein coupl	2,85E-11	BAX,BDNF,CCL2,DRD1,EDNRB,FOS,GHRH,IGF1,IGFBP3,JUN,KCNJ4,PCSK1,PCSK2,POMC,PRL,TGFB1,TGFBR2,VEGFA	778 (19)
MAPK11	kinase	2,85E-11	CAV1,CHGA,FAS,FOS,HMOX1,IL10,IL12B,IL6,INS,NPPA,NPR1,PPARGC1A,PTGS2,RELA,TIMP1,TIMP2,VDR,VIP	901 (21)
Nuclear factor 1	group	2,85E-11	ADRA1B,AR,CHI3L1,CIITA,COL1A1,CYP1A1,CYP1A2,CYP2A6 (includes others),GSS,GUCY1B1,HGF,HSD11B2,HSD17B7,LOX,mir-217,SERPINA3,SLC2A4,TP53	
MAFB	transcription reg	2,93E-11	ADA,ADGRE1,CACNA2D3,CCL2,CD28,CRHBP,CXCL12,F13A1,FPR1,GATM,GCG,HTR2B,IGF1,IL10,IL7R,INS,ITGA2B,LILRB5,MMP9,NFATC1,NPHS1,NPHS2,OLFML2B,PCK1,PCSK2,PDX1,PTGIR,RETN,SLC2A2,SLC7A8,TP53	
GHR	transmembrane	3,00E-11	ADIPOQ,GHR,GHRH,GHRHR,GHSR,IGF1,IGFBP1,IGFBP3,IL1B,IL6,LEP,LHCGR,LPL,NPY,PRL,RELA,SOCS3,SPP1,SST,TNF,TP53	1065 (24)
Laminin (compl	complex	3,00E-11	ACTA2,CCL2,CCND1,CDK5R1,CHGB,COL1A1,DBH,EGFR,ETV5,FN1,IGF2,ITGB1,MMP1,MMP9,NPPA,PGR,PTGS2,SDC4,SERPINE1,TGFB2,WNT5A	1049 (21)
DNMT1	enzyme	3,01E-11	CDKN2A,CIDEA,CNR1,CYP24A1,ESR1,FBN1,FOXP3,GATA4,GSTP1,IFNG,IGF2,IL10,IL13,IL2,IL3,IL4,IL5,KIT,LRP8,MT-CO1,PLEKHA6,POU5F1,PPARG,PRDM16,PTGS2,PTN,SFRP2,SOCS1,SOX17,TIMP3,UCP1,WNT5A	906 (19)
TCF	group	3,01E-11	ABCB1,BMP4,CCND1,CRYBG1,CYP24A1,DBH,DIO2,EDN3,F13A1,FGF9,FOS,GJA1,HTRA1,ID3,IL1R1,IRS1,KLK2,LGR5,LHCGR,MME,MMP2,MMP7,PCSK6,PTGS2,QPCT,SAA1,SERPINA1,SERPINA3,SERPINE1,SLC6A2,TSC22D1,TSPAN8	911 (16)
PSEN1	peptidase	3,05E-11	ABCG2,AGER,APOE,ATP1A2,ATP1B1,ATP2A2,AXL,BAX,BDNF,C3,CCL5,CCND1,CCR5,CDK5R1,CLEC16A,COX8A,CPLX2,CTNNB1,DBP,DNM1L,EGFR,F2R,FOS,FOXO3,FZD4,GAS5,GJA1,GSTP1,HBA1/HBA2,HES1,HES5,HSPA8,HSPD1,IDE,IFNG,IGF1,IL10,IL1B,IL4,IL6,INSR,IRF5,LRP1,LRP1B,LRP8,MAPK1,MME,MMP9,MSR1,MT-CO1,MTHFD1L,NCAM1,NOS1,NOS2,NOTCH1,PAFAH1B2,PDGFRA,PDGFRB,PIK3R1,PPARG,PRC1,PSEN1,PTGS2,RBPJ,RYR2,RYR3,SCARB1,SCN10A,SELPLG,SNAP25,SOCS1,SOD1,TGFB1,TGFBR2,TH,TNF,TP53,TP73,TXN,TYRP1,WARS	991 (20)
ADAM17	peptidase	3,23E-11	CCND1,COL3A1,CXCL8,DUOX2,EFNB2,EGFR,FN1,HES1,IL6,IL6R,IL6ST,MMP2,MMP7,MYH7,NOTCH1,NRG1,REG3A,SAA1,SCARB1,SELL,SOCS3,TBX4,TF,TNF,TNFRSF11B,TNFSF11,TSLP,WNT5A	906 (17)
GNA14	enzyme	3,23E-11	ABCB1,ADM,AGTR1,AKAP12,ANPEP,ARG1,ATF3,AVPR1A,BMP2,BMP4,CXCL8,ENPP1,GJA4,GRB14,HAS2,HBEGF,IL1RN,IL6,NPR3,OLR1,PDLIM5,PLAT,PLAUR,PTGS2,SELENBP1,SGK1,VEGFA,XDH	780 (21)
IFNAR1	transmembrane	3,25E-11	ARG1,ATF3,AXL,CCL17,CCL5,CD40,CIITA,F10,F7,HLA-A,HMGCR,IFIH1,IFNG,IFNL3,IL10,IL12A,IL12B,IL15,IL17A,IL18,IL1A,IL1B,IL6,ITGAV,Ly6a (includes others),NOS2,OAS3,OASL,PLA2G7,PLAT,PTGS2,SERPINE1,SOCS1,SOCS3,SOD2,SREBF2,THBS1,TLR2,TLR7,TNF,TNFAIP3,TNFSF10,VCAM1	675 (14)
BRD4	kinase	3,45E-11	ABLIM1,ACSM3,ACTA2,ALDH1B1,CCND1,CDKN2B,COL1A1,COL1A2,COL4A1,CXCR4,FADS1,FBN1,FN1,FOS,HMOX1,ICAM1,IL2RA,IL7R,ITGA4,ITGB1,LOX,LOXL2,MMACHC,MTHFD1L,MYB,NQO1,PDGFRB,PLAT,PTPN22,RAC1,RREB1,SELE,SLC19A1,SLC7A2,SMARCA4,SRM,STC2,THBS1,THBS2,TIMP1,WNT5A	909 (17)
CYP19A1	enzyme	3,65E-11	AR,BDNF,CCND1,CYP17A1,CYP7A1,EGF,EGFR,ESR1,ESR2,GHRHR,HSD11B2,IL6,IRS1,JUN,KISS1,LEP,LHCGR,LPL,PGR,PPARG,PRL,SCARB1,SLC2A4,SSTR3,TGFB1,TNF,TP53,UCP1,VEGFA	1006 (22)
GLI2	transcription reg	3,80E-11	BMP4,CCL11,CCL17,CCL5,CCND1,CCR5,CLU,CXCR2,GATA4,IFNG,IL10,IL13,IL15,IL1B,IL1RL1,IL4,IL6,IL6R,ITGB1,JAG1,KLK2,MEF2C,MITF,MMP3,MMP9,MYOD1,NKX2-5,PAX2,PI3,PRKCH,SALL1,SPP1,TERT,TNF,VDR	1085 (24)
mir-8	microRNA	3,80E-11	ABCG2,AFP,AKT1,ATF3,BAX,BMP2,CCND1,CTNNB1,EP300,FN1,HIF1A,HMGB1,HMOX1,IFNG,IL1B,IL6,ITGB1,JAZF1,KDR,LEPR,LRP1,MMP1,MOK,PGR,PKD1,PTEN,RAC1,ROCK2,SERPINE2,SIRT1,SMAD2,SMAD5,SOX17,STAT4,STAT5A,SULF2,TGFB2,TGFBR1,TIMP2,TNF,ZFP36,ZFPM2	968 (22)
IL17F	cytokine	4,02E-11	CCL2,CSF2,CXCL5,CXCL8,CXCR4,ICAM1,IFNG,IGF1,IL2,IL6,LEP,LPL,LTA,MMP1,MMP3,PTGS2,TGFB1,TNFRSF1B,TRAF3IP2	890 (14)
SETD2	enzyme	4,02E-11	ANG,ANGPTL3,CAV1,CCN2,ENG,FLT1,FOXO3,GJA4,HHEX,IGF1,IGF1R,JUN,MEF2C,PLG,PTEN,RBPJ,SERPINE1,SOX17,WNT5A	636 (7)
SLPI	other	4,53E-11	CCL5,CCND1,CD40,ELANE,ICAM1,IFNG,IGFBP3,IL2,IL4,IL5,IL6,LOX,NFKBIA,SMAD2,TGFB1,TNF	677 (17)
BACH2	transcription reg	4,58E-11	AHR,CDKN2A,EGLN3,ETV5,FOXO1,FOXP3,HMOX1,ID3,IFNG,IL10,IL12RB2,IL13,IL17A,IL2,IL4,IL5,IL6,MAF,RARA,RARB,STAT4,TNFRSF4,TNFSF4,TP53	952 (17)
NPFF	other	4,67E-11	ACE,ADRB1,ADRB2,ADRB3,CTF1,ID3,INSR,PIK3R1,SLC2A1,SLC2A4,SREBF1,SREBF2	535 (7)
CCN3	growth factor	4,79E-11	ALPL,BGLAP,BMP4,CCL2,CCN2,COL1A1,HES1,HES5,ITGA2,ITGB1,MMP1,MMP2,MMP9,MYOD1,SERPINE1	888 (22)
ETS	group	4,79E-11	CDKN2A,CHI3L1,ENG,ERBB2,FLT1,FOS,ICAM1,IL12B,ITGA2B,PRL,SERPINE1,TERT,TIMP1,TNF,VWF	
LRPAP1	other	4,79E-11	CYP17A1,IL1B,IL6,LDLR,LPL,LRP1,MAPK1,MAPK3,MMP2,PTGES,PTGS2,SERPINA3,SERPINE1,SORL1,TNF	830 (20)
JAG2	growth factor	4,88E-11	BMP2,BMP7,C3,CCL5,CXCL5,HES1,IL10RA,IL1A,IL1B,IL1R1,IL1RN,IL6,JAG1,MIF,MMP1,MMP12,NOTCH1,NOTCH3,SPP1,TNF	395 (9)
SERPINE2	other	4,88E-11	BDNF,CCL17,CCL5,CD34,CSF2,CXCL13,IFNG,IL10,IL17A,IL1A,IL1B,IL2,IL4,IL6,ITGB2,LTA,MMP9,SELE,TNF,TSLP	934 (17)
TNFRSF9	transmembrane	4,88E-11	ANPEP,BCL2A1,CD14,CD28,CD40,CXCL8,FAS,HLA-DQB1,IFNG,IL13,IL1B,IL2,IL4,IL5,IL6,ITGAM,MMP9,NFATC1,PTPRC,TNF	718 (19)
TSC22D3	transcription reg	5,08E-11	ADIPOQ,BGLAP,CCL2,CCL5,CCND1,COL1A1,CXCL8,EDIL3,ICAM1,IL10,IL1B,IL2,IL2RA,IL6,LEP,NFKB1,PPARG,PTGS2,SELE,SGK1,TLR2,TNF,TP53	627 (15)
HDAC2	transcription reg	5,11E-11	ALOX5,APOA1,BRCA1,CD34,CDKN2A,COL1A2,CXCL8,CYBB,DPT,ESR1,FABP1,FABP2,FAS,IGF1,IL12B,IL13,IL1A,IL6,IL9,ITGB8,LGR5,LHCGR,LIG1,MMP9,NFATC1,NFKBIA,NOS2,NR3C1,PAX2,PRIM2,PTGS2,RARB,SLC12A5,SLC8A1,TERT,TFF1,TNF,TNFSF10,TP53,TRPC6	989 (24)
PRKCE	kinase	5,28E-11	ABCB1,ACTA2,BAX,CAV1,CCND1,CRP,CSF2,CXCL8,EGFR,FOS,IL1B,IL2RA,IL2RB,IL6,IL6ST,ITGA2B,JUN,LDLR,MMP9,NFKB1,NOS2,POMC,PTGER3,PTGS2,RGS2,STAT3,TNF,VCAM1,VEGFA	736 (16)

PIK3CG	kinase	5,33E-11	ABCB1,CALCR,HAMP,HMOX1,ICAM1,IFNG,IL17A,IL17RA,IL1B,IL2,IL4,IL5,IL6,ITGB3,MMP3,NFATC1,NOS3,PGR,PIK3CG,SELE,TNF	655 (16)
Brd4	kinase	5,36E-11	ACTA2,CCR2,COL1A1,COL1A2,COL3A1,COL4A1,COL6A3,EDNRB,HBA1/HBA2,HGF,IL6,LIN28A,LOX,LOXL2,PLAT,SELE,SLC4A1,SPTA1,TIMP1,TLR4,TLR6,TLR8	
SIM1	transcription reg	5,65E-11	AGER,AKR1B1,ANG,ANGPTL4,APOA5,APOC4,APOE,AQP4,ARID1A,CACNG1,CYBA,DNASE1,EGF,EGFR,EPO,FCGR2A,GATA2,GDNF,GPX3,HGFAC,HLA-A,ICAM1,IL5,IL6R,ITGB3,ITIH3,JAK2,KCNQ1,LCAT,LEP,LTF,MC3R,MTPN,MYH7,NMBR,PLA2G5,POMC,POSTN,POU5F1,PTPN22,RYR2,SELENBP1,SHH,SIRT1,SLC12A3,SMAD3,SST,STRN,SYT9,TNF,TRH,UBA1,UGT1A6	805 (7)
SP110	transcription reg	5,66E-11	ANXA5,AQP3,ATF3,ATM,BMP4,CDKN2B,CLU,DAB2IP,DICER1,ERCC1,F2R,IFIH1,IL18,IL1R1,IL4R,IL6R,ITGAV,ITGB1,LMNA,MAOA,MTHFR,MYH9,NR1I2,OAS3,P2RX7,PPARG,PRKCA,RAC1,ROCK2,RXRA,SERPINA1,SMAD2,SMARCA4,STAT5A,TBX3,TCF7,TGFBR3,TIMP1,TNFRSF1A,TXNIP,WWOX	
Fc gamma recep	group	5,93E-11	CCL17,CCL18,CCND1,CD40,CXCL8,HES1,ICAM1,IL10,IL12A,IL12B,IL2,IL6,NOS1,NOS2,SOCS3,TGFB1,TNF,TNFAIP3	696 (17)
FANCC	other	6,12E-11	AQP9,ATP1B1,CXCL12,FGFR1,FZD4,GDF15,HES1,HHEX,HNF1B,HSPA4,IGFBP3,IL1B,IL1R1,JAG1,MMP7,MYRF,NOS2,NR3C1,PRKCB,PTGS2,PTPRC,RLN2,SKAP2,TNF,TNFSF4,TP53,UGT2B7	743 (20)
JAK1	kinase	6,12E-11	CCL2,CD14,CD40,CHI3L1,FOS,HAMP,HIF1A,HLA-A,HLA-C,ICAM1,IL10,IL1B,IL4R,IL6ST,MMP2,MYOD1,OSMR,PSMB9,REG3A,RUNX1,SAA1,SFTPB,SOCS3,STAT3,TAP1,TF,TNF	671 (15)
MRTFB	transcription reg	7,23E-11	ACTA2,ADM,CALD1,CCL5,CMA1,COL3A1,CXCR4,CYBA,EDN1,EDNRA,ELANE,EYA2,F11R,F2R,FADS2,GP1BA,GPR37,GSTM5,HLA-A,ITGB1,LCN2,LTF,MYH9,NFKBIZ,P2RY1,PDGFRA,PGLYRP1,POSTN,PTPRO,RAMP1,RHOBTB1,RUNX1,SCARB1,SELP,SLC20A1,SLC6A4,SLPI,TBXAS1,THBS1,TPM1,VCL	
KDM1A	enzyme	7,40E-11	ACSM1,AFP,AGT,ARNTL2,BLM,BMP2,BRCA1,BRCA2,CAD,CCL5,CDH4,CIITA,COL1A1,COL1A2,CTNNB1,CXADR,DDR2,EBF1,FGF10,FOXO1,GATA4,HBB,HSD11B1,IGF1R,LGR5,MPC2,NFE2L3,NOS3,POU5F1,PRICKLE1,PTEN,RARB,RARG,RASGRP3,RETN,SERPINE1,SFRP2,SIRT1,SIX5,SLC22A3,SNAP25,SREBF1,TERT,TIMELESS,UCP1,UHRF1	1133 (23)
TSC1	other	7,71E-11	ALOX15,BAX,CCN2,CTNNB1,CYP1A2,CYP2E1,FOXO1,FOXO3,FOXP3,GLRX,GSR,HMOX1,IFNG,IL12B,IL17A,IL6,IRS1,IRS2,LGR5,MLXIPL,NQO1,PDGFRA,PDGFRB,SREBF1,TNF,TP53	972 (22)
ACVRL1	kinase	7,74E-11	BMPR2,CXCL12,CXCL8,CXCR4,EFNB2,ENG,GDF15,ICAM1,IL1RL1,KDR,PLAT,PLAUR,SELE,SERPINE1,SMAD1,SMAD6,TLR4,VCAM1,VEGFA	689 (18)
ETV4	transcription reg	7,74E-11	ACTA2,ARID3B,BAX,CAV1,CDKN2A,CTNNB1,CXCL8,CXCR4,ERBB2,FN1,MET,MMP14,MMP7,MMP9,MYB,PTGS2,SHH,SPP1,TGFBR2	778 (7)
IGFBP3	other	7,74E-11	ADIPOQ,BAX,CCL11,CCL5,ICAM1,IGF1,IL13,IL1B,IL4,IL5,NOS3,RETN,SERPINE1,SMAD2,SMAD4,THBS2,TNC,TNF,VCAM1	942 (19)
SAA1	transporter	7,74E-11	ALPL,ARG1,BGLAP,CCL11,CCL17,CCL5,CCND1,CXCL8,IL10,IL12B,IL1B,IL1RN,IL6,MMP2,MMP3,MMP9,PPARG,SREBF1,TNF	805 (16)
FCGR2A	transmembrane	8,27E-11	C5,CCL18,CCL2,CCL5,CXCL8,F2RL1,FAS,IFNG,IL10,IL12B,IL1B,IL23A,IL6,PTGS2,SERPINE1,TNF,VEGFA	740 (17)
MTORC1	complex	8,27E-11	AHR,CCND1,CYP11A1,CYP17A1,FGF21,FOXP3,HMGCR,IFNG,IL17A,IL22,IL4,INSIG1,LDHA,NOS2,NOX4,PFKP,PPARGC1A,PTGS2,SLC2A1,SLC2A4,SREBF1,SREBF2,TNF	939 (18)
PTGS1	enzyme	8,88E-11	ANGPT1,ARG1,ATF3,CFTR,CYBB,IL1B,IL6,MMP2,MMP9,NOS2,NOS3,NRG1,PTGER2,PTGER3,PTGER4,PTGES,PTGS1,PTGS2,TNF,VEGFA	949 (19)
PXR ligand-PXR-	complex	8,88E-11	ABCB1,ABCB11,ABCC2,CAT,CYP1A2,CYP2A6 (includes others),CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,CYP7A1,GSTA1,GSTM1,GSTM2,SLCO1B1,SLCO1B3,UGT1A1,UGT1A7 (includes others)	
CSHL1	growth factor	9,51E-11	ACTA2,AR,BMP2,CCN2,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP4A11,FOS,GHRH,GHRHR,GHRL,HNF4A,IGF1,IGFBP1,NPY,PIK3R1,SLC22A1,SLC2A1,SOCS3,SRD5A2,SST,STAT5B,TOX	1014 (24)
IL19	cytokine	9,69E-11	CCL2,CXCR4,FN1,HMOX1,IFNG,IL10,IL13,IL4,IL6,MMP1,MMP9,SOCS1,TNF	758 (17)
TNFRSF6B	transmembrane	9,69E-11	CSF2,CXCL8,ICAM1,IFNG,IL10,IL12B,IL2,IL4,IL5,IL6,MMP2,TNF,VCAM1	721 (20)
PTGER2	G-protein coupl	9,85E-11	ADGRE1,AURKA,BRCA1,CXCL8,CXCR2,CXCR4,CYP19A1,FOXP3,FPR1,HAMP,IFNG,IL10,IL17A,IL1A,IL1B,IL23A,IL6,MMP9,NOS2,NUF2,PGR,PRC1,PTGER3,PTGES,PTGS2,SERPINE1,SPP1,THBS1,TIMP1,TIMP2,TIMP3,TIMP4,TNF,VEGFA	814 (18)
ELK1	transcription reg	1,14E-10	BMP2,BMPR2,CDKN2A,FOS,FUT4,GH1,GRK2,INSIG2,ITGAV,ITGB1,ITGB6,JUN,MECOM,MMP9,MYLK,PRKCA,PRL,PTGS2,SLC2A1,SPP1,THBS1,TLR9,TNF,ZFP36	1000 (22)
Map3k7	kinase	1,16E-10	AFP,BMP4,CCL5,CSF2,EDN1,FGF10,H19,HAS2,HBEGF,IFNG,IL10,IL15,IL15RA,IL1B,IL6,JUN,MLLT3,MMP9,MVK,NFKBIZ,NOD2,OSR1,PTGS2,TNF,TSC22D1,VCAM1	925 (18)
SGK1	kinase	1,16E-10	CCN2,CDK6,CFTR,HBEGF,HES5,IL12B,IL6,KCNA5,KCNJ1,KCNQ1,PPARG,PRL,SCNN1A,SCNN1B,SCNN1G,SLC12A1,SLC12A2,SLC15A2,SLC1A6,SLC1A7,SLC2A3,SLC2A4,SLC5A1,SLC9A3,TNF,TRPV5	837 (17)
TSH	complex	1,16E-10	CCND1,CXCL8,DIO1,DUOX1,FOS,FOXO1,GCH1,IGFBP3,IL1RN,IL6,INSR,KDR,LRP5,NOS2,NOS3,NOX4,PPARD,PTEN,SLC2A1,SLC2A4,SOCS1,SOCS3,SOD2,TNF,TSHR,WNT5A	849 (18)
IL17RA	transmembrane	1,19E-10	CCL11,CXCL12,CXCL8,CXCR2,HAMP,IL13,IL17A,IL1A,IL1B,IL5,IL6,MMP3,MMP9,REG3A,SELE,SELP,TIMP1,TNF	747 (18)
IL23A	cytokine	1,19E-10	CSF2,CXCL13,HP,ICOS,IFNG,IL10,IL13,IL17A,IL18R1,IL1B,IL22,IL23R,IL6,IL9,NFATC1,NOS2,STAT3,TNF	670 (16)
TIMP1	cytokine	1,19E-10	A4GALT,CD40,FLT1,HGF,IGF2,IGFBP3,IL33,MET,MME,MMP2,MMP3,MMP9,PLAT,PLAUR,PLTP,TIMP2,TIMP3,TP53	844 (20)
MBP	other	1,25E-10	CCL2,CD40,FOXP3,GCG,IFNG,IL10,IL12RB2,IL2,IL4,IL5,IL6,LEPR,PTPRC,TGFB1,TNF	899 (17)
TRAIP	enzyme	1,25E-10	C5,CCL11,CXCL13,IFNG,IL10,IL13,IL17A,IL1A,IL1B,IL2,IL23A,IL4,IL6,TNF	587 (15)
ZNF202	transcription reg	1,25E-10	ABCA1,ADRB3,APOA4,APOC3,APOE,CDKN2A,HNF4A,LCAT,LIPC,LPL,PLTP,PNMT,VEGFA,ZFP36	
Rock	group	1,33E-10	ACTA2,BMP2,CCL2,CCN2,CCND1,CDC42,COL1A1,COL3A1,CXCL8,DES,FN1,FOS,ICAM1,IL17A,MYOD1,NOS3,NPPA,PPARG,SORT1,SPP1,TGFB1,THBS1,VCAM1	913 (23)
CAMK4	kinase	1,45E-10	ABCA1,ATF3,BDNF,CDKN2A,CPT1B,CYP11B2,FMR1,FOS,FOXP3,IFNG,IL2,IL4,IL6,JUN,MT-CYB,NPPA,PPARGC1A,TNF,TP53	1011 (24)
miR-17-5p (and	mature microRN	1,45E-10	BMP2,BMPR2,CAMTA1,CCND1,CXCL8,ESR1,ITGB8,MEF2D,MMP3,MYLIP,NCOA3,PKD2,PPARA,PPARG,PTEN,RGS5,RHOC,RUNX1,STAT3,TGFBR2,TLR7,TNF,TP73,TXNIP,VEGFA	804 (17)
SERPINE1	other	1,45E-10	ACTA2,CDKN2A,CXCL8,DLK1,FLT1,FN1,FOS,HGF,IFNG,IL10,IL6,ITGAV,ITGB3,NPY2R,PLAUR,PLG,TGFB1,TGFBR2,UCP3	996 (23)
STAT	group	1,45E-10	AGT,CEBPD,CRP,FOS,HAMP,IL22,IL2RA,IL6ST,LBP,MMP1,NPPA,POMC,PTGER2,SERPINA3,SOCS1,SOCS3,TIMP1,TNF,VIP	832 (11)
THBS1	other	1,45E-10	CCN2,CD69,COL1A1,COL1A2,COL3A1,COL4A1,FN1,IL1B,IL6,LRP1,MMP2,MMP9,PARP1,TGFB1,TGFB2,THBS1,TIMP1,TNF,VEGFA	934 (20)
ITGA5	transmembrane	1,49E-10	APOE,CCND1,CD40,ERBB2,FOS,GJA1,IGF2,IL12A,IL12B,IL1B,IL6,JUN,MMP14,MMP2,MMP9,NOS2,PLAUR,RAC2,SELP,SHH,TGFBR2,TNF	833 (21)
LRP1	transmembrane	1,49E-10	ABCG5,ABCG8,ADGRE1,CD14,COL3A1,GRIA1,IDE,IL1B,IL6,INSR,ITGB1,LRP1,MMP2,MMP9,NOS2,PDGFRB,PTGS2,SHH,SLC2A3,SLC2A4,TNF,WNT5A	932 (22)
PTPN6	phosphatase	1,49E-10	BAX,CCND1,CDK6,CDKN2A,CXCL8,CYBB,DHFR,FN1,GP1BA,IL10,IL12B,IL13,IL1B,IL2,IL4,IL6,ITGB2,NCF2,POMC,STAT3,TIMP1,TNF	816 (21)
T3-TR-RXR	complex	1,58E-10	ADRB1,AKR1C3,APOA5,COL6A3,CYP7A1,F10,FGA,GH1,HP,LDLR,PCK1,PFKP,SCARB1,SLC2A1,SREBF1,SREBF2,TRH,UCP1,UCP2,UCP3	
SMARCA2	transcription reg	1,72E-10	ALPL,CD36,CIITA,CXCL13,CYP7A1,DES,DHFR,EPO,FKBP5,HES1,HES5,IFNG,IL6,ITGAM,KDR,MEF2C,MYLK,MYT1L,PCK1,PHEX,PPARG,SLC6A2,TBX2,TYMS,TYRP1,VDR	792 (16)
ARNT2	transcription reg	1,89E-10	AGER,AKR1B1,ANG,ANGPTL4,APOA5,APOC4,APOE,AQP4,ARID1A,CACNG1,CYBA,DNASE1,EGF,EGFR,FCGR2A,GATA2,GDNF,GPX3,HGFAC,HLA-A,ICAM1,IL5,IL6R,ITGB3,ITIH3,JAK2,KCNQ1,LCAT,LTF,MC3R,MTPN,MYH7,NMBR,PLA2G5,POSTN,POU5F1,PTPN22,RYR2,SELENBP1,SIM1,SIRT1,SLC12A3,SLC2A1,SLC2A3,SMAD3,STRN,SYT9,TNF,UBA1,UGT1A6,VEGFA	
PTHLH	other	1,93E-10	ADAMTS7,ANGPT1,AR,BGLAP,BMPR1A,CCND1,CDKN2A,CDKN2B,CTNNB1,CXCL8,EFNB2,FN1,FOS,HSPA1A/HSPA1B,IGF1,IL6,KISS1,MMP9,PTGS2,RGS2,RUNX1,SERPINE1,TNC,TNFRSF11B,TNFSF11,VDR,VEGFA	1070 (24)
NKX3-1	transcription reg	2,10E-10	AR,CA2,CTNNB1,CTNNBL1,CX3CR1,CXCL13,FES,FOS,FOXO3,IGFBP3,MMP9,PIK3R1,POU5F1,PRKCB,PTPRC,RAMP1,RUNX1,SDC4,SMAD1,SMAD2,STAT3,VAV3,VNN1	977 (19)
ENPP2	enzyme	2,13E-10	ADIPOQ,CIDEA,HAMP,IL6,ITGAM,LEP,PPARG,PPARGC1A,PRDM16,SLC2A1,TNF,UCP1	721 (12)
H2AFY	other	2,15E-10	ABCA1,AKT1,BRCA2,CD36,CDK5R1,CDKN2B,EDN1,ERBB2,FGF1,FN1,GCK,HIF3A,IL16,IL6,IRS1,let-7,LPL,PARP1,POU5F1,PPARG,PTPRO,SERPINE1,SLC2A1,SLC2A2,SLC2A4,SLC7A2,TBX3,TERT,TFF1	1031 (19)
NOX4	enzyme	2,29E-10	AGT,CCL2,CTH,CXCL8,EPAS1,FN1,HAS2,HIF1A,ICAM1,KIT,MMP2,NOS3,NOX4,POU5F1,SERPINE1,SLC2A1,TP53,VEGFA	933 (18)
BGN	other	2,40E-10	BAX,BMP2,CCL2,CCN4,CCND1,CXCL13,CXCL8,EGFR,FBN1,IL1B,LRP6,MMP14,PLTP,SERPINE1,SMAD3,TNF	1003 (16)

ICOSLG/LOC102	other	2,40E-10	CD28,CSF2,FOXP3,ICOS,IFNG,IL10,IL12B,IL13,IL1B,IL1RL1,IL3,IL4,IL5,IL6,TGFB1,TNF	707 (19)
IL-1R	group	2,40E-10	COL3A1,CSF2,IFNG,IL17A,IL1A,IL1B,IL22,IL6,MMP1,MMP14,MMP3,MMP9,NOS2,SELE,SMAD6,TNF	657 (14)
IRF6	transcription reg	2,74E-10	CCL2,CD14,CXCL8,IL10,IL12B,IL17A,IL18,IL1B,IL23A,IL6,LCN2,NLRP3,NOS2,P2RX4,PTGES,PTGS2,SLC7A2,SOCS1,SOD2,TLR4	786 (17)
YBX1	transcription reg	2,88E-10	ABCB1,ABCC1,ACTA2,CCL5,CDK6,CDKN2A,COL1A1,COL1A2,CSF2,CYP11A1,CYP19A1,EGFR,FGFR1,FOS,HBB,HLA-DQB1,HLA-DRA,IGFBP3,IRF5,LHCGR,mir-1290,MMP2,MMP3,PAPPA,PTGS2,SLC2A3,STC2,SV2C,TGFB1,TP53,ZNF607	1126 (21)
TGFBR1	kinase	2,97E-10	ACTA2,AHR,BMP4,CCN2,CCND1,CD40,COL1A1,COL1A2,EDN1,FGF10,FGF21,FGF9,FMOD,FN1,FOXP3,FURIN,GJA4,HAS2,HMOX1,HNF4A,IL12B,IL17A,JAG1,OSR1,PDK4,RUNX1,SERPINE1,SFTPB,VEGFC,ZFP36	909 (18)
COL4A3	other	3,04E-10	CCN2,COL1A1,COL1A2,COL3A1,COL4A1,FN1,ITGA2,ITGB3,MMP14,MMP2,MMP9,PTGS2,TGFB1,TIMP1,TIMP2	799 (16)
ACTN4	transcription reg	3,18E-10	ANGPTL4,CCL2,CCND1,CXCL8,FOS,IL1B,MMP1,MMP3,MMP9,NPHS1,PGR,SERPINE1,TFF1	897 (21)
FDFT1	enzyme	3,18E-10	ABCA1,ABCG5,ABCG8,APOB,CYP7A1,HMGCR,LRP1,MTTP,NR1H3,PCSK9,SCARB1,SREBF1,SREBF2	563 (11)
KLRC4-KLRK1/K	transmembrane	3,18E-10	CD69,IFNG,IL10,IL13,IL17A,IL9,PPARG,RXRA,TCF7,TNF,TNFSF10,TNFSF4,VEGFA	865 (24)
mir-24	microRNA	3,29E-10	AHR,CDKN2B,FN1,FURIN,HNF1A,HNF1B,IFNG,IL12B,IL17A,IL2RA,IL4,IL6,KDR,MAF,NDST1,PARP1,PDX1,RORA,SERPINE1,SLC4A1,TGFB1,TNF,TRIB3	998 (17)
PIM1	kinase	3,29E-10	ABCB1,ABCG2,AKT1,ATP2A2,CAV2,CDKN2A,CTLA4,DNM1L,ERBB2,ERBB3,IFNG,IGF1R,IL10,IL12RB2,IL2,IL2RA,IL6,INSR,MET,PPARGC1A,SOCS1,STAT4,TP53	953 (23)
Aldose Reducta	group	3,42E-10	CCND1,CSF2,CXCL8,G6PD,ICAM1,IL10,IL13,IL1B,IL4,IL5,IL6,ITGAM,MSR1,TNF	795 (17)
Collagen type IV	complex	3,42E-10	ACTA2,CCL2,ITGB1,ITGB3,MMP14,MMP2,MMP9,PLAUR,PTGS2,PTH1R,RELA,SERPINE1,THBS1,TIMP2	955 (20)
Lymphotoxin	complex	3,42E-10	CCL2,CCL5,CSF2,CXCL13,CXCL8,ICAM1,IL1A,IL1B,IL6,MMP1,MMP3,TIMD4,TNF,VCAM1	730 (14)
SCGB1A1	cytokine	3,42E-10	C3,CCL11,COL4A1,FN1,IFNG,IL13,IL4,IL5,ITGB2,MMP14,MMP2,MMP9,PTGS2,SELL	938 (20)
APEX1	enzyme	3,50E-10	ABCB1,ABCC1,ALOX5,CAD,FOS,GFRA1,HTRA1,IL10,IL1A,IL4,IL6,PTGS2,RGS2,RGS4,SIRT1,TP53,VEGFA	1059 (25)
TAB1	enzyme	3,50E-10	CCL5,CFB,CXCL8,GCH1,IFIH1,IL1B,IL2,IL6,JUN,NFKB1,PTGS2,RELA,RGS2,SAA1,SELE,SERPINE1,TNFSF10	537 (14)
corticotropin	biologic drug	2,60E-02	FURIN,PCSK6	
cosyntropin	biologic drug	3,45E-02	CYP11A1,CYP11B2,VEGFA	
TNFSF15	cytokine	3,50E-10	CD40,CSF2,CXCL8,HAMP,IFNG,IL13,IL17A,IL2,IL22,IL2RA,IL2RB,IL4,IL5,IL6,IL9,LEP,MMP9	684 (20)
VTN	other	3,50E-10	COL1A1,COL1A2,EFNB2,IL1B,IRS1,ITGA4,ITGAM,ITGAV,ITGB1,ITGB3,MMP1,MMP2,MMP9,PLAUR,PTGS2,SERPINE1,TNF	895 (20)
IL12 (family)	group	3,55E-10	AQP3,ATF3,CCL5,CCR5,CD69,CSF2,CTH,DICER1,ETV5,FOXP3,FURIN,ICOS,IFNG,IL10,IL12RB2,IL13,IL17A,IL18R1,IL18RAP,IL1B,IL2,IL22,IL2RA,IL4,IL5,IL6,IL9,MAPK1,MAPK3,NCR3,NFKBIZ,SERPINB1,SLC2A3,STAT4,TFRC,TNF,TNFSF10	775 (23)
CALCA	other	3,90E-10	ADD3,AQP4,CALCA,CALCR,CARD14,CCL2,COL3A1,CTNNB1,CXCL8,CXCR4,CYBA,CYP24A1,EDN1,FLT1,FOS,IGF1,IL6,IL9,KDR,LMNA,MAX,MME,NOS2,POMC,PRL,SLC12A1,SLC2A4,SLC9A3,SORT1,TNF,UCP1	990 (23)
FGFR1	kinase	3,90E-10	BAX,BGLAP,BMP4,BMP7,CCND1,COL1A1,COL3A1,FGF1,FGF10,FGF5,FGFR1,FGFR3,FOS,HAMP,HAS2,HES1,HGF,IL2,IL6,JUN,MMP1,MMP14,MMP3,NOTCH1,NR1H3,PCSK1,PLAUR,PTGS1,PTGS2,SLC2A2,TH	976 (18)
miR-199a-5p (a	mature microRN	3,98E-10	ALOX5AP,APOL1,C3,CALD1,CELSR1,COL1A1,COL4A1,FN1,HIF1A,ID3,ITGB3,JAG1,LCN2,MMP1,MMP7,MYRF,NFKB1,PADI4,PTGS2,RELA,RND1,SIRT1,SMTN,TGFBR1,TGFBR2,TGFBR3,VPS11	
TCF3	transcription reg	4,07E-10	ABCC8,ADA,ADIPOQ,AGRP,AP3D1,ATF3,AURKA,BTNL2,CA2,CD2,CDK6,CDKN2A,CDKN2B,CELA1,CKM,COL1A1,CPT1B,CYP11A1,DAB2IP,DOCK1,EBF1,ELANE,ENPP1,FGFR2,FGFR3,FLT3,FOXO1,FOXP3,GATA2,GPLD1,GRIA1,GYPA,HSD11B1,ICOS,ID3,IL1B,IL2RA,IL7R,INS,JUN,KIT,LHCGR,Ly6a (includes others),MEF2C,mir-329,MSMO1,MYOD1,NELL1,NOTCH1,NPPA,NR0B2,NR4A3,NUF2,OPTN,PAX5,PFKP,PML,PRC1,PTGS1,RORA,SELL,SEMA3F,SERPINB1,SLC12A2,SOCS1,SOCS3,TF,TNF,TOX,TYMS	750 (20)
CXCR4	G-protein coupl	4,11E-10	AXL,C5,CCL2,CCND1,CD69,CSF2,CTNNB1,CXCL12,CXCL8,CXCR2,CXCR4,DPP4,EGFR,IL24,IL2RA,IL6,let-7,MMP2,PGR,SHH,TFF1,TNFSF10,TNNC1,TP53	969 (18)
GPS2	transcription reg	4,11E-10	ABCA1,ADIPOR2,BIN1,CCND1,CD14,CDK6,CXCL8,CYP7A1,FOXO1,HEBP1,HP,IL12B,IL6,LTA,NFKBIA,NOS2,PGR,PLA2G3,SGK1,SOCS1,TFF1,TNF,VCAM1,XYLT1	864 (23)
CRY1	enzyme	4,18E-10	ARNTL,DBP,FOS,IL1B,IL6,PCK1,PER1,PER2,PRL,SGK1,TNF	912 (18)
CRY2	enzyme	4,18E-10	ARNTL,CRY1,DBP,FOS,IL1B,IL6,PCK1,PER1,PER2,SGK1,TNF	1014 (18)
DOCK2	other	4,18E-10	ADIPOQ,CIDEA,IL10,IL6,LEP,LIPE,PPARA,PPARGC1A,PRDM16,TNF,UCP1	387 (7)
PTGER1	G-protein coupl	4,18E-10	ANGPTL4,CXCL8,FN1,FOS,GDNF,ICAM1,IL10,IL6,POMC,PTGS2,VEGFC	956 (18)
SYK/ZAP	group	4,18E-10	CD69,IL10,IL2,IL6,MMP1,NFATC1,PTGS2,TIMP1,TNF,VCAM1,VEGFC	656 (18)
DMD	other	4,45E-10	AQP4,CACNA2D1,CAMTA1,CDH13,COL1A2,COL23A1,COL3A1,CSRP3,DES,EGF,GATM,GJA5,GRHL1,H19,HSPA8,HTR2B,IGF1,IGF2,IL12A,IMPA2,KCNK3,KCNMA1,KCNN3,LDB3,LPIN1,MEF2C,MLLT3,MT-ND1,MYBPC3,MYH7,MYOD1,MYT1L,NOS1,P2RY2,PADI2,PDK4,PLPP3,POSTN,PPARGC1A,PROX1,RCSD1,SERPINA1,SERPINB1,SLC2A4,SLC9A2,SORT1,SPTB,TCAP,TMOD4,TP53BP1,UCK2,WWC1	
MEOX2	transcription reg	4,67E-10	ANGPT1,CCL2,CD69,CXCL8,EDN1,HBEGF,ICAM1,ID3,IL6,ITGAV,ITGB3,LRP1,MMP14,SELE,TNFAIP3,TNFSF4,TRAF1,VCAM1,VEGFC	772 (13)
PNPLA2	enzyme	4,67E-10	ACAA2,CD36,CPT1A,CPT1B,FGF21,GSTK1,ICAM1,INSR,IRS1,LEP,MTTP,PCK1,PDK4,PPARA,PPARG,PPARGC1A,SREBF1,UCP1,UCP2	841 (18)
BSCL2	other	4,81E-10	ADIPOQ,ADRB3,AKR1C3,CCND1,CD36,CYP2E1,GCK,GRIA1,HMGA1,IL1RL1,IL33,IL6,LEP,LPIN1,LPL,MMP3,NOS2,PPARG,PSMB9,PTGS1,PTGS2,RETN,SLC2A4,SLPI,TIMP1	980 (21)
mir-223	microRNA	4,95E-10	ABCA1,ABCB1,ACTA2,ATM,CA4,CCR3,CD34,CD36,CRHBP,DNAJC6,EGF,ELANE,FOXO3,GALC,GSTM5,ICAM1,IGF1,IGF1R,IL1A,IL1B,IL1RN,IL23A,IL6,LPL,Ly6a (includes others),MEF2C,MSMO1,NFIA,NLRP3,NQO1,PADI4,PARP1,POSTN,SCARB1,SLC2A4,STAT3,TLR4,TLR7	974 (19)
BIRC5	other	5,07E-10	BAX,CCN2,CHUK,COL1A1,COL3A1,CTNNB1,CXCL13,DPT,FBN1,FCGR2B,FMOD,FN1,HLA-DQA1,HLA-DQB1,IL13,IL4,IL5,IL9,MMP2,TP53,TP73,VEGFC,VWF	978 (20)
CX3CR1	G-protein coupl	5,09E-10	ANXA5,CD14,CD36,HAMP,HMOX1,ICAM1,IGF1,IL1A,IL1B,IL6,MSR1,NOS2,PDX1,SLC2A2,TGFB1,TNF	778 (16)
RPTOR	other	5,26E-10	ADGRE1,CCND1,CDK6,CTLA4,CTNNB1,DHCR7,FDFT1,HIF1A,HMGCR,HSD17B7,ICOS,IL10,IL12B,IL1B,IL6,IRS1,ITGAM,LDHA,LSS,MSMO1,MT-CO1,MVK,NLRP3,NOS2,PTEN,SLC2A1,SLC2A4,SREBF1,SREBF2,TFF1,TNF	1000 (24)
Bvht	other	5,65E-10	ACTA2,ACTC1,ACVRL1,AGTR1,ANGPT1,CSRP3,EBF1,FOXF1,GATA4,GUCY1B1,HBA1/HBA2,IGF2,ITGA4,KDR,LSP1,MEF2C,MYBPC3,MYH7,MYL2,MYL3,NKX2-5,SLC8A1,TBX2,TCF21,TIE1,TNNT2,TTN	531 (11)
ALKBH5	enzyme	5,74E-10	AXL,BRCA2,CAV1,CELSR2,CLU,CYP11A1,CYP17A1,DNM1L,FGFR1,FYN,GJA1,GSTM5,HSPA8,IGF2,LHCGR,MYO6,NCOR1,PAFAH1B1,RARA,RGS2,SBF1,SDHD,SLC4A2,SLC7A8,SMAD5,SOD1,SOX6,UBA1,UHRF1	
DDIT3	transcription reg	6,06E-10	ATF3,CEBPD,CXCL8,DDR2,FN1,FOXO1,HMOX1,HSPD1,IFNG,IL12A,IL12B,IL17A,IL1B,IL4,IL6,ITGA2,ITGAM,JAG1,LCN2,LOX,NPAS2,PER1,PLAT,PPARG,PPARGC1A,RGS4,SELE,SRSF2,STAT3,STAT5A,TGFB2,THBS2,TRIB3,TXNIP,WARS	961 (17)
CCN5	growth factor	6,08E-10	ACTA2,ADIPOQ,BGLAP,CCN2,CTNNB1,ERBB2,ESR1,FN1,HIF1A,JUN,LPL,PPARG,PROCR,SDC4,SERPINE1,SLC2A4,SMAD3,TFF1,TGFB1,TGFBR1,TGFBR2,TGFBR3	806 (21)
CDKN2A	transcription reg	6,25E-10	ACTA2,BAX,BLM,C3,CCL11,CCL18,CCL2,CCL5,CCN2,CCND1,CDKN2A,CDKN2B,CEBPD,COL1A2,CRP,CXCL13,CXCL14,CXCR2,DHFR,EBF1,FGFR1,FOS,GAS7,GNAS,IFNG,IL15,IL1A,IL1B,IL5RA,IL6,ITGAV,ITGB3,JAK2,JUN,KRAS,LTA,MCM8,mir-146,mir-27,MMP1,MMP2,MMP3,MYL2,NFKB2,NR3C1,PDGFRB,PLAGL1,PML,POU5F1,PSMB9,PTEN,PTGS2,PTK2B,RFC1,SERPINE1,SERTAD1,SOX17,TLR4,TNF,TNFRSF1A,TNFRSF1B,TP53,TPM1,VEGFA	905 (17)
Atrial Natriureti	group	6,74E-10	ADIPOQ,CCN2,EDN1,LEP,NOS3,NPR1,NPR2,POU5F1,SERPINE1,TNC	1004 (21)
PPP3R1	phosphatase	6,80E-10	ADRB2,AQP1,ATP2A2,C5,CACNA1C,CACNB2,CPT1B,DLK1,LRP2,MYH7,PON1,PPARA,RYR2,SCNN1G,SFTPB,SLC12A5,SLC8A1	123 (7)
ACKR3	G-protein coupl	6,93E-10	ADM,AKR1C3,AXL,C5,CCND1,CFH,CXCL12,CXCR4,ELN,FMOD,HBEGF,IL24,MMP14,TNNC1,VWF	900 (19)
CCL3	cytokine	6,93E-10	CCL2,CCR5,FOS,IFNG,IL12A,IL1B,IL6,ITGAM,ITGB1,RYR2,RYR3,SELE,STAT3,TNF,TNFSF11	719 (18)
HSPD1	enzyme	6,93E-10	BAX,ICAM1,IFNG,IGF1R,IL10,IL12A,IL12B,IL15,IL1B,IL5,IL6,SELE,SOCS3,TNF,VCAM1	680 (17)
WWTR1	transcription reg	7,03E-10	BGLAP,BMP2,CCN2,CKM,COL1A1,CXCL8,FGF10,FN1,GJA1,ICAM1,IL1A,IL1B,IL6,ITGB2,NEGR1,NPPA,POU5F1,SERPINE1,SPP1,TYMS,VCAM1	561 (12)
IRF3	transcription reg	7,52E-10	ABCC2,CCL2,CCL5,CD40,CD69,CXCL8,FAS,FGF1,FN1,FUT2,IFIH1,IFNG,IFNK,IFNL3,IL10,IL12A,IL12B,IL15,IL17A,IL1B,IL23A,IL4,IL6,IRF5,LCN2,MFAP2,MMP3,MMP9,NECTIN2,NOS2,NR3C1,NRAP,OAS3,OASL,PAH,PML,PVR,RASA1,SORL1,TAP1,TIMP3,TLR4,TNF,TNFAIP3,TNFRSF4,TNFSF10,TNFSF4,TSLP,TYRP1	611 (16)
NCOR1	transcription reg	7,53E-10	ABCB11,ADIPOQ,AFP,CCND1,CDKN2A,COX8A,CYP7A1,DIO1,HAS2,HP,IGFBP1,IGFBP3,IL1B,MME,MMP9,MYOD1,NCOR2,PDK4,PLIN1,PPARG,PTGS2,RARA,RARB,RELA,SREBF1,STK39,TFF1,TRH,TSLP,UCP3	912 (25)
RASSF1	other	7,53E-10	ABCB1,APOE,BMPR2,CARD8,CAV1,CAV2,CCND1,CLU,COL13A1,COL4A1,CPE,CREG1,CXCR4,DACH1,DPEP3,EFNB2,EGFR,ESR1,FOS,GDF15,GHR,GSN,HBEGF,HLA-DPA1,IGFBP3,KISS1,MMP2,MRAS,PTGS2,SPP1	1022 (21)
ALB	transporter	7,76E-10	ACTA2,AGT,CCL2,CCL5,COL1A1,CXCL8,CYBA,EDN1,EDNRA,EDNRB,HNF1A,IL1B,IL6,NOS2,NPHS1,PTGS2,RELA,TGFB1,TNF,VEGFA	871 (16)

ANGPT1	growth factor	7,76E-10	ADAMTS9,APLN,BAX,BMPR1A,CCL2,CCND1,CDKN2A,COL3A1,EFNB2,ICAM1,IL1R1,ITGB1,JAG1,MYH7,NFKB1,NOS3,NPPA,SELE,VCAM1,VEGFA	729 (15)
IRAK1	kinase	7,76E-10	ABCA1,CCL5,CXCL8,FOXP3,IFNG,IL10,IL15,IL17A,IL1B,IL2,IL23A,IL23R,IL6,MMP1,NOX1,RARA,RELA,SELE,TNF,VCAM1	648 (15)
NFkB (family)	group	7,76E-10	CCND1,CXCL8,HNF4A,IL6,LPL,MMP9,NCAM1,PTEN,PTGS2,RELA,TNFAIP3,TNFSF10	642 (13)
HNF1B	transcription reg	7,82E-10	AFP,CA2,CPN1,F11R,FGB,FN1,GSTA1,HGFAC,HNF1A,HNF4A,ID3,IGFBP1,IGFBP3,ITGB6,JAG1,MET,MMP2,MMP7,NR1H4,PCSK9,PDX1,PKD1,PKD2,PKHD1,PLAUR,PTGIS,S100A4,SERPINA1,SGK2,SLC22A12,SLC2A2,SLC5A1,TTR,UGT1A7 (includes others),UMOD	779 (11)
Il3	cytokine	7,96E-10	ADGRE1,AKT1,ANPEP,CD14,CSF2,ELANE,FAS,FOS,IGF1,IL4,IL5,IL5RA,IL6,ITGAM,LCN2,LTF,Ly6a (includes others),MMP3,MPO,MYB,PLA2R1,SOCS1,SPP1,TNFRSF1A,TNFRSF1B,TNFSF11,TP53	868 (22)
ENG	transmembrane	8,10E-10	ACTA2,CCN2,CXCR4,ELN,FN1,ITGB3,KDR,MMP1,NOS3,PECAM1,RAC2,SERPINE1,SIRT1,SMAD2,SMAD6,TGFB1,TGFBR1,TGFBR2,THBS1	900 (20)
CRHR2	G-protein coupl	8,57E-10	CRHR1,IL6,KCNMA1,KCNMB1,NR3C1,RBP4,SLC2A1,SLC2A3,SLC6A4,TH,TPH2,UCP1,UTS2,VEGFA	876 (20)
JUN/JUNB/JUN	group	8,57E-10	BDKRB1,C3,CYP11B1,DBH,FOS,HMOX1,ICOS,IL2,IL6,JUN,MMP1,PTEN,PTPRO,STAT3	657 (12)
OXT	other	8,57E-10	ACTC1,ESR1,FOS,GATA4,GJA1,MEF2C,MYH7,MYL2,NKX2-5,NPPA,NR3C1,PTGS2,RGS2,TNNI3	976 (24)
EGR2	transcription reg	8,99E-10	ABCC1,BGLAP,CAST,CYP19A1,DHCR7,DIO2,EPHA4,ERBB2,FOS,GHR,GHRH,HMGCR,ID3,IFNG,IGF2,IL10,IL17A,IL1A,IL1B,IL2,IL4,IL6R,IL7R,IL9,JUN,KDR,MME,MYB,NOTCH1,RORA,SLC12A2,SMAD1,SOCS1,SOCS3,STAT5A,TFRC,TGFBR3,TNFSF10,TNFSF11,TXNRD2,UCP3,VEGFA	966 (18)
let-7a-5p (and c	mature microRN	8,99E-10	ACTA2,ADGRG1,BDNF,CCND1,CDK6,CDKAL1,CDKN2A,COL1A1,COL1A2,COL3A1,DICER1,DRD3,F2,FADS2,GYS1,HBA1/HBA2,HMGA1,HMOX1,IGF2BP2,ITGA4,ITGB3,KRAS,LIN28A,MMP9,MTPN,MTRR,NEDD4,PRRC2A,PTGS2,PXDN,RABGAP1L,S100A4,SLC1A4,SMAD2,STAT3,TGFBR1,TGFBR3,THBS1,TLR4,TNF,TYMS,UHRF1	591 (7)
IL6ST	transmembrane	9,14E-10	ATP2A2,CALCA,CCND1,CYP3A4,FGA,FGB,HAMP,HP,ICOS,IL6,IL6R,JUN,LTF,MAF,NOTCH1,RET,SOCS1,SOCS3,STAT3,TNFRSF1A,TNFRSF1B,TNFSF11,VCAM1,VIP	848 (22)
DBP	transcription reg	9,18E-10	ADH1B,ADH1C,AGT,AQP4,CYP3A5,CYP7A1,F8,F9,KISS1,NQO1,PER1,PPARA,SCNN1A	
NOX1	enzyme	9,18E-10	CXCL8,EGFR,EPAS1,FLT1,IL13,KDR,MMP9,NFKB1,NFKBIA,NOS2,NOX1,TNF,VEGFA	718 (14)
TNFRSF11B	transmembrane	9,18E-10	BGLAP,BMP2,CA2,IGF1,IGF1R,IL6,ITGAV,MMP9,NOS2,SPP1,TNFRSF11A,TNFRSF11B,TNFSF11	778 (18)
NPC2	transporter	1,03E-09	AKR1C3,BMP2,IL18,IL6,PPARG,PTGDS,PTGER2,PTGER4,PTGES,PTGS1,PTGS2,STAT3,STAT4,TCF21,TLR4,TNF	696 (14)
NPPA	other	1,03E-09	ADM,CCND1,CDKN2A,CYP11B1,EDN1,FLT4,HMOX1,IL10,IL12A,IL12B,IL1B,NOS2,NPPA,PTGS2,TNF,TP53	922 (18)
HIPK2	kinase	1,09E-09	ALOX5AP,BDNF,CIDEA,GATA2,GCLC,GNB3,GSTM5,HBA1/HBA2,HIF1A,HMOX1,NKX2-5,NOX1,NQO1,NTRK1,PECAM1,PPARGC1A,RAC1,RAC2,SLC4A1,SPTB,SST,TFR2,TP53,TRPM5,UCP1,VEGFA	858 (19)
PPARGC1B	transcription reg	1,09E-09	ABCA1,C3,CCND1,CIDEA,CPT1B,DIO2,EGLN3,ERBB2,FDFT1,GCK,HMGCR,LSS,MITF,MT-ATP6,MT-CO1,MT-CO2,MT-ND1,MT-ND2,MTTP,MVK,NPPA,PCK1,PDK4,SLC2A4,UCP1,VEGFA	969 (20)
SIRT6	enzyme	1,16E-09	AKT1,CXCL8,CYP2C18,DBP,HMGCR,IGF1,IGF1R,IGF2R,IL1A,IL1RL1,IL6,IRS2,LSS,MAPK3,PCK1,PLPP3,PPARGC1A,PTEN,PTGS2,SOD2,SREBF1,SREBF2,TNF	1061 (25)
MYOD1	transcription reg	1,19E-09	ACTA2,ACTC1,ADORA1,AGT,BIN1,BRCA1,CAV3,CDH15,CKM,COL4A1,CTNNB1,DES,DHFR,ESR1,FYN,GYS1,IGF1,IGF2,LDB3,MEF2A,MEF2C,MEF2D,mir-378,MMP2,MYBPH,MYH7,MYOD1,PNMT,POSTN,PPARGC1A,PRDM16,PSMB4,RUNX1,RYR1,SLC12A2,SLC2A1,SLC2A4,SST,TGFB1,TGFBR3,TKT,TNNC1,TNNT2,TNNT3,TTN,UCP1,UCP3	975 (23)
mir-146	microRNA	1,27E-09	CAT,CCL2,CD40,CXCL8,EGFR,FOXP3,IL10,IL1B,IL2,IL6,IRAK1,KIT,MMP2,PDGFRA,PTGS2,RELA,RUNX1,SOCS1,TLR4,TNF	841 (16)
Fgf	group	1,28E-09	ACE,CCND1,FOS,IGF1,IGF1R,IL6,JUN,KDR,MITF,MMP2,MMP9,NKX2-5,NPPB,PER1,PRL,PTGS2,VCAM1	906 (21)
NFATC4	transcription reg	1,28E-09	ADIPOQ,ALPL,BDNF,CALCR,COL1A1,COL3A1,IL2,MYH7,NFATC1,NPPB,PPARG,PPP3R1,PTEN,SPP1,TFF1,TNF,TRPC6	818 (12)
SOST	other	1,28E-09	ACADS,CA2,CD36,CPT1A,CYP27B1,IL1B,LPL,MLXIPL,NOX4,PLIN1,PPARA,PPARG,PPARGC1A,SOD1,SOD2,SREBF1,TNFSF11	495 (7)
IKZF2	transcription reg	1,39E-09	CD2,CD28,CD69,CSF2,FOXP3,ICAM1,ICOS,IFNG,IL10,IL10RA,IL1R1,IL2,IL4R,IL5,KLF7,Ly6a (includes others),STAT4,TNFSF4	
IL27RA	transmembrane	1,39E-09	CCR5,CD69,CXCL13,FAS,IFNG,IL10,IL12B,IL13,IL17A,IL1B,IL2,IL2RA,IL4,IL5,IL6,LTA,SOCS3,TNF	634 (15)
CASP8	peptidase	1,45E-09	CCL17,CCR5,CD14,CD69,FAS,FOS,IFNG,IL13,IL18,IL1A,IL1B,IL2RA,IL33,IL4,IL5,IL6,IL9,mir-143,MMP9,NLRP3,TNF,TSLP	659 (17)
IL4R	transmembrane	1,45E-09	ALOX15,ARG1,CCL11,CCL17,CD14,FAS,IL12RB2,IL13,IL13RA2,IL17A,IL1B,IL2RA,IL4,IL5,IL6,IL9,NOS2,PPARG,PPARGC1A,SOCS3,TIMP4,UCP1	749 (16)
mir-15	microRNA	1,47E-09	AR,CCL2,CCL5,CCND1,CD69,CDC42,CDK6,DICER1,EGFR,FGF1,HSPA1A/HSPA1B,IFNG,IL1B,IL6,MAPK3,MMP9,MYB,PLAUR,PTGS2,SIRT1,SLC6A4,TIMP1,TNF,TP53,UCP2	894 (19)
PIK3CA	kinase	1,47E-09	ATP1A1,CALD1,CCND1,CD14,CEBPD,GCK,GSR,GSS,HIF1A,IRS1,IRS2,ITGAM,ITGB1,JAG1,NOS2,PDGFRA,PDGFRB,PIK3CG,POU5F1,PROCR,SERPINE1,SREBF1,SREBF2,TGFB1,TNFSF10	999 (25)
CXCL10	cytokine	1,49E-09	CCL5,CXCR2,FOS,IFNG,IL13,IL1A,IL1B,IL2,IL4,IL5,IL6,ITGA2,MMP9,TGFB1,TNF	844 (20)
mir-148	microRNA	1,49E-09	ABCA1,ACTA2,AQP4,COL1A1,IGF1R,IKZF1,IL6,LDLR,PTEN,RELA,ROCK1,SOCS1,TGFBR1,TGFBR2,TNF	751 (11)
Mt1	other	1,49E-09	ATF3,CCND1,FOS,GSTM3,GSTP1,IL1B,IL6,JUN,LEP,LPL,NFKBIA,OPRM1,RELA,SERPINE1,TNF	911 (16)
RCAN1	transcription reg	1,49E-09	BDNF,CD36,CXCL8,FOS,ICAM1,IL2,IL6,MYH7,NOS3,NPPA,PTGS2,SELE,SOD1,TNF,VCAM1	901 (26)
TRAF2	enzyme	1,52E-09	ADM,AURKA,CCL2,CCL5,CDKN2A,CSF2,CXCL8,EGFR,FAS,ICAM1,IFNG,IKBKE,IL17A,IL2,IL22,IL4,IL6,IL9R,ITGB1,MAPK8,MMP9,NFKB1,NOS2,PPARGC1A,RELA,SELE,TNF,TNFAIP3	530 (14)
Calcineurin prot	complex	1,53E-09	ATP2A2,BDNF,CCL18,CCL5,CKM,CPT1B,CXCL8,FOS,IL2,IL4,MYH7,NPPA,NR4A3,PPARA,PPARGC1A,PTGS2,RGS2,RYR1,SERPINE1,SLC8A1,SLC8A2,SPP1,STAT3,TNF,TNNI3,TRPC6	749 (22)
SOX1	transcription reg	1,53E-09	ACVR2A,ANGPT1,ANKRD17,APCDD1,BMPR1A,COBLL1,CTNNB1,EVX1,EXT2,FABP1,FABP2,FGF5,FOXF1,HES1,IRS1,PDGFRA,PECAM1,PITX2,SMAD1,SMAD4,SOX17,TGFB2,TXNRD1,VEGFA,WNT3,WNT5A	
ACOX1	enzyme	1,63E-09	ACAA1,CAT,CD36,CXCL12,CYP1A2,CYP2C8,CYP4A11,DIO1,DPP4,EGFR,FABP2,GPX4,GSTP1,HLA-DQA1,HLA-DRB5,HSD11B1,HSD3B1,IGF1,IGFBP1,IL1RAP,ITLN1,LCN2,LPL,MBL2,NR1H3,OTC,PAH,PDK4,QPCT,RGS2,SELENBP1,SERPINA1,SGK1,SLC20A1,SLC4A4,SLCO2B1,TP53,TRIB3,UCP2	422 (7)
Alpha catenin	group	1,65E-09	CCN3,COL1A1,COL1A2,COL3A1,COL6A3,CXCL12,ELN,ENG,IGF1,IGF2,IGFBP1,IL1B,IL6,IL6ST,ITGAM,MMP12,MMP2,MMP9,NFKBIA,NFKBIZ,PDGFRA,PTGS2,RHOC,SAA1,SELE,SGK1,SOCS3,STEAP4,THBS2,TIMP1,TNC,TNF,TNFAIP3,TSPAN8,VCAM1	809 (18)
NLRX1	other	1,75E-09	AGT,CD40,CHUK,IFNG,IKBKB,IL10,IL17A,IL1A,IL1B,IL1R1,IL6,IRAK1,NFKB1,NFKB2,NFKBIA,PIK3R1,REL,RELA,SLC2A1,TNF,TNFAIP3	825 (14)
RARB	ligand-depende	1,89E-09	APOA1,BCL2A1,CDKN2A,CDKN2B,CXCL12,CXCL8,DRD1,DRD2,EGFR,FGF21,FOLR2,GATA4,HLA-C,HNF1B,ICAM1,ID3,IGFBP3,IL1B,IL6,ITGAV,JUN,MMP1,NR2F1,PITX2,POU5F1,PTGS2,RARA,RARB,RET,SLC10A1,SLC2A1,SPP1,TGFB1,THBD,VEGFA,VEGFC,ZMAT4	1038 (22)
RB1	transcription reg	1,93E-09	ACTC1,ACTN2,AKT1,ALPL,ATP1A1,ATP1B1,BAX,BGLAP,BLM,BRCA1,CACNA1S,CALCRL,CCN2,CCND1,CDK5R1,CDKN2A,CELSR1,CKM,CXCL8,CYP27B1,DHFR,DIO2,DLK1,EDNRA,FABP2,FAS,FLT1,FN1,FOS,GNRHR,GPR160,GPR83,IGF1,IGF1R,IL6,KDR,KIT,LGR5,LIG1,MAF,MAPK1,MAPK3,MCM8,MEF2C,MEIS1,MET,MFN2,MMP2,MYB,MYH7,NFKB2,NKX2-5,NPY,OPA1,PARP1,POMC,PPARG,PPARGC1A,PTGS1,PYY,RYR1,RYR3,SDHB,SDHC,SDHD,SERPINE1,SOD2,TCAP,TERT,TGFB1,TGFB2,TNF,TNNC1,TNNT2,TOMM7,TOPBP1,TP53,TP73,TXN2,TYMS,UCP1,VEGFA	1015 (23)
JINK1/2	group	1,99E-09	CYP7A1,FAS,FOXO1,IL6,MLXIPL,MMP2,PARP1,PLG,PTGES,PTGS2,SLC2A4,SREBF1,TNF,TNFRSF1A	1015 (25)
MGP	other	1,99E-09	ACTA2,AFP,CELA1,FLT1,GATA4,HGF,HHEX,HNF1A,HNF4A,JAG1,MET,PAH,SPP1,TTR	33 (3)
LPIN1	phosphatase	2,02E-09	APOE,CPT1A,DLK1,HMGCR,IL12B,IL1B,IL6,LPIN1,NOS2,PPARA,PPARG,PPARGC1A,PTGS2,RETN,SREBF1,TNF	878 (21)
FYN	kinase	2,05E-09	EGFR,FOS,FOXP3,GRIA1,IFNG,IL13,IL17A,IL1B,IL2,IL23R,IL4,IL5,IL5RA,IL6,NOTCH1,PTGS2,RORA,SOCS3,TNF,TP53	759 (25)
ICOS	transmembrane	2,05E-09	CCR3,CSF2,CTLA4,CXCR4,ICOS,IFNG,IL10,IL13,IL17A,IL1A,IL2,IL2RA,IL2RB,IL3,IL4,IL5,IL6,MAF,NFATC1,TNF	669 (18)
LTA	cytokine	2,05E-09	CRP,CXCL13,EGFR,ERBB2,FOXP3,HAS2,IFNG,IL10,IL17A,IL1B,IL4,IL5,IL6,ITGAV,ITGB1,ITGB3,LTA,PTGS2,SELL,TNFRSF11B	906 (15)
STK40	kinase	2,05E-09	ABCB1,APOE,C5,CCL2,CCR5,CKM,CXCL5,CXCL8,DES,DLK1,FGF1,FUT4,HLA-DQA1,IL1B,PPARG,PTGS2,SFTPB,SHH,TLR4,TLR5	656 (14)
NFKB2	transcription reg	2,14E-09	AKR1B1,ANXA5,AR,BMP2,CCL5,CCND1,CXCL12,CXCL13,CXCL8,CXCR4,FOS,HAMP,HLA-DQA1,IL2,IL23A,MMP2,MMP9,MYB,NFKB2,PTEN,PTGS2,RELA,SELL,SOD2,TNF,TRAF1,VCAM1	634 (14)
SREBF2	transcription reg	2,14E-09	ABCA1,ACAA2,APOA2,BMP4,CAMK1D,CXCL8,CYP4F2,DHCR7,FADS2,FDFT1,G6PD,HMGCR,INSIG1,IRS2,LDLR,LIPA,LRP1,LSS,MSMO1,MTTP,MVK,NLRP3,PCSK9,PDX1,PPARG,SREBF1,SREBF2	914 (22)
cyanovirin-N	biologic drug	2,60E-02	CD69,IL2RA	
CD2	transmembrane	2,28E-09	CCL11,CCND1,CD40,CSF2,FAS,HLA-DPA1,ICAM1,IFNG,IL10,IL13,IL2,IL4,IL5,PTEN,PTPRC,SELL,STAT4,TNF,TP53	680 (25)
PKM	kinase	2,28E-09	CCND1,CYP19A1,IL18,IL1B,IL6,ITGB1,LDHA,MAP2K5,MMP2,MMP9,MT-ATP6,MT-CO1,MT-CO2,PPARGC1A,SDHB,SLC2A1,STAT3,TGFBR1,VEGFC	946 (19)

ABCB4	transporter	2,32E-09	ACTA2,AFP,CCN2,COL1A1,COL1A2,COL4A1,H19,MMP2,NFKB1,NFKB2,PDGFRB,SERPINE1,SLC10A1,SPP1,TGFB1,TGFB2,TIMP1	703 (7)
cyclic des-acyl g	biologic drug	9,27E-03	PPARGC1A,UCP1	
CDC42	enzyme	2,32E-09	ATF3,CCN2,CCND1,CKM,ESR1,FOS,IFNG,ITGB1,JUN,MAPK8,MMP1,MYH7,PRL,SCARB1,STAT3,TNF,TP53	831 (19)
CIDEC	other	2,39E-09	ACADS,CCL2,CIDEA,CPT1A,CPT1B,DIO2,IL6,LEP,LIPE,PLIN1,PPARA,PPARG,PPARGC1A,SERPINE1,SREBF1,SREBF2,TNF,UCP1	984 (19)
cyclosporin	biologic drug	2,32E-02	CCND1,CXCL8,ICAM1	
cyclosporin A	biologic drug	4,79E-62	ABCC2,ABLIM1,ACTA2,ADORA1,ADORA2A,ADORA2B,AGT,AGTR1,AGTR2,AKR1B1,ANG,APOB,APOE,ATF3,ATP1A1,AVPR1A,BAX,BCAT1,BDNF,BMP2,C4A/C4B,CARD8,CASR,CAV1,CCL11,CCL2,CCL5,CCN2,CCND1,CCR5,CD14,CD200,CD40,CLU,COL1A1,CTLA4,CX3CR1,CXCL8,CXCR4,CYBA,CYP2C9,CYP3A4,CYP3A5,CYP7A1,EDIL3,EDN1,EDNRA,EDNRB,EGF,EGFR,EPO,F5,FAS,FCGR2A,FDFT1,FGA,FGB,FKBP5,FLT1,FN1,FOS,FOXO1,FOXP3,FYN,GAS5,GCGR,GJA1,GSTM3,HIF1A,HMGCR,HMOX1,HNF4A,HSPD1,ICAM1,ICOS,ID3,IFNG,IGFBP1,IL10,IL12A,IL12B,IL12RB2,IL13,IL16,IL17A,IL1A,IL1B,IL2,IL22,IL2RA,IL4,IL5,IL6,INS,ITGAV,ITGB6,ITPR2,JUN,KCNA5,KCNK3,KDR,KL,LAMA3,LCN2,LDLR,LTA,MAF,MIF,MMP1,MMP14,MMP2,MMP3,MMP9,MYH7,NCR3,NFATC1,NFKB1,NFKBIA,NOS1,NOS2,NOS3,NPPA,NR3C1,PAM,POSTN,PRKCA,PRKCH,PRL,PSMB8,PTEN,PTGS2,RAB11B,REL,REN,RUNX1,RXRA,SELE,SELL,SERPINE1,SHH,SLC10A2,SLC12A1,SLC12A3,SLC14A2,SLC23A2,SLC8A1,SLC8A2,SMTN,SNRNP70,SNRPN,SOCS1,SOD1,SPP1,SREBF1,SREBF2,STAT5A,TERT,TGFB1,TGFBR1,TGFBRAP1,TIMP1,TNF,TNFSF10,TNFSF11,TNFSF14,TP53,TSPAN8,TSPAN9,TTN,VCAM1,VEGFA,WNT5A,XCL1	917 (16)
FOXA3	transcription reg	2,39E-09	CD40,CIDEA,CPT1A,CYP2C18,CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,HAMP,PCK1,PPARGC1A,PRDM16,SLC2A2,TF,TTR,UCP1	824 (13)
mir-19	microRNA	2,39E-09	ABCA1,ALOX5,CCN2,ESR1,FZD4,IFNG,LRP6,MSMO1,MYH7,MYLIP,NPPA,PTEN,SMAD4,TGFBR2,THBS1,TLR7,TNF,TNFAIP3	712 (7)
TLR1	transmembrane	2,39E-09	CSF2,CXCL8,CYP27B1,HAMP,IFNG,IL12B,IL15,IL15RA,IL1B,IL6,TNF,TNFAIP3,VDR	656 (16)
IL1RAP	transmembrane	2,40E-09	CD14,CD40,CSF2,CXCL8,IL13,IL1RL1,IL2,IL4,IL5,IL6,KIT,TNF	732 (17)
LAT	other	2,40E-09	CD69,CTLA4,FOXP3,IL10,IL13,IL2,IL2RA,IL4,IL6,NFATC1,SELP,TNF	696 (22)
PCSK1	peptidase	2,40E-09	CCK,GHRH,GIP,IFNG,IGF1,IL10,IL1B,IL2,IL6,LEP,POMC,TNF	879 (22)
SMPD1	enzyme	2,40E-09	ACTA2,CCL5,COL1A1,CYP7A1,DIO1,IL6,MAT1A,MMP1,SLC2A2,SPTA1,TGFB1,TNF	963 (20)
DGCR8	enzyme	2,71E-09	ACTA2,BDNF,CCND1,CNP,ERBB2,ERBB3,FOS,GDNF,GJA1,HES1,JAG1,KRAS,let-7,MITF,NCAM1,NFATC1,NOTCH1,RARA,SHH,TCF7L2,TNC	781 (18)
SOX3	transcription reg	2,93E-09	ACVR2A,ANGPT1,ANKRD17,APCDD1,BMPR1A,COBLL1,CTNNB1,EVX1,EXT2,FABP1,FABP2,FGF5,FOXF1,IRS1,LMX1B,PDGFRA,PECAM1,PITX2,RET,SMAD1,SMAD4,SOX17,TGFB2,TXNRD1,VEGFA,WNT3,WNT5A	
BMPR2	kinase	3,06E-09	CSF2,CTNNB1,CXCL12,CXCL8,EFNB1,EFNB2,EPHA4,FN1,HAMP,ICAM1,SELE,SPP1,TNFRSF11B,TNFSF11,VCAM1	812 (17)
DPP4	peptidase	3,06E-09	CTNNB1,IFNG,IL10,IL1RN,IL2,LRP1,MMP14,MMP2,SLC2A4,SREBF1,TGFB1,THBS1,TIMP1,TIMP2,TNF	795 (20)
EBI3	cytokine	3,29E-09	CCL11,CIITA,FOS,HLA-A,HLA-B,HLA-C,HLA-DPA1,HLA-DQA1,HLA-DRA,ICAM1,IFNG,IL10,IL12RB2,IL13,IL17A,IL2,IL22,IL4,IL5,NFATC1,TAP1,TNFSF10	727 (16)
PITX2	transcription reg	3,37E-09	ADH1C,ATP1A1,ATP1B1,CCND1,COL1A2,DACH1,FOXO1,FZD4,GATA2,GPX4,GRHPR,IDH2,ITGAV,ITGB1,KCNJ11,KCNQ1,LDHA,MSRA,NDUFB3,NPPA,PITX2,POMC,PRL,SDHC,SOD1,SOD2,TBX15,TBX2,TBX3,TBX4,TBX5,TCF21,TXN2,UCP3,WNT5A	1097 (23)
ALOX12	enzyme	3,69E-09	CYP11B2,FN1,IFNG,IL12B,JUN,MMP2,NOS3,PDGFRA,TGFBR2,VEGFA	874 (19)
NPY2R	G-protein coupl	3,69E-09	AGRP,CARTPT,GHRH,IGF1,IL6,LEP,NPY,NPY2R,POMC,TNF	942 (23)
mir-30	microRNA	3,72E-09	AR,BAX,CCN2,CDKN2A,IL12B,IL1B,IL6,ITGA2,ITGB3,LIN28A,MYH7,NEDD4L,NPPA,SERPINE1,SMAD1,SMAD2,STK39,TNF,TP53	889 (17)
CLU	other	3,80E-09	AKT1,BAX,CCL2,CDKN2A,CLU,CXCL8,IL6,MMP2,MMP9,NFKBIA,RELA,SMAD2,SMAD3,SREBF1,TNF,TP53	926 (18)
HSF1	transcription reg	3,97E-09	ABCB1,BAX,BMP4,BMP7,CCN2,CCT2,CD36,CELSR1,CLU,COL18A1,CTNNB1,DLGAP1,DPT,FGF1,FKBP4,FMOD,HMGB1,HMOX1,HSPA1A/HSPA1B,HSPA4,HSPA8,HSPB2,HSPD1,ICAM1,IL1B,IL6,IL7R,JUN,LDHA,LDLR,LPL,MITF,NCOR1,NCOR2,NFKB1,POSTN,POU5F1,PPARG,PPARGC1A,PPP3CA,RELA,SREBF1,TNF,TNFSF11,TRPV1,TTR,UCP3,VCAM1,VCAN,WNT3	871 (16)
TLR7	transmembrane	3,97E-09	ACTC1,AGT,ATF3,BCL2A1,CALCA,CCL2,CCL5,CCND1,CD40,CD69,CFH,CXCL13,CXCL8,DIO2,ETV5,GCGR,ICAM1,IFNG,IFNK,IL10,IL10RA,IL12A,IL12B,IL13,IL1B,IL1R1,IL21R,IL23A,IL4I1,IL6,KCNMA1,LTA,MCOLN2,MYOC,NFKB1,NFKBIA,NR1H4,OAS3,PLAT,RGS4,SELE,SLC12A3,SOCS1,SOD2,TAFA4,TLR7,TNF,TNFAIP3,TP53,TRPM2	669 (16)
NEDD9	other	4,05E-09	ADM,ALOX5,BMP2,FABP1,FOS,GDF15,ITGA2,KIT,LRP1,MMP14,MMP2,MMP9,PCK1,PFKP,SERPINE1,SLC2A1,TF,TXNIP	820 (20)
AXL	kinase	4,11E-09	GNRH1,IFNG,IL10,IL12A,IL13,IL17A,IL18,IL1B,IL4,IL6,MMP1,MMP2,MMP3,MMP9,NOS2,RELA,TNF	986 (18)
ZC3H12A	enzyme	4,11E-09	ADIPOQ,CCL2,CEBPD,ICOS,IFNG,IL12B,IL1B,IL2,IL6,LPL,MAF,NOS2,PPARG,REL,TNF,TNFRSF1B,TNFRSF4	686 (15)
GPER1	G-protein coupl	4,13E-09	ATF3,BAX,CACNA1D,CCN2,CCND1,CEBPD,CYP19A1,EDN1,EDN2,ESR1,FOS,IGF1,JUN,LTF,NFKBIA,PTGER4,RND1,SFRP2,TNF,TNFAIP3,ZFP36	1135 (20)
BMPER	other	4,36E-09	ACTA2,ACVRL1,BMP4,EFNB2,HAMP,HNF4A,ICAM1,MGP,NKX2-5,NOS3,PECAM1,TBX5,TGFBR1,VCAM1	151 (6)
ETV1	transcription reg	4,36E-09	ADRB2,BRCA1,CXCR4,ERBB2,HSD17B7,ITGAV,ITGB3,MITF,MMP1,MMP7,PLAUR,POMC,TERT,TGFBR2	436 (7)
Ikb	group	4,36E-09	BLVRA,CCL2,CCND1,CFB,HHEX,ICAM1,IL6,MMP1,NFKB1,PTEN,PTGS2,TNF,TNFAIP3,TP73	915 (16)
STAT4	transcription reg	5,04E-09	ACSS1,ACVRL1,C3,CAPN5,CCL2,CCR5,DDAH2,ETV5,FDX1,FURIN,GAS5,GJA1,HLA-DQB1,IFIH1,IFNG,IL10,IL10RA,IL12RB1,IL12RB2,IL13,IL17A,IL18R1,IL18RAP,IL2,IL22,IL2RA,IL6,LPIN1,LRP1,MLLT3,PER1,PRDM16,RAMP1,RORA,S100A4,SELE,SELENBP1,SELPLG,SERPINB1,SERPINE1,SERTAD1,SH2B1,SLC2A3,SOCS3,STC2,SUN1,TGFB3,TIMP1,TNF,VEGFA,ZNF524	924 (22)
TYROBP	transmembrane	5,40E-09	CCL2,CD40,CD69,CXCL8,FCGR2B,GPX1,ICAM1,IFNG,IL10,IL10RA,IL18,IL1B,IL6,ITGAM,ITGB1,NCF2,NOD2,SFT2D2,SH2B3,SPP1,TGFB1,TNF,TNFRSF1B	701 (15)
GNA12	enzyme	5,67E-09	ACTA2,CXCL8,DDR2,EGFR,F2R,FOS,G6PD,GCLC,GCLM,GSR,GSTA1,GSTP1,IRS1,mir-143,MMP2,NOS2,NOS3,PDGFRA,PIK3R1,PTGS2,TRPC6,TXNRD1,VAV2,VAV3,VCL,VEGFA	960 (20)
ADM2	other	5,72E-09	ARG1,COX5B,FGF21,FOS,IGFBP3,IL10,LEP,NOS2,PPARGC1A,SDHB,TBX15,TH,UCP1	986 (19)
ADORA3	G-protein coupl	5,72E-09	CCL2,CCL5,CCL8,CSF2,CXCL8,HAMP,IL10,IL24,IL3,NOS2,NPPA,SPP1,VEGFA	728 (18)
CYP2J2	enzyme	5,72E-09	CYP2J2,EGFR,ICAM1,IL1B,IL6,MMP9,NFKBIA,NOS3,NPPA,PIK3CG,PPARG,SELE,VCAM1	1006 (22)
darbepoetin alf	biologic drug	3,31E-03	ICAM1,NOS3,SELP	
FBN1	other	5,72E-09	CCN2,COL1A2,COL3A1,COL6A3,FBN1,MMP1,MMP2,MMP3,MMP9,PPARG,SERPINE1,TGFBR2,TIMP3	1099 (20)
Ras homolog	group	5,72E-09	ABCA1,CCN2,CCND1,FOS,IL16,ITGAV,ITGB1,ITGB3,MMP9,NOS3,PDGFRA,PTGS2,TNFSF11	982 (19)
SRA1	transcription reg	5,72E-09	ADIPOQ,CAV1,DIO2,HES1,LIPE,MMP1,MMP9,PPARA,PPARG,PRDM16,SLC2A3,TGFB2,THBS1	991 (21)
TNFRSF18	transmembrane	5,72E-09	CCL2,CD247,CXCL8,ICAM1,IFNG,IL17A,IL2,IL6,IL9,MMP9,NOS2,PTGS2,TNF	704 (17)
FGF7	growth factor	5,77E-09	CAD,CCND1,CDKN2A,CEBPD,CYP7A1,EGFR,ETV5,FGF1,FGFR1,FGFR2,FOXF1,HAS2,HAS3,IL1A,INS,LTA,MMP2,MMP9,NFE2L3,SERPINE1,SFTPB,SHH,SREBF1,TP53,VEGFA	1015 (19)
TNC	other	5,95E-09	CCL2,CXCL12,EDNRA,EGFR,FOS,HTRA1,IFNG,IL1A,IL1B,IL6,LGR5,MET,MMP1,MMP14,MMP2,TLR4,TNF,TNFSF11,TPM1	941 (20)
HOXA10	transcription reg	5,97E-09	ADIPOQ,ADM,ALOX5AP,ALPL,APOE,AQP1,ATP1A2,BCHE,CDKN2B,COL3A1,CYBB,CYP11B1,CYP2E1,DBP,DPP4,EGFR,FLT1,FN1,GAS6,GJA1,HBG1,HLA-DQA1,HLA-DQB1,HMGCR,IDH2,IGFBP3,IL1R1,ITGB3,LCN2,LEPR,LTF,MAX,MIR99AHG,MYLK,NCAM1,NCF2,PIK3R1,PTGER3,PTGER4,RELA,TGFBR3,THBD,TP53,XDH	
BATF	transcription reg	5,99E-09	AHR,CTLA4,IL10,IL12RB1,IL13,IL17A,IL17RA,IL1R1,IL2,IL22,IL4,IL5,ITGA4,RORA,TCF7	738 (21)
ELOVL5	enzyme	5,99E-09	ABCG8,CYP4A11,ELOVL2,FADS1,FADS2,FGF21,FOXO1,HMGCS2,INSIG2,MLXIPL,PCK1,PDK4,PLTP,PPARGC1A,TRIB3	806 (20)
TRADD	other	5,99E-09	AR,BCL2A1,CCL2,CSF2,CXCL8,ICAM1,IL18R1,IL6,MMP9,NFKBIA,RND1,TNF,TNFAIP3,TRAF1,VCAM1	664 (14)
BDKRB2	G-protein coupl	6,09E-09	BDKRB1,CCN2,EDN1,FOXO1,ICAM1,ITGAM,NOS3,PTGS2,REN,TGFB1,TP53	937 (17)
C1q	complex	6,09E-09	CCL2,CTNNB1,CXCL8,GAS6,ICAM1,IFNG,IL10,IL6,PECAM1,SELE,VCAM1	650 (15)
CNOT3	other	6,09E-09	ALDH1B1,CPT1B,EBF1,IGFBP1,LEPR,PAX5,PDK4,PPARGC1A,TFF1,TNFRSF11A,UCP2	156 (3)
IL18R1	transmembrane	6,09E-09	IFNG,IL10,IL12A,IL1A,IL1B,IL4,IL5,IL6,SOCS1,SOCS3,TNF	622 (13)
PARK7	enzyme	6,09E-09	AR,BAX,CXCL8,HIF1A,ICAM1,NOX4,PTEN,RET,SOD2,TH,TXN	911 (19)
Hbb-b1	transporter	6,13E-09	CCR2,CCR5,CIITA,COX8A,CXCR2,CYBA,CYBB,EGLN3,FN1,HFE,HIF1A,ICAM1,IL10RA,IL16,IL1B,IL2RB,ITGAM,LY86,NCF2,PECAM1,RET,TF,TFRC,TH,TLR2,UCP2,VCAM1,VEGFC,VHL	670 (10)
SFRP1	transmembrane	6,23E-09	ACTA2,BAX,CCND1,COL1A1,CTNNB1,FN1,IL6,MLXIPL,MMP1,MMP2,MMP3,MMP9,NAMPT,NR1H3,PCK1,SERPINE1,SLC2A2,SLC2A4,SREBF1,TGFB2,TP53	937 (22)
B4GALT6	enzyme	6,40E-09	CCL2,CCL5,CSF2,IL1B,IL6,NOS2,PTGS2,TLR2,TNF	498 (7)
ITGA4	transmembrane	6,40E-09	IL1B,IL1RN,ITGA4,ITGAV,MMP2,MMP9,RAC2,TNF,TNFAIP3	777 (21)
LTB4R2	G-protein coupl	6,40E-09	AR,CXCL8,IL13,IL4,MMP1,MMP2,MMP9,NOX1,NOX4	942 (19)
CRHR1	G-protein coupl	6,58E-09	AQP4,EDN1,HAMP,HSD11B1,HSD11B2,KCNMA1,KCNMB1,SLC2A1,SLC2A3,TH,UTS2,VEGFA	768 (15)

ITGAL	transmembrane	6,58E-09	CD69,HES1,IL10,IL12RB2,IL13,IL2,IL4,IL5,ITGA4,ITGB2,NOTCH1,TNF	682 (19)
TACR1	G-protein coupl	6,58E-09	ADIPOR1,ADIPOR2,FOS,IFNG,IL10,IL17A,IL1B,IL23A,IL6,LEP,PTGS2,TNF	810 (19)
histone deacety	complex	6,70E-09	CCND1,CDKN2A,CXCR4,CYP24A1,IL24,KL,LHCGR,MMP9,NOTCH1,PER1,PLAT,PPARGC1A,PRSS8,PTGIS,SLC7A8,TERT,THBS1,TNF	1111 (25)
defibrotide	biologic drug	2,60E-02	PLAT,SERPINE1	
miR-27a-3p (an	mature microRN	6,70E-09	ADORA2B,BAX,CYP1B1,EFNB2,EPHB4,FOXO1,GCA,IGF1,MEF2C,MYH7,NOTCH1,PPARG,RUNX1,RXRA,SMAD3,SMAD4,SMAD5,SRM	
CARD9	other	6,91E-09	C3,CCL5,CCR5,IFNG,IL10,IL12B,IL1A,IL1B,IL2,IL22,IL23A,IL6,MPO,TLR2,TLR9,TNF	731 (16)
IHH	enzyme	6,91E-09	ALPL,BMP4,CCND1,CTNNB1,FLT1,HSD17B7,KDR,MEF2C,MET,NR2F2,PECAM1,PTGFR,PTH1R,SPP1,TNFRSF11B,VEGFA	
PLP1	other	7,09E-09	ATF3,CCL2,FOXP3,ICOS,IFNG,IL10,IL17A,IL2,IL4,IL5,MMP3,NOTCH1,NOTCH3,PRKCQ,SHH,TIMP1,TNF	739 (16)
desmopressin	biologic drug	5,60E-05	ADCY3,ADD3,ADM,AKR1B1,ATP1A1,CARD14,CTNNB1,CYBA,F8,FOS,HSPA1A/HSPA1B,HSPA8,LMNA,MME,PAX2,SCN1B,SCNN1G,SLC12A1,SLC2A4,SLC9A3,SORT1,VWF	
FBXW7	enzyme	7,14E-09	CD36,CDKN2A,COL1A1,FDFT1,FGFBP1,HMGB1,HMGCR,HSPA8,IVD,JUN,KLF5,LDLR,NFE2L3,NFKB2,NOTCH1,NQO1,NR3C1,PPARG,PPARGC1A,SERPINE1,SREBF1,TLR4	956 (23)
IL5	cytokine	7,14E-09	ACAA2,ATP1B1,CA4,CCL2,CCR2,CCR3,CCR5,CD40,CD69,CDC123,CIITA,CSF2,CX3CR1,CXCL8,CXCR2,CXCR4,CYP1A2,EGLN3,FAS,FCGR2B,GCLM,HBEGF,HIF1A,HMGCR,ICAM1,IFI30,IFNG,IL10,IL13,IL1RL1,IL2RA,IL4,IL4R,IL5,IL5RA,IL6R,IL9,ITGAM,ITGAV,ITGB6,LTA,MMP9,MS4A2,NOS2,PAX5,PFKP,PRRC2A,PSMB4,PTPRC,RHOH,S100A4,SGK1,SLC2A1,SLC39A8,SOCS1,STK39,TGFB1,TNF,TNFRSF4,UCK2	809 (15)
GMNN	transcription reg	7,30E-09	ACVR2A,ANGPT1,ANKRD17,APCDD1,BMPR1A,COBLL1,CTNNB1,EVX1,EXT2,FABP1,FABP2,FGF5,FOXF1,IRS1,PDGFRA,PECAM1,PITX2,POU5F1,SMAD1,SMAD4,SOX17,TGFB2,TP53,TXNRD1,VEGFA,WNT3,WNT5A	700 (10)
Havcr1	other	7,30E-09	IL10,IL12A,IL13,IL17A,IL1B,IL4,IL5,IL6	
GLI1	transcription reg	7,65E-09	ABCG2,AKT1,BCL2A1,CAV1,CCND1,CLU,COL1A1,CRHR1,DIO2,FAS,FGF1,FGF10,GALNT2,GATA4,GPER1,IGF1,IGF2,IL2RA,IL6,IMPA2,INSIG1,IRS1,KLK2,LMNA,MEF2C,MMP2,MMP9,NR2F2,PAX2,PDGFRA,POMC,PTH1R,PVR,RXRA,SALL1,SH2B3,SOCS1,SOX6,SPP1,SYNE1,TERT,TFF1,TIMP3,TNC,TP53,TSC22D1,VEGFA,VEGFC	1099 (23)
SPDEF	transcription reg	8,00E-09	CCN2,CD34,CD40,COL13A1,COL1A1,COL4A1,COL6A3,CXCL8,EGFR,FGFR1,HIF1A,PLAUR,PRKCA,SCGB1A1,SERPINE1,SMAD1,SMAD2,SMAD3,SMAD4,SOX17,TGFB1,TNC,UCP3,WNT5A	825 (20)
miR-125b-5p (a	mature microRN	8,06E-09	ACSS1,ALOX5,APLN,ARG1,ARID3B,CBLN2,CCR5,CDK6,CDKN2A,CYP1A1,DICER1,DIO3,ERBB2,ERBB3,GPR160,GSS,ID3,IGFBP3,IL1RN,IL6R,JUN,LIN28A,LIPA,NOS2,OSBPL9,TENM2,TNF,TP53,TSPAN8	982 (19)
STK11	kinase	8,18E-09	ACE,AHCY,ALDH9A1,ATF3,BCL7B,CARTPT,CCL18,CCL2,CCND1,CDC42,CHGB,COL3A1,COX8A,CPS1,CTNNB1,ELOVL2,FGFR2,FGG,FN1,HIF1A,IFNG,IGFBP1,IL17A,IL1A,IL1RAP,IL2RB,IL33,IL4,IL5,IL6,LDHA,MMP2,MMP9,NFKB2,NOS2,PDYN,POLR1D,PRIM2,PTEN,PTGS2,REN,SDHB,SDHD,SERPINE1,SORL1,SPP1,SRM,TFF1,TKT,TNFAIP3,TNFRSF4,TNFSF10,TNFSF4,TXNRD1,TYMS,UCK2,VAV3,VEGFA,VIPR2,WNT5A	987 (19)
BTG2	transcription reg	9,03E-09	BRCA1,CAT,CCND1,HMOX1,IL1B,MMP3,NCAM1,NOX4,NQO1,PDX1,RARA,RARB,SOD1,SOD2	996 (22)
FXR ligand-FXR-	complex	9,03E-09	ABCB11,ABCC2,ABCG5,ABCG8,APOC2,APOC3,APOE,LIPC,NR0B2,NR1I2,PLTP,PPARA,SCARB1,SLCO1B3	
IFNGR1	transmembrane	9,37E-09	CCL17,CCL5,CXCL12,EGF,FAS,ICAM1,IFNG,IL17A,IL1A,IL1B,IL2,IL23A,IL6,MMP2,MMP9,PDGFRB,PRKCG,TNF,TNFRSF1A	722 (17)
ZMPSTE24	peptidase	9,37E-09	ATF3,CXCL14,CXCR2,DIO1,ETNPPL,GHR,ICAM1,IGF1,IGF1R,IGFBP1,IGFBP3,IL6,JAK2,LMNA,SIRPA,SOCS1,SOCS3,STAT5B,TNF	868 (21)
IRAK4	kinase	1,05E-08	ATF3,CCL17,CXCL8,EDN1,FOS,IDE,IFNG,IFNL3,IL10,IL12A,IL12B,IL1B,IL23A,IL4,IL6,IRF5,JUN,NFKBIA,NFKBIZ,NOS2,OLR1,PPARG,SOCS1,TNF,TNFAIP3,ZFP36	665 (16)
TAF4	transcription reg	1,05E-08	AR,BDNF,CCN2,CCND1,COL6A3,DRD2,EGFR,FMOD,GAS5,GAS6,HBEGF,IL1RN,KLF5,LRRC15,MMP2,MMP3,PPARGC1A,PTN,RUNX1,SFRP2,SPP1,TFF1,TGFB1,TGFB3,THBS1,THBS2,VAV3,VEGFC,WWC1	371 (7)
HNRNPA2B1	other	1,07E-08	ABCB1,ADORA2B,CACNB2,CPS1,ELOVL2,ERBB3,FN1,GDF15,GJA1,GPRC5B,GSN,H19,IFNG,IL6,LEPR,MSRB3,NPR3,NR2F1,NR3C2,NTRK3,PAPPA,PBX1,PCSK9,PDE1A,PLCB4,PPARGC1A,RYR1,SERPINA1,SLC2A4,SNAP25,ST8SIA4,STK32B,SULT1A1,TFPI2,TGFB2,TOX3,VCAN,WWOX	
ANXA1	enzyme	1,09E-08	AKT1,CCL2,CD69,COL18A1,CXCR4,IL17A,IL1B,IL2RA,IL6,ITGAM,ITGB2,MMP2,NOS2,POMC,PTGS2,SELL,TIMP2,TLR4	655 (14)
ANXA7	ion channel	1,11E-08	ALOX15,BRCA1,BRCA2,DCC,FGF9,FYN,GCM1,GDNF,GSR,GSTP1,HGF,IGF1,IL12B,ITGA2,ITGAM,ITPR2,NFIA,NR3C1,PDX1,PML,PTEN,SLC2A2,TNFRSF1B,VHL	366 (7)
ZFHX3	transcription reg	1,18E-08	AFP,APOA1,APOA2,CCND1,DRD1,EBF1,F2RL1,GPR50,GSTP1,HLA-A,ID3,MIF,MYH7,MYOD1,NPR1,PAX2,PLA2G7,POMC,PRL,PTGER3,RGS2,RORA,SERPINA1,SIM1,SST,TRH,VIP,VIPR2	
POSTN	other	1,19E-08	ACTA2,BGLAP,DLK1,EGFR,FN1,HES1,LOX,LOXL2,LOXL3,MEF2C,MMP9,NOTCH1,PHEX,PTN,SPP1,TGFB1,TSLP	985 (22)
HEY2	transcription reg	1,22E-08	ACTA2,ALPL,BGLAP,BMP2,CACNA1C,GATA4,GJA5,IL6,MYH7,NKX2-5,NPPA,NR2F2,PROX1,SMTN,TBX2,TBX5	621 (13)
ITGAV	transmembrane	1,22E-08	BAX,CD36,COL1A1,COL1A2,FN1,FOS,HAS2,ITGAV,ITGB3,LDLR,MMP1,MMP2,MMP9,SERPINE1,TGFB1,TIMP1	835 (18)
KEAP1	transcription reg	1,22E-08	AHR,GCLC,GNAI2,GSTP1,HIF1A,HMOX1,IL18,IL1B,IL6,MMP9,NQO1,PPARG,SELP,TBXAS1,UGT1A1,VCAM1	804 (20)
MMP14	peptidase	1,22E-08	ATF3,CCL5,CSF2,CTNNB1,IL10,IL12B,IL6,JAG1,LRP1,MMP14,NR3C1,PTGS2,SLCO2A1,SMARCA1,STK38,VEGFA	821 (19)
ADIPOR1	transmembrane	1,27E-08	ARG1,CAT,IL10,IL4R,IL6,MEF2C,MMP3,MT-CO2,NOS2,PPARGC1A,SLC2A4,SOD2,TP53	1037 (21)
Cbp/p300	group	1,27E-08	ABCA1,BCL2A1,BRCA1,CKM,EPO,HP,IL1B,IL4,MYH7,PTGS2,RELA,TNF,UCP3	1031 (27)
CYP27A1	enzyme	1,27E-08	ABCA1,ABCC2,ABCG8,AGT,ANPEP,APOE,CYP3A5,CYP46A1,CYP7A1,HMGCR,SLC2A4,SREBF1,SREBF2	714 (16)
Gm21596/Hmg	transcription reg	1,27E-08	AFP,AGER,CXCL12,CXCR4,H19,HIF1A,IL10,IL1B,IL1RL1,IL6,NOS2,TLR4,TNF	731 (18)
MAPK12	kinase	1,27E-08	CCND1,FOS,IL10,IL12A,IL12B,IL17A,IL1B,ITGB8,JUN,MMP9,PPARGC1A,TNF,VDR	857 (19)
P2RX7	ion channel	1,27E-08	BAX,CCL2,IL1B,IL23A,IL23R,IL6,NLRP3,NOS2,TGFB1,TNF,TNFRSF1A,TNFSF10,TNFSF11	732 (15)
SFTPD	other	1,27E-08	CCL2,CD14,CTLA4,IL10,IL1B,IL2,MMP1,MMP12,MMP2,MMP3,MMP9,TGFB1,TNF	972 (20)
Tnf receptor	group	1,27E-08	C3,CCN2,CXCL8,ELANE,IL10,IL2,IL6,MMP9,NOS2,SELE,SERPINE1,TGFB1,TIMP1	756 (15)
ADORA2A	G-protein coupl	1,32E-08	ABCA1,ATP1A2,ATP2A2,ATP2B1,ATP2B3,BDNF,CCL17,CD28,COL3A1,FOS,GPLD1,HBA1/HBA2,HMOX1,IFNG,IL10,IL12B,IL2,IL4,IL6,KCNB1,KIF5A,KLC1,MMP9,NFKBIA,NOS2,NR4A3,PCSK1,PDYN,PPP3R1,PTGS2,ROCK1,SELE,STK38,TGFB1,TNF,VEGFA	760 (15)
ARHGDIA	other	1,46E-08	AR,ESR1,ESR2,FOS,IL5,NR3C1,RAC1,SCNN1A,SCNN1B,SCNN1G	742 (11)
CCL21	cytokine	1,46E-08	CCL2,CSF2,CXCL8,IFNG,IL13,IL2,IL4,IL5,P2RX4,TGFB1	751 (15)
HIF3A	transcription reg	1,46E-08	APLN,EDN1,EPAS1,HIF1A,PDGFRB,PLAUR,RARB,SLC2A1,STAT3,VEGFA	976 (14)
RLN2	other	1,46E-08	ACTA2,CD36,EDNRB,FOS,MMP1,MMP2,MMP3,TGFB2,TIMP1,VEGFA	641 (13)
cyclooxygenase	group	1,63E-08	ARG1,FOS,HMOX1,IGF1,IL10,IL13,IL5,IL6,MMP3,PTGS2,RGS2,UCP1	949 (18)
GSK3A	kinase	1,63E-08	BAX,FTO,GATA4,IRS1,KDR,NKX2-5,SELP,SERPINE1,TNF,TNFSF10,TNNC1,TNNI3	999 (20)
HDAC7	transcription reg	1,63E-08	CCND1,CTNNB1,EDN1,ETNPPL,IGFBP1,IL12B,IL2,IL6,NFATC1,NPPA,PTEN,SCNN1A	948 (17)
NT5E	phosphatase	1,63E-08	COL1A1,COL3A1,IL13,IL13RA2,IL1B,IL4,IL6,SERPINE1,SPP1,TGFB1,TIMP1,TNF	911 (17)
Pde4	group	1,63E-08	CCL2,CD14,CD40,CXCL5,HMGCR,ICAM1,IL2,IL2RA,IL6,LDLR,TNF,TP53	797 (17)
S1PR1	G-protein coupl	1,63E-08	CCND1,HGF,ICAM1,IFNG,IGF1,IL1A,IL4,IL6,MAF,PTGS2,TNF,VCAM1	983 (22)
SUMO2	enzyme	1,73E-08	ABCB11,AGT,CAV1,CAV2,CCN3,CD59,CTH,GRB14,HLA-G,HMGA1,HSPA8,IL6,IRS1,MMP14,NR0B2,PIK3R1,PLA2G3,TNC	913 (14)
EPHB4	kinase	1,76E-08	BMP2,BMP4,BMP7,CXCR4,FGFR2,GATA2,IGF2,KDR,KIT,NCAM1,POU5F1,RUNX1,SMAD6,STAT5B,TBX2,TGFB1,TGFB2,TGFBR1,TGFBR2,WNT5A	
IGFBP2	other	1,76E-08	AKT1,CCND1,DDAH1,EGFR,EPHA4,ESR1,FN1,GDF15,GHR,IGFBP1,IGFBP3,LGR5,MMP2,NF1,NUP210,POSTN,PTEN,STAT3,TGFB3,THBS2	1086 (23)
BMP6	growth factor	1,78E-08	ACTA2,ADD3,BMP4,CCN2,CYP11A1,CYP11B1,CYP1B1,EPHX1,ETV5,FSHR,HAMP,HBEGF,HMOX1,ID3,IL1A,IL6,MBL2,PCSK6,PITX2,POMC,PTGS2,SERPINE1,SLC20A1,SMARCA1,TIMP1,TMPRSS6,TXNRD1,VCL,VEGFA	745 (19)
CD69	transmembrane	1,78E-08	CCL5,CD69,IL13,IL17A,IL1B,IL2,IL23R,IL2RA,IL4,IL5,SOCS3,TGFB1,TGFB2,TNF	887 (18)
GRK2	kinase	1,78E-08	BAX,CD46,CDKN2B,FOS,IL6,INSR,LHCGR,NPPA,TNF,TNFRSF11B,TNFSF11	873 (19)
IRAK3	kinase	1,78E-08	ACTA2,BCL2A1,CCN2,COL1A1,IL12B,IL6,IRF5,NFKBIA,NOS2,SOCS1,SOD2,TGFB1,TNF,TNFAIP3	637 (18)
MAP2K2	kinase	1,78E-08	ALDH1L1,CDKN2A,ETV5,FOS,HIF1A,ICOS,IL1B,IL6,INS,IRS1,ITGA2B,ITGB3,PDGFRA,VEGFA	1033 (19)
NOS1	enzyme	1,78E-08	ADIPOQ,BDNF,EPO,FOS,HIF1A,IL1A,IL1B,IL6,OGG1,PDE5A,RELA,SLC2A1,SOCS1,TNF	832 (20)
Ren2	peptidase	1,78E-08	COL3A1,CYBA,CYBB,CYP11B1,GNAI2,MT-CO1,RAC1,REN,SPP1,TIMP1,VEGFA	770 (9)
MECP2	transcription reg	1,90E-08	ABCB1,APOE,BDNF,BRCA1,CDKN2A,CDKN2B,DPP4,ESR1,FKBP5,FOXP3,GABBR2,GRIA1,GSTO1,GSTP1,HBA1/HBA2,IFNG,IGFBP3,IRAK1,IVD,KCNJ6,LMNA,NPY1R,PTGS2,RARB,S100A4,SGK1,SLC12A5,SLC2A3,SLC6A2,TFPI2,TH,TPH2,VEGFA	891 (20)
SUMO3	other	1,97E-08	AGT,CAV1,CAV2,CCN3,CD59,CTH,GRB14,HLA-G,HMGA1,HSPA8,IL6,IRS1,MMP14,PLA2G3,PML,TAP1,TNC	863 (13)
RPSA	translation regu	2,06E-08	CCL5,CSF2,IL1A,IL1B,IL1R1,IL6,MMP2,NOS2,PTGS2,REL,TAP1,TLR4,TNF,TOLLIP,TRAF1	987 (17)
SUMO1	enzyme	2,06E-08	ABCB11,ATP2A2,CCND1,CRYBB3,DHFR,HBB,HP,IL6,NOS2,NPPA,NR0B2,NR3C1,PDX1,PLIN1,TAP1	930 (24)
drotrecogin alfa	biologic drug	8,91E-04	NPPA,NPPB,TNNI3	

ANXA2	other	2,10E-08	AKT1,ANG,BAX,CDK6,FAS,IGFBP3,IL6,JUN,MMP1,MMP2,PCSK9,PLG,PTEN,PTGS2,TNF,TP53	971 (20)
NDRG1	kinase	2,10E-08	ATF3,CCND1,CTNNB1,CXCL5,CXCL8,FOS,IL1A,JUN,MMP1,PARP1,PML,SMAD2,SMAD3,SMAD4,TP53,VEGFA	1062 (22)
SELP	transmembrane	2,10E-08	APOL3,BCL2A1,CCL2,CSF2,CXCL8,CXCR4,CYP1B1,IGF1,IL1B,IL4R,IL6,PLAUR,RELA,SELP,THBD,TNF	842 (18)
ZBTB7B	transcription reg	2,10E-08	AHR,COL1A1,COL1A2,CSF2,IFNG,IL10,IL13,IL17A,IL1R1,IL2,IL2RA,IL2RB,IL4,MAF,TNF,TNFRSF4	649 (13)
MUC1	other	2,11E-08	ABCC1,ARG1,CAT,CCND1,CD40,CTNNB1,CXCL8,EGLN3,GCLC,HGF,HIF1A,HLA-DRA,IKBKB,IL10,IL6,NFKBIA,OASL,RELA,SOD1,SOD2,TERT,TNF	989 (18)
NRIP1	transcription reg	2,11E-08	ACAA2,APOA1,CCND1,CDKN2A,CIDEA,CPT1B,CYP2C8,HAS2,IL1B,IL6,OPLAH,PDK4,PGR,PRL,PTGS2,RARB,SDHB,SLC36A2,SMAD6,TNF,TNFSF4,UCP1	951 (24)
ID1	transcription reg	2,12E-08	CCN2,CCND1,CDKN2A,EVX1,FGFR3,FN1,ICAM1,IGF2,IL2,Ly6a (includes others),MMP14,MMP2,MMP9,MYOD1,NOTCH1,POU5F1,PPARGC1A,SIRT1,TERT,TF,THBS1,TMPRSS6,TNF,TYMS	936 (20)
KAT2B	transcription reg	2,22E-08	ABCB1,CCL2,CCN2,CKM,COL1A2,FOXP3,HBB,HLA-B,IL9,ITGAM,NPPA,NR1H3,PKHD1,PTGS2,RARB,TFF1,TGFBR2,TNF,TP53	1096 (23)
MTA1	transcription reg	2,22E-08	ACTC1,ADRB2,BRCA1,CCN4,CCND1,CDKN2A,CTNNB1,ESR1,MMP2,MMP9,MT-CO2,PAX5,PGR,PIK3R1,PITX2,SERPINB1,SIRT1,STAT3,TNF	1049 (21)
TBK1	kinase	2,30E-08	ATM,CCL5,CD40,CXCL8,EDN1,ICAM1,IFNG,IFNL3,IL10,IL12A,IL12B,IL15,IL15RA,IL18,IL1A,IL1B,IL6,NFKB1,NFKBIZ,OAS3,OASL,PTGS2,RELA,SELE,SLCO3A1,TLR2,TNF,TSC22D1,VEGFA	787 (18)
BCL3	transcription reg	2,60E-08	AGT,CCL5,CCND1,CD40,CD69,CXCL8,FABP3,HLA-DQB1,ICAM1,IFNG,IL10,IL13,IL1B,IL23A,IL4,IL5,JUN,PDK4,PLAUR,TNF	786 (17)
ADCY	group	2,67E-08	COL3A1,CYP1B1,FOS,GJA1,IL1B,IL6,ITGA2B,LEP,NFATC1,PER1,TNF,TP53,TXN	973 (23)
CETP	enzyme	2,67E-08	APOA1,APOB,APOE,CETP,HMGCR,LCAT,LDLR,LPL,NR0B2,PLIN1,PPARG,SREBF1,TNF	906 (21)
IL17a dimer	complex	2,67E-08	CCL2,CCL5,CSF2,IFNG,IL10,IL13,IL1A,IL1B,IL3,IL6,IL9,LCN2,TNF	614 (10)
MAP2K5	kinase	2,67E-08	CCND1,CXCL8,CYP24A1,FOS,JUN,KLF5,MEF2A,MMP9,NPPA,NR4A3,PTGS2,TH,THBS1	772 (20)
JAK	group	2,71E-08	CCL2,CD40,HIF1A,IFIH1,IGF1,IL10,IL12B,IL17A,IL33,IL6,MMP9,PTGER2,PTGER4,PTGS2,REG3A,SOCS1,SOCS3,STAT5A	856 (20)
SELPLG	other	2,71E-08	APOL3,BCL2A1,CCL2,CXCL8,CXCR4,CYP1B1,FOS,IFNG,IGF1,IL10,IL1B,IL2,IL4R,ITGAM,PLAUR,RELA,THBD,TNF	873 (18)
GNRH1	other	2,86E-08	CYP11A1,CYP17A1,CYP19A1,FOS,FSHR,GNRH1,GNRHR,HSD11B1,HSD3B1,IGF1,IL1B,IL2RA,JUN,NOS1,PGR,PLAT,PPP3CA,PRKCQ,PRL,PSEN1,PTGS2	928 (16)
TBP	transcription reg	2,98E-08	BCL2A1,COL1A1,EDNRA,FN1,FOS,FOXP3,GATA4,HLA-A,HMGCR,IGF1R,IGF2,IL2,LDLR,NF1,NFKBIA,PPARG,PTGS2,SCGB1A1,TFF1,TNF,TNFAIP3,TNFSF11,XDH	1074 (22)
BCR (complex)	complex	3,02E-08	BCL2A1,CCND1,CD69,CDK6,CDKN2A,CTNNB1,CXCR4,EP300,FAS,FOS,FOXO1,IFNG,IL10,IL12RB1,IL13,IL2,IL23A,IL24,IL2RA,IL2RB,IL4,IL6,ITGA4,ITGB1,JAK2,NAMPT,NFKB2,PLA2G5,PTGS2,PTPN22,REL,RELA,SELL,SLC2A1,TLR9	620 (17)
INPP5D	phosphatase	3,17E-08	ARG1,CCND1,CD69,CXCL8,FAS,FOXP3,HAMP,IFNG,IL10,IL12B,IL2,IL2RA,IL4,IL6,MITF,SELP,TNF	887 (19)
miR-182-5p (an	mature microRN	3,17E-08	ADCY6,CDH4,CDK6,CLDN17,FN1,FOXO1,FOXO3,IGF1R,ITGA4,ITGB1,LRP6,MITF,NCAM1,RAC1,RARG,SERPINE2,VWF	
LXR ligand-LXR-	complex	3,22E-08	ABCA1,ABCG5,ABCG8,APOE,CETP,CYP7A1,PLTP,SCARB1,SREBF1	
SLC30A7	transporter	3,22E-08	AKT1,ALOX12,CD36,EPHX1,EPHX2,FABP3,INSR,IRS2,SLC27A4	532 (7)
VLDLR	transporter	3,22E-08	ABCA1,APOB,FOS,IL6,SERPINE1,SLC2A1,STAT3,TNF,TNFAIP3	955 (20)
SCAP	other	3,32E-08	ABCA1,ACAA2,ATF3,C5,CYP4F2,DHCR7,DLK1,FADS2,FDFT1,HMGCR,HMGCS2,INSIG1,LDLR,LSS,MSMO1,MVK,OLR1,PCSK9,PLA2G4C,PON1,PTGER4,PTGS2,SLC7A1,SREBF1,SREBF2,TRIB3	723 (16)
ESRRG	ligand-depende	3,34E-08	CYP19A1,FGF1,HGF,KCNE1,KCNH2,KCNJ1,KCNQ1,KLK1,LDHA,LPIN1,LPL,NR0B2,NR3C1,PCK1,PDK4,PPARA,TFF1,UCP3,VEGFA	872 (16)
CRYAB	other	3,37E-08	BMP2,CCND1,DES,HAMP,HSPB2,HTT,IFNG,IL12B,IL17A,IL2,IL6,MME,MYOD1,VEGFA	627 (16)
CTSB	peptidase	3,37E-08	ACTA2,ARG1,CCND1,COL1A1,CYBB,IL10,IL1B,IL4,KDR,NOS2,PLAUR,RAC1,TNF,VEGFA	1034 (21)
ECSIT	transcription reg	3,37E-08	CXCL8,HMOX1,IL1B,IL1RN,IL6,NFKB1,NFKB2,NFKBIA,PLAUR,PTGS2,SOD2,STAT5A,TNFAIP3,TRAF1	596 (13)
Ifnar	group	3,41E-08	AXL,C3,CCL2,CCL5,CD40,HLA-A,HLA-G,IFIH1,IFNG,IL12B,IL15,IL1B,IL6,ITGA4,MMP9,NLRP3,OASL,PSMB8,PSMB9,RNF213,SPP1,TAP1,TGFBR1,TLR2,TLR7,TNF,TNFSF10,VCAM1	687 (15)
ELF3	transcription reg	3,63E-08	ANGPT1,ANGPTL4,CSF2,ERBB2,FN1,FOLH1,IL12B,IL6,MET,MMP3,NFKB1,NOS2,PTGS2,TGFBR2,TIMP3	804 (18)
FECH	enzyme	3,63E-08	APOA4,CCND1,COL3A1,COL4A1,COL6A3,CYP1A2,CYP2C8,CYP2E1,CYP2J2,CYP3A5,CYP4A11,CYP7A1,FABP1,HMOX1,SLC10A1	
KRT17	other	3,63E-08	CCL11,CCL17,CCL5,CCR5,CXCR2,IL10,IL13,IL15,IL1B,IL4,IL6,MMP3,MMP9,SPP1,TNF	125 (4)
PRKAR1A	kinase	3,63E-08	BAX,BGLAP,CCND1,CDC42,EGFR,ERBB2,ERBB3,GATA4,IL2,LEP,NKX2-5,PPARG,SMAD3,SST,VDR	699 (18)
TIRAP	other	3,63E-08	CCL5,CD40,CXCL8,ICAM1,IFNG,IL10,IL12B,IL15,IL1B,IL6,PTGS2,RELA,SELE,TNF,VCAM1	643 (18)
TNFSF14	cytokine	3,63E-08	CCL5,CD40,CSF2,CXCL12,CXCL5,F2RL1,ICAM1,IFNG,IL13,IL6,LIPC,MMP9,TGFB1,TNF,VCAM1	944 (18)
VAV1	transcription reg	3,63E-08	BAX,BCL2A1,CCND1,CD69,FOS,IFNG,IL2,IL4,IL6,JUN,PTGS2,REL,RELA,TNF,VEGFA	955 (19)
MC4R	G-protein coupl	3,71E-08	FOS,GRIA1,HAMP,IL10,IL13,IL6,LEP,MTTP,NPY,PSMA4,TNF,TRH	934 (24)
CEBPE	transcription reg	3,80E-08	ALOX5AP,CD14,CDK6,ELANE,F7,IL10,IL12A,IL18,IL1RN,IL5RA,IL6,ITGAM,LCN2,LTF,MMP2,MMP9,PTGS2,SELL,TLR9,TNF	544 (10)
PTPRJ	phosphatase	3,80E-08	CD69,CEBPD,EDN1,FOS,HBEGF,IL12A,IL18,IL1A,IL6,LTA,MET,NFKBIZ,OASL,PLAGL1,PLAT,PLAUR,PTGS2,TNF,TSC22D1,TSHR	703 (15)
CLOCK	transcription reg	3,87E-08	ACVR2B,ANGPTL4,AVPR1A,CA1,CALD1,CCN2,CCND1,CLOCK,DBP,EGFR,F2R,F7,FGF1,FKBP5,GCK,GDNF,GJA1,HAMP,HAS2,HLA-DQB1,HMGCS2,ICAM1,IKBKE,ITM2C,KCNN3,LPIN1,MAPK8,MGP,MMP7,MSMO1,MTPN,MYLK,NPAS2,NR0B2,OAS3,OXSR1,PAFAH1B2,PDGFRB,PER1,PER2,PICALM,POR,PPARA,RGS5,SLC12A3,SLC20A1,SRR,THBD,THBS1,TIMP4,TNFAIP1,TP53BP1,WNK1,WNK4	703 (11)
EGR3	transcription reg	4,17E-08	EFNB1,GDNF,ID3,IFNG,IL2RA,IRAK1,JUN,MYB,NF1,NOTCH1,PTPN11,RET,RORA,SLC15A2,SLIT2,SOCS1,SOCS3,TNFSF11	829 (15)
HBEGF	growth factor	4,17E-08	ANGPTL4,AR,BMP2,CCND1,CXCR4,EGFR,ELN,GJA1,IGFBP3,ITGB1,LDHA,MAPK1,MMP9,NOS2,NPPB,PDK4,PTGS2,VEGFA	1000 (20)
mir-1	microRNA	4,31E-08	ADD1,BDNF,CACNB2,CCL2,CSF2,CXCL8,DHX15,EDN1,ESR1,FN1,GJA1,HSPD1,IGF1,IGF1R,IL1B,KRAS,MET,MMP9,MYLK,MYOD1,NELFCD,NOTCH3,PICALM,POGK,RASA1,SMARCA4,SRSF9,TNF,TNNT2,VEGFA,VEGFC	851 (17)
Angiotensin II re	group	4,59E-08	ATP1A1,CCL2,CXCL8,EDN1,GLP1R,NOS3,NPY,SERPINE1,TH,TIMP1,VEGFA	889 (24)
GIP	other	4,59E-08	ADIPOQ,BAX,CALCA,FOS,GCG,GIP,IL6,LPL,RGS2,SPP1,TNF	817 (20)
HDC	enzyme	4,59E-08	CYP24A1,CYP27B1,FOS,IFNG,IL6,LEP,PTGS1,PTGS2,SELP,TNF,UCP1	886 (16)
Integrin	complex	4,59E-08	AHR,CCND1,ESR1,FOS,JUN,MMP1,MMP14,MMP9,SOCS3,TGFB2,VEGFA	795 (17)
PSMB8	peptidase	4,59E-08	GJA1,IL1A,IL6,IRS1,NFKB1,NFKB2,NFKBIA,NOS2,PTGFR,PTGS2,TNFAIP3	890 (17)
S1PR2	G-protein coupl	4,59E-08	ACTA2,CCL5,FOS,ICAM1,JUN,NOS3,PTGS2,SELE,TGFB1,TIMP1,VCAM1	777 (16)
ACE2	peptidase	4,67E-08	ACTA2,AGT,CCN2,FN1,IL1B,IL6,NOS1,NOS3,SERPINE1,TNF	1002 (21)
APOA4	transporter	4,67E-08	APOB,FABP2,FOS,FOXO1,IFNG,IL4,MTTP,SCARB1,SELP,TNF	722 (13)
F10	peptidase	4,67E-08	CCL2,CCN2,CXCL8,ICAM1,IL6,MIF,MMP2,SELE,VCAM1,VEGFA	740 (17)
NHLH2	transcription reg	4,67E-08	ADGRE1,ADRB2,ADRB3,GNRH1,IL6,PCSK1,POMC,TRH,UCP1,UCP2	
TFAP2B	transcription reg	4,67E-08	EDN1,EPAS1,ERBB2,IGF2,KISS1,KIT,MMP2,SLC19A1,SOD2,TERT	995 (24)
TRAF4	other	4,67E-08	CCL11,CCL5,CCND1,HAMP,IL13,IL4,IL5,IL6,IL9,STEAP4	599 (14)
CBFB	transcription reg	4,85E-08	ARL4C,CCR5,CTLA4,FOXP3,GPLD1,GPR83,HTRA1,ICAM1,IL2RA,IL2RB,IL4,ITGA2B,MPO,PPARG,PTGER4,RUNX1,SPP1,STAT4,TBL2,TGFBR1,TGFBR2,TGFBR3,TLR7,TNFRSF4,TNFSF11	855 (14)
CEACAM1	transporter	5,02E-08	ANG,ANGPT1,CD40,COL18A1,CXCL8,CXCR4,ICAM1,IFNG,IGF1R,IL2,IL2RB,KDR,LEP,NOTCH3,TIE1,VEGFA,VEGFC	889 (20)
DACH1	transcription reg	5,02E-08	BMP4,CXCL8,FGF5,FGFR1,FOS,IGFBP3,IL6,JUN,MEF2C,MMP3,PLAT,POU5F1,PTGS2,SERPINE1,STC2,TGFB1,TNFAIP3	1065 (17)
FCER1G	transmembrane	5,02E-08	CCL5,CD247,CD69,CSF2,CXCL8,IL10,IL12B,IL13,IL1B,IL1RN,IL2,IL4,IL5,IL6,KIR2DL4,PTGS2,TNF	759 (19)
Ciap	group	5,31E-08	CCL11,CCL5,CCND1,CSF2,IL10,IL12B,IL17A,IL1A,IL1B,IL22,IL6,IL9,TNF	890 (14)
IL36B	cytokine	5,31E-08	CD40,CXCL8,IFNG,IL12A,IL12B,IL17A,IL18,IL1B,IL23A,IL4,IL6,NFKBIZ,TNF	712 (15)
Mt2	other	5,31E-08	ATF3,CCND1,FOS,GSTM3,GSTP1,IL1B,IL6,JUN,LEP,LPL,RELA,SERPINE1,TNF	971 (18)
Relaxin	group	5,31E-08	AQP3,CD36,EDN1,GATA4,GJA1,HAS2,MMP1,MMP9,NKX2-5,NOS1,NOS3,TIMP1,TNFRSF1A	914 (20)
ZEB2	transcription reg	5,50E-08	ALPL,AXL,CCND1,CDKN2A,CDKN2B,CX3CR1,CYP4F3,ELANE,GAB2,GATM,IL2,IL7R,LTA4H,MPO,MS4A2,MYB,PTEN,SELL,TERT,VCAM1	849 (19)
Raf	group	5,59E-08	ANPEP,BGLAP,CCND1,CDKN2A,EDN1,EGF,ETV5,FOS,GDF15,HAMP,HAS2,IGF1R,JUN,PLPP3,PPARGC1A,PRL,PTEN,RARB,RET,SEMA6A,SH2B3,SLC20A1,TNFAIP3	1071 (23)
SOX9	transcription reg	5,59E-08	AR,CCN2,COL1A1,CTNNB1,CXCR4,FOS,GAS7,H19,KIT,LBP,LRP6,MAPK3,MITF,PHEX,PPARG,PRKCA,PTGDS,SCGB1A1,TCF7L2,UCP3,VEGFA,VNN1,WNT3	931 (24)

HSP90B1	other	5,76E-08	CD40,CDC42,CXCL5,ESR1,GP1BA,IFNG,IL12B,IL17A,IL18,IL1B,IL22,IL23A,IL6,ITGA4,ITGB2,NOS2,TLR2,TLR4,TLR9,TNF,VAMP8	707 (17)
Agtr1b	G-protein coupl	6,01E-08	AGT,CCN2,FOS,NOS2,PTGS2,SLC2A4,SLC6A2,VCAM1	860 (19)
Ferritin	complex	6,01E-08	BMP6,CCL5,HAMP,HBB,ICAM1,IL1B,NFKBIA,NOS2	721 (14)
Ighg2b	other	6,01E-08	IFNG,IL10,IL12B,IL1B,IL2,IL4,IL6,TNF	597 (7)
elcatonin	biologic drug	3,31E-03	MMP2,TNFRSF11B,TNFSF11	463 (7)
IL12RB2	transmembrane	6,01E-08	CSF2,IFNG,IL17A,IL18,IL18R1,IL23A,TNF,VCAM1	778 (20)
MAP3K2	kinase	6,01E-08	CSF2,CTNNB1,IFNG,IL2,IL4,IL6,TERT,TNF	735 (17)
MYDGF	cytokine	6,01E-08	IL10,IL13,IL17A,IL22,IL4,IL5,IL9,MAF	
UTS2R	G-protein coupl	6,01E-08	ABCA1,ACAT1,HAMP,MSR1,NR1H3,PPARD,PPARG,SCARB1	
RC3H1	enzyme	6,15E-08	CCL25,CCL5,CXCL13,ICOS,IFNG,IL13,IL17A,IL1A,IL1B,IL4,IL5RA,IL6ST,SPP1,TNFRSF1B	551 (10)
BECN1	other	6,23E-08	BAX,CCL5,HTT,IL12B,IL13,IL1B,IL23A,IL4,IL5,IL6,MYH7,NPPA,SOD2,SPP1,TNF	830 (19)
mir-10	microRNA	6,52E-08	ALOX5,AR,ARG1,BAX,BMPR2,CCL2,CD40,ERBB2,ERBB3,FGFR3,GAB2,GJA1,HIF1A,IGF1R,IGF2,IL6,IL6R,let-7,LIN28A,MAF,NF1,SMAD2,SMAD4,TGFBR1,TNF,TP53,VEGFA	847 (18)
ADAM12	peptidase	7,04E-08	ADAMTSL5,ADIPOQ,BGLAP,CCN2,COL6A3,CSF2,DPT,EGFR,FBN1,GAS6,GDF15,HGF,IGFBP3,IL1RL1,IL33,MGP,MMP3,MYOD1,OLR1,PPARG,SERPINE1,SERPINE2,SFRP2,VWF	889 (18)
NTRK2	kinase	7,04E-08	ABCB1,ABCG2,ANGPT1,BDNF,BMP2,CCND1,CDKN2B,FOS,HGF,JAG1,NOS2,PIK3R1,POMC,PTEN,SERPINE1,SERTAD1,SLC12A5,SNAP25,SPP1,TGFBR1,THBS1,TNF,TNFSF10,VEGFA	1032 (23)
TFAP2C	transcription reg	7,04E-08	ADA,CCN2,CYP11A1,EGFR,ERBB2,ESR1,F2R,FKBP4,FOXC1,GPX1,JAG1,MMP14,MMP2,MMP9,PITX2,RARA,RASA1,RET,SLC19A1,SOD2,TFF1,THBS1,TIMP1,TNFAIP3	977 (19)
enalapril	biologic drug	1,22E-12	ABCC2,ACE,AGT,AGTR2,C4A/C4B,CDKN2A,CLU,FGA,GCGR,GSTM3,HGF,IGFBP1,KDR,LCN2,PDX1,PRL,PTH1R,REN,SERPINE1,SPP1,TGFB1,TGFBR2,TIMP1,UCP2,VCAM1	874 (14)
DUSP10	phosphatase	7,60E-08	IFNG,IL2,IL4,IL6,KLF5,TNF,TP53	603 (14)
TBXA2R	G-protein coupl	7,60E-08	GDNF,ICAM1,IL2,PTGS2,TBXA2R,TGFB1,VCAM1	763 (19)
TLR7/8	group	7,81E-08	BCL2A1,CA2,CCL2,EDN1,IL10,KCNMA1,MCOLN2,NFKBIA,NFKBIZ,NPR1,PLAUR,PTGS2,RGS20,TNF,TNFAIP3,TRIB3,VDR	874 (16)
CYP2E1	enzyme	7,90E-08	CAT,CD14,COL1A2,CYP4A11,GCLC,HMOX1,IL6,NCF2,PON1,PTGS2,TLR4,TNF	818 (18)
DDX5	enzyme	7,90E-08	ACTA2,BAX,CCND1,FOS,HTRA1,JUN,LCN2,S100A4,TGFB1,TIMP1,TP53,WNT5A	1055 (21)
enterotoxin B	biologic drug	4,14E-10	BDNF,CCL11,CCL17,CCL2,CCL5,CD40,CD69,CTLA4,CXCL12,CXCL13,CXCR4,ICAM1,IFNG,IL10,IL10RB,IL12A,IL12B,IL17A,IL1B,IL2,IL2RA,IL33,IL4,IL5,IL6,mir-146,SERPINA3,TNF	880 (12)
entolimod	biologic drug	1,10E-03	HMOX1,IL10,IL1B,IL6	507 (11)
GNAI3	enzyme	7,90E-08	CCL2,CCL5,CCL8,CSF2,CXCL8,IL24,IL3,IL6,RGS19,SPP1,TNF,VEGFA	830 (21)
HMGA2	enzyme	7,90E-08	BCL2A1,CXCR4,IGF2BP2,IL15,IL2,IL2RA,LPL,MMP1,SCNN1A,SPP1,SREBF1,TERT	811 (14)
PDGFC	growth factor	7,90E-08	ACTA2,CCND1,COL1A2,CTNNB1,FLT1,KDR,PDGFRA,PDGFRB,TGFB1,TIMP1,TIMP2,VEGFA	921 (18)
PRDM16	transcription reg	7,90E-08	AGT,CIDEA,DIO2,FGF21,GPX3,HGF,MYH7,MYOD1,PPARGC1A,RETN,SERPINE1,UCP1	551 (14)
RPS6KA5	kinase	7,90E-08	CDKN2A,CDKN2B,FOS,IL10,IL12A,IL12B,IL1B,IL2RA,IL6,JUN,PTGS2,TNF	942 (21)
SLC2A4	transporter	7,90E-08	BDNF,GCK,GRIA1,INSR,LNPEP,MLXIPL,NPPA,RBP4,SLC2A1,SLC2A3,SLC2A4,SREBF1	913 (24)
SOCS6	other	7,90E-08	CEBPD,HBEGF,IL12A,IL18,IL1B,IL2,IL23A,PLAT,PTGS2,STAT3,STAT5A,TNF	773 (15)
BCL2L1	other	7,93E-08	ALOX5AP,BAX,CXCL8,DHFR,EPO,FAS,FN1,GSR,IL1B,LTA,Ly6a (includes others),MMP9,NOS1,NQO1,PTPRC,TH,THBS1,TIMP1,TNF,TNFRSF11B,TNFRSF1A,TNFSF10	911 (18)
FOXL2	transcription reg	7,93E-08	ATF3,BCL2A1,BMP2,CDKN2A,CYP17A1,FAS,FOS,GNRHR,GPRC5B,ICAM1,IGF1,IL12A,NR4A3,PPARGC1A,PTGS2,RGS2,RSPO3,RXFP3,SMAD6,SOD2,TNFAIP3,TNFRSF1A	749 (14)
AIRE	transcription reg	8,05E-08	BMP2,BMP4,CCL17,CCL5,CYP1A2,FABP1,FABP2,FOXP3,GDF2,GIP,IFNG,IGF2,INS,ITIH3,LTF,MGAT5,MMP9,NPY,PTGDR,TLR8,TPH1	
miR-155-5p (mi	mature microRN	8,06E-08	AGTR1,CCL18,CCND1,CD69,CTLA4,CTNNB1,CXCL8,EGFR,F2,FADS1,FOXO3,IFNG,IKBKE,IL12A,IL12B,IL1A,IL1B,IL23A,IL6,KRAS,LPL,MAF,MEIS1,MET,MPZL1,MYB,NOS2,PDLIM5,PICALM,PIK3R1,PTGS2,RAC1,SERPINE1,SMAD1,SMAD2,SOCS1,TCF7L2,TNF,TXNRD1	792 (20)
IFN alpha/beta	group	8,43E-08	AXL,BAX,CCL2,CCL5,CCR2,CD40,CD69,CXCL14,GAS7,HLA-A,IFNG,IL10,IL15,IL15RA,IL6,ITGA2B,Ly6a (includes others),NOS2,SLPI,SOCS1,TLR2,TLR5,TLR7,TNFSF10,TNFSF13	813 (17)
TAL1	transcription reg	9,02E-08	ADCY3,ADGRG1,ARVCF,BHMT2,C3,CD69,CDK6,CDKN2A,CMA1,DOCK1,EVI5,FBN1,GATA2,GUCY1A1,GYPA,HBB,HLA-A,HLA-B,HLA-C,ICAM1,IL10RA,JUN,KIT,MPO,MS4A2,MYB,NFKB1,NFKBIZ,NOS1,NOTCH1,NR4A3,P2RY1,PPP3CA,PRSS8,PTGER4,PTK2B,RAPGEF5,REL,RELA,RUNX1,SLC2A3,TCF7,TNFAIP1,TNFAIP3,TNFSF10,TNFSF4,TOX,TSHR	789 (18)
26s Proteasome	complex	9,06E-08	ADARB2,AHR,AR,ARG1,BAX,BMP2,BRCA2,CCL2,CXCL8,EGF,EGFR,ESR1,FOXO1,GAS5,GCH1,GRIA1,HBEGF,HSD3B1,ICAM1,IL6,MMP12,NFKB1,NFKB2,NOTCH1,PGR,PKD1,PRKCA,PTEN,PTGS2,SFTPB,SMAD2,SOCS3,STAT5A,TNFSF10,TP53,TXNIP,VPS11	1115 (20)
EIF2AK2	kinase	9,16E-08	ARG1,ATF3,BAX,BCL2A1,BDNF,CCND1,CEBPD,CXCL8,ERAP2,FAS,FOS,IFNG,IL1A,IL1B,IL6,IRS2,MMP9,NFKB2,NFKBIA,NNMT,NOS2,OAS3,SELE,SOCS3,SOD2,TNF,TNFAIP3,TP53	770 (13)
CD4	transmembrane	9,27E-08	BAX,CXCL13,FAS,HIF1A,ID3,IFNG,IL10,IL15,IL2,IL22,IL2RA,IL4,MME,NOS2,TNF,TNFSF10	789 (24)
CD80	transmembrane	9,27E-08	BAX,CD28,CSF2,FAS,ICAM1,ICOS,IFNG,IGF1R,IL10,IL1B,IL2,IL2RA,IL4,IL5,IL6,TNF	711 (21)
MSX2	transcription reg	9,27E-08	ABCG2,ALPL,AQP3,AQP4,BGLAP,BMP4,CCND1,CTNNB1,EPHA4,HAMP,PPARG,PROX1,PTH1R,SPP1,TGFB2,TGFB3	886 (23)
PGF	growth factor	9,27E-08	ALOX5,ALOX5AP,ANGPTL4,CCL2,CXCL8,CXCR4,EDN1,FLT1,HIF1A,IL1B,IL6,JAK2,KIT,MMP9,SERPINE1,TNF	827 (17)
Hbb-b2	other	9,46E-08	CCR2,CCR5,CIITA,CXCR2,CYBA,CYBB,FN1,HFE,IL10RA,IL16,IL1B,IL2RB,ITGAM,LY86,NCF2,TF,TFRC,TLR2	587 (10)
MEF2A	transcription reg	9,46E-08	ACTC1,AQP4,ATP2A2,BDNF,CKM,CPT1B,EDN1,FOS,JUN,MEF2A,NPPA,PPARGC1A,SLC2A4,TGFB1,TGFB2,TGFB3,THBD,TNNC1	213 (4)
SERPINA1	other	9,46E-08	ANGPTL4,CCL2,CD36,CXCL8,CYP7A1,ELANE,HAMP,IL10,IL1A,IL1RN,IL2,IL6,LDLR,NFKB1,SCARB1,TLR2,TLR4,TNF	856 (17)
calpain	complex	1,01E-07	AQP4,CCL5,CCND1,CTNNB1,CUL9,GJA1,IL17A,IL2,IL2RA,IL6,NFKBIA,TLR4,TP53	924 (20)
TNFRSF4	transmembrane	1,01E-07	BCL2A1,CTLA4,FOXP3,IFNG,IL10,IL13,IL17A,IL2,IL4,IL5,IL6,IL9,SOCS1	668 (17)
IL36A	cytokine	1,04E-07	CD40,CSF2,CXCL8,IFNG,IL12A,IL12B,IL17A,IL1A,IL1B,IL23A,IL4,IL6,LCN2,NFKBIZ,TNF	712 (15)
RXRG	ligand-depende	1,04E-07	ACAA2,APOA1,APOC3,BGLAP,CYP24A1,CYP4A11,DRD2,FABP1,FABP3,LPL,PCK1,PDK4,POU5F1,TIMP2,TIMP3	802 (17)
CFLAR	other	1,08E-07	CTNNB1,CXCL8,FOS,HMOX1,IFNG,IL17A,IL1B,IL2,IL2RA,IL4,IL5,NFKB1,PDX1,TNF	612 (15)
DHX9	enzyme	1,08E-07	ABCB1,APOE,CCND1,CDKN2A,IL18,IL6,NOS2,PARP1,SST,TGFBR2,TNF	835 (19)
ELF1	transcription reg	1,08E-07	BRCA2,CD247,ERBB2,FES,IFNG,IL10,IL2,IL2RA,IL4,IL5,NCF2,SOD3,TLR9,TOLLIP	714 (22)
FZD8	G-protein coupl	1,08E-07	ACTA2,BMP2,BMP4,CCN2,COL1A1,CTNNB1,FN1,GATA4,TBX5,TP53,VCAN	844 (15)
GLIS2	transcription reg	1,08E-07	C3,CCN2,CCND1,COL1A1,IFNG,INS,LTBP2,MGP,MMP14,SERPINE1,TGFB1	762 (13)
hemoglobin	complex	1,08E-07	ADM,CXCL8,EDN1,GCLM,HMOX1,IL2,IL6,NOS3,NQO1,REN,TFRC	726 (17)
LEF1	transcription reg	1,08E-07	AR,BGLAP,CCND1,CDKN2A,CXCR4,ELANE,FAS,FGF10,FN1,HAS2,IL13,IL4,IL5,IL7R,MITF,MMP2,MMP7,NCAM1,PTGS2,SGK1,SPP1,TP53	1042 (26)
mir-221	microRNA	1,08E-07	ATM,CCN2,KDR,KIT,MAPK8,MMP2,MMP9,PIK3R1,PTEN,STAT5A,TGFBR1,TGFBR2,TIMP3,TP53	
NCR2	transmembrane	1,08E-07	CSF2,IFNG,IL2,IL22,NR4A3,PTGS2,THBS1,TNF,TNFSF11,TNFSF14,XCL1	651 (20)
PDK4	kinase	1,08E-07	ARG1,ASIC3,CPT1B,HIF1A,IL10,IL1B,IL6,KRAS,NOS2,PPARGC1A,TNF	1057 (24)
PLA2G4A	enzyme	1,08E-07	ANXA5,CCL2,CXCL8,GSTM5,ICAM1,IL1B,IL6,NOS2,PLA2G5,PTGS2,TNF	807 (20)
SP4	transcription reg	1,08E-07	CCND1,CHRNA3,EGFR,FLT1,IGF1R,IL2RB,LHCGR,mir-27,MYH7,NFKB1,RELA,SOD2,STAT3,VEGFA	636 (7)
Ngf	group	1,12E-07	AGTR2,BDNF,CALCA,CCND1,CHGB,CLU,FOS,HTT,JUN,MMP3,MYB,NCAM1,NOS1,NOS2,PLAUR,PRKCA,RARB,SERPINE1,TH,TP53,TRPV1	986 (22)
CXCL1	cytokine	1,18E-07	CXCR2,ICAM1,IL1B,IL6,KRAS,LEP,MRAS,SOCS3,TNF	920 (22)
ELN	other	1,18E-07	ELN,FN1,IL1B,IL6,MMP1,MMP12,MMP2,MMP9,TNF	1011 (23)
G6PD	enzyme	1,18E-07	ADIPOQ,G6PD,IGFBP1,IL10,PPARG,PRL,RETN,SREBF1,TNF	834 (18)
etanercept	biologic drug	1,31E-11	BMP7,CCL2,CD247,CXCL8,CYBB,ICAM1,IFNG,IL12B,IL1B,IL23A,IL6,MMP12,NOS2,NOX1,PTGES,PTGS2,SLC10A1,TNF	693 (16)
GATA5	transcription reg	1,18E-07	ACTC1,EDN1,HBA1/HBA2,MYH7,NPPA,PGR,SLC5A1,SLC9A3,TNNC1	
HSPB8	kinase	1,18E-07	BMP4,BMPR1A,BMPR2,CCL2,CXCL8,ICAM1,IL6,MITF,NPPA	779 (18)
LMO4	transcription reg	1,18E-07	ALK,CCND1,HP,PGR,PPARG,PPARGC1A,RYR2,SOD2,TFF1	1164 (26)
MZF1	transcription reg	1,18E-07	AXL,CD34,MS4A2,MYB,NOS1,PRKCA,SELL,SOD3,TGFB1	
NKX2-5	transcription reg	1,19E-07	ACTA2,ADORA1,BAX,DIO2,ECE1,GATA4,GJA1,GJA5,MEF2C,MYL2,MYLK,NKX2-5,NPPA,PITX2,RYR2,SCGB1A1,TBX5	871 (18)
PTPRC	phosphatase	1,19E-07	BCL2A1,CCL5,CCND1,CCR3,CXCR2,ICAM4,IFNG,IL10,IL13,IL17A,IL1B,IL2,IL22,IL4,IL5,TNF,VCAM1	661 (22)
IRF5	transcription reg	1,25E-07	AKT1,BAX,CCL5,COL1A1,COL3A1,COL4A1,CXCR4,EP300,FOXO1,IFIH1,IL12A,IL12B,IL23A,IL4,IL6,IRF5,NAMPT,NFKB1,OASL,PTGS2,RAC1,RELA,TGFB1,TNF,TNFSF10,VEGFA	865 (17)
AIMP1	cytokine	1,28E-07	CCL2,CCL5,CXCL8,ICAM1,IFNG,IL10,IL12A,IL12B,IL1B,TNF	845 (20)

FABP1	transporter	1,28E-07	ABCG5,ABCG8,AGER,CD36,CYP7A1,FAAH,HMOX1,NR1H4,PPARA,SLC10A2	717 (22)
KDM3A	transcription reg	1,28E-07	ACTA2,ADM,CCND1,CTNNB1,EDN1,GDF15,HMOX1,LEP,MMP9,SERPINE1	632 (12)
miR-19b-3p (an	mature microRN	1,28E-07	ALOX5,BMPR2,CCN2,CCND1,ESR1,MYLIP,PTEN,STAT3,THBS1,VEGFA	569 (7)
exenatide	biologic drug	5,20E-17	ABCA1,AGER,ARG1,BAX,CCN2,FOS,GCG,GLP1R,HMOX1,ICAM1,IL10,IL4,IL6,IRS2,ITGAM,MMP9,NOS2,PCSK1,PDX1,PER1,POMC,PTGS2,SIRT1,TXNIP	900 (22)
miR-96-5p (and	mature microRN	1,28E-07	ADCY6,CELSR2,FN1,FOXO1,HTR1B,IRS1,ITGB1,KRAS,MITF,SERPINE2	
ezatiostat	biologic drug	8,91E-04	ABCC1,GCLC,GCLM	
TNFSF9	cytokine	1,28E-07	CD14,CXCL8,ICAM1,IFNG,IL2,IL4,IL6,TNF,TNFRSF1A,VCAM1	775 (18)
ADRA1B	G-protein coupl	1,40E-07	ADRA1A,ADRA1D,BDNF,CCND1,CEBPD,COL3A1,DDAH1,FN1,FOS,IL6,IL6ST,JUN,LEP,LOX,NPPA,NPY,PPP3CA,VEGFA	828 (16)
TCF7	transcription reg	1,40E-07	BCL11B,CEBPD,CTNNB1,FOS,HNF1B,HNF4A,IL17A,IL2,MET,PPARA,PPARD,PPARG,RARA,RARB,RORA,SPP1,TCF7,UCP1	712 (13)
TWIST2	transcription reg	1,46E-07	BCL11A,BIN1,CCND1,CKM,CTNNB1,FN1,H19,IL1B,MAF,MGST3,MMP9,OSGIN1,POSTN,TERT,TGFB1,TNF	862 (16)
miR-29b-3p (an	mature microRN	1,47E-07	ACVR2A,ANGPTL4,CAV2,CCND1,CDC42,CDK6,COL1A1,COL1A2,COL3A1,COL4A1,FBN1,GAS7,GPR37,INSIG1,LOXL2,PIK3R1,PPIC,PTEN,TGFB3,TNFAIP3,TP53,VEGFA	685 (7)
FSHR	G-protein coupl	1,52E-07	ADIPOQ,ADIPOR1,ADIPOR2,AR,CPE,CYP11A1,CYP19A1,ESR2,FDX1,GATA4,HSD3B1,IGFBP3,LHCGR,NPPA,NPR3,PCK1,PGR,PLAT,VEGFA	930 (22)
FLT3LG	cytokine	1,54E-07	CCR5,CD40,CXCL12,FLT3,FOXP3,ICAM1,IFNG,IL10,IL15RA,IL1RL1,IL2,IL2RA,IL2RB,IL7R,ITGAM,MPO,PAX5,PTPRC,ROCK1,SOCS1,TERT	757 (20)
SIN3A	transcription reg	1,54E-07	BDNF,CARTPT,COL1A1,COL1A2,CYP1A1,ESR1,FOXP3,GSTP1,HLA-DRA,IFNG,LHCGR,MAP4,MMP9,PTGS2,RARB,SERPINE1,TERT,TFF1,TGFBR2,TP53BP1,TXNIP	920 (16)
NOTCH3	transcription reg	1,56E-07	ACTA2,DES,EPAS1,FN1,FOXP3,GUCY1B1,HES1,HES5,IL10,IL22,MMP9,MSR1,NOS2,NOTCH1,PBX1,PDGFRB,PRKCQ,RGS5,SMTN,TP53	752 (18)
LILRB1	transmembrane	1,58E-07	ADM,CAV1,CXCL8,FGFR3,FOXO3,IFNG,IL12B,ITGB1,MAF,MMP2,MMP9,TNF	714 (16)
LINC00963	other	1,58E-07	BAX,CXCR4,EGFR,FN1,FOXO3,ICAM1,IL4I1,IL6,ITGA9,TGFB1,TNF,TRIB3	743 (13)
MAPK13	kinase	1,58E-07	FOS,HAMP,IL10,IL12A,IL12B,IL1B,IL6,PPARGC1A,TNF,TP53,VDR,VEGFA	1005 (22)
Pkg	group	1,58E-07	BDNF,CAT,CTNNB1,EDN1,FOS,JUN,LGR5,PTGES,SLC6A4,SOD2,TXN,VCL	988 (18)
PYCARD	transcription reg	1,58E-07	ACTA2,CXCL8,IFNG,IL10,IL18,IL1B,IL22RA2,IL6,MMP9,NOTCH1,PTGS2,TNF	776 (18)
TCL1A	transcription reg	1,60E-07	CTSH,CXCR2,CYBB,ELANE,FCGR2B,FKBP5,FOS,FPR1,GDF15,HMOX1,IL17RA,IL1B,ITGAM,ITGB2,LCN2,LTF,Ly6a (includes others),MMP12,MMP9,MPO,MSR1,MYO5A,PTPRO,SLC11A1,STEAP4,TLR7	1039 (19)
NFYB	transcription reg	1,64E-07	ABCG2,ACTA2,BCL11B,BRD2,CACNA2D3,CAV1,CBS/CBSL,CDKN2A,CHEK2,CHPT1,COL1A1,COL1A2,CTC1,CTNNB1,DCC,DPP4,EPAS1,F8,FAS,FGFR2,GALNT2,GLA,GPR160,GRK3,HLA-DQB1,HLA-DRA,IGF1,ITM2C,LPIN1,LRP2,MSRA,MTAP,MTPN,MVK,NPR1,OGG1,PAX2,PCK1,PDGFRB,S100A4,SCARB1,SDF2,SLC39A8,SLC8A2,ST8SIA4,TBC1D22A,TGFBR2,TIMP3,TPM1,TTC39B,TYMS,UHRF1,VWF,ZNF524	145 (4)
GAB2	other	1,70E-07	ANGPT1,CD34,CD69,FOS,GSN,HAMP,HIF1A,IL13RA2,IL2,IL6,ITGA2B,ITGB3,KDR,SERPINE1,TNF	954 (20)
PAK1	kinase	1,70E-07	CCND1,CDKN2A,CTNNB1,CYP19A1,FN1,GCG,HES1,ITGAM,ITGB2,MMP14,MMP9,PGR,SCARB1,TP53,VEGFA	836 (18)
IFNL3	cytokine	1,84E-07	IFNG,IFNLR1,IL12A,IL12B,IL15,IL23A,IL2RA,IL5RA,MMP9,SOCS1,TLR2,TLR4,TNF	859 (18)
MTA2	transcription reg	1,84E-07	ACTC1,CDKN2A,FSHR,GATA2,HBB,HBG1,IFNG,IL2,IL4,JUN,KIT,MS4A2,SLC4A1	692 (7)
NCOA4	transcription reg	1,85E-07	ADH1B,AKR1B1,AR,CCN2,FABP2,FGFR2,FGFR3,FYN,GATA4,JAG1,MME,NR3C1,PLTP,TFF1	1039 (10)
WNT11	other	1,85E-07	CCN4,CTNNB1,GATA4,GDNF,MYH7,MYOD1,NKX2-5,NPPA,PHEX,POU5F1,TGFB2,THBD,TNNC1,TNNT2	
Hsp70	group	2,03E-07	CD14,CD40,CXCL8,HIF1A,ICAM1,IL12B,IL15,IL17A,IL1B,IL6,NFKBIA,NOD2,NOS2,NPC1,SCNN1B,SELE,TNF,VCAM1	564 (14)
CD3 group	group	2,15E-07	FOXP3,FYN,IFNG,IL10,IL13,IL17A,IL1B,IL2,IL22,IL2RA,IL4,IL5,LDHA,mir-146,NR1I2,PLA2G4C,STAT3,TFRC,TNF	622 (23)
TSC2	other	2,27E-07	ATF3,ATP6AP2,BAX,CCND1,CREG1,CTNNB1,FOS,GALC,GLA,GSN,HIF1A,HMGCS2,HMOX1,IFNG,IRS1,IRS2,LGR5,MGP,NTRK3,OGG1,PDGFRA,PDGFRB,PDK4,PRELP,PRKCA,PTEN,RELA,SLC14A1,SLC2A1,SOD2,UCP2,VAMP8,ZFP36	929 (19)
CDK5R1	kinase	2,34E-07	CD14,CXCL8,FOS,IL1B,IL6,MMP2,SERPINE1,SIRT1,SOX6,TH,TNF	1056 (23)
MST1R	kinase	2,34E-07	ACTA2,ARG1,CCND1,CTNNB1,FOS,IFNG,JUN,POU5F1,ROS1,SMAD2,TNF	840 (21)
Ncoa-Nr1i2-Rxr	complex	2,34E-07	ABCB1,ABCC2,CAT,CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,NOS2,SLCO1B1	
RARRES2	transmembrane	2,34E-07	ADIPOQ,CCL5,CYP11A1,CYP19A1,IL1B,IL6,LEP,LIPE,PLIN1,SLC2A4,TNF	834 (13)
CTLA4	transmembrane	2,63E-07	AHR,CD40,CD69,CXCL8,FOXP3,ICAM1,ICOS,IFNG,IL10,IL12RB1,IL12RB2,IL13,IL2,IL2RA,IL4,IL5,NFATC1,PADI2,SELE,SELP,SOD2,TGFB1	701 (22)
TCF7L2	transcription reg	2,72E-07	ACAA1,ADD1,ADGRG1,ADIPOR2,ALOX5,AQP3,AQP9,BIN1,BMP4,CASR,CCN2,CCND1,CDKN2A,CNP,CYP2C8,CYP2E1,CYP3A7,CYP7A1,EGFR,EPAS1,ERBB3,FGF21,FGFR2,GCLM,GLP1R,GSN,GSS,HMGCS2,HSPA2,ID3,IL10,IL12RB1,IL1RAP,IL23A,INS,IRS1,IRS2,JAG1,LDLRAP1,MMP1,MMP7,MYO6,MYRF,NCOR2,NINJ2,NPC1,PCK1,PDX1,PICALM,PKD1,PLAT,PLEKHG1,POLR1D,PPARGC1A,PRICKLE1,PTPN11,ROCK1,SLC12A2,SPP1,STK39,STRN,VEGFA	1141 (25)
AEBP1	peptidase	2,75E-07	ABCA1,ACTA2,APOE,CD36,COL1A2,NOS2,NR1H3,PPARG	943 (18)
CYBA	enzyme	2,75E-07	CYBB,EPAS1,FN1,IL6,SERPINE1,SOD2,TNF,VEGFA	793 (17)
FFAR1	G-protein coupl	2,75E-07	CD36,CYP1A1,HAMP,IRS2,NFATC1,PDX1,PPARGC1A,SLC2A1	945 (21)
HBB	transporter	2,75E-07	COL1A2,CXCL8,HBA1/HBA2,ICAM1,PECAM1,SERPINE1,TGFB1,VCAM1	682 (14)
HOXB5	transcription reg	2,75E-07	HAMP,ITGAV,ITGB3,MMP1,MMP2,PLAUR,RET,SHH	
CDK19	kinase	2,77E-07	ATF3,BAX,CDKN2A,CLU,CXCL8,DHCR7,DRAM1,EPHX1,FADS2,FAS,FDFT1,HBEGF,HMOX1,IL1A,JUN,LSS,MVK,NOTCH1,OSGIN1,PROCR,RXRA,TCN2,TGFB1,TRIB3,TSC22D1,TXNIP,VDR	
TNFSF13B	cytokine	2,84E-07	ADIPOQ,BAX,BCL2A1,CCL2,CD40,CSF2,CXCL8,FCGR2B,FOXO1,HLA-DQA1,ICAM1,IL10,IL15,JUN,LEP,MMP9,NAMPT,NFKB2,SELL,SPP1,TP53	939 (23)
CD86	transmembrane	2,92E-07	CD28,CD40,CD69,CSF2,CTLA4,FAS,ICAM1,ICOS,IFNG,IL10,IL2,IL4,IL5,IL6,NFKBIA,TNF,TNFAIP3,TNFRSF11A	683 (22)
BHLHE40	transcription reg	3,02E-07	ATP1B1,BDNF,CSF2,IFNG,IL10,IL2,IL2RA,MEF2C,MITF,MYOD1,PER1,SREBF1	1041 (21)
mir-33	microRNA	3,02E-07	ABCA1,ADIPOQ,AGT,CDK6,CPT1A,FRS2,GCK,IRS2,LPL,PPARG,PPARGC1A,SLC2A4	380 (6)
SAFB	other	3,02E-07	CCL5,CCN3,CDKN2A,CNTNAP2,CXCL8,FOS,HLA-C,HLA-DPA1,HLA-DPB1,HLA-DRA,HMOX1,IGF1,JUN,MLLT3,PSMB9,TBX2,TFF1,TNFRSF11B,TNFSF10	845 (9)
FEV	transcription reg	3,06E-07	ADRA1B,CALCR,CHGB,CXCR4,FOS,HCRTR1,HTRA1,ICAM1,ITGB1,NFIA,NPY,NR2F2,NR3C1,PDYN,PROX1,PYGB,SLC18A2,SLC22A3,SLC6A4,SLC7A8,SLIT2,SST,TCF7L2,TPH2,VCAM1	
SMAD5	transcription reg	3,07E-07	ALPL,BMP2,CCN2,DIDO1,GATA2,HAMP,ICAM1,ID3,RUNX1,SELE,SERPINE1,SMAD6,VCAM1,VEGFA	748 (13)
TRPM2	ion channel	3,07E-07	CXCL8,EPAS1,FOXO3,HIF1A,IFNG,IL12B,LDHA,NOS2,PTEN,SLC2A1,SOD2,TNF,VEGFA,VHL	992 (20)
BCL10	transcription reg	3,11E-07	CCL5,CSF2,CXCL8,IFNG,IL2,IL2RA,IL6,NFKB2,TNF,TNFAIP3	742 (15)
BMP10	growth factor	3,11E-07	BMPR2,ENG,ICAM1,MEF2C,NFKBIA,NKX2-5,NPPA,SELE,SMAD6,VCAM1	
DPH5	enzyme	3,11E-07	EGF,EP300,IFNG,IL1B,NFKBIA,RELA,SMAD3,STAT3,TNF,TP53	
LY96	transmembrane	3,11E-07	CCL5,CD40,CXCL8,IL12B,IL6,MMP1,NFKB1,SELE,TLR4,TNF	493 (14)
PIM2	kinase	3,11E-07	CCND1,FOXP3,IFNG,IL12RB2,IL2RA,PPARGC1A,SOCS1,STAT4,TP53,TP73	1009 (20)
PRDX2	enzyme	3,11E-07	AR,BAX,CCL2,CCND1,EPO,FOXO1,FOXP3,HAMP,ICAM1,PTGS2	834 (20)
Retnla	other	3,11E-07	ACTA2,HES1,HIF1A,IL17A,IL23A,JAG1,LEP,MYH7,NOTCH1,NPPA	766 (15)
RHOB	enzyme	3,11E-07	CXCL8,EGFR,ICAM1,IL6,ITGB2,ITGB3,NFKB1,NOS2,PTGS2,TGFBR2	923 (20)
STIM1	ion channel	3,11E-07	C5,GCLC,GPX1,GSTO1,HMOX1,IL10,IL13,IL6,NQO1,TNF	895 (22)
TNFRSF12A	transmembrane	3,11E-07	CCL2,CCL5,CKM,CXCL8,IL6,KL,MMP1,MMP3,MYOD1,PPARGC1A	734 (20)
NEUROG3	transcription reg	3,13E-07	ABCC8,CCK,CHGA,DRD1,EBF1,EFNB2,ERBB3,GCG,GCK,GIP,HAMP,IGF2R,INS,NOTCH2,NR2F1,NTRK1,PCSK1,PDX1,PSEN1,RARB,SREBF1,SST,XRCC1	684 (13)
CCR1	G-protein coupl	3,23E-07	CCL11,CCL5,FOS,IFNG,ITGAM,ITGAV,ITGB3,MMP2,MMP9,NFATC1,SPP1,TNF,TNFRSF11A	843 (18)
CPE	peptidase	3,23E-07	CCK,CHGA,CHGB,CTNNB1,HMGCR,LDLR,LEP,PAM,PCSK2,PDYN,POMC,SREBF2,TRH	928 (21)
NOTCH4	transcription reg	3,23E-07	ACTA2,ANGPT1,DES,EFNB2,FLT4,HES1,HES5,IL10,IL2RA,NOTCH1,RGS5,SERPINE1,TIE1	153 (3)
ABL1	kinase	3,42E-07	BMP2,C3,CAV1,CCND1,CTSL,DHFR,FAS,MMP1,SST,TFF1,TGFB2,TGFB3,TP53,TP73,VEGFA,VIP	995 (21)
CIITA	transcription reg	3,42E-07	CCND1,COL1A1,COL1A2,HLA-A,HLA-B,HLA-DPA1,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,IL10,IL13,IL4,IL5,MMP9	976 (20)
LCK	kinase	3,42E-07	ABCA1,CD2,CD69,FOS,FOXP3,IFNG,IL2,ITGB2,JUN,MMP9,NOTCH2,NR1H3,PPARG,RUNX1,SCARB1,VEGFA	730 (19)
APLNR	G-protein coupl	3,49E-07	AFP,ANGPT1,GATA4,MEF2C,MYL2,NKX2-5,PDGFRB,TBX5,THBS1	
CLEC10A	other	3,49E-07	CRP,CSF2,IFNG,IL10,IL1B,IL6,MMP9,MPO,TNF	508 (7)
CMKLR1	G-protein coupl	3,49E-07	ADIPOQ,IL13,IL4,IL5,IL6,LIPE,PLIN1,SLC2A4,TNF	915 (19)
Collagen Alpha1	group	3,49E-07	CCL18,COL1A1,EGFR,IL1RN,MMP2,MMP9,PLAUR,PTGS2,TIMP2	734 (17)
FABP2	transporter	3,49E-07	ABCA1,ABCG5,ABCG8,CPT1A,HMGCR,LEP,NR1H3,PPARA,PPARG	586 (7)
PON1	phosphatase	3,49E-07	ABCA1,HMOX1,ICAM1,IFNG,IL6,MSR1,PPARG,SCARB1,TNF	885 (21)
RYR2	ion channel	3,49E-07	CAPN10,FOXO1,IL6,MMP2,PCK1,PPARA,PPARGC1A,SIRT1,UCP1	1052 (21)
TIFA	other	3,49E-07	CCL2,CCL5,CSF2,CXCL8,HAMP,ICAM1,IL6,NFKBIA,TNFAIP3	824 (14)

TCF4	transcription reg	3,87E-07	ADA,CCND1,CD2,CDH17,CDKN2A,CDKN2B,CELA1,EDN1,ENPP1,FGF1,FN1,FOS,GCG,HSD11B1,ID3,IRS1,JUN,Ly6a (includes others),MITF,MMP1,MYB,NCOR2,NELL1,NOS2,NUF2,OPTN,PHEX,PITX2,PLAUR,PML,POMC,PPARG,PRC1,SELL,SERPINB1,SGK1,SPP1,STAT3,TCF7L2,TERT,TLR9,TYRP1,VCAN,VHL	990 (24)
FADD	other	3,91E-07	CD34,CDK6,CTNNB1,CXCL8,CXCR4,DES,FAS,FOS,HAMP,ICAM1,IFIH1,IFNG,IL2,IL6,IRF5,JUN,MMP9,NAT1,NFKB1,PLA2G4C,PSMB8,SOCS1,ST8SIA4,TNF,TNFAIP3	765 (20)
Hedgehog	group	4,16E-07	ABCC8,BDNF,CCND1,CDKN2A,FOXF1,GATA4,HES1,IGF2,JAG1,KCNJ11,KIT,KLK2,PDX1,SHH,SLC2A2,SPP1,TFF1,TP53	374 (7)
IL2RG	transmembrane	4,20E-07	CCL11,CRY1,CSF2,FOS,FOXP3,HLA-A,IFNG,IKBKE,IL17A,IL2,IL4,IL6,IL7R,JUN,KLRB1,NEDD4L,RHOH,TNF,VKORC1	656 (19)
CTBP1	enzyme	4,22E-07	BMP7,BRCA1,BRCA2,C8orf44-SGK3/SGK3,CDKN2A,COL1A2,FKBP5,FOS,RAC1,SIRT1,SMAD6,TFF1,THBS1,VCAN,VDR	640 (7)
MMP2	peptidase	4,22E-07	BMP2,CCL11,CCND1,COL18A1,CXCL12,EGFR,FN1,IL1RN,IL4R,IL6ST,JAK2,MMP1,PLG,SOCS1,TGFB1	824 (19)
INHA	growth factor	4,44E-07	ACTA2,BAX,BCAN,CCN2,CCN4,COL1A2,COL3A1,CYP11A1,CYP17A1,CYP19A1,CYP1B1,EGFR,EPHX1,F11R,FGFR1,HAS2,IFNG,IL1R1,ITGA9,KIT,LHCGR,LMNA,MMP2,PIK3R1,PTGS2,SERPINE1,SGK1,SMARCA1	634 (11)
miR-30c-5p (an	mature microRN	4,46E-07	ANPEP,ATP2A2,BDNF,CCN2,DOCK7,F2,GNAI2,IL6,INS,IRS2,ITGA2,JUN,MET,MTTP,NCEH1,NPR3,PAFAH1B2,PPARG,PPP3CA,PPP3R1,SLC4A10,SLC4A7,SLC7A1,STRN,TMCO1,TNF,TP53,UAP1,WNT5A	857 (11)
SASH1	other	4,60E-07	ATM,CD40,EDN1,HHEX,IL12A,IL12B,IL15,IL15RA,IL18,IL6,LTA,MET,NFKBIZ,OASL,PLAT,PML,PTGS2,SLCO3A1,SOCS1,TIMELESS,TNF,TSC22D1	581 (10)
BIRC3	enzyme	4,74E-07	CCL2,CXCL8,ICAM1,IFNG,IL1B,IL2,IL6,NFKB2,NFKBIA,TNF,TP53	650 (16)
GDF15	growth factor	4,74E-07	CCND1,CCR2,GDF15,HAMP,IL6,MYH7,NPPA,PLAUR,SERPINE1,TIMP3,TNF	1028 (21)
HOXA5	transcription reg	4,74E-07	CXCL8,FGF10,IGF1,IGFBP1,PGR,PTN,SHH,SLC6A2,TGFB1,TGFB3,TP53	
LY6E	other	4,74E-07	ABCG2,CCN2,CD14,CD34,CXCL8,HLA-DRA,IL1B,IL6,NFKBIA,SERPINE1,TNF	804 (22)
miR-296-5p (mi	mature microRN	4,74E-07	ABCB1,AKT1,BAX,CCND1,COL1A1,HMGA1,KLK1,MMP1,TNC,TP53,VEGFA	
MSR1	transmembrane	4,74E-07	CCL5,CD40,CTNNB1,IL10,IL1B,IL6,MMP9,NFKB1,NOS2,PGR,TNF	732 (17)
MITF	transcription reg	5,32E-07	APOE,ATP1A1,BRCA1,C8orf44-SGK3/SGK3,CDK5R1,CDKN2A,CMA1,COL1A1,CRYBG1,CXCL8,EDNRB,FMOD,FN1,FOS,GCG,HES1,HIF1A,HPS4,IL6R,INPP4B,ITGA4,KCNN2,KIT,LIG1,MET,MGP,MITF,MMP14,NR3C1,NUF2,PHACTR1,POU5F1,SCARB1,SEMA6A,SERPINE1,SLC14A1,SLC19A2,SLC7A8,SORT1,SOX13,SOX6,TBX2,TERT,TP53,TPH1,TXNIP,TYRP1,XRCC3	1054 (26)
CBX5	transcription reg	5,37E-07	ABCB1,AKR1C3,BCL11A,CDH17,CKM,CXCL5,CYP1B1,CYP2J2,DRD2,ERAP2,FGFBP1,GALC,GSTT1,HBB,KIT,LCN2,MMP7,OLR1,PPARG,PSMB8,QPCT,RORA,SELENBP1,SERPINA3,SLC2A3,SLC7A8,STAT5A,TIMP4,TSPAN8,TXNIP	
CD47	transmembrane	5,50E-07	CALCR,COL1A1,IFNG,IL10,IL12RB2,IL1B,IL2,IL6,KDR,NFATC1,NOS2,TNF,TNFSF11	887 (21)
DKK1	growth factor	5,50E-07	ACTA2,BDNF,BGLAP,BMP4,BMP6,CCND1,CDKN2A,COL1A1,CTNNB1,DPAGT1,HNF4A,IL10,IL13,IL4,MMP9,PPARG,TBX3,TNNC1,TP53,WNT5A	959 (25)
FLI1	transcription reg	5,50E-07	ADGRG1,APOC2,CCL5,CCN2,CCND1,COL1A1,COL1A2,FOXO3,GP1BA,HBB,HSPA8,IL2RA,ITGA2B,LOX,MMP1,POLR1D,RARB,TGFBR2,TNC,VEGFA	697 (15)
PLIN5	other	5,50E-07	ACAA2,CPT1B,GCLC,GPX4,GSS,HMOX1,NQO1,PDK4,POR,PPARA,PPARGC1A,TXNRD1,UCP3	279 (4)
USP7	peptidase	5,50E-07	CD36,CDKN2A,FABP1,FKBP5,FOXP3,IL23A,IL6,KLK2,PPARG,SLC2A2,TNF,TNNT2,TP53	1040 (22)
FOXC1	transcription reg	5,51E-07	CXCR4,EFNB2,FOXO1,HES5,ITGB3,MMP7,MMP9,NOTCH1,PITX2,SERPINE1,TSC22D1,WNT5A	496 (7)
filgrastim	biologic drug	7,49E-16	ADGRG3,ALOX15,ALOX5,ALPL,ANGPT1,ATF3,ATP1A1,ATP2B4,CAST,CCL23,CCL5,CCR3,CCT2,CD46,CD59,CD69,CHIT1,CLU,CR1,CRYBG1,CST3,CXCL8,CXCR4,CYB561,CYBB,CYP1B1,DACH1,DDAH2,F5,FKBP5,GP1BB,HLA-DPA1,HLA-DPB1,HLA-DQB1,HLA-DRA,HLA-DRB1,HLA-DRB5,HMGA1,HP,IGF2BP2,IL10,IL18R1,IL18RAP,IL1R1,IL1RAP,IL2RB,IL4R,IL5RA,ITGA4,ITGAM,ITPK1,JAK2,JUN,KIT,KLRB1,LDHA,LDLR,LGALS2,MEF2A,MEF2C,MLXIP,MME,MMP12,MMP9,MYB,NCOR2,NCR3,NECTIN2,NLRP3,NR4A3,OAS3,OASL,P2RY2,PCSK9,PDE4D,PLAUR,PPP1R12B,PRKAG2,PTGER2,PTGS2,RABGAP1L,RNASE3,S100A4,SERPINB1,SGK1,SLC26A6,SMAD3,SOCS1,SORT1,SPP1,SULF2,TAF4,THRA,TLR4,TLR5,TLR8,TRPM2,TSC22D1,VNN1	
LCAT	enzyme	5,51E-07	APOA1,APOE,CCND1,CLU,HMGCR,LDLR,PON1,PPARG,PPARGC1A,SCARB1,UCP1,UCP3	717 (14)
DGKZ	kinase	5,57E-07	CCND1,CD69,CTNNB1,IFNG,IL12B,IL6,TNF	864 (19)
GHSR	G-protein coupl	5,57E-07	AGRP,GHRH,IGF1,IL1B,IL6,NPY,TNF	925 (22)
IL22RA2	transmembrane	5,57E-07	HAMP,HLA-B,IFNG,IL13,IL4,LCN2,SOCS3	554 (14)
LPA	other	5,57E-07	CXCL8,GHR,ICAM1,NR3C1,SELE,SERPINE1,VCAM1	871 (14)
OCLN	other	5,57E-07	MMP1,MMP14,MMP2,MMP3,MMP7,MMP9,SIRT1	795 (10)
RNF40	enzyme	5,57E-07	ALPL,BGLAP,CXCL12,G6PD,PDK4,PPARG,TFF1	568 (7)
ATM	kinase	6,03E-07	ADIPOQ,ATM,ATR,BAX,BLM,CCN2,CCND1,CHEK2,CLU,CXCL8,FAS,FN1,HMOX1,IGF1R,IL2,IL6,JUN,LEP,LPIN1,SERPINE1,TNFAIP3,TP53	784 (17)
ZFPM1	transcription reg	6,03E-07	ALOX5,ALOX5AP,ANXA5,ENPP1,GATA2,GP1BA,HBB,HEBP1,IFNG,IL10RB,IL12RB2,IL1R1,IL4,IL5,ITGA2B,MPO,MS4A2,PBX1,PTGER3,PTPN22,SELP,TFR2	683 (19)
GDF9	growth factor	6,47E-07	CCN2,CYP11A1,CYP17A1,CYP19A1,HAS2,HSPG2,ID3,ITGAV,KIT,LHCGR,LOX,PTGER2,PTGS2,SMAD6,VCAN	749 (18)
PIAS1	transcription reg	6,47E-07	ABCB11,ACTA2,CCL2,CCND1,CXCL8,CYP11A1,CYP11B1,CYP11B2,CYP17A1,KLF5,NOS3,NPPA,NR0B2,PRL,SREBF1	917 (26)
BRAF	kinase	6,72E-07	CCND1,CCR2,CD40,CDKN2A,CXCL8,EPAS1,HAMP,HIF1A,IFNG,IL1A,IL1B,IL6,ITGB1,mir-122,mir-137,mir-146,mir-335,MITF,MMP1,MMP14,MMP9,RLN3,SERPINE2,THBS1,TSC22D1,TSHR,VHL	917 (19)
ABCC8	transporter	6,91E-07	CAT,CPT1B,FOXO1,IL6,MT-CO1,PPARGC1A,SOD1,SOD2,TNF,UCP3	741 (13)
DDR1	kinase	6,91E-07	CDKN2A,COL1A1,COL3A1,ELN,MMP1,MMP14,MMP2,MMP9,TP53,VCAM1	959 (20)
Fcgr3	group	6,91E-07	BAX,CSF2,CXCL8,IFNG,IL1RN,IL2,ITGAM,ITGB2,TNF,TNFSF4	791 (19)
HAVCR2	other	6,91E-07	CCR5,CTLA4,CXCR4,IFNG,IL13,IL1B,IL2,IL4,IL6,TNF	742 (19)
Hmgb1	transcription reg	6,91E-07	AGER,CCND1,CHGA,CHGB,CXCL8,IL10,IL1B,IL6,NOS2,TNF	935 (19)
IL-17f dimer	complex	6,91E-07	CCL2,CCL5,CSF2,IL10,IL13,IL1A,IL1B,IL6,IL9,LCN2	289 (5)
INHBB	growth factor	6,91E-07	COL3A1,COL4A1,HAMP,HGF,LOXL3,MMP3,SERPINE1,THBS1,TIMP1,TNC	750 (13)
ITGB6	other	6,91E-07	COL1A1,COL1A2,COL3A1,MMP12,MMP2,MMP3,MMP9,SERPINE1,SMAD2,TGFB1	945 (21)
fontolizumab	biologic drug	7,98E-05	CCL8,FAS,IFNG,IL12RB2,IL15RA,IL6,NAMPT,TNF	
KLF10	transcription reg	6,91E-07	BAX,BGLAP,CCND1,EGFR,FOXP3,IL12B,POMC,PTGS1,SERPINE1,TGFB1	877 (14)
KLK5	peptidase	6,91E-07	ICAM1,IL17A,IL18,IL1B,IL22,IL23A,IL4,IL6,TNF,TSLP	775 (22)
MAZ	transcription reg	6,91E-07	CAV1,FGG,HAMP,INS,KRAS,MMP1,MMP9,PNMT,PPARG,STAT3	777 (7)
p85 (pik3r)	group	6,91E-07	HIF1A,IL2,IL6,MMP2,NOS2,NOS3,PPARG,PTGS2,RELA,VEGFA	901 (17)
PHB2	transcription reg	6,91E-07	BMP2,GJA1,IGFBP1,IL6ST,PGR,PRL,SOCS1,SOCS3,STAT3,TXN	791 (7)
PLC	group	6,91E-07	CCL2,CXCL8,FOS,LIPE,NOS2,PTGS2,TH,TNF,TNFRSF11A,TNFRSF11B	761 (16)
JAG1	growth factor	7,51E-07	ACTA2,CCND1,COL1A1,CYP11A1,CYP19A1,GATA2,HES1,IFNG,IL13,ITGAV,ITGB3,NR2F2,PDGFRB,SPP1,TP53,WNT3	748 (18)
S100A4	other	7,51E-07	AGER,BAX,CCL5,CTNNB1,FN1,MMP14,MMP2,MMP9,NOTCH2,PTEN,SAA1,THBS1,TIMP1,TIMP2,TP53,VCAM1	914 (18)
CD274	enzyme	7,89E-07	CD69,CSF2,FOXP3,ICOS,IFNG,IL10,IL13,IL17A,IL2,IL4,IL6,STAT3,TNF,TNFSF10	620 (23)
EIF4EBP1	translation regu	7,89E-07	ARG1,CCND1,CEBPD,CYP2A6 (includes others),HAMP,IL10,IL1RN,LEP,PPARG,PPARGC1A,PTGS2,SLC2A1,SOCS1,UCP1	1006 (25)
EZR	other	7,89E-07	ATF3,BAX,CTNNB1,FAS,IL10,IL1B,IL6,MMP14,MMP2,MMP9,PTGS2,SMOC2,TNF,TRIB3	768 (17)
TERC	other	7,89E-07	ALAD,ARNTL,AURKA,CCL5,CLU,CRY1,CYP2C8,CYP4A11,H19,HMGCR,PRC1,TERT,TGFB1,THRA	930 (16)
ABCD2	transporter	7,92E-07	ALOX5,IL1B,NOS2,PTGS2,RELA,TNF	982 (19)
ATP6AP2	transporter	7,92E-07	AGT,ATP6AP2,CYBB,NOX4,PTGS2,TGFB1	653 (12)
FLT4	transmembrane	7,92E-07	BGLAP,IL1B,IL6,NOS3,SOCS1,TNF	729 (19)
FTO	enzyme	7,92E-07	IGF1,INS,LEP,MYH7,NPPA,UCP1	733 (14)
MIR17-92	group	7,92E-07	FZD4,HNF1B,LRP6,PKD1,PKD2,PKHD1	
PIWIL4	other	7,92E-07	CDKN2A,FGFR2,TGFB1,TGFB3,TGFBR1,TGFBR2	
PPP1R14B	phosphatase	7,92E-07	EPAS1,FLT1,HIF1A,KDR,PECAM1,VEGFA	
SAMD4A	translation regu	7,92E-07	CIDEA,PPARA,PRDM16,UCP1,UCP2,UCP3	
TNFRSF10A	transmembrane	7,92E-07	CD14,IFNG,IL12B,IL6,ITGAM,STAT3	627 (15)
Trbv13-2	other	7,92E-07	FOXP3,IFNG,IL10,IL17A,IL2,IL4	
VAV	group	7,92E-07	CD69,IL10,IL2,IL4,STAT3,TNF	735 (16)
HNRNPK	transcription reg	8,05E-07	AGT,ALOX15,AR,CCK,CCN2,G6PD,KNG1,LDLR,LPIN1,MMP3,PPARG,PRELP,PTGS2,RASA1,TCN2,UCP2,VCAN	644 (10)
Hsp27	group	8,05E-07	BAX,BGLAP,CCND1,CD14,CXCL8,FOS,GBA,GCH1,IL10,IL6,IL6R,NOS2,NOX4,NTRK1,PTGS2,STAT3,TGFB1	754 (18)
ERN1	kinase	8,12E-07	ANG,ATF3,ATP2A2,CAD,CEBPD,CYP1A2,CYP1B1,CYP2E1,FAS,GP1BB,IKBKB,IL1B,IL4,IL6,ITGB6,JUN,LGR5,MLXIPL,MYH7,NOS2,NOX4,NPPA,NR1H3,PADI4,PPARG,PVR,SLC20A1,SLC7A1,TNF,VEGFA,WARS,WFS1,XRCC1	729 (16)
SOX11	transcription reg	8,19E-07	AS3MT,BMP2,BMP4,BMPR1A,CAV1,CCL5,CCND1,CXCR4,EBF1,EP300,FAS,GNRH1,HSPD1,IFIH1,IL6ST,ITGA4,ITGB1,MAPK8,MYOD1,PAX5,PPP3CA,SKAP2,SMAD1,SMAD3,TGFBR1,TNKS	525 (7)

TEAD1	transcription reg	8,88E-07	ACTA2,ADM,CALD1,CCND1,CDK6,COL3A1,DES,EDN1,EDNRA,GPR37,MYH7,NFKBIZ,NPPA,POSTN,PTGS2,PTPRO,RHOBTB1,THBS1,TNNC1,TNNT2,TPM1	717 (14)
ADAM15	peptidase	8,93E-07	CCL5,EGFR,FLT1,IFNG,IL6,ITGAV,KDR,TNF,VEGFA	827 (21)
BMX	kinase	8,93E-07	COL3A1,CXCL8,FOS,HSPA1A/HSPA1B,IL6,MMP2,PPARGC1A,TIMP1,TNFRSF1B	971 (19)
CALC	group	8,93E-07	AQP4,CCL2,EDN1,FOS,MAX,NOS2,SORT1,TNF,VEGFC	891 (20)
Coup-Tf	group	8,93E-07	CYP11B2,CYP2D6,HGF,HNF4A,LTF,OTC,PCK1,POU5F1,RARB	423 (7)
DGAT1	enzyme	8,93E-07	CD36,CPT1A,CPT1B,LEP,LPL,PDK4,PPARA,PPARD,PPARG	892 (20)
elastase	group	8,93E-07	HMOX1,ICAM1,IL1B,MMP12,MMP2,MMP3,MMP9,PSEN1,TGFB1	864 (20)
FPR2	G-protein coupl	8,93E-07	CCL2,CCR5,CXCL8,IL10,IL12A,IL13,IL4,IL5,IL6	766 (21)
HNF4G	transcription reg	8,93E-07	ABCB11,APOA4,APOC3,CYP1A2,CYP7A1,GSTA1,HAMP,OTC,SHBG	
LPAR1	G-protein coupl	8,93E-07	CACNA2D1,CCN2,CXCL8,GDNF,IL6,KLF5,MMP9,PRKCG,PTGS2	829 (18)
PER2	transcription reg	8,93E-07	ARNTL,ATP1A1,CCND1,DBP,LEP,PER1,PER2,PRL,UCP1	267 (9)
Rac	group	8,93E-07	BMP2,CCL2,CCND1,FOS,HIF1A,IL6,MMP1,PTGS2,THBS2	800 (17)
RBP3	transporter	8,93E-07	IFNG,IL10,IL17A,IL22,IL22RA2,IL23R,IL5,TNF,TNFRSF1A	682 (10)
SCAVENGER rec	group	8,93E-07	CCL5,CXCL8,IFNG,IL10,IL12A,IL13,IL4,IL6,TNF	795 (12)
SOCS2	other	8,93E-07	GHR,IFNG,IGF1,LIPE,MYH7,MYOD1,PPARG,STAT3,STAT5A	752 (19)
ST14	peptidase	8,93E-07	CSF2,CXCL8,ICAM1,IFNG,IL1B,MMP1,MMP3,TNF,TSLP	775 (16)
ACSS2	enzyme	9,08E-07	ACAA1,FABP1,FABP2,GC,HMGCR,LSS,PPARA,PPARG,SCARB1,SLC27A4,SREBF1	581 (7)
CCL4	cytokine	9,08E-07	CCL2,CCR5,CD40,IFNG,IL12A,IL4,IL5,IL6,PDYN,TNF,TNFSF11	677 (18)
Fibrinogen	complex	9,08E-07	CCL2,CD40,CXCL8,ICAM1,IL1B,IL6,ITGAM,MMP14,SELP,TLR2,TNF	789 (17)
ITGA9	other	9,08E-07	ACTA2,CXCL12,CXCL14,IL1B,IL6,MMP1,MMP14,MMP3,TGFB1,TNC,TNFSF11	782 (21)
MAFK	transcription reg	9,08E-07	EGLN3,GCLC,GCLM,GSTA1,GSTP1,HBB,HMOX1,ITGA2B,NQO1,TXN,TXNRD1	695 (13)
MGAT5	enzyme	9,08E-07	CXCR2,EGFR,IFNG,IL13,IL4,IL4R,IL5,ITGB1,LGR5,PTPRC,TNF	801 (23)
NLRC5	transcription reg	9,08E-07	CD40,HLA-A,HLA-B,HLA-C,HLA-G,IL10,IL1B,IL6,PSMB9,TAP1,TNF	628 (17)
NTN1	other	9,08E-07	CCL11,DCC,IFNG,IL10,IL13,IL17A,IL2,IL4,IL6,PTGS2,TNF	649 (18)
PER1	transcription reg	9,08E-07	ARNTL,CCND1,CRY1,DBP,LEP,PER1,PER2,PRL,SLC12A3,WNK1,WNK4	886 (18)
SIGIRR	transmembrane	9,08E-07	IFNG,IL10,IL18,IL1A,IL1B,IL1R1,IL6,IRAK1,NFKB1,TLR4,TNF	680 (17)
XRCC6	enzyme	9,08E-07	APOA1,APOE,BAX,CCL5,FKBP5,HSPA4,IFNG,IL6,NFKB1,SIRT1,TNF	924 (18)
B2M	transmembrane	9,09E-07	CSF2,HLA-A,HLA-DQA1,HLA-DQB1,HLA-DRB5,IFNG,IGF1R,IL1B,IL4,IL6,MEF2A,MEF2C,MEF2D	792 (21)
NFIL3	transcription reg	9,09E-07	FAS,FGF21,IFNG,IL10,IL12B,IL13,IL17A,IL22,IL3,IL9,PTGS2,TNF,TNFSF10	700 (21)
RIPK1	kinase	9,09E-07	CAT,CCL2,CCL5,CXCL8,EGFR,HAMP,IL12B,IL1B,IL6,mir-146,NFKB1,TNF,TP53	729 (20)
CEBPG	transcription reg	9,22E-07	ADH1C,CXCL8,ELANE,F7,HBB,IFNG,IL6,PRL	703 (12)
PARP2	enzyme	9,22E-07	ADIPOQ,CD36,FAS,LEP,LPL,PPARG,SFTPB,SIRT1	886 (13)
TCF21	transcription reg	9,22E-07	CKM,COL4A1,CYP11A1,IL6,KISS1,MMP2,PITX2,TIMP1	
VEGFC	growth factor	9,22E-07	CXCR4,FLT4,ITGA4,ITGB1,KDR,PROX1,PTGS2,VEGFC	895 (15)
PRKAG3	other	9,53E-07	ABCA1,ANGPTL4,AQP1,ATP1B1,CD36,CES1,DNASE1,FGFR1,GAS5,GJA1,GLRX,GPX3,HAMP,HFE,IFI30,IL15,LEP,LUC7L2,MAP4,MYOD1,NAMPT,NOS1,NR3C1,PAM,PPARGC1A,RAMP1,SLC2A1,SLC2A3,SLC7A2,SOX17,SREBF1,TFRC,TSPAN8,UGT1A7 (includes others),WNK2,ZC3H11A,ZFP36	
GHRH	other	9,67E-07	CCND1,CTBP1,DRD2,FOS,GH1,GHRH,GHRHR,GHRL,IGF1,LEP,LEPR,SST	960 (22)
NFKBIZ	transcription reg	9,67E-07	CCL17,CEBPD,CSF2,CXCL8,IFNG,IL10,IL12B,IL17A,IL23A,IL6,LCN2,TNF	702 (15)
NODAL	growth factor	9,67E-07	ARG1,CCL5,CCND1,CD34,CD40,FOXO3,IL10,IL12A,IL12B,NOS2,SOX17,TNF	980 (23)
Smad	complex	9,67E-07	ANGPTL4,CCN2,CDKN2A,CDKN2B,COL1A1,COL1A2,ID3,IFNG,SERPINE1,VEGFA,VIP,WNT5A	684 (12)
TRA	transmembrane	9,67E-07	BAX,FAS,IFNG,IL10,IL12B,IL2,IL2RA,IL4,IL5,SELPLG,SOCS3,TNF	678 (18)
XIAP	enzyme	9,67E-07	CCND1,CDK6,CXCL8,IL6,PTEN,PTGS2,RELA,SELE,SERPINE1,SOD2,TNF,TXN2	600 (17)
IL9	cytokine	9,74E-07	CCL11,CCL2,CMA1,GP1BA,IFNG,IL13,IL22,IL4,IL5,IL5RA,IL9,ITGA2B,PECAM1,TGFB1,TNF	727 (19)
LHCGR	G-protein coupl	9,74E-07	AR,CYP11A1,CYP11B2,CYP17A1,CYP19A1,EDN2,ESR1,ESR2,FSHR,GNRH1,HSD3B2,LHCGR,PGR,PTGS1,PTGS2	1104 (22)
MERTK	kinase	9,74E-07	ATM,HGF,IFNG,IL10,IL12A,IL17A,IL18,IL1B,IL2,IL23A,IL6,MYL2,NOS2,PLAGL1,TNF	774 (19)
NQO1	enzyme	9,74E-07	BAX,CCL5,CCND1,CCR2,CXCL12,CXCR4,FPR1,IL6,KIT,MMP9,NOS2,PTGS2,TP53,TP73,VCAM1	804 (15)
SAMSN1	other	9,91E-07	ATM,CD40,EDN1,HBEGF,IFNG,IL12A,IL12B,IL15,IL15RA,IL18,IL23A,IL6,LTA,NFKBIZ,OASL,PLAT,PML,PTGS2,SLCO3A1,SOCS1,SOCS3,STAT5A,TIMELESS,TNF,TSC22D1	785 (19)
EED	transcription reg	1,09E-06	BDNF,CDKN2A,DAB2IP,EGFR,EVX1,FGF5,GATA4,GDNF,MMP2,MMP7,PTGS2,SHH,SLC26A6,TBX3,TBX5,TCF21	1003 (24)
VEGFB	growth factor	1,09E-06	ATF3,ATP2A2,BAX,GPX1,GSR,MMP12,MYH7,NPPA,OLR1,PPARGC1A,SLC27A4,SOD1,SOD2,TNF,TP53,TXNRD1	878 (21)
CD5	transmembrane	1,12E-06	CD69,ICAM1,IL10,IL10RB,IL13,IL17A,IL2,IL23R,IL5,IL5RA,LDLR,MSMO1,MVK,RARA,STAT3,TGFB1,TLR8,TLR9	610 (19)
JAK3	kinase	1,13E-06	BAX,CDK6,FOXP3,IFNG,IL10,IL12B,IL17A,IL2RA,IL6,IL7R,IL9,MAF,SHH,SOCS3,STAT3,TNF,UCP1	963 (20)
CHRNA7	transmembrane	1,22E-06	CHRNA3,IFNG,IL1B,IL1RN,IL6,ITGAM,MAPK1,PPARD,RELA,TGFB1,TIMP2,TIMP3,TNF,TP53	944 (17)
FLCN	other	1,22E-06	CDKN2B,CIDEA,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,PITX2,PPARGC1A,PRDM16,SERPINE1,UCP1,UCP3	419 (8)
MARK2	kinase	1,22E-06	ADIPOQ,IFNG,IGF1,IL12A,IL12B,IL15,IL18,IL4,LEP,LTA,NFKBIZ,PTGS2,SLCO3A1,TNF	691 (10)
ETV5	transcription reg	1,26E-06	AGER,BAX,CAV1,CCND1,CHI3L1,CTNNB1,CXCL12,CXCR4,ETV5,FN1,ICAM1,IL9,ITGB1,LCN2,MAF,MET,MMP14,MMP2,MYB,RET,SCARB1,SFTPB,SHH,SPP1,TIMP3,VEGFA	927 (21)
LHX1	transcription reg	1,26E-06	ANPEP,ATP1B1,BHMT2,CYB561,CYP27B1,DPP4,FABP3,FGF5,GATM,HES5,HHEX,HNF4A,JAG1,KDM5B,KL,LRP2,Ly6a (includes others),NPHS2,PAH,PAX2,SIM1,SLC12A1,SLC22A6,SOX17,TRH,UGT1A3,UMOD	
BCL11B	transcription reg	1,30E-06	ADORA1,CXCL8,FOXP3,GRIA1,IFNG,IL10,IL13,IL17A,IL2,IL22,IL23R,IL2RA,IL4,IL4R,IL7R,LTA,NCEH1,OPRM1,TGFBR1,TNF	999 (15)
IKBKE	kinase	1,30E-06	CCL5,CCND1,CXCL12,CXCL8,FUT2,HLA-A,IFIH1,IFNL3,IKBKE,IL17A,IL1A,IL23A,IL6,MMP3,MMP9,NFKBIA,NOS2,PTGS2,REG3A,TNF	601 (17)
ALDH1A1	enzyme	1,42E-06	BMP2,CNR1,CPT1B,IGF1,MLXIPL,NOTCH1,PCK1,PPARA,PPARD,PPARG	1118 (25)
CD46	other	1,42E-06	C3,CD69,FLT3,FOXP3,IFNG,IL10,IL2RA,MYB,PTGER4,SLC2A1	631 (24)
EGLN3	enzyme	1,42E-06	ADM,EPAS1,EPO,HIF1A,IL1A,IL1B,LDHA,NOS3,TNFRSF11B,VCAM1	824 (20)
Endothelin	group	1,42E-06	APLN,EDN1,FOS,JUN,NPPA,NPPB,PTGS2,RELA,RHO,TNF	828 (21)
Ncoa-Nr1i3-Rxr	complex	1,42E-06	ABCC2,CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,NOS2,SLCO1B1,SOD3	
Pdgf Ab	complex	1,42E-06	ANGPT1,CCND1,CKM,FOS,GRIA1,HBEGF,HIF1A,HMOX1,IL6,VEGFC	803 (18)
RPS6KA3	kinase	1,42E-06	FOS,IFNG,IL10,IL2,INS,LEP,PHEX,PTGS2,RELA,TNF	989 (23)
TAF1	transcription reg	1,42E-06	AR,BCL2A1,DIO1,GHR,HAMP,IGF1,LHCGR,SCARB1,TFF1,TNFSF11	830 (7)
TREM2	transmembrane	1,42E-06	CD40,CX3CR1,IL1A,IL1B,IL6,NFKBIA,NOS2,PTGS2,TNF,TNFAIP3	977 (21)
KLF5	transcription reg	1,43E-06	ACTA2,ARG1,CCND1,CPT1B,CTNNB1,CXCR4,EPAS1,FGFBP1,HIF1A,KLF5,MMP9,NOTCH1,PPARG,PTGES,RUNX1,SORCS2,UCP2,UCP3,WFS1	924 (24)
ACSL4	enzyme	1,46E-06	AR,CALCR,CAMK1D,CDKN2B,ENPP1,ESR1,JAK2,MYO5A,PGR,PPARG,PRKG1,PTGS2,THBD	541 (7)
AGTR2	G-protein coupl	1,46E-06	AGTR1,BAX,COL3A1,DES,FOS,KNG1,NOS2,NOS3,NPPA,OLR1,PIK3R1,POMC,TGFBR1	882 (22)
GNAI2	enzyme	1,46E-06	CCND1,CCR5,CXCR4,F2R,IFNG,IL4,IL5,ITGA4,PRKCA,PTPN1,SELL,STAT3,TNF	816 (18)
SYVN1	transporter	1,46E-06	AHR,ATP1A1,AXL,BCAT1,CCND1,CD46,CYB561,CYP1B1,DIO2,ERCC6,EXT2,FAS,FOLR1,HLA-A,HLA-C,IGF1R,IL7R,ITGAV,ITGB1,NFKB2,OLR1,PLD2,PLPP3,PVR,SLC12A3,SLC20A1,SLC2A1,SLC2A3,SLC4A7,SLC6A6,SLC7A2,TFRC	289 (5)
VAV3	cytokine	1,46E-06	BAX,BCL2A1,C4A/C4B,CAV1,CAV2,CAV3,EGF,HBEGF,HGF,IL2,IL6,REL,RELA	861 (19)
RAC2	enzyme	1,56E-06	CCR5,EFNB2,FOS,IFNG,IL13,IL1B,LDHA,LTA,MIF,NFKB1,NPPB,RAC1,SLPI,STAT4,TKT,TSC22D1	719 (20)
HOXA3	transcription reg	1,58E-06	ALOX5,ENG,EPAS1,HBA1/HBA2,IKZF1,IL17RA,ITGA4,ITGAV,ITGB1,NR2F2,PIK3CG,RAC2,ROCK1,RUNX1,SHANK2,SOX17,TNFRSF1B	
NOTCH2	transcription reg	1,58E-06	ACTA2,COL1A1,CTNNB1,DES,EGFR,HES1,HES5,IL10,IL22,IL6,IL7R,PTEN,RELA,RGS5,TNF,TNFSF11,TP53	752 (18)
CD9	other	1,64E-06	CCN4,CD69,DPP4,ERVW-1,HAMP,IL2,ITGA2,ITGB1,MMP9,TNF,VEGFA,WNT5A	804 (24)
miR-24-3p (and	mature microRN	1,64E-06	BAX,BRCA1,CDKN2A,DHFR,FURIN,IL6,NOTCH1,SMAD3,SMAD4,SMAD5,TGFB1,TNF	
PSMD10	transcription reg	1,64E-06	AKT1,BAX,CCND1,CXCL8,GNAS,HIF1A,ICAM1,IKBKB,IL6,MRAS,PTEN,TP53	890 (19)
SPRY1	other	1,64E-06	ETV5,FGF1,FGF10,FGF9,FGFR3,IGF1,IL2,LOX,LOXL3,MMP14,MMP2,NR2F1	511 (7)
TNFSF4	cytokine	1,64E-06	CXCL13,IFNG,IL10,IL13,IL17A,IL2,IL4,IL5,IL6,MAF,NFATC1,TNF	771 (19)
BTRC	enzyme	1,66E-06	ARNTL,BCL2A1,CCND1,CTNNB1,CXCL8,IL1B,IL6,RELA,SMAD4,SST,TRAF1	905 (18)
CaMKII	complex	1,66E-06	ARG1,BDNF,FOS,HAS2,IL10,IL1B,INSR,NOS3,SLC2A4,SLC8A1,TP53	1108 (25)
CD200	other	1,66E-06	FOXP3,IFNG,IL10,IL1B,IL4R,IL6,MET,NOS2,TLR2,TLR4,TNF	984 (16)
IKK (complex)	complex	1,66E-06	CCL5,CCND1,CXCL8,ICAM1,IFNG,IL1B,IL2,MMP9,PTGS2,TNF,VCAM1	794 (15)
MAP3K5	kinase	1,66E-06	ACE,BAX,CCN2,CCND1,CXCL8,CYBB,HMOX1,IL6,JUN,TGFB1,TP53	778 (15)
PLA2G6	enzyme	1,66E-06	ALOX12,ARG1,NFKB1,NOS2,NOX1,NOX4,PPARG,PTGS2,RELA,RGS2,TNF	978 (22)
PTPN3	phosphatase	1,66E-06	ANGPTL4,CDKN2B,COL1A1,FN1,IL2,ITGAV,JAG1,MMP9,SERPINE1,TGFBR1,VDR	1006 (20)

RAPGEF3	other	1,66E-06	CYP1B1,FN1,LEP,NFATC1,NPPA,PDX1,SLC2A2,SOCS3,SPP1,TGFB1,THBS1	1012 (20)
SLC9A3R1	other	1,66E-06	ABCC2,ACTN4,CCL5,CFTR,EGFR,ERBB2,ERBB3,HAMP,PTEN,S100A4,SCARB1	950 (13)
NEUROG1	transcription reg	1,72E-06	ADD3,C3,CDK5R1,CFH,COL3A1,EPAS1,FABP3,FGF9,FN1,HAS2,IL6,ITGB3,LGR5,MARC2,MMP9,PAPPA,PPIC,PXDN,S100A4,THBS1	541 (7)
MIR124	group	1,86E-06	AR,CAV1,CDK6,IFNG,IL1B,IL2,IL6,NR3C2,PTPRC,RELA,ROCK1,STAT3,TNF,TP53	565 (12)
USP22	peptidase	1,86E-06	BCL2A1,CHI3L1,CYBB,FCGR2A,FCGR2B,FES,IL2,ITGAM,ITGB2,MSR1,NCF2,NF1,PTPRC,TNF	426 (7)
RARG	ligand-depende	1,87E-06	ABCA1,APOA1,BMP2,CCN2,CNR1,COL4A1,CYP19A1,FOLR2,FOS,FOXC1,GATA4,HAS2,HNF1B,IL6,JUN,NR2F1,PITX2,POU5F1,RARA,RARB,SLC10A1,TFF1,THBD,ZMAT4	971 (24)
GLP-1-(7-34)-an	biologic drug	4,79E-11	AGER,CYP7A1,FOS,GCG,HMOX1,IGF1R,LPL,MFN2,NPPB,NQO1,PDX1,PPARG,SIRT1,STAT3,VCAM1	861 (20)
PDLIM2	other	1,91E-06	CCND1,CSF2,CXCL8,F2RL1,GHR,GSTM1,GSTM2,HACD4,HBEGF,IFNG,IGFBP3,KIT,KYNU,MECOM,MME,MYEOV,NPR3,NR2F1,OAS3,SLC22A3,STAT4,STC2,TXNIP,WWOX,ZNF300	705 (16)
STAT2	transcription reg	1,91E-06	CAV1,CCL5,CD40,CIITA,CXCL8,IFNG,IL10,IL12A,IL6,IRF5,NOX1,PITX2,PSMB8,SHH,SOCS1,SOCS3,TNF,TNFSF10,WARS	985 (20)
BTC	growth factor	2,04E-06	CXCL8,HAS2,IL6,IRS2,ITGAM,MMP9,PRL,PTGS2,SREBF1	989 (21)
CRTC1	transcription reg	2,04E-06	BDNF,HAMP,MMP1,MT-CO2,NQO1,PER1,PPARGC1A,PTEN,TIMP1	695 (10)
glucagon	biologic drug	1,24E-05	ADD3,CARD14,CTNNB1,CYBA,CYP7A1,FGF21,FOS,GHRL,LMNA,mir-214,MME,NR4A3,SLC12A1,SLC2A4,SLC9A3,SORT1,SREBF1	640 (17)
GNA13	enzyme	2,04E-06	ACTA2,CXCL8,FOS,GSTA1,mir-143,NOS2,PTGS2,TRPC6,VEGFA	888 (18)
mir-199	microRNA	2,04E-06	ALOX5AP,AXL,EDN1,HIF1A,NOS2,SIRT1,SMAD4,TP53,VEGFA	899 (16)
glutathione eth	biologic drug	2,60E-02	IL12B,MMP1	
PLCG1	enzyme	2,04E-06	CCL2,CCND1,CTNNB1,FOS,IFNG,KDR,PECAM1,SERPINE1,THBS1	906 (17)
STUB1	enzyme	2,10E-06	ACTA2,ERBB2,FOXO1,GATA4,IL2,IL6,NFKB2,NOS1,NOS3,NPPA,RUNX1,TERT,TFF1,TP53,VEGFA	1057 (22)
ADRA1A	G-protein coupl	2,18E-06	BDNF,CEBPD,COL3A1,CYP1A1,DDAH1,FN1,FOS,IL6,IL6ST,JUN,LOX,MMP7,NPPA,PPP3CA,PRIM2,STAT3,VEGFA	741 (16)
MAPT	other	2,21E-06	ABCG2,ANXA5,ATP1A2,ATP1B1,ATR,BDNF,BSN,C3,CAST,CCND1,CDK5R1,CPLX2,DNM1L,FOS,FYN,GAS7,GLO1,GPX4,GSTM5,GSTP1,HBA1/HBA2,HIF1A,HSPA1A/HSPA1B,HSPA8,HSPD1,HTT,IFNG,IL1A,IL1B,IL6,JUN,KLC1,LRP1B,MAPK1,MAPK3,MAPK8,MMP9,MT-CO2,MTHFD1L,NFKB1,NFKB2,NOS1,NOS2,PAFAH1B2,PPP3R1,PSEN1,SERPINE1,SNAP25,SOD1,TH,TNF,TXN,VEGFA	948 (22)
TFRC	transporter	2,26E-06	ADGRG1,ATF3,F13A1,FOS,GAS7,GPX3,HMOX1,ITGAM,ITGB2,JUN,KIT,LDHA,MMP12,PPARG,PTN,SLC2A1,STC2,SULF2,TGFB2,TGFB3,TNFSF10,TP53,TREML2	497 (7)
ANPEP	peptidase	2,30E-06	ANPEP,DPP4,IL1RN,IL2,IL6,TGFB1,TNF	431 (7)
CD48	other	2,30E-06	CCL11,IFNG,IL13,IL2,IL4,IL5,TNF	759 (11)
FBXO42	other	2,30E-06	CCL5,CXCL8,ICAM1,IL6,MMP9,TNF,VCAM1	520 (7)
HISTONE	group	2,30E-06	AHR,CDK6,CIITA,CSF2,FMR1,IL6,KISS1,MAPK1,NOD2,NOS3,PTGIS,SELP,SLPI	527 (11)
HTR7	G-protein coupl	2,30E-06	COL23A1,FOS,IL17A,IL1B,IL6,THBS1,TNF	893 (22)
IL4I1	enzyme	2,30E-06	CCL2,CCL8,CD247,CXCL8,IFNG,IL1A,IL2	727 (16)
NGFR	transmembrane	2,30E-06	CCND1,DRD2,FOS,IL1RL1,JUN,LDLR,NCAM1,NR0B2,PLAT,SERPINE1,SNAP25,SORT1,TNF	924 (21)
PLA2G1B	enzyme	2,30E-06	CD36,CXCL8,LEP,PPARA,PPARD,PPARG,UCP2	929 (18)
PTGDR	G-protein coupl	2,30E-06	CSF2,IFNG,IL1B,IL2,NOS2,PTGS2,TNF	736 (19)
TENM1	transmembrane	2,30E-06	CHL1,EDNRB,ERBB3,MGP,SCARB1,SEMA6A,SLC1A4	
UCN2	other	2,30E-06	AR,CCL2,CXCL8,FOS,POMC,TH,TLR4	1092 (22)
VAV2	transcription reg	2,30E-06	AGTRAP,BCL2A1,CD69,CDC42,EGF,FOS,HBEGF,HGF,IL2,IL6,RAC1,REL,RELA	658 (16)
CDKN1A	kinase	2,51E-06	ACTA2,AURKA,BAX,BRCA1,CCL2,CCN2,CCND1,CDKN2A,CDKN2B,COL1A2,EDNRA,F9,FAS,FN1,HSPA1A/HSPA1B,IFNG,IL1B,IL1R1,IL2,IL6,ITGAM,ITGAV,ITGB3,JAG1,MAF,MMP1,MMP3,MMP9,MTTP,MYOD1,PRC1,PTPRC,SAA1,SERPINE1,SOD2,TCN2,TERT,TNF,TNFSF13,TP53,TYMS,UHRF1,VEGFA,WNT3	930 (17)
CSK	kinase	2,53E-06	FOS,FYN,IL1B,IL2,IL6,ITGB2,NPPA,TNF	672 (21)
CUX1	transcription reg	2,53E-06	CAD,CCL5,CYBB,CYP7A1,ELANE,ERBB2,FTO,HLA-B,ITGB2,KISS1,KLK8,LTF,MMP2,MYH7,NCAM1,NPPA,RASIP1,THBS1,WNT5A	585 (7)
DBI	other	2,53E-06	APOB,HMGCR,LSS,PPARA,PPARD,PPARG,SREBF2,TNF	847 (13)
GnRH analog	biologic drug	1,53E-09	ABCC1,ABO,ACAA2,ACOT7,ACTN4,ADD2,AGER,AKAP10,AP3D1,AP3S2,ATF3,BCL2A1,CACNA1D,CAMKK2,CD40,CLOCK,CTNS,CXCL5,EDNRB,EGF,ESR1,EXT2,FAS,FLT1,FN1,FOS,GNRH1,GPER1,GSTO1,HIF1A,HLA-DPB1,HSPA2,IFNG,JUN,KLF7,KYNU,LCAT,MAPK1,MAPK3,MIA3,NCOA3,NFKBIA,NPPA,NR1I2,NTRK3,NUTF2,PDGFRB,PDLIM5,PLEKHA6,PRCP,PSMA6,PSMB4,PVR,RARA,REG3A,RELA,SDF2,SF1,SKAP2,SLC2A3,SMAD2,SMAD5,SRSF3,THRA,TP53,TPM1,TSC1,VCL	891 (17)
HRH1	G-protein coupl	2,53E-06	IFNG,IL10,IL13,IL5,LEP,PTGS2,SELP,UCP1	829 (21)
goserelin	biologic drug	4,87E-02	IGF1R,VEGFA	
PELI1	enzyme	2,53E-06	CCL5,CXCL8,IFNG,IL12B,IL1B,IL6,NOS2,TNF	655 (18)
PLCL1	enzyme	2,53E-06	DIO2,HAMP,LHCGR,PPARA,PPARD,PPARG,PPARGC1A,UCP1	837 (15)
PLTP	enzyme	2,53E-06	APOA1,APOB,CETP,IL10,IL1B,IL6,LDLR,TNF	778 (20)
PTGIR	G-protein coupl	2,53E-06	CCL11,CCL17,CXCL12,IFNG,IL13,IL1B,IL5,IL6	747 (17)
RGS2	other	2,53E-06	CEBPD,HBEGF,IL18,IL2,LPL,PLAT,PPARG,SREBF1	898 (18)
RPS6KA4	kinase	2,53E-06	FOS,IL10,IL12A,IL12B,IL2RA,IL6,JUN,TNF	747 (20)
ZBTB32	transcription reg	2,53E-06	CIITA,HLA-DQB1,IFNG,IL10,IL13,IL2,IL4,IL5	572 (10)
CARD11	kinase	2,69E-06	CCL5,CSF2,IFNG,IL10,IL13,IL2,IL2RA,IL4,IL5,MME,NFKB1,TNF	606 (17)
GAS6	growth factor	2,69E-06	AXL,IFNG,IL17A,IL1B,IL6,MSR1,NFKB1,PDGFRA,PTGES,SOCS1,SOCS3,TNF	615 (17)
RAG2	enzyme	2,69E-06	ALOX15,BAX,CCL11,CD2,CSF2,IFNG,IL1B,IL2,IL2RA,IL6,KLF5,TNF	915 (22)
CREB3L3	transcription reg	2,74E-06	APOA4,APOA5,APOC2,BGLAP,CRP,FGF21,HAMP,LPIN1,NFATC1,PCK1	
IL1RL1	transmembrane	2,74E-06	CD28,CXCL8,IFNG,IL13,IL4,IL5,IL6,ITGAM,TLR4,TNF	855 (18)
ITCH	enzyme	2,74E-06	CCN2,FOS,FOXP3,IFNG,IL1B,IL4,IL5,IL6,NFATC1,TNF	699 (17)
KLF13	transcription reg	2,74E-06	BMP2,CCL5,HBB,IL10,IL13,IL4,IL5,IL9,PGR,TNF	
PTK2B	kinase	2,74E-06	CXCL8,FOS,IFNG,IL10,IL2,JUN,SOCS1,TERT,TP53,VCL	704 (19)
PTPN2	phosphatase	2,74E-06	BCL11B,CCL17,CCND1,CIDEA,IFNG,IL10,NOS2,PPARGC1A,PRDM16,UCP1	1028 (24)
WWOX	enzyme	2,74E-06	BGLAP,COL1A1,ESR1,IL6,MMP9,TIMP2,TIMP4,TP53,TP73,VEGFA	948 (19)
PCGF2	transcription reg	2,77E-06	CDK6,CDKN2A,GATA4,HES1,IFNG,IL13,IL17A,IL5,JAG1,NFKB1,NOTCH1,NOTCH3,SMAD3,TP53	896 (15)
PSEN2	peptidase	2,85E-06	ANXA5,ATP2A2,BAX,COX8A,CTNNB1,DBP,EGFR,F2R,FOXO3,FZD4,GAS5,GJA1,HBA1/HBA2,HES5,IGF1R,INSR,MT-CO2,NOTCH1,PDGFRA,PDGFRB,PRC1,PSEN1,PTGS2,SCN10A,TP53,TYRP1	976 (20)
FGF4	growth factor	2,90E-06	CTNNB1,FOS,FOXO1,FOXO3,HMGCR,JAG1,MMP14,PRL,SHH,SOX17,VEGFA	849 (19)
miR-18a-5p (an	mature microRN	2,90E-06	CCN2,CCND1,ESR1,FGG,HIF1A,HP,KRAS,PTEN,SOX6,THBS1,WNK2	482 (7)
NFE2	transcription reg	2,90E-06	CAT,HBB,HSD3B1,HSD3B2,ITGA2B,NQO1,SELP,SLC6A4,SPTA1,TBXAS1,TXN	
LGR4	transmembrane	3,02E-06	AHR,AQP9,CD14,CSF2,CYP1A2,CYP2E1,ESR1,IL1A,IL1B,IL6,NR3C2,SLC13A3,SLC22A1,TNF,WNT5A	723 (18)
mir-145	microRNA	3,08E-06	ABCA1,ACTA2,CACNA1C,CD28,CDK6,EGFR,IL10,IL6,IRS1,KLF5,NFATC1,PDGFRA,POU5F1,ROCK1,SOD2,TP53	839 (21)
SMAD1	transcription reg	3,08E-06	ACTA2,ALPL,CCN2,CDKN2B,COL1A1,COL1A2,COL4A1,HHEX,ICAM1,NKX2-5,SELE,SMAD1,SMAD6,SPP1,VCAM1,VEGFA	998 (21)
TEAD3	transcription reg	3,08E-06	ADM,CALD1,COL3A1,DES,EDN1,EDNRA,GPR37,MYH7,NFKBIZ,POSTN,PTPRO,RHOBTB1,THBS1,TNNC1,TNNT2,TPM1	
EOMES	transcription reg	3,34E-06	ACTA2,ACTC1,ADCYAP1,ADM,APLNR,CCK,COL3A1,COL6A3,CXCR4,FOXC1,FOXP3,H19,IFNG,IGFBP3,IL2RB,IL5,ITGA2,KDR,PDGFRA,POU5F1,RGS2,SOX17,STAT3,TFPI2,TNFSF10,TSHZ1,WNT3	342 (7)
SPARC	other	3,34E-06	AKR1C3,ATM,BLM,BRCA1,BRCA2,CEBPD,COL1A1,COL1A2,CPT1B,CTBP1,CYP1A1,FN1,HES1,IL6,LRP8,MMP2,MPZL1,NOTCH1,NOTCH2,NPY,P2RY2,PER2,SERPINE1,SLC22A5,TGFB1,TOPBP1,WNK4	975 (23)
PPP3CA	phosphatase	3,41E-06	ALOX12,ATP2A2,C3,CA2,CD2,CPT1A,FN1,GSTP1,IGF1R,LCAT,NFATC1,NPPA,PLPP3,PPP3R1,PTGFR,PTGS2,S100A4,SDC4,SLC2A4,SPP1,TF,TNF	734 (22)
ALDH1A2	enzyme	3,53E-06	ABCG2,ATF3,CCN2,COL1A2,COL3A1,KIT,Ly6a (includes others),NKX2-5,NPPA,RARB,SPP1,TIMP1,TIMP3	830 (13)
PAX5	transcription reg	3,70E-06	CCND1,CD40,CIITA,CNR2,CTNNB1,DLEU2,FLT3,FN1,G6PD,INSR,MET,MMP2,NR3C1,PAX2,SLC2A1,SLC2A3,TP53,TXNIP	1028 (17)
CUL4B	other	4,06E-06	CDKN2A,COL4A1,FOXO3,GLO1,IGFBP3,KMT2C,MCM8,PTEN,RUNX1,SOCS1,SOD1,TGFB1,TNF,ZFP36	433 (7)
TANK	other	4,06E-06	ATM,CXCL8,IL12B,IL1A,IL23A,IL6,LTA,NFKB1,NFKBIZ,NOS2,PTGS2,TIMELESS,TNF,TSC22D1	563 (14)
LTBR	transmembrane	4,25E-06	ACTA2,CLU,CSF2,CXCL12,CXCL13,FAAH,ICAM1,IL6,LIPC,NFKB2,NFKBIA,NOS2,PDGFRB,SERPINA1,TNF,VCAM1	559 (15)
C1QBP	transcription reg	4,27E-06	ADRA1B,BDKRB1,CCND1,CTNNB1,CXCL8,HAS2,IFNG,MT-CO1,MT-CO2	803 (19)
CABIN1	other	4,27E-06	IFNG,IL13,IL2,IL4,IL6,IL9,MMP2,MYH7,NPPA	774 (21)
DSP	other	4,27E-06	ADIPOQ,COL1A1,COL1A2,COL3A1,CTNNB1,LPL,MMP14,PPARG,TGFB1	514 (7)

EPHX2	enzyme	4,27E-06	BDNF,CCL2,HES1,ICAM1,IL1B,IL6,NOTCH1,SELE,VCAM1	865 (21)
FCER1A	transmembrane	4,27E-06	CSF2,IL13,IL2,IL3,IL4,IL6,LAT2,SIRPA,TNF	639 (24)
IGFBP1	other	4,27E-06	IGF1,IGFBP1,IGFBP3,ITGA2,ITGAV,ITGB1,ITGB3,NOS3,TGFB1	1054 (25)
KLF9	transcription reg	4,27E-06	BMP2,CCND1,COL1A1,CYP7A1,ESR1,GHR,IGFBP1,PGR,TGFB1	1019 (15)
MAFG	transcription reg	4,27E-06	GCLC,GCLM,GSTP1,HMOX1,ITGA2B,NQO1,TBXAS1,TP53,TXNRD1	
MAML1	transcription reg	4,27E-06	CCND1,CKM,CXCL8,HES1,HES5,IL1A,IL1B,IL7R,MYLK	915 (19)
NPY1R	G-protein coupl	4,27E-06	FOS,IL6,LEP,NPY,POMC,TNF,TPH1,UCP1,UCP2	1024 (22)
NREP	other	4,27E-06	ACTA2,COL3A1,MMP2,MMP9,PDGFRA,PDGFRB,TGFB1,TGFBR2,VEGFA	470 (7)
OSBPL8	transporter	4,27E-06	ABCA1,APOE,CYP7A1,FABP2,HMGCR,LIPC,NR1H3,SREBF1,SREBF2	
S1PR3	G-protein coupl	4,27E-06	ACTA2,FOS,HGF,ICAM1,IGF1,IL1B,JUN,PTGS2,VCAM1	861 (19)
PEBP1	other	4,28E-06	ADIPOQ,CIDEA,CSF2,IL13,IL2,IL4,IL5,IL6,IL9,PCK1,PON1,RBP4,RETN,TNF,UCP1	863 (22)
Hif1	complex	4,32E-06	ADM,APLN,CXCR4,EDN1,EPO,FN1,HIF3A,HMOX1,KCNB1,LDHA,LHCGR,LOXL2,LPIN1,NGB,NMBR,NOS2,SLC2A1,TFRC,VEGFA	943 (15)
OSMR	transmembrane	4,32E-06	ADGRE1,BAX,FGB,FOS,IL6,IL6R,IL6ST,JAK2,LBP,OSMR,PSMB9,SERPINA1,SOCS1,SOCS3,SREBF1,STAT3,TIMP1,TNFSF11,ZFP36	688 (16)
mir-133	microRNA	4,80E-06	ATP6AP2,CCN2,CD34,CDC42,FBN2,FN1,GSTP1,HLA-G,IGF1R,ITPR2,KCNH2,KCNQ1,MET,MMP14,PPARG,SLC2A4,TNF,TNFSF10,TNNT2,VCAN	786 (18)
CD81	other	4,89E-06	HAMP,ICAM1,IFNG,IL2,IL2RA,IL4,MMP14,MMP2,TFR2,TNF,VCAM1	906 (21)
HEY1	transcription reg	4,89E-06	ACTA2,BMP2,GATA4,KDR,MMP2,NPPA,NR2F2,PROX1,SMTN,TBX2,TP53	456 (7)
IL36G	cytokine	4,89E-06	CSF2,CXCL8,IFNG,IL12A,IL12B,IL17A,IL22,IL23A,IL4,IL6,TNF	725 (19)
mir-103	microRNA	4,89E-06	CACNA1C,CACNA2D1,CAV1,CDK6,FOXO1,HIF1A,IL23A,MMP12,NOTCH2,OPRM1,TP53	
mir-214	microRNA	4,89E-06	ATM,FGFR1,IGF1R,LDLR,LTF,NFKB1,NOS3,PCK1,PTEN,PTGS2,RELA	374 (7)
Mir122a,b	group	4,89E-06	CCK,CD69,HMGCR,IFNG,IGF1R,IL6,MVK,NOS2,SOCS1,TNF,TP53	1084 (18)
TRIM28	transcription reg	4,89E-06	ALAD,CCL5,DNAJC6,EPAS1,FOXO3,HAMP,IFNG,IL2,IL6,MITF,MMP2,NFKB1,S100A4,SOX6,TP73,TYRP1,WNT5A,ZNF77	1035 (19)
TRPV4	ion channel	4,89E-06	CCL5,FAS,FOS,IL6,PPARGC1A,SOCS3,THBS1,TIMP1,TLR2,UCP1,VCAM1	983 (22)
GABPB1	transcription reg	5,00E-06	AURKA,BRCA1,ELANE,IL16,IL7R,ITGB2,PRL,TNC,TSHR,UCP3	163 (4)
KCNIP3	transcription reg	5,00E-06	CALCA,CCND1,FOS,GCM1,IFNG,IL2,IL4,PDYN,TNFAIP3,TRPV1	975 (25)
LGALS9	other	5,00E-06	CCR5,CXCR4,IFNG,IL10,IL13,IL17A,IL1B,IL2,IL4,TNF	737 (16)
NAB2	transcription reg	5,00E-06	ALOX5AP,FLT1,FN1,FOS,HIF1A,IL2,MMP3,PPARG,TGFB1,TNFSF10	811 (17)
PHB	transcription reg	5,00E-06	BAX,CXCL8,CYP11A1,CYP19A1,H19,IFNG,IGF2,IL1B,RELA,TNF	1090 (18)
apyrase	group	5,08E-06	IL17A,IL2,IL6,MMP2,MMP9,SELP	629 (18)
CCL18	cytokine	5,08E-06	IFNG,MMP2,MMP9,S100A4,TGFB1,TNF	405 (7)
CLIC4	ion channel	5,08E-06	CCL5,IL12B,IL1B,IL6,SLC16A8,TNF	817 (21)
CXCL17	cytokine	5,08E-06	IL12A,IL12B,IL17A,IL22,IL23A,TNF	
CYP4F2	enzyme	5,08E-06	CYBB,FLT1,IL6,KDR,NCF2,VEGFA	680 (14)
DRD5	G-protein coupl	5,08E-06	AGTR1,BDNF,HMOX1,IFNG,IL23A,PLD2	629 (13)
FZD5	G-protein coupl	5,08E-06	CD14,ERVW-1,GCM1,IFNG,SPP1,VEGFA	
HLA-DQ	complex	5,08E-06	CSF2,FOS,IL10,IL1B,IL6,TNF	648 (17)
HTR2A	G-protein coupl	5,08E-06	BDNF,CCN2,EGFR,HTR2A,OPRM1,SLC12A5	461 (9)
KAT5	transcription reg	5,08E-06	AFP,APOA1,BAX,CACNB2,CAD,CCND1,CFTR,CXCL8,CXCR4,EGFR,ERCC1,ERCC2,HNF4A,HSPD1,IFNG,IL10,IL2,IL6,NPPA,PRL,RAD54B,SOD2,SOX17,SRSF2,TFF1,TTR	887 (20)
MT-TE	other	5,08E-06	MT-ATP6,MT-CO2,MT-CYB,MT-ND1,MT-ND4,MT-ND6	
NPAS2	transcription reg	5,08E-06	ARNTL,CLOCK,CRY1,F7,PER1,PER2	437 (7)
P2RY1	G-protein coupl	5,08E-06	FN1,FOS,IL6,LEP,SELE,VCAM1	797 (16)
P2RY4	G-protein coupl	5,08E-06	ICAM1,MMP9,SELE,TIMP1,TIMP4,VCAM1	577 (7)
RBP4	other	5,08E-06	ADCY6,PCK1,RARA,RARB,SHH,TGFB1	544 (9)
SELL	transmembrane	5,08E-06	CXCR4,IFNG,IL1B,IL6,TGFB1,TNF	718 (18)
SERPINC1	enzyme	5,08E-06	HSPG2,IL6,MAPK3,MIF,NOS2,TNF	515 (13)
SLC9A1	ion channel	5,08E-06	CA2,CXCL8,IL9,NOS2,PPP3R1,SLC12A2	
Sphk	group	5,08E-06	CCL2,IL33,IL6,SELE,TNF,VCAM1	770 (19)
TCIM	other	5,08E-06	CXCL8,ICAM1,IL1A,IL6,PTGS2,VCAM1	707 (12)
TP73-AS1	other	5,08E-06	HMGB1,IL1B,IL6,KISS1,MOK,TNF	754 (12)
TPSD1	peptidase	5,08E-06	CXCL8,IFNG,IL10,IL4,IL6,PTGS2	785 (18)
TSC22D1	transcription reg	5,08E-06	CXCL8,FN1,IL1B,IL6,SERPINE1,TP53	931 (19)
UBASH3A	enzyme	5,08E-06	EGFR,IFNG,IL10,IL2,IL4,IL5	602 (19)
UCP1	transporter	5,25E-06	ADGRE1,CCL25,CTH,FGF21,G6PD,GDF15,GPX3,GPX4,GSR,GSTM1,GSTO1,HSD17B7,IFNG,IL1B,IL6,LEP,MT-CO1,MTHFD1,MTHFD1L,OAS3,PCK1,SDHB,SERPINE1,SHMT1,SLC6A9,SRM,TGFB1,TLR7,TLR9,TNF,TRIB3,TXN2,UCP1,UCP2,UCP3	1029 (24)
PLA2G10	enzyme	5,27E-06	ARG1,BMP4,CCL2,CD36,CD40,FAS,HOXC13,HSPA4,IL10,IL13,IL17A,IL1B,IL22,IL4,IL5,IL6,PTGS2,PTPRC,RGS14,SHH,SRM,TDRD5,TNF,VEGFA,VEGFC	909 (17)
HLX	transcription reg	5,31E-06	BMP2,CD34,CDKN2A,CXCL8,CYP1B1,GDF15,HES1,ICAM1,IFNG,IL4R,JUN,KYNU,PAPPA	691 (7)
PDPK1	kinase	5,31E-06	CAV1,CCND1,CST3,CXCL8,FOXO1,FOXO3,IL1B,IL4,IL6,SELL,SERPINE1,TNF,TNFSF11	993 (23)
ISL1	transcription reg	5,42E-06	ACTC1,ADCYAP1,BMP4,CARTPT,CCKAR,DCC,ETV5,GCG,GIP,GNAS,IFNG,IL1A,IL1B,IL6,NPY,NTRK1,NTRK3,RET,RUNX1,SCN7A,TH,TNF,TRPV1	789 (16)
hemocyanin	biologic drug	9,67E-07	CD14,IFNG,IL10,IL13,IL2,IL4,IL5,NOS2,TGFB1,TNF,TNFRSF4,TNFSF4	706 (20)
PRDM5	transcription reg	5,42E-06	ADARB2,ARID3B,CACNA1C,CDH4,CYP3A7,EBF1,EDNRA,GCK,IL6R,mir-143,mir-196,MYB,NOTCH1,NOTCH2,PAX5,PML,POU2F3,POU5F1,PPP1R12B,RARA,RUNX1,SOCS3,TP53	
HOXA9	transcription reg	5,47E-06	ADD3,ADGRG1,ARNTL,BRCA2,CALCRL,CCL2,CD34,CD36,CDKN2A,CPB2,CTH,CYBB,EDNRA,ENPP1,FLT3,GATA2,GLRX,HBG1,IGF1,IL7R,INPPL1,JUN,KIT,LAT2,LY86,MYB,NDUFB3,NFIA,NPPA,PTPRC,PTPRG,SDC4,SELE,SHH,SPP1,TSC22D1,VHL	
PLN	transporter	5,59E-06	APOA1,ATP1A1,ATP2B1,DES,FABP3,GCGR,GNAI2,HES1,ITGB1,MYH7,MYL2,NOTCH1,NPPA,PRKCA,PRKCB,PRKCQ,RYR2,SOD1,SPTB	1042 (23)
KLF15	transcription reg	5,81E-06	ACADS,ACAT1,ACSS1,CCN2,CD36,CPT1B,CPT2,FABP3,NPHS1,NPHS2,NPPA,PDK4,PPARG,PPARGC1A,SLC2A4,UCP3	1028 (19)
CASZ1	enzyme	5,86E-06	ABCC9,CACNA1D,CCL17,CKM,DCC,EDN1,ENPP1,GRIN3A,HTR1B,KCNK3,RAMP1,TGFB3,TNFRSF1B,XYLT1	
NR1D1	ligand-depende	5,86E-06	APOC3,ARNTL,CRY1,FADS2,FGF21,FOS,KLB,MEF2C,NAMPT,RHO,SIRT1,SLC2A1,TH,TLR4	
NSD2	enzyme	5,86E-06	BAX,CA2,CXCR4,ERCC1,FOS,IGF1,IGF2BP2,IL5,ITGB1,JUN,KMT2C,PRKCA,ROCK2,STAT3	873 (11)
SPRY2	other	5,86E-06	EGFR,EPAS1,EPHB4,EPO,ETV5,FGFR3,FOS,HIF1A,MET,NR2F1,PTEN,PTPN1,SFTPB,SLC2A1	965 (17)
CDK2	kinase	5,99E-06	BRCA1,CD34,CDKN2A,CYP3A4,DHFR,FOS,GCK,IL2,KCNJ11,NCOR2,PGR,SNAP25,TERT,TNFAIP3,UCP2	714 (16)
GABPA	transcription reg	5,99E-06	ATM,AURKA,BRCA1,ELANE,FAS,HMOX1,IL16,IL7R,ITGB2,NQO1,PPARG,PRL,SOD3,TNC,TSHR	651 (10)
RPS6KB1	kinase	5,99E-06	ATP1A1,CAV3,CCND1,HAMP,HIF1A,HMGCR,IL10,IL12B,IL17A,IL23R,IRS1,SERPINE1,SLC2A4,SREBF2,TP53	861 (20)
AIF1	other	6,02E-06	ACTA2,CCND1,COL1A1,COL3A1,IL17A,IL4,IL6,TGFB1	736 (11)
DAP3	other	6,02E-06	MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6	
DOK1	kinase	6,02E-06	ADIPOQ,CD69,FOXP3,IL2,IL2RA,LEP,STAT4,TNF	1076 (22)
IgG2a	complex	6,02E-06	CXCL8,HMOX1,IFNG,IL10,IL1B,IL6,LTA,TNF	926 (23)
PDGFRB	kinase	6,02E-06	ACTA2,EGFR,EPO,HAMP,PDGFRB,RGS5,SMAD1,STAT3	880 (22)
PLA2G2D	enzyme	6,02E-06	ARG1,CCR2,IFNG,IL12A,IL1B,IL6,ITGAM,TNF	879 (12)
RNF128	enzyme	6,02E-06	CD247,IFNG,IL2,IL4,IL5,NFATC1,TFR2,TNF	751 (22)
SERPINB5	other	6,02E-06	BAX,CDC42,IL13,IL4,IL5,RAC1,SCNN1B,VEGFA	866 (18)
TRPV1	ion channel	6,02E-06	ADCYAP1,FOS,HLA-DQB1,IL6,PTGS2,TP53,TRPV1,VIP	1043 (23)
VEGFD	growth factor	6,02E-06	BDNF,BGLAP,CCND1,IL18,IL6,MMP12,PTGS2,VEGFC	782 (17)
ZIC3	transcription reg	6,02E-06	GATA4,KLK1,NKX2-5,NPPA,PDGFRA,PITX2,SOX17,TBX5	
GDNF	growth factor	6,12E-06	AR,BDKRB1,BDNF,CCND1,DRD1,DRD2,ETV5,FN1,GATA2,GFRA1,HSD11B2,HTR2A,KIT,KLC1,NNAT,PDYN,SCN10A,SST,TH,TNF	1026 (23)
ADIPOR2	transmembrane	7,01E-06	ADIPOR2,GCK,PPARA,PPARG,PTGS2,UCP1,UCP2	942 (20)
CDK6	kinase	7,01E-06	CDK6,CDKN2A,DHFR,IL10,TP53,TSC1,VEGFA	885 (24)
DBH	enzyme	7,01E-06	AGRP,DRD2,FOS,IFNG,NPY,UCP1,UCP2	
GFPT1	enzyme	7,01E-06	GCK,HAS2,LEP,PPARG,SLC2A2,TGFB1,THBS1	800 (17)
Hmga2	enzyme	7,01E-06	CDKN2A,HNF4A,IL15,IL15RA,IL2,IL2RA,MYOD1	

IL20	cytokine	7,01E-06	IFNG,IL13,IL4,MMP12,MMP9,TNFRSF11A,TNFSF11	658 (15)
IQGAP1	other	7,01E-06	CCND1,CDC42,CXCR4,IFNG,IL2,PGR,TFF1	1154 (24)
KCNA3	ion channel	7,01E-06	CTLA4,FOXO1,IFNG,IL10,IL17A,IL2RA,IL6	745 (10)
LAT2	other	7,01E-06	CXCL8,IL10,IL12B,IL2,IL4,IL6,TNF	657 (21)
NFKBIE	transcription reg	7,01E-06	CCL2,CSF2,CXCL8,ICAM1,SELE,TNF,VCAM1	658 (13)
PDK2	kinase	7,01E-06	ARG1,ASIC3,IL10,IL1B,IL6,NOS2,TNF	880 (23)
PIM3	kinase	7,01E-06	IFNG,IL12RB2,IL1B,PECAM1,PPARGC1A,STAT4,TNF	814 (12)
RAMP1	transporter	7,01E-06	FLT4,IFNG,IL4,IL6,TNF,VEGFA,VEGFC	935 (18)
VASP	other	7,01E-06	ARG1,EPAS1,HIF1A,IL1B,NOS2,SELP,TNF	1007 (25)
SHC1	other	7,19E-06	BAX,CD69,EDN2,FOS,GSTP1,ICAM1,IL2,INS,ITGAM,MEF2A,NQO1,SDC4,SELE,SERPINE1,SOD2,THBD,TXN	894 (16)
GLI3	transcription reg	7,75E-06	AKT1,BMP4,CCND1,CD69,EBF1,FGF10,FOXO1,GNRH1,KLK1,MAPKAPK2,NFKBIZ,PAX2,PAX5,PVR,RUNX1,SALL1,SHH,TERT,TNFAIP3,WNT5A	
ONECUT1	transcription reg	7,75E-06	ABCB11,ABCC2,ADH1B,AFP,AGTR1,APOH,C2,CACNA1D,CD36,CEBPD,CXCL13,CYP7A1,F11,F9,FADS3,FAS,GCG,GLA,GSS,HABP2,HLA-G,HMGCR,HNF1B,HNF4A,HSPA1A/HSPA1B,HTR2B,ITGAV,LPL,MAP2K5,MEIS1,MGST3,MON1B,NFKBIA,NR0B2,NR1I2,NUTF2,PCK1,PON1,PPARD,PTPRN2,RARG,RORA,SEMA6A,SERPINA1,SLC2A2,TBX2,TCF7,TNFSF10,TTR,UGT1A1,WDR12	395 (7)
TYK2	kinase	7,84E-06	CD36,HAMP,HIF1A,IFNG,IL12A,IL12B,IL17A,IL18R1,IL1B,IL23A,OSMR,SOCS3,STAT3	716 (16)
IL24	cytokine	7,86E-06	BAX,CCND1,CXCL8,FAS,FOXP3,HBEGF,IFNG,IL10,IL12A,IL12B,IL23A,IL24,NOS2,PAX5,PTGS2,XRCC4	734 (15)
TEAD2	transcription reg	7,86E-06	ADM,CALD1,CCND1,COL3A1,EDN1,EDNRA,GPR37,NFKBIZ,POSTN,PTPRO,RHOBTB1,THBS1,TNNT2,TP53,TPM1,UHRF1	361 (7)
BMP	group	7,97E-06	CCN2,ERBB3,GATA4,IL6,KDR,LMX1B,NKX2-5,SMAD1,SMAD5,SPP1,TCF21	375 (7)
CDC73	other	7,97E-06	CCND1,GATA2,H19,HMGA1,HMGCS2,IGF1,IGF2,PTGES,RUNX1,SOCS1,TFF1	674 (13)
COMMD1	transporter	7,97E-06	EGLN3,GRHPR,IFNG,LDHA,LGALS2,NFKBIA,PFKP,STC2,TF,TFRC,VEGFA	533 (7)
HEXIM1	transcription reg	7,97E-06	ACE2,ANGPT1,CCND1,COL1A1,FGF9,HIF1A,LOXL2,SLC2A1,TFF1,TGFB2,TP53	982 (22)
NMU	other	7,97E-06	BRCA1,CSF2,DIO2,IL10,IL13,IL4,IL5,IL6,IL9,LEP,MYB	821 (21)
PPIF	enzyme	8,00E-06	BMP6,CCL2,CCL5,CCR2,CCR5,CSF2,CX3CR1,CXCL12,CXCR2,CXCR4,DLK1,HGF,IL13,IL16,IL6,IRF5,MGP,MMP2,PDK4,PITX2,PTN,TNF,WNT5A,XCL1	615 (11)
MAX	transcription reg	8,18E-06	ACTC1,AR,BAX,CAD,CDKN2B,DHFR,DLEU2,EBF1,EDN1,FADS2,GH1,HAMP,HMGA1,MTHFD1,PDGFRB,RARB,SLC2A1,SLC2A3,TERC,TERT,TNNT2,TXNIP,WRN	474 (6)
TRAF3	enzyme	8,18E-06	ADM,CCL5,CXCL12,CXCL13,EGFR,FAS,ICAM1,IFNG,IL10,IL12B,IL1B,IL2,IL2RB,IL4,IL6,IL9R,MAPK8,MET,NFKB2,NFKBIA,TERT,TNF,TNFAIP3	542 (17)
CADM1	other	8,24E-06	GRIA1,IFNG,IL2,IL22,IL4	603 (11)
Cd24a	other	8,24E-06	IFNG,IL12B,IL6,MMP2,TNF	730 (16)
HPGDS	enzyme	8,24E-06	IL2,ITGAM,PTGDS,TGFB1,TNF	618 (10)
NPY5R	G-protein coupl	8,24E-06	HAMP,IL6,NPY,POMC,TNF	810 (15)
SEMA3F	other	8,24E-06	HIF1A,MMP2,MMP9,TP53,VEGFA	703 (18)
SLAMF6	transmembrane	8,24E-06	IFNG,IL12B,IL16,IL17A,TNF	542 (7)
Trbv13-1	other	8,24E-06	IFNG,IL10,IL12B,IL4,TNF	
C5	other	8,29E-06	C5AR2,IL10,IL1B,IL6,ITGB1,ITGB2,SOCS3,STAT3,TNF	799 (19)
FABP5	transporter	8,29E-06	CXCL8,FABP3,FOXP3,IL17A,LEP,PPARG,RORA,SOCS3,VEGFA	859 (18)
HNRNPU	transporter	8,29E-06	BAX,HBB,IL1B,IL6,MYOD1,POU5F1,SPP1,TNF,VCAM1	
HSPB1	other	8,29E-06	ACTA2,IL10,IL1B,IL6,LPL,PECAM1,RELA,TNF,TP53	775 (19)
IFNLR1	transmembrane	8,29E-06	ATF3,CCL5,IFIH1,IFNL3,IL1A,IL1B,IL6,ITGAV,OASL,PTGS2,SOD2,THBS1,TLR2,TNF,TNFAIP3	643 (17)
LBP	transporter	8,29E-06	CD14,CXCL8,CXCR2,IL1B,IL1RN,IL6,LBP,TLR2,TNF	840 (18)
mir-515	microRNA	8,29E-06	ANGPTL4,AR,CXCL8,HIF1A,IL6,RELA,SERPINE1,SMAD4,TGFBR2	644 (12)
P2RY2	G-protein coupl	8,29E-06	CXCL8,HAS2,ICAM1,PTGS2,SCNN1A,SERPINE1,SLC12A1,TF,VCAM1	760 (19)
SMAD6	transcription reg	8,29E-06	IFNG,IL6,NFATC1,NOS2,PCK1,SERPINE1,SPP1,TGFB1,TGFB3	710 (16)
TARBP2	other	8,29E-06	DCAF6,DICER1,LIN28A,MAF,MYL3,RET,SOX6,THBS1,TNNC1	644 (7)
TNFRSF21	transmembrane	8,29E-06	CD28,CTLA4,IL10,IL13,IL2RA,IL4,IL5,NFATC1,STAT3	767 (19)
CARM1	transcription reg	8,33E-06	ABCB11,C3,CDKN2A,DHFR,EPHX2,FOS,GCLC,ICAM1,MMP3,PCK1,PTGES,SIRT1,STC2,TFF1	1086 (25)
HES1	transcription reg	8,34E-06	CCK,CHGA,DLK1,GAA,GIP,GRIA1,HES1,IL1RL1,IL6,NOTCH1,PAX2,PAX5,PPARG,PTEN,PTGDS,SPP1,SST,TPH1	
ACKR1	G-protein coupl	8,72E-06	BDNF,CCL2,CXCR2,ICAM1,MYO5A,PMS1,SELE,TNFAIP3,TNKS,VCAM1	676 (14)
ITGA2	transmembrane	8,72E-06	COL1A1,GHRH,IGF1,IL17A,IL6,ITGA2,ITGB1,MMP1,MMP3,TNFSF11	840 (21)
ITGAM	transmembrane	8,72E-06	CD28,CXCL8,IL10,IL12A,IL12B,IL1B,IL6,PTGS2,TGFB1,TNF	654 (17)
MAT1A	enzyme	8,72E-06	APOA1,ATP1B1,BAX,CYP2E1,CYP4A11,FAS,LTA4H,MAT1A,SAA1,SOD1	
RNASE1	enzyme	8,72E-06	CCL2,CCL23,CCL5,CCL8,CXCL5,IL12B,IL16,IL2RA,IL6,TNF	
EIF2AK3	kinase	8,80E-06	ANG,ARNTL,ATF3,BDNF,CCND1,DNASE1,GCH1,IGF1,IL1B,IL6,JUN,LARS,MTHFR,NFKB2,NOS2,PON2,SLC1A4,SLC1A7,SPATA5,TNF,TP53,TXNIP,VEGFA,WARS,WFS1,ZFP36	741 (19)
CLEC11A	growth factor	9,48E-06	ALOX5,ALOX5AP,CCR5,CXCL12,CYP17A1,FOS,IL13,IL1B,LDHA,LHCGR,MIF,NFKB1,SLPI,STAT4,TKT,TNF,TSC22D1	920 (19)
miR-34a-5p (an	mature microRN	9,48E-06	ATF3,AXL,CCND1,CDK6,DHFR,ICAM1,JAG1,LIN28A,MET,MYB,NOTCH1,NOTCH2,POU5F1,PPARG,SIRT1,TP53,VEGFA	960 (20)
NKX2-3	transcription reg	9,86E-06	ACTA2,ADM,ALPL,ANGPTL4,BCHE,BMP2,BMP4,C2CD4B,CBS/CBSL,CD300LG,CD34,CD36,CXADR,CXCL8,EDN1,F2RL1,FBN2,FCN3,GCA,GCH1,GDF15,GHR,HFE,HLA-B,HLA-C,IL7R,MMP7,MYO5A,NOS3,NR2F1,POSTN,PSMB8,PSMB9,PTGS2,RNF213,SERPINE2,TAP1,TFPI2,TNFSF4,TRPC6,UCP3,VCAM1	
ADAM10	peptidase	1,00E-05	ACTA2,ATP2A2,CACNA2D1,CALCRL,CCND1,CCR2,CXCL12,DLGAP1,EGFR,FOS,IL6ST,IRAK1,KLRB1,MEF2C,MET,MKKS,NOS1,RGS4,RHO,ROCK1,TGFB1,TH,XCL1	1020 (19)
H2AFZ	other	1,02E-05	AFP,APOA1,CCND1,CD69,CXCR4,HNF4A,MYOD1,NOS3,PPARG,SOX17,TOMM40,TTR	
miR-221-3p (an	mature microRN	1,02E-05	ESR1,FOS,FOXO3,GAS5,ICAM1,KIT,MITF,MMP1,PIK3R1,PTEN,SOD2,TIMP3	707 (7)
PRKCI	kinase	1,02E-05	ABCC8,CCND1,HMOX1,IL10,IL1A,IL6,KCNJ11,PTGS2,SLC2A1,SLC2A2,SLC2A4,SREBF1	1002 (21)
ROCK1	kinase	1,02E-05	CCN2,CCND1,COL1A1,COL3A1,EDN1,FBLN2,FBN1,ICAM1,MYH7,NPPA,TGFB2,VCAM1	976 (25)
HIC1	transcription reg	1,08E-05	ACTA2,ADORA2B,ADRB2,CA2,CCN3,CCND1,CXCL14,CYP24A1,FADS1,GPR161,KCNJ6,LCN2,LRP8,MAP2K5,MMP12,SIRT1,SNAP25,SPP1	575 (7)
ING1	transcription reg	1,14E-05	AFP,ANGPTL4,BAX,CCL2,CCL5,CDKN2A,DIDO1,HSPA1A/HSPA1B,JAK2,SHH,SPP1,TP53,ZFP36	1025 (20)
EIF4E	translation regu	1,19E-05	ATR,CCND1,CDKN2A,EGFR,EP300,FGF5,FN1,GPX3,HIF1A,HMOX1,HMOX2,IFNG,IL15RA,IL18,IL1A,IL2,INSIG1,MAPKAPK2,MMP3,MMP9,NFKBIA,NOS2,PLAUR,POMC,PRL,SERTAD1,SLC6A4,TNC,TNF,TP53,TP53BP1,TPH2,VEGFC,ZPR1	990 (23)
POU2F2	transcription reg	1,22E-05	ADA,ALOX5,CCR5,CD69,EBF1,GATM,HLA-DRA,HNF1B,IL10,IL12A,IL2,IL5RA,JUN,MMAB,MVK,NOS2,PLEKHG1,RYR1,SPP1,STAT3,TERT,TIMP2,VIP	501 (7)
CTCF	transcription reg	1,25E-05	APOA1,APOC3,BAX,BDNF,CDKN2A,GATA4,H19,HLA-DQA1,HLA-DQB1,HLA-DRB1,HLA-DRB5,IGF2,IL12RB1,IL17A,IL1R1,MMP14,MYOD1,NFKB2,TGFB3,TNF,TP53	726 (12)
AKT3	kinase	1,26E-05	ERBB2,ERBB3,IFNG,IGF2,IL17A,IL2,MMP9,MT-CO1,MT-CO2,RAC1,WNK1	994 (22)
CHI3L1	enzyme	1,26E-05	ARL4C,CALD1,CXCL8,MMP9,NAMPT,NNMT,SERPINB1,SERPINE1,TGFBR2,TNC,VEGFA	959 (21)
FGF9	growth factor	1,26E-05	BAX,BMP4,CCND1,CYP11A1,FGF10,GCLC,HMOX1,PECAM1,PITX2,SHH,VEGFA	816 (20)
HMGB2	transcription reg	1,26E-05	BAX,CCND1,CXCL5,CXCL8,IL1B,IL6,MMP1,MMP14,MMP3,NRG1,VEGFC	948 (15)
Pka catalytic su	group	1,26E-05	ABCA1,CXCL8,CYP11A1,CYP17A1,DBH,PCK1,PPARGC1A,PRL,SST,TH,VDR	864 (17)
C5AR2	G-protein coupl	1,29E-05	ATP2A2,C5AR2,IFNG,IL10,IL12B,IL17A,IL5,TNF	892 (16)
COX4I1	enzyme	1,29E-05	PDK4,POSTN,PPP3CA,SFRP2,SLC24A3,SLC2A4,TGFB2,TSPAN8	
GHRHR	G-protein coupl	1,29E-05	CCND1,FOS,GH1,GHRHR,HSD11B1,HSD11B2,IL1B,TNF	987 (22)
HAVCR1	other	1,29E-05	CDK6,IFNG,IL10,IL2,IL2RA,IL4,IL5,TNF	680 (23)
HHEX	transcription reg	1,29E-05	ENG,FLT1,ITGAV,KDR,SLC10A1,SST,TIE1,VEGFA	
HNRNPD	transcription reg	1,29E-05	FLT1,FOS,HBB,IL10,LDLR,TERC,TERT,TNF	490 (7)
PIAS3	transcription reg	1,29E-05	CDKN2B,FGG,HP,MMP3,MMP9,NFATC1,RELA,SERPINA3	680 (11)
PLCE1	enzyme	1,29E-05	CCL2,CCR2,CXCL8,CXCR2,IFNG,IL6,PTGS2,TNF	932 (20)
PRDX1	enzyme	1,29E-05	ARG1,BAX,IFNG,IL12A,IL12B,PTGS2,REL,SELP	910 (16)
PSMB10	peptidase	1,29E-05	IL10,IL1A,IL4,IL6,NFKB2,NFKBIA,NOS2,TNFAIP3	378 (7)
TYR	enzyme	1,29E-05	CCR2,CSF2,CXCR2,CXCR4,IFNG,IL2,KIR2DL1/KIR2DL3,KIR2DS3	734 (7)
SNAI2	transcription reg	1,38E-05	AKT1,AR,AXL,BGLAP,BRCA2,CCN2,CCND1,CDC42,COL1A1,CXCL12,CXCR4,FN1,ITGB1,MEF2C,MMP14,MMP9,STAT3,VDR	750 (21)

BMP15	growth factor	1,46E-05	CYP11A1,CYP19A1,FSHR,HAS2,ID3,LHCGR,PAPPA,PCSK6,PTGS2,SMAD6	577 (14)
CXCR3	G-protein coupl	1,46E-05	CD69,CFTR,COL1A1,FN1,HMOX1,IFNG,IL10,MMP1,MPO,TNC	837 (19)
GRN	growth factor	1,46E-05	ANGPT1,CCND1,GBA,ICAM1,IL10,IL12B,IL1B,IL6,TNF,VEGFA	786 (20)
HSP90AB1	enzyme	1,46E-05	ABCC1,ATF3,EPAS1,ESR1,HIF1A,IL17A,KCNJ11,NOS2,POU5F1,SLC6A4	1000 (20)
IGFBP5	other	1,46E-05	BAX,BGLAP,CCND1,COL1A1,EFNB2,IGF1,IRS1,MYH7,SERPINE1,TNFRSF1A	882 (25)
MFSD2A	transporter	1,46E-05	DHCR7,FADS1,FADS2,FDFT1,INSIG1,LDLR,LSS,RHO,SREBF1,SREBF2	
TRPC1	ion channel	1,46E-05	BAX,CCND1,CDK6,FOXO1,HIF1A,IGFBP1,KDR,MYOD1,PRL,TRPC1	778 (16)
FGF8	growth factor	1,48E-05	BGLAP,BMP2,BMP4,CCL11,CCL2,CCND1,COL18A1,CTNNB1,DDAH2,ETV5,FGF10,FGFR1,FGFR2,LMX1A,PAX5,RGS12,SHH,SLPI,SPP1,TH,THBS1,TNFRSF11B,VDR	838 (21)
Igm	complex	1,48E-05	BCL2A1,CD40,CD69,CDKN2A,CXCL8,FAS,FCGR2B,ID3,IL10,IL17A,IL2RA,JAK2,NFKB1,NFKB2,PAX5,TNF,TNFSF4,TP53,TRAF1	893 (22)
CGA	other	1,51E-05	BAX,BDNF,CCR3,CXCL8,LHCGR,MMP14,MMP2,PTGS2,SGK1,TIMP2,TIMP3,UGT1A1	1136 (25)
EIF2AK4	kinase	1,51E-05	AQP4,ATF3,CAT,CD247,IL10,IL12B,IL1B,IL6,PPARG,PSEN1,SOD2,TNF	832 (22)
Hmgn3	other	1,51E-05	APOA1,APOA2,FGA,INS,KCNJ11,KNG1,POMC,SERPINA1,SLC2A2,TRIB3,TSHR,TTR	255 (4)
PRLR	transmembrane	1,51E-05	AKR1C3,AKT1,BDNF,ESR1,ESR2,GDNF,GHR,HSD3B1,LEP,PRL,TP53,VDR	1001 (21)
SRSF1	other	1,51E-05	AURKA,CD200,COL1A1,DIO1,ENG,FN1,IL2,LMNA,RAC1,SRSF2,TP53,VEGFA	100 (4)
TG	other	1,51E-05	ANGPT1,CPT1A,CYP7A1,DIO1,IFNG,IL10,IL18,IL2,IL4,PDK4,SLC26A4,TRH	899 (20)
WAS	other	1,51E-05	CD69,CSF2,IFNG,IL17A,IL1B,IL2,IL22,IL23R,IL4,IL5,SELPLG,TNF	838 (25)
WNT4	cytokine	1,51E-05	BMP2,CCND1,CTNNB1,CYP11B1,CYP17A1,CYP21A2,DLK1,FKBP4,FKBP5,FOXO1,MYOD1,PTGS2	517 (7)
ADORA1	G-protein coupl	1,52E-05	BAX,CCL17,COL3A1,HAMP,IL13,IL4,MMP12,MMP9,NPPA	815 (18)
CCR6	G-protein coupl	1,52E-05	HAMP,IFNG,IL10,IL12A,IL12B,IL2,IL5,MMP12,TNF	877 (21)
CXCL3	cytokine	1,52E-05	CCL5,GRK2,GRK5,ICAM1,IL1B,IL6,ITGB1,POSTN,TNF	751 (18)
DEF6	other	1,52E-05	FN1,FOS,IFNG,IL17A,IL2,IL4,MMP2,MMP9,NFATC1	720 (21)
FMO3	enzyme	1,52E-05	ABCG5,ABCG8,FGF21,FOXO1,MTTP,PDK4,PPARA,PPARGC1A,SREBF1	
PARG	enzyme	1,52E-05	GDF15,IL1B,MTR,NAT1,NOS2,NVL,PARP1,PTGS2,TNF	885 (16)
MDM2	transcription reg	1,53E-05	ATF3,BAX,CCND1,CDKN2A,CXCL8,ESR2,FOXO3,HIF1A,IGF1R,IL13RA2,IL1RN,IL2,NR0B2,RELA,TERT,THBS1,TIMP1,TNFSF10,TP53,TP73	1023 (20)
Pln	other	1,61E-05	APOA1,ATP1A1,ATP2B1,DES,FABP3,GCGR,GNAI2,ITGB1,MYH7,MYL2,NPPA,PRKCA,PRKCB,PRKCQ,RYR2,SOD1,SPTB	
FOSB	transcription reg	1,62E-05	BDNF,CCND1,FOLR2,FOS,GNRHR,MMP1,MMP2,MMP9,PPARG,SERPINE1,SMAD3,TH,TIMP1	955 (25)
NCSTN	peptidase	1,62E-05	CD14,CEBPD,EGFR,ELANE,FCGR2A,FCGR2B,GATA2,HES1,ITGA2B,Ly6a (includes others),MPO,NOTCH1,PSEN1	857 (15)
PF4	cytokine	1,62E-05	ACTA2,CCL2,CXCL8,ICAM1,IFNG,IL17A,IL1A,IL1B,IL22,IL6,ITGAM,THBD,TNF	757 (18)
PRKAA	group	1,62E-05	BAX,CPT1A,CYP11A1,FOXO3,HSD11B1,IL6,NCF2,NOS2,OGG1,PCK1,PPARGC1A,SREBF1,TNF,TP53	929 (23)
TARDBP	transcription reg	1,62E-05	CD36,CFTR,FIS1,IFNG,IL1B,IL6,LCN2,MEF2D,MFN1,mir-143,MT-ND6,PRKN,TNF	779 (12)
ELAVL1	other	1,70E-05	ABCA1,ACTA2,ATF3,CCL8,CTNNB1,FCGR2A,FOS,GLP1R,GSS,HBB,HLA-A,HLA-DRB5,HMOX1,HSPA2,IFIH1,IL13,IL17A,IL4,IL6,mir-122,MYOD1,NFKBIA,NOS2,NUF2,PLA2G7,PRC1,PSMB4,PTGS2,PTPRC,PTPRN2,REN,SIRT1,STAT3,TNF,TP53,VCAM1,VEGFA,WARS,ZFP36	970 (21)
ATF6	transcription reg	1,76E-05	ATP2A2,AURKA,CPT1A,CPT2,FOS,IL6,INS,LMAN1,NPPA,NR0B2,NUCB2,PCK1,PDX1,PLAT,PPARA,PVR,SRR,VEGFA	1059 (22)
APOH	transporter	1,77E-05	CD36,CD40,F2,IFNG,NFKB1,SELE,TNF	754 (18)
ATP7A	transporter	1,77E-05	ADCYAP1,CCK,CCL2,ELN,PAM,POMC,VEGFA	
DDR2	kinase	1,77E-05	COL1A1,LOXL2,MMP1,MMP14,MMP2,MMP3,MMP7	508 (9)
GPR132	G-protein coupl	1,77E-05	CCL17,CSF2,ICAM1,IFNG,IL5,IL6,SELE	858 (19)
IL17RB	transmembrane	1,77E-05	CCL11,CCL17,HAMP,IL13,IL5,IL6,TGFB1	651 (18)
Kallikrein	group	1,77E-05	AGTR1,BDKRB2,DRD1,EDNRA,ICAM1,TGFB1,VCAM1	552 (11)
MAFF	transcription reg	1,77E-05	GCLC,GSTP1,HBB,HBG1,IL1RN,NQO1,TXNRD1	
icatibant	biologic drug	3,49E-07	AGTR1,BDKRB1,BDKRB2,ICAM1,NOS3,NOTCH1,PTGS2,STAT3,TGFB1	640 (12)
NCOA6	transcription reg	1,77E-05	ABCG5,CYP2C9,CYP7A1,FOS,LPL,SREBF1,SST	950 (19)
NDFIP1	other	1,77E-05	IL1B,IL2,IL2RA,IL4,IL6,PTEN,TNF	624 (19)
PLCL2	enzyme	1,77E-05	DIO2,LHCGR,PPARA,PPARD,PPARG,PPARGC1A,UCP1	740 (11)
TNFSF18	cytokine	1,77E-05	AGTR1,CTLA4,FOXP3,IFNG,IL17A,IL2RA,TNFRSF11A	751 (19)
XPO1	transporter	1,77E-05	CCND1,GATA4,ICAM1,IGFBP3,MET,NOS2,TP53	921 (18)
ALKBH1	enzyme	1,87E-05	MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND2,MT-ND4	
APCS	other	1,87E-05	FCGR2A,FCGR2B,IFNG,IL10,LDLR,SIRPA	560 (10)
CD276	other	1,87E-05	CXCL8,IFNG,IL2,IL4,MMP9,TNF	871 (19)
farnesyl transfe	complex	1,87E-05	GJA1,HBEGF,IL6,MMP7,MPO,NOS2	1007 (20)
GALP	other	1,87E-05	FOS,IL1A,IL1B,IL6,POMC,UCP1	689 (11)
GFER	enzyme	1,87E-05	CYP1A2,CYP3A4,DNM1L,FUT4,IL6,POU5F1	
IL26	cytokine	1,87E-05	CXCL8,ICAM1,IL10,IL1B,IL6,TNF	620 (16)
IL18BP	other	1,87E-05	CXCL8,IFNG,IL23A,IL6,TNF,VEGFA	656 (13)
LITAF	transcription reg	1,87E-05	CCL5,CCL8,IFNG,IL10,IL1A,TNF	751 (21)
MEDAG	other	1,87E-05	CD36,FABP2,LIPE,LPL,PLIN1,PPARG	
NSUN3	enzyme	1,87E-05	MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND2,MT-ND4	
PDZK1	transporter	1,87E-05	AQP1,SCARB1,SLC22A12,SLC26A6,SLC7A2,VCAM1	
PLA2G5	enzyme	1,87E-05	COL1A2,COL3A1,PLA2G5,PTGS2,VEGFA,VEGFC	883 (18)
POU3F3	transcription reg	1,87E-05	BSND,CDK5R1,KCNJ1,PTGER3,SLC12A1,UMOD	
Proinsulin	group	1,87E-05	APOM,CTLA4,FOXO1,GCK,IL10,NFATC1	555 (11)
RBCK1	transcription reg	1,87E-05	ATP1A1,CCND1,ESR1,ICAM1,TNFAIP3,VCAM1	788 (17)
SDC2	other	1,87E-05	ACTA2,MMP7,TGFBR1,TGFBR2,TGFBR3,TP53	1045 (15)
Tlr13	other	1,87E-05	CXCL8,IL12B,IL1B,IL6,NFKB1,TNF	719 (16)
TNFRSF10B	transmembrane	1,87E-05	CXCL8,IFNG,IL2,IL4,IL6,MMP3	636 (19)
IL17C	cytokine	1,94E-05	CXCL8,IFNG,IL17A,IL1A,IL1B,IL2,IL23A,IL6,LCN2,PI3,TNF	788 (9)
LTF	peptidase	1,94E-05	BMP7,CCL5,IL10,IL5,IL6,PGR,PLIN1,TNF,TNFRSF11B,TNFSF11,TP53	743 (17)
PROCR	other	1,94E-05	ANGPT1,CCND1,ICAM1,IL1B,IL1R1,IL23R,IL6,MMP9,ROCK2,TNF,VCAM1	722 (20)
Saa3	other	1,94E-05	APOA1,BMP2,CCL5,COL1A1,CTNNB1,IGF1,MMP2,MMP3,MMP9,TNFRSF11B,TNFSF11	619 (12)
MYCN	transcription reg	2,01E-05	ABCA1,ABCB1,ABCC1,ABCG2,ACTN4,ATXN2,BAX,CAD,CAV1,CCN2,CCND1,CDC42,CIITA,CLU,COL18A1,COL1A1,COL4A1,EGFR,FBN1,FGF5,FGFR2,FN1,GATA4,HLA-A,HMGA1,HSPD1,ITGA2,ITGB1,KDM5B,LDHA,MAP4,MMP2,MSRB3,MYH9,NCAM1,NTRK1,PRKN,RGS5,SERPINE1,SIRT1,SLC2A1,SOX17,TERC,TERT,TH,TIMP2,TNFRSF1A,TP53,TPM1,XRCC3	970 (19)
ADRA1D	G-protein coupl	2,05E-05	ADRA1B,BDNF,CEBPD,COL3A1,DDAH1,FN1,FOS,IL6,IL6ST,JUN,LOX,PPP3CA,PRIM2,STAT3,VEGFA	1037 (22)
ARHGAP31	other	2,21E-05	BMP2,BMP7,CDKN2A,FN1,GDF15,ITGB6,JUN,MMP3,TGFB2,TGFB3,TGFBR1,TGFBR3	448 (7)
DMP1	other	2,21E-05	ADD3,ALPL,BMP2,CDKN2A,CX3CR1,CXCL8,F13A1,FGF1,IL6,LIPG,NPY,SLC6A9,SMAD6,SPP1	378 (7)
HOXC6	transcription reg	2,21E-05	ABCB1,BCO2,BMP7,CARD8,COL23A1,FGFR2,HAMP,IGFBP3,MME,NFKB2,PDGFRA,RFX7,RUNX1,VCAM1	
TRB	transmembrane	2,21E-05	BAX,CCL11,FAS,IFNG,IL10,IL13,IL2,IL2RA,IL4,IL5,SELPLG,TNF	698 (20)
PDCD1	phosphatase	2,23E-05	CD40,CXCL8,FAS,IFNG,IL10,IL12A,IL13,IL17A,IL2,IL22,IL2RA,IL4,IL5,IL6,KIR2DL2,NOS2,PADI2,TNF	628 (16)
GNRH	group	2,28E-05	ADCYAP1,ADIPOQ,ATF3,BMP7,CHGA,FOS,GNRHR,IGFBP3,JUN,MAPK3,PTGS2,SCG3,SGK1	1149 (25)
NPM1	transcription reg	2,28E-05	ALK,CCL2,CTNNB1,IFNG,IL6,IL6ST,let-7,LTF,MMP9,SOD2,TNF,TP53,VEGFA	818 (19)
RNASE2	enzyme	2,28E-05	CCL2,CCL23,CCL5,CCL8,CXCL5,IL10,IL12B,IL13,IL2RA,IL5,IL6,TNF,TNFRSF1A	768 (16)
TRH	other	2,28E-05	DIO2,F2,F2R,FOS,JUN,KCNA5,MITF,POMC,PRL,SFTPB,TRH,TRHR,VIP	923 (25)
MBD3	other	2,32E-05	ACTC1,APOE,CCN4,CCND1,CDKN2A,CTNNB1,DPP4,EP300,FZD4,HTRA1,LGR5,LRP5,MAPK8,MEF2A,PITX2,PPARD,PRICKLE1,SFRP2,SIRT1,TIE1,WNT5A	108 (3)
Fibrin	complex	2,36E-05	ACTA2,CXCL8,FN1,ICAM1,IL6,KDR,mir-146,SERPINE1,TH,TLR4	866 (19)
HSPA9	other	2,36E-05	FOXO1,HES1,NTRK1,PBX1,PRDM16,RARB,RET,SOD2,TH,TP53	559 (11)
CAPN3	peptidase	2,52E-05	CCL5,GCLM,GPX3,HMOX1,NCF2,NOX4,PTGS2,SOD2	493 (7)
CHRNA1	transmembrane	2,52E-05	CD28,CD40,CD69,CTLA4,FAS,IFNG,IL10,IL2	798 (16)
FNDC5	other	2,52E-05	ALPL,BDNF,COL1A1,CTNNB1,LRP5,PRDM16,SPP1,UCP1	
HOXC9	transcription reg	2,52E-05	BMP4,FGF10,MMP9,NOS3,SHH,SPP1,TIMP3,WNT5A	
IGFBP7	transporter	2,52E-05	CCND1,CDKN2A,CYP11A1,MAPK1,MMP2,MMP9,PTGS2,SOD2	1021 (23)
ITIH1	other	2,52E-05	IL10,IL12B,IRF5,NOS2,PPARG,TGFB1,TNF,TNFSF14	63 (3)
Nos	group	2,52E-05	BDNF,CD59,FOS,GCH1,HMOX1,OLR1,TIMP1,VEGFA	719 (18)

PDE5A	enzyme	2,52E-05	ATP2A2,CD247,FOXP3,IL1B,IL6,NOS1,NOS2,PRKG1	724 (18)
PPARÎ±-RXRÎ±	complex	2,52E-05	ABCA1,ACAA1,APOA1,APOA2,CPT1B,IL6,LPL,NFKBIA	570 (7)
RND3	enzyme	2,52E-05	BAX,CCND1,HES1,MMP2,NOTCH1,PTEN,PTGS2,ROCK1	955 (16)
SERTAD2	transcription reg	2,52E-05	ADRB3,CAT,CPT1B,DIO2,LIPE,PPARD,PPARGC1A,UCP1	
SMC3	other	2,52E-05	BMPR2,CXCL12,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,IRS2,THBS1	
TBX3	transcription reg	2,52E-05	CDKN2A,GJA1,GJA5,JDP2,NPPA,POU5F1,TBX2,TP53	
TRAF5	transporter	2,52E-05	FAS,ICAM1,IL10,IL12B,IL17A,IL6,RELA,TNF	635 (18)
CCKBR	G-protein coupl	2,63E-05	ADIPOQ,APLN,CTNNB1,GHSR,HIF1A,LEP,MAPK1,MAPK3,RETN	863 (15)
NOD1	other	2,63E-05	CCL5,CXCL8,IL1A,IL1B,IL6,NFKB1,NOS2,RELA,TNF	814 (18)
NRTN	growth factor	2,63E-05	HAMP,IL13,IL4,IL5,IL6,RET,SLC12A5,TNF,TRPM8	877 (20)
RHOJ	enzyme	2,63E-05	ADIPOQ,AKAP12,ATP2A2,CAV1,GSN,LRP1B,MYH9,PLAT,PTN	
TEK	kinase	2,63E-05	ANGPT1,APLN,IFNG,IL17A,IL1A,IL22,IL6,TNF,VEGFA	817 (19)
TMSB4	group	2,63E-05	BGLAP,BMP2,BMP4,IRAK1,ITGA2,ITGB1,mir-146,SERPINE1,SPP1	738 (14)
Usp17la (includ	peptidase	2,63E-05	ABCG2,CXCL8,IL1B,IL23A,IL6,KIT,MMP2,POU5F1,TNF	511 (12)
POLR2A	enzyme	2,65E-05	CAD,CAV1,CCND1,CXCR4,FOS,GATA4,KISS1,MAGI1,MYOD1,NFKBIA,SELE,SGK1,STC2,TFF1,TNFAIP3,TP73,VEGFA	777 (9)
CDH11	other	2,92E-05	AGT,EGF,IGF1,ITGB2,MMP7,NOS2,PIK3R1,PTK2B,RAC1,SERPINA1,TFF1	517 (7)
collagen type i (	group	2,92E-05	ABCC1,CCL18,CCL2,GPA33,HNF4A,HTR2B,IL1RN,MSR1,MYO7B,NR1I2,SERPINE1	
mir-25	microRNA	3,17E-05	BAX,ESR2,HNF1B,IL6,ITGB3,MYLIP,PTEN,RGS5,TGFBR1,TNF,TP53,TSC1	908 (19)
CHD4	enzyme	3,37E-05	ADORA1,AS3MT,BCL11A,CHEK2,DUOX2,FAS,GNB3,HBB,HBG1,HMOX1,IL12B,IL13,IL4,JUN,NCEH1,TIMP2,TP53	729 (7)
MBD2	transcription reg	3,52E-05	APOE,BRCA1,CDKN2A,CDKN2B,DLK1,DPP4,ELANE,ESR1,FOXP3,G6PD,GSTP1,IL4,MEF2A,MMP2,MMP9,SGK2,SST,TBX19	
FLT1	kinase	3,53E-05	ACTN4,ADD1,AHCY,BCAT1,BCL7B,CTBP1,EPAS1,FOS,HLA-B,HMOX1,ICAM1,MAX,NOS3,NOTCH1,RALB,SDHC,SMARCA4,TGFBR2,THBS1,VWF	894 (20)
miR-141-3p (an	mature microRN	3,57E-05	BAX,CDK6,CLOCK,COL1A2,CTNNB1,CYP1B1,DACH1,ITGAV,ITGB1,JAG1,PITX2,PTPRD,RAC1,STAT5B,TBX5,TGFB2,TP73,WDR37,ZFPM2	473 (7)
NFAT (complex)	complex	3,70E-05	ATF3,CCL2,ICAM1,IL2,IL33,IL4,IL6,OPRM1,SERPINE1,SPP1	
UBE3A	enzyme	3,70E-05	AR,CDKN2A,ESR1,IL1B,PGR,PML,SERPINE1,SNRPN,TERT,TP53	1060 (20)
C9	other	3,89E-05	COL1A1,COL3A1,FN1,ICAM1,IL1B,SELE,VCAM1	621 (10)
CCNT1	transcription reg	3,89E-05	CAD,CCND1,CXCL8,INS,PPARGC1A,SLC2A1,TFF1	689 (12)
FFAR4	G-protein coupl	3,89E-05	CXCL8,IL17A,IL22,INSR,IRS1,LEP,PTGS2	621 (12)
FOXF1	transcription reg	3,89E-05	CACNA1C,HGF,ITGB3,MYLK,PDGFRA,VCAM1,WNT5A	
KRIT1	other	3,89E-05	BMP2,CXCR4,EFNB2,JUN,SOD2,TGFB2,THBS1	
OGG1	enzyme	3,89E-05	CAD,HIF1A,IFNG,IL1A,IL1B,IL6,TNF	1005 (21)
PDE3B	enzyme	3,89E-05	ADIPOQ,IL6,PPARGC1A,SERPINE1,SOCS3,TNF,TRIB3	1069 (24)
RIPK3	kinase	3,89E-05	HAMP,IFNG,IL18,IL1A,IL1B,IL6,TNF	823 (17)
BNIP3L	other	4,00E-05	AURKA,CST3,EIF2AK1,GSN,IL16,IL2RB,LTA,NFKB2,NFKBIA,NUF2,PDGFRB,PTK2B,STAT3,TFRC,TGFB1,TIMP2	608 (7)
TMEM173	other	4,00E-05	CCL5,CSF2,CXCL8,GAS7,GJA4,IL10,IL1A,IL1B,IL22RA2,IL33,IL6,LCN2,NOS2,OASL,PTPRC,TNF	769 (18)
TNFRSF8	transmembrane	4,26E-05	CDC5L,CXCL8,CXCR4,FAS,GCLC,IFNG,IL10,IL13,IL2,IL4,KIR3DL1,NFKB2,RELA,TNF,TNFSF10,TRAF1,VCL	621 (16)
HOXA7	transcription reg	4,30E-05	ADGRG1,CALCRL,CD34,EDNRA,EGFR,FLT3,IL7R,LAT2,LY86,PGR,TSC22D1	
MEF2	group	4,30E-05	CKM,CPT1B,CTNNB1,IL10,IL1RN,IL2,JUN,MEF2A,PPARGC1A,PTGS2,SLC2A4	475 (11)
BMPR1A	kinase	4,33E-05	AGRP,CYP11A1,CYP17A1,HAMP,HHEX,HSD3B1,ID3,NKX2-5,SERPINE1,SOX6,SRD5A2,TBX5,TNF	937 (22)
BID	other	4,38E-05	CTSH,CXCL8,IL1B,IL4,IL5,IL6,MMP12,MT-CO2,TIMP1	860 (17)
IAPP	other	4,38E-05	FDFT1,FOS,HAMP,HMGCR,LEPR,MSMO1,NPY,POMC,STAT3	865 (21)
KISS1R	G-protein coupl	4,38E-05	BMP7,ERBB2,ESR2,FOS,KISS1,let-7,LHCGR,LIN28A,MMP9	1122 (25)
LCP2	other	4,38E-05	CD69,ID3,IFNG,IL2,IL4,ITGAM,MAPK1,SELP,TNF	503 (18)
miR-23a-3p (an	mature microRN	4,38E-05	CXCL12,HES1,IL6R,MET,NOTCH1,PTEN,SMAD3,SMAD4,SMAD5	
SMARCD3	transcription reg	4,38E-05	COL1A1,FMOD,MGP,MITF,NKX2-5,NPPA,PITX2,SOX6,WNT5A	590 (13)
SP100	transcription reg	4,38E-05	BRCA1,CCN2,CD14,FOS,HBB,HSPA1L,HSPA8,ICAM1,MMP1	952 (19)
Sos	group	4,42E-05	ABCC1,ADD2,AKR1C3,APLN,AQP3,CA2,CAST,CASZ1,CAT,CHI3L1,COBLL1,CYP17A1,DOCK1,FOS,GATA4,GBA,GIT2,GSR,HBA1/HBA2,HMOX1,HSD3B1,IRS2,ITGB1,KRAS,LAMA3,LRP8,MAOA,MET,MMP3,MYH9,PTGS2,PTH1R,RALB,RUNX1,SIRPA,SLPI,TGFB1,XDH	1050 (22)
mir-150	microRNA	4,47E-05	ACTA2,CXCR4,FZD4,HIF1A,IFNG,IKZF1,IL2RA,MMP14,MYB,NOTCH3,SLC2A1,SOCS1	582 (10)
MTTP	transporter	4,47E-05	ABCA1,ABCG5,ABCG8,APOA4,APOB,CD36,CPT1A,HMGCR,JUN,MTTP,PPARG,TNF	697 (15)
AQP11	transporter	4,55E-05	EGF,EGFR,MMP12,TGFB1,TIMP1	
BDKRB1	G-protein coupl	4,55E-05	BDKRB1,CCN2,EDN1,IL17A,TGFB1	949 (21)
CASP6	peptidase	4,55E-05	ARG1,HAMP,IL10,MMP2,MMP9	867 (17)
CD300LF	other	4,55E-05	CALCR,CXCL8,IL1A,IL1B,MMP9	712 (16)
CFH	other	4,55E-05	APOA1,APOB,CRP,PPARG,TNF	792 (14)
CLEC4D	other	4,55E-05	IL12B,IL17A,IL1B,IL6,TNF	789 (14)
CLEC6A	transmembrane	4,55E-05	IL10,IL12B,IL1B,IL6,TNF	619 (17)
CMA1	peptidase	4,55E-05	AGT,COL1A1,COL3A1,IL1B,MMP9	900 (20)
CYP4A11	enzyme	4,55E-05	ACE,AGT,MMP9,SGK1,SLC12A3	
DNAJA3	other	4,55E-05	CXCL8,EGFR,ERBB2,STAT5B,VEGFA	756 (15)
Dynamin	group	4,55E-05	FOS,IL6,ITGAV,KDR,TNF	990 (22)
F13A1	enzyme	4,55E-05	IL10,IL1B,IL6,TNF,TNFSF11	
Fcgr2	group	4,55E-05	AGER,CCL5,CSF2,IL5,IL6	746 (17)
MALSU1	other	4,55E-05	MT-CO1,MT-CO2,MT-ND1,MT-ND4,MT-ND6	
MSLN	other	4,55E-05	BAX,IL6,MMP7,MMP9,TP53	667 (12)
PDGFD	growth factor	4,55E-05	CXCR4,MMP1,NFATC1,PTGS2,VEGFA	862 (20)
PHOX2A	transcription reg	4,55E-05	CHRNA3,DBH,RET,SLC6A2,TH	
PRSS8	peptidase	4,55E-05	IL1A,IL1B,MMP9,TLR4,TSLP	228 (3)
SERPINA12	other	4,55E-05	ADIPOQ,LEP,RETN,SLC2A4,TNF	
SH2B3	other	4,55E-05	HMOX1,IL12RB1,NOS3,SELE,VCAM1	722 (14)
SHOX2	transcription reg	4,55E-05	ADRB3,FGF10,FGFR2,HTRA1,NKX2-5	
SMPD2	enzyme	4,55E-05	IL1B,IL6,NOS2,SCARB1,TNF	675 (15)
TPR	other	4,55E-05	CXCL8,IL1A,IL1B,IL6,NOTCH1	
UBE2D1	enzyme	4,55E-05	MARCH1,NOS1,PTGS2,SMAD2,SMAD4	499 (9)
WAC	other	4,55E-05	ALPL,BGLAP,G6PD,PDK4,PPARG	
ZMYND10	other	4,55E-05	MMP14,MMP2,MMP9,THBS1,VEGFA	826 (13)
ACACB	enzyme	4,62E-05	HMGCR,LEP,MLXIPL,PPARA,PPARG,SLC2A4,SREBF1,SREBF2	853 (18)
CGB3 (includes	other	4,62E-05	CYP11A1,ESR2,IL17A,LHCGR,MMP2,PTGS2,RUNX1,SGK1	935 (19)
CNR2	G-protein coupl	4,62E-05	CCL2,CCND1,CXCL8,GRK5,IFNG,IL1B,OPRM1,TNF	828 (20)
COL1A1	other	4,62E-05	CCL2,COL1A1,CXCR4,EDN1,ICAM1,MMP14,SELE,VCAM1	738 (14)
CXCL2	cytokine	4,62E-05	CCL5,CXCR2,ICAM1,IL17A,IL1B,IL6,ITGAM,TNF	777 (18)
FCGR1A	transmembrane	4,62E-05	C5,IL1B,IL1RN,IL6,ITGAM,ITGB2,LSP1,TNF	693 (18)
GC-GCR dimer	complex	4,62E-05	ADRB2,AGT,IL10,IL1RN,NFKBIA,NPPA,SCGB1A1,SLPI	
GPNMB	enzyme	4,62E-05	FOS,IL12B,IL6,ITGB1,MITF,NFATC1,TNF,TNFRSF11A	840 (20)
Hif	complex	4,62E-05	ANGPTL4,CKM,CXCL8,EPO,HAMP,LDHA,TF,TH	
IGHE	other	4,62E-05	CCL5,CSF2,IL10,IL13,IL4,IL6,TNF,ZFP36	667 (20)
IRAK2	kinase	4,62E-05	CXCL8,IL10,IL1B,IL6,NFKB1,NOS2,SELE,TNF	758 (17)
mir-130	microRNA	4,62E-05	ABCB1,AQP4,IL4,KDR,PPARA,ROCK1,TGFBR1,TNF	
miR-223-3p (mi	mature microRN	4,62E-05	CHUK,FOXO3,IRS1,MEF2C,NFIA,NLRP3,SLC2A4,TGFBR3	
PCYT2	enzyme	4,62E-05	ABCA1,CD36,MLXIPL,MTTP,NR1H3,PPARG,SLC27A4,SREBF1	532 (7)
SPOP	other	4,62E-05	BRD2,DHCR7,FDFT1,INS,MMP1,PDX1,RAC1,SST	251 (4)
Stat5 dimer	complex	4,62E-05	BAX,CCND1,EBF1,IFNG,IGF1,IGF2,IGFBP3,SOCS1	
ASCL1	transcription reg	4,70E-05	CACNA2D3,CDCA7,CDK5R1,CIITA,DBH,DCC,HES5,ID3,INS,LMX1B,NPY,PAX2,PCSK6,PDGFRA,PDYN,PRKCQ,PROX1,RET,SLC6A5,SNAP25,TH,ZMAT4	
THPO	cytokine	5,10E-05	AURKA,BAX,CCN3,CCND1,FOS,GP1BA,ITGA2B,ITGB3,KDR,mir-146,NOS3,RUNX1,SELP,SH2B3,TAP1,VEGFA	802 (20)
ABCD1	transporter	5,14E-05	ALOX5,IL1B,NOS2,PTGS2,RELA,TNF	1008 (19)
AGRP	other	5,14E-05	DIO2,FOS,LEP,PSMA4,TRH,UCP1	149 (3)

AIM2	other	5,14E-05	FCGR2B,IFNG,IL10,IL18,IL1B,TNF	811 (18)
ARV1	transporter	5,14E-05	CYP7A1,FGF21,NR0B2,NR1H4,PPARA,SREBF1	
ATG16L1	enzyme	5,14E-05	IL18,IL1A,IL1B,IL6,NFKBIA,SOD2	831 (18)
CBLB	enzyme	5,14E-05	FLT3,FOXP3,IFNG,IL2,IL4,MET	794 (25)
CD80/CD86	group	5,14E-05	CTLA4,IFNG,IFNL3,IL17A,IL2,IL6	507 (11)
EGLN2	enzyme	5,14E-05	CXCL8,EPAS1,EPO,HIF1A,NOS3,TNF	752 (19)
FAT1	other	5,14E-05	IL1B,IL6,JUN,MMP3,PTGS2,VEGFC	638 (9)
FKBP5	enzyme	5,14E-05	ARG1,CXCL8,ICAM1,IL6,KLK2,NOS2	823 (16)
IL10RB	transmembrane	5,14E-05	CXCL8,ICAM1,IL10,SAA1,SOCS3,TNF	602 (16)
KHSRP	enzyme	5,14E-05	IL12B,IL1B,LDLR,let-7,NOS2,WNT5A	920 (19)
MB	transporter	5,14E-05	EPAS1,HIF1A,HSPB2,NPPA,VCAM1,VEGFA	957 (19)
mir-224	microRNA	5,14E-05	API5,CDC42,CYP19A1,DIO1,MMP9,SMAD4	828 (7)
MPL	transmembrane	5,14E-05	FOS,GP1BA,ITGA2B,ITGB3,SELP,SLC2A1	948 (23)
NR1D2	ligand-depende	5,14E-05	APOC3,ARNTL,CD36,FABP3,FGF21,IL6	623 (10)
PI3	other	5,14E-05	ACTA2,CXCL8,IFNG,IL12B,NFKBIA,TNF	582 (12)
PI3Kγ	group	5,14E-05	IFNG,IL10,IL1B,SELE,TLR4,TNF	859 (14)
PPP1CA	phosphatase	5,14E-05	AR,CCN2,FOS,IL10,NUMA1,SPP1	963 (20)
PSMB9	peptidase	5,14E-05	HLA-A,NFKB1,NFKB2,NFKBIA,TAP1,TNFAIP3	837 (16)
RYR1	ion channel	5,14E-05	MT-CO1,MT-CO2,MT-ND1,MT-ND6,TRPC3,TRPC6	
SAV1	other	5,14E-05	CCN2,CCND1,PITX2,PRKN,SPP1,TNF	59 (3)
ST6GAL1	enzyme	5,14E-05	CXCL8,HIF1A,IL6,RELA,SLC2A1,SLC2A3	741 (16)
TEAD	group	5,14E-05	CALD1,CAV2,CCN2,CCND1,FN1,POSTN	267 (4)
TGFBR	group	5,14E-05	ACTA2,NOX1,NOX4,SOCS3,TNFSF11,WNT5A	683 (13)
THBD	transmembrane	5,14E-05	IL18,IL1B,IL6,PECAM1,THBD,TNF	920 (20)
tryptase	group	5,14E-05	BAX,F2R,F2RL1,MMP9,PLAT,TNFAIP3	778 (16)
WNT5B	other	5,14E-05	ACTA2,CCND1,COL1A1,FN1,PROX1,VCAN	543 (9)
XCL1	cytokine	5,14E-05	CD40,IFNG,IL10,IL2,IL2RA,TNF	702 (12)
YBX3	transcription reg	5,14E-05	CCND1,CSF2,ERBB2,ERBB3,HLA-DQB1,JUN	84 (4)
PTP4A1	phosphatase	5,36E-05	ACTN4,AHCY,ANXA5,BAX,CCL5,FMR1,GSTP1,HIF1A,HNF4A,HSPA1A/HSPA1B,ITGA4,ITGB8,MAPK8,MMP14,MMP2,PECAM1,PIK3R1,ROCK1,ROCK2,RUVBL2,SRSF2,SRSF3,TKT,TP53,UBA1,VCAN	
BAG1	other	5,64E-05	CCND1,EGFR,FKBP5,FOS,JUN,NEDD4L,NR3C1,PTGS2,TP73,UAP1	859 (18)
BCL2L11	other	5,64E-05	ADRB2,CCL5,CCND1,CD36,HDAC9,IL10,IL1B,IL6,TGFB1,TNF	801 (14)
infliximab	biologic drug	3,55E-13	BMP2,CCL17,CCL18,CTLA4,CXCL8,CYP27B1,EDN1,FCGR2A,FCGR2B,IFNG,IL12RB2,IL13,IL15,IL1B,IL22,IL2RA,IL5,IL9,LTA,MMP12,NAMPT,NFKB2,NFKBIA,PTGES,PTGS2,TNF,TNFRSF4,TRAF1,VEGFA	915 (18)
SOX6	transcription reg	5,64E-05	BMP6,CCND1,CTNNB1,FGFR3,HSPG2,INS,MYL3,SOCS3,TNNC1,TP53	688 (12)
SSTR2	G-protein coupl	5,64E-05	FOS,GCK,IFNG,LPL,MMP9,POMC,SLC18A2,SST,THBS1,TNFRSF1A	843 (22)
IFN type 1	group	6,01E-05	CCL5,CD69,CXCL13,CXCL8,IFIH1,IFNG,IL12B,IL13,IL5,IL6,MMP9,OASL,PML,TNFSF10,XDH	687 (16)
LMNB1	other	6,01E-05	ACTN4,CXCL12,DHCR7,FBN1,FLT3,GJA1,HBEGF,HMGCR,LDLR,LMNA,MGP,MSMO1,PAPPA,TGFB2,THBS2	
TRIM24	transcription reg	6,14E-05	CA2,CASR,CFHR1,CYP24A1,FBN1,HNF1B,IFIH1,JAK2,Ly6a (includes others),MOV10,NUMA1,OASL,PRKCQ,PSMB8,PSMB9,SERPINE1,SOCS1,SPP1,TAP1,TLR2,TP53,TRPV5,VEGFA	457 (7)
APOB	transporter	6,21E-05	APOA4,APOB,APOE,CD36,LPIN1,NPPA,NR1H3,PPARG,PSMB9,SCARB1,SLC2A4,SREBF1	805 (21)
SUZ12	enzyme	6,56E-05	ATP2A2,CDKN2A,CNR1,DAB2IP,EVX1,GATA4,H19,HNF4A,IGFBP3,ILF3,INSIG1,KDM5B,MFN2,MMP2,MMP7,NKX2-5,PGR,PLCB4,POU2F3,POU5F1,PTEN,RARB,SMARCA4,TBX3,TGFB1,TNFRSF11B,TNFRSF1B,VTA1	760 (13)
NRF1	transcription reg	6,69E-05	ATP1A1,ATP1B1,COX5B,COX8A,CXCL8,FMR1,GCLC,GCLM,HBB,HMOX1,HPCAL1,IDE,IL1A,IL1RN,NQO1,PVR,SDHD,TP53	
EPHB6	kinase	6,95E-05	BMPR1A,BMPR2,CSF2,FKBP5,IFNG,IL10,IL6,let-7,mir-27,mir-335,TGFB1,TNF,TRIB1,TRIB3	754 (20)
DNA-methyltra	group	7,01E-05	CDKN2A,CDKN2B,DIO3,EPHX2,ICOS,IFNG,mir-217,MMP1,PTGS2	913 (12)
IDO1	enzyme	7,01E-05	HLA-G,IFNL3,IL10,IL12B,IL6,mir-143,SLC1A4,SLC6A9,TNF	673 (16)
IL37	cytokine	7,01E-05	BMP2,CSF2,IFNG,IL1A,IL1B,IL1RN,IL6,TIMP1,TNF	673 (14)
PCDH11Y	other	7,01E-05	BMP4,CCND1,CHGA,EP300,GJA1,JUN,PTGS2,RET,SFRP2	516 (7)
SENP1	peptidase	7,01E-05	IL12B,MFN2,MMP2,MMP9,NOS2,PML,POMC,PPARG,UCP2	1060 (27)
ST8SIA1	enzyme	7,01E-05	C3,C4A/C4B,EGFR,HMGCR,IL1A,IL1B,MMP9,POU5F1,TNF	996 (23)
insulin glargine	biologic drug	4,87E-02	IL6,NPY	
TNFRSF11A	transmembrane	7,01E-05	CD40,CXCL13,FN1,MME,POU5F1,RELA,TFAP2B,TNFRSF11A,VCAM1	912 (19)
SBDS	other	7,15E-05	ADD2,AKR1C3,CCN2,CTH,ERBB3,FOS,GABBR2,HES5,IL4R,LGR5,MAOA,PLAGL1,PTPRO,RAC1,RAC2,RGS4,SORCS1,SPP1,TNC,TRIB3,XCL1	
MKNK1	kinase	7,23E-05	ACOT7,ANXA5,AP3D1,ARVCF,CPLX2,FOS,HSPA2,KIF5A,KLC1,LCN2,MAPK1,MYO5A,MYO6,NR4A3,PAFAH1B1,PDLIM5,PLTP,SMAD2,SNAP25,THRA,TNF,TP53BP1,TXNIP	
FFAR3	G-protein coupl	7,60E-05	ANPEP,BAX,BCL11A,CACNA1C,CBS/CBSL,FADS2,FCGR2B,GAS6,ICAM1,IL1A,IL1B,IL1RAP,LAX1,LEP,LOXL2,LY86,PCSK9,TLR7,TLR8,TP53	283 (5)
interferon beta	biologic drug	2,88E-03	CCR2,CCR5,COX5B,CXCR4,FPR1,GSTP1,HLA-DPB1,HLA-DRB5,IL16,IL1RN,IL2RB,JAK2,LTF,MMP9,NCF2,NFKBIA,NOTCH1,PLAUR,PSMB8,SERPINA1,TBXAS1,TNFRSF1B	652 (7)
ASIP	other	7,72E-05	AGRP,CYP11B1,HTR1B,HTR2C,NPY,TRPC1,TYRP1	574 (10)
ipilimumab	biologic drug	9,27E-03	ICOS,IFNG	453 (14)
B4GALNT1	enzyme	7,72E-05	C3,C4A/C4B,FOS,IL1A,IL1B,TNF,VEGFA	641 (12)
CCL3L3	cytokine	7,72E-05	CCL5,CD40,IFNG,IL1B,IL5,IL6,TNF	675 (16)
CRBN	enzyme	7,72E-05	IL1B,IL2,IL6,JUN,LEP,NOS2,PTGS2	1061 (22)
CSF2RA	transmembrane	7,72E-05	ADGRE1,FOS,IL5,IL5RA,ITGAM,JUN,PIK3CG	821 (20)
CTSG	peptidase	7,72E-05	CCL2,CXCL5,CYP11A1,FPR1,IL1B,MMP7,TNF	600 (18)
CYP51A1	enzyme	7,72E-05	HMGCR,LSS,MSMO1,NKX2-5,RARA,RXRA,SREBF2	
DUSP14	phosphatase	7,72E-05	IFNG,IL12A,IL18,IL2,IL4,NFKBIZ,PLAT	716 (17)
MMP8	peptidase	7,72E-05	CXCL8,HGF,IL10,IL6,MET,NR3C1,TGFB1	776 (19)
NPPC	other	7,72E-05	GUCY1A1,GUCY1B1,NOS2,NOS3,PRKG1,UCP1,XYLT1	349 (5)
PEX5L	ion channel	7,72E-05	CYP7A1,DHCR7,FDFT1,HMGCR,LSS,MVK,SREBF2	
PTBP1	enzyme	7,72E-05	CDC42,DRD2,FGFR1,KRAS,LDLR,NOS2,SERPINA3	
SIRPA	phosphatase	7,72E-05	CCL5,CXCL8,IL13,IL1B,IL4,IL6,TNF	594 (15)
MEN1	transcription reg	7,83E-05	AKT1,BGLAP,CCND1,CDKN2B,CTNNB1,FOS,FOXC1,IRS2,let-7,MEIS1,PTN,TERT,TGFBR2	1011 (24)
DDX17	enzyme	7,98E-05	ABCA1,CCND1,HTRA1,JUN,LCN2,mir-515,S100A4,TFF1	791 (7)
FKBP4	enzyme	7,98E-05	C3,IL15RA,NOS2,NOS3,PDK4,PPARG,SREBF1,TNF	861 (16)
HRH2	G-protein coupl	7,98E-05	CXCR2,IFNG,IL10,IL13,IL17A,IL4,IL6,TNF	813 (23)
IL13RA2	transmembrane	7,98E-05	CCL11,IL13,IL13RA2,MMP12,MMP14,MMP9,TGFB1,VNN1	765 (16)
ITPR1	ion channel	7,98E-05	BDNF,ERBB2,FOS,IL2,NOS1,NOS3,PCK1,RYR2	987 (19)
mir-208	microRNA	7,98E-05	ENG,IL24,MYH7,MYL3,NPPA,SOX6,TNF,TNNC1	
miR-205-5p (an	mature microRN	7,98E-05	ABCC2,ATP1A1,ERBB3,INPPL1,KLK2,NCOR2,PTEN,VEGFA	
PDGFRA	kinase	7,98E-05	ACTA2,BGLAP,COL1A1,FOS,KIT,PDGFRA,PRKCQ,TP53	1002 (25)
isotretinoin	biologic drug	1,49E-08	ABCA1,AGTR1,CCL2,CXCL8,CYP1B1,IFNG,IGFBP3,IL12B,IL6,LCN2,MMP1,MMP9,NFKB2,OLR1,PRKCA,PTGIS,PTGS2,RARA,RARB,RARG,SERPINA3,TFRC,TLR2,TNFSF10,VCAM1	995 (21)
PPP2R5C	other	7,98E-05	BCL2A1,CD69,CXCL8,IFNG,IL2,NFKB1,REL,TNFAIP3	873 (18)
UCP2	transporter	7,98E-05	ADIPOQ,EPAS1,IFNG,IL1B,IL6,LPL,NOS2,TNF	905 (24)
mir-34	microRNA	8,21E-05	AR,AXL,CCND1,CDK6,CPLX2,EFNB1,ITGA2B,KCNH2,LIN28A,MET,MLLT3,MYB,NOTCH1,NOTCH2,SIRT1,SOX17,TNF,TP53	956 (23)
MMP12	peptidase	8,28E-05	ACTN4,CCL5,CSF2,CXCR2,DNM1L,HNF4A,IL6,IL6ST,MAP4,MMP14,MMP2,MMP9,MYH9,NFKBIA,PSMA6,SHH,VCL	949 (20)
HAND1	transcription reg	8,37E-05	ANGPT1,CPT1A,EDN1,EFNB2,FLT1,KDR,LIPE,NOTCH1,NPPA,TIE1	
KAT2A	enzyme	8,37E-05	CCND1,IL2,IL9,JUN,NR1H3,PCK1,PIK3R1,PPARGC1A,RHO,TFF1	1023 (25)
TAF4B	transcription reg	8,37E-05	CCN2,FN1,JUN,MMP3,NFKBIA,RET,SPP1,TGFB1,TGFB3,TNFAIP3	
ZBTB7A	transcription reg	8,37E-05	ADA,CDKN2A,FOS,H19,IL2RA,NFATC1,PFKP,RELA,SELE,SLC2A3	1042 (19)
GTF2B	transcription reg	8,50E-05	BCL2A1,CYP24A1,DIO1,GHR,IGF1,LHCGR,NFKBIA,PPARG,TERT,TFF1,TNFAIP3,TNFSF11	896 (17)
ABCC9	ion channel	8,57E-05	HIF1A,PPARGC1A,SLC2A1,XDH	371 (7)
APOC3	transporter	8,57E-05	APOA1,APOC3,NOS2,VCAM1	736 (10)
ARID2	transcription reg	8,57E-05	ALPL,BGLAP,BMP4,FGFR2	

ATP8B1	transporter	8,57E-05	ABCB11,CFTR,NR1H4,SLC10A2	82 (3)
B3GNT2	enzyme	8,57E-05	CD14,IL1B,IL6,TNF	601 (9)
BATF3	transcription reg	8,57E-05	IFNG,IL12B,IL2,MMP1	587 (7)
Bvr	group	8,57E-05	HMOX1,HMOX2,NOS2,RELA	753 (13)
CALM1 (include	other	8,57E-05	HTT,PGR,TFF1,TNFAIP3	
Carlr	other	8,57E-05	IL1A,IL1B,NFKB2,PTGS2	
CD163	transmembrane	8,57E-05	HMOX1,IL1B,IL6,TNF	708 (13)
COPA	transporter	8,57E-05	IL12B,IL1B,IL23A,IL6	
CRLF1	other	8,57E-05	CD69,ICAM1,IFNG,IL17A	573 (14)
CTNNAL1	other	8,57E-05	CCND1,FN1,ITGAV,ITGB3	498 (7)
CYP11B2	enzyme	8,57E-05	IGF1R,KCNMA1,KCNMB1,VEGFA	493 (7)
CYP8B1	enzyme	8,57E-05	ABCA1,ABCG5,ABCG8,CYP7A1	473 (9)
DGKA	kinase	8,57E-05	CD69,IL1B,IL2,LIPE	773 (21)
EGFL7	other	8,57E-05	ICAM1,NFKBIA,SELE,VCAM1	
ENPP1	enzyme	8,57E-05	ALPL,BGLAP,LEP,SPP1	
GIPC1	other	8,57E-05	HAMP,PROX1,SERPINE1,TGFBR3	
HLA-E	transmembrane	8,57E-05	IFNG,IL13,IL4,TNF	563 (12)
IFIT2	other	8,57E-05	IL12B,IL1B,IL6,TNF	833 (14)
IL2ORB	other	8,57E-05	IFNG,IL10,IL2,IL4	752 (18)
IL36RN	cytokine	8,57E-05	CXCL8,IL17A,IL1B,IL6	492 (8)
IRAK1BP1	other	8,57E-05	IL10,IL6,NFKB1,RELA	561 (13)
ITPR	group	8,57E-05	CYP1B1,IL1B,MAPK1,MAPK3	
LNPEP	peptidase	8,57E-05	ADIPOQ,LEP,NOS2,SLC2A4	476 (7)
LPAR3	G-protein coupl	8,57E-05	CXCL8,EGFR,IL6,KLF5	450 (7)
LRP4	other	8,57E-05	BMP4,BMP7,SHH,TNFSF11	
miR-718 (miRN	mature microRN	8,57E-05	IRAK1,PTEN,TLR4,TNF	
MUC2	other	8,57E-05	IL1B,IL6,PTGS2,TNF	
Nppb	other	8,57E-05	ACE,COL1A1,NPPA,TGFB3	
NUCB2	other	8,57E-05	FOS,IL6,PTGS2,TRH	987 (21)
ORM1	other	8,57E-05	HAMP,IL1RN,IL6,TNF	911 (20)
P2RX4	ion channel	8,57E-05	BDNF,IL1B,MMP3,MMP9	744 (15)
PGRMC1	transmembrane	8,57E-05	BCL2A1,EGFR,LCN2,PGR	643 (7)
PPP1CC	phosphatase	8,57E-05	BAX,BDNF,IL6,TNF	911 (21)
RAB11FIP3	other	8,57E-05	FOS,IFNG,IL2,JUN	571 (10)
Rps6ka5	kinase	8,57E-05	IL1B,IL6,NOS2,TNF	
SERPING1	other	8,57E-05	BDKRB1,IL10,IL6,TNF	935 (14)
TNIP3	other	8,57E-05	CXCL8,IL12B,IL6,TNF	711 (9)
TRIL	other	8,57E-05	CCL5,CXCL8,IL6,TNF	878 (9)
UMOD	other	8,57E-05	IL12B,TNF,TRPV5,UMOD	
ZXDC	transcription reg	8,57E-05	CCL2,CD14,HLA-DRA,ITGAM	
SOX4	transcription reg	8,61E-05	ALDH1B1,BAX,BMPR2,CACNA1H,CCN3,CD2,CSRP3,CTNNB1,DDAH2,DICER1,FN1,FOS,GLDC,GNRH1,HAMP,HLA-DQB1,IFI30,IGF1,IGF2,KLK8,KYNU,Ly6a (includes others),MAGI1,MYOD1,NCAM1,OVOS2,PECAM1,PITRM1,PPIC,SELL,SERPINE2,SMAD1,SORT1,TBXA2R,TPH1	785 (13)
PBX1	transcription reg	8,78E-05	CDKN2B,COL1A1,CYBB,GCK,GNRH1,MMP9,NCF2,REN,SST,STAT3,TCF7L2	580 (12)
SOX10	transcription reg	8,78E-05	CHRNA3,EDNRB,ERBB3,FOS,GAS7,KCNB1,MITF,NOTCH1,PTN,RET,SOD3	
JAK1/2	group	1,00E-04	BCL11B,CCK,CCL2,CCN3,CD69,CIITA,GLDC,HLA-DQA1,HLA-DRA,HLA-DRB5,IL2,IL6,NOS2,PRKCG,PSMB9,PTK2B,RGS14,TNF	924 (19)
1810019D21Rik	other	1,02E-04	ABCB1,BDKRB2,EDN1,F5,GPR87,GPX1,HGF,IL13RA2,ITGA2,ITGB2,KCNH2,MMP9,PLA2G7,SYNE1,THBD,UGT1A6	
OTX2	transcription reg	1,02E-04	BMP4,CDH4,GNRH1,MITF,MYOD1,NCAM1,PAX2,POMC,RHO,SLC14A1,SLC16A8,SREBF2,TF,THBS4,TNC,TTR,TYRP1	
NFYC	transcription reg	1,03E-04	CDKN2A,COL1A1,COL1A2,FGFR2,HLA-DRA,LPIN1,MTPN,NPR1,PCK1,PDGFRB,SDF2,SGK1,TYMS	57 (3)
EIF4G2	translation regu	1,08E-04	HIF1A,IGF2,JUN,KLF5,PLAT,POU5F1,PTGS2,SERPINE2,TBX3	598 (7)
HFE	transmembrane	1,08E-04	ADIPOQ,BMP6,FURIN,HAMP,INS,SLC2A2,TF,TFR2,TFRC	377 (6)
IgG1	complex	1,08E-04	BAX,CD14,CD40,CXCL8,IL13,IL4,ITGA4,ITGAV,TNF	613 (13)
IL15RA	transmembrane	1,08E-04	CD226,EDN1,IL10,IL17A,IL2,IL2RA,IL6,PTPRC,TNF	629 (19)
miR-199a-3p (a	mature microRN	1,08E-04	FN1,MET,NFKB1,PON2,PTGS2,RELA,RUNX1,SMAD1,VCAN	598 (7)
NFIX	transcription reg	1,08E-04	ADRA1B,CCND1,CHI3L1,CKM,CXCL8,HGF,POSTN,SERPINA3,SERPINE1	776 (7)
PTAFR	G-protein coupl	1,08E-04	CCL2,CXCL8,EGFR,IL1B,IL6,MMP2,MMP9,PTGS2,TNF	933 (22)
WDR5	transcription reg	1,08E-04	CTNNB1,ERBB2,ESR1,IGF2R,KLK2,POU5F1,SFRP2,SPP1,TP53	812 (13)
FGFR3	kinase	1,15E-04	BMP4,CCND1,CDKN2A,COL1A1,COL3A1,FOS,HES1,MAF,MMP9,PECAM1,PROX1,SPP1	835 (18)
HSF2	transcription reg	1,15E-04	CCT2,CDK5R1,CLU,HIF1A,HSPA1A/HSPA1B,HSPA4,IL1B,JUN,LHCGR,TNF,TNFSF11,TXN	
ADCY7	enzyme	1,18E-04	CHUK,IL1RL1,IRAK1,TLR4,TLR9,TNF	
ANG	enzyme	1,18E-04	ANG,BAX,CCL5,CCL8,IL6,TP53	805 (13)
ANGPTL2	other	1,18E-04	CD34,IL12A,IL12B,IL1B,IL6,TNF	504 (7)
COP1	enzyme	1,18E-04	ETV5,FAS,ICAM1,PPARGC1A,SREBF1,TRIB3	922 (14)
FANCD2	other	1,18E-04	CAT,GPX1,SOD1,SOD2,TNF,TXNRD1	504 (7)
GPC1	transmembrane	1,18E-04	ITGB3,MYOD1,PTGS2,PTK2B,SOX17,VEGFA	874 (16)
HOXB7	transcription reg	1,18E-04	ANGPT1,CXCL8,HAMP,MMP9,REN,VEGFA	1044 (23)
HSD11B2	enzyme	1,18E-04	ATP2A2,BGLAP,CCN2,COL1A1,SCNN1A,SLC12A3	557 (11)
IGF2R	transmembrane	1,18E-04	DDAH1,IGF2,IL2,NPC1,POSTN,TGFB3	
LGALS8	other	1,18E-04	CCL2,CCL5,CSF2,CXCL8,IL6,VWF	890 (17)
LGALS3BP	transmembrane	1,18E-04	FN1,IFNG,IL6,MMP14,MMP3,TNF	807 (9)
LUM	other	1,18E-04	FAS,IL1B,IL6,MMP14,TGFB1,TNF	511 (9)
NAP1L1	other	1,18E-04	AFP,APOA1,CXCR4,HNF4A,SOX17,TTR	
NCF4	enzyme	1,18E-04	FUT4,IFNG,IL17A,IL1B,IL6,TNF	554 (14)
NQO2	enzyme	1,18E-04	CCND1,CXCL12,CXCR4,MMP9,NOS2,PTGS2	915 (17)
PHLPP2	enzyme	1,18E-04	IRS1,MMP2,NPPA,PRKCA,PRKCB,TNF	917 (20)
PPBP	cytokine	1,18E-04	COL18A1,COL6A3,CXCR2,PDGFRB,SERPINE1,VEGFA	508 (7)
PPP5C	phosphatase	1,18E-04	AHR,CCND1,CD36,PLIN1,SGK1,TFF1	849 (15)
Sry	transcription reg	1,18E-04	GPX1,IL1B,NOS2,PTGDS,SOD2,TCF21	
AMH	growth factor	1,21E-04	BMPR1A,CDKN2A,CYP11A1,CYP17A1,CYP19A1,LHCGR,MMP2,SMAD5,SMAD6,SMAD9	854 (13)
MAC	complex	1,21E-04	AKR1C3,CD59,FN1,MMP3,PTGER2,PTGS2,SPP1,THBS1,TNF,ZFP36	841 (19)
miR-22-3p (miR	mature microRN	1,21E-04	ARID3B,BIN1,BMP7,ESR1,MAX,MECOM,POGK,PPARA,RGS14,ZNF618	
PTPN22	phosphatase	1,21E-04	ARG1,FOS,IL10,IL1B,IL2,IL23A,IL6,NOS2,OSMR,TNF	724 (19)
SLC9A3	ion channel	1,21E-04	CCL5,CCND1,CELA1,ELANE,IFNG,NOS2,PSMB8,PSMB9,REG3A,SLC5A1	601 (7)
PAX8	transcription reg	1,22E-04	DHFR,DIO1,DIO2,DIO3,HBB,NCAM1,POMC,PRL,TERC,TERT,TH	
EREG	growth factor	1,32E-04	HAS2,HBEGF,IL12B,IL18,IL6,PTGS2,TNC,TNF	1026 (23)
IFITM1	transmembrane	1,32E-04	ACBD4,DDAH2,EDIL3,LEPR,MAPK1,MMP12,SERPINE2,TP53	
ITGB4	transmembrane	1,32E-04	BAX,CCL5,CCND1,GPX4,IL6,MMP1,TP53,VEGFA	1077 (25)
NFIA	transcription reg	1,32E-04	CYP1A2,CYP2A6 (includes others),EFNB1,HSD17B7,LOX,NFIA,PCK1,SLIT2	
PAEP	other	1,32E-04	CCL5,CXCL5,EDN1,HBEGF,IFNG,IL1RL1,IL2,VEGFA	647 (16)
PLCG2	enzyme	1,32E-04	BCL2A1,FOXO1,ICAM1,IL6,NFATC1,PTGS2,TNF,TNFSF10	947 (19)
S100B	other	1,32E-04	AGER,CHGA,CHGB,FOS,IL1B,JUN,TNF,TP53	930 (18)
SH3BP2	other	1,32E-04	CALCR,FOS,IL2,ITGAV,ITGB3,KIT,MITF,NFATC1	914 (21)
TFEC	transcription reg	1,32E-04	BCL11A,COL6A3,F13A1,IGF1R,IL6,LGALS2,MYH9,PSMA6	
YY2	transcription reg	1,32E-04	CSF2,CXCR4,FOS,MYL2,NKX2-5,POU5F1,TET2,TP53	
IFNE	cytokine	1,35E-04	ANGPTL3,CD40,HSD11B1,IFIH1,IFNG,IL10,IL4,PTGER2,PTGER4,PTGS2,SLC2A1,SLC7A2,STAT4	825 (20)
ESRRA	ligand-depende	1,39E-04	ATP2A2,CD36,COL1A1,CPT1B,CYP17A1,CYP19A1,EPAS1,ERBB2,FABP3,GPR37,GSDMB,HAMP,HMGCR,LDHA,LIPA,LIPE,LPL,LTF,MTCH2,MYH7,NR0B2,PDK4,PLIN1,PNMT,PPARA,PPARG,PPARGC1A,RARA,SIRT1,SMARCA4,SPP1,TCAP,TFF1,THRA	999 (21)

BET	group	1,42E-04	GCLC,HMOX1,IL6,MECOM,NQO1,SLC4A1,STAT3	
Betacatenin/TC	complex	1,42E-04	ALPL,CCND1,FGF9,GJA1,JUN,MMP7,TNFRSF11B	
CCL19	cytokine	1,42E-04	CSF2,IFNG,IL10,IL13,IL4,IL5,TNF	779 (20)
CSF3R	transmembrane	1,42E-04	CD14,CXCL12,FOS,ITGAM,LTF,MPO,SELE	507 (7)
GABBR1	G-protein coupl	1,42E-04	BMP2,CASR,IL6,POMC,PRL,SPP1,TNF	919 (21)
GALNT6	enzyme	1,42E-04	ANPEP,CTNNB1,DPP4,FN1,LGR5,TERT,TFF1	537 (7)
MEG3	other	1,42E-04	ACTA2,COL1A1,FN1,GDF15,HIF1A,JUN,TP53	871 (11)
OPA1	enzyme	1,42E-04	AGER,FGF21,IL1B,IL6,NLRP3,TLR2,TNF	644 (12)
PECAM1	other	1,42E-04	CCND1,CD36,IL6,MMP2,SELP,THBS1,TNF	750 (21)
PIAS4	transcription reg	1,42E-04	FABP1,IL12B,IL1B,ITGB8,PDK4,SERPINE1,VHL	1040 (25)
RALA	enzyme	1,42E-04	CTNNB1,MMP2,MMP9,NPPA,PLAUR,TP53,VEGFC	827 (18)
SPHK2	kinase	1,42E-04	CCL5,FYN,IFNG,IL6,STAT4,TNF,TP53	695 (19)
SURF1	enzyme	1,42E-04	CPT2,INSR,MT-CO1,MT-CO2,PPARA,PPARGC1A,SLC2A4	
TAC4	other	1,42E-04	IFNG,IL17A,IL1B,IL6,MMP14,MMP2,TNF	872 (18)
TFCP2	transcription reg	1,42E-04	CFH,FGA,IL2,IL4,MMP9,SPP1,TYMS	457 (7)
Tnfsf9	other	1,42E-04	IFNG,IL12A,IL2,IL6,NOS2,TNF,VCAM1	839 (19)
TPT1	other	1,42E-04	BAX,FOXO1,IL13,IL2,IL4,IL6,TP53	874 (13)
VCP	enzyme	1,42E-04	CCL2,CCL5,CXCL8,ERCC6,NFKB2,NOS2,VCAM1	833 (20)
ARID5A	transcription reg	1,46E-04	IFNG,IL10,IL6,STAT3,TNF	945 (17)
Collagen type II	complex	1,46E-04	GP1BA,ITGA2,ITGAV,ITGB1,ITGB3	500 (9)
CXCL6	cytokine	1,46E-04	HAMP,IL1B,IL6,MMP9,TNF	492 (7)
CYP11A1	enzyme	1,46E-04	CYP11A1,CYP21A2,HSD11B1,PNMT,POMC	428 (7)
DAB2	other	1,46E-04	CCND1,CTNNB1,FOS,HMGCR,LRP2	852 (21)
lanreotide	biologic drug	9,27E-03	IGF1,IGFBP3	
lapatinib/trastu	biologic drug	9,27E-03	CRP,TNNI3	
ERCC2	enzyme	1,46E-04	CPT1B,CYP4A11,TFF1,UCP1,UCP3	670 (14)
ERCC4	enzyme	1,46E-04	DIO1,EP300,FN1,GHR,IGF1	926 (18)
FIRRE	other	1,46E-04	IL12B,IL1A,IL1B,TNF,VCAM1	
IL18RAP	transmembrane	1,46E-04	CXCL8,IFNG,IL1A,IL6,PTGS2	798 (15)
KCNMA1	ion channel	1,46E-04	CXCL8,KCNMA1,KCNMB1,MMP2,POMC	
KLKB1	peptidase	1,46E-04	BDKRB2,ICAM1,MAS1,SIRT1,VCAM1	453 (7)
Klrk1	transmembrane	1,46E-04	CCL5,CSF2,IFNG,IL10,TNF	857 (18)
LGALS7/LGALS7	other	1,46E-04	COL1A2,GSTM3,MMP9,RYR2,SERPINE1	635 (7)
LPCAT3	enzyme	1,46E-04	ABCA1,ABCG8,CD36,CPT1A,MTTP	
LRPPRC	other	1,46E-04	MT-ATP6,MT-CO1,MT-ND1,MT-ND2,MT-ND6	
LTC4S	enzyme	1,46E-04	IFNG,IL10,IL13,IL4,IL5	832 (23)
MRPL14	other	1,46E-04	MT-CO1,MT-CO2,MT-ND1,MT-ND4,MT-ND6	
Muscarinic chol	group	1,46E-04	ALPL,FMR1,FOS,JUN,RGS2	806 (18)
Pde4d	enzyme	1,46E-04	ADCYAP1,ITGB2,PGR,PTGS2,TNF	470 (7)
PDE6B	enzyme	1,46E-04	CAT,FOS,GPX1,HMOX1,SOD1	432 (7)
PGK1	kinase	1,46E-04	CTNNB1,CXCR4,MMP2,MMP3,PLG	883 (17)
PLA2G2A	enzyme	1,46E-04	CD69,CXCL8,IL6,NOS2,PTGS2	903 (19)
PRCP	peptidase	1,46E-04	NOS3,PECAM1,THBD,TRH,UCP1	854 (12)
RASGRP4	other	1,46E-04	IL13RA2,IL2,IL4,IL6,TNF	787 (10)
SERPINA3	other	1,46E-04	CCN2,EGFR,HMGCR,LDLR,NOX4	881 (12)
SLC22A1	transporter	1,46E-04	CPT1A,CPT1B,CPT2,SLC22A5,SLC2A2	718 (7)
SNED1	other	1,46E-04	IGF1,IGFBP1,IGFBP3,SLC2A1,SLC2A4	
sphingomyelina	group	1,46E-04	IL2,JUN,MMP1,PTGS2,TERT	801 (20)
STRA6	transporter	1,46E-04	PPARG,RARA,RXRA,SOCS3,TGFB1	798 (12)
Tlr11	transmembrane	1,46E-04	CXCL8,IFNG,IL1B,IL6,TNF	701 (19)
ZNF423	transcription reg	1,46E-04	ADCY3,BRCA1,PPARG,RARB,SMAD6	470 (7)
ZNF652	other	1,46E-04	EGFR,SMAD2,TGFB1,TGFB2,TGFBR2	
leuprolide	biologic drug	2,34E-07	BAX,CYP19A1,GNRHR,MMP1,MMP14,MMP2,MMP3,MMP9,NR4A3,TGFB1,TIMP1	966 (22)
AIP	transcription reg	1,48E-04	ADGRL4,ADRA1D,AHR,CX3CR1,CYP1A1,CYP1B1,F2RL1,GPR39,NPR3,NPY1R,PLAGL1,PPARA,RGS2,RGS4	
IRF9	transcription reg	1,48E-04	CD69,CIITA,CXCL8,IFNG,IL12A,IL18,IL1A,IL6,IRF5,SIRT1,SOCS1,SOCS3,TNF,TNFSF10	655 (17)
REST	transcription reg	1,59E-04	BDNF,CACNA1H,CARTPT,CHGB,CXCL12,DRD3,FGF5,GATA4,HNF1A,KCNJ6,LIN28A,mir-137,mir-27,NELL1,NPPA,NRXN3,NTRK3,OPRM1,PCSK1,POU5F1,SCG3,SCN10A,SLC12A5,SLC26A4,SNAP25,TERT,TPH2,TRPM2,USP37,VIP	717 (9)
HTATIP2	transcription reg	1,63E-04	ANGPT1,CCND1,EGFR,FOS,MMP2,POU5F1,SPP1,TP53,VEGFA	816 (21)
TGFB1I1	transcription reg	1,63E-04	AR,CD36,FABP1,FN1,FOS,HAMP,LTBP2,NOX4,SERPINE1	922 (18)
OGT	enzyme	1,66E-04	ATP2A2,BAX,CCND1,DNM3,DUOXA1,FGF5,FOS,GDNF,HAMP,HMGA1,IL2,INS,INSR,JUN,LPL,MMP2,PPARGC1A,SHH,SREBF1,TNC,TP53	911 (21)
RAD21	transcription reg	1,67E-04	APOC3,BDNF,BMPR2,CXCL12,HLA-DQA1,HLA-DQB1,HLA-DRA,HLA-DRB1,IGF2,IRS2,THBS1	
USP18	peptidase	1,73E-04	CCL5,IFIH1,IFNG,IL15,IL2,IL6,NFATC1,SOCS1,SOCS3,TNFSF10	558 (20)
EHMT2	transcription reg	1,75E-04	C8orf44-SGK3/SGK3,CXCL12,CYP7A1,FN1,IL13,IL17A,NCOA3,PGR,PTGS2,SNRPN,SREBF1,TFF1,TGFB1	1088 (23)
NME1	kinase	1,75E-04	BAX,CCN2,CCND1,MET,MMP14,MMP2,PGR,PTGS2,PTN,RAC1,SERPINE1,TIMP1,TP53	975 (21)
IL7R	transmembrane	1,82E-04	AHR,CXCL8,DPP4,EBF1,ETNK2,FOXP3,IFNG,IL17A,IL2,IL2RA,IL6,PAX5,PCSK6,RYR3,SELE,SELL,SLC35F3,TIRAP,TNFSF11,VCAM1	740 (22)
CUL3	enzyme	1,88E-04	ACE,ACSS1,DBP,EFNB3,GSTK1,IL6,MMP1,MYH7,MYL2,MYL3,NQO1,PDLIM5,SLC25A31,UCP3	473 (7)
NRL	transcription reg	1,88E-04	ABCA4,ADRB1,BMP4,CNGB3,GNB3,GRB14,IGF1R,INSR,MEF2C,OSGEP,PIK3R1,PTPN1,RHO,SMAD4	
RHO	G-protein coupl	1,92E-04	AQP1,CACNB2,CEBPD,COL1A2,DRD4,FOS,HFE,KCNB1,MEF2C,NCAM1,PDC,PLA2G7,SGK1,SHH,TNFAIP3,TRPC1	535 (7)
ZEB1	transcription reg	1,92E-04	CDKN2A,CDKN2B,COL1A1,COL1A2,CXADR,FN1,IL2,mir-214,NFKB1,PTGS2,RELA,SERPINE1,SFTPB,TF,TP73,XDH	1013 (19)
FOLR1	transporter	1,95E-04	ACTN4,ADA,ADH1C,AQP4,ATR,B3GNT3,CAT,CAV1,GAS5,GBA,GLRX,LSP1,NPHP1,S100A4,SIX5,SLC13A2,SLC15A2,ST3GAL4,TNFRSF11A,TYMS,XCL1	
NEUROD1	transcription reg	2,02E-04	ABCC8,CDK5R1,CHGA,GCK,INS,NCAM1,NR0B2,NTRK3,PCSK1,PCSK2,POMC,SLIT2	
PRC2	complex	2,02E-04	BMP2,CDKN2A,EVX1,FGF5,GATA4,IFNL3,KDR,MMP2,MMP7,PECAM1,SOX17,TBX3	964 (17)
BACH1	transcription reg	2,08E-04	CXCR4,GCLM,GSTA1,HBB,HMOX1,MMP1,NQO1,SPP1	426 (7)
EPHA2	kinase	2,08E-04	BAX,EGFR,MAPK1,MAPK3,MMP9,SELE,SLIT2,VCAM1	966 (18)
MAPK8IP1	other	2,08E-04	BDNF,CCND1,FOS,IFNG,IL6,JUN,SLC2A2,TNF	794 (18)
MED30	transcription reg	2,08E-04	LPL,MT-CO1,NDUFB3,PPARGC1A,SDHB,SDHC,SDHD,SOD2	
PDCD4	other	2,08E-04	IL1B,IL6,JUN,LOX,MMP3,PLAUR,PTGS2,VEGFC	857 (17)
CD24	other	2,11E-04	ADD3,ADRB2,ATF3,CAV1,CFTR,CXCL8,EPHB6,FOS,GDF15,ICAM1,IRAK1BP1,JUN,LAT2,NCOA3,OASL,OGG1,RASA1,SLC4A4,TFPI2,THBS1,TIMP4,TP53,VDR	763 (16)
BTNL2	transmembrane	2,12E-04	CSF2,FOXP3,IFNG,IL17A,IL1RL1,IL2,IL4,IL6,LDLRAD4,NTRK3,S100A4,SELL,SLC15A2,TGFBR1,TNF,TNFRSF1B,TNFSF10,XDH	928 (21)
COLQ	other	2,25E-04	BDNF,BMP4,COL4A1,COL6A3,FN1,HSPG2,LTBP4,MFAP2,MMP2,MMP9,PRELP,SDC4,SGCD,TGFB1,TGFB3,TIMP1,VCAN	
DOCK8	other	2,25E-04	ATM,CD40,EDN1,IL12B,IL15,IL15RA,IL18,IL6,LTA,NFKBIZ,PLAT,PTGS2,REL,SLCO3A1,SOCS1,TNF,TSC22D1	
TLR8	transmembrane	2,25E-04	CCL2,CD40,CXCL8,CYP27B1,IFNG,IFNK,IL12A,IL12B,IL1B,IL6,NR1H4,TNF,VDR	585 (16)
PRMT1	enzyme	2,26E-04	ALOX12,CCL11,CNP,CTNNB1,CYP3A4,GCLC,GYPA,ITGA2B,PPARG,RARB,TFF1	936 (21)
SOX17	transcription reg	2,26E-04	AFP,CCND1,COL4A1,CTNNB1,FOS,GATA4,HNF4A,IFNK,KDR,NR2F1,POU5F1	821 (13)
lisinopril	biologic drug	3,33E-13	ACE,CAST,FOS,IL13,IL1B,JUN,KDR,LDLR,MMP2,NOS2,PDGFRB,REN,TGFB1,TNF,VEGFA	631 (16)
ACE	peptidase	2,38E-04	ACE,AGT,CCN2,LDHA,REN,SERPINE1	907 (17)
Adaptor protein	complex	2,38E-04	IFNG,IL10,MMP9,NOS2,PTGS2,SOD2	
Adaptor protein	complex	2,38E-04	AGXT,CD28,HMOX1,IFNG,LHCGR,NOS1	
AIMP2	other	2,38E-04	CDKN2A,EGFR,KRAS,SLC2A1,SLC2A2,SLC2A4	413 (7)
CAMKK2	kinase	2,38E-04	ADRB2,BDNF,CCND1,KCNB1,LEP,PPARGC1A	988 (23)
CPT1C	enzyme	2,38E-04	CPT1A,CPT1B,MT-CO2,NPY,PDK4,PPARGC1A	370 (7)
CRLF2	transmembrane	2,38E-04	IL10,IL12A,IL12B,IL13,IL4,IL5	650 (18)
DUSP4	phosphatase	2,38E-04	CYP11A1,IL1RL1,IL6,MMP1,PCK1,SMAD2	880 (17)

ELK3	transcription reg	2,38E-04	ERBB2,FOS,HMOX1,MMP3,NOS2,SERPINE1	441 (7)
EPHB1	kinase	2,38E-04	FOS,IL6ST,JUN,PCK1,PTGS2,SERPINE1	890 (17)
HIPK1	kinase	2,38E-04	GCLC,GSTM5,NKX2-5,NQO1,PECAM1,VEGFA	
HIST2H3C	other	2,38E-04	ADGRL3,HBB,IL1B,LRP2,RUNX1,THBS4	
HTR2B	G-protein coupl	2,38E-04	BAX,COL23A1,ERBB2,MYH7,NPPA,TGFB1	840 (12)
IL1R2	transmembrane	2,38E-04	CSF2,CXCL8,IL1B,IL6,MPO,TNF	596 (15)
MAFA	transcription reg	2,38E-04	G6PC2,GCKR,INS,PDX1,SLC2A2,TNF	
MALT1	peptidase	2,38E-04	IL10,IL17A,IL2,IL2RA,IL6,TNF	618 (18)
MAS1	G-protein coupl	2,38E-04	CYBB,IL1B,IL6,NOS2,NOS3,TNF	919 (19)
miR-135a-5p (a	mature microRN	2,38E-04	ALOX5AP,JAK2,NR3C2,PPARG,SLC6A4,SMAD5	
MMP7	peptidase	2,38E-04	BMP7,FAS,FLT1,MMP2,MMP3,TNFSF11	958 (20)
MYZAP	other	2,38E-04	ATP2A2,DES,FOS,GJA1,MYL2,NPPA	596 (11)
PIAS2	transcription reg	2,38E-04	AR,CDKN2B,FOS,ITGA2,LDLR,SLC11A1	991 (19)
PTCSC3	other	2,38E-04	CCND1,CTNNB1,LRP6,MMP9,S100A4,STAT3	
SART1	other	2,38E-04	EPO,HIF1A,MMP9,POU5F1,SERPINE1,VEGFA	530 (7)
SLC51A	transporter	2,38E-04	ABCC2,CYP3A5,CYP7A1,NR0B2,SLC10A2,UGT1A1	
TXK	kinase	2,38E-04	HAMP,IFNG,IL2,IL2RB,KLRB1,TNF	732 (20)
MECOM	transcription reg	2,39E-04	GATA2,ITGA2B,ITGB3,ITPR2,Ly6a (includes others),PBX1,PML,SERPINE1,ZFPM2	
NTRK1	kinase	2,39E-04	BDNF,FOS,IGF2,MMP9,RET,SOD2,TP53,TSC22D1,WNT5A	986 (21)
PDGF-AA	complex	2,39E-04	ACTA2,FOS,HBEGF,HGF,IGF1,IL6,LDLR,PDGFRA,TGFB1	949 (23)
TRPS1	transcription reg	2,39E-04	ALPL,BGLAP,ENPP1,KCNMA1,PHEX,RAMP1,RUNX1,SEMA6A,VDR	
CHADL	other	2,41E-04	FAS,IGFBP3,IL6,MEF2C,MET,NTRK3,PHEX,PTH1R,STEAP4,VCAM1	
CRTC2	other	2,41E-04	CCND1,CDK6,CYP19A1,MT-CO2,PCK1,PPARGC1A,SDS,SMAD6,SMARCA2,SMARCA4	787 (13)
DLL1	enzyme	2,41E-04	EFNB2,EPHA4,GATA2,HES1,HES5,IFNG,IL10,IL13,IL17A,JAG1	493 (12)
GRP	growth factor	2,41E-04	CCND1,CXCL8,FOS,GCG,IL33,JUN,PRKCA,PTGS2,TSLP,VEGFA	870 (20)
mir-135	microRNA	2,41E-04	ALOX5AP,AR,CXCL12,EDN1,HIF1A,IL1B,IL1R1,SLC6A4,SMAD5,SPP1	
SND1	enzyme	2,41E-04	ANGPTL4,DHFR,IL13RA2,JAG1,KISS1,KYNU,NR2F1,PTGS2,PTPRN2,QPCT	
APBB1	transcription reg	2,43E-04	ACTA2,CCND1,EGFR,HES1,TP73,TPM1,TYMS	1061 (23)
INSIG2	other	2,43E-04	FDFT1,G6PD,HMGCR,INSIG1,LDLR,SREBF1,SREBF2	525 (9)
mir-154	microRNA	2,43E-04	BAX,CCND1,HMOX1,KIT,PLAUR,PTEN,STAT3	797 (16)
SLC18A3	transporter	2,43E-04	ADRB1,DRD2,GRK2,GRK5,GRK6,MYH7,NPPA	
SP2	transcription reg	2,43E-04	BGLAP,CCND1,DHFR,FOS,GNAI2,PTGS1,SERPINE1	
EIF3E	other	2,64E-04	ANGPT1,CCND1,CD36,CD40,COL18A1,DYNC1H1,EPAS1,LIG1,LPA,SAA1,THBS1,TNC	726 (7)
FLT3	kinase	2,64E-04	BAX,CYBA,CYBB,IFNG,IL10,IL12B,IL6,MPO,NOX1,NOX4,SLC2A1,TNF	773 (20)
FOXP1	transcription reg	2,64E-04	GJA1,IFNG,IL6,ITGAM,JUN,MEF2C,MYH7,NFIA,NKX2-5,NPPA,POU5F1,SCGB1A1	552 (7)
Tcf7	transcription reg	2,64E-04	BCL11B,FYN,GPA33,IFNG,IL17A,IL22,IL2RA,IL4,IL7R,KIT,TNF,TOX	517 (7)
RRP1B	transcription reg	2,81E-04	AURKA,BMP7,BRCA1,BRCA2,CCND1,CYP24A1,DHFR,EP300,FOXO1,ITGB2,MRAS,NCOA1,PRKCA,RABIF,RARA,RARG,SERPINE2,SMAD6,SPP1,TGFB1,TOPBP1,VDR,VEGFC	
TFE3	transcription reg	2,86E-04	CIDEA,GCK,INSIG1,IRS2,MT-ATP6,MT-CO1,MT-CYB,MT-ND1,MT-ND2,MYH9,PPARGC1A,SERPINE1,TYRP1	711 (12)
miR-16-5p (and	mature microRN	2,88E-04	BDNF,CACNA2D1,CARD8,CCND1,CDK6,CRHBP,EGFR,F2,FGFR1,FLT3,GALNT13,GSTM4,HMGA1,HMOX1,HSPA1A/HSPA1B,IGF1,IGF1R,IGF2R,IL6,ITGA2,JUN,MAPK3,MYB,NFIA,NOTCH2,NPR3,PAFAH1B2,PMS1,PTGS2,SERPINE2,SKAP2,SLC12A2,SLC7A1,TXN2,UCP2,VEGFA	
Rar	group	3,01E-04	ABCG2,AQP3,ARG1,CYP4F2,ITGB2,MGP,MMP1,RARB,SFTPB,SLC10A1,UCP1	571 (17)
SFPQ	transcription reg	3,01E-04	ADARB2,AR,CYP11A1,CYP17A1,ECE1,EPHX1,LPIN1,PPARG,SEMA6A,SF1,TH	832 (7)
RBL1	transcription reg	3,02E-04	CCND1,CDKN2A,DHFR,FAS,FOS,HES1,LHCGR,MET,NOTCH1,POMC,PPARGC1A,TERT,THBS1,TNF,TP53,TP73,TYMS,UCP1	986 (21)
ADRB1	G-protein coupl	3,18E-04	ACTC1,COL3A1,GNAS,IRAK1,LEP,RYR2,SLC9A1,THBS1	786 (12)
ERVW-1	other	3,18E-04	CCL5,CDKN2A,CNP,CXCL8,IL6,NOS2,SLC1A4,TP53	892 (14)
HOXD3	transcription reg	3,18E-04	CDKN2A,COL1A1,HAMP,IGFBP3,ITGB3,MMP2,SERPINE1,THBS1	
IL11RA	transmembrane	3,18E-04	ACTA2,CCL11,CCL17,FOS,MMP12,MMP2,POSTN,TGFB1	834 (14)
mir-192	microRNA	3,18E-04	ACTA2,CXCL8,FN1,IGF1,IGF1R,NOD2,TP53,TYMS	938 (18)
MLX	transcription reg	3,18E-04	CCN3,DIO1,FGF21,IGF2,IL1RN,SLC2A2,THBS2,TXNIP	
STAP2	other	3,18E-04	CCND1,CCR2,CXCR2,CXCR4,EGFR,FGB,IL6,TNF	747 (17)
TIMP2	other	3,18E-04	MMP14,MMP2,NFKBIA,PDX1,RELA,SLC2A2,TIMP2,VEGFA	938 (19)
ARID1A	transcription reg	3,31E-04	ALPL,BMP4,FZD4,HES1,LRP5,LRP6,MEF2C,TERT,WNT3,WNT5A	175 (4)
CASP3	peptidase	3,31E-04	BAX,HTT,IL16,mir-143,MMP9,MYOD1,NOS2,PTEN,TNF,TP53	929 (22)
Focal adhesion	group	3,31E-04	EFNB2,FZD4,ICAM1,IL6,ITGB2,MMP2,MMP9,SELL,TP53,VCAM1	824 (19)
mir-22	microRNA	3,31E-04	BMP6,BMP7,ERAL1,ERBB3,ESR1,IL6,MECOM,RGS2,TGFBR2,TNF	691 (11)
mir-132	microRNA	3,31E-04	BDNF,CCL2,EP300,FOXO3,GRIA1,IFNG,PTEN,RASA1,STAT4,TNF	1079 (21)
SIAH2	transcription reg	3,31E-04	AKR1C3,ANGPT1,CHEK2,CYP24A1,DCC,EGLN3,FGF1,HIF1A,MME,NCOR1	
ZNF281	transcription reg	3,31E-04	BLM,CCL11,CCL2,CXCR4,IL6,LGR5,PTGS1,PTGS2,XRCC3,XRCC4	
HOTAIR	other	3,41E-04	ACTA2,COL1A1,GDF15,HIF1A,ICAM1,IFNL3,MAPK1,MMP2,MMP9,NPPA,PTEN,TP53	977 (24)
KCNK9	ion channel	3,41E-04	CA1,CYP11B1,HP,HSD3B1,HTR1B,KCNK3,LCN2,REN,SEZ6L,SLC14A1,SPTA1,SV2C	
mir-124	microRNA	3,41E-04	ABCC8,BAX,CAMTA1,IL2,KCNJ11,NFATC1,PDX1,RELA,STAT3	648 (15)
NR0B1	ligand-depende	3,41E-04	AR,CYP11A1,CYP17A1,CYP19A1,CYP7A1,HSD3B2,KCNN2,MLXIPL,NOS1,PCK1,SCARB1,SREBF1	768 (20)
NR2C2	ligand-depende	3,41E-04	APOE,CCND1,CD36,CYP24A1,ERCC6,LHCGR,POMC,RARB,TFF1	775 (13)
EGLN	group	3,54E-04	ADM,ANGPTL3,APLN,APOA4,BCL11B,CCL2,DIO3,EGLN3,EPO,FYN,GRHPR,GYS1,HLA-B,HLA-DQB1,IFNG,IGFBP1,KDM5B,LCN2,LDHA,MIF,PAM,PFKP,PPFIA4,SAA1,SELENBP1,SERPINE1,STC2,TH,VEGFA,VKORC1	930 (26)
miR-1-3p (and c	mature microRN	3,57E-04	AGMAT,ANPEP,AP3D1,ARID1A,AXL,BDNF,DHX15,EGFR,ESR1,F2,FBLN2,G6PD,GCH1,GJA1,GNPDA2,HPS4,IGF1,LRP1,MEF2A,MET,MOV10,NELFCD,NOTCH2,NOTCH3,PICALM,POGK,RABGAP1L,SDC4,SRSF9,SYNE1,THBS1,TIMP3,TPM1,UHRF1	
ABCC1	transporter	3,59E-04	CYBA,CYBB,NCF2,NOX1,NQO1	
AQP4	transporter	3,59E-04	AQP4,CYP2E1,IL1B,IL6,SLC2A1	521 (7)
CD5L	transmembrane	3,59E-04	CCL5,IL1B,TLR2,TLR4,TNF	895 (14)
CHCHD5	other	3,59E-04	CPT1B,PPARA,PPARG,PPARGC1A,SREBF1	
CXCL16	cytokine	3,59E-04	CXCL8,FN1,IFNG,IL4,TNF	976 (19)
CYP3A4	enzyme	3,59E-04	CYP3A7,GCLC,HMOX1,SLC10A2,SLCO1B3	601 (9)
DLG4	kinase	3,59E-04	FOS,HTR2A,HTR2C,LRP8,MAS1	
FYB1	other	3,59E-04	CD69,IFNG,IL2,IL2RA,ITGAM	813 (20)
GPR84	G-protein coupl	3,59E-04	IL12B,IL1B,IL6,NOS2,TNF	691 (14)
GRB10	other	3,59E-04	FOS,IGF1,IRS1,KDR,MMP12	1066 (26)
HDAC10	transcription reg	3,59E-04	MITF,MMP2,MMP9,TXNIP,TYRP1	824 (13)
HDAC11	transcription reg	3,59E-04	IL10,IL17A,IL1B,TNF,TNFSF4	983 (20)
HYOU1	other	3,59E-04	IL12B,IL6,NOS2,PECAM1,TNF	973 (26)
IL23R	transmembrane	3,59E-04	IFNG,IL10,IL17A,IL2,IL22	789 (20)
immune comple	complex	3,59E-04	IFNG,IL1RN,SOCS1,SOCS3,VCAM1	665 (18)
L-type Calcium	complex	3,59E-04	APOE,BDNF,CACNA1D,ENPP1,FOS	837 (25)
Lefty	group	3,59E-04	CCN2,FOXO1,IGFBP1,PRL,SMAD5	
LGALS9B	other	3,59E-04	IFNG,IL10,IL2,IL5,TNF	
MLANA	other	3,59E-04	CSF2,IFNG,IL2,KIR2DL1/KIR2DL3,KIR2DS3	467 (7)
MRPL12	other	3,59E-04	MT-CO1,MT-CO2,MT-ND1,MT-ND2,MT-ND6	
NCR3	transmembrane	3,59E-04	CCL5,CSF2,IFNG,NCR3,TNF	831 (17)
PKP2	other	3,59E-04	COL3A1,FN1,GJA1,IL1A,TGFB1	818 (9)
PRTN3	peptidase	3,59E-04	CCL2,CXCL8,IL18,IL6,TNF	787 (19)
RAB1A	enzyme	3,59E-04	ADRA1A,ADRA1B,ADRB1,ADRB2,PRKCA	
REL/RELA/RELB	group	3,59E-04	CSF2,IFNG,IL12B,IL2,IL3	
RLN1	other	3,59E-04	AQP3,ESR1,HAS2,MYH7,NPPA	
S100a7a	other	3,59E-04	CCND1,CSF2,CXCL8,IL1A,MMP2	726 (13)
TBL1XR1	transcription reg	3,59E-04	DIO1,HP,MMP12,RARB,TFF1	421 (7)

ULBP1	transmembrane	3,59E-04	CD69,HLA-A,IFNG,IL2RA,TNF	638 (13)
VIPR2	G-protein coupl	3,59E-04	IFNG,IL2,IL4,IL5,MAF	748 (17)
VTCN1	other	3,59E-04	CCND1,IFNG,IL10,IL2,TNF	822 (18)
ZNF382	transcription reg	3,59E-04	CDK6,IKBKE,MITF,STAT3,STAT5B	
IFNL1	cytokine	3,83E-04	ATF3,CD40,CXCL8,F2R,HLA-B,HLA-C,IFIH1,IFNG,IL10,IL12B,IL13,IL5,IL6,mir-122,OAS3,OASL,PML,PSMB9,TLR2	671 (17)
SMO	G-protein coupl	3,83E-04	CCND1,DIO1,DIO3,ENPP1,ERVW-1,FAS,FBLN2,FOXF1,HBB,KLK2,LGALS13,LGR5,MYOD1,NCAM1,NFATC1,RUNX1,TGFB3,VCAM1,VCAN	914 (20)
7S NGF	complex	3,96E-04	CLU,FOS,GCLC,GCLM	
ACAN	other	3,96E-04	FOXP3,IFNG,IL10,TNF	587 (12)
ACOT13	enzyme	3,96E-04	PPARA,PPARG,PPARGC1A,UCP1	
ADAM8	peptidase	3,96E-04	CCL5,IL4,IL5,TNF	800 (11)
ALDH3A2	enzyme	3,96E-04	GCLC,GCLM,HMOX1,SOD1	
AOPEP	peptidase	3,96E-04	IL1B,IL6,RELA,TNF	
ATPase	group	3,96E-04	CD40,ICAM1,MMP14,VCAM1	
BBS12	other	3,96E-04	ADIPOQ,IL6,LEP,TNF	830 (16)
Beta Arrestin	group	3,96E-04	FOS,IFNG,IL2,LHCGR	1048 (23)
BPI	transporter	3,96E-04	CXCL8,ICAM1,IL6,TNF	896 (10)
BUD23	enzyme	3,96E-04	CXCL8,FKBP5,IL6,PLAGL1	496 (7)
CD6	transmembrane	3,96E-04	FOXP3,IFNG,IL6,TNF	783 (16)
CITED1	transcription reg	3,96E-04	CYP24A1,ERBB2,IGF1,IGF2	
CLDN2	other	3,96E-04	CCND1,ITGA2,ITGB1,MMP9	584 (10)
Collagen type V	complex	3,96E-04	ITGA2,ITGAV,ITGB1,ITGB3	468 (7)
CYP	group	3,96E-04	CYP27B1,GCLM,HMOX1,NQO1	896 (16)
DRD3	G-protein coupl	3,96E-04	FOS,LEP,SLC9A3,TH	703 (16)
ELMO1	other	3,96E-04	EDN1,IL10,NOX4,TGFB1	804 (11)
Erm	group	3,96E-04	CAV1,ICAM1,IFNG,IL2	726 (18)
FGG	other	3,96E-04	IL1B,IL6,NOS2,TNF	621 (14)
FOXI1	transcription reg	3,96E-04	ATP6V1B1,SLC12A3,SLC26A4,SLC4A1	
FUT4	enzyme	3,96E-04	BAX,MMP12,PARP1,SELE	532 (7)
Gata	group	3,96E-04	EDN1,ITGA2B,KDR,NPPA	
GLS	enzyme	3,96E-04	ACTA2,COL1A1,FN1,HIF1A	850 (11)
Hottip	other	3,96E-04	SMAD2,SMAD3,TGFBR1,TGFBR2	
HSD17B1	enzyme	3,96E-04	CYP11A1,CYP17A1,HSD17B7,LHCGR	
HTR4	G-protein coupl	3,96E-04	ANGPT1,CARTPT,CXCL12,VCAM1	366 (7)
ICAM5	other	3,96E-04	CD69,IFNG,IL2RA,TGFB1	
IL12RB2/IL23R	group	3,96E-04	IL17A,IL1B,IL22,TNF	440 (9)
ILF2	transcription reg	3,96E-04	EGFR,FOS,IL13,ILF3	568 (7)
Integrinî±	group	3,96E-04	ITGAM,ITGB2,TLR2,TLR4	719 (7)
KIDINS220	transcription reg	3,96E-04	CD69,FOS,IFNG,IL2	680 (11)
KLK8	peptidase	3,96E-04	IFNG,IL10,IL5,IL6	479 (9)
LRRC32	other	3,96E-04	FOXP3,IFNG,TGFB1,TGFB3	822 (11)
03-mar	other	3,96E-04	CXCL8,FCGR2B,NFKBIA,TNF	830 (14)
MCF2	other	3,96E-04	CCND1,HAMP,ITGA2,ITGB1	863 (19)
mir-637	microRNA	3,96E-04	AKT1,CCND1,CTNNB1,FOXO1	
MLYCD	enzyme	3,96E-04	CD36,CPT1B,PDK4,UCP3	370 (7)
MYCL	transcription reg	3,96E-04	CAD,CIITA,HSPD1,TERT	
NAA10	enzyme	3,96E-04	EGFR,EPO,TGFBR3,VEGFA	531 (7)
Orm1 (includes	other	3,96E-04	IL1B,IL6,NOS2,TNF	
PDE4D	enzyme	3,96E-04	IFNG,IL5,MITF,PLAT	850 (21)
PILRB	other	3,96E-04	IFNG,IL1B,IL6,TNF	926 (19)
PINK1	kinase	3,96E-04	HIF1A,SLC2A1,TH,VEGFA	530 (7)
PLIN2	other	3,96E-04	LEP,PCK1,UCP1,UCP2	570 (11)
RAB4A	enzyme	3,96E-04	ADRB1,KCNH2,MYH7,NEDD4L	
RFXANK	transcription reg	3,96E-04	COL1A2,HLA-A,HLA-B,HLA-DRA	
RIDA	enzyme	3,96E-04	IFNG,IL10,IL4,TNF	
SENP6	peptidase	3,96E-04	CXCL8,ICAM1,IL6,TNF	586 (10)
SLC22A2	transporter	3,96E-04	CPT1A,CPT1B,CPT2,SLC22A5	717 (7)
SMPD3	enzyme	3,96E-04	FOXO1,ICAM1,IGF1,VCAM1	854 (20)
SPIC	transcription reg	3,96E-04	FCGR2B,IL2RA,KIT,NFKB1	521 (7)
SSBP1	other	3,96E-04	FGA,HLA-DRA,TGFB1,TSHR	
STX11	transporter	3,96E-04	IFNG,IL1B,IL6,TNF	909 (17)
TAF9	transcription reg	3,96E-04	CXCL8,HAMP,HLA-DRA,TP53	
Tlr12	other	3,96E-04	CXCL8,IL1B,IL6,TNF	729 (17)
TNFAIP8	other	3,96E-04	IL17A,IL1B,IL6,MMP1	424 (7)
VCAM1	transmembrane	3,96E-04	ABCG2,CCND1,MMP9,VCAM1	722 (16)
DIRAS3	enzyme	3,97E-04	CCND1,F2,HLA-DQA1,HMGA1,PARP1,PRL,TFPI2	
EFNB2	kinase	3,97E-04	ANGPT1,BGLAP,IL7R,MAPK1,MAPK3,PTH1R,TNFSF11	
MAPK10	kinase	3,97E-04	CXCL8,FOS,IL6,JUN,MMP1,PTGS2,TNF	850 (18)
mir-204	microRNA	3,97E-04	BDNF,CXCL8,FOXC1,IGF2R,IL1B,IL6,PTPN11	950 (12)
RCOR1	transcription reg	3,97E-04	CARTPT,COL1A1,COL1A2,NOS2,PTGS2,SERPINE1,TNF	690 (7)
SMURF2	enzyme	3,97E-04	CCN2,CDKN2A,FN1,JUN,SERPINE1,SMAD1,SMAD2	720 (16)
Srebp	group	3,97E-04	CYP4F2,FOS,G6PD,H19,LDLR,NPC1,UCP2	
IRF7	transcription reg	4,19E-04	C5,CCL5,CCL8,CD40,CD69,CTLA4,FOXP3,IFIH1,IFNK,IFNL3,IL12A,IL15,IL15RA,IL33,IL4I1,IRF5,ITGAM,JAK2,Ly6a (includes others),NAMPT,NRAP,OAS3,OASL,PSMB8,PSMB9,SOCS1,TAP1,TLR4,TLR8,TNFSF10,TRAF1	791 (19)
DYSF	other	4,22E-04	ABCA1,CTSH,CYBA,FCGR2B,FN1,HLA-A,HLA-DQA1,HLA-DQB1,HLA-DRB5,HSPA1A/HSPA1B,ITGB1,ITGB3,MMP12,PDGFRA,S100A4,SERPINA3,TIMP1,UGT1A6	
CACNA1A	ion channel	4,38E-04	CACNA1A,IL10,IL1B,IL6,ITGAM,TNF	665 (12)
CST3	other	4,38E-04	CALCR,FOS,HAMP,IL1B,NFATC1,NFKBIA	669 (13)
DDB2	other	4,38E-04	BAX,MMP9,NFKBIA,SOD2,TP53,VEGFA	1051 (24)
EDNRB	G-protein coupl	4,38E-04	FLT4,HIF1A,NPPA,TPM1,VEGFA,VEGFC	947 (18)
GREM1	other	4,38E-04	COL1A1,ELN,GDNF,RET,SHH,TNF	624 (11)
HNRNPAB	enzyme	4,38E-04	ACTA2,HBB,HTRA1,PTGS2,S100A4,SPP1	540 (7)
HPSE	enzyme	4,38E-04	CCL2,HGF,IRS1,MMP9,PLAUR,PTGS2	860 (18)
IL16	cytokine	4,38E-04	CMA1,FOS,FOXP3,IFNG,IL2RA,TGFB1	751 (20)
Il8r	group	4,38E-04	BAX,CXCL8,EGFR,ITGAM,MMP2,MMP9	852 (19)
ITGA3	other	4,38E-04	FN1,ITGA2,MMP2,PTGS2,SERPINE1,VCL	711 (18)
L1CAM	other	4,38E-04	IL1B,LGR5,MMP2,MMP9,NOS2,SMOC2	933 (18)
LECT2	other	4,38E-04	C3,IFNG,IL10,IL1B,IL6,TNF	852 (14)
LILRB4	other	4,38E-04	IFNG,IL17A,IL1A,IL1B,IL6,TNF	788 (16)
miR-148a-3p (a	mature microRN	4,38E-04	ACTA2,COL1A1,IL6,NR1I2,TGFBR2,TNF	
miR-451a (and	mature microRN	4,38E-04	ABCB1,AKT1,CCND1,MIF,MMP2,MMP9	
PCSK2	peptidase	4,38E-04	CARTPT,CCK,PCSK1,PDX1,POMC,SST	825 (20)
PLD1	enzyme	4,38E-04	CTNNB1,IL13,IL13RA2,IL2,NOS2,PTGS2	636 (14)
PTGDR2	G-protein coupl	4,38E-04	CCL5,IL13,IL2,IL4,IL5,ITGAM	921 (25)
RASGRF1	other	4,38E-04	FOS,IGF1,IL6,KRAS,MMP3,MMP9	982 (18)
STAR	transporter	4,38E-04	ABCA1,CCL5,CD36,NR1H3,POMC,SPP1	
STAT1/3/5 dime	complex	4,38E-04	CHI3L1,EPAS1,MMP1,MMP3,SOCS3,TIMP3	
TIGIT	other	4,38E-04	IFNG,IL10,IL13,IL4,IL5,IL9	845 (20)
VGLL3	other	4,38E-04	ADM,COL1A1,COL1A2,MMP3,SPP1,THBS1	
caspase	group	4,46E-04	BAX,CCND1,CD14,CDK6,EGFR,IL1A,IL2RA,PTEN,THBS1,TNF	908 (20)

mir-126	microRNA	4,46E-04	CXCL12,DLK1,FOXP3,IRS1,KIT,MITF,MMP7,PTPRC,VCAM1,VEGFA	568 (7)
PTH1R	G-protein coupl	4,46E-04	AR,CCND1,COL1A1,KL,MGP,PHEX,SPP1,TNFRSF11A,TNFRSF11B,TNFSF11	734 (15)
mir-182	microRNA	4,52E-04	ADCY6,CDH4,CDK6,CLDN17,FN1,FOXO1,FOXO3,GHR,ITGA4,LRP6,NCAM1,RASA1,VWF	
CAR ligand-CAR	complex	4,70E-04	ABCC2,CYP2C19,CYP2C8,CYP2C9,CYP3A4,CYP3A5,CYP3A7,SOD3	
CDK8	kinase	4,70E-04	CXCL8,CXCR4,DIO1,MAGI1,NOTCH1,RARB,STC2,TP73	783 (13)
EIF4EBP2	translation regu	4,70E-04	ARG1,CEBPD,CYP2A6 (includes others),GRIA1,IL10,IL1RN,PPARG,PTGS2	549 (9)
EPCAM	other	4,70E-04	ATF3,CCND1,FOS,GCG,INS,JUN,POU5F1,TP53	760 (12)
FGFR4	kinase	4,70E-04	CCND1,CTNNB1,CYP7A1,FOS,KDR,MMP1,MMP14,SERPINE1	771 (18)
FUT8	enzyme	4,70E-04	ALDH2,CYP1B1,ELN,GSTM3,GSTM5,GYPA,MMP12,TFRC	
miR-31-5p (and	mature microRN	4,70E-04	CASR,CDKN2A,CXCL5,CXCL8,FGF10,FOXP3,HIF1A,IL1B	
SMARCC1	transcription reg	4,70E-04	EBF1,HBG1,IL7R,KDR,NCOA1,PAX5,TFF1,TP53	784 (12)
TRIM21	enzyme	4,70E-04	IL12B,IL17A,IL1B,IL2,IL22,IL6,SALL1,TNF	609 (16)
ADAMTS12	peptidase	4,78E-04	CCL11,CHI3L1,IL22,IL33,IL6,LCN2,MGP,MMP3,SELP	
CASR	G-protein coupl	4,78E-04	ABCC2,CASR,GABBR2,GATA4,NKX2-5,PON1,PTGS2,TYMS,VDR	853 (18)
NCL	other	4,78E-04	DICER1,HBB,HIF1A,HSPA1A/HSPA1B,ILF3,PTEN,RET,TNF,TP53	885 (16)
thyroid hormon	group	4,78E-04	ABCA1,CPT1A,CYP7A1,FOS,GH1,NTRK1,POR,PRL,UCP1	958 (24)
MTDH	transcription reg	5,15E-04	ANGPT1,CXCL8,DIO1,FABP1,HIF1A,HTRA1,MMP2,NR0B2,RARB,SOCS1,TYMS	1124 (24)
ROCK2	kinase	5,15E-04	CXCL8,DES,FAS,ICAM1,MYOD1,PI3,PPARG,PRKG1,SERPINE1,SPP1,VCAM1	913 (16)
KMT2A	transcription reg	5,39E-04	ADRA1A,ADRA1B,ARSG,CDKN2A,EPHB4,FOXC1,HAMP,MECOM,MEIS1,mir-196,PBX1,PGR,PITX2,PRDM16,RGS4,SCARB1,SMAD1,TFF1,TRIB1,ZMAT4	886 (12)
ARHGAP21	other	5,52E-04	ATM,IL12A,IL15,IL15RA,IL18,LTA,NFKBIZ,PLAT,PTGS2,SLCO3A1,TNF,TSC22D1	
PRMT5	enzyme	5,52E-04	ADIPOQ,CDKN2A,CYP7A1,LEP,NPPA,POU5F1,PPARA,PPARG,PPARGC1A,PTPRO,RETN,SREBF1	959 (24)
SRSF2	transcription reg	5,52E-04	ABCC9,AURKA,CCND1,CES1,COL1A1,EP300,MLXIPL,NR1H4,PPARA,RYR2,SREBF1,SRSF2	
H2AFX	transcription reg	5,93E-04	CLU,GATA4,MT-CO1,PLEKHA6,PPARGC1A,PTN,SDHB,SFRP2,TIMP3,TP53BP1	762 (7)
IFT88	other	5,93E-04	ACAT1,ACAT2,ADIPOQ,COL1A2,HAMP,HMGCR,LSS,PPARG,SHH,TIMP3	515 (7)
mir-193	microRNA	5,93E-04	ACTN4,CCL2,CKM,KIT,MYOD1,NOTCH1,NPHS1,NPHS2,PTEN,VEGFA	643 (7)
CFB	peptidase	6,19E-04	C3,C4A/C4B,C5,ITGAM,SREBF1,TGFB2,THBD	
Iga	complex	6,19E-04	CXCL8,FCGR2B,IL10,IL12A,IL12B,TGFB1,TNF	899 (16)
PHLPP1	enzyme	6,19E-04	CEBPD,FOXO1,IL15,IL18,IRS1,PRKCA,PRKCB	712 (7)
PKNOX1	transcription reg	6,19E-04	CCL2,GNRH1,PBX1,PPARGC1A,REN,SLC2A4,SST	
PPP1R1B	phosphatase	6,19E-04	ATF1,CCND1,CTNNB1,ERBB2,FOS,LRRK2,SRSF3	956 (20)
TF	transporter	6,19E-04	CCL2,CCL5,CCND1,COL1A1,CXCL8,EGFR,TFR2	922 (20)
TNK1	kinase	6,19E-04	IFIH1,IL10,IL6,NOS2,TLR8,TLR9,TNFSF10	505 (11)
ASAH1	enzyme	6,56E-04	CCL5,CERS6,CYP11A1,CYP17A1,CYP21A2,ELOVL2,LIPE,NR4A3,SCARB1	39 (3)
FSHB	other	6,77E-04	CCN2,CYP19A1,EGFR,FSHR,ITGB3,PLAT,SGK1,SHBG	
IL2RA	transmembrane	6,77E-04	FOS,IFNG,IL10,IL15RA,IL2,IL4,JUN,TNF	725 (20)
PARPBP	other	6,77E-04	CNTNAP2,CPEB4,CYP2E1,ELN,KISS1,REN,TIMP1,TNC	
PAX2	transcription reg	6,77E-04	ERBB2,GCG,ITGAV,ITGB3,MITF,PAX2,PAX5,SFRP2	
STK4	kinase	6,77E-04	FAS,FOXO1,HAMP,IL6,IL7R,MMP2,SFTPB,TNF	846 (20)
TERF2IP	other	6,77E-04	CCL2,CCN2,CXCL8,H19,IGF2,NFKBIA,NNMT,TNF	580 (12)
CD38	enzyme	7,03E-04	ACTA2,ATP1B1,COL1A1,EGLN3,EVI5,FN1,ICAM1,IFI30,IL2,IL2RA,IL5RA,IL6,IL6R,LTA,NCAM1,PAX5,PFKP,PPARGC1A,PPP3CA,S100A4,SELL,SLC2A1,SLC39A8,SOCS1,SOCS3,STK39,TGFB1,UCK2,VCAM1	933 (22)
MAVS	other	7,03E-04	ALPL,CCL5,CXCL8,IFNG,IL12B,IL1B,IL6,NFKB1,OASL,SOCS1,SOCS3,SPP1,TLR7,TNF,TNFRSF11B,TNFSF11	654 (18)
POU4F1	transcription reg	7,15E-04	ACTC1,ADCYAP1,BAX,CARTPT,CCKAR,CHRNA3,DCC,ETV5,GNAS,IL2,KCNMA1,NPY,NTRK1,NTRK3,RET,RUNX1,SCN7A,SNAP25,SYT9,TFAP2B,TH,TRPV1	
AGTRAP	G-protein coupl	7,44E-04	FOS,GJA1,HMOX1,SLC6A2,VEGFA	738 (17)
AKAP12	transporter	7,44E-04	ANGPT1,CCND1,HIF1A,MMP2,TNF	958 (23)
APC/APC2	group	7,44E-04	CTNNB1,JAG1,MMP14,NOS2,TRAF1	586 (11)
ARF6	transporter	7,44E-04	CCL5,IL1B,IL2,IL6,TNF	768 (20)
Bcl9-Cbp/p300-	complex	7,44E-04	CCND1,GJA1,HNF1A,MMP7,PPARD	
CAPN1	peptidase	7,44E-04	IL17A,IL6,MMP2,PTPN1,TNF	876 (21)
CD160	transmembrane	7,44E-04	FOS,IFNG,IL6,JUN,TNF	696 (9)
CD244	transmembrane	7,44E-04	CCL5,CSF2,FOS,IFNG,TNF	1024 (22)
CD200R1	transmembrane	7,44E-04	HIF1A,IFNG,IL2,IL4,TNF	626 (21)
HCAR1	G-protein coupl	7,44E-04	IL10,IL1B,IL6,PPARGC1A,TNF	743 (16)
IL22RA1	transmembrane	7,44E-04	CXCL8,HBEGF,IL24,NOS2,SOD2	
KCNJ11	ion channel	7,44E-04	CPT1B,FOXO1,MT-CO1,NPPA,PPARGC1A	
MEMO1	other	7,44E-04	CA2,CCND1,FOS,JUN,STC2	985 (16)
miR-126a-5p (a	mature microRN	7,44E-04	CYP2A6 (includes others),DLK1,KIT,MITF,MMP7	
miR-142-3p (an	mature microRN	7,44E-04	F9,HMGB1,IL12B,PRKCA,TNF	472 (7)
MSGN1	transcription reg	7,44E-04	CLOCK,HES1,NOTCH1,NOTCH2,PPARG	
NPC1L1	transporter	7,44E-04	ABCA1,FOXO1,HMGCR,MTTP,SREBF2	768 (12)
RALBP1	enzyme	7,44E-04	COL1A2,COL4A1,IL6,MMP2,TNF	888 (19)
Rap1	group	7,44E-04	DBH,FOS,IL2,MMP3,SORL1	928 (20)
RECK	other	7,44E-04	CCND1,CDKN2A,EGFR,MMP9,TP53	973 (19)
RGS4	other	7,44E-04	KDR,MYH7,MYL2,NPPA,PPP3R1	429 (12)
RSPO3	kinase	7,44E-04	CYP11B1,IL6,PTGS2,SHH,TNF	843 (12)
RUNX1T1	transcription reg	7,44E-04	CD34,CD69,CDKN2A,ELANE,NTRK1	
SLC16A3	transporter	7,44E-04	IL1B,IL6,MMP9,NOS2,TNF	
SPN	transmembrane	7,44E-04	CD69,IFNG,IL2,TNF,TP53	769 (22)
TOLLIP	other	7,44E-04	IL10,IL6,NFKB1,TLR4,TNF	577 (15)
TPSAB1/TPSB2	peptidase	7,44E-04	CMA1,FN1,IL1B,IL6,MMP3	534 (12)
TRG	other	7,44E-04	CAV1,CAV2,HLA-DQB1,IFNG,IL1B	529 (7)
UCHL3	peptidase	7,44E-04	ADIPOQ,BAX,SLC2A4,SREBF1,TP53	969 (21)
ZIC2	transcription reg	7,44E-04	APOE,CCND1,DRD1,EPHA4,SHH	483 (9)
CDK7	kinase	7,47E-04	EGFR,MET,STC2,TFF1,TGFB1,TNFAIP3	893 (11)
Complement	complex	7,47E-04	C5,CLU,ITGAM,PDGFRB,SELP,VCAM1	582 (11)
EN1	transcription reg	7,47E-04	CCND1,PAX5,PLCB4,SLC18A2,TH,TNFSF11	
FSTL1	other	7,47E-04	GDF15,IL1B,IL6,NFKB1,NLRP3,TNF	914 (18)
HSPA1A/HSPA1	enzyme	7,47E-04	CXCL8,FOS,IL1B,KCNH2,PSIP1,TNF	819 (17)
ID4	transcription reg	7,47E-04	BAX,BRCA1,CDKN2A,CDKN2B,MMP2,PPARG	
MBTPS1	peptidase	7,47E-04	FDFT1,HMGCR,LDLR,PTH1R,SREBF1,SREBF2	387 (7)
mir-127	microRNA	7,47E-04	ARG1,IL10,IL1B,IL6,NOS2,TNF	506 (7)
mir-373	microRNA	7,47E-04	ANGPTL4,CXCL8,IL6,RELA,SERPINE1,TGFBR2	
Mmp	group	7,47E-04	AXL,FAS,ITGAM,MMP9,PLG,VEGFA	805 (22)
OPRM1	G-protein coupl	7,47E-04	ADM,EGFR,IFNG,IL6,MMP9,OPRM1	830 (20)
Pdgfr	group	7,47E-04	ACTA2,CCL2,FN1,HBEGF,POU5F1,TNC	862 (20)
RBP1	transporter	7,47E-04	GCK,PDX1,PPARG,RARA,RXRA,SLC2A2	761 (15)
SOX5	transcription reg	7,47E-04	BMP6,FGFR3,HAMP,HSPG2,IL10,LIPE	
trypsin	group	7,47E-04	CXCL8,ELN,FOS,ICAM1,MIF,PTGS2	935 (22)
CD247	transmembrane	7,62E-04	ANG,CYBA,EDIL3,FCGR2A,HAMP,IFNG,IL10,IL2,IL4,KCNK3,NKTR,PLA2G5,QPCT,SLC23A2,SNRNP70	560 (22)
E2F3	transcription reg	8,45E-04	AKR1C3,CAV2,CCND1,CDKN2A,COL18A1,DHFR,ECE1,EDN1,FGFR2,HSPD1,ID3,IGF1,IGF2,KRAS,LEP,let-7,LPL,mir-143,mir-27,MYB,PLCB4,PTGER3,PTN,SERPINE1,SMG6,TERT,THBD,THBS1,TIMP3,TOPBP1,TP73	913 (21)
BRD2	kinase	8,49E-04	CDKN2A,HBA1/HBA2,HMOX1,IL1B,IL5RA,IL6,IL7R,NQO1,SLC4A1,SPTA1,STAT4,TNF,VAV3	
IDH1	enzyme	8,49E-04	BCAT1,CTNNB1,EPAS1,FN1,LEP,LPL,PCK1,PPARG,RETN,SLC2A1,SLC2A4,TGFB2,TP53	835 (16)
PPP2CA	phosphatase	8,63E-04	CCND1,CD36,CFB,FOXO3,IL17A,IL1A,IL2,IL23R,NOS2,PTGS2,RARB,TNF	635 (17)
CDX2	transcription reg	8,64E-04	ABCB1,CAV1,CCK,CCL25,CDH17,CLU,FGF1,FUT2,GIP,HNF1B,HNF4A,JUN,KLF5,LMX1A,MEIS1,MLLT3,NR1H4,NR2F2,POU5F1,PTEN,SLC26A6,SLC5A1,SLC7A8,SOX17,TCF7L2,TGFB1,UGT1A7 (includes others)	469 (7)
LIN28B	other	8,84E-04	BCL11A,CA1,let-7,LGR5,POU5F1,SMAD2,TGFBR1,TGFBR3,WNT3	
ABCB11	transporter	8,91E-04	CYP7A1,NR0B2,SLC10A2	892 (23)

ACAT1	enzyme	8,91E-04	ABCA1,HMGCR,ITGB1	475 (7)
AHCY	enzyme	8,91E-04	GPX1,ICAM1,VCAM1	
ARHGEF2	other	8,91E-04	CCND1,IL6,TNF	819 (19)
ATP1A2	transporter	8,91E-04	ATP1A1,ATP1A2,FOS	268 (4)
atypical protein	group	8,91E-04	CTNNB1,IL10,SREBF1	728 (16)
BAG4	other	8,91E-04	APOB,IL1B,IL6	549 (10)
C1QTNF1	other	8,91E-04	IL1B,IL6,TNF	824 (18)
CACNA1S	ion channel	8,91E-04	IL10,IL4,IL5	555 (7)
CEACAM3	other	8,91E-04	IFNG,IL2,TNF	
CEACAM6	other	8,91E-04	IL17A,IL1B,IL6	567 (7)
CEACAM7	other	8,91E-04	IL17A,IL1B,IL6	
CEACAM21	other	8,91E-04	IL17A,IL1B,IL6	
CHIA	enzyme	8,91E-04	CCL17,CCL2,CXCL8	
CLCN3	ion channel	8,91E-04	NFKB1,TGFB1,VCAM1	
CNTFR	transmembrane	8,91E-04	CXCL8,GJA1,IL1A	639 (12)
COL3A1	other	8,91E-04	CCL18,FN1,IL1RN	
COQ7	enzyme	8,91E-04	ARG1,HIF1A,TNF	708 (10)
DAPK1	kinase	8,91E-04	CXCL8,IL1B,TP53	902 (18)
DDX6	enzyme	8,91E-04	LPIN1,mir-143,PPARG	
Dexamethasone	complex	8,91E-04	NR1I2,RXRA,SGK1	
DHCR7	enzyme	8,91E-04	HMGCR,IL6,TNF	1021 (18)
DMBT1	transmembrane	8,91E-04	EFNB2,EPHB4,HAMP	
DSG1	other	8,91E-04	IL5,TNF,TSLP	531 (7)
DUB	group	8,91E-04	ABCA1,LDLR,MYLIP	477 (5)
Eotaxin	group	8,91E-04	ITGAM,MAPK1,MAPK3	490 (6)
EPX	enzyme	8,91E-04	IL10,IL4,IL5	
ERC1	other	8,91E-04	CXCL8,NFKBIA,PTGS2	550 (11)
GBP1	enzyme	8,91E-04	KDR,MMP1,VWF	179 (3)
GJC1	ion channel	8,91E-04	IL1B,TGFB1,TNF	675 (11)
GLUD1	enzyme	8,91E-04	LPL,MAPK3,SLC2A1	476 (7)
GNLY	other	8,91E-04	CCL2,CCL5,TNF	
GPS1	other	8,91E-04	FOS,HAMP,MAPK8	
H60a	other	8,91E-04	HLA-A,IFNG,TNF	858 (12)
HAP1	other	8,91E-04	CACNA1C,LEP,TSC1	542 (7)
HDGF	growth factor	8,91E-04	COL1A1,SERPINE1,TGFB1	
HSPB3	other	8,91E-04	CCL2,CXCL8,ICAM1	
HSPBP1	other	8,91E-04	HSPA1A/HSPA1B,HSPA1L,HSPA2	
IL10R	group	8,91E-04	IL12RB1,IL23R,SOCS3	534 (11)
IL20RA	transmembrane	8,91E-04	CXCL8,ICAM1,IL10	649 (14)
Il3r	complex	8,91E-04	CXCL8,NECTIN2,SELE	507 (7)
INAVA	other	8,91E-04	IL10,IL1B,IL6	
lipoxygenase	group	8,91E-04	CCL2,IL10,RGS2	695 (13)
LOC290071	other	8,91E-04	CCL11,IL13,IL4	
MAGEA3/MAGE	other	8,91E-04	IFNG,IL2,TNF	
mir-368	microRNA	8,91E-04	AR,HES5,SMAD4	
mir-431	microRNA	8,91E-04	CD34,FN1,VCAN	
miR-125b-1-3p	mature microRN	8,91E-04	IL13,IL1B,TNF	
miR-22-5p (and	mature microRN	8,91E-04	IL6,TGFBR2,TNF	
miR-222-5p (mi	mature microRN	8,91E-04	ACTA2,AR,ROCK2	
miR-520g-3p (a	mature microRN	8,91E-04	ABCG2,SMAD6,VEGFA	
miR-543-3p (an	mature microRN	8,91E-04	IL6,TGFBR2,TNF	
myosin-light-ch	group	8,91E-04	CCND1,EGFR,IL13	711 (16)
NFAM1	transmembrane	8,91E-04	IL13,IL2,TNF	167 (7)
NLRC3	other	8,91E-04	IL1B,IL6,TNF	836 (15)
NOP58	enzyme	8,91E-04	CCND1,LTF,PGR	
NR2F6	ligand-depende	8,91E-04	CYP19A1,LHCGR,LPL	
PDK	group	8,91E-04	IL1B,IL6,TNF	956 (18)
potassium chan	group	8,91E-04	FOS,JUN,SCNN1A	322 (7)
PRDX4	enzyme	8,91E-04	ICAM1,MAPK8,NOS2	507 (7)
PRR7	other	8,91E-04	CD69,IL2,JUN	534 (14)
Raet1b	other	8,91E-04	HLA-A,IFNG,TNF	858 (12)
SCT	other	8,91E-04	AQP1,CD36,VIP	
SIPA1	other	8,91E-04	IL2,ITGB1,MMP9	860 (19)
SLC48A1	transporter	8,91E-04	IGF1R,ITGB1,SLC2A1	
SLN	other	8,91E-04	PPARG,PPARGC1A,UCP1	720 (13)
SPATA2	other	8,91E-04	IL1B,IL6,TNF	543 (10)
SPON2	other	8,91E-04	IL6,NFKB1,TNF	542 (7)
SRFBP1	other	8,91E-04	ACTC1,MYL2,NPPA	
STARD7	other	8,91E-04	IL13,IL4,IL5	487 (7)
STIP1	other	8,91E-04	GRK2,STAT3,TP53	
STK16	kinase	8,91E-04	NPPC,SERPINE1,VEGFA	
TMBIM1	other	8,91E-04	FAS,MMP2,MMP9	454 (7)
UBE2D2	enzyme	8,91E-04	ESR1,SMAD2,SMAD4	498 (9)
UBE2D3	enzyme	8,91E-04	CCND1,SMAD2,SMAD4	498 (9)
Zfp35	other	8,91E-04	IL13,IL4,IL5	
FBXO32	enzyme	9,16E-04	CSF2,FGF9,GCLC,HSPB7,IL1B,IL1R1,IL2,IL6,KLF5,LBP,MMP3,PPP3CA,PTGER3,PTGES,PTGIS,PTGS2,SOD2,TFPI2	
ATR	kinase	9,29E-04	ATM,ATR,BAX,FAS,HAMP,MET,WRN	961 (22)
BARX2	transcription reg	9,29E-04	ACTA2,ESR1,MMP9,MYL3,NCAM1,TIMP1,TIMP3	322 (7)
ITGA6	transmembrane	9,29E-04	BAX,CTNNB1,ITGA2,LGR5,RELA,TP53,VEGFA	1108 (22)
NMDA Recepto	complex	9,29E-04	ATF3,BDNF,FOS,GRIA1,NCAM1,NOS1,NOS2	810 (21)
PADI2	enzyme	9,29E-04	ADAMTS9,CXCL8,IL6,let-7,PTGS2,RELA,TNFRSF1B	492 (7)
CTR9	other	9,51E-04	CXCL12,CYP1A1,ELOVL2,EPAS1,IL17A,PGR,PTGES,TFF1	634 (8)
FAM3B	cytokine	9,51E-04	CAV1,CCN4,FN1,GJA1,IGFBP3,LCN2,LDHA,PTN	
KDM6B	enzyme	9,51E-04	CCL5,CD40,FN1,IL12B,IL6,ITGA2B,NOS3,OASL	918 (18)
LTB	cytokine	9,51E-04	CRP,CXCL13,IFNG,IL1B,IL4,IL5,IL6,SELL	653 (19)
MBD1	transcription reg	9,51E-04	ABCB1,APOE,BRCA1,CDKN2A,DPP4,ESR1,SLCO3A1,SNRPN	
mir-9	microRNA	9,51E-04	AR,CAMTA1,CDKN2A,CTNNB1,CXCR4,JAK2,NFKB1,RUNX1	
KLF1	transcription reg	1,07E-03	ADD2,ALAD,AQP1,BCL11A,HBB,ICAM4,IL12B,ITGA2B,PECAM1,SLC2A1,SPTB,TFRC	496 (7)
NRG2	growth factor	1,08E-03	ATF1,BIN1,CCN2,CYP11B1,EDN1,EGFR,ERBB2,HES1,HMOX1,IGF2,NR4A3,PAFAH1B1,PLG,TGFBR1,VEGFA	967 (18)
GSTP1	enzyme	1,09E-03	CBS/CBSL,CXCL13,CXCR2,CYP2A6 (includes others),CYP2E1,DIO3,ESR1,ETNPPL,FKBP5,GPR83,GSTP1,HMOX1,IL1B,IL22RA2,ITGA2,JUN,MMP7,MTRR,NQO1,NTRK1,PER1,PON1,PTPRG,SERPINB7,SERPINE1,SFRP2,SLC6A7,TNF,UGT1A6,UTS2	1112 (24)
antigen	group	1,10E-03	IL13,IL22,IL4,IL5	540 (13)
ATP6V0A2	transporter	1,10E-03	ARG1,IL10,MMP9,TGFB1	
BARD1	transcription reg	1,10E-03	BRCA1,CYP1A1,CYP3A4,TP53	723 (7)
BCL2A1	other	1,10E-03	BCL2A1,CD69,CXCL8,Ly6a (includes others)	588 (7)
BLVRA	enzyme	1,10E-03	HMOX1,JUN,PPARA,TNFSF10	968 (18)
CASP4	peptidase	1,10E-03	IFNG,IL18,IL1A,IL1B	761 (17)
CCAR1	transcription reg	1,10E-03	CEBPD,EPAS1,PPARG,RGS2	
CD33	other	1,10E-03	CSF2,IFNG,IL2,TNF	733 (21)

Dgk	group	1,10E-03	CCL2,CXCL8,CYP17A1,NOS2	772 (15)
DRD4	G-protein coupl	1,10E-03	DRD2,DRD4,GNAS,HAMP	429 (8)
EFEMP2	other	1,10E-03	CCN2,ELN,FBLN2,MMP9	445 (7)
EIF5A	translation regu	1,10E-03	BAX,CDK5R1,NOS2,TP53	
ELP1	other	1,10E-03	BMP4,CTNNB1,FLT1,VEGFA	975 (20)
ETV3	transcription reg	1,10E-03	MMP1,MYB,PRIM2,SPP1	
F2RL3	G-protein coupl	1,10E-03	CALCA,FOS,SELP,TNF	732 (14)
Gm35986	other	1,10E-03	FDFT1,HMGCR,MVK,SREBF2	
GPIIB-IIIA	complex	1,10E-03	CD40,MMP14,MMP9,PLAUR	898 (21)
GRM5	G-protein coupl	1,10E-03	FOS,NOS2,SOD2,TNF	1004 (22)
GUCY2C	kinase	1,10E-03	GUCA2B,IFNG,LEP,TNF	
Hrg	other	1,10E-03	ARG1,CCL2,IL10,MMP9	
HSPB2	other	1,10E-03	CCL2,CXCL8,ICAM1,TGFB1	12 (2)
HTR2C	G-protein coupl	1,10E-03	BDNF,LEP,PPARA,PPARG	745 (16)
HTRA1	peptidase	1,10E-03	EGFR,HTRA1,MMP1,MMP3	640 (11)
IKZF4	transcription reg	1,10E-03	IL17A,IL2,IL2RA,POMC	
INPPL1	phosphatase	1,10E-03	GCK,IL13,IL4,SLC2A4	671 (11)
ITGA11	other	1,10E-03	ACTA2,GHRH,IGF1,MMP14	589 (7)
KCNK2	ion channel	1,10E-03	CCL2,ICAM1,PECAM1,VCAM1	613 (11)
LRIG1	other	1,10E-03	EGFR,ERBB2,ERBB3,TNF	563 (7)
MAGED1	transcription reg	1,10E-03	CDKN2A,JUN,NTRK1,TNF	918 (17)
MN1	other	1,10E-03	CYP24A1,TNFRSF11B,TNFSF11,TP53	
MYH6	enzyme	1,10E-03	IFNG,IL17A,IL2,MYH7	
NET1	other	1,10E-03	FN1,ITGB1,MMP14,SERPINE1	614 (10)
Nisch	other	1,10E-03	FAS,FOS,MLXIPL,SREBF1	568 (7)
Npy4r	G-protein coupl	1,10E-03	GHRH,GNRH1,IGF1,LEP	743 (12)
OBP2B	transporter	1,10E-03	CPT1A,MLXIPL,PPARG,SREBF1	
OPRK1	G-protein coupl	1,10E-03	FOS,HAMP,KDR,SLC6A4	
OTUD7B	peptidase	1,10E-03	ACTA2,CXCL8,ICAM1,RARA	725 (15)
muromonab-CD	biologic drug	1,78E-09	CD69,FOXP3,ICOS,IFNG,IL13,IL17A,IL2,IL2RA,IL5,TFRC,TNF	646 (19)
OXSR1	kinase	1,10E-03	SLC12A1,SLC12A2,SLC12A3,STK39	48 (3)
PRKAB1	kinase	1,10E-03	HIF1A,IL6,LEP,NOS2	988 (23)
PROK2	other	1,10E-03	FOS,HIF1A,IL1B,VEGFA	676 (11)
PSMD4	other	1,10E-03	CD14,CD36,CD69,TERT	792 (16)
Pzp	other	1,10E-03	APOE,LDLR,LPL,LRP1	
RAB7B	peptidase	1,10E-03	IGF2R,IL6,TLR4,TNF	925 (23)
SERPIND1	other	1,10E-03	F2R,IL1B,IL6,KLF5	503 (9)
SF1	transcription reg	1,10E-03	ACTA2,COL1A1,FN1,ICAM1	
SLC12A2	transporter	1,10E-03	SCNN1A,SCNN1B,SCNN1G,SLC4A2	
SLC16A1	transporter	1,10E-03	CYBB,IFNG,IL2,IL6	882 (15)
SOX18	transcription reg	1,10E-03	IL6ST,PROX1,RXRA,VCAM1	
STX2	transporter	1,10E-03	BMP2,BMP4,CCND1,MMP2	801 (18)
SULT1E1	enzyme	1,10E-03	CYP17A1,PTGS2,SCARB1,SULF2	
TAB2	other	1,10E-03	MMP9,NOS2,PTGS2,TFF1	1061 (24)
TAF10	transcription reg	1,10E-03	DIO1,GHR,HLA-DRA,IGF1	815 (9)
TLR10	transmembrane	1,10E-03	CXCL8,IL1B,IL6,TNF	701 (19)
TLR2/TLR4	group	1,10E-03	IL12B,IL23A,IL6,TNF	814 (18)
TNFRSF14	transmembrane	1,10E-03	F2RL1,MMP1,MMP9,TNF	762 (17)
TRIM33	transcription reg	1,10E-03	GATA2,RUNX1,SERPINE1,TGFBR2	
TRPM7	kinase	1,10E-03	NOS3,TRPM6,TRPM7,VCAM1	402 (5)
USP11	peptidase	1,10E-03	BAX,CDKN2A,CHUK,TP53	776 (16)
XPA	other	1,10E-03	FOS,PTGS1,PTGS2,TNF	
ZMIZ1	other	1,10E-03	HES1,IL2RA,NOTCH1,SERPINE1	
CCND1	transcription reg	1,13E-03	AQP3,AR,AURKA,BRCA1,CCND1,CDCA7,CDK6,CDKN2A,CDKN2B,COL1A1,EGFR,ERBB2,FGFR1,GATA4,HSPA1A/HSPA1B,HSPA8,ID3,ITGAV,ITGB3,ITGB6,KLHDC1,KLK2,MACF1,MC4R,MMP2,MMP3,MYLK,NCOA3,NOTCH1,PAH,PGR,PPARG,PRIM2,PSRC1,PTPRC,RGS2,ROR2,SELENBP1,SLC4A4,SPP1,TGFB3,TGFBR2,TNF,TP53,TRPM8,TSC1,TYMS,UAP1,UHRF1,WWOX	1067 (23)
ASXL2	other	1,17E-03	ATP1A2,HSD11B1,LIPE,LPL,PLIN1,PPARG,SERPINE1,SLC2A4,VEGFA	642 (11)
miR-26a-5p (an	mature microRN	1,17E-03	CDK6,CDKN2A,FGF9,HGF,PGR,PTEN,PTGS2,SMAD1,TGFBR2	453 (7)
NF2	other	1,17E-03	CCND1,CTNNB1,HMOX1,let-7,mir-196,MMP2,MMP9,PLAUR,SEMA3F	849 (17)
TCF12	transcription reg	1,17E-03	CDKN2A,CDKN2B,CELA1,FLT3,FN1,FOXO1,GJA1,IL10RA,IL7R,NOTCH1,NR4A3,PAX5,POMC,TNFAIP1	548 (10)
Actin	group	1,20E-03	ABCC1,GRIA1,HBG1,IL18,IL1B,KCNB1	427 (7)
BTLA	other	1,20E-03	IL12A,IL12B,IL17A,IL2,IL5,TNF	762 (16)
CD1D	other	1,20E-03	CD40,IFNG,IL10,IL12A,IL2,IL4	822 (19)
growth factor	group	1,20E-03	CLU,FGFR1,FOS,IL7R,PTGS2,SELL	926 (20)
natriuretic pept	biologic drug	8,91E-04	ADIPOQ,PPARD,PPARGC1A	511 (7)
GTF2I	transcription reg	1,20E-03	CAT,CCND1,FOS,KDR,SIRT1,THBS1	895 (13)
Hnf3	group	1,20E-03	CYP2C9,HNF1A,IGFBP1,PCK1,SLC2A2,TTR	
HNF4Î± dimer	complex	1,20E-03	CYP7A1,FABP1,FABP2,HNF1A,PON1,SLC2A2	
LAMC1	other	1,20E-03	ACTA2,ETV5,FN1,IGF2,TGFB2,WNT5A	881 (15)
MGAT3	enzyme	1,20E-03	APOB,HES1,ITGA2,MTTP,NOTCH1,NOTCH3	456 (7)
MVP	other	1,20E-03	CXCL8,ICAM1,IL1B,IL6,JUN,TNF	1009 (20)
NKX2-2	transcription reg	1,20E-03	GCK,GHRL,INS,PDX1,SLC2A2,SST	488 (8)
ORAI1	ion channel	1,20E-03	C5,IFNG,IL17A,IL2,IL6,NFATC1	764 (19)
CYP1A1	enzyme	1,22E-03	CCND1,CYP17A1,CYP1A1,GSTA1,GSTM2,GSTM3,IFNLR1,IGF1,LMNA,NQO1,SDHB,SHANK2,SMARCA4,SMTN,ST3GAL4,TNNT2,TRPM8,TSC22D1,UGT1A6,VAMP8	938 (19)
SMYD1	transcription reg	1,25E-03	MIF,MT-CO1,MT-ND1,NAMPT,NDUFAB1,NT5C2,OGDHL,PPARA,PPARGC1A,PYGB,RXRA,SDHD,TKT	
PRKN	enzyme	1,29E-03	ACTA2,CCND1,CDK6,CTNNB1,EGFR,GLO1,KDR,MAOA,NOS1,PSEN1	815 (20)
GNL3	other	1,31E-03	CDKN2A,CDKN2B,EDNRA,FGF5,GATA4,NKX2-5,POU5F1,TP53	791 (10)
SIX5	transcription reg	1,31E-03	ATP1A1,COL9A2,IGF2,PLTP,PTN,SFRP2,SIM1,SLC6A13	
WNT7A	cytokine	1,31E-03	ESR1,FGF1,LMX1B,MMP1,MMP9,MYOD1,PLAUR,WNT5A	718 (12)
XBP1	transcription reg	1,31E-03	AFP,APOA1,ATP2A2,BLZF1,CAT,CCL5,CXCL8,CYP1A2,CYP2E1,ESR1,FAS,FKBP1B,FN1,GCC1,GOSR2,HLA-DRA,HMOX1,ICAM1,IFNG,IL24,IL6,INS,LMAN1,NOS2,NR1H3,NUCB2,PDX1,RELA,SERPINA1,SOD1,SREBF1,TNF,TNFSF11,TTR,TXN,VCAM1,WFS1	752 (18)
RCE1	peptidase	1,33E-03	ACTN4,CXCL12,FBN1,FLT3,GJA1,HBEGF,LMNA,MGP,PAPPA,TGFB2,THBS2	
C2CD5	other	1,35E-03	CIDEA,CPT1A,DIO2,HAMP,PPARGC1A,PRDM16,UCP1	
CBX7	other	1,35E-03	BMP2,CDKN2A,CXCL8,CYP1B1,GDF15,KYNU,PAPPA	657 (7)
CCK	other	1,35E-03	CARTPT,CNR1,FOS,MET,NPY,NPY2R,VEGFA	988 (23)
FLNA	other	1,35E-03	GP1BA,GP1BB,IL2,ITGB1,MMP9,OPN4,SCNN1A	746 (20)
mir-143	microRNA	1,35E-03	COL3A1,KRAS,mir-143,MMP2,PDGFRA,PTGS2,SLC2A1	569 (7)
SCP2	transporter	1,35E-03	ACAA1,CYP7A1,FABP1,HMGCR,LDLR,PCK1,SCARB1	715 (17)
SIRT2	transcription reg	1,35E-03	CDKN2A,DHCR7,FDFT1,HMGCR,LSS,MVK,NEDD4	161 (5)
TBXT	transcription reg	1,35E-03	COL1A1,FMOD,KDR,MGP,MITF,SHH,SOX6	
TET3	enzyme	1,35E-03	ADAMTS9,APLN,EPAS1,GSS,LRP2,POR,SLC12A5	
BCL6B	transcription reg	1,37E-03	ATM,S100A4,TNFRSF1A,TP53,VEGFA	
CCL1	cytokine	1,37E-03	IL6,ITGA2,ITGB2,MMP2,SERPINE1	682 (12)
EEF1A2	translation regu	1,37E-03	CYBA,CYBB,IL10,ITGB2,NOX1	
EXT1	enzyme	1,37E-03	CCND1,CTNNB1,EVX1,NDST1,SHH	678 (10)
FRMD6	other	1,37E-03	BMP2,CCN2,FGF1,IGFBP3,PRL	
ITGB5	other	1,37E-03	COL1A2,IL10,KDR,MMP2,MMP9	906 (19)

KCNN4	ion channel	1,37E-03	CCL11,CCL5,FOS,MMP9,NFATC1	496 (7)
KDM5A	transcription reg	1,37E-03	ACTC1,ACTN2,ATP1A1,ATP1B1,CACNA1S,CCND1,COL1A2,HMOX1,ITGB1,MFN2,MYH7,OPA1,RYR1,RYR3,SDHB,SDHC,SDHD,SOD2,TCAP,TERT,TNNC1,TNNT2,TOMM7,TXN2	
KLB	enzyme	1,37E-03	CYP7A1,FOS,HMGCR,NR0B2,SREBF2	400 (6)
LAIR1	transmembrane	1,37E-03	IFNG,IL17A,IL2,IL6,TNF	876 (20)
LCOR	transcription reg	1,37E-03	ADORA1,ESR1,FKBP5,IGFBP1,TFPI2	
MEOX1	transcription reg	1,37E-03	BMP4,CDKN2A,GATA4,MEF2C,NKX2-5	
METRNL	other	1,37E-03	DIO2,IL10,IL4,PPARGC1A,UCP1	
mir-185	microRNA	1,37E-03	AR,FDFT1,HMGCR,LDLR,SREBF2	
miR-125b-2-3p	mature microRN	1,37E-03	API5,BAX,KLK1,MMP9,TP53	
NCR1	transmembrane	1,37E-03	CCL5,CD69,CSF2,IFNG,TNF	698 (19)
PDE4B	enzyme	1,37E-03	CCL5,IFNG,IL2,ITGB2,TNF	909 (18)
neuropeptide Y	biologic drug	9,27E-03	NOS2,UCP2	
PPM1D	phosphatase	1,37E-03	CCND1,CDKN2A,PGR,RELA,TP53	1043 (19)
PRKRA	other	1,37E-03	DCAF6,DICER1,MAF,RET,THBS1	641 (7)
NF-kappaB deco	biologic drug	7,68E-03	IL6,NOS2,PTGS2	825 (18)
PTGER3	G-protein coupl	1,37E-03	AR,HAMP,IL10,IL6,LEP	657 (16)
SELE	transmembrane	1,37E-03	CSF2,FOS,IL1B,IL6,TNF	899 (20)
SETD7	enzyme	1,37E-03	CCND1,GCK,NOS2,SLC2A2,TNF	1019 (22)
SLC6A1	transporter	1,37E-03	IFNG,IL17A,IL23A,IL6,TNF	806 (18)
TEC	kinase	1,37E-03	FOS,HAMP,IL2,IL4,SELP	627 (24)
TRAF1	other	1,37E-03	IL4,IL6,NFKB2,TNF,TRAF1	781 (17)
USP8	peptidase	1,37E-03	EGFR,ERBB3,GRIA1,MET,POMC	660 (12)
CLDN7	other	1,43E-03	ABLIM1,AGT,APOE,C3,CCN2,CXCL8,CYP11B2,F5,FADS3,HLA-B,LTA4H,MMP2,MMP9,NNMT,NRG1,PANX2,PRSS8,SCGB1A1,SERPINB1,SERPINB7,SLCO2A1,TIMP2,TMCO1	533 (7)
GNAS	enzyme	1,50E-03	CDC42,CYP19A1,CYP27B1,FOS,LEP,LHCGR,PCSK1,PPARG,PPARGC1A,PRL,SCG3,SPP1,TNFSF11	948 (19)
CDK5	kinase	1,53E-03	BDNF,CD14,IGFBP3,JUN,KCNMA1,LPL,RALB,TH,TNFAIP3	860 (19)
FAAH	enzyme	1,53E-03	ERBB2,FAAH,FOS,HMOX1,MAEL,PECAM1,POU5F1,PTK2B,TRH	885 (15)
TCF7L1	transcription reg	1,53E-03	ATF3,FGF5,GPA33,JUN,KIT,NKX2-5,PPARG,SOX17,TBX3	903 (15)
MED13	transcription reg	1,59E-03	ACSM3,CD36,CIDEA,CYP2A6 (includes others),ELN,GYS1,HMGCR,KNG1,PCSK9,PPARG,SLC2A4,TKT	575 (7)
PPRC1	transcription reg	1,59E-03	ALOX5AP,BMP6,CXCL8,FBXL13,GDF15,IL13RA2,IL1A,LCN2,NAMPT,NFKBIZ,PTGS2,VIP	
Smad2/3	group	1,65E-03	ABCG2,APOA1,CDKN2A,CDKN2B,FOXP3,FUT7,mir-329,POU5F1,RUNX1,SELPLG,SERPINE1,SOX17,TIMP3,TNC	
KCNE3	ion channel	1,75E-03	ACE2,AKR1C3,BCAT1,CCL17,CHL1,CXCL13,HMGCS2,HSD17B7,HSPA1A/HSPA1B,IL23R,OSGIN1,PER1,PTGS2,SLC2A5,STAT4	
CHD7	enzyme	1,76E-03	BAX,CDKN2A,EGFR,HES5,JAG1,NOTCH3,RBPJ,TP53	
NFIC	transcription reg	1,76E-03	CCND1,CDKN2A,CYP17A1,HMGB1,HTRA1,LHCGR,PDGFRA,TP53	
PLAG1	transcription reg	1,80E-03	ACVR2B,AQP1,EFNB1,IGF2,KCNJ4,LSP1,MLXIP,MYRF,NFATC1,PPIC,TNNT3,TRAF1,VEGFA	
AURKA	kinase	1,84E-03	CTNNB1,MMP2,PTEN,TERT,TP53,TP73	1051 (21)
CLCN5	ion channel	1,84E-03	IL12B,IL17A,IL6,LRP2,SOD1,TXN	
FOXG1	transcription reg	1,84E-03	CDKN2B,GCK,NCOA3,PAX2,PCK1,SERPINE1	446 (7)
miR-128-3p (an	mature microRN	1,84E-03	ADORA2B,LDLR,NTRK3,SNAP25,TGFBR1,TXNIP	
NRP1	transmembrane	1,84E-03	ACTA2,CD40,HLA-DQB1,IL1B,IL6,TNF	855 (23)
PCK1	kinase	1,84E-03	IL1B,IL6,IRS2,PCK1,SLC2A4,TNF	955 (25)
PLAGL1	transcription reg	1,84E-03	ANGPTL4,FABP1,LDHA,PPARG,PTEN,SLC2A4	531 (7)
PTGFR	G-protein coupl	1,84E-03	FOS,GDNF,NOX1,NPPA,PTGS1,PTGS2	988 (23)
RXFP2	G-protein coupl	1,84E-03	AR,CTNNB1,LRP1,LRP5,NOTCH1,SOX17	
SLC2A1	transporter	1,84E-03	FN1,HMOX1,MMP2,NQO1,PPARA,SERPINE1	968 (21)
SP7	transcription reg	1,84E-03	ALPL,BGLAP,COL1A1,IL6,SPP1,TNFSF11	
SPINT1	other	1,84E-03	APCDD1,CTNNB1,PROX1,ROR2,SOX17,WNT5A	
SPTLC2	enzyme	1,84E-03	CCN2,COL1A1,MMP2,NPPA,THBS1,TIMP1	763 (11)
TAP1	transporter	1,84E-03	CXCL8,HLA-A,IL1B,IL6,PSMB9,TNF	861 (18)
ZNF148	transcription reg	1,84E-03	CDKN2A,CXCL5,FDX1,FN1,ITGAM,RNLS	
CAST	peptidase	1,90E-03	IL17A,MEF2A,MEF2D,MMP9,NPPA,SLC2A4,TP53	978 (19)
SIM2	transcription reg	1,90E-03	EPO,IKBKB,MMP2,MMP3,MYOD1,SHH,TIMP2	481 (7)
VIM	other	1,90E-03	AXL,BGLAP,CCL2,IL17A,IL4,ITGB1,TGFB1	839 (23)
DIO3	enzyme	1,98E-03	ABCC8,GCK,INS,ITIH3,KCNJ11,PDX1,SHH,SLC2A2,TRH	438 (7)
THBS4	other	1,98E-03	CD40,CHUK,COL3A1,ICAM1,PECAM1,SELE,TGFB2,TNC,VCAM1	
Ubiquitin	group	1,98E-03	BMP2,HSPA4,HSPD1,IL4,MMP2,NOS1,RARA,TIMP2,TNFSF10	811 (18)
ACKR2	G-protein coupl	2,02E-03	CCL11,CCL5,CCR2,IFNG,IL17A,IL1A,IL1B,IL22,OAS3,OASL,TNF	701 (18)
CDK2AP1	other	2,02E-03	CCN4,CTNNB1,EP300,LRP5,MAPK8,PITX2,PPARD,PRICKLE1,SFRP2,TIE1,WNT5A	863 (13)
NORAD	other	2,05E-03	CCN2,COL4A1,ID3,IGFBP3,JUN,NCOR2,SGK1,SMAD6,SMTN,THBS1	468 (7)
ATN1	transcription reg	2,10E-03	ATP1A1,ATP1B1,BDNF,CA4,CHGB,CHUK,CNR1,DBP,EBF1,FGF1,GAS7,GRK2,GRK5,GSN,HBEGF,HPCAL1,KCNK3,LTBP2,MAX,NR2F1,PRKCG,PTPN22,SPP1,THRA	
CYP1B1	enzyme	2,14E-03	CCND1,CYP17A1,CYP1B1,GSTM2,GSTM3,HMOX1,IFNLR1,NQO1,SHANK2,ST3GAL4,TNFSF10,TRPM8,UGT1A6	1122 (17)
IFNA1/IFNA13	cytokine	2,14E-03	AR,CCL8,CD40,CD69,CYP1A1,CYP1A2,CYP2E1,IFIH1,IFNG,IL1B,PTGS2,SOCS1,STAT4	777 (20)
ABCA4	transporter	2,31E-03	AGER,C3,CFB,GLO1,IFNG	
ACVR2A	kinase	2,31E-03	BGLAP,HAMP,ICAM1,SELE,VCAM1	519 (11)
AFP	transporter	2,31E-03	FOS,GNRH1,GNRHR,MMP9,TSC22D1	734 (11)
APOA2	transporter	2,31E-03	ABCA1,APOA1,APOB,CXCL8,SCARB1	697 (17)
C9orf72	other	2,31E-03	CXCL8,EDN1,EDN2,EDNRA,EDNRB	
CHRM3	G-protein coupl	2,31E-03	FOS,HMOX1,ITGA2,LEP,MMP9	946 (18)
DHTKD1	enzyme	2,31E-03	ABCC8,GLP1R,IGF1,INS,KCNJ11	
ENTPD1	enzyme	2,31E-03	CXCL8,IFNG,IL12B,SERPINE1,TNF	724 (16)
HLF	transcription reg	2,31E-03	AQP4,F9,HIF1A,PPARA,SCNN1A	
LNX2	other	2,31E-03	HES1,HES5,JAG1,NOTCH1,TCF7L2	
MCL1	transporter	2,31E-03	BAX,CCND1,KDR,NOS3,NQO1	832 (18)
miR-208a-3p (a	mature microRN	2,31E-03	CD14,MYH7,PTGIR,SPP1,TBXA2R	
Ncoa6	transcription reg	2,31E-03	CYP7A1,FOS,LPL,SERPINE1,SREBF1	732 (15)
RASGRP1	other	2,31E-03	CD69,CSF2,IFNG,IL2,TNF	919 (23)
S100A7	other	2,31E-03	CSF2,CXCL8,IL1A,MMP9,VEGFA	884 (18)
TNNI3	transporter	2,31E-03	CCL11,CCL5,CCR2,CCR5,MYH7	
Traj18	other	2,31E-03	CCL5,CD40,IFNG,IL6,TNF	895 (16)
WWP2	enzyme	2,31E-03	CCL5,IL2,IL6,PTEN,TNF	812 (13)
ZFP57	transcription reg	2,31E-03	DLK1,H19,IGF2,IGF2R,SNRPN	
PROX1	transcription reg	2,33E-03	CD34,CYP7A1,FGFR3,FLT4,ITGA9,KDR,RGS4,TNNT3	
ABL2	kinase	2,36E-03	CTSL,MMP1,MMP14,MMP3	
ANKRD42	transcription reg	2,36E-03	CSF2,IL1B,IL6,TNF	492 (7)
APOBEC1	enzyme	2,36E-03	APOB,IFNG,IL12B,PTGS2	706 (11)
BANCR	other	2,36E-03	CCND1,MMP1,MMP2,TSHR	849 (14)
BGLAP	other	2,36E-03	ADIPOQ,DIO2,PRDM16,UCP1	
cAMP-Gef	group	2,36E-03	CCL2,CXCL5,CYP1B1,NOS2	468 (7)
Cd209b	other	2,36E-03	IL18,IL1B,IL6,TNF	799 (11)
CHGA	other	2,36E-03	GCG,IL1B,SERPINE2,TH	531 (7)
DLC1	other	2,36E-03	CDK6,CDKN2A,CDKN2B,SERPINE1	532 (7)
Glucocorticoid-(	complex	2,36E-03	BGLAP,POMC,PRL,VIPR1	757 (11)
GNMT	enzyme	2,36E-03	ABCA1,CYP1A1,NPC1,SCARB1	555 (7)
GPRC6A	G-protein coupl	2,36E-03	CIDEA,DIO2,PRDM16,UCP1	
HESX1	transcription reg	2,36E-03	GATA2,IL17A,MYB,RUNX1	
HIST4H4	other	2,36E-03	GSTP1,PGR,RUNX1,TFF1	
HIVEP3	transcription reg	2,36E-03	IL2,S100A4,TNF,TNFSF11	699 (18)

Inhibin	complex	2,36E-03	CYP17A1,GHRH,GNRHR,IFNG	
KLRB1	transmembrane	2,36E-03	CCL5,CSF2,IFNG,TNF	739 (16)
LGI1	other	2,36E-03	GRIA1,MMP1,MMP12,MMP3	499 (7)
LPAR2	G-protein coupl	2,36E-03	CXCL8,FN1,IL6,PTGS2	898 (19)
MARCO	transmembrane	2,36E-03	IL1B,IL6,NFKB1,TNF	784 (18)
MFAP2	other	2,36E-03	ITGA4,ITGB3,TNFSF11,VCAN	
MGLL	enzyme	2,36E-03	HAMP,IL1A,IL6,TNF	974 (22)
MIB1	enzyme	2,36E-03	BLM,HES1,HES5,NOTCH1	129 (6)
mir-320	microRNA	2,36E-03	AQP1,AQP4,IGF1,TFRC	
miR-139-5p (mi	mature microRN	2,36E-03	FOXO1,IGF1R,KIT,RUNX1	
MLLT3	transcription reg	2,36E-03	EDN1,SCNN1A,SCNN1G,SGK1	
NDST1	enzyme	2,36E-03	BMP2,FGF9,KDR,TGFB1	826 (11)
PPM1A	phosphatase	2,36E-03	ITGAV,ITGB1,MMP2,TP53	653 (10)
PPM1B	phosphatase	2,36E-03	CEBPD,HBEGF,PLAGL1,TP53	
PRLH	cytokine	2,36E-03	CXCL8,IL6,LEP,PRL	1048 (25)
PTK	group	2,36E-03	IL6,NR3C1,TGFB1,TNF	746 (19)
QRFP	other	2,36E-03	CD36,LPL,NPY,PPARG	493 (7)
RIOX1	enzyme	2,36E-03	AKT1,BGLAP,IGF1,IGF1R	628 (7)
SFRP5	transmembrane	2,36E-03	CCL2,CXCR4,IL1B,TNF	642 (10)
SNTA1	other	2,36E-03	AQP4,IGF1,KIDINS220,NOS1	
SNW1	transcription reg	2,36E-03	BGLAP,CCND1,MMP9,SERPINE1	493 (7)
TH2 Cytokine	group	2,36E-03	ARG1,CCR5,SOCS3,TLR9	
TRIM8	other	2,36E-03	CCL5,IL6,SOCS1,TNF	626 (15)
TSPO	transmembrane	2,36E-03	ICAM1,SOD2,TNF,VCAM1	731 (15)
ULBP2	transmembrane	2,36E-03	CSF2,IFNG,LTA,TNF	721 (17)
VGF	growth factor	2,36E-03	AGRP,CHGB,FOS,NPY	668 (12)
WNK1	kinase	2,36E-03	KCNJ1,SERPINE1,SLC12A3,SMAD2	716 (13)
ZNF521	transcription reg	2,36E-03	NFATC1,PPARG,TNFRSF11A,TNFSF11	425 (6)
LONP1	peptidase	2,41E-03	ACADS,ACAT1,COX8A,HSPD1,MRPS22,MT-ATP6,MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-ND2,MT-ND4,MT-ND6,PTGS2,SOD1,SOD2	
Rb	group	2,41E-03	CCL2,CCND1,CDKN2A,CYP1A1,DHFR,EPO,FGFR2,H19,MMP3,PPARGC1A,SOD2,TERT,TP53,TP73,TYMS,UCP1	1070 (23)
SPIB	transcription reg	2,41E-03	APOE,ATF3,BMP6,CCR2,CCR5,CD200,HSPA1A/HSPA1B,IL2RA,KDR,KIT,LGR5,MARCH1,MEF2C,NFKB1,P2RY12,SLC22A12,TNFRSF11B	
miR-483-3p (mi	mature microRN	2,47E-03	ADIPOR2,BRCA1,CTNNB1,DCAF6,GJA1,IGF2,KLHL12,MAPKAPK2,SLC7A1,SMAD4,SOCS3	
SKIL	transcription reg	2,47E-03	ACTA2,AFP,COL1A2,COL4A1,CXCL12,RHOBTB1,SERPINE1,SOX17,THBS2,TMCO1,WDR37	847 (13)
Wnt	group	2,47E-03	CD34,CDH15,CTNNB1,EGFR,GATA4,KDR,MMP9,PITX2,PPARG,PPARGC1A,TNFSF11	612 (16)
UXT	transcription reg	2,52E-03	ATR,CTLA4,CXCL8,F5,FKBP5,IL2RA,NCOR1,NFKBIA,TNFAIP3	389 (7)
ZAP70	kinase	2,53E-03	ANG,CD69,CYBA,EDIL3,FKBP5,IFNG,IL2,IL4,KCNA5,KCNK3,QPCT,SLC23A2,SNRNP70	550 (20)
KDM2B	enzyme	2,55E-03	BDNF,CCL5,CDKN2A,CDKN2B,FOS,let-7,PDGFRA,SFRP2,SOX17,TP53	1103 (27)
KDM5B	transcription reg	2,57E-03	ARL6IP5,AURKA,BRCA1,CAV1,CCN2,CCND1,ERBB2,ERBB3,ESR1,FGFR2,GATA4,GCA,INSIG1,let-7,MIA3,NKX2-5,PGR,PSIP1,SCNN1A,SMARCA2,STAT5A,TGFB1,TGFB2,TNFSF13	887 (13)
COL2A1	other	2,62E-03	COL1A1,COL3A1,CXCR4,IFNG,IL1B,IL2,TNF	776 (19)
EDN3	other	2,62E-03	CCND1,CDKN2A,CTNNB1,FOS,ITGA2,ITGB1,ITGB3	990 (20)
LGR5	transmembrane	2,62E-03	AHR,AKR1C3,AQP9,CYP1A2,CYP2E1,SLC13A3,SLC22A1	
mir-26	microRNA	2,62E-03	CDKN2A,FGF9,PTEN,PTGS2,SMAD1,SMAD4,STK39	
MSX1	transcription reg	2,62E-03	BGLAP,BMP2,BMP4,EPHA4,GNRHR,MYOD1,SHH	
SIN3B	transcription reg	2,62E-03	CAD,COL1A2,DHFR,HES1,LDHA,TXNIP,TYMS	768 (7)
SPZ1	transcription reg	2,62E-03	CCND1,FN1,HIF1A,MAPK1,MAPK3,VEGFA,WNT5A	
HDAC9	transcription reg	2,71E-03	BAX,JUN,MYH7,NPPA,SLC2A4,SMARCA2	695 (17)
HIF1AN	enzyme	2,71E-03	ADM,EGLN3,EPO,LDHA,SLC2A1,VEGFA	775 (13)
HPX	transporter	2,71E-03	AGTR1,IL23A,IL6,ITGAM,NOS2,TFRC	
IL2RB	transmembrane	2,71E-03	CCL2,FOS,IL10,IL2RA,IL4,JUN	862 (23)
MESP1	transcription reg	2,71E-03	FOXC1,GATA4,MEF2C,NKX2-5,PRICKLE1,RASGRP3	
mir-194	microRNA	2,71E-03	ACTA2,DACH1,PLAUR,RAC1,THBS1,TP53	798 (13)
miR-100-5p (an	mature microRN	2,71E-03	CCND1,FGFR3,IGF1R,IGF2,RPTOR,SOX17	
NKX6-1	transcription reg	2,71E-03	GCG,GFRA1,HNF1A,NR4A3,PDX1,SST	
OMA1	peptidase	2,71E-03	CPT1B,DNM1L,LEP,MFN2,OPA1,PPARGC1A	
PRF1	transporter	2,71E-03	IFNG,IL10,IL18,IL1B,IL6,TNF	775 (17)
Rhox5	transcription reg	2,71E-03	ADIPOQ,INS,JAZF1,PPARG,PPARGC1A,RETN	821 (16)
SLAMF1	transmembrane	2,71E-03	CXCL8,IFNG,IL12RB2,IL4,IL6,TNF	536 (20)
STK3	kinase	2,71E-03	CCN2,CCND1,IL6,SFTPB,SPP1,TNF	928 (18)
UBD	other	2,71E-03	IL10,PPARA,PPARGC1A,PSMB9,UCP2,UCP3	760 (7)
ZFPM2	transcription reg	2,71E-03	ATP2A2,CYP11A1,CYP17A1,KDR,MYH7,NPPA	546 (10)
A2M	transporter	2,98E-03	CCND1,FOXO1,IL1B,IL6,LRP1,NFKB1,SLC2A1,SREBF1,SREBF2,TNF,WNT5A	981 (21)
miR-145-5p (an	mature microRN	2,98E-03	ACTA2,CES1,F11R,IGF1R,IRS1,KLF5,MMP1,POU5F1,PPP3CA,RASA1,SERPINE1,SOD2,SPTB	
RBM5	other	2,98E-03	CD69,CDKN2A,GPER1,ICAM1,INSIG1,ITPA,NCOA3,STAT5B,TRAF1,UBA1,UCP2	
BCAP31	transporter	3,04E-03	ADGRE1,CFTR,GCK,IL1B,INSIG1,SAA1,SREBF1,TNF	722 (15)
BMPR1B	kinase	3,04E-03	CYP19A1,HAMP,ID3,POSTN,PPARG,PTGS2,SERPINE1,SOX6	817 (17)
CTSS	peptidase	3,04E-03	COL4A1,FAS,IFNG,IL1B,ITGB1,MMP9,TNF,TNFSF10	715 (16)
oblimersen	biologic drug	3,54E-02	ADM,ATF3,BRD2,CEBPD,CXCL8,EFNB2,IL24,OASL,PRKCA,ZPR1	
ESRRB	ligand-depende	3,04E-03	ADIPOR1,GCKR,MEF2C,NR0B2,PCSK6,RHO,SLC6A6,TFF1	
IGF2BP1	translation regu	3,04E-03	COL1A1,COL1A2,COL6A3,IGF2,KRAS,PTEN,TNC,WNT3	
octreotide	biologic drug	2,40E-10	ABCC2,BMPR1A,BMPR2,EGFR,FOS,IGF1,IGFBP1,KIT,NOS2,NOS3,PLAGL1,POMC,PPARG,PRL,SMAD6,TP53	1110 (24)
NTF3	growth factor	3,04E-03	ERBB2,FOS,GJA1,JUN,RELA,SST,TH,TRPV1	1048 (24)
PLK4	kinase	3,04E-03	ATM,CD40,EDN1,IL15,IL15RA,IL1B,MMP3,PLAT	497 (7)
PRKDC	kinase	3,04E-03	AHR,APOE,ATM,CCND1,FKBP5,ROCK2,TFF1,VCAM1	768 (18)
TICAM2	other	3,04E-03	CCL5,IFNG,IL12B,IL1B,IL4,IL6,MMP14,TNF	648 (19)
mir-122	microRNA	3,05E-03	BICD1,CYP1A2,CYP2C9,CYP7A1,G6PD,GNPDA2,GYS1,IGF1R,IL6,INSIG1,MAP4,MMP7,MVK,NUTF2,PTPN1,SLC7A1,VAV3,WARS	
BMI1	transcription reg	3,10E-03	ATM,AURKA,CDKN2A,CDKN2B,FAS,JPH3,let-7,LOX,MET,NFKB1,SMAD3,TERT,TP53,VEGFC	1061 (23)
ATP7B	transporter	3,14E-03	CYP7A1,FDFT1,H19,HMGCR,LDLR,LPIN1,LSS,MSMO1,PPARA,SREBF2	
A4GALT	enzyme	3,31E-03	IL6,NOS2,TNF	
omalizumab	biologic drug	2,60E-02	CSF2,TNF	
ACOT11	enzyme	3,31E-03	PPARG,PPARGC1A,UCP1	370 (7)
ADRA2B	G-protein coupl	3,31E-03	CCND1,FLT1,SHH	
AKAP13	other	3,31E-03	FKBP5,FOS,MEF2C	550 (13)
AMACR	enzyme	3,31E-03	IFNG,IL17A,IL4	
ANKRD13C	other	3,31E-03	ADRB2,PTGDR,TBXA2R	
ASCC1	transcription reg	3,31E-03	CXCL8,TNF,TNFSF10	492 (7)
ATP6V0D2	transporter	3,31E-03	IL12B,IL6,TNF	520 (7)
BAG2	other	3,31E-03	IL1B,IL6,TNF	954 (24)
CACTIN	other	3,31E-03	CCL5,CXCL8,TNF	574 (12)
CANX	other	3,31E-03	ABCA1,BAX,NOX4	
CD151	other	3,31E-03	CD69,IL2,MMP9	847 (21)
CD300C	transmembrane	3,31E-03	CXCL8,IL12B,TNF	567 (7)
CEACAM5	other	3,31E-03	IL17A,IL1B,IL6	
CELF2	other	3,31E-03	BAX,SIRT1,TP53	641 (7)
chitinase	group	3,31E-03	CCL2,CCL5,CXCL8	
CMIP	other	3,31E-03	IFNG,IL4,MAF	382 (7)
COL1A2	other	3,31E-03	COL1A2,SERPINE1,TGFB1	444 (7)

CPB2	peptidase	3,31E-03	IFNG,IL10,IL6	730 (15)
P144	biologic drug	9,27E-03	CCL2,IL10	
CTSD	peptidase	3,31E-03	ABCA1,ROCK2,TXN	
CXCL9	cytokine	3,31E-03	IFNG,IL10,MMP9	804 (20)
CYP2C8	enzyme	3,31E-03	IL1B,IL6,SELE	743 (17)
DGCR5	other	3,31E-03	AKT1,CTNNB1,EGFR	
DNM2	enzyme	3,31E-03	CFTR,MMP14,MMP2	503 (9)
EAF2	transcription reg	3,31E-03	HIF1A,THBS1,VHL	
FEZF1	other	3,31E-03	KRAS,MMP1,TIMP1	
FGA	other	3,31E-03	IL1B,IL6,TNF	496 (7)
FLII	other	3,31E-03	CXCL8,TFF1,TNF	386 (7)
G0S2	other	3,31E-03	CDCA7,HSPD1,SLC19A1	
GCLC	enzyme	3,31E-03	FOS,JUN,SLC39A8	
Gzmb	peptidase	3,31E-03	IL13,IL4,IL5	
HECTD3	enzyme	3,31E-03	IL1B,IL6,TNF	
HSPB6	other	3,31E-03	CCL2,CXCL8,ICAM1	957 (19)
Il12 receptor	complex	3,31E-03	IFNG,IL4,TNF	737 (17)
IRF2BP2	transcription reg	3,31E-03	IL2,IL4,TNF	
ITPRID2	other	3,31E-03	ADIPOQ,IGF1,LEP	
LAMA4	enzyme	3,31E-03	HIF1A,UCP1,VEGFA	
LAMP2	enzyme	3,31E-03	HIF1A,IGF2R,M6PR	
LRRC8C	ion channel	3,31E-03	LPL,PPARG,SREBF1	
MBNL1	other	3,31E-03	ABLIM1,NEDD4,PTEN	
Meg3	other	3,31E-03	FLT1,HES1,VEGFA	369 (7)
parathyroid hor	biologic drug	4,36E-03	BMP6,FN1,FOS,TNFSF11	555 (7)
MEP1A	peptidase	3,31E-03	CXCL8,IL1B,IL6	
MIR129	group	3,31E-03	CDK6,MAPK1,MAPK3	
miR-342-3p (mi	mature microRN	3,31E-03	IL6,TGFBR2,TNF	
miR-495-3p (an	mature microRN	3,31E-03	IL6,TGFBR2,TNF	
NCF2	enzyme	3,31E-03	SELE,SOD2,VCAM1	467 (7)
NFX1	transcription reg	3,31E-03	HSD17B7,NFKB1,TERT	
NOX5	ion channel	3,31E-03	CDKN2A,PTGES,PTGS2	751 (11)
pasireotide	biologic drug	1,46E-04	BMPR1A,BMPR2,POMC,PRL,SMAD6	
NPLOC4	other	3,31E-03	CCL2,CCL5,NFKB2	417 (10)
PAPOLA	enzyme	3,31E-03	MT-ATP6,MT-CO1,MT-CO2	
PDCD10	other	3,31E-03	CTNNB1,THBD,VEGFA	597 (7)
PDCD6IP	other	3,31E-03	DRD1,DRD3,ESR1	
PELI2	enzyme	3,31E-03	CXCL8,IL6,TNF	712 (18)
PFKFB4	kinase	3,31E-03	NCOA3,TKT,XDH	779 (13)
PKIA	other	3,31E-03	FN1,IGF1,PCK1	526 (10)
PLAGL2	transcription reg	3,31E-03	IGF2,LDHA,NCF2	
PMEL	enzyme	3,31E-03	CSF2,IFNG,IL2	
PTP4A2	phosphatase	3,31E-03	CTNNB1,PTEN,VCL	
RAB11A	enzyme	3,31E-03	KCNMB1,SCARB1,SLC2A5	
RAPGEF4	other	3,31E-03	NFATC1,SPP1,THBS1	661 (7)
RAR ligand-RAR	complex	3,31E-03	ABCC2,SLC10A1,SLCO1B3	
RBBP5	transcription reg	3,31E-03	CDKN2A,POU5F1,TFF1	628 (7)
RGD1560225	other	3,31E-03	EDN1,ITPR2,PTGS2	
RRM2	enzyme	3,31E-03	HIF1A,MMP9,THBS1	863 (13)
SCIN	other	3,31E-03	GSN,ITGA2B,RAC2	
SCTR	G-protein coupl	3,31E-03	AQP4,CD36,HAMP	
09-sep	enzyme	3,31E-03	CCND1,HIF1A,TYRP1	
Serine Protease	group	3,31E-03	IFNG,IL6,NOS2	965 (18)
SERPINB7	other	3,31E-03	CCL2,ICAM1,TGFB1	
SIGLEC1	other	3,31E-03	IL6,TGFB1,TNF	806 (19)
SIRT4	enzyme	3,31E-03	ADGRE1,IL1B,TNF	371 (7)
SLC12A3	transporter	3,31E-03	IFNG,IL6,TRPM6	
SLC39A4	transporter	3,31E-03	CCND1,IL6,NELL1	791 (13)
SLC7A5	transporter	3,31E-03	IFNG,IL17A,IL4	690 (13)
Slfn1	enzyme	3,31E-03	CCND1,PDGFRA,PDGFRB	
SOS1	other	3,31E-03	CD69,IL2,SELL	728 (14)
SPRED1	other	3,31E-03	IL13,IL5,KRAS	
TAOK2	kinase	3,31E-03	GSTP1,PGR,SOD2	
TEX11	other	3,31E-03	BAX,CCND1,FOS	704 (11)
THAP11	transcription reg	3,31E-03	GATA4,POU5F1,PRKN	
TIAM1	other	3,31E-03	JUN,RAC1,TIMP1	543 (9)
TRHR	G-protein coupl	3,31E-03	LEP,LEPR,SOCS3	673 (11)
TXN2	enzyme	3,31E-03	CYBA,CYBB,RAC1	
tyrosine kinase	group	3,31E-03	CYP1A1,HMOX1,INSR	783 (11)
UFD1	peptidase	3,31E-03	CCL2,CCL5,NFKB2	417 (10)
VLDL	complex	3,31E-03	PON2,SERPINE1,VCAM1	506 (7)
KISS1	other	3,53E-03	FOS,GNRH1,GSTP1,MMP9,MT-ND2,NPY,PPARGC1A	916 (18)
LOX	enzyme	3,53E-03	COL3A1,ELN,IGF1R,LRP5,PDGFRA,PDGFRB,RELA	813 (16)
miR-103-3p (an	mature microRN	3,53E-03	CACNA1C,CACNA2D1,CDK6,ICOS,NFIA,OPRM1,PIK3CG	
miR-7a-5p (and	mature microRN	3,53E-03	EGFR,FOS,IGF1R,IRS1,IRS2,MAPKAP1,SYNE1	
MYBL2	transcription reg	3,59E-03	AURKA,CCND1,CDKN2A,CLU,ELN,GATA2,HSPA8,IFNG,ITGB1,MPO,PPP3CA	789 (21)
ANGPTL4	other	3,66E-03	CD36,LPIN1,LPL,SREBF1,UCP1	696 (13)
CD19	transmembrane	3,66E-03	IFNG,IL10,IL4,IL6,TNF	542 (18)
FCMR	other	3,66E-03	HAMP,IFNG,IL6,NFKB2,TNF	712 (18)
FGF23	growth factor	3,66E-03	ATP1A2,CYP24A1,CYP27B1,KL,TRPV5	570 (13)
MTORC2	complex	3,66E-03	CCL2,FOXP3,IFNG,IL4,SREBF1	945 (19)
PDCD1LG2	enzyme	3,66E-03	IFNG,IL10,IL13,IL2,IL4	795 (19)
PIK3CB	kinase	3,66E-03	APLN,AR,HAMP,NOS2,SLC2A1	973 (19)
PITX1	transcription reg	3,66E-03	CCND1,POMC,PRL,TBX4,TFF1	1057 (18)
TCIRG1	enzyme	3,66E-03	CTLA4,IFNG,IL2,IL4,SELL	
Tcrd	other	3,66E-03	IFNG,IL15,IL17A,IL22,TNF	889 (17)
UNC93B1	transporter	3,66E-03	CSF2,IFNG,IL12B,IL17A,TLR7	617 (17)
ARG1	enzyme	3,84E-03	CDK5R1,IGF1,IL12B,IL6,NOS2,RPTOR	724 (12)
CCAT2	other	3,84E-03	ACTA2,BAX,CCND1,MMP7,SMAD2,TGFB1	
CD70	cytokine	3,84E-03	BCL2A1,CD69,FAS,IFNG,IL2RA,SELL	827 (18)
Cyclin E	group	3,84E-03	CD34,DHFR,HIF1A,KRAS,PGR,ROCK2	168 (8)
Cyp2c23	enzyme	3,84E-03	CCR2,CX3CR1,F5,ITGAM,TGFB2,TIMD4	
DAXX	transcription reg	3,84E-03	CCND1,CYP11A1,IL6,MMP1,SERPINE1,SMAD4	903 (18)
DDX25	enzyme	3,84E-03	ACE,DROSHA,EP300,HMGCR,NFKBIA,SREBF2	
GAL	other	3,84E-03	FOS,GCG,GH1,LEP,PRL,SORT1	997 (23)
peptide T	biologic drug	4,55E-05	ICAM1,IL10,ITGAV,TGFB1,TNF	
GPI	enzyme	3,84E-03	CAV1,CCND1,CXCL8,FN1,RAC1,STEAP4	862 (15)
LAMA5	other	3,84E-03	MMP14,MMP9,NPY2R,SHH,TNF,TNFRSF1B	833 (17)
mir-7	microRNA	3,84E-03	ABCC1,BAX,IGF1R,MAPKAP1,RELA,SLC2A3	
NEDD4	enzyme	3,84E-03	ERBB3,FN1,MMP9,PTEN,TP53,TRPV5	1018 (22)

PLD2	enzyme	3,84E-03	ABCB11,IL13RA2,NOS2,NR1H4,PTGS2,SCARB1	814 (18)
QKI	other	3,84E-03	CHGB,ERCC2,ITGB8,PTPRO,TNC,VCAM1	
SMYD3	enzyme	3,84E-03	AR,CEBPD,NKX2-5,PSMD9,TERT,TFF1	1002 (17)
Sod	group	3,84E-03	HLA-DRA,HMOX1,ICAM1,MMP2,TP53,VCAM1	949 (19)
THY1	other	3,84E-03	AXL,CLU,GAS6,MMP2,TGFB1,VEGFA	897 (19)
HMGN1	transcription reg	3,90E-03	ATP6AP2,CBR3,FGA,FOS,IL4I1,KNG1,TFF1,TTR	
P2RY14	G-protein coupl	3,90E-03	CACNA1C,CACNA1H,CARTPT,CASR,GHRL,GLP1R,SLC2A2,SST	
SIX1	transcription reg	3,90E-03	BMP4,DACH1,FGF10,MYOD1,PAX2,SALL1,TGFBR1,VEGFC	469 (7)
TLX1	transcription reg	3,90E-03	CCK,ERBB2,GATA2,GRIN3A,KDR,MYB,NPY1R,SST	
ELF4	transcription reg	3,96E-03	ABCB1,CA2,CDKN2A,CXCL8,IL3,KIT,SELL,SPP1,TP53	600 (7)
FHIT	enzyme	3,96E-03	IPO7,MMP14,MMP2,MMP9,RAB6C/RAB6D,RABIF,RAC1,RHOC,TGFB3	
TFDP1	transcription reg	3,96E-03	ATM,CCND1,CDKN2A,DHFR,FGFR1,FGFR2,MYB,TP53,TP73	803 (16)
ZBED6	transcription reg	3,96E-03	ARL4C,COL13A1,GCK,IGF2,PDX1,ROCK2,SGK1,TCF7,WWC1	
AREG	growth factor	4,00E-03	C3,CCND1,CXCR4,EGFR,FOS,FOXP3,HAS2,IL6,ITGB8,JUN,MMP1,MMP9,NPPC,PRC1,PTGS2,RUNX1,TXNRD1	760 (18)
CDKN1B	kinase	4,16E-03	AGTRAP,APCDD1,BCL11A,CCND1,GAB2,GYPA,HSPB2,IL2RA,IL4,ITGAM,MMP9,MYOD1,PAX5,RUNX1,RYR2,SERPINE1,SHMT1,SLC9A1,STAT3,TYRP1,WNT3	887 (18)
ADGRF5	G-protein coupl	4,36E-03	IL1RN,MMP2,MMP9,TNF	681 (14)
ARID3B	transcription reg	4,36E-03	POU5F1,TNF,TNFRSF1B,TNFSF10	
CLCF1	cytokine	4,36E-03	IL12B,MSR1,POMC,SOCS3	723 (17)
collagen	group	4,36E-03	IL10,IL17A,MAPK3,SELP	365 (7)
Cyp4a14	enzyme	4,36E-03	CD36,IL1A,IL1B,TNF	370 (7)
CYSLTR1	G-protein coupl	4,36E-03	FOS,HAMP,NFATC1,SOD1	
CYSLTR2	G-protein coupl	4,36E-03	CXCL8,KIT,MITF,TYRP1	
FANCA	other	4,36E-03	GNRHR,HES1,IL1B,TNF	660 (13)
FCGR3A/FCGR3	transmembrane	4,36E-03	F2RL1,IFNG,SELL,TNF	770 (13)
FOXD2-AS1	other	4,36E-03	CDC42,CTNNB1,HES1,NOTCH1	
GABP	complex	4,36E-03	ELANE,ERBB2,IL7R,SOD3	
GPAT3	enzyme	4,36E-03	LPL,PPARG,SLC2A4,SREBF1	330 (5)
GRK5	kinase	4,36E-03	HTR2A,NFKB1,RELA,TP53	828 (11)
HEYL	transcription reg	4,36E-03	GATA4,MMP2,NPPA,SMTN	
HINT1	enzyme	4,36E-03	BAX,FADS1,FADS2,TP53	450 (7)
HRH3	G-protein coupl	4,36E-03	IFNG,LEP,UCP1,UCP3	804 (17)
HS6ST1	enzyme	4,36E-03	CXCL8,IL6,SMAD2,VEGFA	687 (13)
IL-2R	complex	4,36E-03	FOS,IL2RA,IL4,IL5	847 (17)
LIPC	enzyme	4,36E-03	APOA1,APOA2,APOB,SCARB1	611 (12)
LTBP4	growth factor	4,36E-03	BMP4,TGFB1,TGFB2,TGFB3	768 (12)
MAOA	enzyme	4,36E-03	CCND1,HTR2A,HTR2C,SLC18A2	
MIA	other	4,36E-03	FN1,ITGB3,MMP14,PLAT	
miR-138-5p (mi	mature microRN	4,36E-03	RHOC,ROCK2,TERT,VCAN	
miR-192-5p (an	mature microRN	4,36E-03	DHFR,IGF1,IGF1R,TYMS	
N-Cadherin	group	4,36E-03	CCL2,CCND1,MMP9,VCAM1	790 (18)
NUP155	transporter	4,36E-03	ANGPTL4,CACNA1C,CSRP3,SLC8A1	250 (7)
PFKFB3	kinase	4,36E-03	ADIPOQ,IL6,RETN,TNF	702 (11)
PLP2	transporter	4,36E-03	EPHB4,HLA-C,ICAM1,PECAM1	
PRKCG	kinase	4,36E-03	ADORA2A,CCND1,MYH7,NPY	143 (5)
RC3H2	enzyme	4,36E-03	ICOS,IFNG,IL17A,IL4	758 (9)
RGS19	other	4,36E-03	BMP4,GATA4,MEF2C,MYH7	385 (7)
RNF41	enzyme	4,36E-03	ERBB3,HAMP,IL1B,TNF	819 (20)
S100A10	other	4,36E-03	IL6,MMP1,PLG,TNF	962 (22)
SLC2A2	transporter	4,36E-03	GCGR,IRS2,PCK1,PDX1	673 (11)
TBL1X	transcription reg	4,36E-03	DIO1,MMP12,RARB,TFF1	562 (14)
TFIIA	complex	4,36E-03	FOS,IL2,NF1,TFF1	570 (7)
TXNRD1	enzyme	4,36E-03	BAX,FAS,GPX3,TP53	997 (19)
ZNF91	transcription reg	4,36E-03	DDAH1,FCGR2B,POSTN,TGFB3	
ZNF384	transcription reg	4,36E-03	COL1A1,MMP1,MMP3,MMP7	
RNASEH2A	enzyme	4,63E-03	IFIH1,IL6,IRF5,NFKB1,NFKB2,NFKBIA,OASL,PTGS2,TLR2,TLR4	
ALDH2	enzyme	4,66E-03	CALCA,CTH,GCLC,GCLM,GSS,SHMT1,SLC1A4	
miR-204-5p (an	mature microRN	4,66E-03	ATP2B1,EFNB1,FBN2,MMP3,MMP9,PPARG,PTPN11	
TSPYL5	other	4,66E-03	CAST,CNTNAP2,CYP11B1,CYP19A1,F11R,NR3C1,NR3C2	
GAPDH	enzyme	4,88E-03	C2,CCL2,ENPP1,HLA-C,IL10,OAS3,SPP1,TXNIP,WARS	
HOXB13	transcription reg	4,94E-03	AR,ATP10D,BCHE,CCND1,CDKN2A,EPHA4,NFKBIA,UGT2B7	524 (7)
NF1	other	4,94E-03	CBS/CBSL,CCND1,CTNNB1,KRAS,MAF,MYH7,NPPA,PCK1	906 (16)
RNASEL	enzyme	4,94E-03	IL1B,MT-ATP6,MT-CO2,MYOD1,NR3C1,PTGS2,TNF,TP53	633 (18)
SUB1	transcription reg	4,94E-03	BAX,CCND1,FOS,KCNJ4,NDUFAB1,RXFP3,VEGFA,VEGFC	462 (4)
TET2	enzyme	5,25E-03	ADORA2B,AQP8,CPN1,FN1,FOXC1,FOXP3,GRK5,IGF1R,IL1B,IL1R1,IL6,ITGA2,ITGB2,P2RY2,PDGFRB,SH2B3,SLC20A1,SLC6A4,SORL1,TIMP1,TNFSF14,XYLT1	
CREB3L1	transcription reg	5,30E-03	BGLAP,COL1A1,COL1A2,NOS2,SLC1A4,SPP1	
Fgfr	group	5,30E-03	FGFR1,FOS,GDNF,HMOX1,LGR5,SPP1	975 (24)
GCGR	G-protein coupl	5,30E-03	FGF21,LEP,PCK1,SLC6A2,SLC6A4,SREBF1	723 (14)
HCAR2	G-protein coupl	5,30E-03	IL12B,IL1B,IL23A,IL6,PTGS2,TNF	777 (19)
HOXB9	transcription reg	5,30E-03	CXCL8,NCAM1,NRG1,REN,SHH,TGFB2	
IL17R	complex	5,30E-03	CCL2,CCL5,CXCL5,CXCL8,MMP1,TIMP1	660 (13)
POU1F1	transcription reg	5,30E-03	GH1,GHR,GHRHR,NPY,PRL,TP53	1079 (25)
RFX3	transcription reg	5,30E-03	BBS4,DNAH11,GCK,HLA-DRA,IL5RA,SLC2A2	
SMURF1	enzyme	5,30E-03	NOS2,SMAD1,SMAD2,SMAD5,SMAD6,WFS1	375 (7)
BCAR1	enzyme	5,47E-03	CCND1,CDKN2B,ESR1,MMP7,RAC1	938 (21)
BPIFA1	other	5,47E-03	IL1B,IL6,LTF,PTEN,SCGB1A1	
CD180	other	5,47E-03	BCL2A1,IL10,IL6,TLR9,TNF	734 (20)
CLEC4E	other	5,47E-03	IL10,IL17A,IL6,NOS2,TNF	711 (15)
FH	enzyme	5,47E-03	HMOX1,LDHA,LTBP2,NQO1,TKT	
HLA-A	other	5,47E-03	HLA-A,IFNG,MEF2A,MEF2C,MEF2D	
IL1RL2	transmembrane	5,47E-03	CXCL8,IL22,IL23A,IL6,REG3A	526 (10)
LILRA2	other	5,47E-03	CD40,CXCL8,IL10,IL6,TNF	734 (16)
MDGA2	other	5,47E-03	ATR,BCL2A1,CDKN2A,FAS,IL6	
POLR3G	enzyme	5,47E-03	AURKA,LMNA,RAC1,S100A4,TP53	
PPIA	enzyme	5,47E-03	IL4,IL5,MMP9,POU5F1,RARB	760 (19)
SAMHD1	enzyme	5,47E-03	IL6,NFKB1,NFKB2,NFKBIA,TNF	711 (9)
TCF/LEF	group	5,47E-03	CCND1,FN1,ITGB1,MMP2,PTGS2	
TIA1	other	5,47E-03	HBB,PTGS2,SIRT1,TNF,VEGFA	
TLE1	transcription reg	5,47E-03	ATF3,BCL2A1,CDKN2A,FOS,ROCK2	691 (7)
TRIM38	other	5,47E-03	CCL5,CXCL8,IL1B,IL6,TNF	570 (17)
UGCG	enzyme	5,47E-03	ABCB1,BAX,ICAM1,PCK1,SLC12A1	934 (17)
XRCC5	enzyme	5,47E-03	APOE,FKBP5,NFKB1,TP53,XDH	883 (16)
ASXL1	transcription reg	5,57E-03	ATP1A2,HSD11B1,LIPE,LPL,PLIN1,PPARG,RARB,SERPINE1,SLC2A4,VEGFA	470 (7)
NFIB	transcription reg	5,57E-03	BMP6,EDN2,EFNB1,GFRA1,HSD17B7,JCAD,LOX,MYOC,NCAM1,STEAP4	
NANOG	transcription reg	5,76E-03	ABCB1,AHR,CDK6,COL3A1,FGF5,FOS,GATA4,GCK,HSPA1A/HSPA1B,IGF1R,IGFBP1,KDR,MAX,MEIS1,PDX1,POU5F1,RAPGEF5,SOX17,TBX3,TET2,TP53,ZFHX3	683 (11)
HSPG2	enzyme	5,96E-03	ACTA2,APOB,CXCR4,DRAM1,FGFR3,IGF1,PRKN,SIRT1,TCHP	629 (7)
PAF1	other	6,00E-03	CCL5,IFNL3,NFKBIZ,OAS3,OASL,PLAUR,SDC4,SERPINE1,SERTAD1,SOD2,ZFP36	
GRHL2	transcription reg	6,04E-03	BMP2,ERBB3,MMP1,MMP14,MYB,NOTCH3,TERT	

SAFB2	other	6,04E-03	CNTNAP2,FOS,HLA-C,HLA-DPB1,JUN,MLLT3,PSMB9	
GCK	kinase	6,17E-03	CPT1A,CPT2,IRS2,NPY,PCK1,POMC,SLC2A2,SREBF1	992 (21)
HOXD10	transcription reg	6,29E-03	AGXT2,DOT1L,FMR1,HBEGF,HEBP1,ICAM1,MMP14,REN,RHOC,SERPINE1,TFR2,TIMP1,TIMP2	
PAX6	transcription reg	6,62E-03	ATOH7,CCND1,CDCA7,CDK6,EFNB2,F2,G6PC2,GAA,GCG,GCK,GIPR,GLP1R,HAS2,HES1,INS,MAF,MET,MITF,MMP9,NCAM1,PAX2,PCSK1,PCSK2,PDX1,PIGG,SLC2A2,SMAD2,SMAD4,SOCS1,SST,TNC,VEGFA	594 (13)
ABCB6	transporter	6,64E-03	ALAD,CAT,CYP1A1,CYP1A2,CYP2A6 (includes others),CYP2R1,CYP3A5,CYP4A11,CYP4F2,TXNRD2	
HSPA5	enzyme	7,03E-03	BAX,CCL5,CLU,CPT1A,ESR1,HSPA8,IL6,NQO1,PTEN,SREBF1,SREBF2	905 (22)
DDX58	enzyme	7,11E-03	ALPL,CCL2,CCL5,CXCL8,IFIH1,IFNL3,IL1B,IL6,PTGS2,SOCS1,SOCS3,SPP1,TNF,TNFSF10	600 (18)
COPS5	transcription reg	7,13E-03	BAX,CD247,HIF1A,LHCGR,STAT3,TP53	934 (20)
CSNK2A1	kinase	7,13E-03	AHR,CCND1,FN1,RELA,TP53,ZFP36	889 (16)
GAS5	other	7,13E-03	CCND1,CDK6,FGF1,IL1B,IL6,TNF	970 (19)
mir-31	microRNA	7,13E-03	AR,FOXP3,IL2,ITGA2,MET,SPP1	
polaprezinc	biologic drug	3,45E-02	CXCL8,IL2,TNF	
MNT	transcription reg	7,13E-03	CAD,IFNG,IL2,TERT,TNF,TXNIP	
MUC4	other	7,13E-03	CCND1,EGFR,ERBB2,ERBB3,MMP9,PRKCG	960 (17)
poly rI:rC-RNA	biologic drug	6,87E-45	ABCA1,APOL1,APOL3,ATF3,AXL,BAX,BMP2,C2,C3,CCL11,CCL17,CCL2,CCL5,CCL8,CD14,CD200,CD36,CD40,CD69,CEBPD,CFB,CNP,CRP,CSF2,CTNNB1,CXCL8,CXCR4,CYP27B1,CYP4F2,DIO1,DIO2,DUOX1,EDN1,EFNB3,ELANE,FAS,FCGR2B,FN1,FOS,FPR1,GATM,GCH1,GDF15,HBEGF,HFE,HIF1A,HLA-A,HLA-B,HLA-C,HLA-G,HSPB2,HSPD1,ICAM1,IFIH1,IFNG,IFNK,IFNL3,IGF1,IL10,IL10RA,IL12A,IL12B,IL13,IL13RA2,IL15,IL15RA,IL17A,IL18,IL1A,IL1B,IL2,IL23A,IL2RA,IL33,IL4I1,IL4R,IL6,IRAK1,IRF5,ITGAM,JAG1,JAK2,JUN,KYNU,LIG1,LIMK1,LIPG,LPL,LTA,LTA4H,LTF,M6PR,MBL2,MEIS1,MMP1,MMP2,MMP3,MMP9,MPO,MRAS,MSR1,MYB,MYOC,NAMPT,NAT1,NFKB1,NFKB2,NFKBIA,NLRP3,NOS2,NOTCH1,NOTCH3,NR4A3,OAS3,OASL,OLR1,PLA2G4C,PLAUR,POU5F1,PRKCQ,PSIP1,PSMB8,PSMB9,PTGS2,PTPN2,REL,RELA,RGS2,SCARB1,SDC4,SELE,SLC26A4,SLC2A2,SLPI,SOCS1,SOD2,SRSF2,ST8SIA4,TAP1,TET2,TFPI2,TGFB1,THBS1,TIRAP,TLR2,TLR4,TLR5,TLR6,TNF,TNFAIP3,TNFRSF11B,TNFSF10,TNFSF13,TNFSF4,TOLLIP,TP53,TRAF1,TRPV1,TSHR,TSLP,USF1,VCAM1,VEGFA,VEGFC,WNT5A,ZFP36	915 (15)
polymyxin B	biologic drug	6,40E-09	CXCL8,HGF,IL10,IL12B,IL1B,IL6,LDLR,TNF,VCAM1	965 (15)
TLX3	transcription reg	7,13E-03	CCK,GRIN3A,NPY1R,RET,SST,VIP	
MSC	transcription reg	7,21E-03	BMP7,CCL2,CHL1,CKM,FUT7,HGF,ITGA9,PAX5,SELL,SPP1,TLR7,TRIB1	145 (5)
NFE2L1	transcription reg	7,22E-03	CYP4A11,GCLC,GCLM,GSTP1,HMOX1,LEP,NQO1,PSMA6,SNRPN	
AP3B1	transporter	7,26E-03	AP3D1,IL12B,TNF,TNFRSF1A	566 (12)
BANP	other	7,26E-03	BAX,CCND1,STAT3,TP53	1035 (21)
BCKDK	kinase	7,26E-03	AQP4,CAT,SOD2,TNF	
BRMS1	transcription reg	7,26E-03	CXCR4,GJA1,IL6,SPP1	786 (15)
C7	other	7,26E-03	ICAM1,IL1B,SELE,VCAM1	621 (10)
C8	complex	7,26E-03	ICAM1,IL1B,SELE,VCAM1	621 (10)
CAMK2G	kinase	7,26E-03	CTNNB1,NFKB1,NPPA,TP53	769 (13)
Ccl6	cytokine	7,26E-03	MMP2,MMP9,SERPINA1,TIMP4	
Ck2	complex	7,26E-03	CYBB,FOS,INSR,ZFP36	1015 (24)
COCH	other	7,26E-03	IL18,IL1B,IL6,TNF	
CRTC3	other	7,26E-03	LEP,MT-CO2,PPARGC1A,RGS2	
FGF3	growth factor	7,26E-03	CTNNB1,MMP2,MMP9,PLAT	869 (17)
FUS	transcription reg	7,26E-03	ATF3,HSPD1,ICAM1,TBL2	729 (7)
GDF11	growth factor	7,26E-03	ATP2A2,ICAM1,NPPA,VCAM1	
GPBAR1	G-protein coupl	7,26E-03	CCND1,DIO2,GCG,PCSK1	
HAS2	enzyme	7,26E-03	ACTA2,IL6,MMP9,TIMP1	999 (20)
HGS	other	7,26E-03	EGFR,ESR1,FOS,SCNN1A	1073 (26)
MC1R	G-protein coupl	7,26E-03	HAMP,MITF,NR4A3,TNF	601 (9)
MHC Class II (co	complex	7,26E-03	IFNG,IL2,IL6,TNF	758 (26)
mir-217	microRNA	7,26E-03	HMOX1,IRS1,PTEN,SIRT1	
MIRLET7	group	7,26E-03	BCL11A,IL6,KRAS,LIN28A	
MKX	transcription reg	7,26E-03	COL1A1,COL1A2,COL3A1,SOX6	
OLFM4	other	7,26E-03	IL12A,IL1B,IL5,TNF	492 (7)
Pde	group	7,26E-03	FOS,HMOX1,NR4A3,PTGS1	
PLCB3	enzyme	7,26E-03	HAMP,IL13,IL6,TNF	751 (20)
RASSF6	other	7,26E-03	BAX,CDKN2A,TP53,TP73	746 (15)
RFXAP	transcription reg	7,26E-03	COL1A2,HLA-B,HLA-DQA1,HLA-DRA	144 (4)
RTKN	other	7,26E-03	BCL2A1,FOS,TNF,TNFAIP3	711 (9)
SASH3	other	7,26E-03	IFNG,IL10,IL4,TNF	924 (18)
SCUBE3	other	7,26E-03	MMP2,MMP9,SERPINE1,TGFB1	574 (10)
SIAH1	enzyme	7,26E-03	CTNNB1,DCC,EGLN3,HIF1A	241 (4)
SLC11A1	transporter	7,26E-03	HAMP,IFNG,IL10,IL3	481 (7)
TFCP2L1	transcription reg	7,26E-03	CYP11A1,GRHL1,SIRPA,SLC27A4	
TNFRSF17	transmembrane	7,26E-03	BAX,CD40,CSF2,ICAM1	671 (15)
TPM3	other	7,26E-03	IGF1,MMP1,MMP2,VEGFA	523 (7)
UBA7	enzyme	7,26E-03	IL10,IL12A,IL23A,TNF	515 (10)
UNC5B	transmembrane	7,26E-03	CCL11,IL10,IL6,TNF	
voltage-gated c	complex	7,26E-03	CD34,ITGAM,ITPR2,PTPRC	
ZBTB10	other	7,26E-03	CAD,ESR1,FLT1,SP4	
E2f	group	7,45E-03	BRCA1,CAV1,CDKN2A,CYP27B1,DHFR,DLEU2,DROSHA,DUOX2,EPAS1,HIF1A,IGF1,ITGB1,LIG1,MTHFD1,MYB,NPPA,POMC,SERPINE1,TP53,TYMS,USP37	582 (11)
IFRD1	other	7,63E-03	CCN2,CTH,DES,IGF1,MTTP,MYOD1,NFATC1,SPP1	644 (11)
UPF2	other	7,63E-03	CACNA1D,CACNB2,CLU,PTGS2,TFR2,TNFAIP3,TNFRSF11B,TSPAN8	
ACOD1	enzyme	7,68E-03	IL6,TNF,TNFAIP3	505 (10)
ADAM9	peptidase	7,68E-03	ITGB1,SLIT2,TIMP1	454 (7)
AHSG	other	7,68E-03	CXCL8,IL6,TNF	830 (19)
ARG2	enzyme	7,68E-03	BAX,NOS2,TNF	705 (10)
arginase	group	7,68E-03	ARG1,NOS2,OLR1	
ARHGEF25	other	7,68E-03	CDC42,JUN,RAC1	468 (7)
ARLNC1	other	7,68E-03	AR,FKBP5,KLK2	
Asc2	other	7,68E-03	CYP1A2,CYP3A5,GSTP1	
BRCA2	transcription reg	7,68E-03	BAX,SERPINE1,TP53	
CC2D1A	transcription reg	7,68E-03	CCL5,DRD2,IL6	492 (7)
CD59	other	7,68E-03	CD69,IL2,IL2RA	735 (19)
CDCA2	other	7,68E-03	CDKN2A,CDKN2B,NUMA1	180 (4)
CDH4	other	7,68E-03	MMP1,MMP2,PTGS2	
CDR2	other	7,68E-03	EGLN3,SLC2A1,TF	
CEL	enzyme	7,68E-03	BAX,CCND1,TP53	895 (21)
CES1	enzyme	7,68E-03	ADIPOQ,IL1B,IL6	291 (4)
Cox5b	other	7,68E-03	POSTN,PPP3CA,TGFB2	
Cpla2	group	7,68E-03	AR,PTGS2,VEGFA	803 (17)
CSF	group	7,68E-03	BCL2A1,C3,IL2	
CSNK1A1	kinase	7,68E-03	CXCR4,HAMP,IL2	607 (11)
DNM1	enzyme	7,68E-03	CXCR2,GLP1R,MMP14	
EIF2AK1	kinase	7,68E-03	IL1B,IL6,TNF	675 (11)
FGF13	growth factor	7,68E-03	MMP3,MMP9,VEGFA	659 (12)
Foxe3	transcription reg	7,68E-03	PDGFRA,PROX1,TTR	
FUT7	enzyme	7,68E-03	SELE,SELP,SELPLG	
GAS7	transcription reg	7,68E-03	BGLAP,ITGB1,SPP1	
GCH1	enzyme	7,68E-03	GCH1,HMOX1,TNC	16 (3)
GCLM	enzyme	7,68E-03	FOS,GCLM,JUN	

Gpcr	group	7,68E-03	EGFR,FOS,JUN	816 (20)
GRAP2	other	7,68E-03	CD69,IL2,IL2RA	610 (17)
HAMP	other	7,68E-03	HAMP,IL6,TNF	200 (4)
Hbb	other	7,68E-03	ICAM1,PECAM1,VCAM1	
HLA-DRB1	transmembrane	7,68E-03	IFNG,IL2,TNF	
Ho	group	7,68E-03	CXCR2,ICAM1,ITGAM	
Igf	group	7,68E-03	FN1,HIF1A,PYY	584 (7)
IgG2b	complex	7,68E-03	IL1B,IL6,TNF	496 (7)
KIR2DL4	transmembrane	7,68E-03	CD69,IFNG,KIR2DL4	
KLK1	peptidase	7,68E-03	IL6,KLK1,TRPV5	
KRT10	other	7,68E-03	CCND1,IKBKB,TNF	883 (16)
LILRB3	transmembrane	7,68E-03	CSF2,IL1B,IL6	662 (20)
LOC102724788/	enzyme	7,68E-03	NFATC1,PTGS2,TNFSF10	757 (15)
LRP8	transmembrane	7,68E-03	ABCA1,CLU,GPX4	
LSP1	other	7,68E-03	GATA2,ITGB1,PECAM1	
Mamld1	other	7,68E-03	CYP11A1,CYP17A1,HSD3B2	
MC3R	G-protein coupl	7,68E-03	HMOX1,LEP,TNF	900 (24)
Mcpt1	peptidase	7,68E-03	AGT,IL10,TNF	
protamine zinc	biologic drug	8,91E-04	IGF1,IGFBP1,UCP3	411 (7)
mir-365	microRNA	7,68E-03	AR,CKM,MYOD1	
mir-506	microRNA	7,68E-03	GFRA1,RHOC,TNF	
miR-183-5p (mi	mature microRN	7,68E-03	FOXO1,IDH2,SRSF2	
miR-292b-5p (a	mature microRN	7,68E-03	AR,BCL11A,BCL11B	
MPO	enzyme	7,68E-03	EDNRB,NOS2,VCAM1	823 (21)
Mst/krs	group	7,68E-03	IL12B,NFKB2,OPA1	
MTF2	transcription reg	7,68E-03	CDKN2A,POU5F1,TBX3	919 (19)
MYBBP1A	transcription reg	7,68E-03	MMP3,PPARGC1A,SLC2A4	759 (7)
Nfatc	group	7,68E-03	IL2,PPARGC1A,PTGS2	
P4HTM	enzyme	7,68E-03	EPAS1,EPO,HIF1A	752 (11)
PENK	other	7,68E-03	CDKN2A,FOS,UCP1	826 (16)
Pik3r	group	7,68E-03	CXCL8,EPO,TP53	659 (11)
PLAA	other	7,68E-03	CLU,IL6,PTGS2	715 (16)
PRMT2	enzyme	7,68E-03	CCND1,IL6,TNF	905 (18)
PSAP	enzyme	7,68E-03	CCND1,ESR1,GBA	627 (11)
PTGIS	enzyme	7,68E-03	CYP2E1,NOS1,NOS2	
PTPRN2	phosphatase	7,68E-03	IRS2,PTPRN2,TH	
RAD51C	enzyme	7,68E-03	ESR1,PGR,XRCC3	
RAP1B	enzyme	7,68E-03	CCL5,CSF2,IFNG	837 (20)
RAR-RXR	complex	7,68E-03	PRDM16,UCP1,VEGFA	
RBM14	transcription reg	7,68E-03	CCND1,HTRA1,SOX6	
RECQL4	enzyme	7,68E-03	ABCB1,CSF2,HBB	427 (7)
RNF187	enzyme	7,68E-03	CCND1,HBEGF,JUN	
RPE65	enzyme	7,68E-03	FOS,OPN4,RHO	
RPS3	enzyme	7,68E-03	CXCL8,IL2,NFKBIA	812 (14)
RUBCN	other	7,68E-03	IL10,IL1B,IL6	627 (11)
SCNN1B	ion channel	7,68E-03	KCNJ1,SCNN1A,SCNN1G	
sGC	complex	7,68E-03	BDNF,FOS,FOXP3	1005 (20)
SGMS1	enzyme	7,68E-03	IL6,SCARB1,TNF	425 (7)
SLC39A8	transporter	7,68E-03	MMP12,MMP3,MMP9	411 (3)
SLC40A1	transporter	7,68E-03	IL6,TGFB1,TNF	528 (10)
SMARCA5	transcription reg	7,68E-03	HAMP,IL2,IL3	
SNCG	other	7,68E-03	ESR1,IGF1R,PGR	1015 (15)
SRSF6	other	7,68E-03	LMNA,TNC,VEGFA	
SWI-SNF	complex	7,68E-03	MET,PPARG,SELE	307 (7)
TH1 Cytokine	group	7,68E-03	CCR5,HIF1A,NOS2	422 (6)
TIMP4	other	7,68E-03	MMP14,TIMP2,TIMP4	
TPPP2	other	7,68E-03	ATM,CDKN2A,TP53	
TRA2B	other	7,68E-03	LPIN1,NQO1,RGS4	
TRIM27	transcription reg	7,68E-03	HAMP,IFNG,TNF	466 (7)
TTYH1	ion channel	7,68E-03	HES1,HES5,NOTCH1	
TYMS	enzyme	7,68E-03	FAS,TP53,TYMS	705 (7)
Wfdc17	other	7,68E-03	ARG1,IL1B,IL6	
WNK4	kinase	7,68E-03	CFTR,SLC12A3,WNK4	505 (7)
ZC3H10	other	7,68E-03	MT-CO1,MT-CO2,SDHB	
HSD17B4	enzyme	7,70E-03	ACAA1,ALOX5,BMP2,CD36,CYP4A11,PDK4,PTGS2	
PCYT1A	enzyme	7,70E-03	ABCA1,AXL,FGFR1,GFRA1,GSN,MAPKAPK2,MAT1A	
Ahr-aryl hydroc	complex	7,85E-03	BAX,CYP1A1,CYP1A2,CYP1B1,FAS	
CAMK2D	kinase	7,85E-03	BDNF,IL1RL1,IL6,MYH7,NPPA	844 (24)
CBS/CBSL	enzyme	7,85E-03	APOA1,APOB,CCL2,LOX,SCARB1	471 (7)
CBX2	transcription reg	7,85E-03	AHR,CDKN2A,GATA4,HBB,RUNX1	
ILF3	transcription reg	7,85E-03	EGFR,FOS,HLA-DRA,IL13,IL2	568 (7)
LOXL2	enzyme	7,85E-03	ESR1,FN1,MMP14,MMP9,PECAM1	
miR-132-3p (an	mature microRN	7,85E-03	EP300,GRIA1,IFNG,IL17A,MMP9	
NFKBID	transcription reg	7,85E-03	CSF2,IFNG,IL10,IL2,IL6	699 (18)
POU3F2	transcription reg	7,85E-03	CDK5R1,CHGA,IL3,MITF,NCAM1	
RGCC	other	7,85E-03	ACTA2,FN1,IL1B,NOS2,SREBF1	589 (10)
SAT1	enzyme	7,85E-03	DHFR,IGFBP3,LEP,LPL,PPARGC1A	
SRSF3	other	7,85E-03	CCND1,CXCL8,JUN,TP53,VEGFA	549 (7)
TNFAIP8L2	other	7,85E-03	IL10,IL12B,IL1B,IL6,TNF	799 (21)
GPD1	enzyme	7,94E-03	ALPL,APOA4,CCND1,CD36,CXCL13,CYP2C8,EGFR,F11,FADS3,FMO3,MTHFD1L,NQO1,NVL,PTK2B,SERPINA3,SERPINB1,SERPINE2	
12 lipoxygenase	group	9,27E-03	MMP9,NOX1	
15-LOX	group	9,27E-03	CD36,PPARG	468 (7)
ACADS	enzyme	9,27E-03	GLO1,UCP1	
Acp5	phosphatase	9,27E-03	IL1B,TNF	649 (11)
ADAMTS9	peptidase	9,27E-03	MMP9,VEGFA	234 (4)
ADGRG1	G-protein coupl	9,27E-03	IGF1,VEGFA	
ADGRL2	G-protein coupl	9,27E-03	ADRB2,HAMP	
ADGRV1	G-protein coupl	9,27E-03	HAMP,HBA1/HBA2	
ADNP	transcription reg	9,27E-03	TNF,TP53	
ADRM1	other	9,27E-03	NFKBIA,NOS2	663 (7)
AFAP1L2	other	9,27E-03	CXCL8,IL6	925 (19)
AGXT	enzyme	9,27E-03	COL3A1,NPPA	
AHSA1	other	9,27E-03	CYP19A1,MC4R	
AKAP10	other	9,27E-03	IL10,IL6	
alpha-adrenerg	group	9,27E-03	GCG,SLC8A1	
ANO6	ion channel	9,27E-03	IFNG,IL2RA	527 (7)
ARHGDIB	enzyme	9,27E-03	IL5,PTGS2	568 (17)
ARL11	other	9,27E-03	IL6,TNF	806 (13)
ARNTL2	transcription reg	9,27E-03	HAMP,THBD	

ATP1A1	transporter	9,27E-03	HMGCR,LDLR	198 (4)
ATP9A	transporter	9,27E-03	VEGFA,VEGFC	
BAZ1A	other	9,27E-03	IGFBP3,TNFSF11	628 (7)
BCLAF1	transcription reg	9,27E-03	CCND1,TP53	
BORCS8-MEF2B	transcription reg	9,27E-03	GNRH1,JUN	
BTBD7	other	9,27E-03	MMP2,MMP9	
CADPS2	other	9,27E-03	BDNF,HAMP	
Camkk	group	9,27E-03	ABCA1,GRIA1	
CBP-ICSBP-IRF-1	complex	9,27E-03	CYBB,NCF2	
CCNG1	other	9,27E-03	TP53,TP73	832 (11)
Cd200r3	other	9,27E-03	IL2,IL4	
CD200R1L	other	9,27E-03	IL2,IL4	
CD300E	other	9,27E-03	IL6,TNF	
CD8B	other	9,27E-03	IL1B,TNF	465 (7)
CDKN2B-AS1	other	9,27E-03	CDKN2A,CDKN2B	
CDO1	enzyme	9,27E-03	IGF1,MYOD1	
CELA1	peptidase	9,27E-03	HLA-A,HSPA1A/HSPA1B	
CFP	other	9,27E-03	HAMP,ITGAM	
Cg Beta	group	9,27E-03	ADCYAP1,PGR	469 (7)
Clock-Bmal1	complex	9,27E-03	CLOCK,NAMPT	
COL17A1	other	9,27E-03	CXCL8,IL6	467 (7)
Convulxin	complex	9,27E-03	CXCL8,SELP	366 (7)
COX6A2	enzyme	9,27E-03	UCP1,UCP2	643 (7)
CRADD	other	9,27E-03	CCL2,IL6	
Cry-Period	complex	9,27E-03	ARNTL,CLOCK	
CYP4A	group	9,27E-03	SGK1,SLC12A3	
cytochrome-c o	complex	9,27E-03	AQP1,MAOA	
DAZAP2	other	9,27E-03	IL13,IL5	563 (10)
DDT	enzyme	9,27E-03	IL6,TNF	643 (7)
DDX20	transcription reg	9,27E-03	IGF2,TP53	
DENND1A	other	9,27E-03	CYP11A1,CYP17A1	
DNAJB1	transcription reg	9,27E-03	IL17A,RORA	
DPP10-AS1	other	9,27E-03	CTNNB1,TIMP3	
E2f-Dp1	complex	9,27E-03	BRCA1,PPARG	
ECI1	enzyme	9,27E-03	CYP4A11,PPARA	
EDF1	transcription reg	9,27E-03	MEF2C,NR0B2	
EDIL3	other	9,27E-03	IL17A,TP53	
EIF4E2	translation regu	9,27E-03	EGFR,PDGFRA	
EIF4H	translation regu	9,27E-03	CCND1,EIF4H	
ETS-ELK1	complex	9,27E-03	CCND1,CDKN2A	
ETV7	transcription reg	9,27E-03	BMP6,RARA	
FAM120B	other	9,27E-03	ADIPOQ,PLIN1	468 (7)
FBLIM1	other	9,27E-03	EGFR,TNFSF11	563 (7)
FBXO44	enzyme	9,27E-03	ADRB2,BRCA1	
FCAR	transmembrane	9,27E-03	IL12B,TNF	870 (18)
FGB	other	9,27E-03	HAMP,ICAM1	
FOXQ1	transcription reg	9,27E-03	DACH1,NRXN3	
FRAT1	other	9,27E-03	CTNNB1,JUN	585 (11)
GAD1	enzyme	9,27E-03	FOS,GNRH1	839 (14)
GAS5-AS1	other	9,27E-03	ACTA2,SMAD2	
GATAD2B	transcription reg	9,27E-03	CXCL8,PTGS2	
GH2	other	9,27E-03	INSR,PIK3R1	510 (7)
GJA3	transporter	9,27E-03	GJA1,GJA8	
GNAT3	enzyme	9,27E-03	AGRP,SLC5A1	
GPR4	G-protein coupl	9,27E-03	ICAM1,VCAM1	532 (7)
GPR32	G-protein coupl	9,27E-03	CXCL8,IL6	464 (7)
GPR34	G-protein coupl	9,27E-03	ITGAM,ITGB2	597 (7)
GRAP	other	9,27E-03	FOS,IL2	
GSDMB	other	9,27E-03	ALOX5,TGFB1	
GUCY	group	9,27E-03	IL4,IL5	
Hat	complex	9,27E-03	NOS2,SLC8A1	587 (7)
HIST3H3	other	9,27E-03	PGR,TFF1	
HLTF	transcription reg	9,27E-03	HBB,SERPINE1	
HNRNPF	other	9,27E-03	LPIN1,PPARG	
HOXC5	transcription reg	9,27E-03	HAMP,SHH	
IBSP	other	9,27E-03	MMP2,THBS1	222 (3)
ICAM3	transmembrane	9,27E-03	IFNG,PPARG	669 (12)
Id	group	9,27E-03	ACTC1,CKM	
IGFALS	other	9,27E-03	IGF1,PPARG	589 (7)
Igtp	enzyme	9,27E-03	IFNG,IL12B	567 (7)
IL17D	cytokine	9,27E-03	CXCL8,IL6	
IL1RAPL1	transmembrane	9,27E-03	IL6,TNF	385 (7)
Inflammasome	complex	9,27E-03	IL18,IL1B	704 (11)
ING2	transcription reg	9,27E-03	SERPINE1,SPP1	719 (7)
Integrin alpha V	complex	9,27E-03	MMP1,TGFB1	783 (21)
INTERLEUKIN	group	9,27E-03	FOS,NOS2	
ITGAE	other	9,27E-03	IFNG,TNF	506 (10)
ITGB7	transmembrane	9,27E-03	IFNG,TNF	468 (7)
IVNS1ABP	other	9,27E-03	PML,SOD2	
KALRN	kinase	9,27E-03	HAMP,RAC1	
KCP	other	9,27E-03	PPARGC1A,UCP1	250 (7)
KIR2DS4 (includ	transmembrane	9,27E-03	CD69,IFNG	506 (7)
Klf16	transcription reg	9,27E-03	DRD1,DRD2	254 (5)
L3MBTL1	other	9,27E-03	MMP3,RUNX1	
l9Rl3	other	9,27E-03	HMOX1,NOS2	604 (7)
LAMA3	other	9,27E-03	IL1B,MMP1	702 (12)
LCTL	enzyme	9,27E-03	KL,KLB	
LEFTY2	growth factor	9,27E-03	MMP3,MMP7	434 (7)
LPAR5	G-protein coupl	9,27E-03	CCK,PTGS2	660 (7)
LPIN2	phosphatase	9,27E-03	IL6,LPIN1	
LRP1B	transmembrane	9,27E-03	ABCA1,NCEH1	
MAML2	transcription reg	9,27E-03	HES1,HES5	
MAML3	transcription reg	9,27E-03	HES1,HES5	
MAP4	other	9,27E-03	HIF1A,VEGFA	658 (11)
MAPK8IP2	other	9,27E-03	BDNF,FOS	884 (20)
MAPKAPK2/3	group	9,27E-03	IL13,IL6	579 (10)
MDC1	other	9,27E-03	CLU,TP53	469 (7)
MED23	transcription reg	9,27E-03	KISS1,TFF1	455 (4)
mir-95	microRNA	9,27E-03	AR,BRCA1	
mir-134	microRNA	9,27E-03	BDNF,LIMK1	

mir-622	microRNA	9,27E-03	HIF1A,PLAUR	
mir-663	microRNA	9,27E-03	CXCR4,HSPG2	
mir-3473	microRNA	9,27E-03	IL10,PTEN	
miR-1195 (miR	mature microR	9,27E-03	IGF1,STAT3	
miR-509-3p (mi	mature microR	9,27E-03	AR,NTRK3	
miR-758-5p (an	mature microR	9,27E-03	AR,TP53	
Mitochondrial c	complex	9,27E-03	MAOA,PPARGC1A	
MMUT	enzyme	9,27E-03	LCN2,MMUT	
MR1	transmembrane	9,27E-03	CSF2,IL17A	
MTNR1A	G-protein coupl	9,27E-03	DIO2,DIO3	586 (7)
MTNR1B	G-protein coupl	9,27E-03	DIO2,DIO3	586 (7)
NCR3LG1	other	9,27E-03	IL13,IL5	
Nedd4	enzyme	9,27E-03	THBS1,TP53	400 (7)
NMB	other	9,27E-03	FOS,JUN	1146 (25)
NOXO1	other	9,27E-03	NOX1,SOD2	
rituximab	biologic drug	7,13E-03	ADORA2A,BAX,BCL2A1,FAS,IL10,TP53	898 (17)
NPBWR1	G-protein coupl	9,27E-03	NPY,POMC	476 (7)
NPS	other	9,27E-03	FOS,ITGAM	499 (5)
P2RY11	G-protein coupl	9,27E-03	HAMP,REN	468 (7)
PAK6	kinase	9,27E-03	HAMP,MMP9	
PARM1	other	9,27E-03	BMP2,BMP4	
PCNA	enzyme	9,27E-03	EP300,HAMP	
PDE4A	enzyme	9,27E-03	IFNG,TNF	796 (20)
PGLYRP3	transmembrane	9,27E-03	HAMP,IFNG	
PIEZO1	ion channel	9,27E-03	CD69,IL2RA	
PLA2	group	9,27E-03	FOS,TNF	860 (13)
PLA2G2F	enzyme	9,27E-03	PTGES,PTGS2	680 (7)
Plc beta	group	9,27E-03	IL6,NFKB1	623 (11)
PLCD4	enzyme	9,27E-03	EGFR,ERBB2	
PLSCR3	enzyme	9,27E-03	ADIPOQ,LEP	
POPDC2	other	9,27E-03	IL1B,TNF	520 (8)
PREB	transcription reg	9,27E-03	ABCA1,PRL	
PRG2	other	9,27E-03	IL10,IL4	784 (11)
PRKCSH	enzyme	9,27E-03	PKD1,PKD2	
PSG1	other	9,27E-03	TGFB1,VEGFA	
PTPase	group	9,27E-03	ABCA1,IRS1	531 (7)
PTPRG	phosphatase	9,27E-03	CD34,KIT	772 (7)
PYGO2	other	9,27E-03	ABCB1,HAMP	
romidepsin	biologic drug	6,12E-11	BAX,BCL2A1,CASZ1,CCND1,CDC42,CDKN2A,CDKN2B,CXADR,CXCL8,EGFR,ERBB2,FOS,GSN,HIF1A,ICAM1,INSR,ITGAV,JUN,MMP9,PLAUR,PTGS2,RAC1,RHOC,TERT,TIMP3,TP53,VHL	781 (18)
PYY	other	9,27E-03	FABP2,LEP	
Rab5	group	9,27E-03	ADRB2,IL6	348 (9)
RAD51	enzyme	9,27E-03	CHEK2,TP53	4 (2)
Raet1a	other	9,27E-03	HLA-A,IFNG	
RAI1	other	9,27E-03	BDNF,LEP	
RBM17	other	9,27E-03	ERBB2,FN1	
Rbp	group	9,27E-03	PPARG,SOCS3	43 (3)
RECQL5	enzyme	9,27E-03	PARP1,XRCC1	
REG3A	enzyme	9,27E-03	REG3A,SOCS3	
RelA-CRel	complex	9,27E-03	IL12A,IL12B	
REM2	enzyme	9,27E-03	CCND1,CDKN2A	429 (7)
RNF11	enzyme	9,27E-03	MMP9,SERPINE1	360 (9)
Rps15a-ps4	other	9,27E-03	NFKB2,NFKBIA	733 (9)
RRAD	enzyme	9,27E-03	CCND1,LPL	
RYR3	ion channel	9,27E-03	ADIPOQ,ATF3	
SCIMP	other	9,27E-03	IL6,TNF	652 (10)
SCNN1A	ion channel	9,27E-03	KCNJ1,SCNN1G	504 (7)
SCNN1G	ion channel	9,27E-03	KCNJ1,SCNN1A	
SEC63	transporter	9,27E-03	PKD1,PKD2	
SEMA6A	transmembrane	9,27E-03	HAMP,KDR	
SH2D3C	other	9,27E-03	IL2,IL6	506 (7)
SIGLEC11	other	9,27E-03	IL1B,NOS2	431 (7)
SLC22A3	transporter	9,27E-03	IL4,IL6	
SLC33A1	transporter	9,27E-03	IL17A,IL18	
SLC4A2	transporter	9,27E-03	IL2,IL2RA	
SLC7A11	transporter	9,27E-03	IL1B,TNF	935 (16)
SLC8A1	transporter	9,27E-03	EDN1,SLC8A1	531 (7)
Smr3b/Vcsa2	other	9,27E-03	ADORA2B,HIF1A	
SOCS7	other	9,27E-03	IRS1,PPARG	
SORCS3	transporter	9,27E-03	AGRP,HAMP	
sPla2	group	9,27E-03	PTGES,PTGS2	680 (7)
SPR	enzyme	9,27E-03	lGF1,TH	
STAG2	transcription reg	9,27E-03	CD69,TNF	520 (7)
TAGLN	other	9,27E-03	MMP9,TP53	441 (7)
TBX4	transcription reg	9,27E-03	FGF10,TBX2	
TH	enzyme	9,27E-03	FOS,NPY	
TIMM50	phosphatase	9,27E-03	HSD3B1,HSD3B2	
TMEM9B	other	9,27E-03	CXCL8,IL6	520 (7)
TNNT2	other	9,27E-03	MYH7,NPPA	555 (7)
TUSC2	other	9,27E-03	IL10,IL17A	
VENTX	transcription reg	9,27E-03	CCND1,CDKN2A	489 (7)
VPS33B	transporter	9,27E-03	SELP,VWF	
ZFP90	transcription reg	9,27E-03	IFNG,IL2	
ZFP36L1	transcription reg	9,27E-03	TNF,VEGFA	
ZG16	other	9,27E-03	IFNG,IL6	
ZMAT3	other	9,27E-03	BAX,TP53	745 (11)
ZP3	other	9,27E-03	IFNG,IL4	
ZRANB1	peptidase	9,27E-03	IFNG,IL17A	
HOXC8	transcription reg	9,33E-03	HAMP,Ly6a (includes others),NQO1,PLAGL1,RARB,REN,SPP1,SRD5A2	
KDM4C	enzyme	9,33E-03	DHFR,FGF5,KLF5,MFN1,PITX2,POC1B,POU5F1,WNT3	
miR-92a-3p (an	mature microR	9,33E-03	BMPR2,CCND1,IKZF1,IL6,ITGB3,MYLIP,PTEN,TNF	703 (12)
NRXN1	transporter	9,33E-03	CXCL12,F11R,LMX1B,MGP,PAX2,TGFB1,THBS1,TNC	
AXIN1	other	9,37E-03	APCDD1,CCND1,CTNNB1,FOS,PITX2,PPARG	849 (17)
CYB5R4	enzyme	9,37E-03	ATF3,CD36,GCLC,HMOX1,LPL,PPARGC1A	586 (11)
sargramostim	biologic drug	4,87E-02	CYBB,ITGAM	
DTNBP1	other	9,37E-03	ACTC1,DRD2,NPPA,SLC6A12,SNAP25,SST	
EPOR	transmembrane	9,37E-03	GATA2,JUN,MPO,SOCS1,SOCS3,TNF	694 (20)
HRG	other	9,37E-03	CXCL14,CXCR4,HLA-DQA1,SPP1,TIMP1,TIMP3	
Klra7 (includes	transmembrane	9,37E-03	CCL5,CSF2,IFNG,SERPINE2,TNF,XCL1	688 (16)
TFAM	transcription reg	9,37E-03	ACADS,CPT2,FABP3,IL1B,PFKP,PPARA	477 (7)

EFNA1	other	9,39E-03	CCN2,CD69,EP300,ETV5,FN1,IL2,IL2RA,IL4,ITGB6,KRAS,NEDD4L,PLAT,SLC20A1	989 (22)
miR-122-5p (mi	mature microRN	9,39E-03	ATP1A2,CERS6,EGLN3,GYS1,HJV,HMGB1,NCAM1,NFATC1,OSMR,RABIF,SLC7A1,TBX19,TRIB1	
LTBP1	other	9,67E-03	IL17A,IL9,SERPINE1,SMAD2,SMAD3,TGFB1,VWF	415 (7)
PLK2	kinase	9,67E-03	ATM,CD40,EDN1,IL15,IL15RA,IL1B,PLAT	
SKP2	other	9,67E-03	CCND1,CDKN2A,FOXO3,FOXP3,POU5F1,SLC2A1,TP73	991 (21)
SLC25A13	transporter	9,79E-03	ALPL,APOA4,CCND1,CD36,CXCL13,CYP2C8,EGFR,F11,FADS3,FMO3,MTHFD1L,NQO1,NVL,PTK2B,SERPINA3,SERPINB1,SERPINE2	
TRAP1	enzyme	1,04E-02	COX5B,COX8A,CRCP,ERBB2,HIF1A,HSPB2,HSPD1,ITGB1,LSS,NCAM1,PECAM1,PTGS2,SMAD4,SOD1,TXN2,VHL	
CD83	transmembrane	1,08E-02	IFNG,IL10,IL2,IL4,PTGS2	
CD209	other	1,08E-02	IL10,MMP2,MMP9,PTGS2,TNF	
CYP1A2	enzyme	1,08E-02	CCND1,CYP17A1,GSTM2,GSTM3,IFNLR1,NQO1,SHANK2,ST3GAL4,TRPM8,UGT1A6	
FOXF2	transcription reg	1,08E-02	ACTA2,CTNNB1,FOXF1,PDGFRA,WNT5A	
Foxo	group	1,08E-02	ABCB1,ABCC2,CDKN2B,IL7R,TRIB3	
Foxp1	transcription reg	1,08E-02	CNR1,GJA1,IFNG,IL2,MYH7,NPPA,PCK1,PPARGC1A,RYR1,SCGB1A1	
IFNA4	cytokine	1,08E-02	ATP2B4,CCL8,CD69,IFIH1,IFNG,Ly6a (includes others),OASL,SLCO3A1,STAT4,TREML2	
IFNA8	cytokine	1,08E-02	CCL8,HAMP,IFIH1,IFNG,STAT4	
IFNA16	cytokine	1,08E-02	CCL8,HAMP,IFIH1,IFNG,STAT4	
MT-TM	other	1,08E-02	MT-CO1,MT-CO2,MT-CYB,MT-ND1,MT-TL1	
RFX5	transcription reg	1,08E-02	COL1A1,COL1A2,HLA-B,HLA-DRA,HLA-DRB1	
SELENOS	other	1,08E-02	ADIPOQ,CAV1,IL6,PPARG,TNF	
THRAP3	transcription reg	1,08E-02	ADIPOQ,CCND1,HAS2,NR3C1,TXNIP	
TOPBP1	other	1,08E-02	BAX,BLM,CDKN2B,IGFBP3,MMP3	
AMBP	transporter	1,12E-02	ACTA2,IL1B,RELA,TNFRSF1A	
ATF5	transcription reg	1,12E-02	GAS5,PLAT,SAA1,TXNIP	
CAMK2A	kinase	1,12E-02	BDNF,FOS,HAMP,WNT3	
CARTPT	other	1,12E-02	CARTPT,FOS,HAMP,TRH	
CXCL13	cytokine	1,12E-02	IL10,LTA,MMP1,TNFSF11	
FTH1	enzyme	1,12E-02	HBB,IL10,SHMT1,TFRC	
HBP1	transcription reg	1,12E-02	CCND1,CDKN2A,MYOD1,PTGS2	
HLA-G	other	1,12E-02	CXCR4,FAS,IFNG,KIR2DL4	
HOXA1	transcription reg	1,12E-02	FGF5,GATA4,Ly6a (includes others),SLC14A1	
IL9R	transmembrane	1,12E-02	IL13,IL5,IL6,SELL	
LINC01139	other	1,12E-02	ANGPTL4,IGFBP3,LDHA,MAPK1	
LY6K	other	1,12E-02	ABCG2,CCN2,CD34,SERPINE1	
MIR320	group	1,12E-02	EDN1,FN1,MMP9,TFRC	
miR-378a-3p (a	mature microRN	1,12E-02	CDK6,FOXO1,FOXO3,IGF1R	
NCK1	kinase	1,12E-02	CD69,FOS,IL2,PRL	
PA2G4	transcription reg	1,12E-02	AR,ERBB2,GDF15,KLK2	
PARP	group	1,12E-02	APOE,CDKN2A,NOS2,TP53	
PLCB1	enzyme	1,12E-02	MAPK1,MAPK3,NPPA,PTGS2	
RANBP9	other	1,12E-02	FOS,JUN,PTK2B,TP73	
RLIM	enzyme	1,12E-02	CCN2,CDKN2B,FN1,SERPINE1	
SH2B1	other	1,12E-02	AGRP,NPY,PDX1,PLAUR	
TAF5	transcription reg	1,12E-02	DIO1,GHR,HAMP,IGF1	
TDGF1	growth factor	1,12E-02	MYH7,MYL2,NPPA,STAT3	
TEF	transcription reg	1,12E-02	AQP4,MYLK,PPARA,SCNN1A	
TP53BP2	other	1,12E-02	BAX,CCN2,CTNNB1,FAS	
TRPM8	ion channel	1,12E-02	GPX4,HSPA1A/HSPA1B,SOD1,UCP3	
TYRO3	kinase	1,12E-02	IL1B,IL6,MITF,TNF	
ZGPAT	transcription reg	1,12E-02	EGFR,FGF5,PTEN,VCAM1	
Cdk	group	1,13E-02	CCL2,CCL5,CXCL8,IL6,PPARGC1A,RGS2,TXNIP,UCP2	
SLC16A2	transporter	1,13E-02	DIO1,DIO3,SHH,SLC7A8,SLCO1B3,SLCO1C1,SLCO3A1,TRH	
ATG5	other	1,20E-02	HTT,IFIH1,IFNG,IKBKE,PSEN1,RELA,SCARB1	
mir-142	microRNA	1,20E-02	ABCG2,IL6,IL6ST,MYB,NFKB2,TGFBR1,TNF	
TRIB3	kinase	1,20E-02	BGLAP,CTH,GDF15,PPARG,PRKN,STC2,TRIB3	
SCX	transcription reg	1,21E-02	COL1A1,MMP3,POSTN,SPP1,TIMP3,TNC	
SMARCE1	transcription reg	1,21E-02	BGLAP,BRCA1,BRCA2,FOS,PGR,TFF1	
YWHAZ	enzyme	1,21E-02	CTNNB1,MMP1,MMP7,PPARG,SMAD3,TP53	
ZNF217	transcription reg	1,29E-02	ADM,ATL1,ATP10D,CCL2,CDKN2B,DPP6,ERBB3,EVX1,GATA4,IGFBP3,MAP2K5,NRXN3,PLAT,RGS20	
Secretase gamn	complex	1,36E-02	HES1,IL10,IL17A,IL22,IL2RA,MME,NOTCH1,SLC2A1	
Ampa Receptor	complex	1,43E-02	BDNF,EGFR,ERBB2	
ANGPTL6	other	1,43E-02	ANGPT1,LEP,VEGFA	
ANKHD1/ANKH	other	1,43E-02	CCND1,mir-196,VEGFA	
BICC1	other	1,43E-02	EGF,EGFR,HBEGF	
C4A/C4B	other	1,43E-02	C4A/C4B,C5,TNF	
CACNA1C	ion channel	1,43E-02	CACNA1C,CAV1,PTGS2	
CALCB	other	1,43E-02	lL4,IL9,PRL	
Camk	complex	1,43E-02	CCK,KDR,MYL2	
Casp12	peptidase	1,43E-02	IL18,MMP3,TNF	
CCL15	cytokine	1,43E-02	CXCL8,ICAM1,IL6	
CDH13	other	1,43E-02	ADIPOQ,CCND1,CTNNB1	
CR1	transmembrane	1,43E-02	C3,IFNG,IL2	
CTSC	peptidase	1,43E-02	IL1B,IL6,TNF	
CXCL5	cytokine	1,43E-02	ITGAM,TNF,TNFSF11	
CXXC4	other	1,43E-02	CCND1,MMP7,TET2	
CXXC5	other	1,43E-02	ACTA2,CTNNB1,KDR	
DBH-AS1	other	1,43E-02	CCND1,CDK6,CDKN2A	
DKK2	other	1,43E-02	CD69,IFNG,SPP1	
DLX4	transcription reg	1,43E-02	BRCA1,HBB,VEGFA	
DNM1L	enzyme	1,43E-02	FUT4,MFN1,POU5F1	
DYNLL1	other	1,43E-02	FOS,NOS1,TFF1	
ERCC1	enzyme	1,43E-02	DIO1,GHR,IGF1	
ERCC3	enzyme	1,43E-02	DIO1,GHR,IGF1	
EZH1	enzyme	1,43E-02	IL6,TNF,TOLLIP	
FKBP8	other	1,43E-02	HIF1A,MMP9,SHH	
GMFG	growth factor	1,43E-02	IL6,ITGB1,TNF	
GPR119	G-protein coupl	1,43E-02	ABCA1,GCG,GLP1R	
Hmgb2 (include	transcription reg	1,43E-02	MMP14,NFKB2,TGFB3	
Irs3	other	1,43E-02	IRS2,LEP,SREBF1	
KCNQ1OT1	other	1,43E-02	KCNQ1,mir-214,SMAD4	
LDL-cholesterol	complex	1,43E-02	CXCR4,ICAM1,THBD	
MC2R	G-protein coupl	1,43E-02	HAMP,IL6,POMC	
miR-219a-5p (a	mature microRN	1,43E-02	ALOX5,CD14,TNFRSF1B	
miR-320b (and	mature microRN	1,43E-02	AQP1,AQP4,IGF1	
MMP13	peptidase	1,43E-02	COL1A1,TGFB1,TNF	
Msx3	transcription reg	1,43E-02	IGF1,PPARG,TNF	
P110	group	1,43E-02	ABCC1,COL4A1,IL6	
PAPPA	peptidase	1,43E-02	ABCA1,PAPPA,SCARB1	
PDZK1IP1	other	1,43E-02	MSRA,PTGS1,SCARB1	
PEBP4	other	1,43E-02	ESR1,TFF1,TP53	

PIP5K1B	kinase	1,43E-02	IL1B,IL6,TNF	
PITX3	transcription reg	1,43E-02	BDNF,POMC,TH	
PMCH	other	1,43E-02	GRIA1,LEP,POMC	
PRKAB2	kinase	1,43E-02	IL6,INS,NFKB1	
PRKD2	kinase	1,43E-02	CXCL8,ITGA2,KDR	
PXN	other	1,43E-02	CCND1,FSHR,VCL	
RBBP4	enzyme	1,43E-02	HBG1,KRAS,LHCGR	
RFC1	transcription reg	1,43E-02	PPARG,RELA,VIPR1	
Rhox4b (include	transcription reg	1,43E-02	CD34,KDR,NKX2-5	
SIX3	transcription reg	1,43E-02	CCND1,PDGFRA,RHO	
SLC7A11-AS1	other	1,43E-02	CCND1,GCLM,JUN	
SMARCD1	transcription reg	1,43E-02	BAX,KLK2,MMP1	
SNIP1	other	1,43E-02	CAD,CCND1,SMAD1	
SOX15	transcription reg	1,43E-02	CCN2,CKM,MYOD1	
SPTAN1	other	1,43E-02	ITGAV,ITGB3,SPTBN4	
SPTBN2	other	1,43E-02	NCAM1,NPY,SLC1A6	
SRPK1	kinase	1,43E-02	INSR,RAC1,VEGFA	
TADA3	transcription reg	1,43E-02	PGR,RARB,TFF1	
THBS2	other	1,43E-02	HES1,HES5,MMP2	
TRPC3	ion channel	1,43E-02	CCND1,TRPC1,VCAM1	
UBA1	enzyme	1,43E-02	CCND1,NOS1,TP53	
UBP1	transcription reg	1,43E-02	CD40,CYP11A1,GRHL1	
VIPAS39	other	1,43E-02	SELP,THBS1,VWF	
WIF1	other	1,43E-02	CTNNB1,MITF,SFRP2	
WRN	enzyme	1,43E-02	CXCL8,HIF1A,POU5F1	
AQP1	transporter	1,45E-02	AKR1B1,CES1,CTNNB1,LCN2,TH	
CREB3	transcription reg	1,45E-02	FKBP4,INSIG1,INSIG2,MMP9,SREBF1	
CSF2RB	transmembrane	1,45E-02	ADGRE1,FOS,IL6,ITGAM,JUN	
GAS2L3	other	1,45E-02	EPHX1,F2R,FAS,SLC19A2,TP53	
IFT57	other	1,45E-02	BDNF,MT-ND1,MT-ND4,SDHB,SHH	
MDK	growth factor	1,45E-02	ACE,ACTA2,PLAT,PTPRC,RELA	
TGIF1	transcription reg	1,45E-02	CXCL8,DRD1,IL1B,IL6,RARB	
VIPR1	G-protein coupl	1,45E-02	CCL5,CD40,IL10,NOS2,TNF	
mir-181	microRNA	1,46E-02	AR,CD69,CDKN2A,MME,MMP14,PTEN,PTPN11,PTPN22,RGS5,TIMP3	
PRKAR2B	kinase	1,47E-02	FOS,IL2,LEP,NR4A3,PDYN,PPARG,UCP1	
TAF6	transcription reg	1,47E-02	ATF3,BCL11B,HAMP,HES1,HLA-DRA,JUN,SRSF3	
CISH	other	1,53E-02	ID3,IFNG,IL2,IL2RA,IL4,TNF	
EIF4G1	translation regu	1,53E-02	ATM,BRCA1,BRCA2,HIF1A,TP53,TP53BP1	
RAG1	enzyme	1,53E-02	CD2,IFNG,IL2,IL23A,IL2RA,TLR7	
RBL2	other	1,59E-02	AURKA,BRCA1,CAMKK2,CCND1,CDKN2A,DHFR,FAS,GRK6,MYOD1,PRIM2,TERT,TNF,TP73,TYMS,UCK2,VEGFA,XRCC3	
PIK3CD	kinase	1,61E-02	CXCL8,IFNG,IL17A,IL2,IL4,IL5,MAF,TNF	
CDKN2C	transcription reg	1,63E-02	CCL2,CDKN2A,CDKN2B,MMP3	
Cebp	complex	1,63E-02	CXCL8,IL10,IL6,MYOD1	
CIC	transcription reg	1,63E-02	CCND1,ETV5,ITGA2,SLC20A1	
CLEC4A	transmembrane	1,63E-02	IL10,IL17A,IL4,TNF	
DRD1	G-protein coupl	1,63E-02	BDNF,DRD3,FOS,HTR1B	
HCK	kinase	1,63E-02	CD36,IL6,MAOA,TNF	
HSP90AA1	enzyme	1,63E-02	CYP1B1,FN1,GJA1,GRK3	
KLRD1	transmembrane	1,63E-02	IFNG,IL2RA,NCR3,TNF	
LIMA1	other	1,63E-02	IL13RA2,MMP7,VCAN,VDR	
LINC-ROR	other	1,63E-02	FAS,NOTCH1,POU5F1,TP53	
MAP3K11	kinase	1,63E-02	CXCL8,IL4,MMP7,RELA	
MED14	transcription reg	1,63E-02	CD36,IGFBP1,NR3C1,TFF1	
METTL3	enzyme	1,63E-02	SERPINE2,SOCS1,SOCS3,TIMP1	
mGluR	group	1,63E-02	BDNF,EGFR,ERBB2,FMR1	
miR-130a-3p (a	mature microRN	1,63E-02	AQP4,DICER1,SMAD4,ZFPM2	
NTS	other	1,63E-02	CXCL8,FOS,PRL,TH	
RFX2	transcription reg	1,63E-02	COL1A2,HLA-DRA,IL5RA,LMNA	
SFRP4	transmembrane	1,63E-02	CCND1,CTNNB1,FN1,HAMP	
TBX1	transcription reg	1,63E-02	BMP4,FGF10,FLT4,PITX2	
VSIR	other	1,63E-02	CCL11,IFNG,IL17A,TNF	
RICTOR	other	1,71E-02	AR,ATP6V1B1,BAX,CD69,COX8A,DRD2,FOXP3,GCK,HIF1A,IFNG,IGFBP1,IL17A,IL4,IL7R,IRS2,LEPR,NAT8,NDUFAB1,NDUFB3,PRKCA,PRKCB,PRKCG,PSMA4,PSMA6,PSMB4,PSMB8,PSMB9,PTEN,PTGS2,RAC1,SDHB,SDHC,SDHD,SGK1,SLC10A2,SREBF1,VCAM1	
mir-210	microRNA	1,72E-02	ARG1,BDNF,CCN2,CDKN2A,CXCL12,DHFR,FOXP3,GIT2,IL16,KDR,NCAM1,NUP210,PTPN1,SDF2,SDHD,TCF7L2	
FCGR2B	transmembrane	1,78E-02	CCL5,IL10,IL1A,SOCS1,SOCS3,TNF,VEGFA	
PTCH1	transmembrane	1,78E-02	CCND1,FOXF1,IGF2,MYOD1,PDGFRA,PDX1,TNNT3	
EFNA2	kinase	1,87E-02	BDNF,CCN2,CD247,CDC5L,CSF2,ETV5,NEDD4L,NOS1,PLAT,RUNX1,SLC20A1	
CXCR2	G-protein coupl	1,90E-02	IL10,IL12A,IL6,NOS2,PPARG,TNF	
DNAJB6	transcription reg	1,90E-02	CTNNB1,GCM1,KISS1,SPP1,TNF	
DROSHA	enzyme	1,90E-02	KRAS,let-7,mir-143,mir-27,THBS1	
E2F2	transcription reg	1,90E-02	CCND1,CDKN2A,DHFR,ECE1,FGFR2,IL6,let-7,mir-27,MYB,SERPINE1,TERT,TOPBP1,TP53	
GAB1	other	1,90E-02	ANGPT1,ARG1,CCL5,IL1B,IL6	
mir-451	microRNA	1,90E-02	CD69,IL2RA,KLF7,RAC1,RASA1	
MYCBP2	enzyme	1,90E-02	BAZ1B,MYO5A,MYO6,PRKCB,ROCK2	
NBEAL2	other	1,90E-02	GATA2,MITF,SELP,THBS1,VWF	
NCAM1	other	1,90E-02	EGFR,HSPA4,NCAM1,NFKBIA,THBS1	
SDCBP	enzyme	1,90E-02	CTNNB1,EGFR,MMP2,TGFBR1,TP53	
SGPL1	enzyme	1,90E-02	ABCA1,ABCB1,ABCC1,BAX,PPARG,PTGS2	
Smad2/3-Smad	complex	1,90E-02	CDKN2B,COL1A1,COL1A2,IGFBP3,SERPINE1	
SS18	transcription reg	1,90E-02	FGFR2,GCH1,IGF2,NFATC1,RET,SALL1,SOCS3,SYNE1	
ZC3H14	other	1,90E-02	IL15,IL15RA,LTA,PLAT,TSC22D1	
ACVR1	kinase	1,94E-02	ALPL,CCN3,EDIL3,HNF4A,ICAM1,IL33,SELE,TSLP,VCAM1	
IFIH1	enzyme	1,94E-02	CCL2,CCL5,FAS,IL12B,IL1B,IL6,Ly6a (includes others),NFKBIA,TNF	
MYOC	other	2,03E-02	CA2,CNP,FBN1,FN1,ITGB1,JDP2,MFAP2,PGR,PRKCB,PTEN,PTGER4,PXDN,SLC2A3,SPP1,STC2	
miR-124-3p (an	mature microRN	2,06E-02	ACAA2,AHR,ALDH9A1,BDNF,CAV1,CCL2,CCN2,CD59,CDCA7,CDK6,CYP1B1,DRAM1,F11R,GSN,HES1,ITGB1,JAG1,LDLR,LDLRAP1,MTPN,MYH9,NFATC1,NR3C2,RARG,RELA,RNPEPL1,SLC17A5,SLC22A5,SMAD5,STAT3,UHRF1,USP49	
MLXIPL	transcription reg	2,13E-02	CPT1A,FGF21,GCK,HIF1A,PPARA,SLC2A2,TXNIP	
HDL-cholestero	complex	2,23E-02	APOB,DDR2,DHCR7,FDFT1,MSMO1,RPTOR,SLC2A2,TRIB3	
ACO1	enzyme	2,26E-02	IGF1,IGFBP1,IGFBP3,TFRC	
AVPR1A	G-protein coupl	2,26E-02	BGLAP,IL4,NPPA,PPP3CA	
CLEC1B	transmembrane	2,26E-02	CXCL12,IL10,SPP1,TNC	
CTNNBIP1	other	2,26E-02	CCND1,HMGCR,KLK2,RAC1	
DMRT1	transcription reg	2,26E-02	AR,BMPR1A,DHCR7,FGF10,FGFR2,HLA-DQA1,IGF1R,IGF2R,IGFBP3,MAPK1,NR1H3,POU5F1,RET,SHBG,TOX2,VCL	
G protein alpha	group	2,26E-02	F2R,FCGR2A,FCGR2B,mir-146	
LRAT	enzyme	2,26E-02	HGF,PDK4,PPARD,RARB	
miR-375-3p (mi	mature microRN	2,26E-02	ADIPOR2,HNF1B,JAK2,MTPN	
NRG4	growth factor	2,26E-02	ABCA1,APOC4,GCK,SREBF1	

PAWR	transcription reg	2,26E-02	CCL11,IL2RA,MAPK1,MAPK3	
PIK3R2	kinase	2,26E-02	FOXO1,IFNG,IL2,PIK3R1	
RB1CC1	other	2,26E-02	CCL5,CCND1,CDKN2B,SERPINE1	
S100A12	other	2,26E-02	CCND1,IL22,IL6,MMP2	
SH3KBP1	other	2,26E-02	BCL2A1,FN1,HIF1A,SERPINE1	
SORT1	G-protein coupl	2,26E-02	ACTN2,SLC2A1,SLC2A4,TNF	
WWC1	transcription reg	2,26E-02	BMP2,CCN2,FGF1,TFF1	
ADCYAP1R1	G-protein coupl	2,32E-02	BDNF,FOS,PER2	
AFF1	transcription reg	2,32E-02	IGF1,PTEN,TERT	
AGR2	other	2,32E-02	CDKN2A,EGFR,FOS	
AKIRIN2	other	2,32E-02	CCND1,IL6,MMP9	
AMELY	growth factor	2,32E-02	ALPL,BGLAP,SPP1	
ASCL2	transcription reg	2,32E-02	CXCR4,CYP19A1,TFF1	
ATE1	enzyme	2,32E-02	CCND1,JUN,MYH7	
CASQ2	other	2,32E-02	CASQ2,NPPA,RYR2	
CBR3-AS1	other	2,32E-02	CCND1,ERBB2,TGFB1	
CCN4	other	2,32E-02	CCND1,CTNNB1,MMP1	
CD2AP	other	2,32E-02	IL2,NPHS1,TGFB1	
CTSE	peptidase	2,32E-02	CD40,IL18,IL1B	
DEFB4A/DEFB4I	other	2,32E-02	IL13,IL18,IL4	
DLG1	kinase	2,32E-02	IFNG,PTEN,TNF	
DMTF1	transcription reg	2,32E-02	ANPEP,CDKN2A,TP53	
ERBIN	other	2,32E-02	CDKN2B,ERBB2,SERPINE1	
FNIP1	other	2,32E-02	MYH7,PPARGC1A,TNNC1	
GABBR2	G-protein coupl	2,32E-02	CASR,GABBR2,GRIA1	
GLP1R	G-protein coupl	2,32E-02	ABCA1,FOS,IL6	
HIST1H4C	other	2,32E-02	AFP,PGR,TGFBR2	
HMGCR	enzyme	2,32E-02	CCN2,HMGCR,IL1B	
HNRNPC	other	2,32E-02	CD40,HBB,HBG1	
HP	peptidase	2,32E-02	ADIPOQ,HMOX1,REN	
IGFBP4	other	2,32E-02	ACTA2,IGF1,IGFBP3	
KHDRBS1	transcription reg	2,32E-02	CCND1,ECE1,LEP	
LAX1	other	2,32E-02	IL6,LAT2,TNF	
LHB	other	2,32E-02	HAMP,HSD3B1,HSD3B2	
LRP2	transporter	2,32E-02	BMP4,NLRP3,SHH	
MARCKSL1	other	2,32E-02	CTNNB1,MYH7,NPPA	
miR-197-3p (an	mature microRN	2,32E-02	IL6,TGFBR2,TNF	
miR-491-5p (an	mature microRN	2,32E-02	AR,MMP2,MMP9	
miR-494-3p (mi	mature microRN	2,32E-02	HMOX1,KIT,PTEN	
MRC1	transmembrane	2,32E-02	CCL5,IFNG,NOS2	
NACC1	transcription reg	2,32E-02	BAX,HMGB1,TP53	
nicotinic acetyld	complex	2,32E-02	FOS,JUN,PNMT	
NKX3-2	transcription reg	2,32E-02	FGF10,FGFR3,POSTN	
OGN	growth factor	2,32E-02	BGLAP,CRHR1,CTNNB1	
OXTR	G-protein coupl	2,32E-02	BGLAP,FOS,HAMP	
PCSK9	peptidase	2,32E-02	APOB,CYP7A1,LDLR	
PILRA	other	2,32E-02	IL1B,IL6,TNF	
PRKG2	kinase	2,32E-02	FOS,GRIA1,PDGFRA	
PROK1	growth factor	2,32E-02	CCN2,CXCL8,PTGS2	
PSENEN	peptidase	2,32E-02	HES5,PSEN1,TP53	
PTGDS	enzyme	2,32E-02	BAX,PTGDR,PTPN11	
PTK6	kinase	2,32E-02	CYP11A1,EGFR,FABP2	
PTPRS	phosphatase	2,32E-02	IGF1,PRL,SST	
RAP1GAP	other	2,32E-02	CCND1,CDK6,FOS	
RASSF8	other	2,32E-02	DDAH1,POSTN,TGFB3	
SCGB3A2	other	2,32E-02	MMP12,MMP14,MMP2	
SDHA	enzyme	2,32E-02	HMOX1,SLC2A1,SLC2A4	
SERPINA4	other	2,32E-02	CCL2,NOS3,VCAM1	
Sfk	group	2,32E-02	ICAM1,IL1B,NOS2	
SLC19A1	transporter	2,32E-02	CALCR,Ly6a (includes others),PSMB8	
SLC5A8	transporter	2,32E-02	BAX,TNFSF10,TP53	
Smad1/5/8-Sma	complex	2,32E-02	NKX2-5,PTGS2,SMAD6	
TDO2	enzyme	2,32E-02	AHR,PTGS2,SLC1A4	
TIMD4	other	2,32E-02	IL13,IL4,IL6	
TMPO	other	2,32E-02	COL1A1,COL3A1,TIMP2	
TNIK	kinase	2,32E-02	CCND1,GRIA1,TCF7	
TRKC-miR2	microRNA	2,32E-02	CCND1,CTNNB1,TNF	
TRPA1	transporter	2,32E-02	IL1B,IL4,IL6	
ZNF43	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF85	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF100	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF254	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF429	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF431	transcription reg	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF528	other	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF665	other	2,32E-02	DDAH1,POSTN,TGFB3	
ZNF708	other	2,32E-02	DDAH1,POSTN,TGFB3	
miR-181a-5p (a	mature microRN	2,33E-02	CD69,ESR1,KRAS,MMP14,PGR,TIMP3	
Calmodulin	group	2,38E-02	BDNF,EPHB6,FLT3,HTT,KDR,KLF5,MYLK,NOS1,NPAS2,SMAD2,SYT9	
ZBTB17	transcription reg	2,41E-02	CCND1,CD46,CDKN2B,JUN,KIT,KLK8,LDLR,NTRK1,NUF2,OSMR,PRC1,PSRC1,SOCS1,ZFP36	
AGPAT2	enzyme	2,43E-02	ADIPOQ,LEP,PLIN1,PPARG,SLC2A4	
AKR1B1	enzyme	2,43E-02	CCND1,CPT1A,MMP2,NOS2,PPARG	
DLK1	other	2,43E-02	IGF1R,IL6,NOTCH1,PPARG,REL	
GFI1B	transcription reg	2,43E-02	FOXO1,GATA2,SOCS1,SOCS3,TGFBR3	
LYL1	transcription reg	2,43E-02	ADGRG1,BRCA1,ID3,ITGA2,NFKB1	
miR-9-5p (and c	mature microRN	2,43E-02	FOXO1,GCM1,JAK2,NFKB1,NTRK3	
stallimycin	biologic drug	3,08E-06	BMP7,CXCL8,IFIH1,IFNG,IL1A,IL1B,IL24,IL6,IL7R,IL9,NOS2,PML,PYHIN1,TNF,TNFSF10,TNFSF4	906 (15)
NFASC	other	2,43E-02	BCAN,DCTN5,KIF5A,KLC1,SPTBN4	
SEL1L	other	2,43E-02	HES5,NOTCH1,PTEN,TIMP1,TIMP2	
SLC6A3	transporter	2,43E-02	CDK5R1,DRD2,GHRH,GRIA1,TH	
RTN4	other	2,49E-02	BDNF,DYNC1H1,FGF1,IL12B,IL6,JUN,MYL2,NQO1,RHO,VEGFA	
KDR	kinase	2,57E-02	CTLA4,HAMP,HMOX1,KDR,MMP14,NOTCH1,PAX2,PTGS2,SELE	
14-3-3	group	2,60E-02	CDKN2A,ZFP36	
ABCG2	transporter	2,60E-02	ABCG2,GSR	
AGAP2	enzyme	2,60E-02	CCND1,TP53	
Akr1b7	enzyme	2,60E-02	ADIPOQ,LEP	
Aldosterone-MI	complex	2,60E-02	KRAS,SGK1	
ALPL	phosphatase	2,60E-02	ALPL,SPP1	
Ap1 gamma	group	2,60E-02	CD28,HLA-A	
APBB2	other	2,60E-02	LRP1,TYMS	

ARHGAP1	other	2,60E-02	CDKN2A,TP53	
ARHGEF11	other	2,60E-02	ABCA1,FOS	
ARID1B	transcription reg	2,60E-02	ALPL,FOS	
ASH1L	transcription reg	2,60E-02	IL6,TNFAIP3	
ASH2L	transcription reg	2,60E-02	ESR1,MMP9	
ATF7IP	transcription reg	2,60E-02	CDKN2A,SNRPN	
AZU1	peptidase	2,60E-02	IL1B,TNF	
BCAT2	enzyme	2,60E-02	ADIPOQ,LEP	
BCKDHA	enzyme	2,60E-02	CDKN2A,RARB	
BIRC6	enzyme	2,60E-02	BAX,TP53	
BTG1	transcription reg	2,60E-02	JUN,NR3C1	
BTN3A1	other	2,60E-02	IFNG,IL2	
BUB3	other	2,60E-02	CDKN2A,TP53	
C1QTNF6	other	2,60E-02	IL10,TNF	
C1QTNF12	other	2,60E-02	IL1B,TNF	
CACNA1D	ion channel	2,60E-02	CACNA1C,RYR2	
CARD8	other	2,60E-02	BCL2A1,IL1B	
CASP10	peptidase	2,60E-02	IL6,TNF	
CCL25	cytokine	2,60E-02	IL17A,MMP1	
CCNL2	other	2,60E-02	BAX,TP53	
CD7	other	2,60E-02	IFNG,TNF	
CD34	other	2,60E-02	IL10,TNF	
CDK5R2	other	2,60E-02	BDNF,FOS	
CHCHD4	enzyme	2,60E-02	HIF1A,MT-CO2	
CHST15	enzyme	2,60E-02	CCL5,IL6	
CHTOP	other	2,60E-02	LTF,TFF1	
CIDEB	other	2,60E-02	ADIPOQ,LEP	
CISD1	other	2,60E-02	ADIPOQ,SIRT1	
CLASP2	other	2,60E-02	GRIA1,SNAP25	
CLIP1	other	2,60E-02	IL6,TNF	
CLTRN	other	2,60E-02	ATP1A1,SCNN1A	
CNP	enzyme	2,60E-02	NOS2,NPPB	
Col17a1	other	2,60E-02	ELANE,SERPINA1	
COL7A1	other	2,60E-02	THBS1,WNT5A	
CPEB3	translation regu	2,60E-02	EGFR,GRIA1	
CRIP2	other	2,60E-02	CXCL8,IL6	
CSNK1E	kinase	2,60E-02	PER1,SERPINE1	
CTBP1-DT	other	2,60E-02	SMAD3,TP53	
CYCS	transporter	2,60E-02	IFNG,IL2	
CYP2C9	enzyme	2,60E-02	CCND1,HBA1/HBA2	
DDX54	transcription reg	2,60E-02	ERBB2,TFF1	
DERL1	other	2,60E-02	ABCC8,MMP2	
DGKH	kinase	2,60E-02	CCL2,CXCL8	
DHPS	enzyme	2,60E-02	CDK5R1,IL2RA	
DHX15	enzyme	2,60E-02	IL6,TNF	
DLST	enzyme	2,60E-02	JUN,PIK3R1	
DNAJA2	enzyme	2,60E-02	IL17A,RORA	
DUSP9	phosphatase	2,60E-02	IL12B,PCK1	
EBF3	transcription reg	2,60E-02	ADCY3,SLC2A4	
EID2	other	2,60E-02	CDKN2B,CKM	
EPHA4	kinase	2,60E-02	HAMP,IGF1	
Ewsr1	other	2,60E-02	DROSHA,LMNA	
FAM49B	other	2,60E-02	CD69,IFNG	
Fascin	group	2,60E-02	CCN2,MMP9	
taspoglutide	biologic drug	4,55E-05	CPT1A,FABP1,FABP2,LIPC,PLIN1	
FDPS	enzyme	2,60E-02	ADRB2,CD69	
Fetal Hemoglob	complex	2,60E-02	HIF1A,HMOX1	
FKBP1B	enzyme	2,60E-02	FKBP1B,RYR2	
FKHR	group	2,60E-02	CCND1,VCAM1	
GC	transporter	2,60E-02	CYP24A1,CYP27B1	
GCA	other	2,60E-02	IL6,TNF	
GCDH	enzyme	2,60E-02	ANG,HAMP	
GCNT1	enzyme	2,60E-02	FOS,IL2	
GIMAP1-GIMAP	other	2,60E-02	HSPD1,IFNG	
GNG2	enzyme	2,60E-02	F2R,NFKB1	
GOPC	transporter	2,60E-02	ADRB1,CFTR	
GPC3	other	2,60E-02	CCND1,LDLR	
GPX4	enzyme	2,60E-02	IL6,MMP1	
GRK3	kinase	2,60E-02	ADRA2B,CD46	
GZMA	peptidase	2,60E-02	CCL2,CXCL8	
GÎ±12/13	group	2,60E-02	IGF1,MMP1	
HAO1	enzyme	2,60E-02	PDGFRA,PPARGC1A	
HES6	transcription reg	2,60E-02	HNF4A,MMP1	
HOXB8	transcription reg	2,60E-02	HAMP,MYLK	
HPRT1	enzyme	2,60E-02	IL4,P2RY1	
HSD17B14	enzyme	2,60E-02	IL23A,IL6	
HSPA4	other	2,60E-02	IDE,TGFB1	
Hspg	group	2,60E-02	MMP1,VEGFA	
IGF2-AS	other	2,60E-02	BDNF,IGF2	
IGF2BP3	translation regu	2,60E-02	ABCG2,IGF2	
IGHG1	other	2,60E-02	IFNG,TNF	
INPP5K	phosphatase	2,60E-02	IGF2,LEP	
ITGB8	other	2,60E-02	SMAD3,TGFB1	
JMY	transcription reg	2,60E-02	BAX,HTRA1	
JPH4	other	2,60E-02	IFNG,IL17A	
KIR2DL1/KIR2D	other	2,60E-02	IFNG,IL6	
KLF14	transcription reg	2,60E-02	FOXP3,PPARGC1A	
KLF16	transcription reg	2,60E-02	CYP1A1,HAMP	
KLHL2	other	2,60E-02	CCND1,JUN	
KLHL21	other	2,60E-02	NFKBIA,NFKBIZ	
KPNA2	transporter	2,60E-02	IL2,STK35	
KRT5	other	2,60E-02	ICAM1,VEGFA	
LAPTM4B	other	2,60E-02	BAX,TGFB1	
LDLRAP1	transporter	2,60E-02	HMGCR,LRP2	
LSS	enzyme	2,60E-02	ABCA1,LDLR	
Madcam1	other	2,60E-02	IFNG,TNF	
MAGI2	kinase	2,60E-02	NPHS1,PTEN	
MAP1LC3	group	2,60E-02	IL12B,TNF	
MAPK15	kinase	2,60E-02	AR,JUN	
MAT2B	enzyme	2,60E-02	CCND1,HMOX1	

MCHR1	G-protein coupl	2,60E-02	LEP,TRH	
MED24	transcription reg	2,60E-02	HAMP,HTRA1	
MGAT4A	enzyme	2,60E-02	CCND1,SLC2A2	
MGMT	enzyme	2,60E-02	ATM,TP53	
Miat	other	2,60E-02	FURIN,TGFB1	
Miat	other	2,60E-02	ICAM1,TNF	
mir-361	microRNA	2,60E-02	IL6,TNF	
mir-379	microRNA	2,60E-02	HIF1A,TP53	
mir-489	microRNA	2,60E-02	AR,PTPN11	
mir-497	microRNA	2,60E-02	CCND1,MAPK3	
mir-499	microRNA	2,60E-02	MYH7,PPP3CA	
mir-541	microRNA	2,60E-02	AR,PTPRN2	
mir-1180	microRNA	2,60E-02	AKT1,CTNNB1	
miR-485-3p (an	mature microRN	2,60E-02	KMT2C,NTRK3	
miR-615-3p (mi	mature microRN	2,60E-02	AR,PPARG	
miR-625-5p (an	mature microRN	2,60E-02	NTRK3,PTEN	
MUC5AC	peptidase	2,60E-02	IFNG,MMP7	
MYLIP	enzyme	2,60E-02	LDLR,LRP8	
N4BP1	other	2,60E-02	JUN,TP73	
NAAA	enzyme	2,60E-02	IL1B,TNF	
Naip1 (includes	other	2,60E-02	IL1B,NOS2	
NDUFAF3	other	2,60E-02	CCND1,ESR1	
NEU1	enzyme	2,60E-02	MTTP,SREBF2	
TGAL copolyme	biologic drug	2,91E-12	BDNF,CCL5,CXCL8,FOXP3,IFNG,IGF1,IL10,IL1B,IL1RN,IL4,NRG1,P2RX7,TGFB1,TNF	746 (16)
NEURL1	enzyme	2,60E-02	GRIA1,JAG1	
NFATC2IP	other	2,60E-02	IL4,NFATC1	
NIK	group	2,60E-02	CXCL8,IL6	
NKRF	transcription reg	2,60E-02	CXCL8,NOS2	
NRP2	kinase	2,60E-02	CTNNB1,S100A4	
OSR2	transcription reg	2,60E-02	OSR1,TGFB3	
PAG1	other	2,60E-02	FYN,IL2	
PDCD5	other	2,60E-02	ATP2A2,FOXP3	
PES1	other	2,60E-02	CCND1,HMOX1	
PIK3C3	kinase	2,60E-02	CDKN2A,IGF2	
PLEC	other	2,60E-02	CXCR4,IL6	
POFUT1	enzyme	2,60E-02	NOTCH1,NOTCH2	
POU3F4	transcription reg	2,60E-02	EPHA4,GCG	
PPP1R3C	phosphatase	2,60E-02	LEP,SLC2A1	
Prl3b1	growth factor	2,60E-02	ESR1,ESR2	
PSMC3	enzyme	2,60E-02	CDKN2A,TP53	
PTPN12	phosphatase	2,60E-02	IL6,TNF	
PTTG1IP	other	2,60E-02	CCND1,TSHR	
PURB	transcription reg	2,60E-02	ACTA2,HTRA1	
PVT1	other	2,60E-02	let-7,LIN28A	
RAB10	enzyme	2,60E-02	IL6,TNF	
RACGAP1	transporter	2,60E-02	CD14,CDC42	
RECQL	enzyme	2,60E-02	CSF2,HBB	
REG3G	other	2,60E-02	IL33,TSLP	
RING1	transcription reg	2,60E-02	FOS,JUN	
RNF8	enzyme	2,60E-02	RARA,RARB	
RNF144B	enzyme	2,60E-02	BAX,TP73	
RPS7	other	2,60E-02	PIK3R1,TP53	
S100A1	other	2,60E-02	NPPA,SLC8A1	
SCARB2	transmembrane	2,60E-02	IL6,TNF	
SERPINB3	other	2,60E-02	IL6,LRP1	
SKAP1	kinase	2,60E-02	IFNG,IL2	
SLC1A1	transporter	2,60E-02	DRD1,FOS	
SLC27A1	transporter	2,60E-02	MYH7,PPARG	
SLC2A5	transporter	2,60E-02	SLC2A5,SLC9A3	
SLC6A14	transporter	2,60E-02	IL1A,IL4	
SMCR8	other	2,60E-02	IL6,TNF	
SNX1	transporter	2,60E-02	AGTR1,EGFR	
SPEN	transcription reg	2,60E-02	BGLAP,HES1	
SPTBN1	other	2,60E-02	FOS,STAT3	
SRGAP1	other	2,60E-02	CCND1,CTNNB1	
SRSF5	other	2,60E-02	NR3C1,VEGFA	
STAB1	transporter	2,60E-02	IL10,TNF	
STK38	kinase	2,60E-02	IL6,TNF	
STRAP	other	2,60E-02	JUN,SERPINE1	
SUCO	other	2,60E-02	COL1A1,COL1A2	
TACR2	G-protein coupl	2,60E-02	IFNG,IL2	
TBC1D4	other	2,60E-02	ADIPOQ,SCNN1A	
TERF1	transcription reg	2,60E-02	CDKN2A,TP53	
TFPI2	other	2,60E-02	ABCB1,CCND1	
TH17 Cytokine	group	2,60E-02	CXCL8,IL6	
TIGAR	enzyme	2,60E-02	CCL2,TNFAIP3	
TOR2A	other	2,60E-02	ACAT1,FOS	
TPM1	other	2,60E-02	CALD1,TPM1	
TPSG1	peptidase	2,60E-02	IL13,IL6	
Trim30a/Trim3(	other	2,60E-02	IL6,TNF	
Trk Receptor	group	2,60E-02	AKT1,EDN1	
TSIX	other	2,60E-02	COL1A1,COL1A2	
TTC5	other	2,60E-02	BAX,TP53	
TUT4	enzyme	2,60E-02	IL6,let-7	
UBE2L3	enzyme	2,60E-02	NR3C1,TFF1	
urate oxidase	group	2,60E-02	IL13,IL5	
USP6	peptidase	2,60E-02	BMP4,MMP9	
VRK1	kinase	2,60E-02	HAMP,MMP1	
YEATS4	transcription reg	2,60E-02	CDKN2A,TP53	
ZNF300	transcription reg	2,60E-02	CXCL8,IL6	
ZNF335	transcription reg	2,60E-02	HAMP,MEF2C	
ZNF451	enzyme	2,60E-02	CDKN2B,SERPINE1	
BAX	transporter	2,81E-02	BAX,CCL5,CTSH,HLA-A,IL15,IL6,MMP12,MMP9,TIMP1,TNF	
TBX2	transcription reg	2,87E-02	ATF3,AURKA,CDKN2A,DBP,LIG1,NPPA,PRC1,PRIM2,PTEN,SREBF2,TGFB2,TRIB3,TYRP1	
PTF1A	transcription reg	2,98E-02	CACNA2D3,CELA1,ELANE,LMX1B,NPHS1,NPY,PAX2,PRKCQ,SLC6A5,TFAP2B,ZMAT4	
GNB1	enzyme	3,00E-02	AHR,APOA5,CNNM2,F2R,IL1B,NFKB1,PTGER4,THBD	
TFEB	transcription reg	3,00E-02	CCL17,CCL5,GBA,GLA,IL1B,IL6,TYRP1,VEGFA	
ALK	kinase	3,02E-02	FOXP3,IL10,POU5F1,SHH	
ATXN3	peptidase	3,02E-02	CXCL12,IL1RL1,MMP2,SOD2	
BCO1	enzyme	3,02E-02	BCO2,ELOVL2,PPARG,SCARB1	

BHLHE41	transcription reg	3,02E-02	ANGPTL4,IL4,MEF2C,MYOD1	
CD74	transmembrane	3,02E-02	BDNF,CXCL8,HIF1A,TPH2	
CDC37	other	3,02E-02	CDK6,CDKN2A,ERBB2,KIT	
ERFE	other	3,02E-02	CD36,FABP1,HAMP,SMAD6	
FRS2	other	3,02E-02	ACTA2,BMP4,ERBB2,Ly6a (includes others)	
JARID2	transcription reg	3,02E-02	CCND1,GATA2,NOTCH1,PTEN	
LAMA2	other	3,02E-02	ACTA2,CSK,DES,MMP9	
NLRC4	other	3,02E-02	IL17A,IL18,IL1B,NOS2	
PEMT	enzyme	3,02E-02	COL1A1,GCGR,TIMP1,TNF	
RBBP7	transcription reg	3,02E-02	GATA2,KIT,MS4A2,SLC4A1	
SLC4A1	transporter	3,02E-02	AQP1,C5,FCGR2A,ICAM4	
SPINT2	other	3,02E-02	HABP2,HAMP,PAPPA,TGFB1	
YWHAQ	other	3,02E-02	IL2,MMP1,MMP7,TP73	
BIRC2	enzyme	3,04E-02	CCL2,CXCL8,IL6,NFATC1,TNF	
BRD7	transcription reg	3,04E-02	BAX,CYP1A1,DICER1,ESR1,VCAN	
HOXA13	transcription reg	3,04E-02	AR,BMP2,BMP7,EPHA4,WNT5A	
IL31	other	3,04E-02	CCL2,CDK6,EGF,SOCS1,SOCS3	
IL21R	transmembrane	3,04E-02	IFNG,IL10,IL21R,IL4,SOCS3	
mir-101	microRNA	3,04E-02	ATM,COL1A1,COL3A1,PTGS2,TGFBR1	
mir-144	microRNA	3,04E-02	CD34,KLF7,RAC1,RASA1,VCAN	
PTP4A3	phosphatase	3,04E-02	CSK,FN1,IGF1R,ITGB3,PTEN	
SUV39H1	enzyme	3,04E-02	CDKN2B,FOXP3,HBB,IL2,RARB	
TNFRSF13C	transmembrane	3,04E-02	BCL2A1,CXCL8,IFNG,IL10,NFKB2	
MAP4K4	kinase	3,34E-02	ACAA2,ACADS,CHPT1,GRHPR,GYS1,IVD,MLXIPL,NDUFAB1,NT5C2,PDX1,PLCB4,PNPLA3,PON2,PPARG,PTGES,SLC2A4,SREBF1,ST3GAL4	
LHX2	transcription reg	3,38E-02	BDNF,COL1A1,DIO2,EDN2,GPR50,NQO1	
mir-183	microRNA	3,38E-02	FN1,IRS1,ITGB1,LRP1,PTEN,SERPINE2	
miR-203a-3p (a	mature microRN	3,38E-02	CDK6,F2RL1,PRKCA,SIRT1,SOCS3,VEGFA	
SGPP2	phosphatase	3,38E-02	HSPA4,HSPA8,HSPB7,IL1B,IL6,TNF	
Cdc42	enzyme	3,44E-02	ACTA2,CTSH,EDN2,FAS,GATA2,MYH9,NPPA,TNF	
ACTA2	other	3,45E-02	ACTA2,CCN2,MET	
Ahr-Arnt	complex	3,45E-02	CYP1A1,CYP1A2,CYP1B1	
AQP7	transporter	3,45E-02	BAX,INS,PRKCB	
tocilizumab	biologic drug	5,57E-07	CCL2,CCL5,CXCL8,IFNG,IL10,IL6,LPA	405 (8)
ARHGEF1	other	3,45E-02	CCND1,FOS,TRPC6	
AZI2	other	3,45E-02	IFNG,IL6,TNF	
C4BP	complex	3,45E-02	FDFT1,HMGCR,MSMO1	
CBX1	transcription reg	3,45E-02	CDKN2A,CKM,FOXP3	
CCDC80	other	3,45E-02	CCND1,LEP,PPARG	
CCL7	cytokine	3,45E-02	ICAM1,IL10,VCAM1	
CD82	other	3,45E-02	IL10,IL2,TIMP1	
CD8A	other	3,45E-02	IFNG,IL1B,TNF	
CERS6	transcription reg	3,45E-02	LEP,NOS2,TNF	
CSNK2A2	kinase	3,45E-02	CTNNB1,ESR1,FOXO3	
CXCR1	G-protein coupl	3,45E-02	BAX,CCND1,CXCL8	
DEPTOR	other	3,45E-02	CCL5,ICAM1,VCAM1	
DES	other	3,45E-02	ACE,SPP1,TGFB1	
DVL1	other	3,45E-02	CTNNB1,NPPA,PTGS2	
EFEMP1	enzyme	3,45E-02	RELA,SERPINE1,VEGFA	
ERRFI1	other	3,45E-02	IL1B,NFKB1,TNF	
FBLN5	other	3,45E-02	MMP2,SERPINA1,TGFB1	
FEM1A	transcription reg	3,45E-02	IL1B,IL6,TNF	
GADD45GIP1	other	3,45E-02	GCLC,HMOX1,HSPD1	
GAL3ST1	enzyme	3,45E-02	ITGB1,PCK1,SLC12A1	
GRIP1	transcription reg	3,45E-02	IGF1,PTGS2,TFF1	
GSN	other	3,45E-02	DNASE1,HAMP,NOS3	
GSTK1	enzyme	3,45E-02	ADIPOQ,IL18,TNF	
HSP	group	3,45E-02	IFNG,KCNH2,TNF	
HSPA8	enzyme	3,45E-02	HIF1A,MEF2D,TNF	
KSR1	kinase	3,45E-02	CDKN2A,CDKN2B,TP53	
LASP1	transporter	3,45E-02	CTNNB1,ITGA4,S100A4	
LATS1	kinase	3,45E-02	BAX,CCN2,PRL	
MAP3K12	kinase	3,45E-02	CRP,JUN,STAT3	
miR-140-5p (an	mature microRN	3,45E-02	CXCL12,SMAD3,VEGFA	
trastuzumab	biologic drug	3,04E-02	CCND1,CXCL8,ERBB2,IL6,NOS2	
miR-217-5p (an	mature microRN	3,45E-02	PPARA,PPARGC1A,SIRT1	
NDP	growth factor	3,45E-02	BDNF,EDN2,PSIP1	
NEU3	enzyme	3,45E-02	AR,MMP1,MMP7	
PADI4	enzyme	3,45E-02	IL6,OSGIN1,TNF	
PBX2	transcription reg	3,45E-02	CCL2,FOS,PDGFRA	
PDLIM7	other	3,45E-02	BGLAP,BMP2,SPP1	
PON2	enzyme	3,45E-02	CXCR2,IL6,TNF	
Ptgs2os2	other	3,45E-02	CCL5,IL6,TRAF1	
RBM38	other	3,45E-02	CDKN2A,TP53,TP73	
RGS16	other	3,45E-02	FABP1,FGF21,IL13	
RHOG	enzyme	3,45E-02	MAPK8,MYH7,RELA	
SENP7	peptidase	3,45E-02	CACNA1C,CXCL8,DHFR	
SMAD1/5	group	3,45E-02	HAMP,ID3,PLAUR	
TAPBP	transporter	3,45E-02	HLA-A,HLA-B,TAP1	
TERF2	transcription reg	3,45E-02	CDKN2A,MIF,TP53	
TNFAIP6	other	3,45E-02	ACTA2,HAMP,MMP9	
U1 snRNP	complex	3,45E-02	CCL5,IFNG,TNF	
UCA1	other	3,45E-02	CCND1,NPPA,PTEN	
triptorelin	biologic drug	1,77E-05	CYP19A1,FOS,GNRH1,GNRHR,JUN,NOS1,PGR	931 (19)
USP2	peptidase	3,45E-02	RARA,SERPINE1,TP53	
VCL	enzyme	3,45E-02	IL6,ITGB1,PTEN	
WNT7B	other	3,45E-02	CCND1,SHH,VEGFA	
ACVR1C	kinase	3,74E-02	CCND1,CDKN2B,FOS,NPY,SERPINE1	
ATXN1	transcription reg	3,74E-02	ATP2A2,PRKCG,SLC1A6,TRPC3,VEGFA	
C1QA	other	3,74E-02	F2R,IFNG,IL6,SERPINE1,TNF	
DUSP5	phosphatase	3,74E-02	CA2,CSF2,NPPA,SLPI,ZFP36	
EIF2S1	translation regu	3,74E-02	CAT,CCND1,GCLC,IFNG,NOS2	
HNRNPA1	enzyme	3,74E-02	FGG,IL6,KRAS,SREBF1,TNF	
NONO	transcription reg	3,74E-02	CDKN2A,CYP17A1,NOS3,PDE11A,PDE4D	
PPP1R13L	transcription reg	3,74E-02	CTNNB1,GJA1,ITGAV,ITGB1,SLC2A1	
RFX1	transcription reg	3,74E-02	COL1A1,COL1A2,HLA-DRA,IL5RA,LMNA	
WLS	other	3,74E-02	BMP4,BMPR2,CXCR2,FGF9,SHH	
TCOF1	transporter	3,76E-02	ACVR2A,ADM,AKR1B1,EGLN3,FABP3,GRHPR,HACD4,NAF1,RASA1,SLC2A1,TBX2,TXNRD1	
BCR	kinase	3,91E-02	HBB,IL24,NFATC1,POU5F1	
COL6A1	other	3,91E-02	CKM,COL6A5,ROCK1,TNC	

COL9A1	other	3,91E-02	FMOD,FN1,HSPG2,THBS4	
DEFB103A/DEFB	other	3,91E-02	IL13,IL18,IL4,PTGS2	
FCER2	transmembrane	3,91E-02	CXCL8,IL2RA,NOS2,TNF	
IDH2	enzyme	3,91E-02	ADIPOQ,FN1,PPARG,TGFB2	
IFNA5	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
IFNA6	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
IFNA7	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
IFNA10	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
IFNA14	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
IFNA21	cytokine	3,91E-02	CCL8,IFIH1,IFNG,STAT4	
MAPKAP1	other	3,91E-02	FOXP3,HIF1A,PTEN,SREBF1	
mir-322	microRNA	3,91E-02	CDKN2A,FGFR1,FN1,IGF1R	
NAE1	enzyme	3,91E-02	AURKA,BRCA1,CCND1,CDKN2B	
Ptprd	phosphatase	3,91E-02	CCL2,CEBPD,CXCL14,PSMB9	
PTPRE	phosphatase	3,91E-02	IL18,MET,STAT5A,TSC22D1	
SGPP1	phosphatase	3,91E-02	IL1B,IL6,PTGS2,TNF	
TGFBR3	kinase	3,91E-02	BAX,FN1,PTEN,SERPINE1	
WNT3	other	3,91E-02	CTNNB1,POSTN,PTGS2,WNT3	
GTF2IRD1	transcription reg	3,93E-02	ERAP1,FOS,KDR,PDC,POSTN,PPARA,RHO,STAT3	
mir-23	microRNA	4,01E-02	GATM,PTEN,PTK2B,SEMA6A,SOD2,SPP1	
DNASE2	enzyme	4,03E-02	IFNG,IL10,IL18,Ly6a (includes others),OAS3,TNF,TNFSF10	
EWSR1	other	4,03E-02	CCND1,CHEK2,ERBB2,F2RL1,FOS,KIT,NPY	
PCGEM1	other	4,46E-02	CYP11A1,G6PD,GSR,IDH2,LDHA,LSS,PDK4,SLC2A1	
DCAF1	kinase	4,53E-02	CCN3,PTGES,SOCS3,TNFSF10,TXNIP	
GLIS3	transcription reg	4,53E-02	GHRL,INS,PDX1,SLC2A2,SST	
miR-293-5p (an	mature microRN	4,53E-02	ADORA1,MADD,MAPK1,MMP9,SYNE1	
PAX7	transcription reg	4,53E-02	ABCA1,AHR,CAMK1D,CXCR4,F2RL1,GALNT13,GCH1,ID3,LRPAP1,NQO1,PLAGL1,PPARG	
SH2D1A	other	4,53E-02	ICOS,IFNG,IL17A,IL2,IL4	
TUG1	other	4,53E-02	BAX,BDNF,FUT4,IL6,TNF	
PLK1	kinase	4,64E-02	BAX,CTNNB1,EGFR,ESR1,PIK3R1,PLA2R1,TERT	
MEP1B	peptidase	4,70E-02	NDST1,PITX2,RBPJ,SLC12A5,TFRC,TLR6	
SFN	other	4,70E-02	CTNNB1,ERBB2,FKBP5,IL1R1,PDK4,SGK1	
APH1A	peptidase	4,81E-02	EGFR,PSEN1,TP53	
ASF1A	other	4,81E-02	POU5F1,SOX17,VCAM1	
CCND2	other	4,81E-02	CCND1,CDKN2A,VEGFA	
CD99	other	4,81E-02	CAV1,MMP9,PTPRC	
CDKN3	phosphatase	4,81E-02	DLK1,H19,IGF2R	
DDB1	other	4,81E-02	CDKN2A,FMOD,PTEN	
DUSP6	phosphatase	4,81E-02	ERCC1,ESR1,PCK1	
DUSP16	phosphatase	4,81E-02	IFNG,IL4,VCAM1	
ESRP1	other	4,81E-02	FGFR2,POU5F1,RAC1	
GLRX	enzyme	4,81E-02	HIF1A,ICAM1,VEGFA	
GRM1	G-protein coupl	4,81E-02	FMR1,HAMP,HIF1A	
Gulo	enzyme	4,81E-02	let-7,mir-143,mir-27	
ISGF3	complex	4,81E-02	HIF1A,IFIH1,TNFSF10	
JMJD6	transmembrane	4,81E-02	CCND1,IL12A,IL12B	
LIMS1	other	4,81E-02	GJA1,ITGB1,TGFB2	
LRRK2	kinase	4,81E-02	IL1B,NOS2,TNF	
MCAM	other	4,81E-02	ATF3,FN1,MMP2	
Mir218	microRNA	4,81E-02	CXCR4,SFRP2,SPP1	
miR-126a-3p (a	mature microRN	4,81E-02	IRS1,VCAM1,VEGFA	
miR-185-5p (an	mature microRN	4,81E-02	AKT1,CDC42,CDK6	
MNX1	transcription reg	4,81E-02	MET,PDX1,SLC2A2	
MSI2	other	4,81E-02	FN1,SMAD3,TGFBR1	
Mup1 (includes	other	4,81E-02	MLXIPL,PPARG,PPARGC1A	
urotensin II	biologic drug	1,46E-04	ALOX5,CXCL8,GHRH,SMAD3,UTS2R	
NDRG2	other	4,81E-02	BAX,MITF,MYH7	
NEK7	kinase	4,81E-02	EDN1,IL12A,PTGS2	
PHEX	peptidase	4,81E-02	PHEX,TNFRSF11B,TNFSF11	
Pki	group	4,81E-02	ACE,GNRHR,PRL	
Presenilin	group	4,81E-02	INSR,PML,RYR2	
PRRX1	transcription reg	4,81E-02	FOS,SHH,TNC	
PTMA	other	4,81E-02	IL1B,MMP9,TNF	
SERPINB2	other	4,81E-02	BAX,CD14,TP73	
SOX8	transcription reg	4,81E-02	DLK1,PHEX,VNN1	
SRD5A1	enzyme	4,81E-02	CYP11A1,CYP19A1,LCN2	
STK25	kinase	4,81E-02	CPT1B,GCK,HAMP	
UCHL5	peptidase	4,81E-02	PARP1,TOPBP1,TP73	
USP17L2 (includ	peptidase	4,81E-02	ABCG2,KIT,POU5F1	
VWF	other	4,81E-02	F8,HES1,SELP	
ACP1	phosphatase	4,87E-02	CTNNB1,FOS	
Activin	complex	4,87E-02	ACVR2B,GNRH1	
valspodar	biologic drug	4,87E-02	AVPR1A,SLC8A2	
vancomycin	biologic drug	1,25E-07	C3,C4A/C4B,CAT,CD14,CLU,CSF2,FCGR2A,FGA,FGB,GAS5,GCGR,GSTK1,GSTM3,HMOX1,IFNG,IGFBP1,IL10,IL17A,LCN2,NOX4,PSMB8,SOD2,SOD3,SPP1,TIMP1,TSPAN8	545 (10)
ADD2	other	4,87E-02	ADD1,ADD3	
vapreotide	biologic drug	3,31E-03	CCL2,CXCL8,THBS1	523 (7)
vasoactive intes	biologic drug	4,89E-06	CCL2,CXCL8,EGF,FOS,IL12A,IL17RA,MMP3,SNAP25,TLR4,TNFRSF11B,VEGFA	859 (19)
ADRA2A	G-protein coupl	4,87E-02	CYP1A1,TNF	
AMFR	transmembrane	4,87E-02	MFN1,MFN2	
ANKH	transporter	4,87E-02	SPP1,WNT5A	
APLP2	other	4,87E-02	EGFR,TP53	
ARID5B	transcription reg	4,87E-02	ACTA2,IFNG	
Bc1	translation regu	4,87E-02	ACTA2,SMAD3	
BRS3	G-protein coupl	4,87E-02	AGRP,LEP	
BST2	other	4,87E-02	IL6,TNF	
C1GALT1	enzyme	4,87E-02	BAX,GP1BA	
CALCR	G-protein coupl	4,87E-02	FOS,TP53	
Casein	group	4,87E-02	ICAM1,IL1B	
CBFA2T2	transcription reg	4,87E-02	CHGA,HES1	
CCDC134	other	4,87E-02	IFNG,TNF	
CCDC88B	enzyme	4,87E-02	IFNG,TNF	
CCKAR	G-protein coupl	4,87E-02	LEP,MET	
CCNA1	other	4,87E-02	MMP2,VEGFA	
Cd1	group	4,87E-02	IFNG,IL4	
CD300LD	other	4,87E-02	IL6,TNF	
CDC25B	phosphatase	4,87E-02	CCND1,TP53	
CDH3	other	4,87E-02	CDH15,HAMP	
CEBPZ	transcription reg	4,87E-02	COL1A2,CRP	
CELA2A	peptidase	4,87E-02	CDKN2A,SLPI	

CFL1	other	4,87E-02	ICAM1,JUN	
CHFR	enzyme	4,87E-02	AURKA,PARP1	
CHST2	enzyme	4,87E-02	IL10,IL4	
CHST4	enzyme	4,87E-02	IL10,IL4	
Cmtm2a	transcription reg	4,87E-02	CYP11A1,CYP17A1	
Collagen type V	complex	4,87E-02	BAX,CCND1	
CSH1/CSH2	other	4,87E-02	CYP2E1,PDX1	
DLL3	other	4,87E-02	HES1,HES5	
EDAR	transmembrane	4,87E-02	BMP4,SHH	
endothelin rece	group	4,87E-02	FOS,NPPA	
EPC1	transcription reg	4,87E-02	CKM,MYOD1	
F8	other	4,87E-02	IL2RA,TNF	
FAM57A	other	4,87E-02	CCND1,TP53	
FBLN2	other	4,87E-02	MMP2,VEGFA	
Fc receptor	group	4,87E-02	IFNG,IL10	
FDX2	transporter	4,87E-02	IREB2,TFRC	
FDXR	enzyme	4,87E-02	IREB2,TFRC	
FGF16	growth factor	4,87E-02	MMP2,MMP9	
FZD1	G-protein coupl	4,87E-02	ABCB1,CTNNB1	
GALR1	G-protein coupl	4,87E-02	CCND1,HAMP	
GGT1	enzyme	4,87E-02	EGFR,TNFSF11	
GIT1	kinase	4,87E-02	MMP2,MMP9	
GLIPR2	other	4,87E-02	ACTA2,EGFR	
GLRX3	enzyme	4,87E-02	PPP3R1,TFRC	
GNL3L	other	4,87E-02	ADRB2,BAX	
H19	other	4,87E-02	IGF2,IRS1	
HHIP	other	4,87E-02	EBF1,PAX5	
HINT2	other	4,87E-02	ADIPOQ,LEP	
HLA-C	other	4,87E-02	IL6,TNF	
HMX2	transcription reg	4,87E-02	BMP4,PAX2	
HOXD11	transcription reg	4,87E-02	GDNF,ITGA8	
HRH4	G-protein coupl	4,87E-02	IFNG,IL17A	
HS6ST2	enzyme	4,87E-02	CXCL8,IL6	
IFNGR	complex	4,87E-02	SOCS3,TNF	
IK	cytokine	4,87E-02	CIITA,HLA-DRA	
IL17B	cytokine	4,87E-02	IL6,MMP9	
ITGAX	transmembrane	4,87E-02	CXCL8,IL1B	
K Channel	complex	4,87E-02	POU5F1,TP53	
KLF7	transcription reg	4,87E-02	HBB,NTRK1	
KLK3	peptidase	4,87E-02	KNG1,REN	
LETM1	transporter	4,87E-02	MT-CO1,MT-ND6	
LETMD1	other	4,87E-02	BAX,TP53	
LSINCT5	other	4,87E-02	IL1B,STAT3	
MAL	other	4,87E-02	IFNG,IL2	
Metalloproteas	group	4,87E-02	FN1,ITGAM	
miR-191-5p (an	mature microRN	4,87E-02	CRP,IL6	
miR-331-3p (mi	mature microRN	4,87E-02	ERBB2,PLAUR	
miR-515-5p (an	mature microRN	4,87E-02	FGFR2,PIK3C2B	
miR-516a-3p (a	mature microRN	4,87E-02	AR,WNT5A	
Mt3	other	4,87E-02	CEBPD,GSTP1	
Nc2	complex	4,87E-02	HLA-A,IL2	
NDST2	enzyme	4,87E-02	CMA1,FN1	
NME2	kinase	4,87E-02	PTGS2,TERT	
NUDT2	phosphatase	4,87E-02	KIT,TPH1	
P2RY6	G-protein coupl	4,87E-02	CXCL8,VCAM1	
PAK2	kinase	4,87E-02	CD69,IL2	
PDE8A	enzyme	4,87E-02	HMGCR,LDLR	
PER3	other	4,87E-02	DBP,PRL	
PHLDA1	other	4,87E-02	FAS,ITGA2	
PLA2G16	enzyme	4,87E-02	ADIPOQ,LEP	
PLAC8	other	4,87E-02	CCND1,TP53	
Pld	group	4,87E-02	FN1,HIF1A	
PLK3	kinase	4,87E-02	FAS,PTEN	
PODXL	kinase	4,87E-02	MMP1,MMP9	
Prl3d1 (includes	other	4,87E-02	ESR1,ESR2	
PTCH2	transmembrane	4,87E-02	CXCL12,JAG1	
RAPSN	other	4,87E-02	JAK2,SOCS3	
RASAL3	other	4,87E-02	IFNG,IL4	
RGL2	other	4,87E-02	NPPA,RALB	
RNF122	other	4,87E-02	IL6,TNF	
RNF139	enzyme	4,87E-02	FDFT1,HMGCR	
RPL5	other	4,87E-02	PTEN,TP53	
RPS6KA1	kinase	4,87E-02	HAMP,IL10	
SERPINH1	other	4,87E-02	COL1A1,SERPINE1	
SIGMAR1	transmembrane	4,87E-02	BDNF,KCNH2	
SLA2	other	4,87E-02	CD69,IL2	
SLAMF7	other	4,87E-02	LTA,TNF	
SLC2A8	transporter	4,87E-02	FGF21,PPARA	
SLC34A1	transporter	4,87E-02	CYP27B1,CYP46A1	
SLC9A3R2	transporter	4,87E-02	CCND1,SCARB1	
SNRK	kinase	4,87E-02	CCND1,CTNNB1	
Stat dimer	complex	4,87E-02	FOS,IL6	
TAF12	transcription reg	4,87E-02	HLA-DRA,SELE	
TBPL1	transcription reg	4,87E-02	FOS,NF1	
TBX20	transcription reg	4,87E-02	TBX2,TBX5	
Tcrb-V3	group	4,87E-02	CD69,IL2RA	
TEC/BTK/ITK/TX	group	4,87E-02	CD69,IL2RA	
TMEM119	other	4,87E-02	BGLAP,CTNNB1	
TMSB10/TMSB4	other	4,87E-02	FAS,MMP7	
TOP3A	enzyme	4,87E-02	BLM,TP53	
TSPAN33	other	4,87E-02	NOS1,PTGS2	
UNG	enzyme	4,87E-02	BDNF,TP53	
USP4	peptidase	4,87E-02	ADORA2A,IL17A	
USP28	peptidase	4,87E-02	GATA4,TP53	
Vacuolar H+ AT	complex	4,87E-02	IL6,TNF	
VAPB	other	4,87E-02	let-7,mir-196	
VSNL1	other	4,87E-02	CYP11B2,ITGAV	
XPO5	transporter	4,87E-02	DICER1,let-7	
ZFP64	transcription reg	4,87E-02	IL6,TNF	
ZFYVE9	peptidase	4,87E-02	ACTA2,SMAD2	

ZNF282	transcription reg	4,87E-02	PGR,TFF1	
48s	complex	4,93E-02	CCND1,IGF1R,SREBF1,VEGFA	
CDH2	other	4,93E-02	ACTA2,CCND1,KCNA5,MMP9	
CPEB1	translation regu	4,93E-02	IL13,IL6,MMP9,TP53	
EHHADH	enzyme	4,93E-02	ACAA1,CD36,CYP4A11,PDK4	
HOXB4	transcription reg	4,93E-02	GPX3,ITGB3,PGR,RARB	
mir-290	microRNA	4,93E-02	LIN28A,POU5F1,RELA,TGFBR2	
ODC1	enzyme	4,93E-02	PDGFRA,PDGFRB,SERPINE1,TLR2	
PMP22	other	4,93E-02	APOE,HMGCR,JUN,NOTCH1	
PNN	other	4,93E-02	GDF15,JUN,MMP7,TIMP1	
zoptarelin doxo	biologic drug	9,27E-03	EGFR,GNRHR	
PURA	transcription reg	4,93E-02	ACTA2,AR,DHFR,ITGAM	
TNFAIP2	other	4,93E-02	IL15RA,LTA,PLAT,SLCO3A1	
ZBTB33	transcription reg	4,93E-02	BAX,FAS,MMP7,S100A4	

Annexed Table2A. Proteins involved in Hypertension that are related to IFNG. The Upstream Regulator Analysis tool from Ingenuity Pathway Analysis (IPA) was applied to the 2206 hypertension-related proteins obtained from the Phenopedia. IFNG interacts with 932 of the proteins involved in hypertension. Of these, with 410 it does so directly and with the rest it does so indirectly through Master Regulators (IFNG,IL10,IL4,IL1B,TNF,CEBPB,PPARG,NFkB (complex),STAT6,Ap1,HIF1A,NFKB1,RELA,STAT3, NFKBIA).

Affected **indicates direct connection between both proteins**

		Master regulator														
Target	**Molecule Type**	**IFNG**	**IL10**	**IL4**	**IL1B**	**TNF**	**CEBPB**	**PPARG**	**NFkB (compl**	**STAT6**	**Ap1**	**HIF1A**	**NFKB1**	**RELA**	**STAT3**	**NFKBIA**
A4GALT	enzyme				Affected	Affected										
ABCA1	transporter	Affected	Affected	Affected		Affected		Affected								
ABCB1	transporter	Affected					Affected		Affected			Affected	Affected	Affected		
ABCB11	transporter				Affected	Affected										
ABCC1	transporter	Affected				Affected										
ABCC2	transporter				Affected	Affected										
ABCC8	transporter											Affected				
ABCG2	transporter				Affected	Affected		Affected						Affected		
ABLIM1	other			Affected						Affected						
ACAA1	enzyme							Affected								
ACAA2	enzyme							Affected								
ACADS	enzyme					Affected		Affected								
ACE	peptidase	Affected				Affected					Affected					
ACSS1	enzyme	Affected														
ACTA2	other	Affected	Affected	Affected	Affected	Affected	Affected	Affected				Affected		Affected	Affected	
ACTN4	transcription regulator													Affected		
ADAMTS7	peptidase					Affected										
ADAMTS8	peptidase	Affected				Affected										
ADAMTS9	peptidase	Affected							Affected							
ADGRE1	G-protein coupled receptor			Affected					Affected							
ADGRG1	G-protein coupled receptor	Affected														
ADH1C	enzyme						Affected									
ADIPOQ	other	Affected				Affected	Affected	Affected				Affected			Affected	
ADIPOR2	transmembrane receptor							Affected								
ADM	other	Affected	Affected		Affected	Affected	Affected		Affected			Affected			Affected	
ADORA1	G-protein coupled receptor	Affected				Affected							Affected			
ADORA2A	G-protein coupled receptor	Affected				Affected										
ADORA2B	G-protein coupled receptor	Affected		Affected	Affected	Affected			Affected			Affected				
ADRA2A	G-protein coupled receptor	Affected							Affected							
ADRA2C	G-protein coupled receptor								Affected							
ADRB1	G-protein coupled receptor					Affected										
ADRB2	G-protein coupled receptor				Affected	Affected		Affected								
ADRB3	G-protein coupled receptor					Affected	Affected	Affected								
AFP	transporter											Affected		Affected		
AGER	transmembrane receptor	Affected	Affected		Affected	Affected			Affected							
AGRP	other														Affected	
AGT	growth factor	Affected				Affected	Affected	Affected	Affected			Affected		Affected	Affected	
AGTR1	G-protein coupled receptor	Affected			Affected	Affected										Affected
AHCY	enzyme	Affected														
AHR	ligand-dependent nuclear receptor	Affected		Affected					Affected					Affected	Affected	
AKAP12	transporter					Affected						Affected				
AKR1B1	enzyme				Affected	Affected							Affected			
AKR1C3	enzyme						Affected									
AKT1	kinase											Affected			Affected	
ALAD	enzyme					Affected										
ALDH1B1	enzyme								Affected							
ALDH1L1	enzyme	Affected														
ALDH2	enzyme			Affected		Affected				Affected						
ALDH9A1	enzyme							Affected								
ALOX12	enzyme	Affected		Affected				Affected								
ALOX15	enzyme	Affected		Affected	Affected					Affected					Affected	
ALOX5	enzyme			Affected		Affected										
ALOX5AP	other	Affected	Affected	Affected		Affected	Affected					Affected		Affected		
ALPL	phosphatase	Affected			Affected											
ANGPT1	growth factor				Affected	Affected										
ANGPTL4	other	Affected			Affected	Affected		Affected				Affected			Affected	
ANPEP	peptidase					Affected										
APCDD1	other						Affected									
APLN	other					Affected	Affected					Affected				
APLNR	G-protein coupled receptor						Affected									
APOA1	transporter					Affected		Affected								Affected
APOA2	transporter							Affected								
APOA4	transporter														Affected	
APOB	transporter				Affected		Affected									
APOC2	transporter				Affected	Affected										
APOC3	transporter						Affected									
APOC4	transporter					Affected										
APOE	transporter			Affected	Affected	Affected		Affected	Affected	Affected		Affected	Affected	Affected		
APOL1	transporter	Affected				Affected										
AQP1	transporter	Affected				Affected			Affected							
AQP11	transporter	Affected														
AQP3	transporter					Affected		Affected								
AQP4	transporter				Affected							Affected				
AQP9	transporter	Affected				Affected						Affected				
AR	ligand-dependent nuclear receptor					Affected							Affected	Affected		
ARG1	enzyme	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected			Affected		Affected	
ARL6IP5	other	Affected			Affected	Affected										
ARNTL2	transcription regulator			Affected						Affected						
ASIC3	ion channel				Affected											
ATF3	transcription regulator	Affected			Affected	Affected			Affected		Affected					
ATM	kinase						Affected									
ATP1A1	transporter	Affected			Affected	Affected										
ATP1B1	transporter	Affected														
ATP2A2	transporter	Affected			Affected	Affected		Affected	Affected			Affected				
ATP2B1	transporter					Affected										
ATP2B4	transporter					Affected										
ATP6AP2	transporter								Affected		Affected		Affected	Affected		
ATP6V1B1	transporter															Affected
ATR	kinase						Affected									
AURKA	kinase											Affected				
AVPR1A	G-protein coupled receptor	Affected			Affected	Affected										
AXL	kinase											Affected				Affected
BAX	transporter	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected		Affected	Affected	Affected		Affected
BCAN	other	Affected														
BCL11A	transcription regulator			Affected					Affected							Affected
BCL2A1	other	Affected	Affected		Affected	Affected	Affected		Affected		Affected		Affected	Affected		Affected
BDKRB1	G-protein coupled receptor		Affected		Affected	Affected										
BDKRB2	G-protein coupled receptor					Affected										
BDNF	growth factor	Affected		Affected		Affected	Affected		Affected		Affected					
BGLAP	other				Affected	Affected	Affected	Affected			Affected					
BHMT	enzyme						Affected									
BIN1	other			Affected				Affected								
BLVRA	enzyme					Affected			Affected					Affected		
BMP2	growth factor		Affected		Affected	Affected			Affected			Affected	Affected	Affected		Affected
BMP4	growth factor				Affected	Affected										
BMP6	growth factor	Affected	Affected													
BMPR1A	kinase		Affected			Affected										
BRCA1	transcription regulator							Affected				Affected				
BRCA2	transcription regulator	Affected											Affected	Affected		
C2	peptidase	Affected														
C3	peptidase	Affected		Affected	Affected	Affected	Affected	Affected	Affected					Affected		Affected
C4A/C4B	other	Affected														
C5	cytokine					Affected									Affected	
CA2	enzyme			Affected		Affected		Affected		Affected						
CAD	enzyme			Affected												
CALCA	other	Affected			Affected	Affected										
CALCR	G-protein coupled receptor			Affected												
CAMK1D	kinase			Affected						Affected						

CARD8	other					Affected			Affected					Affected		
CASR	G-protein coupled receptor				Affected								Affected	Affected		
CAT	enzyme	Affected		Affected	Affected	Affected		Affected							Affected	
CAV1	transmembrane receptor	Affected				Affected		Affected				Affected		Affected		
CAV2	other							Affected								
CAV3	enzyme								Affected							
CAVIN3	other					Affected										
CBR3	enzyme					Affected			Affected							
CBS/CBSL	enzyme													Affected		
CCDC86	other			Affected						Affected						
CCK	other					Affected			Affected							
CCKAR	G-protein coupled receptor	Affected			Affected				Affected							
CCL11	cytokine	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected			Affected	Affected	Affected	Affected
CCL16	cytokine		Affected													
CCL17	cytokine	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected			Affected		Affected	
CCL18	cytokine	Affected	Affected	Affected		Affected										
CCL2	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected
CCL23	cytokine	Affected	Affected	Affected						Affected						
CCL25	cytokine	Affected		Affected												
CCL5	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
CCL8	cytokine	Affected		Affected	Affected				Affected	Affected						
CCN2	growth factor	Affected		Affected	Affected	Affected		Affected	Affected		Affected	Affected	Affected	Affected	Affected	
CCN3	growth factor					Affected						Affected				
CCN4	other					Affected										
CCND1	transcription regulator	Affected		Affected		Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
CCR2	G-protein coupled receptor	Affected	Affected		Affected	Affected			Affected			Affected				
CCR3	G-protein coupled receptor	Affected		Affected		Affected										Affected
CCR5	G-protein coupled receptor	Affected	Affected	Affected	Affected	Affected	Affected			Affected		Affected			Affected	
CD14	transmembrane receptor	Affected	Affected	Affected	Affected	Affected	Affected							Affected		
CD2	transmembrane receptor	Affected	Affected	Affected						Affected						
CD200	other	Affected		Affected		Affected										
CD226	other														Affected	
CD247	transmembrane receptor					Affected										
CD28	transmembrane receptor		Affected			Affected										
CD36	transmembrane receptor	Affected		Affected		Affected		Affected	Affected			Affected				
CD40	transmembrane receptor	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected
CD46	other														Affected	
CD59	other					Affected							Affected	Affected		
CD69	transmembrane receptor			Affected	Affected	Affected			Affected	Affected				Affected		Affected
CDC42	enzyme					Affected										
CDH13	other	Affected	Affected			Affected										Affected
CDK5R1	kinase	Affected				Affected										
CDK6	kinase		Affected	Affected				Affected								
CDKN2A	transcription regulator	Affected				Affected					Affected	Affected		Affected	Affected	
CDKN2B	transcription regulator	Affected					Affected								Affected	
CDKN2B-AS1	other	Affected			Affected	Affected										
CEBPD	transcription regulator	Affected			Affected	Affected	Affected		Affected						Affected	Affected
CELSR1	G-protein coupled receptor	Affected														
CELSR2	G-protein coupled receptor	Affected														
CERS6	transcription regulator	Affected				Affected										
CES1	enzyme							Affected								
CETP	enzyme								Affected							
CFB	peptidase	Affected			Affected	Affected			Affected				Affected	Affected	Affected	
CFTR	ion channel	Affected			Affected	Affected	Affected		Affected				Affected	Affected		Affected
CHI3L1	enzyme				Affected	Affected							Affected	Affected	Affected	Affected
CHIT1	enzyme						Affected									
CHUK	kinase		Affected													
CIDEA	other							Affected								
CIITA	transcription regulator	Affected	Affected	Affected	Affected	Affected			Affected				Affected	Affected	Affected	
CKM	kinase					Affected										
CLU	other					Affected			Affected		Affected					Affected
CNP	enzyme					Affected										
CNR1	G-protein coupled receptor	Affected														
CNR2	G-protein coupled receptor			Affected	Affected	Affected				Affected						
COBLL1	other			Affected						Affected						
COL18A1	other			Affected					Affected							
COL1A1	other	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected			Affected	Affected	Affected	
COL1A2	other	Affected		Affected		Affected	Affected	Affected	Affected	Affected			Affected	Affected	Affected	Affected
COL3A1	other					Affected									Affected	Affected
COL6A3	other			Affected												
CORIN	peptidase							Affected								
CPB2	peptidase				Affected		Affected									
CPLX2	other							Affected								
CPT1A	enzyme					Affected	Affected	Affected		Affected						
CPT1B	enzyme					Affected		Affected								
CPT2	enzyme					Affected		Affected								
CR1	transmembrane receptor		Affected													
CRCP	transmembrane receptor					Affected										
CRHR1	G-protein coupled receptor				Affected	Affected			Affected							
CRP	other				Affected	Affected	Affected		Affected				Affected	Affected	Affected	
CRY1	enzyme					Affected										
CSF2	cytokine	Affected	Affected	Affected	Affected	Affected			Affected		Affected		Affected	Affected	Affected	Affected
CSK	kinase	Affected														Affected
CTF1	cytokine														Affected	
CTLA4	transmembrane receptor		Affected			Affected									Affected	
CTNNB1	transcription regulator	Affected			Affected	Affected	Affected	Affected	Affected							Affected
CTNS	transporter			Affected						Affected						
CTSH	peptidase	Affected														
CTSL	peptidase							Affected							Affected	
CX3CR1	G-protein coupled receptor	Affected	Affected		Affected	Affected										
CXADR	transmembrane receptor	Affected														
CXCL12	cytokine	Affected	Affected		Affected	Affected			Affected		Affected	Affected				Affected
CXCL13	cytokine		Affected		Affected	Affected									Affected	
CXCL14	cytokine							Affected								
CXCL5	cytokine	Affected	Affected		Affected	Affected	Affected	Affected	Affected					Affected		
CXCL8	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
CXCR2	G-protein coupled receptor					Affected									Affected	
CXCR4	G-protein coupled receptor	Affected	Affected	Affected	Affected	Affected	Affected		Affected			Affected		Affected	Affected	Affected
CYB561	enzyme	Affected														
CYBA	enzyme	Affected			Affected	Affected		Affected								Affected
CYBB	enzyme	Affected		Affected	Affected	Affected			Affected	Affected			Affected	Affected		
CYP11A1	enzyme	Affected			Affected	Affected	Affected									
CYP11B1	enzyme					Affected										
CYP11B2	enzyme				Affected											
CYP17A1	enzyme					Affected	Affected							Affected		
CYP19A1	enzyme				Affected	Affected	Affected	Affected				Affected		Affected		
CYP1A1	enzyme				Affected	Affected	Affected							Affected		
CYP1A2	enzyme	Affected			Affected											
CYP1B1	enzyme					Affected										Affected
CYP24A1	enzyme	Affected					Affected									
CYP27B1	enzyme				Affected	Affected	Affected									
CYP2A6 (incl	enzyme						Affected									
CYP2C19	enzyme				Affected											
CYP2C8	enzyme					Affected										
CYP2C9	enzyme	Affected			Affected									Affected		
CYP2E1	enzyme	Affected		Affected	Affected	Affected	Affected									
CYP3A4	enzyme	Affected			Affected		Affected		Affected					Affected		
CYP3A5	enzyme				Affected				Affected							
CYP46A1	enzyme											Affected				
CYP4A11	enzyme							Affected		Affected						
CYP4F3	enzyme											Affected				
CYP7A1	enzyme				Affected	Affected										
DBP	transcription regulator	Affected			Affected				Affected							
DCD	other					Affected										

DDAH1	enzyme			Affected						Affected						
DDR2	kinase	Affected														
DHCR7	enzyme						Affected									
DHFR	enzyme						Affected									
DICER1	enzyme												Affected			
DIO1	enzyme	Affected			Affected	Affected			Affected							
DIO2	enzyme													Affected		
DLK1	other							Affected								
DNASE1	enzyme											Affected				
DPP4	peptidase	Affected		Affected	Affected	Affected									Affected	
DRD2	G-protein coupled receptor								Affected							
DROSHA	enzyme												Affected			
DUOX1	enzyme			Affected												
DUOX2	enzyme	Affected														
DYNC1H1	peptidase			Affected												
ECE1	peptidase	Affected														
EDN1	cytokine	Affected			Affected	Affected		Affected	Affected		Affected	Affected		Affected	Affected	
EDN2	growth factor							Affected								
EDNRA	transmembrane receptor	Affected														
EDNRB	G-protein coupled receptor	Affected				Affected			Affected			Affected				
EFL1	translation regulator			Affected						Affected						
EFNB2	kinase	Affected				Affected	Affected									
EGF	growth factor	Affected														
EGFR	kinase					Affected		Affected	Affected			Affected	Affected			
EGLN3	enzyme	Affected			Affected	Affected		Affected				Affected				
ELANE	peptidase						Affected									
ELN	other	Affected			Affected									Affected		
ENG	transmembrane receptor				Affected	Affected						Affected				
ENPP1	enzyme				Affected				Affected							
EP300	transcription regulator				Affected											
EPAS1	transcription regulator			Affected	Affected			Affected	Affected			Affected		Affected	Affected	
EPHB4	kinase			Affected												
EPHX1	peptidase			Affected				Affected		Affected						
EPO	cytokine				Affected	Affected						Affected				Affected
ERAP1	peptidase	Affected							Affected					Affected		Affected
ERAP2	peptidase	Affected							Affected					Affected		Affected
ERBB2	kinase	Affected			Affected	Affected			Affected			Affected		Affected		Affected
ERCC1	enzyme					Affected					Affected					
ERGIC1	other											Affected				
ERVFRD-1	other					Affected										
ESR1	ligand-dependent nuclear receptor				Affected	Affected									Affected	
ESR2	ligand-dependent nuclear receptor														Affected	
ETV5	transcription regulator					Affected										
EVI5	other			Affected												
F11R	other	Affected				Affected		Affected								
F13A1	enzyme			Affected	Affected											
F2R	G-protein coupled receptor	Affected		Affected												
F2RL1	G-protein coupled receptor	Affected		Affected	Affected	Affected			Affected		Affected					
F7	peptidase						Affected									
F8	other						Affected									
FAAH	enzyme	Affected	Affected	Affected												
FABP1	transporter				Affected	Affected		Affected		Affected						
FABP2	transporter							Affected								
FABP3	transporter							Affected								
FADS1	enzyme			Affected		Affected				Affected						
FAM13A	other											Affected				
FAS	transmembrane receptor	Affected	Affected	Affected	Affected	Affected	Affected		Affected				Affected	Affected	Affected	Affected
FCGR2A	transmembrane receptor	Affected	Affected	Affected						Affected						
FCGR2B	transmembrane receptor	Affected	Affected	Affected	Affected	Affected										
FGA	other														Affected	
FGB	other				Affected										Affected	
FGF1	growth factor	Affected						Affected	Affected							
FGF10	growth factor					Affected								Affected		
FGF21	growth factor							Affected		Affected						
FGF5	growth factor					Affected			Affected							
FGFR1	kinase					Affected										
FGFR2	kinase				Affected	Affected	Affected									
FGFR3	kinase				Affected											
FGG	other	Affected			Affected	Affected			Affected				Affected		Affected	
FKBP5	enzyme	Affected	Affected	Affected	Affected					Affected						
FLT1	kinase	Affected		Affected	Affected	Affected						Affected			Affected	
FLT4	transmembrane receptor	Affected				Affected										
FMR1	translation regulator				Affected											
FN1	enzyme	Affected		Affected	Affected	Affected		Affected	Affected		Affected	Affected		Affected	Affected	Affected
FOS	transcription regulator	Affected	Affected	Affected	Affected	Affected	Affected		Affected		Affected	Affected	Affected	Affected	Affected	Affected
FOXF1	transcription regulator					Affected			Affected							
FOXO1	transcription regulator	Affected			Affected	Affected										
FOXO3	transcription regulator						Affected									
FOXP3	transcription regulator	Affected	Affected	Affected		Affected			Affected	Affected			Affected	Affected	Affected	
FPR1	G-protein coupled receptor		Affected			Affected										
FURIN	peptidase	Affected			Affected							Affected				
FUT4	enzyme					Affected									Affected	
FUT7	enzyme			Affected	Affected	Affected						Affected				
FYN	kinase					Affected						Affected				
G6PD	enzyme				Affected											
GAS5	other	Affected			Affected	Affected										Affected
GAS6	growth factor	Affected			Affected				Affected							
GATA2	transcription regulator					Affected		Affected								
GATM	enzyme			Affected						Affected						
GCH1	enzyme	Affected			Affected	Affected			Affected					Affected		Affected
GCK	kinase	Affected			Affected			Affected				Affected				
GCLC	enzyme				Affected	Affected			Affected							
GCLM	enzyme					Affected										
GDF15	growth factor	Affected			Affected	Affected		Affected	Affected					Affected		
GDNF	growth factor	Affected				Affected			Affected							
GFRA1	transmembrane receptor												Affected			
GHR	transmembrane receptor				Affected	Affected						Affected				
GHRL	growth factor					Affected										
GIPR	G-protein coupled receptor							Affected								
GJA1	transporter	Affected		Affected	Affected	Affected						Affected	Affected		Affected	
GJA5	transporter	Affected														
GLA	enzyme	Affected			Affected				Affected							
GNA14	enzyme	Affected		Affected						Affected						
GNAI2	enzyme	Affected				Affected										
GNAS	enzyme	Affected			Affected		Affected		Affected							
GNRH1	other				Affected											Affected
GNRHR	G-protein coupled receptor										Affected					
GOSR2	transporter					Affected										
GP1BA	transmembrane receptor					Affected										
GP1BB	other													Affected		
GPER1	G-protein coupled receptor	Affected										Affected				
GPR83	G-protein coupled receptor	Affected														
GPRC5B	G-protein coupled receptor	Affected	Affected			Affected										
GPX1	enzyme					Affected										
GPX3	enzyme															Affected
GPX4	enzyme			Affected		Affected										
GRIA1	ion channel	Affected			Affected	Affected										
GRK2	kinase	Affected														
GRK5	kinase								Affected				Affected	Affected		Affected
GSS	enzyme										Affected					
GSTA1	enzyme				Affected	Affected	Affected	Affected						Affected		
GSTM2	enzyme					Affected										
GSTM5	enzyme															Affected
GSTP1	enzyme	Affected				Affected					Affected					

GYS1	enzyme				Affected											
H19	other				Affected	Affected										
HAMP	other				Affected		Affected		Affected	Affected		Affected			Affected	
HAS2	enzyme	Affected			Affected	Affected	Affected		Affected				Affected	Affected	Affected	
HAS3	enzyme					Affected										
HAVCR1	other														Affected	
HBB	transporter						Affected				Affected				Affected	
HBEGF	growth factor	Affected		Affected	Affected	Affected										
HBG1	other														Affected	
HDAC9	transcription regulator	Affected	Affected			Affected			Affected							
HEBP1	other							Affected								
HES1	transcription regulator				Affected	Affected		Affected						Affected		Affected
HES5	transcription regulator								Affected				Affected		Affected	
HGF	growth factor			Affected	Affected	Affected	Affected	Affected							Affected	
HGFAC	peptidase								Affected							
HIF1A	transcription regulator	Affected			Affected	Affected			Affected			Affected		Affected	Affected	Affected
HIF3A	transcription regulator								Affected			Affected				
HLA-A	other	Affected			Affected	Affected	Affected		Affected						Affected	Affected
HLA-B	transmembrane receptor	Affected				Affected								Affected		
HLA-C	other	Affected														
HLA-DQA1	transmembrane receptor	Affected													Affected	
HLA-DQB1	other	Affected														
HLA-DRA	transmembrane receptor	Affected			Affected	Affected										
HLA-DRB1	transmembrane receptor	Affected														
HLA-DRB5	transmembrane receptor	Affected													Affected	
HLA-G	other	Affected	Affected													
HMGA1	transcription regulator	Affected			Affected		Affected									Affected
HMGB1	transcription regulator	Affected			Affected	Affected										
HMGCR	enzyme	Affected		Affected		Affected		Affected		Affected						
HMGCS2	enzyme							Affected		Affected						
HMOX1	enzyme	Affected	Affected		Affected	Affected		Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
HNF1B	transcription regulator				Affected											
HNF4A	transcription regulator				Affected	Affected			Affected					Affected	Affected	
HP	peptidase				Affected	Affected	Affected	Affected				Affected			Affected	
HSD11B1	enzyme			Affected	Affected	Affected	Affected									
HSD17B7	enzyme					Affected										
HSD3B1	enzyme			Affected						Affected						
HSD3B2	enzyme			Affected		Affected	Affected									
HSPA1A/HSP	enzyme	Affected		Affected	Affected	Affected										
HSPA1L	other	Affected			Affected				Affected							
HSPA4	other					Affected						Affected				
HSPA8	enzyme	Affected				Affected	Affected									Affected
HSPD1	enzyme	Affected				Affected	Affected									
HSPG2	enzyme	Affected			Affected	Affected										
HTR2A	G-protein coupled receptor														Affected	
HTRA1	peptidase	Affected														
ICAM1	transmembrane receptor	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected				Affected	Affected	Affected	Affected
ICOS	transmembrane receptor			Affected		Affected			Affected	Affected					Affected	
ID3	transcription regulator			Affected	Affected	Affected										
IDE	peptidase	Affected		Affected		Affected										
IDH2	enzyme					Affected										
IFI30	enzyme	Affected		Affected											Affected	
IFIH1	enzyme	Affected		Affected		Affected				Affected					Affected	
IFNG	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IFNK	cytokine	Affected							Affected							
IFNLR1	transmembrane receptor			Affected												
IGF1	growth factor	Affected		Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected		Affected		
IGF1R	transmembrane receptor	Affected		Affected		Affected								Affected	Affected	
IGF2	growth factor					Affected						Affected				Affected
IGF2R	transmembrane receptor			Affected						Affected						Affected
IGFBP1	other				Affected	Affected	Affected	Affected							Affected	
IGFBP3	other				Affected	Affected	Affected	Affected			Affected	Affected	Affected			
IKBKB	kinase		Affected										Affected			
IKBKE	kinase	Affected			Affected	Affected	Affected		Affected				Affected	Affected	Affected	
IL10	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL10RA	transmembrane receptor	Affected	Affected	Affected	Affected	Affected			Affected	Affected						
IL12A	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected				Affected	Affected		Affected
IL12B	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected	
IL12RB1	transmembrane receptor	Affected		Affected		Affected									Affected	
IL12RB2	transmembrane receptor	Affected	Affected	Affected												
IL13	cytokine	Affected	Affected	Affected		Affected		Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected
IL13RA2	transmembrane receptor	Affected	Affected	Affected		Affected			Affected	Affected					Affected	
IL15	cytokine	Affected		Affected	Affected	Affected			Affected	Affected		Affected				Affected
IL15RA	transmembrane receptor	Affected		Affected	Affected	Affected			Affected					Affected		Affected
IL16	cytokine			Affected	Affected	Affected										
IL17A	cytokine	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected		Affected			Affected	
IL17RA	transmembrane receptor	Affected	Affected									Affected				
IL18	cytokine	Affected	Affected	Affected	Affected	Affected			Affected				Affected			
IL18R1	transmembrane receptor	Affected		Affected	Affected	Affected				Affected					Affected	
IL18RAP	transmembrane receptor	Affected		Affected	Affected											
IL1A	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected		Affected		Affected
IL1B	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
IL1F10	cytokine					Affected										
IL1R1	transmembrane receptor	Affected	Affected	Affected	Affected	Affected									Affected	
IL1RAP	transmembrane receptor				Affected											
IL1RL1	transmembrane receptor	Affected		Affected	Affected	Affected										
IL1RN	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected			Affected	Affected	Affected	Affected
IL2	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected		Affected	Affected	Affected	Affected
IL21R	transmembrane receptor					Affected										
IL22	cytokine		Affected		Affected	Affected			Affected			Affected		Affected	Affected	
IL23A	cytokine	Affected	Affected		Affected	Affected		Affected	Affected		Affected		Affected	Affected	Affected	
IL23R	transmembrane receptor	Affected			Affected							Affected			Affected	
IL24	cytokine		Affected	Affected	Affected	Affected	Affected		Affected	Affected						
IL2RA	transmembrane receptor	Affected		Affected	Affected	Affected		Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected
IL2RB	transmembrane receptor			Affected											Affected	
IL3	cytokine		Affected	Affected		Affected					Affected					
IL33	cytokine		Affected	Affected	Affected	Affected		Affected		Affected						Affected
IL4	cytokine	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	
IL4I1	enzyme	Affected		Affected	Affected	Affected				Affected						
IL4R	transmembrane receptor	Affected	Affected	Affected		Affected				Affected					Affected	
IL5	cytokine	Affected	Affected	Affected		Affected	Affected		Affected	Affected	Affected		Affected		Affected	Affected
IL5RA	transmembrane receptor			Affected						Affected						
IL6	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL6R	transmembrane receptor	Affected			Affected										Affected	
IL6ST	transmembrane receptor		Affected	Affected						Affected					Affected	
IL7R	transmembrane receptor	Affected	Affected	Affected		Affected			Affected					Affected		Affected
IL9	cytokine	Affected	Affected	Affected	Affected	Affected		Affected		Affected				Affected	Affected	
IL9R	transmembrane receptor														Affected	
INS	other	Affected			Affected	Affected	Affected	Affected								
INSIG1	other					Affected		Affected								
INSIG2	other							Affected				Affected				
INSR	kinase	Affected			Affected	Affected	Affected	Affected								
IRAK1	kinase	Affected	Affected		Affected											Affected
IREB2	translation regulator	Affected														
IRF5	transcription regulator	Affected		Affected		Affected									Affected	
IRS1	enzyme	Affected			Affected	Affected	Affected	Affected								
IRS2	enzyme	Affected			Affected	Affected	Affected	Affected		Affected		Affected				
ITGA2	transmembrane receptor			Affected		Affected					Affected					Affected
ITGA2B	transmembrane receptor											Affected				
ITGA4	transmembrane receptor	Affected	Affected	Affected		Affected										
ITGAM	transmembrane receptor	Affected	Affected		Affected	Affected			Affected						Affected	
ITGAV	transmembrane receptor	Affected		Affected	Affected	Affected			Affected			Affected			Affected	Affected
ITGB1	transmembrane receptor	Affected		Affected	Affected	Affected			Affected						Affected	Affected
ITGB2	transmembrane receptor	Affected		Affected		Affected						Affected			Affected	

ITGB3	transmembrane receptor	Affected		Affected	Affected	Affected						Affected				
ITGB6	other					Affected									Affected	
ITGB8	other				Affected	Affected			Affected							
ITPA	enzyme			Affected												
ITPK1	kinase	Affected		Affected						Affected						
ITPR2	ion channel					Affected										
IVD	enzyme							Affected								
JAG1	growth factor	Affected		Affected		Affected			Affected	Affected			Affected		Affected	
JAK2	kinase	Affected		Affected						Affected					Affected	
JDP2	transcription regulator															Affected
JUN	transcription regulator	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected		Affected		Affected
KCNH2	ion channel				Affected	Affected										Affected
KCNJ1	ion channel	Affected			Affected	Affected										
KCNMA1	ion channel	Affected														
KCTD7	ion channel	Affected														
KDR	kinase	Affected			Affected	Affected			Affected						Affected	
KIDINS220	transcription regulator			Affected						Affected						
KIT	transmembrane receptor			Affected		Affected			Affected					Affected		
KL	enzyme					Affected										
KLB	enzyme					Affected		Affected								
KLF5	transcription regulator					Affected										Affected
KLF7	transcription regulator					Affected										
KLK2	peptidase				Affected											
KLRB1	transmembrane receptor			Affected	Affected	Affected										
KRAS	enzyme	Affected														
KYNU	enzyme	Affected				Affected			Affected							
LAMA3	other				Affected	Affected										
LAT2	other	Affected														
LBP	transporter				Affected	Affected	Affected								Affected	
LCAT	enzyme					Affected									Affected	
LCN2	transporter	Affected			Affected	Affected	Affected		Affected							Affected
LDHA	enzyme	Affected			Affected	Affected						Affected			Affected	
LDLR	transporter				Affected	Affected	Affected	Affected								
LEP	growth factor	Affected			Affected	Affected	Affected	Affected				Affected			Affected	
LEPR	transmembrane receptor						Affected								Affected	
let-7	microRNA												Affected			
LGALS2	other			Affected												
LGR5	transmembrane receptor					Affected								Affected		
LHCGR	G-protein coupled receptor					Affected	Affected		Affected		Affected					
LIMK1	kinase	Affected														
LIPE	enzyme					Affected		Affected		Affected						
LIPG	enzyme			Affected												
LNPEP	peptidase							Affected								
LOX	enzyme	Affected			Affected	Affected						Affected			Affected	
LOXL2	enzyme											Affected				
LPL	enzyme	Affected		Affected		Affected		Affected			Affected					
LRP1	transmembrane receptor			Affected												
LRP2	transporter														Affected	
LRP6	transmembrane receptor					Affected										
LSP1	other			Affected					Affected							
LSS	enzyme					Affected										
LTA	cytokine	Affected		Affected	Affected				Affected	Affected			Affected	Affected	Affected	
LTA4H	enzyme			Affected												
LTBP2	other					Affected										
LTC4S	enzyme			Affected		Affected			Affected				Affected	Affected		
LTF	peptidase														Affected	
Ly6a (include	other	Affected		Affected						Affected						
MAEA	other					Affected										
MAF	transcription regulator		Affected	Affected						Affected					Affected	
MAGI1	kinase					Affected										
MAOA	enzyme			Affected												
MAP2K5	kinase														Affected	
MAP4	other			Affected												
MAPK1	kinase			Affected		Affected										
MAPK3	kinase			Affected												
MAPKAP1	other					Affected										
MAX	transcription regulator	Affected														
MBL2	other					Affected	Affected		Affected							
MECOM	transcription regulator					Affected										
MEF2C	transcription regulator				Affected	Affected						Affected				
MEFV	other	Affected	Affected	Affected	Affected	Affected										
MET	kinase					Affected					Affected	Affected				
MFAP2	other				Affected											
MGAT5	enzyme														Affected	
MGP	other					Affected	Affected									Affected
MIF	cytokine	Affected			Affected	Affected						Affected		Affected		
mir-143	microRNA						Affected									
mir-146	microRNA	Affected			Affected	Affected	Affected		Affected				Affected	Affected		
mir-27	microRNA					Affected										
MITF	transcription regulator	Affected				Affected						Affected			Affected	
MMP1	peptidase	Affected	Affected	Affected	Affected	Affected	Affected		Affected		Affected	Affected		Affected		Affected
MMP12	peptidase	Affected		Affected	Affected	Affected				Affected	Affected				Affected	
MMP14	peptidase				Affected	Affected		Affected		Affected						Affected
MMP2	peptidase	Affected	Affected	Affected	Affected	Affected			Affected	Affected	Affected	Affected			Affected	
MMP3	peptidase	Affected		Affected	Affected	Affected	Affected		Affected		Affected		Affected	Affected	Affected	Affected
MMP7	peptidase				Affected	Affected					Affected	Affected	Affected	Affected	Affected	
MMP9	peptidase	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
MOB3C	other					Affected										
MOV10	enzyme			Affected						Affected						
MPO	enzyme					Affected		Affected								
MRAS	enzyme	Affected													Affected	
MS4A2	transmembrane receptor		Affected	Affected												
MSR1	transmembrane receptor	Affected	Affected	Affected		Affected	Affected				Affected		Affected			
MT-ATP6	transporter														Affected	
MT-CO1	enzyme														Affected	
MT-CO2	enzyme				Affected	Affected			Affected		Affected				Affected	
MT-CYB	enzyme					Affected								Affected	Affected	Affected
MT-ND1	enzyme											Affected			Affected	
MT-ND2	enzyme														Affected	
MT-ND1	enzyme											Affected			Affected	
MT-ND2	enzyme														Affected	
MT-ND4	enzyme														Affected	
MT-ND6	enzyme														Affected	
MTTP	transporter					Affected		Affected								
MVK	kinase			Affected						Affected						
MYB	transcription regulator	Affected								Affected			Affected	Affected	Affected	
MYH7	enzyme					Affected		Affected				Affected			Affected	
MYH9	enzyme	Affected		Affected		Affected										
MYLK	kinase				Affected	Affected			Affected							
MYO6	other									Affected						
MYOD1	transcription regulator	Affected		Affected	Affected	Affected		Affected			Affected			Affected	Affected	Affected
NAMPT	cytokine	Affected			Affected	Affected			Affected					Affected	Affected	
NCAM1	other	Affected				Affected			Affected							
NCF2	enzyme	Affected				Affected			Affected							
NCOA1	transcription regulator					Affected										
NCOA3	transcription regulator			Affected						Affected						
NCOR2	transcription regulator					Affected										
NCR3	transmembrane receptor	Affected														
NF1	other	Affected														
NFATC1	transcription regulator		Affected	Affected		Affected				Affected			Affected	Affected		
NFE2L3	transcription regulator	Affected														
NFKB1	transcription regulator	Affected		Affected	Affected	Affected			Affected				Affected	Affected	Affected	Affected
NFKB2	transcription regulator	Affected		Affected	Affected	Affected			Affected				Affected	Affected		Affected
NFKBIA	transcription regulator	Affected		Affected	Affected	Affected			Affected	Affected			Affected	Affected		Affected
NFKBIZ	transcription regulator	Affected			Affected	Affected	Affected		Affected						Affected	
NLRP3	other	Affected				Affected										

NNMT	enzyme					Affected										
NOD2	other	Affected	Affected			Affected							Affected	Affected		Affected
NOS1	enzyme	Affected			Affected	Affected			Affected							
NOS2	enzyme	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
NOS3	enzyme	Affected	Affected		Affected	Affected		Affected				Affected			Affected	Affected
NOTCH1	transcription regulator	Affected			Affected	Affected			Affected			Affected		Affected	Affected	
NOTCH3	transcription regulator	Affected													Affected	
NOX1	enzyme	Affected			Affected	Affected								Affected	Affected	
NOX4	enzyme	Affected				Affected		Affected				Affected				
NPHS1	other		Affected			Affected										
NPPA	other				Affected	Affected		Affected	Affected			Affected			Affected	Affected
NPPB	other					Affected		Affected	Affected				Affected	Affected		
NPY	other				Affected										Affected	
NPY2R	G-protein coupled receptor	Affected														
NQO1	enzyme	Affected			Affected	Affected					Affected					
NR0B2	ligand-dependent nuclear receptor				Affected	Affected										
NR1H3	ligand-dependent nuclear receptor				Affected	Affected	Affected	Affected								
NR1H4	ligand-dependent nuclear receptor				Affected	Affected										
NR1I2	ligand-dependent nuclear receptor					Affected										
NR2F2	ligand-dependent nuclear receptor							Affected								
NR3C1	ligand-dependent nuclear receptor			Affected		Affected					Affected					
NR4A3	ligand-dependent nuclear receptor		Affected	Affected	Affected	Affected						Affected	Affected	Affected		
NTRK1	kinase	Affected			Affected											
NUCB2	other					Affected										
NUMA1	other			Affected												
OAS3	enzyme	Affected		Affected		Affected				Affected					Affected	
OASL	enzyme	Affected		Affected		Affected				Affected					Affected	
OLFML2B	other					Affected										
OLR1	transmembrane receptor				Affected	Affected		Affected	Affected					Affected		
OPRM1	G-protein coupled receptor			Affected		Affected			Affected	Affected	Affected					
OPTN	other	Affected				Affected										
OSBPL10	transporter					Affected										
OSMR	transmembrane receptor				Affected	Affected										
P2RY1	G-protein coupled receptor	Affected														
P2RY2	G-protein coupled receptor								Affected					Affected		
PADI4	enzyme										Affected					
PAM	enzyme	Affected	Affected													
PAPPA	peptidase	Affected			Affected	Affected										
PARP1	enzyme					Affected								Affected		
PAX2	transcription regulator													Affected		
PAX5	transcription regulator			Affected											Affected	
PCK1	kinase	Affected				Affected	Affected	Affected			Affected			Affected	Affected	
PCSK1	peptidase	Affected			Affected										Affected	
PCSK2	peptidase	Affected			Affected											
PCSK6	peptidase				Affected	Affected										
PCSK9	peptidase					Affected									Affected	
PDGFRA	kinase				Affected	Affected	Affected									
PDK4	kinase						Affected	Affected		Affected						
PDX1	transcription regulator	Affected			Affected	Affected		Affected	Affected							
PECAM1	other	Affected				Affected		Affected	Affected					Affected	Affected	
PER2	transcription regulator					Affected										
PFKP	kinase			Affected	Affected											
PGR	ligand-dependent nuclear receptor														Affected	
PHACTR1	other	Affected														
PI3	other				Affected	Affected	Affected						Affected	Affected		
PICALM	other															Affected
PIK3C2B	kinase					Affected										
PIK3CG	kinase		Affected			Affected										
PIK3R1	kinase															Affected
PLA2G3	enzyme				Affected	Affected		Affected								
PLA2G4C	enzyme			Affected		Affected										
PLA2G5	enzyme	Affected			Affected	Affected										
PLA2G7	enzyme	Affected														
PLAT	peptidase				Affected	Affected										Affected
PLAUR	transmembrane receptor	Affected				Affected	Affected					Affected			Affected	
PLG	peptidase						Affected									
PLIN1	other					Affected		Affected								
PML	transcription regulator	Affected				Affected									Affected	
PMS1	enzyme			Affected						Affected						
POLG	enzyme			Affected								Affected				
POMC	other	Affected	Affected		Affected	Affected	Affected								Affected	
POSTN	other			Affected	Affected	Affected										
POU2F1	transcription regulator					Affected		Affected							Affected	
POU5F1	transcription regulator											Affected		Affected	Affected	
PPARA	ligand-dependent nuclear receptor	Affected			Affected	Affected	Affected	Affected	Affected	Affected		Affected				
PPARD	ligand-dependent nuclear receptor	Affected				Affected	Affected	Affected								
PPARG	ligand-dependent nuclear receptor	Affected		Affected	Affected	Affected	Affected	Affected	Affected					Affected		
PPARGC1A	transcription regulator	Affected		Affected	Affected	Affected	Affected	Affected		Affected					Affected	
PPFIA4	phosphatase											Affected				
PPIC	enzyme							Affected								
PRKCA	kinase	Affected		Affected		Affected				Affected		Affected				
PRKCQ	kinase	Affected														
PRL	cytokine	Affected				Affected	Affected				Affected					Affected
PROCR	other														Affected	
PRSS8	peptidase	Affected		Affected			Affected									
PSEN1	peptidase				Affected	Affected										
PSIP1	transcription regulator														Affected	
PSMA4	peptidase	Affected														
PSMA6	peptidase	Affected		Affected			Affected									
PSMB8	peptidase	Affected		Affected	Affected	Affected									Affected	
PSMB9	peptidase	Affected	Affected		Affected	Affected			Affected					Affected	Affected	
PTEN	phosphatase					Affected		Affected				Affected		Affected		Affected
PTGDS	enzyme				Affected									Affected		
PTGES	enzyme	Affected			Affected	Affected	Affected	Affected	Affected					Affected		Affected
PTGFR	G-protein coupled receptor				Affected	Affected	Affected									
PTGIS	enzyme				Affected							Affected				
PTGS1	enzyme				Affected	Affected	Affected									
PTGS2	enzyme	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
PTN	growth factor	Affected													Affected	
PTPN1	phosphatase	Affected	Affected	Affected												
PTPN11	phosphatase	Affected				Affected										
PTPN2	phosphatase		Affected												Affected	
PTPRC	phosphatase					Affected										
RAC1	enzyme					Affected										Affected
RAC2	enzyme	Affected			Affected		Affected									
RAPGEF5	other					Affected										
RARA	ligand-dependent nuclear receptor				Affected	Affected										
RARB	ligand-dependent nuclear receptor				Affected			Affected								
RASGRP3	other			Affected						Affected						
RBP4	other							Affected								
RBPJ	transcription regulator								Affected						Affected	
REG3A	enzyme		Affected											Affected	Affected	
REL	transcription regulator				Affected	Affected			Affected							
RELA	transcription regulator	Affected		Affected	Affected	Affected		Affected	Affected			Affected	Affected	Affected		Affected
REN	peptidase				Affected			Affected							Affected	
RET	kinase											Affected			Affected	
RETN	other					Affected		Affected								
RGS14	other					Affected										
RGS2	other					Affected										
RGS20	other					Affected										
RGS4	other					Affected	Affected									Affected
RGS5	other					Affected										
RND1	enzyme					Affected										
RNF213	enzyme			Affected						Affected						

RNLS	enzyme														Affected	
ROCK1	kinase															Affected
RORA	ligand-dependent nuclear receptor				Affected	Affected	Affected								Affected	
RSPO3	kinase										Affected					
RUNX1	transcription regulator								Affected						Affected	
RXRA	ligand-dependent nuclear receptor				Affected	Affected										
S100A4	other										Affected					
SAA1	transporter				Affected	Affected	Affected	Affected	Affected					Affected	Affected	
SBF1	phosphatase	Affected												Affected		
SCARB1	transporter	Affected	Affected		Affected	Affected	Affected	Affected								
SCNN1A	ion channel	Affected			Affected	Affected										
SCNN1B	ion channel	Affected			Affected	Affected										
SCNN1G	ion channel	Affected			Affected	Affected		Affected								
SDC4	other	Affected			Affected	Affected			Affected			Affected	Affected	Affected		Affected
SELE	transmembrane receptor	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected		Affected	Affected		Affected
SELENBP1	other									Affected						
SELL	transmembrane receptor	Affected	Affected	Affected		Affected										
SELP	transmembrane receptor	Affected		Affected		Affected				Affected			Affected	Affected		
SELPLG	other		Affected	Affected		Affected			Affected							
SEMA3F	other															Affected
SERPINA1	other	Affected					Affected	Affected		Affected					Affected	
SERPINA3	other				Affected	Affected			Affected						Affected	
SERPINB1	other					Affected									Affected	
SERPINE1	other	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected			Affected	
SERPINE2	other					Affected								Affected	Affected	Affected
SFRP2	transmembrane receptor								Affected							
SFTPB	other					Affected		Affected							Affected	
SGK1	kinase					Affected	Affected	Affected							Affected	Affected
SHBG	other					Affected		Affected						Affected		
SHH	peptidase	Affected			Affected	Affected			Affected			Affected		Affected	Affected	Affected
SIRPA	phosphatase			Affected												
SIRT1	transcription regulator				Affected	Affected	Affected	Affected								
SIRT6	enzyme					Affected										
SLC10A1	transporter				Affected	Affected	Affected									
SLC10A2	transporter				Affected											
SLC11A1	transporter	Affected				Affected										
SLC12A1	transporter	Affected			Affected	Affected										
SLC12A2	transporter	Affected					Affected									Affected
SLC14A1	transporter	Affected			Affected	Affected										
SLC14A2	transporter	Affected			Affected	Affected										
SLC1A4	transporter					Affected										
SLC20A1	transporter				Affected	Affected										
SLC27A4	transporter							Affected								
SLC2A1	transporter	Affected		Affected	Affected	Affected		Affected	Affected			Affected			Affected	
SLC2A2	transporter	Affected			Affected	Affected		Affected	Affected							
SLC2A3	transporter											Affected				
SLC2A4	transporter	Affected			Affected	Affected		Affected	Affected			Affected		Affected		
SLC2A5	transporter								Affected					Affected		
SLC2A9	transporter				Affected											
SLC3A1	transporter	Affected			Affected				Affected							
SLC4A2	transporter	Affected														
SLC4A4	transporter	Affected														
SLC4A7	transporter			Affected						Affected						
SLC6A4	transporter		Affected		Affected											
SLC6A6	transporter	Affected														
SLC7A1	transporter					Affected	Affected		Affected							
SLC7A2	transporter			Affected		Affected										
SLC7A8	transporter					Affected										
SLC8A1	transporter	Affected				Affected					Affected					
SLC9A1	ion channel							Affected								
SLC9A3	ion channel	Affected			Affected	Affected									Affected	
SLCO1B1	transporter				Affected									Affected		
SLCO2B1	transporter					Affected										
SLIT2	other								Affected							
SLPI	other	Affected				Affected			Affected							
SMAD1	transcription regulator	Affected				Affected										
SMAD2	transcription regulator						Affected									
SMAD3	transcription regulator	Affected				Affected			Affected							
SMAD4	transcription regulator	Affected												Affected		Affected
SMAD6	transcription regulator														Affected	
SMAD9	transcription regulator														Affected	
SMOC2	other													Affected		
SMTN	other	Affected														
SNAP25	transporter	Affected			Affected											
SOCS1	other	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected					Affected	
SOCS3	phosphatase	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected			Affected			Affected	Affected
SOD1	enzyme					Affected		Affected								Affected
SOD2	enzyme	Affected			Affected	Affected			Affected			Affected	Affected	Affected	Affected	Affected
SOD3	enzyme	Affected				Affected			Affected							Affected
SORBS1	other					Affected		Affected								
SORL1	transporter															Affected
SORT1	G-protein coupled receptor	Affected														
SOX13	transcription regulator			Affected						Affected						
SOX6	transcription regulator														Affected	
SPP1	cytokine	Affected		Affected	Affected	Affected	Affected	Affected	Affected							
SREBF1	transcription regulator	Affected			Affected	Affected	Affected	Affected						Affected	Affected	
SREBF2	transcription regulator	Affected												Affected		
SRM	enzyme			Affected												
SST	other						Affected									
ST8SIA4	enzyme					Affected										
STAT3	transcription regulator	Affected	Affected		Affected		Affected					Affected			Affected	
STAT4	transcription regulator	Affected	Affected	Affected	Affected	Affected			Affected	Affected						
STAT5A	transcription regulator			Affected	Affected	Affected			Affected	Affected				Affected		
STAT5B	transcription regulator			Affected				Affected		Affected						
STC2	other											Affected			Affected	
STEAP4	enzyme					Affected										
STK39	kinase			Affected						Affected						
TAP1	transporter	Affected	Affected			Affected			Affected					Affected	Affected	
TBX5	transcription regulator											Affected				
TBXA2R	G-protein coupled receptor							Affected								
TBXAS1	enzyme	Affected				Affected		Affected								
TCF7	transcription regulator			Affected						Affected						
TCF7L2	transcription regulator	Affected														
TERC	other	Affected			Affected	Affected						Affected				
TERT	enzyme	Affected	Affected			Affected			Affected			Affected	Affected	Affected	Affected	
TF	transporter					Affected	Affected									
TFF1	other				Affected											
TFPI2	other				Affected	Affected			Affected					Affected	Affected	
TFRC	transporter	Affected	Affected	Affected		Affected			Affected			Affected				Affected
TGFB1	growth factor	Affected	Affected	Affected	Affected	Affected	Affected		Affected		Affected	Affected	Affected	Affected	Affected	Affected
TGFB2	growth factor	Affected				Affected						Affected				Affected
TGFB3	growth factor			Affected	Affected	Affected			Affected			Affected				
TGFBR1	kinase	Affected		Affected		Affected		Affected								
TGFBR2	kinase	Affected		Affected	Affected	Affected		Affected								
TGFBR3	kinase	Affected														
TH	enzyme					Affected					Affected					
THBD	transmembrane receptor			Affected	Affected	Affected									Affected	
THBS1	other	Affected			Affected	Affected						Affected			Affected	
THBS2	other					Affected										
TIE1	kinase					Affected										
TIMP1	cytokine	Affected	Affected	Affected	Affected	Affected			Affected	Affected	Affected				Affected	Affected
TIMP2	other			Affected	Affected	Affected			Affected							Affected
TIMP3	other	Affected		Affected	Affected	Affected										Affected
TIMP4	other	Affected			Affected	Affected	Affected									

TKT	enzyme							Affected								
TLR2	transmembrane receptor	Affected	Affected	Affected	Affected	Affected			Affected			Affected	Affected	Affected		Affected
TLR4	transmembrane receptor	Affected	Affected	Affected	Affected	Affected		Affected	Affected		Affected					Affected
TLR5	transmembrane receptor	Affected	Affected			Affected										
TLR6	transmembrane receptor	Affected										Affected				
TLR7	transmembrane receptor	Affected	Affected		Affected	Affected										
TLR8	transmembrane receptor	Affected	Affected		Affected	Affected	Affected									
TLR9	transmembrane receptor	Affected	Affected				Affected						Affected	Affected		
TMPRSS6	peptidase											Affected				
TNC	other			Affected		Affected										Affected
TNF	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
TNFAIP3	enzyme				Affected	Affected			Affected				Affected	Affected		Affected
TNFRSF11A	transmembrane receptor	Affected	Affected	Affected	Affected	Affected				Affected						
TNFRSF11B	transmembrane receptor	Affected		Affected	Affected	Affected			Affected			Affected		Affected		Affected
TNFRSF1A	transmembrane receptor	Affected	Affected			Affected	Affected		Affected							
TNFRSF1B	transmembrane receptor	Affected	Affected		Affected	Affected									Affected	Affected
TNFRSF4	transmembrane receptor			Affected		Affected			Affected				Affected	Affected		
TNFSF10	cytokine	Affected	Affected		Affected	Affected		Affected	Affected				Affected		Affected	Affected
TNFSF11	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected					Affected	
TNFSF13	cytokine	Affected														
TNFSF14	cytokine					Affected			Affected							Affected
TNFSF4	cytokine			Affected					Affected							
TNNC1	other					Affected										
TOLLIP	other								Affected							Affected
TOX	transcription regulator					Affected										
TP53	transcription regulator	Affected		Affected		Affected	Affected	Affected	Affected			Affected	Affected	Affected	Affected	Affected
TP73	transcription regulator	Affected												Affected		
TRAF1	other				Affected	Affected			Affected				Affected	Affected		Affected
TRH	other	Affected			Affected				Affected						Affected	
TRIB3	kinase						Affected	Affected	Affected							
TRPC1	ion channel					Affected										Affected
TRPC3	ion channel					Affected			Affected							
TRPC6	ion channel					Affected			Affected					Affected		
TSHR	G-protein coupled receptor	Affected														
TSHZ1	transcription regulator					Affected										
TSLP	cytokine			Affected	Affected	Affected		Affected	Affected	Affected	Affected		Affected	Affected		
TTN	kinase											Affected				
TXN	enzyme					Affected						Affected				
TXN2	enzyme					Affected										
TXNIP	other	Affected			Affected	Affected										
TXNRD1	enzyme					Affected										
TYRP1	enzyme	Affected														
UAP1	enzyme				Affected											
UBA1	enzyme															Affected
UCP1	transporter			Affected		Affected	Affected	Affected		Affected						
UCP2	transporter					Affected		Affected								
UCP3	transporter				Affected	Affected		Affected								
UGT1A1	enzyme				Affected									Affected		
UGT1A6	enzyme						Affected									
UGT1A7 (inc	enzyme							Affected								
VAMP8	transporter							Affected								
VAV3	cytokine					Affected										
VCAM1	transmembrane receptor	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected
VCAN	other		Affected		Affected		Affected								Affected	
VCL	enzyme					Affected										
VDR	transcription regulator	Affected		Affected	Affected	Affected	Affected	Affected			Affected					
VEGFA	growth factor	Affected	Affected	Affected	Affected	Affected		Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected
VEGFC	growth factor	Affected			Affected	Affected			Affected			Affected				Affected
VHL	transcription regulator													Affected		
VIP	other					Affected					Affected				Affected	
VIPR1	G-protein coupled receptor	Affected		Affected		Affected										
VIPR2	G-protein coupled receptor			Affected		Affected										
VNN1	enzyme							Affected								
WARS	enzyme	Affected													Affected	
WNT5A	cytokine	Affected			Affected	Affected			Affected						Affected	
XCL1	cytokine	Affected	Affected	Affected												
XDH	enzyme				Affected	Affected	Affected									
XYLT1	enzyme				Affected			Affected			Affected					
ZFP36	transcription regulator	Affected	Affected	Affected	Affected	Affected			Affected	Affected					Affected	
ZPR1	other	Affected														

Annexed Table 2B. Proteins involved in Hypertension that are related to UBA7. The Upstream Regulator Analysis tool from Ingenuity Pathway Analysis (IPA) was applied to the 2206 hypertension-related proteins obtained from the Phenopedia.

Affected **indicates direct connection between both proteins**

		Master regulator									
Target	**Molecule Type**	**UBA7**	**RAC1**	**TRAF6**	**NFkB (compl**	**Ap1**	**RELA**	**NFKBIA**	**STAT3**	**NFKB1**	**HIF1A**
ABCB1	transporter		Affected		Affected		Affected			Affected	Affected
ABCC8	transporter										Affected
ABCG2	transporter						Affected				
ACE	peptidase					Affected					
ACTA2	other		Affected				Affected		Affected		Affected
ACTN4	transcription regulator						Affected				
ADAMTS9	peptidase				Affected						
ADGRE1	G-protein coupled receptor				Affected						
ADIPOQ	other								Affected		Affected
ADM	other				Affected				Affected		Affected
ADORA1	G-protein coupled receptor									Affected	
ADORA2B	G-protein coupled receptor				Affected						Affected
ADRA2A	G-protein coupled receptor				Affected						
ADRA2C	G-protein coupled receptor				Affected						
AFP	transporter						Affected				Affected
AGER	transmembrane receptor				Affected						
AGRP	other								Affected		
AGT	growth factor		Affected		Affected		Affected		Affected		Affected
AGTR1	G-protein coupled receptor							Affected			
AHR	ligand-dependent nuclear receptor				Affected		Affected		Affected		
AKAP12	transporter										Affected
AKR1B1	enzyme									Affected	
AKT1	kinase		Affected						Affected		Affected
ALDH1B1	enzyme				Affected						
ALOX15	enzyme								Affected		
ALOX5AP	other						Affected				Affected
ANGPTL4	other								Affected		Affected
APLN	other										Affected
APOA1	transporter							Affected			
APOA4	transporter								Affected		
APOE	transporter				Affected		Affected			Affected	Affected
AQP1	transporter				Affected						
AQP4	transporter										Affected
AQP9	transporter										Affected
AR	ligand-dependent nuclear receptor						Affected			Affected	
ARG1	enzyme								Affected	Affected	
ATF3	transcription regulator		Affected		Affected	Affected					
ATP2A2	transporter				Affected						Affected
ATP6AP2	transporter				Affected	Affected	Affected			Affected	
ATP6V1B1	transporter							Affected			
AURKA	kinase										Affected
AXL	kinase							Affected			Affected
BAX	transporter				Affected		Affected	Affected		Affected	Affected
BCL11A	transcription regulator				Affected			Affected			
BCL2A1	other				Affected	Affected	Affected	Affected		Affected	
BDNF	growth factor				Affected	Affected					
BGLAP	other					Affected					
BLVRA	enzyme				Affected		Affected				
BMP2	growth factor				Affected		Affected	Affected		Affected	Affected
BRCA1	transcription regulator										Affected
BRCA2	transcription regulator						Affected			Affected	
C3	peptidase				Affected		Affected	Affected			
C5	cytokine								Affected		
CARD8	other				Affected		Affected				
CASR	G-protein coupled receptor						Affected			Affected	
CAT	enzyme								Affected		
CAV1	transmembrane receptor						Affected				Affected
CAV3	enzyme				Affected						
CBR3	enzyme				Affected						
CBS/CBSL	enzyme						Affected				
CCK	other				Affected						
CCKAR	G-protein coupled receptor				Affected						
CCL11	cytokine				Affected		Affected	Affected	Affected	Affected	
CCL17	cytokine			Affected	Affected				Affected	Affected	
CCL2	cytokine			Affected	Affected	Affected	Affected	Affected	Affected	Affected	
CCL5	cytokine				Affected	Affected	Affected	Affected	Affected	Affected	Affected
CCL8	cytokine				Affected						
CCN2	growth factor		Affected		Affected	Affected	Affected		Affected	Affected	Affected
CCN3	growth factor										Affected
CCND1	transcription regulator		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
CCR2	G-protein coupled receptor				Affected						Affected
CCR3	G-protein coupled receptor							Affected			
CCR5	G-protein coupled receptor								Affected		Affected
CD14	transmembrane receptor						Affected				
CD226	other								Affected		
CD36	transmembrane receptor				Affected						Affected
CD40	transmembrane receptor				Affected	Affected	Affected	Affected	Affected	Affected	
CD46	other								Affected		
CD59	other						Affected			Affected	
CD69	transmembrane receptor				Affected		Affected	Affected			
CDH13	other							Affected			
CDKN2A	transcription regulator					Affected	Affected		Affected		Affected
CDKN2B	transcription regulator								Affected		
CEBPD	transcription regulator				Affected			Affected	Affected		
CETP	enzyme				Affected						

CFB	peptidase				Affected		Affected		Affected	Affected	
CFTR	ion channel				Affected		Affected	Affected		Affected	
CHI3L1	enzyme						Affected	Affected	Affected	Affected	
CIITA	transcription regulator		Affected		Affected		Affected		Affected	Affected	
CKM	kinase		Affected								
CLU	other				Affected	Affected		Affected			
COL18A1	other				Affected						
COL1A1	other						Affected		Affected	Affected	
COL1A2	other		Affected		Affected		Affected	Affected	Affected	Affected	
COL3A1	other							Affected	Affected		
CRHR1	G-protein coupled receptor				Affected						
CRP	other		Affected	Affected	Affected		Affected		Affected	Affected	
CSF2	cytokine			Affected	Affected	Affected	Affected	Affected	Affected	Affected	
CSK	kinase							Affected			
CTF1	cytokine								Affected		
CTLA4	transmembrane receptor								Affected		
CTNNB1	transcription regulator		Affected	Affected	Affected			Affected			
CTSL	peptidase								Affected		
CXCL12	cytokine				Affected	Affected		Affected			Affected
CXCL13	cytokine			Affected					Affected		
CXCL5	cytokine			Affected	Affected		Affected				
CXCL8	cytokine		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
CXCR2	G-protein coupled receptor								Affected		
CXCR4	G-protein coupled receptor				Affected		Affected	Affected	Affected		Affected
CYBA	enzyme							Affected			
CYBB	enzyme			Affected	Affected		Affected			Affected	
CYP17A1	enzyme						Affected				
CYP19A1	enzyme						Affected				Affected
CYP1A1	enzyme						Affected				
CYP1B1	enzyme							Affected			
CYP2C9	enzyme						Affected				
CYP3A4	enzyme				Affected		Affected				
CYP3A5	enzyme				Affected						
CYP46A1	enzyme										Affected
CYP4F3	enzyme										Affected
DBP	transcription regulator				Affected						
DICER1	enzyme									Affected	
DIO1	enzyme				Affected						
DIO2	enzyme						Affected				
DNASE1	enzyme										Affected
DPP4	peptidase								Affected		
DRD2	G-protein coupled receptor				Affected						
DROSHA	enzyme									Affected	
EDN1	cytokine				Affected	Affected	Affected		Affected		Affected
EDNRB	G-protein coupled receptor				Affected						Affected
EGFR	kinase			Affected	Affected					Affected	Affected
EGLN3	enzyme										Affected
ELN	other						Affected				
ENG	transmembrane receptor										Affected
ENPP1	enzyme				Affected						
EPAS1	transcription regulator				Affected		Affected		Affected		Affected
EPO	cytokine							Affected			Affected
ERAP1	peptidase				Affected		Affected	Affected			
ERAP2	peptidase				Affected		Affected	Affected			
ERBB2	kinase				Affected		Affected	Affected			Affected
ERCC1	enzyme					Affected					
ERGIC1	other										Affected
ESR1	ligand-dependent nuclear receptor		Affected						Affected		
ESR2	ligand-dependent nuclear receptor								Affected		
F2RL1	G-protein coupled receptor				Affected	Affected					
FAM13A	other										Affected
FAS	transmembrane receptor		Affected		Affected		Affected	Affected	Affected	Affected	
FGA	other								Affected		
FGB	other								Affected		
FGF1	growth factor				Affected						
FGF10	growth factor						Affected				
FGF5	growth factor				Affected						
FGG	other				Affected				Affected	Affected	
FLT1	kinase								Affected		Affected
FN1	enzyme		Affected		Affected	Affected	Affected	Affected	Affected		Affected
FOS	transcription regulator		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
FOXF1	transcription regulator				Affected						
FOXP3	transcription regulator				Affected		Affected		Affected	Affected	
FURIN	peptidase										Affected
FUT4	enzyme								Affected		
FUT7	enzyme										Affected
FYN	kinase										Affected
GAS5	other							Affected			
GAS6	growth factor				Affected						
GCH1	enzyme				Affected		Affected	Affected			
GCK	kinase										Affected
GCLC	enzyme				Affected						
GDF15	growth factor				Affected		Affected				
GDNF	growth factor				Affected						
GFRA1	transmembrane receptor									Affected	
GHR	transmembrane receptor										Affected
GJA1	transporter								Affected	Affected	Affected
GLA	enzyme				Affected						
GNAS	enzyme				Affected						
GNRH1	other							Affected			
GNRHR	G-protein coupled receptor					Affected					

GP1BB	other						Affected				
GPER1	G-protein coupled receptor										Affected
GPX3	enzyme							Affected			
GRK5	kinase				Affected		Affected	Affected		Affected	
GSN	other		Affected								
GSS	enzyme					Affected					
GSTA1	enzyme						Affected				
GSTM5	enzyme							Affected			
GSTP1	enzyme					Affected					
HAMP	other				Affected				Affected		Affected
HAS2	enzyme				Affected		Affected		Affected	Affected	
HAVCR1	other								Affected		
HBB	transporter					Affected			Affected		
HBG1	other								Affected		
HDAC9	transcription regulator				Affected						
HES1	transcription regulator						Affected	Affected			
HES5	transcription regulator				Affected				Affected	Affected	
HGF	growth factor								Affected		
HGFAC	peptidase				Affected						
HIF1A	transcription regulator		Affected	Affected	Affected		Affected	Affected	Affected		Affected
HIF3A	transcription regulator				Affected						Affected
HLA-A	other				Affected			Affected	Affected		
HLA-B	transmembrane receptor						Affected				
HLA-DQA1	transmembrane receptor								Affected		
HLA-DRB5	transmembrane receptor								Affected		
HMGA1	transcription regulator							Affected			
HMOX1	enzyme		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
HNF4A	transcription regulator				Affected		Affected		Affected		
HP	peptidase								Affected		Affected
HSD11B2	enzyme		Affected								
HSPA1L	other				Affected						
HSPA4	other										Affected
HSPA8	enzyme							Affected			
HTR2A	G-protein coupled receptor								Affected		
ICAM1	transmembrane receptor		Affected	Affected	Affected		Affected	Affected	Affected	Affected	
ICOS	transmembrane receptor				Affected				Affected		
IFI30	enzyme								Affected		
IFIH1	enzyme								Affected		
IFNG	cytokine		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
IFNK	cytokine				Affected						
IGF1	growth factor					Affected	Affected				Affected
IGF1R	transmembrane receptor						Affected		Affected		
IGF2	growth factor							Affected			Affected
IGF2R	transmembrane receptor							Affected			
IGFBP1	other								Affected		
IGFBP3	other					Affected				Affected	Affected
IKBKB	kinase									Affected	
IKBKE	kinase				Affected		Affected		Affected	Affected	
IL10	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL10RA	transmembrane receptor				Affected						
IL12A	cytokine	Affected			Affected		Affected	Affected		Affected	
IL12B	cytokine			Affected	Affected	Affected	Affected		Affected	Affected	Affected
IL12RB1	transmembrane receptor								Affected		
IL13	cytokine		Affected		Affected	Affected	Affected	Affected	Affected	Affected	
IL13RA2	transmembrane receptor				Affected				Affected		
IL15	cytokine			Affected	Affected			Affected			Affected
IL15RA	transmembrane receptor				Affected		Affected	Affected			
IL17A	cytokine				Affected				Affected		Affected
IL17RA	transmembrane receptor										Affected
IL18	cytokine				Affected					Affected	
IL18R1	transmembrane receptor								Affected		
IL1A	cytokine				Affected	Affected	Affected	Affected			Affected
IL1B	cytokine		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL1R1	transmembrane receptor								Affected		
IL1RN	cytokine				Affected		Affected	Affected	Affected	Affected	
IL2	cytokine		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	
IL22	cytokine				Affected		Affected		Affected		Affected
IL23A	cytokine	Affected	Affected		Affected	Affected	Affected		Affected	Affected	
IL23R	transmembrane receptor								Affected		Affected
IL24	cytokine				Affected						
IL2RA	transmembrane receptor				Affected	Affected	Affected	Affected	Affected	Affected	
IL2RB	transmembrane receptor								Affected		
IL3	cytokine					Affected					
IL33	cytokine		Affected					Affected			
IL4	cytokine		Affected		Affected	Affected	Affected		Affected		Affected
IL4R	transmembrane receptor								Affected		
IL5	cytokine		Affected		Affected	Affected		Affected	Affected	Affected	
IL6	cytokine		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL6R	transmembrane receptor		Affected						Affected		
IL6ST	transmembrane receptor								Affected		
IL7R	transmembrane receptor				Affected		Affected	Affected			
IL9	cytokine						Affected		Affected		
IL9R	transmembrane receptor								Affected		
INSIG2	other										Affected
IRAK1	kinase							Affected			
IRF5	transcription regulator			Affected					Affected		
IRS2	enzyme										Affected
ITGA2	transmembrane receptor					Affected		Affected			
ITGA2B	transmembrane receptor										Affected
ITGAM	transmembrane receptor				Affected				Affected		
ITGAV	transmembrane receptor				Affected			Affected	Affected		Affected

ITGB1	transmembrane receptor		Affected		Affected			Affected	Affected		
ITGB2	transmembrane receptor								Affected		Affected
ITGB3	transmembrane receptor										Affected
ITGB6	other								Affected		
ITGB8	other				Affected						
JAG1	growth factor				Affected				Affected	Affected	
JAK2	kinase								Affected		
JDP2	transcription regulator							Affected			
JUN	transcription regulator		Affected		Affected	Affected	Affected	Affected			Affected
KCNH2	ion channel							Affected			
KDR	kinase				Affected				Affected		
KIR3DL2	other		Affected								
KIT	transmembrane receptor				Affected		Affected				
KLF5	transcription regulator							Affected			
KYNU	enzyme				Affected						
LBP	transporter								Affected		
LCAT	enzyme								Affected		
LCN2	transporter				Affected			Affected			
LDHA	enzyme								Affected		Affected
LEP	growth factor								Affected		Affected
LEPR	transmembrane receptor								Affected		
let-7	microRNA									Affected	
LGR5	transmembrane receptor						Affected				
LHCGR	G-protein coupled receptor				Affected	Affected					
LOX	enzyme								Affected		Affected
LOXL2	enzyme										Affected
LPL	enzyme					Affected					
LRP2	transporter								Affected		
LSP1	other				Affected						
LTA	cytokine				Affected		Affected		Affected	Affected	
LTC4S	enzyme				Affected		Affected			Affected	
LTF	peptidase								Affected		
MAF	transcription regulator								Affected		
MAP2K5	kinase								Affected		
MAPK8	kinase		Affected								
MBL2	other				Affected						
MEF2C	transcription regulator										Affected
MET	kinase					Affected					Affected
MGAT5	enzyme								Affected		
MGP	other							Affected			
MIF	cytokine						Affected				Affected
mir-146	microRNA				Affected		Affected			Affected	
MITF	transcription regulator								Affected		Affected
MMP1	peptidase		Affected		Affected	Affected	Affected	Affected			Affected
MMP12	peptidase					Affected			Affected		
MMP14	peptidase		Affected					Affected			
MMP2	peptidase		Affected		Affected	Affected			Affected		Affected
MMP3	peptidase				Affected	Affected	Affected	Affected	Affected	Affected	
MMP7	peptidase					Affected	Affected		Affected	Affected	Affected
MMP9	peptidase		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
MRAS	enzyme								Affected		
MSR1	transmembrane receptor					Affected				Affected	
MT-ATP6	transporter								Affected		
MT-CO1	enzyme								Affected		
MT-CO2	enzyme				Affected	Affected			Affected		
MT-CYB	enzyme						Affected	Affected	Affected		
MT-ND1	enzyme								Affected		Affected
MT-ND2	enzyme								Affected		
MT-ND4	enzyme								Affected		
MT-ND6	enzyme								Affected		
MYB	transcription regulator						Affected		Affected	Affected	
MYH7	enzyme		Affected						Affected		Affected
MYLK	kinase				Affected						
MYOD1	transcription regulator					Affected	Affected	Affected	Affected		
NAMPT	cytokine				Affected		Affected		Affected		
NCAM1	other				Affected						
NCF2	enzyme			Affected	Affected						
NFATC1	transcription regulator						Affected			Affected	
NFKB1	transcription regulator			Affected	Affected		Affected	Affected	Affected	Affected	
NFKB2	transcription regulator				Affected		Affected	Affected		Affected	
NFKBIA	transcription regulator				Affected		Affected	Affected		Affected	
NFKBIZ	transcription regulator				Affected				Affected		
NOD2	other						Affected	Affected		Affected	
NOS1	enzyme				Affected						
NOS2	enzyme			Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
NOS3	enzyme							Affected	Affected		Affected
NOTCH1	transcription regulator				Affected		Affected		Affected		Affected
NOTCH3	transcription regulator								Affected		
NOX1	enzyme						Affected		Affected		
NOX4	enzyme										Affected
NPPA	other		Affected		Affected			Affected	Affected		Affected
NPPB	other		Affected		Affected		Affected			Affected	
NPY	other								Affected		
NQO1	enzyme					Affected					
NR3C1	ligand-dependent nuclear receptor					Affected					
NR4A3	ligand-dependent nuclear receptor						Affected			Affected	Affected
OAS3	enzyme								Affected		
OASL	enzyme								Affected		
OLR1	transmembrane receptor				Affected		Affected				
OPRM1	G-protein coupled receptor				Affected	Affected					
P2RY2	G-protein coupled receptor				Affected		Affected				

PADI4	enzyme					Affected					
PARP1	enzyme						Affected				
PAX2	transcription regulator						Affected				
PAX5	transcription regulator								Affected		
PCK1	kinase					Affected	Affected		Affected		
PCSK1	peptidase								Affected		
PCSK9	peptidase								Affected		
PDX1	transcription regulator				Affected						
PECAM1	other				Affected		Affected		Affected		
PGR	ligand-dependent nuclear receptor								Affected		
PI3	other						Affected			Affected	
PICALM	other							Affected			
PIK3R1	kinase							Affected			
PLAT	peptidase							Affected			
PLAUR	transmembrane receptor		Affected						Affected		Affected
PML	transcription regulator								Affected		
POLG	enzyme										Affected
POMC	other								Affected		
POU2F1	transcription regulator								Affected		
POU5F1	transcription regulator						Affected		Affected		Affected
PPARA	ligand-dependent nuclear receptor				Affected						Affected
PPARG	ligand-dependent nuclear receptor				Affected		Affected				
PPARGC1A	transcription regulator								Affected		
PPFIA4	phosphatase										Affected
PRKCA	kinase										Affected
PRKG1	kinase		Affected								
PRL	cytokine		Affected			Affected		Affected			
PROCR	other								Affected		
PSIP1	transcription regulator								Affected		
PSMB8	peptidase								Affected		
PSMB9	peptidase				Affected		Affected		Affected		
PTEN	phosphatase						Affected	Affected			Affected
PTGDS	enzyme						Affected				
PTGES	enzyme				Affected		Affected	Affected			
PTGIS	enzyme										Affected
PTGS2	enzyme		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
PTN	growth factor								Affected		
PTPN2	phosphatase								Affected		
RAC1	enzyme		Affected					Affected			
RBPJ	transcription regulator				Affected				Affected		
REG3A	enzyme						Affected		Affected		
REL	transcription regulator				Affected						
RELA	transcription regulator			Affected	Affected		Affected	Affected		Affected	Affected
REN	peptidase								Affected		
RET	kinase								Affected		Affected
RGS4	other							Affected			
RNLS	enzyme								Affected		
ROCK1	kinase							Affected			
RORA	ligand-dependent nuclear receptor								Affected		
RSPO3	kinase					Affected					
RUNX1	transcription regulator				Affected				Affected		
S100A4	other					Affected					
SAA1	transporter				Affected		Affected		Affected		
SBF1	phosphatase						Affected				
SDC4	other				Affected		Affected	Affected		Affected	Affected
SELE	transmembrane receptor			Affected	Affected	Affected	Affected	Affected		Affected	
SELP	transmembrane receptor						Affected			Affected	
SELPLG	other				Affected						
SEMA3F	other							Affected			
SERPINA1	other								Affected		
SERPINA3	other			Affected	Affected				Affected		
SERPINB1	other								Affected		
SERPINE1	other				Affected	Affected			Affected		Affected
SERPINE2	other						Affected	Affected	Affected		
SFRP2	transmembrane receptor				Affected						
SFTPB	other								Affected		
SGK1	kinase							Affected	Affected		
SHBG	other						Affected				
SHH	peptidase				Affected		Affected	Affected	Affected		Affected
SLC12A2	transporter							Affected			
SLC2A1	transporter				Affected				Affected		Affected
SLC2A2	transporter				Affected						
SLC2A3	transporter										Affected
SLC2A4	transporter				Affected		Affected				Affected
SLC2A5	transporter				Affected		Affected				
SLC3A1	transporter				Affected						
SLC7A1	transporter				Affected						
SLC8A1	transporter					Affected					
SLC9A3	ion channel								Affected		
SLCO1B1	transporter						Affected				
SLIT2	other				Affected						
SLPI	other				Affected						
SMAD3	transcription regulator				Affected						
SMAD4	transcription regulator						Affected	Affected			
SMAD6	transcription regulator								Affected		
SMAD9	transcription regulator								Affected		
SMOC2	other						Affected				
SOCS1	other				Affected				Affected		
SOCS3	phosphatase				Affected			Affected	Affected		Affected
SOD1	enzyme							Affected			
SOD2	enzyme		Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected

SOD3	enzyme				Affected			Affected			
SORL1	transporter							Affected			
SOX6	transcription regulator		Affected						Affected		
SPP1	cytokine				Affected						
SREBF1	transcription regulator						Affected		Affected		
SREBF2	transcription regulator						Affected				
STAT3	transcription regulator		Affected						Affected		Affected
STAT4	transcription regulator				Affected						
STAT5A	transcription regulator				Affected		Affected				
STC2	other								Affected		Affected
TAP1	transporter				Affected		Affected		Affected		
TBX5	transcription regulator										Affected
TERC	other										Affected
TERT	enzyme				Affected		Affected		Affected	Affected	Affected
TFPI2	other				Affected		Affected		Affected		
TFRC	transporter				Affected			Affected			Affected
TGFB1	growth factor		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
TGFB2	growth factor							Affected			Affected
TGFB3	growth factor				Affected						Affected
TH	enzyme					Affected					
THBD	transmembrane receptor								Affected		
THBS1	other								Affected		Affected
TIMP1	cytokine				Affected	Affected		Affected	Affected		
TIMP2	other				Affected			Affected			
TIMP3	other							Affected			
TLR2	transmembrane receptor				Affected		Affected	Affected		Affected	Affected
TLR4	transmembrane receptor				Affected	Affected		Affected			
TLR6	transmembrane receptor										Affected
TLR9	transmembrane receptor						Affected			Affected	
TMPRSS6	peptidase										Affected
TNC	other							Affected			
TNF	cytokine	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
TNFAIP3	enzyme			Affected	Affected		Affected	Affected		Affected	
TNFRSF11B	transmembrane receptor				Affected		Affected	Affected			Affected
TNFRSF1A	transmembrane receptor				Affected						
TNFRSF1B	transmembrane receptor							Affected	Affected		
TNFRSF4	transmembrane receptor				Affected		Affected			Affected	
TNFSF10	cytokine				Affected			Affected	Affected	Affected	
TNFSF11	cytokine				Affected				Affected		
TNFSF14	cytokine				Affected			Affected			
TNFSF4	cytokine				Affected						
TOLLIP	other				Affected			Affected			
TP53	transcription regulator				Affected		Affected	Affected	Affected	Affected	Affected
TP73	transcription regulator						Affected				
TRAF1	other				Affected		Affected	Affected		Affected	
TRH	other				Affected				Affected		
TRIB3	kinase				Affected						
TRPC1	ion channel							Affected			
TRPC3	ion channel				Affected						
TRPC6	ion channel				Affected		Affected				
TSLP	cytokine				Affected	Affected	Affected			Affected	
TTN	kinase										Affected
TXN	enzyme										Affected
UBA1	enzyme							Affected			
UGT1A1	enzyme						Affected				
VCAM1	transmembrane receptor		Affected		Affected	Affected	Affected	Affected		Affected	Affected
VCAN	other								Affected		
VDR	transcription regulator					Affected					
VEGFA	growth factor		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected
VEGFC	growth factor				Affected			Affected			Affected
VHL	transcription regulator						Affected				
VIP	other					Affected			Affected		
WARS	enzyme								Affected		
WNT5A	cytokine		Affected		Affected				Affected		
XYLT1	enzyme					Affected					
ZFP36	transcription regulator				Affected				Affected		

Annexed Table 2C. Proteins involved in Hypertension that are related to USP18. The Upstream Regulator Analysis tool from Ingenuity Pathway Analysis (IPA) was applied to the 2206 hypertension-related proteins obtained from the Phenopedia. USP18 interacts with 558 of the proteins involved in hypertension. Of these, with 10 it does so directly (CCL5,IFIH1,IFNG,IL15,IL2,IL6,NFATC1,SOCS1,SOCS3,TNFSF10) and with the rest it does so indirectly through Master Regulators (TAB1, STAT1,NFATC2, MAP3K7,RCAN1,Ikb,ATF2,IRF8,NFKB1,NFKBIA, NFKB(compex),Ap1,NFATC3,NFATC1, STAT3, STAT2, RELA, STAT4, IRF9).

Affected **indicates direct connection between both proteins**

		Master regulator																		
Target	**Molecule Type**	**USP18**	**TAB1**	**STAT1**	**NFATC2**	**MAP3K7**	**RCAN1**	**Ikb**	**ATF2**	**IRF8**	**NFKB1**	**NFKBIA**	**NFkB (compl**	**Ap1**	**NFATC3**	**NFATC1**	**STAT3**	**STAT2**	**RELA**	**STAT4**	**IRF9**
ABCA1	transporter			Affected	Affected																
ABCB1	transporter										Affected		Affected						Affected		
ABCG2	transporter																		Affected		
ACE	peptidase													Affected							
ACSS1	enzyme																			Affected	
ACTA2	other														Affected		Affected		Affected		
ACTN4	transcription regulator																		Affected		
ACVRL1	kinase									Affected										Affected	
ADAMTS9	peptidase												Affected								
ADGRE1	G-protein coupled receptor									Affected			Affected								
ADIPOQ	other																Affected				
ADM	other												Affected				Affected				
ADORA1	G-protein coupled receptor										Affected										
ADORA2B	G-protein coupled receptor												Affected								
ADRA2A	G-protein coupled receptor												Affected								
ADRA2C	G-protein coupled receptor												Affected								
AFP	transporter																		Affected		
AGER	transmembrane receptor												Affected								
AGRP	other																Affected				
AGT	growth factor			Affected									Affected				Affected		Affected		
AGTR1	G-protein coupled receptor											Affected									
AHR	ligand-dependent nuclear receptor												Affected			Affected	Affected		Affected		
AKR1B1	enzyme										Affected										
AKT1	kinase																Affected				
ALDH1B1	enzyme												Affected								
ALOX15	enzyme			Affected													Affected				
ALOX5AP	other																		Affected		
ALPK1	kinase			Affected																	
ANGPTL4	other																Affected				
APOA1	transporter											Affected									
APOA4	transporter																Affected				
APOC2	transporter			Affected																	
APOC3	transporter								Affected												
APOE	transporter			Affected							Affected		Affected						Affected		
APOL4	other			Affected																	
AQP1	transporter												Affected								
AR	ligand-dependent nuclear receptor										Affected								Affected		
ARG1	enzyme			Affected							Affected						Affected				
ATF3	transcription regulator								Affected	Affected			Affected	Affected	Affected						
ATM	kinase				Affected																
ATP2A2	transporter												Affected								
ATP6AP2	transporter										Affected		Affected	Affected					Affected		
ATP6V1B1	transporter											Affected									
AXL	kinase			Affected								Affected									
BAX	transporter			Affected						Affected	Affected	Affected	Affected						Affected		
BCL11A	transcription regulator											Affected	Affected								
BCL2A1	other								Affected		Affected	Affected	Affected	Affected					Affected		
BDNF	growth factor						Affected						Affected	Affected							
BGLAP	other													Affected							
BLVRA	enzyme							Affected					Affected						Affected		
BMP2	growth factor										Affected	Affected	Affected		Affected				Affected		
BMP7	growth factor															Affected					
BRCA2	transcription regulator										Affected								Affected		
C3	peptidase			Affected								Affected	Affected						Affected	Affected	
C4A/C4B	other			Affected																	
C5	cytokine																Affected				
CALCR	G-protein coupled receptor															Affected					
CAPN5	peptidase																			Affected	
CARD8	other												Affected						Affected		
CASR	G-protein coupled receptor										Affected								Affected		
CAT	enzyme																Affected				
CAV1	transmembrane receptor																	Affected	Affected		
CAV3	enzyme												Affected								
CBR3	enzyme												Affected								
CBS/CBSL	enzyme																		Affected		
CCK	other												Affected								
CCKAR	G-protein coupled receptor												Affected								
CCL11	cytokine										Affected	Affected	Affected				Affected		Affected		
CCL17	cytokine				Affected						Affected		Affected				Affected				
CCL2	cytokine			Affected				Affected			Affected	Affected	Affected	Affected			Affected		Affected	Affected	
CCL5	cytokine	Affected	Affected	Affected	Affected	Affected				Affected	Affected	Affected	Affected	Affected			Affected	Affected	Affected		
CCL8	cytokine												Affected								
CCN2	growth factor										Affected		Affected	Affected			Affected		Affected		
CCND1	transcription regulator			Affected				Affected	Affected		Affected	Affected	Affected	Affected		Affected	Affected		Affected		
CCR2	G-protein coupled receptor									Affected			Affected								
CCR3	G-protein coupled receptor											Affected									
CCR5	G-protein coupled receptor				Affected												Affected			Affected	
CD14	transmembrane receptor			Affected		Affected				Affected									Affected		
CD226	other																Affected				
CD36	transmembrane receptor						Affected						Affected								
CD40	transmembrane receptor			Affected	Affected					Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected		
CD46	other																Affected				
CD59	other										Affected								Affected		
CD69	transmembrane receptor											Affected	Affected		Affected				Affected		Affected
CDH13	other											Affected									
CDKN2A	transcription regulator								Affected					Affected			Affected		Affected		
CDKN2B	transcription regulator																Affected				
CEBPD	transcription regulator			Affected								Affected	Affected				Affected				
CETP	enzyme												Affected								
CFB	peptidase		Affected	Affected		Affected		Affected		Affected	Affected		Affected				Affected		Affected		
CFTR	ion channel										Affected	Affected	Affected						Affected		
CHI3L1	enzyme										Affected	Affected					Affected		Affected		
CIITA	transcription regulator			Affected						Affected	Affected		Affected				Affected	Affected	Affected		Affected
CLU	other											Affected	Affected	Affected							
COL18A1	other												Affected								
COL1A1	other										Affected				Affected	Affected	Affected		Affected		
COL1A2	other										Affected	Affected	Affected				Affected		Affected		
COL3A1	other											Affected					Affected				
CRHR1	G-protein coupled receptor												Affected								
CRP	other										Affected		Affected				Affected		Affected		
CSF2	cytokine			Affected	Affected						Affected	Affected	Affected	Affected		Affected	Affected		Affected		
CSK	kinase											Affected									
CTF1	cytokine																Affected				
CTLA4	transmembrane receptor				Affected												Affected				
CTNNB1	transcription regulator								Affected			Affected	Affected								
CTSL	peptidase																Affected				
CX3CR1	G-protein coupled receptor			Affected	Affected											Affected					
CXCL12	cytokine											Affected	Affected	Affected							
CXCL13	cytokine																Affected				
CXCL5	cytokine												Affected						Affected		
CXCL8	cytokine		Affected	Affected		Affected	Affected		Affected		Affected	Affected	Affected	Affected			Affected	Affected	Affected		Affected
CXCR2	G-protein coupled receptor																Affected				
CXCR4	G-protein coupled receptor											Affected	Affected				Affected		Affected		
CYBA	enzyme											Affected									
CYBB	enzyme									Affected	Affected		Affected			Affected			Affected		
CYP11B2	enzyme								Affected												
CYP17A1	enzyme																		Affected		
CYP19A1	enzyme																		Affected		
CYP1A1	enzyme															Affected			Affected		
CYP1A2	enzyme			Affected																	
CYP1B1	enzyme											Affected				Affected					
CYP2C8	enzyme			Affected																	
CYP2C9	enzyme																		Affected		
CYP2E1	enzyme			Affected																	
CYP3A4	enzyme												Affected						Affected		
CYP3A5	enzyme			Affected									Affected								
CYP4A11	enzyme			Affected																	
DBP	transcription regulator												Affected								
DDAH2	enzyme																			Affected	
DICER1	enzyme										Affected										
DIO1	enzyme												Affected								
DIO2	enzyme																		Affected		
DPP4	peptidase			Affected													Affected				
DRD2	G-protein coupled receptor												Affected								
DROSHA	enzyme										Affected										
DUOX2	enzyme			Affected																	
EDN1	cytokine			Affected	Affected								Affected	Affected	Affected	Affected	Affected		Affected		
EDNRB	G-protein coupled receptor												Affected								
EGFR	kinase										Affected		Affected								
EGLN3	enzyme			Affected																	
ELN	other																		Affected		
ENPP1	enzyme												Affected								
EPAS1	transcription regulator												Affected				Affected		Affected		
EPO	cytokine											Affected									
ERAP1	peptidase											Affected	Affected						Affected		
ERAP2	peptidase											Affected	Affected						Affected		
ERBB2	kinase											Affected	Affected						Affected		
ERCC1	enzyme													Affected							
ESR1	ligand-dependent nuclear receptor																Affected				

ESR2	ligand-dependent nuclear receptor															Affected					
ETV5	transcription regulator																			Affected	
F2RL1	G-protein coupled receptor												Affected	Affected							
FAS	transmembrane receptor			Affected	Affected					Affected	Affected	Affected	Affected			Affected	Affected		Affected		
FCGR2B	transmembrane receptor			Affected																	
FDX1	transporter																			Affected	
FGA	other															Affected					
FGB	other															Affected					
FGF1	growth factor												Affected								
FGF10	growth factor																	Affected			
FGF21	growth factor								Affected												
FGF5	growth factor												Affected								
FGG	other										Affected		Affected			Affected					
FLT1	kinase															Affected					
FN1	enzyme								Affected			Affected	Affected	Affected				Affected		Affected	
FOS	transcription regulator			Affected			Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected			Affected		Affected	
FOXF1	transcription regulator												Affected								
FOXO1	transcription regulator			Affected																	
FOXP3	transcription regulator			Affected	Affected						Affected		Affected			Affected	Affected		Affected		
FURIN	peptidase			Affected																Affected	
FUT4	enzyme															Affected					
GAS5	other											Affected								Affected	
GAS6	growth factor												Affected								
GATA4	transcription regulator					Affected															
GCG	other				Affected																
GCH1	enzyme		Affected			Affected						Affected	Affected						Affected		
GCK	kinase			Affected												Affected					
GCLC	enzyme												Affected								
GDF15	growth factor												Affected						Affected		
GDNF	growth factor												Affected								
GFRA1	transmembrane receptor										Affected										
GIP	other								Affected												
GJA1	transporter										Affected				Affected		Affected			Affected	
GLA	enzyme												Affected								
GNAS	enzyme												Affected								
GNRH1	other											Affected									
GNRHR	G-protein coupled receptor													Affected							
GP1BB	other																	Affected			
GPX3	enzyme											Affected									
GRK5	kinase										Affected	Affected	Affected					Affected			
GSS	enzyme													Affected							
GSTA1	enzyme																	Affected			
GSTM5	enzyme											Affected									
GSTP1	enzyme													Affected							
HAMP	other												Affected			Affected					
HAS2	enzyme										Affected		Affected			Affected		Affected			
HAVCR1	other															Affected					
HBB	transporter													Affected		Affected					
HBG1	other			Affected												Affected					
HDAC9	transcription regulator												Affected								
HES1	transcription regulator			Affected								Affected						Affected			
HES5	transcription regulator										Affected		Affected			Affected					
HGF	growth factor															Affected					
HGFAC	peptidase												Affected								
HHEX	transcription regulator							Affected													
HIF1A	transcription regulator			Affected								Affected	Affected			Affected		Affected			
HIF3A	transcription regulator												Affected								
HLA-A	other											Affected	Affected			Affected					
HLA-B	transmembrane receptor																	Affected			
HLA-DQA1	transmembrane receptor			Affected												Affected					
HLA-DQB1	other																			Affected	
HLA-DRB5	transmembrane receptor			Affected												Affected					
HMGA1	transcription regulator											Affected									
HMOX1	enzyme					Affected					Affected	Affected	Affected	Affected		Affected		Affected			
HNF1A	transcription regulator															Affected					
HNF1B	transcription regulator															Affected					
HNF4A	transcription regulator												Affected			Affected	Affected		Affected		
HP	peptidase																Affected				
HSPA1L	other												Affected								
HSPA8	enzyme											Affected									
HTR2A	G-protein coupled receptor																Affected				
HTRA1	peptidase			Affected																	
ICAM1	transmembrane receptor			Affected			Affected	Affected		Affected	Affected	Affected	Affected			Affected	Affected		Affected		
ICOS	transmembrane receptor				Affected								Affected			Affected	Affected				
ID3	transcription regulator									Affected											
IFI30	enzyme			Affected													Affected				
IFIH1	enzyme	Affected	Affected	Affected		Affected											Affected			Affected	
IFNG	cytokine	Affected		Affected	Affected				Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IFNK	cytokine									Affected			Affected								
IFNL3	cytokine			Affected																	
IGF1	growth factor			Affected										Affected				Affected			
IGF1R	transmembrane receptor			Affected													Affected		Affected		
IGF2	growth factor											Affected									
IGF2R	transmembrane receptor											Affected									
IGFBP1	other																Affected				
IGFBP3	other										Affected			Affected							
IKBKB	kinase										Affected										
IKBKE	kinase										Affected		Affected				Affected		Affected		
IKZF1	transcription regulator				Affected																
IL10	cytokine			Affected	Affected				Affected		Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	
IL10RA	transmembrane receptor												Affected							Affected	
IL12A	cytokine			Affected	Affected					Affected	Affected	Affected	Affected					Affected	Affected		Affected
IL12B	cytokine			Affected	Affected	Affected				Affected	Affected		Affected	Affected	Affected	Affected	Affected		Affected		
IL12RB1	transmembrane receptor																Affected			Affected	
IL12RB2	transmembrane receptor			Affected	Affected															Affected	
IL13	cytokine				Affected				Affected		Affected	Affected	Affected	Affected	Affected		Affected		Affected	Affected	
IL13RA2	transmembrane receptor												Affected				Affected				
IL15	cytokine	Affected		Affected	Affected					Affected		Affected	Affected								
IL15RA	transmembrane receptor			Affected								Affected	Affected						Affected		
IL17A	cytokine			Affected	Affected								Affected			Affected	Affected			Affected	
IL17RA	transmembrane receptor									Affected											
IL18	cytokine			Affected	Affected					Affected	Affected		Affected								Affected
IL18R1	transmembrane receptor																Affected			Affected	
IL18RAP	transmembrane receptor																			Affected	
IL1A	cytokine				Affected							Affected	Affected	Affected					Affected		Affected
IL1B	cytokine		Affected	Affected	Affected	Affected				Affected	Affected	Affected	Affected	Affected		Affected	Affected		Affected		
IL1R1	transmembrane receptor			Affected													Affected				
IL1RL1	transmembrane receptor								Affected												
IL1RN	cytokine										Affected	Affected	Affected				Affected		Affected		
IL2	cytokine	Affected	Affected	Affected	Affected	Affected	Affected		Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	
IL22	cytokine				Affected								Affected			Affected	Affected		Affected	Affected	
IL23A	cytokine								Affected		Affected		Affected	Affected			Affected		Affected		
IL23R	transmembrane receptor																Affected				
IL24	cytokine												Affected								
IL2RA	transmembrane receptor				Affected						Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	
IL2RB	transmembrane receptor																Affected				
IL3	cytokine													Affected							
IL33	cytokine											Affected				Affected					
IL4	cytokine			Affected	Affected					Affected			Affected	Affected	Affected	Affected	Affected		Affected		
IL4R	transmembrane receptor																Affected				
IL5	cytokine				Affected					Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected				
IL6	cytokine	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
IL6R	transmembrane receptor																Affected				
IL6ST	transmembrane receptor																Affected				
IL7R	transmembrane receptor											Affected	Affected						Affected		
IL9	cytokine				Affected	Affected											Affected		Affected		
IL9R	transmembrane receptor																Affected				
INS	other			Affected												Affected					
IRAK1	kinase											Affected									
IRF5	transcription regulator			Affected						Affected							Affected	Affected			Affected
ITGA2	transmembrane receptor											Affected		Affected							
ITGAM	transmembrane receptor									Affected			Affected				Affected				
ITGAV	transmembrane receptor											Affected	Affected			Affected	Affected				
ITGB1	transmembrane receptor					Affected						Affected	Affected				Affected				
ITGB2	transmembrane receptor																Affected				
ITGB3	transmembrane receptor															Affected					
ITGB6	other																Affected				
ITGB8	other								Affected				Affected								
ITPR2	ion channel															Affected					
JAG1	growth factor										Affected		Affected				Affected				
JAK2	kinase			Affected													Affected				
JDP2	transcription regulator											Affected									
JUN	transcription regulator		Affected	Affected	Affected	Affected			Affected			Affected	Affected	Affected	Affected				Affected		
KCNH2	ion channel											Affected									
KDR	kinase												Affected				Affected				
KIT	transmembrane receptor												Affected						Affected		
KLF5	transcription regulator											Affected									
KYNU	enzyme												Affected								
LBP	transporter																Affected				
LCAT	enzyme																Affected				
LCN2	transporter			Affected								Affected	Affected								
LDHA	enzyme				Affected												Affected				
LEP	growth factor																Affected				
LEPR	transmembrane receptor																Affected				
let-7	microRNA										Affected										
LGR5	transmembrane receptor																		Affected		

LHCGR	G-protein coupled receptor												Affected	Affected							
LOX	enzyme																Affected				
LPIN1	phosphatase																			Affected	
LPL	enzyme													Affected							
LRP1	transmembrane receptor																			Affected	
LRP2	transporter																Affected				
LSP1	other									Affected			Affected								
LTA	cytokine										Affected		Affected				Affected		Affected		
LTC4S	enzyme										Affected		Affected						Affected		
LTF	peptidase																Affected				
Ly6a (include	other			Affected																	
MAF	transcription regulator				Affected					Affected							Affected				
MAP2K5	kinase																Affected				
MAPK3	kinase				Affected																
MBL2	other												Affected								
MET	kinase													Affected							
MGAT5	enzyme																Affected				
MGP	other											Affected									
MIF	cytokine																		Affected		
mir-146	microRNA										Affected		Affected						Affected		
mir-27	microRNA			Affected																	
MITF	transcription regulator				Affected												Affected				
MLLT3	transcription regulator																			Affected	
MMP1	peptidase					Affected		Affected	Affected			Affected	Affected	Affected					Affected		
MMP12	peptidase													Affected			Affected				
MMP14	peptidase											Affected									
MMP2	peptidase												Affected	Affected			Affected				
MMP3	peptidase					Affected					Affected	Affected	Affected	Affected	Affected		Affected		Affected		
MMP7	peptidase										Affected			Affected			Affected		Affected		
MMP9	peptidase			Affected						Affected	Affected	Affected	Affected	Affected			Affected		Affected		
MRAS	enzyme																Affected				
MSR1	transmembrane receptor									Affected	Affected			Affected							
MT-ATP6	transporter																Affected				
MT-CO1	enzyme																Affected				
MT-CO2	enzyme												Affected	Affected			Affected				
MT-CYB	enzyme											Affected					Affected		Affected		
MT-ND1	enzyme																Affected				
MT-ND2	enzyme																Affected				
MT-ND4	enzyme																Affected				
MT-ND6	enzyme																Affected				
MYB	transcription regulator										Affected						Affected		Affected		
MYH7	enzyme					Affected	Affected		Affected						Affected	Affected	Affected				
MYLK	kinase								Affected				Affected								
MYOD1	transcription regulator					Affected						Affected		Affected			Affected		Affected		
NAMPT	cytokine												Affected				Affected		Affected		
NCAM1	other												Affected								
NCF2	enzyme												Affected								
NF1	other									Affected											
NFATC1	transcription regulator	Affected			Affected					Affected	Affected				Affected	Affected			Affected		
NFKB1	transcription regulator		Affected		Affected	Affected		Affected			Affected	Affected	Affected				Affected		Affected		
NFKB2	transcription regulator										Affected	Affected	Affected						Affected		
NFKBIA	transcription regulator				Affected						Affected	Affected	Affected						Affected		
NFKBIZ	transcription regulator				Affected								Affected				Affected				
NKX2-5	transcription regulator					Affected															
NOD2	other										Affected	Affected							Affected		
NOS1	enzyme												Affected								
NOS2	enzyme			Affected					Affected	Affected	Affected	Affected	Affected	Affected			Affected		Affected		
NOS3	enzyme						Affected					Affected					Affected				
NOTCH1	transcription regulator								Affected				Affected				Affected		Affected		
NOTCH3	transcription regulator																Affected				
NOX1	enzyme			Affected													Affected	Affected	Affected		
NOX4	enzyme			Affected	Affected											Affected					
NPPA	other			Affected		Affected	Affected		Affected			Affected	Affected		Affected		Affected				
NPPB	other								Affected		Affected		Affected						Affected		
NPY	other																Affected				
NQO1	enzyme													Affected		Affected					
NR3C1	ligand-dependent nuclear receptor													Affected							
NR4A3	ligand-dependent nuclear receptor										Affected								Affected		
OAS3	enzyme			Affected													Affected				
OASL	enzyme			Affected	Affected	Affected											Affected				
OLR1	transmembrane receptor												Affected						Affected		
OPRM1	G-protein coupled receptor												Affected	Affected							
P2RY2	G-protein coupled receptor												Affected						Affected		
PADI4	enzyme													Affected							
PARP1	enzyme																		Affected		
PAX2	transcription regulator																		Affected		
PAX5	transcription regulator																Affected				
PCK1	kinase								Affected					Affected			Affected		Affected		
PCSK1	peptidase																Affected				
PCSK9	peptidase																Affected				
PDGFRA	kinase								Affected												
PDGFRB	kinase			Affected																	
PDX1	transcription regulator			Affected									Affected			Affected					
PECAM1	other			Affected									Affected				Affected		Affected		
PER1	transcription regulator																			Affected	
PGR	ligand-dependent nuclear receptor																Affected				
PHACTR1	other			Affected																	
PI3	other										Affected								Affected		
PICALM	other											Affected									
PIK3R1	kinase											Affected									
PITX2	transcription regulator																	Affected			
PLAT	peptidase				Affected							Affected									
PLAUR	transmembrane receptor																Affected				
PML	transcription regulator				Affected					Affected							Affected				
POMC	other			Affected													Affected				
POU2F1	transcription regulator																Affected				
POU5F1	transcription regulator																Affected		Affected		
PPARA	ligand-dependent nuclear receptor												Affected								
PPARG	ligand-dependent nuclear receptor			Affected	Affected				Affected				Affected		Affected	Affected			Affected		
PPARGC1A	transcription regulator				Affected				Affected								Affected				
PPP3R1	phosphatase				Affected										Affected	Affected					
PRDM16	transcription regulator																			Affected	
PRL	cytokine			Affected								Affected		Affected							
PROCR	other																Affected				
PSEN1	peptidase								Affected												
PSIP1	transcription regulator																Affected				
PSMB8	peptidase			Affected													Affected	Affected			
PSMB9	peptidase			Affected									Affected				Affected		Affected		
PTEN	phosphatase							Affected	Affected			Affected				Affected			Affected		
PTGDS	enzyme																		Affected		
PTGES	enzyme											Affected	Affected						Affected		
PTGS2	enzyme		Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected	Affected	Affected	Affected	Affected	Affected	Affected		Affected		
PTN	growth factor			Affected													Affected				
PTPN1	phosphatase				Affected																
PTPN2	phosphatase																Affected				
RAC1	enzyme											Affected									
RAMP1	transporter																			Affected	
RARB	ligand-dependent nuclear receptor			Affected																	
RBPJ	transcription regulator												Affected				Affected				
REG3A	enzyme																Affected		Affected		
REL	transcription regulator				Affected								Affected								
RELA	transcription regulator		Affected			Affected			Affected		Affected	Affected	Affected						Affected		
REN	peptidase																Affected				
RET	kinase																Affected				
RGS2	other		Affected		Affected	Affected															
RGS4	other											Affected									
RNF213	enzyme			Affected																	
RNLS	enzyme																Affected				
ROCK1	kinase											Affected									
RORA	ligand-dependent nuclear receptor																Affected			Affected	
RSPO3	kinase													Affected							
RUNX1	transcription regulator			Affected									Affected				Affected				
S100A4	other													Affected						Affected	
SAA1	transporter		Affected			Affected							Affected				Affected		Affected		
SBF1	phosphatase																		Affected		
SDC4	other										Affected	Affected	Affected						Affected		
SELE	transmembrane receptor		Affected		Affected	Affected	Affected				Affected	Affected	Affected	Affected					Affected	Affected	
SELENBP1	other																			Affected	
SELL	transmembrane receptor															Affected					
SELP	transmembrane receptor										Affected								Affected		
SELPLG	other												Affected			Affected				Affected	
SEMA3F	other											Affected									
SERPINA1	other																Affected				
SERPINA3	other			Affected									Affected				Affected				
SERPINB1	other																Affected			Affected	
SERPINE1	other		Affected			Affected							Affected	Affected			Affected			Affected	
SERPINE2	other											Affected					Affected		Affected		
SERTAD1	transcription regulator																			Affected	
SFRP2	transmembrane receptor												Affected								
SFTPB	other														Affected		Affected				
SGK1	kinase											Affected					Affected				
SH2B1	other																			Affected	
SHBG	other																		Affected		
SHH	peptidase			Affected								Affected	Affected				Affected	Affected	Affected		
SIRT1	transcription regulator																				Affected
SLC12A2	transporter											Affected									

SLC2A1	transporter												Affected				Affected				
SLC2A2	transporter			Affected									Affected			Affected					
SLC2A3	transporter																			Affected	
SLC2A4	transporter												Affected						Affected		
SLC2A5	transporter												Affected						Affected		
SLC3A1	transporter												Affected								
SLC7A1	transporter												Affected								
SLC8A1	transporter			Affected										Affected							
SLC9A3	ion channel																Affected				
SLCO1B1	transporter																		Affected		
SLCO3A1	transporter				Affected																
SLIT2	other												Affected								
SLPI	other					Affected							Affected								
SMAD2	transcription regulator			Affected																	
SMAD3	transcription regulator			Affected									Affected								
SMAD4	transcription regulator											Affected							Affected		
SMAD6	transcription regulator																Affected				
SMAD9	transcription regulator																Affected				
SMOC2	other																		Affected		
SOCS1	other	Affected		Affected	Affected								Affected				Affected	Affected			Affected
SOCS3	phosphatase	Affected		Affected	Affected							Affected	Affected				Affected	Affected		Affected	Affected
SOD1	enzyme						Affected					Affected									
SOD2	enzyme								Affected		Affected	Affected	Affected				Affected		Affected		
SOD3	enzyme											Affected	Affected								
SORL1	transporter											Affected									
SORT1	G-protein coupled receptor			Affected																	
SOX6	transcription regulator																Affected				
SPP1	cytokine												Affected			Affected					
SREBF1	transcription regulator			Affected													Affected		Affected		
SREBF2	transcription regulator																		Affected		
SST	other								Affected												
STAT3	transcription regulator			Affected													Affected				
STAT4	transcription regulator												Affected								
STAT5A	transcription regulator				Affected								Affected						Affected		
STC2	other																Affected			Affected	
SUN1	other																			Affected	
TAP1	transporter			Affected									Affected				Affected		Affected		
TERT	enzyme				Affected	Affected				Affected	Affected		Affected				Affected		Affected		
TF	transporter								Affected												
TFF1	other			Affected																	
TFPI2	other												Affected				Affected		Affected		
TFRC	transporter											Affected	Affected								
TGFB1	growth factor				Affected						Affected	Affected	Affected	Affected			Affected		Affected		
TGFB2	growth factor								Affected			Affected									
TGFB3	growth factor												Affected							Affected	
TH	enzyme								Affected					Affected							
THBD	transmembrane receptor																Affected				
THBS1	other																Affected				
TIGD6	other			Affected																	
TIMP1	cytokine											Affected	Affected	Affected			Affected			Affected	
TIMP2	other											Affected	Affected								
TIMP3	other											Affected									
TLR2	transmembrane receptor				Affected						Affected	Affected	Affected						Affected		
TLR4	transmembrane receptor			Affected						Affected		Affected	Affected	Affected							
TLR8	transmembrane receptor			Affected																	
TLR9	transmembrane receptor			Affected						Affected	Affected								Affected		
TNC	other											Affected									
TNF	cytokine			Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected	Affected
TNFAIP3	enzyme							Affected			Affected	Affected	Affected							Affected		
TNFRSF11B	transmembrane receptor											Affected	Affected							Affected		
TNFRSF1A	transmembrane receptor												Affected									
TNFRSF1B	transmembrane receptor											Affected					Affected					
TNFRSF4	transmembrane receptor										Affected		Affected						Affected			
TNFSF10	cytokine	Affected	Affected	Affected		Affected					Affected	Affected	Affected			Affected	Affected	Affected				Affected
TNFSF11	cytokine			Affected									Affected		Affected	Affected	Affected					
TNFSF14	cytokine											Affected	Affected									
TNFSF4	cytokine												Affected									
TNNI3	transporter														Affected							
TOLLIP	other											Affected	Affected									
TP53	transcription regulator			Affected						Affected	Affected	Affected	Affected				Affected		Affected			
TP73	transcription regulator							Affected											Affected			
TRAF1	other				Affected						Affected	Affected	Affected						Affected			
TRH	other												Affected				Affected					
TRIB3	kinase												Affected									
TRPC1	ion channel											Affected										
TRPC3	ion channel												Affected									
TRPC6	ion channel												Affected						Affected			
TSC22D1	transcription regulator				Affected																	
TSHR	G-protein coupled receptor								Affected													
TSLP	cytokine										Affected		Affected	Affected					Affected			
UBA1	enzyme											Affected										
UCP1	transporter								Affected													
UGT1A1	enzyme																		Affected			
VCAM1	transmembrane receptor						Affected		Affected		Affected	Affected	Affected	Affected		Affected			Affected			
VCAN	other																Affected					
VDR	transcription regulator													Affected								
VEGFA	growth factor										Affected	Affected	Affected	Affected			Affected		Affected	Affected		
VEGFC	growth factor											Affected	Affected									
VHL	transcription regulator					Affected													Affected			
VIP	other													Affected			Affected					
WARS	enzyme			Affected													Affected	Affected				
WNT5A	cytokine					Affected							Affected				Affected					
XYLT1	enzyme													Affected								
ZFHX3	transcription regulator									Affected												
ZFP36	transcription regulator												Affected				Affected					
ZNF524	other																			Affected		
ZNF652	other			Affected																		