

Supplemental Data

Endothelial Dysfunction at the Cellular Level in 3 Dimensions: Severity, Acuteness, and Distribution

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Abbreviated title: Endothelial dysfunction in 3D

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Supplementary Data Analysis Methods

Word Frequency analysis

To obtain an overall view of the diseases and pathophysiological processes in which ED has been studied over time, we performed a word frequency analysis on the titles of the 10,000 earliest (spanning 1950–1997) and 10,000 latest (spanning 2018–2020) results in PubMed. To this end, we used the search term “endothelial dysfunction”, sorted by date of publication; at the time of writing of the review, this search term resulted in more than 85,000 reports. The titles of the 10,000 earliest and 10,000 latest hits were separately downloaded from PubMed in CSV format. Both files were separately analyzed with an online word counter (countwordsfree.com). In total, there were 117,900 words in the file with the earliest publications and 142,552 words in the file with the latest publications. We kept the top 500 words with the highest counts and only kept words referring to diseases, tissues, organs, or pathophysiological processes. Words with similar meanings or referring to similar processes were grouped. Next, we compared the earliest with the latest publications and assigned color codes using Excel.

This strategy allows one to analyze overall trends in publications on a specific topic without selection bias. However, the analysis is highly dependent on the intensity of research on a specific disease, is hampered by diseases consisting of two or more separate words (high blood pressure), and does not take into account the relevance of the papers for the topic.

Analysis of gene expression in freshly isolated endothelial cells

An excellent tool to explore the endothelial transcriptome has been developed by Khan and coworkers (1). They developed a database called EndoDB that combines transcriptomic data from 360 datasets. Using this tool, we selected all experiments in which the endothelial transcriptome was determined in freshly isolated endothelial cells—i.e., without in vitro culturing steps and thus resembling the in vivo endothelial phenotype. We only selected experiments from EndoDB in which a healthy state was compared to a disease state in vascular endothelial cells—excluding studies studying lymphatic, embryonic, or corneal endothelial cells. This resulted in 24 studies from EndoDB supplemented with two other studies outside EndoDB (2, 3). The identity of these datasets is presented in **Suppl. Table 7** (except for data from (2)). Datasets were downloaded from EndoDB in CSV format, with false discovery rate set at a cutoff of 0.1, providing log fold change values for all genes with significantly differential expression between disease state to health state. Genes coded “NA” or “Gm0000000” were removed from datasets. Genes were considered upregulated if fold change > 1.5 and downregulated if fold change < 0.666. Upregulated genes of all datasets were combined in a single table, and downregulated genes of all datasets were combined in a separate table (**Suppl. Dataset 1**).

We downloaded a list of protein-coding human genes from the HUGO Gene Nomenclature Committee website (<https://www.genenames.org/>). Next, we counted the frequency of significant up- or downregulation of each known protein-coding human gene in the data table (**Suppl. Dataset 1**) and ranked them. Out of 48375 genes, 10908 were upregulated in at least one dataset and 11285 downregulated in at least one dataset; 3006 were upregulated and 3055 were downregulated in at least three datasets. For reference, *NOS2* (coding for inducible NOS or iNOS) was upregulated in four datasets, and *NOS3* (coding for endothelial NOS or eNOS) was downregulated in five datasets.

Gene ontology enrichment analysis was performed using g:Profiler (<https://biit.cs.ut.ee/gprofiler/gost>) on 104 genes upregulated in at least 8/26 datasets and on 98 downregulated in at least 7/25 datasets. Results are summarized in **Suppl. Table 5** and **6**.

Supplementary Table 1. Frequency of title words associated with “endothelial dysfunction”.

Diseases, organ systems, pathophysiology	1950–1997	2018–2021	Difference
vascular, coronary, artery, arteries, arterial, aorta, aortic, carotid, vessels	3614	1746	-1868
ischemia, reperfusion, hypoxia, ischemic, hypoxic, infarction, angina	1174	185	-989
lung(s), respiratory, pulmonary	1001	577	-424
vasodilation, vasoconstriction, vasospasm, vasodilator, vasoactive, vasoconstrictor	478	56	-422
inflammation, leukocyte(s), inflammatory, neutrophil(s), lymphocytes, immune	1130	716	-414
hypertension, hypertensive, normotensive	910	519	-391
nitric	552	344	-208
muscle, skeletal	348	152	-196
tumo(u)r, cancer, metastasis	330	143	-187
growth, proliferation	384	219	-165
thrombosis, thrombotic, platelet(s)	496	378	-118
atherosclerosis, atherosclerotic, atherogenesis	452	351	-101
transplantation	173	77	-96
liver, hepatic, intestinal, gastric	277	183	-94
shock	147	62	-85
microvascular, -circulation, -circulatory, -vessels, capillary	486	409	-77
brain, cognitive, cerebral	380	319	-61
edema	105	68	-37
sepsis, endotoxin, infection, septic	212	212	0
wound	39	50	11
preeclampsia	76	88	12
bone	41	67	26
venous, vein	157	184	27
acute	303	331	28
corneal, retinal	232	265	33
rheumatoid, arthritis, lupus	100	135	35
Alzheimer		54	54
sleep		78	78
angiogenesis, angiogenic, neovascular, neovascularization	305	395	90
chronic	254	347	93
fibroblast, fibrosis, sclerosis	48	169	121
erectile		147	147
barrier	150	324	174
apoptosis, autophagy		222	222
heart(s), myocardial, cardiovascular, cardiac, circulation, myocardium	1074	1296	222
covid-19		234	234
renal, glomerular, kidney, nephropathy	302	537	235
obesity, obese		261	261
age-related, aging, senescence, older, aged	29	360	331
lipoprotein(s), hypercholesterolemia, lipid, cholesterol	274	655	381
stroke, cerebrovascular, neurovascular	36	465	429

diabetic, diabetes, insulin	491	962	471
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Supplementary Table 2. Gene ontology enrichment analysis of brain endothelial cells in various disorders of the central nervous system

MF_Term_name	MF_term_id	Intersections
ECM structural constituent	GO:0005201	COL12A1, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, DCN, EMILIN1, FBLN1, FBN1, LAMB1, LUM, POSTN, PXDN, TNC
cell adhesion molecule binding	GO:0050839	COL3A1, EMILIN1, FBLN1, FBN1, ITGB3, LAMB1, MMP14, POSTN, SPP1, THBS1, THY1, VWF
fibronectin binding	GO:0001968	FBLN1, IGFBP5, ITGB3, LOXL3, THBS1, TNC
PDGF binding	GO:0048407	COL1A1, COL1A2, COL3A1, COL5A1
protein-lysine 6-oxidase activity	GO:0004720	LOX, LOXL2, LOXL3
insulin-like growth factor I binding	GO:0031994	IGFBP4, IGFBP5, ITGB3
metalloendopeptidase activity	GO:0004222	ADAM12, ADAM19, ADAMTS4, ADAMTS8, BMP1, MMP14
BP_Term_name	BP_term_id	Intersections
cell migration	GO:0016477	ANLN, ANXA1, ASPM, CCL2, CD44, CH25H, COL1A1, COL3A1, COL5A1, CXCL10, CYP1B1, DCN, DPYSL3, EMILIN1, FBLN1, FSCN1, IFITM1, IGFBP5, IGSF10, ITGB3, KIF20B, KIT, LAMB1, LBP, LGMN, LOX, LOXL2, LRG1, MMP14, MYC, PDLIM1, PGF, PLEKHO1, POSTN, PTGS2, ROBO1, SELE, SELP, SERPINE1, SPP1, SULF1, THBS1, THY1, TIMP1
ECM organization	GO:0030198	ADAMTS4, ADAMTS8, AEBP1, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, CYP1B1, EMILIN1, FBLN1, FKBP10, FSCN1, ITGB3, LAMB1, LOX, LOXL2, LOXL3, LUM, MMP14, POSTN, PXDN, SULF1, SULF2
vasculature development	GO:0001944	ADAM12, ALDH1A2, ANXA1, APLN, APLNR, CCL2, COL1A1, COL1A2, COL3A1, COL5A1, CXCL10, CYP1B1, DCN, EMILIN1, FKBP10, ITGB3, KIT, LOX, LOXL2, LRG1, MMP14, PGF, PTGS2, PXDN, ROBO1, SERPINE1, SULF1, THBS1, THBS2, THY1
circulatory system development	GO:0072359	ADAM12, ADAM19, ALDH1A2, ANXA1, APLN, APLNR, BICC1, CCL2, CDK1, COL1A1, COL1A2, COL3A1, COL5A1, CXCL10, CYP1B1, DCN, EMILIN1, FBN1, FKBP10, ITGB3, KIT, LOX, LOXL2, LRG1, MMP14, PDLIM1, PGF, PTGS2, PXDN, ROBO1, SERPINE1, SULF1, THBS1, THBS2, THY1
response to stress	GO:0006950	ADAMTS4, ANXA1, CASP4, CCL2, CCNA2, CD14, CD44, CDK1, CH25H, CHST1, COL1A1, COL3A1, COL5A1, CXCL10, CYP1B1, DPYSL3, EMILIN1, FBLN1, FKBP10, GJB2, IFITM1, IGFBP4, ITGB3, KIT, LBP, LGALS1, LOX, LOXL2, LOXL3, LRG1, MCM5, MMP14, MYC, PARP3, PDLIM1, PGF, PTGS2, PXDN, SELP, SERPINE1, SERPING1, SLC7A11, SLFN9, SPP1, SULF2, THBS1, THY1, TIMP1, TLR2, TNC, TNFRSF23, TNFSF8, TOP2A, UPP1, VWF
angiogenesis	GO:0001525	ADAM12, ANXA1, APLN, APLNR, CCL2, CXCL10, CYP1B1, DCN, EMILIN1, ITGB3, LOXL2, LRG1, MMP14, PGF, PTGS2, PXDN, ROBO1, SERPINE1, SULF1, THBS1, THBS2, THY1
mitotic cell cycle	GO:0000278	ANLN, ANXA1, BUB1B, CCL2, CCNA2, CCNB2, CDK1, CENPE, CENPF, CKAP2, CKS1B, KIF11, KIF15, KIF20B, LGMN, MKI67, MYC, NDC80, PARP3, PRC1, RRM2, TACC3, TPX2, TUBB6, UBE2C
wound healing	GO:0042060	ANXA1, CCL2, CD44, COL1A1, COL3A1, COL5A1, FBLN1, FKBP10, ITGB3, LOX, LRG1, SELP, SERPINE1, SERPING1, SLC7A11, THBS1, TIMP1, VWF
leukocyte migration	GO:0050900	ANXA1, CCL2, CH25H, CXCL10, EMILIN1, ITGB3, KIT, LBP, LGMN, MMP14, PGF, SELE, SELP, SERPINE1, SPP1, THY1

response to cytokine	GO:0034097	<i>ALDH1A2,ANXA1,CASP4,CCL2,CD14,CD44,CH25H,COL1A1,COL3A1,CXCL10,CYP1B1,DPYSL3,IFITM1,KIT,LOX,MYC,NFIL3,PTGS2,ROBO1,SELE,SELP,SPP1,THBS1,TIMP1,TLR2,TNFRSF23</i>
ECM assembly	GO:0085029	<i>COL1A2,COL3A1,EMILIN1,FKBP10,LAMB1,LOX,PXDN</i>
TM receptor protein TK signaling pathway	GO:0007169	<i>APLN,CCL2,COL1A1,DCN,EMILIN1,IGFBP4,IGFBP5,ITGB3,KIT,LCP2,LGMN,LOX,PGF,ROBO1,SULF1,SULF2,THBS1</i>
regeneration	GO:0031099	<i>ANXA1,CCL2,CCNA2,CDK1,IGSF10,MYC,PGF,PTGFRN,SULF2,THY1,TNC</i>
connective tissue development	GO:0061448	<i>BMP1,CD44,COL1A1,COL3A1,COL5A1,ITGB3,LOX,LOXL2,SULF1,SULF2,TIMP1</i>
reg. of nitrogen compound metabolic process	GO:0051171	<i>AEBP1,APLN,APLNR,ATP8B1,BUB1B,CCNA2,CCNB2,CD44,CDK1,CENPE,CENPF,CKAP2,CKS1B,COL1A1,CYP1B1,DCN,DKK3,EMILIN1,FBLN1,FBN1,IGFBP5,ITGB3,KIT,LCP2,LGMN,LOX,LOXL2,LOXL3,LUM,MEOX1,MMP14,MYC,NFIL3,PARP3,PDLIM1,PGF,PTGS2,ROBO1,RUNX1,SERPINE1,SERPING1,SLC7A11,SLC7A7,SPP1,THBS1,THY1,TIMP1,TLR2,TNFRSF23,TNFSF8,TPX2,ZFP521</i>
defense response	GO:0006952	<i>ADAMTS4,ANXA1,CASP4,CCL2,CD14,CH25H,CHST1,CXCL10,EMILIN1,IFITM1,IGFBP4,KIT,LBP,LGALS1,LOXL3,MYC,PTGS2,SELP,SERPINE1,SERPING1,SLFN9,THBS1,TIMP1,TLR2,TNC,TNFSF8</i>
muscle structure development	GO:0061061	<i>APLNR,CDK1,CENPF,COL3A1,CXCL10,FLNC,IGFBP5,KIT,LGALS1,LOX,MMP14,MYC,PDLIM1,PLEKHO1,PTGFRN,SCGB3A1</i>
chemotaxis	GO:0006935	<i>ANXA1,CCL2,CH25H,CMTM3,CXCL10,ITGB3,KIT,LBP,LGMN,LOX,PGF,ROBO1,SERPINE1,SPP1,THBS1</i>
cell communication	GO:0007154	<i>ALDH1A2,ANXA1,APLN,APLNR,ASPM,BICC1,BMP1,BUB1B,CASP4,CCL2,CCNA2,CD14,CD44,CDK1,CMTM3,COL1A1,COL1A2,COL3A1,CXCL10,CYP1B1,DCN,DKK3,EMILIN1,FBLN1,FBN1,GJB2,IFITM1,IGFBP4,IGFBP5,ITGB3,KIT,LBP,LCP2,LGMN,LOX,LOXL3,LRG1,MMP14,MYC,NDC80,PGF,POSTN,PTGS2,ROBO1,RUNX1,SCGB3A1,SELP,SERPINE1,SLC7A11,SPP1,SULF1,SULF2,SYNPO,THBS1,THY1,TIMP1,TLR2,TNC,TNFRSF23,TNFSF8,UPP1,VWF</i>
regulation of VEGF production	GO:0010574	<i>CCL2,CYP1B1,PTGS2,SULF1,SULF2</i>
CC_Term_name	CC_term_id	Intersections
extracellular region	GO:0005576	<i>ADAMTS4,ADAMTS8,AEBP1,ANXA1,APLN,BMP1,CASP4,CCL2,CD14,CENPE,CMTM3,COL12A1,COL1A1,COL1A2,COL3A1,COL5A1,COL5A2,CXCL10,DCN,DKK3,DPYSL3,EMILIN1,FBLN1,FBN1,IGFBP4,IGFBP5,IGSF10,ISLR,KIF2OB,KIT,LAMB1,LBP,LGALS1,LGMN,LOX,LOXL2,LOXL3,LRG1,LUM,MMP14,PARP3,PGF,POSTN,PRC1,PXDN,SCGB3A1,SELE,SELP,SERPINE1,SERPING1,SPP1,SULF1,SULF2,THBS1,THBS2,TIMP1,TNC,TNFSF8,TPX2,TUBB6,VCAN,VWF</i>
collagen-containing ECM	GO:0062023	<i>ADAM19,ADAMTS4,ADAMTS8,ANXA1,BMP1,COL12A1,COL1A1,COL1A2,COL3A1,COL5A1,COL5A2,DCN,EMILIN1,FBLN1,FBN1,LAMB1,LGALS1,LOX,LOXL2,LUM,POSTN,PXDN,S100A6,SERPINE1,SERPING1,THBS2,TIMP1,TNC,VWF</i>
fibrillar collagen trimer	GO:0005583	<i>COL1A1,COL1A2,COL3A1,COL5A1,COL5A2,LUM</i>
basement membrane	GO:0005604	<i>COL5A1,FBLN1,FBN1,LAMB1,LOXL2,PXDN,THBS2,TIMP1,TNC</i>
cytoplasm	GO:0005737	<i>ACOT7,ADAM19,AEBP1,ALDH18A1,ALDH1A2,ANLN,ANXA1,APLN,APRT,ASPM,ATP8B1,B3GNT3,BICC1,BMP1,BUB1B,CASP4,CCL2,CCNA2,CCNB2,CD14,CD44,CDK1,CENPF,CH25H,CHST1,CKAP2,CMTM3,COL1A1,COL1A2,CYP1B1,DPYSL3,FBLIM1,FKBP10,FLNC,FSCN1,GJB2,HMMR,IFITM1,ITGB3</i>

		, KIF11, KIF15, KIF20B, KIT, LAMB1, LCP2, LGALS1, LGMN, LOXL2, LOXL3, MARCKSL1, MCM5, MEOX1, MKI67, MMP14, MYC, NDC80, PARP3, PDLIM1, PLEKH O1, POSTN, PRC1, PTGFRN, PTGS2, PXDN, ROBO1, RRM2, S100A6, SELE, SELP, SLC7A11, SLFN9, SPP1, SULF1, SULF2, SYNPO, TACC3, THBS1, THBS2, THY1, TLR2, TNFRSF23, TOP2A, TPX2, TUBB6, UBE2C, UPP1, VWF
mitotic spindle	GO:0072686	ASPM, CDK1, CENPE, CKAP2, KIF11, KIF20B, PRC1, TPX2, TUBB6
cytoskeleton	GO:0005856	ANLN, ANXA1, ASPM, BUB1B, CCNB2, CDK1, CENPE, CENPF, CKAP2, DPYSL3, FBLIM1, FLNC, FSCN1, HMMR, KIF11, KIF15, KIF20B, MARCKSL1, MMP14, MYC, NDC80, PDLIM1, PRC1, SELE, SLC7A11, SYNPO, TACC3, TOP2A, TPX2, TUBB6
cell surface	GO:0009986	ANXA1, CD14, CD44, CXCL10, HMMR, ITGB3, KIT, LBP, LGALS1, PXDN, ROBO1, SELP, SLC7A11, SULF1, SULF2, THBS1, THY1, TLR2, TNFRSF23
microtubule	GO:0005874	ASPM, CDK1, CENPE, CKAP2, KIF11, KIF15, KIF20B, PRC1, TPX2, TUBB6
protein complex involved in cell adhesion	GO:0098636	EMILIN1, ITGB3, LGALS1, TNC
cyclin-dependent PK holoenzyme complex	GO:0000307	CCNA2, CCNB2, CDK1, CKS1B

Gene ontology enrichment analysis (G:Profiler) of genes upregulated in endothelial cells in at least 3 different neurological disorders. Data are derived from Supplementary File 6 of (2). Here, the most important non-redundant molecular functions (MF), biological processes (BP), and cellular compartments (CC) are shown. ECM, extracellular matrix; PDGF, platelet-derived growth factor; PK, protein kinase; TK, tyrosine kinase; TM, transmembrane; VEGF, vascular endothelial derived growth factor.

Supplementary Table 3. Most frequently upregulated genes in endothelial cells in various disorders

<i>Gene Symbol</i>	<i>Freq UP</i>	<i>Gene name</i>
<i>FKBP10</i>	12/26	FK506 binding protein 10
<i>NME1</i>	12/26	NME/NM23 nucleoside diphosphate kinase 1
<i>SPP1</i>	12/26	secreted phosphoprotein 1
<i>COL4A1</i>	11/26	collagen, type IV, alpha 1
<i>COL5A2</i>	11/26	collagen, type V, alpha 2
<i>LAMB1</i>	11/26	laminin B1
<i>MCAM</i>	11/26	melanoma cell adhesion molecule
<i>MMP14</i>	11/26	matrix metalloproteinase 14
<i>TOP2A</i>	11/26	topoisomerase (DNA) II alpha
<i>ACOT7</i>	10/26	acyl-CoA thioesterase 7
<i>COL15A1</i>	10/26	collagen, type XV, alpha 1
<i>COL18A1</i>	10/26	collagen, type XVIII, alpha 1
<i>FHL2</i>	10/26	four and a half LIM domains 2
<i>IGFBP3</i>	10/26	insulin-like growth factor binding protein 3
<i>MYCN</i>	10/26	v-myc avian myelocytomatosis viral related oncogene
<i>PRC1</i>	10/26	protein regulator of cytokinesis 1
<i>PTGFRN</i>	10/26	prostaglandin F2 receptor negative regulator
<i>SPC25</i>	10/26	SPC25, NDC80 kinetochore complex component, homolog
<i>TGFBI</i>	10/26	transforming growth factor, beta induced
<i>ALDH18A1</i>	9/26	aldehyde dehydrogenase 18 family, member A1
<i>APLNR</i>	9/26	apelin receptor
<i>ASPM</i>	9/26	abnormal spindle microtubule assembly
<i>ATP8B1</i>	9/26	ATPase, class I, type 8B, member 1
<i>BIRC5</i>	9/26	baculoviral IAP repeat-containing 5
<i>BUB1B</i>	9/26	BUB1B, mitotic checkpoint serine/threonine kinase
<i>C1QTNF6</i>	9/26	C1q and tumor necrosis factor related protein 6
<i>CCNB1</i>	9/26	cyclin B1
<i>CCNB2</i>	9/26	cyclin B2
<i>CD276</i>	9/26	CD276 antigen
<i>CDCA7</i>	9/26	cell division cycle associated 7
<i>CDKN3</i>	9/26	cyclin-dependent kinase inhibitor 3
<i>COL1A2</i>	9/26	collagen, type I, alpha 2
<i>COL8A1</i>	9/26	collagen, type VIII, alpha 1
<i>FN1</i>	9/26	fibronectin 1
<i>HMMR</i>	9/26	hyaluronan mediated motility receptor (RHAMM)
<i>LGALS1</i>	9/26	lectin, galactose binding, soluble 1
<i>LOX</i>	9/26	lysyl oxidase
<i>MKI67</i>	9/26	antigen identified by monoclonal antibody Ki 67
<i>NHP2</i>	9/26	NHP2 ribonucleoprotein
<i>OLFML2B</i>	9/26	olfactomedin-like 2B
<i>PCLAF</i>	9/26	PCNA clamp associated factor

<i>PFKP</i>	9/26	phosphofructokinase, platelet
<i>PLA2G7</i>	9/26	phospholipase A2, group VII
<i>PLOD2</i>	9/26	procollagen lysine, 2-oxoglutarate 5-dioxygenase 2
<i>PLP2</i>	9/26	proteolipid protein 2
<i>RACGAP1</i>	9/26	Rac GTPase-activating protein 1
<i>RRM2</i>	9/26	ribonucleotide reductase M2
<i>THY1</i>	9/26	thymus cell antigen 1, theta
<i>TIMP1</i>	9/26	tissue inhibitor of metalloproteinase 1
<i>TPX2</i>	9/26	TPX2, microtubule-associated
<i>AEBP1</i>	8/26	AE binding protein 1
<i>APRT</i>	8/26	adenine phosphoribosyl transferase
<i>ARMCX2</i>	8/26	armadillo repeat containing, X-linked 2
<i>BAMBI</i>	8/26	BMP and activin membrane-bound inhibitor
<i>CDC20</i>	8/26	cell division cycle 20
<i>CENPF</i>	8/26	centromere protein F
<i>CEP55</i>	8/26	centrosomal protein 55
<i>CKS1B</i>	8/26	CDC28 protein kinase 1b
<i>COL1A1</i>	8/26	collagen, type I, alpha 1
<i>COL4A2</i>	8/26	collagen, type IV, alpha 2
<i>COL6A3</i>	8/26	collagen, type VI, alpha 3
<i>DPYSL3</i>	8/26	dihydropyrimidinase-like 3
<i>ECT2</i>	8/26	ect2 oncogene
<i>ESM1</i>	8/26	endothelial cell-specific molecule 1
<i>FAM167B</i>	8/26	family with sequence similarity 167, member B
<i>FIGL1</i>	8/26	fidgetin-like 1
<i>FKBP14</i>	8/26	FK506 binding protein 14
<i>FSCN1</i>	8/26	fascin actin-bundling protein 1
<i>GPNMB</i>	8/26	glycoprotein (transmembrane) nmb
<i>GPR176</i>	8/26	G protein-coupled receptor 176
<i>HDC</i>	8/26	histidine decarboxylase
<i>IGF1</i>	8/26	insulin-like growth factor 1
<i>IGFBP5</i>	8/26	insulin-like growth factor binding protein 5
<i>KNSTRN</i>	8/26	kinetochore-localized astrin/SPAG5 binding
<i>LAMC1</i>	8/26	laminin, gamma 1
<i>LCN2</i>	8/26	lipocalin 2
<i>LGALS3</i>	8/26	lectin, galactose binding, soluble 3
<i>LTBP2</i>	8/26	latent transforming growth factor beta binding protein 2
<i>LURAP1L</i>	8/26	leucine rich adaptor protein 1-like
<i>MCM2</i>	8/26	minichromosome maintenance complex component 2
<i>MCM5</i>	8/26	minichromosome maintenance complex component 5
<i>MGP</i>	8/26	matrix Gla protein
<i>MIF</i>	8/26	macrophage migration inhibitory factor
<i>MRPL52</i>	8/26	mitochondrial ribosomal protein L52
<i>NDC80</i>	8/26	NDC80 kinetochore complex component

<i>NID2</i>	8/26	nidogen 2
<i>NOX4</i>	8/26	NADPH oxidase 4
<i>NUDT5</i>	8/26	nudix (nucleoside diphosphate linked moiety X)-type motif 5
<i>P3H4</i>	8/26	prolyl 3-hydroxylase family member 4
<i>PDGFRB</i>	8/26	platelet derived growth factor receptor, beta polypeptide
<i>POSTN</i>	8/26	periostin, osteoblast specific factor
<i>PPIC</i>	8/26	peptidylprolyl isomerase C
<i>PSAT1</i>	8/26	phosphoserine aminotransferase 1
<i>SERPINE1</i>	8/26	serine (or cysteine) peptidase inhibitor, clade E, member 1
<i>SLC6A6</i>	8/26	solute carrier family 6, member 6
<i>TCF19</i>	8/26	transcription factor 19
<i>TMEM176A</i>	8/26	transmembrane protein 176A
<i>TMEM263</i>	8/26	transmembrane protein 263
<i>TNC</i>	8/26	tenascin C
<i>TNFRSF11B</i>	8/26	tumor necrosis factor receptor superfamily, member 11b
<i>TPD52L1</i>	8/26	tumor protein D52-like 1
<i>UBE2C</i>	8/26	Ubiquitin Conjugating Enzyme E2 C
<i>UCK2</i>	8/26	uridine-cytidine kinase 2
<i>UHRF1</i>	8/26	ubiquitin-like, containing PHD and RING finger domains, 1

Most frequently upregulated genes in endothelial cells derived from 26 separate datasets, covering 26 different experimental setups.

Supplementary Table 4. Most frequently downregulated genes in endothelial cells in various disorders

<i>Gene Symbol</i>	<i>Freq DOWN</i>	<i>Gene name</i>
<i>KLF4</i>	10/25	kruppel-like factor 4
<i>FAM107A</i>	10/25	family with sequence similarity 107, member A
<i>GNA14</i>	10/25	guanine nucleotide binding protein, alpha 14
<i>SOX17</i>	10/25	SRY (sex determining region Y)-box 17
<i>SYNE1</i>	10/25	spectrin repeat containing, nuclear envelope 1
<i>PTH1R</i>	10/25	parathyroid hormone 1 receptor
<i>CAVIN2</i>	9/25	caveolae associated 2
<i>MKNK2</i>	9/25	MAP kinase-interacting serine/threonine kinase 2
<i>ENPP4</i>	9/25	ectonucleotide pyrophosphatase/phosphodiesterase 4
<i>EZH1</i>	9/25	enhancer of zeste 1 polycomb repressive complex 2 subunit
<i>FRY</i>	9/25	FRY microtubule binding protein
<i>SGMS1</i>	9/25	sphingomyelin synthase 1
<i>KLF2</i>	9/25	Kruppel-like factor 2 (lung)
<i>PECAM1</i>	9/25	platelet/endothelial cell adhesion molecule 1
<i>JAM2</i>	8/25	junction adhesion molecule 2
<i>ENTPD1</i>	8/25	ectonucleoside triphosphate diphosphohydrolase 1
<i>GATM</i>	8/25	glycine amidinotransferase
<i>RNF144B</i>	8/25	ring finger protein 144B
<i>USP54</i>	8/25	ubiquitin specific peptidase 54
<i>BMX</i>	8/25	BMX non-receptor tyrosine kinase
<i>CBX7</i>	8/25	chromobox 7
<i>CDKN1C</i>	8/25	cyclin-dependent kinase inhibitor 1C (P57)
<i>FGFR3</i>	8/25	fibroblast growth factor receptor 3
<i>ICAM2</i>	8/25	intercellular adhesion molecule 2
<i>JUN</i>	8/25	jun proto-oncogene
<i>NPY1R</i>	8/25	neuropeptide Y receptor Y1
<i>PDE2A</i>	8/25	phosphodiesterase 2A, cGMP-stimulated
<i>PK4</i>	8/25	pyruvate dehydrogenase kinase, isoenzyme 4
<i>RASGRP2</i>	8/25	RAS, guanyl releasing protein 2
<i>SHE</i>	8/25	src homology 2 domain-containing transforming protein E
<i>TXNIP</i>	8/25	thioredoxin interacting protein
<i>BTG2</i>	8/25	BTG anti-proliferation factor 2
<i>CHCHD7</i>	8/25	coiled-coil-helix-coiled-coil-helix domain containing 7
<i>HNRNPH3</i>	8/25	heterogeneous nuclear ribonucleoprotein H3
<i>KBTBD2</i>	8/25	kelch repeat and BTB (POZ) domain containing 2
<i>MTURN</i>	8/25	maturin, neural progenitor differentiation regulator homolog
<i>NR3C1</i>	8/25	nuclear receptor subfamily 3, group C, member 1
<i>NR3C2</i>	8/25	nuclear receptor subfamily 3, group C, member 2
<i>PRKD2</i>	8/25	protein kinase D2
<i>RNF125</i>	8/25	ring finger protein 125
<i>RAB27A</i>	7/25	RAB27A, member RAS oncogene family

<i>STMN2</i>	7/25	stathmin-like 2
<i>EHD3</i>	7/25	EH-domain containing 3
<i>INSIG1</i>	7/25	insulin induced gene 1
<i>LMO7</i>	7/25	LIM domain only 7
<i>MAP3K6</i>	7/25	mitogen-activated protein kinase kinase kinase 6
<i>MTMR10</i>	7/25	myotubularin related protein 10
<i>PFKFB3</i>	7/25	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3
<i>RASGEF1A</i>	7/25	RasGEF domain family, member 1A
<i>ST6GALNAC3</i>	7/25	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 3
<i>DUSP8</i>	7/25	dual specificity phosphatase 8
<i>MYLIP</i>	7/25	myosin regulatory light chain interacting protein
<i>NR4A2</i>	7/25	nuclear receptor subfamily 4, group A, member 2
<i>PGM5</i>	7/25	phosphoglucomutase 5
<i>SCN2B</i>	7/25	sodium channel, voltage-gated, type II, beta
<i>SLC52A3</i>	7/25	solute carrier protein family 52, member 3
<i>SRGN</i>	7/25	serglycin
<i>TIE1</i>	7/25	tyrosine kinase with immunoglobulin-like and EGF-like domains 1
<i>TPPP3</i>	7/25	tubulin polymerization-promoting protein family member 3
<i>UTRN</i>	7/25	utrophin
<i>ABCA9</i>	7/25	ATP-binding cassette, sub-family A (ABC1), member 9
<i>ADRB2</i>	7/25	adrenergic receptor, beta 2
<i>AIF1L</i>	7/25	allograft inflammatory factor 1-like
<i>B4GALT4</i>	7/25	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 4
<i>COL4A4</i>	7/25	collagen, type IV, alpha 4
<i>FAM110A</i>	7/25	family with sequence similarity 110, member A
<i>FCHSD2</i>	7/25	FCH and double SH3 domains 2
<i>HBEGF</i>	7/25	heparin-binding EGF-like growth factor
<i>ITPR3</i>	7/25	inositol 1,4,5-triphosphate receptor 3
<i>LMBRD1</i>	7/25	LMBR1 domain containing 1
<i>MBP</i>	7/25	myelin basic protein
<i>MCF2L</i>	7/25	mcf.2 transforming sequence-like
<i>P2RY14</i>	7/25	purinergic receptor P2Y, G-protein coupled, 14
<i>PMP22</i>	7/25	peripheral myelin protein 22
<i>PRDM16</i>	7/25	PR domain containing 16
<i>RNF167</i>	7/25	ring finger protein 167
<i>S1PR1</i>	7/25	sphingosine-1-phosphate receptor 1
<i>SIK1</i>	7/25	salt inducible kinase 1
<i>ABHD4</i>	7/25	abhydrolase domain containing 4
<i>ANKRD44</i>	7/25	ankyrin repeat domain 44
<i>ATP8A1</i>	7/25	ATPase, aminophospholipid transporter, class I, type 8A, member 1
<i>ATP10A</i>	7/25	ATPase, class V, type 10A
<i>CTNNA3</i>	7/25	catenin (cadherin associated protein), alpha 3
<i>CYTH3</i>	7/25	cytohesin 3
<i>DENND3</i>	7/25	DENN/MADD domain containing 3

<i>EPB41L2</i>	7/25	erythrocyte membrane protein band 4.1 like 2
<i>EXOC6</i>	7/25	exocyst complex component 6
<i>IER2</i>	7/25	immediate early response 2
<i>KANK3</i>	7/25	KN motif and ankyrin repeat domains 3
<i>KCNK7</i>	7/25	potassium channel, subfamily K, member 7
<i>KLF3</i>	7/25	Kruppel-like factor 3 (basic)
<i>LRRC49</i>	7/25	leucine rich repeat containing 49
<i>MFSD6</i>	7/25	major facilitator superfamily domain containing 6
<i>NDEL1</i>	7/25	nudE neurodevelopment protein 1 like 1
<i>PODXL</i>	7/25	podocalyxin-like
<i>RNF19A</i>	7/25	ring finger protein 19A
<i>TAL1</i>	7/25	T cell acute lymphocytic leukemia 1
<i>TOB1</i>	7/25	transducer of ErbB-2.1

Most frequently downregulated genes in endothelial cells derived from 25 separate datasets, covering 25 different experimental setups.

Supplementary Table 5. Gene ontology enrichment analysis of upregulated genes in endothelial cells in various disorders

MF_Term_name	MF_term_id	Intersections
ECM structural constituent	GO:0005201	<i>COL4A1, COL5A2, LAMB1, COL15A1, COL18A1, TGFB1, COL1A2, COL8A1, FN1, AEBP1, COL1A1, COL4A2, COL6A3, LAMC1, LTBP2, MGP, NID2, POSTN, TNC</i>
structural molecule activity	GO:0005198	<i>COL4A1, COL5A2, LAMB1, COL15A1, COL18A1, TGFB1, COL1A2, COL8A1, FN1, AEBP1, COL1A1, COL4A2, COL6A3, LAMC1, LTBP2, MGP, MRPL52, NID2, POSTN, TNC</i>
integrin binding	GO:0005178	<i>SPP1, LAMB1, MMP14, TGFB1, FN1, THY1, ESM1, GPNMB, IGF1</i>
PDGF binding	GO:0048407	<i>COL4A1, COL1A2, COL1A1, PDGFRB</i>
collagen binding	GO:0005518	<i>TGFB1, FN1, LOX, AEBP1, NID2, P3H4</i>
GF binding	GO:0019838	<i>COL4A1, IGFBP3, COL1A2, COL1A1, IGFBP5, LTBP2, PDGFRB</i>
BP_Term_name	BP_term_id	Intersections
ECM organization	GO:0030198	<i>FKBP10, COL4A1, COL5A2, LAMB1, MMP14, COL15A1, COL18A1, TGFB1, COL1A2, COL8A1, LOX, OLFML2B, AEBP1, COL1A1, COL4A2, FSCN1, LAMC1, NID2, P3H4, POSTN, TNFRSF11B</i>
mitotic cell cycle process	GO:1903047	<i>PRC1, SPC25, BUB1B, CCNB1, CCNB2, CDKN3, MKI67, RACGAP1, RRM2, TPX2, CDC20, CENPF, CEP55, CKS1B, ECT2, GPNMB, IGF1, KNSTRN, MCM2, NDC80, PDGFRB, TPD52L1, UBE2C</i>
collagen fibril organization	GO:0030199	<i>FKBP10, COL4A1, COL5A2, COL15A1, COL1A2, LOX, AEBP1, COL1A1, COL4A2, P3H4</i>
organelle fission	GO:0048285	<i>TOP2A, PRC1, ASPM, BUB1B, CCNB1, CCNB2, MKI67, RACGAP1, TPX2, CDC20, CENPF, FIGNL1, IGF1, KNSTRN, NDC80, P3H4, PDGFRB, UBE2C</i>
blood vessel development	GO:0001568	<i>FKBP10, COL4A1, MCAM, MMP14, COL15A1, COL18A1, TGFB1, APLNR, COL1A2, COL8A1, FN1, LOX, THY1, COL1A1, COL4A2, ESM1, GPNMB, PDGFRB, SERPINE1</i>
circulatory system development	GO:0072359	<i>FKBP10, COL4A1, MCAM, MMP14, COL15A1, COL18A1, FHL2, TGFB1, APLNR, COL1A2, COL8A1, FN1, LOX, THY1, COL1A1, COL4A2, ESM1, GPNMB, IGF1, NOX4, PDGFRB, SERPINE1</i>
ossification	GO:0001503	<i>SPP1, COL5A2, MMP14, FHL2, IGFBP3, COL1A2, LOX, BAMBI, COL1A1, FIGNL1, IGF1, IGFBP5, MGP, TNC</i>
angiogenesis	GO:0001525	<i>COL4A1, MCAM, MMP14, COL15A1, COL18A1, TGFB1, APLNR, COL8A1, FN1, THY1, COL4A2, ESM1, GPNMB, PDGFRB, SERPINE1</i>
endodermal cell differentiation	GO:0035987	<i>COL5A2, LAMB1, MMP14, COL8A1, FN1, COL4A2</i>
cell migration	GO:0016477	<i>LAMB1, MCAM, MMP14, IGFBP3, ASPM, FN1, LOX, PLA2G7, THY1, TIMP1, BAMBI, COL1A1, DPYSL3, FSCN1, GPNMB, IGF1, IGFBP5, KNSTRN, LAMC1, LGALS3, MIF, PDGFRB, SERPINE1</i>
tube morphogenesis	GO:0035239	<i>FKBP10, COL4A1, MCAM, MMP14, COL15A1, COL18A1, TGFB1, APLNR, COL8A1, FN1, LOX, THY1, COL4A2, ESM1, GPNMB, PDGFRB, SERPINE1</i>
cell adhesion	GO:0007155	<i>SPP1, LAMB1, MCAM, MMP14, COL15A1, COL18A1, TGFB1, CD276, COL8A1, FN1, LGALS1, THY1, COL1A1, COL6A3, GPNMB, IGF1, LAMC1, LGALS3, NID2, POSTN, SERPINE1, TNC</i>
positive regulation of fibroblast proliferation	GO:0048146	<i>CCNB1, FN1, IGF1, MIF, PDGFRB</i>
regulation of cell communication	GO:0010646	<i>SPP1, MMP14, FHL2, IGFBP3, APLNR, ASPM, BIRC5, CCNB1, FN1, LGALS1, LOX, RACGAP1, THY1, TIMP1, BAMBI, CDC20, CEP55, COL1A1, ECT2, ESM1, FIGNL1</i>

		,GPNMB,IGF1,IGFBP5,LGALS3,LURAP1L,MIF,NDC80,NOX4,PDGFRB,POSTN,SERPINE1,SLC6A6,TPD52L1
muscle structure development	GO:0061061	MMP14,FHL2,IGFBP3,PTGFRN,APLNR,LGALS1,LOX,CENPF,COL6A3,IGF1,IGFBP5,NOX4,PDGFRB
peptidyl-lysine hydroxylation	GO:0017185	FKBP10,PLOD2,P3H4
regulation of SMC migration	GO:0014910	IGFBP3,IGF1,IGFBP5,PDGFRB,SERPINE1
response to wounding	GO:0009611	FKBP10,SPP1,MCAM,FN1,LOX,TIMP1,COL1A1,DPYSL3,IGF1,PDGFRB,SERPINE1,TNC
regulation of signal transduction	GO:0009966	MMP14,FHL2,IGFBP3,APLNR,ASPM,CCNB1,FN1,LGALS1,LOX,RACGAP1,THY1,TIMP1,BAMBI,CEP55,COL1A1,ECT2,ESM1,FIGNL1,GPNMB,IGF1,IGFBP5,LGALS3,LURAP1L,MIF,NDC80,NOX4,PDGFRB,POSTN,SERPINE1,TPD52L1
CC_Term_name	CC_term_id	Intersections
ECM	GO:0031012	COL4A1,COL5A2,LAMB1,MMP14,COL15A1,COL18A1,TGFBI,COL1A2,COL8A1,FN1,LGALS1,LOX,OLFML2B,TIMP1,AEBP1,COL1A1,COL4A2,COL6A3,LAMC1,LGALS3,LTBP2,MGP,NID2,POSTN,SERPINE1,TNC,TNFRSF11B
extracellular space	GO:0005615	NME1,SPP1,COL4A1,COL5A2,LAMB1,MCAM,MMP14,ACOT7,COL15A1,COL18A1,IGFBP3,TGFBI,C1QTNF6,COL1A2,COL8A1,FN1,LGALS1,LOX,OLFML2B,PFKP,PLA2G7,PLOD2,RACGAP1,THY1,TIMP1,AEBP1,APRT,COL1A1,COL4A2,COL6A3,DPYSL3,FIGNL1,FSCN1,IGF1,IGFBP5,LAMC1,LCN2,LGALS3,LTBP2,MGP,MIF,NID2,NUDT5,POSTN,PPIC,PSAT1,SERPINE1,TNC,TNFRSF11B
basement membrane	GO:0005604	COL4A1,LAMB1,COL15A1,COL18A1,TGFBI,COL8A1,FN1,TIMP1,COL4A2,LAMC1,NID2,TNC
extracellular vesicle	GO:1903561	NME1,SPP1,LAMB1,ACOT7,COL15A1,COL18A1,TGFBI,COL1A2,FN1,LGALS1,PFKP,PLOD2,RACGAP1,THY1,TIMP1,AEBP1,APRT,COL4A2,COL6A3,FIGNL1,FSCN1,LAMC1,LCN2,LGALS3,LTBP2,MGP,MIF,NID2,NUDT5,PPIC,PSAT1,SERPINE1
IGF ternary complex	GO:0042567	IGFBP3,IGF1,IGFBP5
endoplasmic reticulum	GO:0005783	FKBP10,SPP1,COL4A1,COL5A2,LAMB1,COL15A1,COL18A1,IGFBP3,PTGFRN,ATP8B1,COL1A2,COL8A1,FN1,LGALS1,PLOD2,PLP2,THY1,TIMP1,COL1A1,COL4A2,COL6A3,FKBP14,IGFBP5,LAMC1,NOX4,P3H4,TNC
cytoplasm	GO:0005737	FKBP10,NME1,SPP1,COL4A1,COL5A2,LAMB1,MMP14,TOP2A,ACOT7,COL15A1,COL18A1,FHL2,IGFBP3,PRC1,PTGFRN,SPC25,TGFBI,ALDH18A1,ASPM,ATP8B1,BIRC5,BUB1B,CCNB1,CCNB2,CDCA7,CDKN3,COL1A2,COL8A1,FN1,HMMR,LGALS1,PCLAF,PFKP,PLA2G7,PLOD2,PLP2,RACGAP1,RRM2,THY1,TIMP1,TPX2,AEBP1,APRT,ARMCX2,BAMBI,CDC20,CENPF,CEP55,COL1A1,COL4A2,COL6A3,DPYSL3,ECT2,FIGNL1,FKBP14,FSCN1,GPNMB,HDC,IGF1,IGFBP5,KNSTRN,LAMC1,LCN2,LGALS3,MCM2,MCM5,MIF,MRPL52,NDC80,NOX4,NUDT5,P3H4,PDGFRB,POSTN,PPIC,PSAT1,SERPINE1,TNC,TPD52L1,UBE2C,UCK2
kinetochore	GO:0000776	SPC25,BIRC5,BUB1B,CCNB1,CENPF,KNSTRN,NDC80

Gene ontology enrichment analysis (G:Profiler) of genes upregulated in endothelial cells derived from 26 separate databases, covering 26 different experimental setups. Here, the most important non-redundant molecular functions (MF), biological processes (BP), and cellular compartments (CC) are shown. ECM, extracellular matrix; GF, growth factor; IGF, insulin-like growth factor; PDGF, platelet-derived growth factor; PK, protein kinase; SMC, smooth muscle cell.

Supplementary Table 6. Gene ontology enrichment analysis of downregulated genes in endothelial cells in various disorders

BP_Term_name	BP_term_id	Intersections
response to endogenous stimulus	GO:0009719	FAM107A,GNA14,KLF2,CDKN1C,FGFR3,JUN,PDE2A,PDK4,TXNIP,BTG2,KBTD2,NR3C1,NR3C2,PRKD2,STMN2,INSIG1,NR4A2,ADRB2,MBP,PRDM16,IER2,KLF3,NDEL1,TOB1
positive regulation of biological process	GO:0048518	KLF4,FAM107A,SOX17,PTH1R,ENPP4,EZH1,KLF2,PECAM1,JAM2,GATM,RNF144B,BMX,CBX7,CDKN1C,FGFR3,JUN,PDE2A,TXNIP,BTG2,MTURN,NR3C1,NR3C2,PRKD2,RAB27A,STMN2,EHD3,LMO7,RASGEF1A,MYLIP,NR4A2,TIE1,TPPP3,UTRN,ADRB2,FCHSD2,HBEGF,ITPR3,MBP,MCF2L,PRDM16,S1PR1,SIK1,ATP8A1,ATP10A,CYTH3,EPB41L2,IER2,NDEL1,PODXL,RNF19A,TAL1,TOB1
signaling	GO:0023052	KLF4,FAM107A,GNA14,SOX17,PTH1R,MKNK2,SGMS1,KLF2,PECAM1,BMX,CDKN1C,FGFR3,JUN,NPY1R,PDE2A,PDK4,RASGRP2,TXNIP,KBTD2,MTURN,NR3C1,NR3C2,PRKD2,RNF125,EHD3,INSIG1,LMO7,MAP3K6,RASGEF1A,DUSP8,NR4A2,SCN2B,SRGN,TIE1,ADRB2,FCHSD2,HBEGF,ITPR3,MBP,MCF2L,P2RY14,PMP22,PRDM16,S1PR1,SIK1,CTNNA3,CYTH3,DENND3,NDEL1,RNF19A,TAL1,TOB1
positive regulation of cellular process	GO:0048522	KLF4,FAM107A,SOX17,PTH1R,EZH1,KLF2,PECAM1,JAM2,RNF144B,CBX7,CDKN1C,FGFR3,JUN,TXNIP,BTG2,MTURN,NR3C1,NR3C2,PRKD2,RAB27A,STMN2,EHD3,LMO7,RASGEF1A,NR4A2,TIE1,TPPP3,UTRN,ADRB2,FCHSD2,HBEGF,ITPR3,MBP,MCF2L,PRDM16,S1PR1,SIK1,ATP8A1,ATP10A,CYTH3,EPB41L2,IER2,NDEL1,PODXL,RNF19A,TAL1,TOB1
developmental process	GO:0032502	KLF4,SOX17,SYNE1,PTH1R,MKNK2,EZH1,FRY,KLF2,PECAM1,JAM2,BMX,CBX7,CDKN1C,FGFR3,JUN,NPY1R,PDE2A,TXNIP,BTG2,HNRNPH3,MTURN,PRKD2,RAB27A,STMN2,INSIG1,PFKFB3,MYLIP,NR4A2,PGM5,SCN2B,SRGN,TIE1,TPPP3,UTRN,ADRB2,COL4A4,HBEGF,LMBRD1,MBP,PMP22,PRDM16,S1PR1,SIK1,ATP10A,IER2,KLF3,NDEL1,PODXL,TAL1,TOB1
tissue development	GO:0009888	KLF4,SOX17,PTH1R,KLF2,PECAM1,BMX,CDKN1C,FGFR3,JUN,PDE2A,TXNIP,BTG2,HNRNPH3,PRKD2,PGM5,SRGN,TIE1,TPPP3,ADRB2,HBEGF,S1PR1,SIK1,PODXL,TAL1
cell communication	GO:0007154	KLF4,FAM107A,GNA14,SOX17,PTH1R,MKNK2,SGMS1,KLF2,PECAM1,BMX,CDKN1C,FGFR3,JUN,NPY1R,PDE2A,PDK4,RASGRP2,TXNIP,KBTD2,MTURN,NR3C1,NR3C2,PRKD2,RNF125,INSIG1,MAP3K6,RASGEF1A,DUSP8,NR4A2,SCN2B,SRGN,TIE1,ADRB2,FCHSD2,HBEGF,ITPR3,MBP,MCF2L,P2RY14,PMP22,PRDM16,S1PR1,SIK1,CTNNA3,CYTH3,DENND3,NDEL1,RNF19A,TAL1,TOB1
regulation of biological quality	GO:0065008	FAM107A,GNA14,SOX17,PTH1R,ENPP4,KLF2,PECAM1,JAM2,ENTPD1,GATM,NPY1R,PDE2A,PDK4,BTG2,RAB27A,EHD3,INSIG1,MYLIP,SCN2B,SRGN,ADRB2,FCHSD2,ITPR3,MBP,PRDM16,S1PR1,ABHD4,ATP8A1,ATP10A,CTNNA3,KANK3,CKNK7,NDEL1,TAL1,TOB1
CC_Term_name	CC_term_id	Intersections
plasma membrane	GO:0005886	FAM107A,GNA14,SYNE1,PTH1R,CAVIN2,ENPP4,SGMS1,PECAM1,JAM2,ENTPD1,BMX,FGFR3,ICAM2,JUN,NPY1R,PDE2A,RASGRP2,PRKD2,RAB27A,EHD3,LMO7,RASGEF1A,MYLIP,PGM5,SCN2B,SLC52A3,TIE1,UTRN,ADRB2,AIF1L,FCHSD2,HBEGF,ITPR3,LMBRD1,MBP,MCF2L,P2RY14,PMP22,S1PR1,ATP8A1,ATP10A,CYTH3,EPB41L2,EXOC6,CKNK7,MFSD6,PODXL
cell periphery	GO:0071944	FAM107A,GNA14,SYNE1,PTH1R,CAVIN2,ENPP4,FRY,SGMS1,PECAM1,JAM2,ENTPD1,BMX,FGFR3,ICAM2,JUN,NPY1R,PDE2A,RASGRP2,PRKD2,RAB27A,EHD3,LMO7,RASGEF1A,MYLIP,PGM5,SCN2B,SLC52A3,TIE1,UTRN,ADRB2,AIF1L,COL4A4,FCHSD2,HBEGF,ITPR3,LMBRD1,MBP,MCF2L,P2RY14

		<i>14,PMP22,S1PR1,ATP8A1,ATP10A,CYTH3,EPB41L2,EXOC6,KCNK7,MFSD6,PODXL</i>
cytoplasm	GO:0005737	<i>KLF4,FAM107A,SYNE1,PTH1R,CAVIN2,MKNK2,ENPP4,FRY,SGMS1,PECAM1,GATM,RNF144B,BMX,CBX7,CDKN1C,FGFR3,PDE2A,PDK4,RASGRP2,TXNIP,BTG2,CHCHD7,MTURN,NR3C1,NR3C2,PRKD2,RNF125,RAB27A,STMN2,EHD3,INSIG1,LMO7,MTMR10,PFKFB3,RASGEF1A,ST6GALNAC3,DUSP8,MYLIP,NR4A2,PGM5,SLC52A3,SRGN,TPPP3,UTRN,ADRB2,AIF1L,B4GALT4,COL4A4,FAM110A,FCHSD2,HBEGF,ITPR3,LMBRD1,MBP,MCF2L,PRDM16,RNF167,S1PR1,SIK1,ABHD4,ATP8A1,ATP10A,CTNNA3,CYTH3,DENND3,EPB41L2,EXOC6,IER2,KANK3,LRRC49,NDEL1,PODXL,RNF19A,TOB1</i>
cell junction	GO:0030054	<i>FAM107A,SYNE1,PECAM1,JAM2,FGFR3,PDE2A,RASGRP2,EHD3,LMO7,PGM5,SCN2B,SRGN,UTRN,AIF1L,FCHSD2,MBP,PMP22,CTNNA3,CYTH3,EPB41L2,NDEL1,PODXL,RNF19A</i>
anchoring junction	GO:0070161	<i>FAM107A,PECAM1,JAM2,FGFR3,EHD3,LMO7,PGM5,AIF1L,PMP22,CTNNA3,CYTH3,EPB41L2,PODXL</i>
cell leading edge	GO:0031252	<i>FAM107A,BMX,RASGRP2,STMN2,AIF1L,CTNNA3,CYTH3,NDEL1,PODXL</i>

Gene ontology enrichment analysis (G:Profiler) of genes downregulated in endothelial cells derived from 25 separate databases, covering 25 different experimental setups. Here, the most important non-redundant biological processes (BP) and cellular compartments (CC) are shown.

Supplementary Table 7. Datasets included in transcriptomic analysis of ED in vivo

Code (Fig. 7)	Dataset ID	Tissue	Intervention inducing ED
Cor.HT	GSE104530	Cardiac	Mouse model of spontaneous hypertension
Liv.Cirrh	GEOD1843	Liver	Rat model of liver cirrhosis
Car.Flow1	GEOD20741	Carotic artery	Partial ligation of mouse carotic artery, 48 h after surgery
Brst.Gen	GEOD24501	Breast	Mouse model of Pten deletion in fibroblasts
Cor.Lip	GEOD24762	Cardiac	High cholesterol diet in porcine coronary arteries
Lung.Gen	GEOD27932	Lung	Broad somatic deletion of all FoxOs leading to a cancer-prone condition
Kidn.Fibr1	GEOD37606	Kidney	Crim1KST264 mice with progressive renal fibrosis
Ao.Lip1	GEOD39264	Aorta	Hyperlipidemic mice
Liv.Flow	GEOD50046	Liver	Partial hepatectomy in mice
Liv.Tum1	GEOD51401	Liver	Human liver tumors vs normal liver
Car.Flow2	GEOD56143	Carotic artery	Partial ligation of mouse carotic artery, 21 d
Ao.Lip2	GEOD57329	Aorta	High-fat diet in mice for 8 w, aortic endothelium
SkM.Lip	GEOD57329SkM	Skeletal muscle	High-fat diet in mice for 8 w, skeletal muscle endothelium
Kidn.Fibr2	GEOD63272	Kidney	Transgenic model of glomerulosclerosis in mice
Ao.Lip3	GEOD6735	Aorta	High-fat diet in mice, aortic endothelium
Bra.Tum1	GEOD73753	Brain	Shh-medulloblastoma model (<i>Ptch</i> ^{+/-} ; <i>Ink4c</i> ^{-/-})
Bra.Tum2	GEOD73753B	Brain	Wnt-medulloblastoma model (<i>Blbp</i> -Cre; mutant <i>Ctnnb1</i> ^{+/-} ; <i>p53</i> ^{-/-} ; mutant <i>Pik3ca</i> ^{+/-})
Bra.Tum3	MTAB3949	Brain	Patient-derived glioblastoma xenografts in mouse brain
Liv.Tum2	MTAB4842	Liver	B19-F10 liver melanoma metastases in mouse
BM.CTx	MTAB6872	Bone marrow	Mouse bone marrow after chemotherapy
BM.RTx	MTAB6872B	Bone marrow	Mouse bone marrow after radiotherapy
SkM.PreE	MTAB7358	Skeletal muscle	Preeclampsia in mouse
Col.Tum	GSE77199	Colon	Human colon tumor vs healthy control tissue
Liv.Tum3	GSE77199B	Liver	Human liver tumor vs healthy control tissue
Kidn.Tum	GSE77199C	Kidney	Human kidney tumor vs healthy control tissue

Codes of different datasets used in Fig. 7.

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