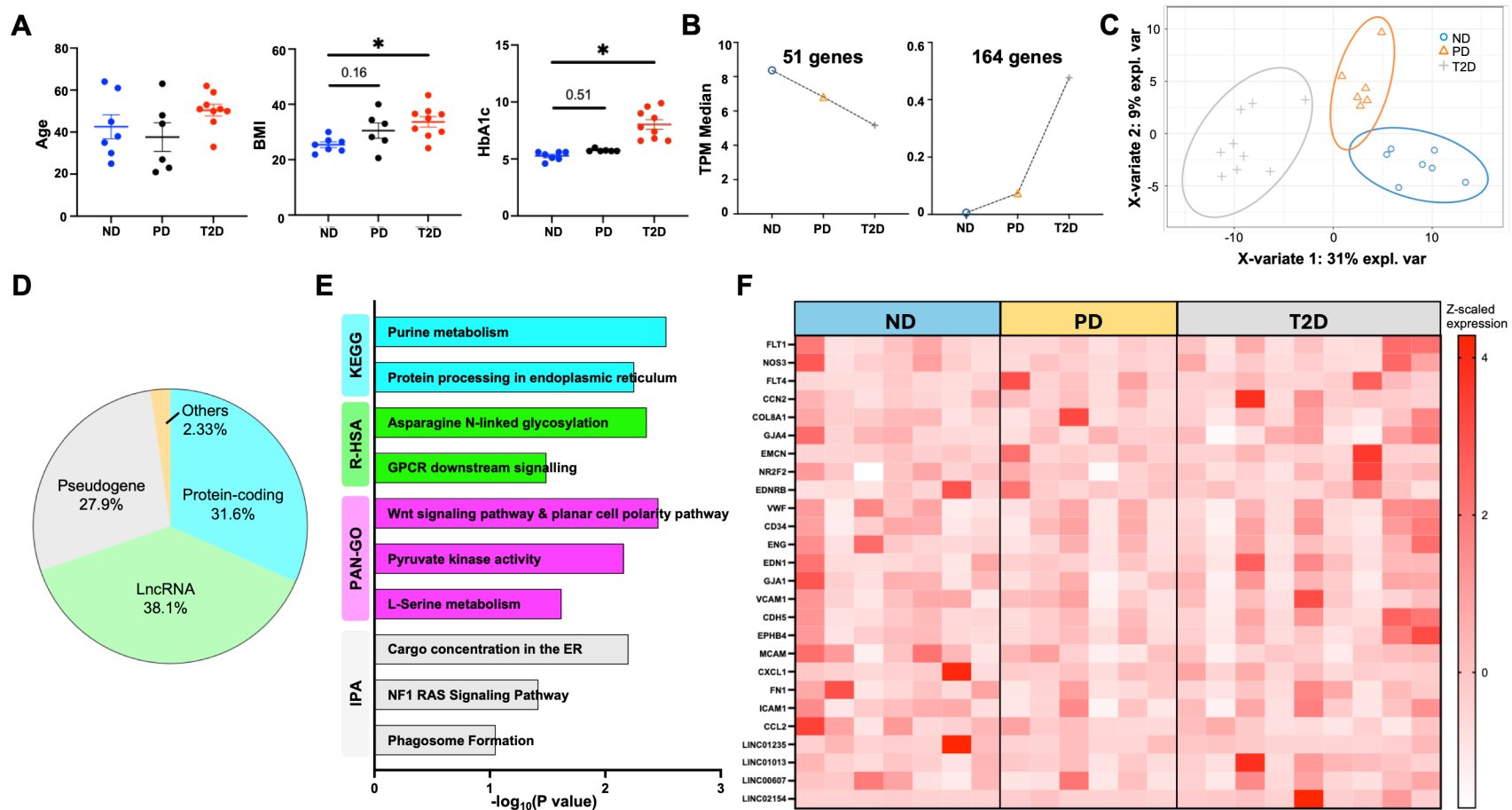
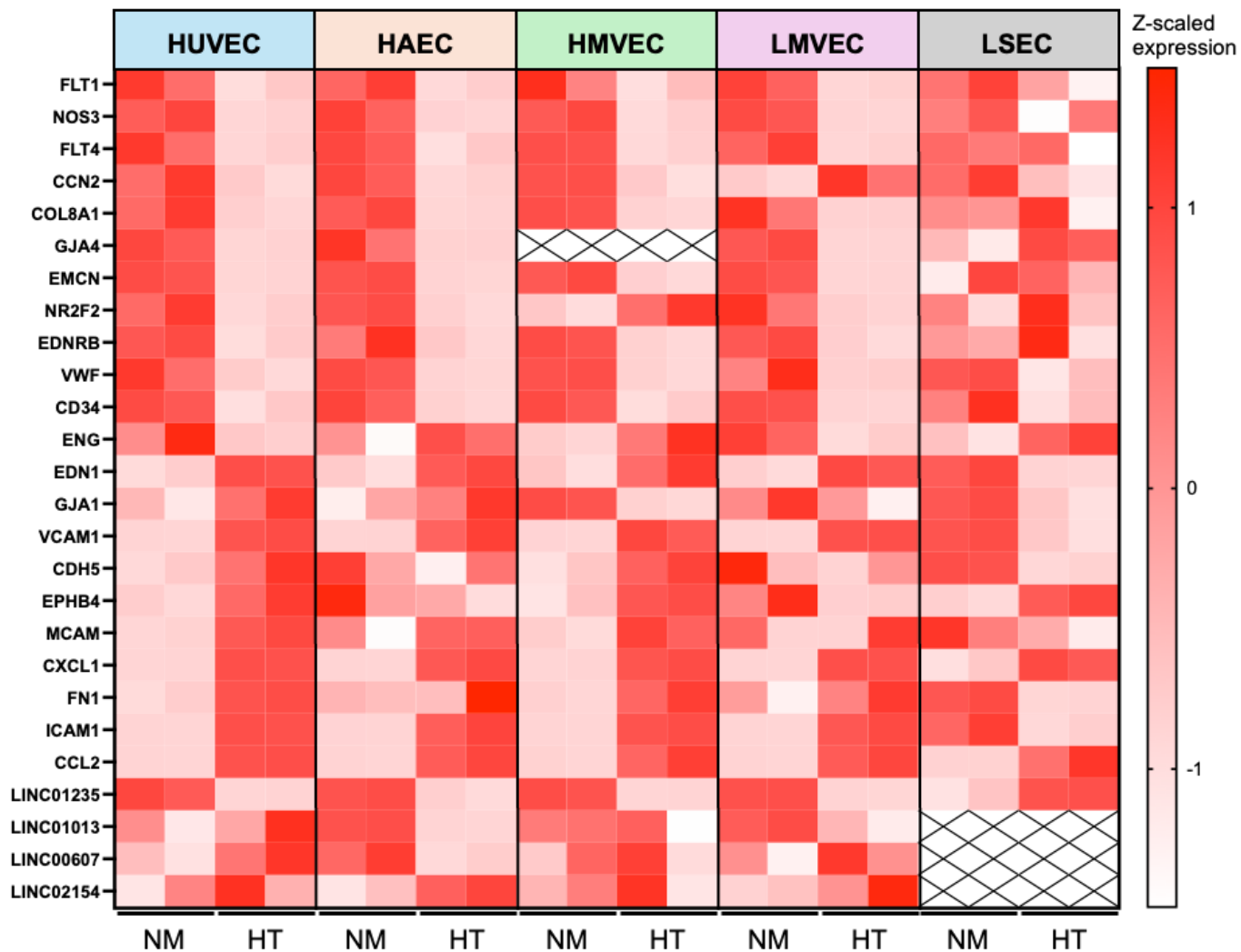
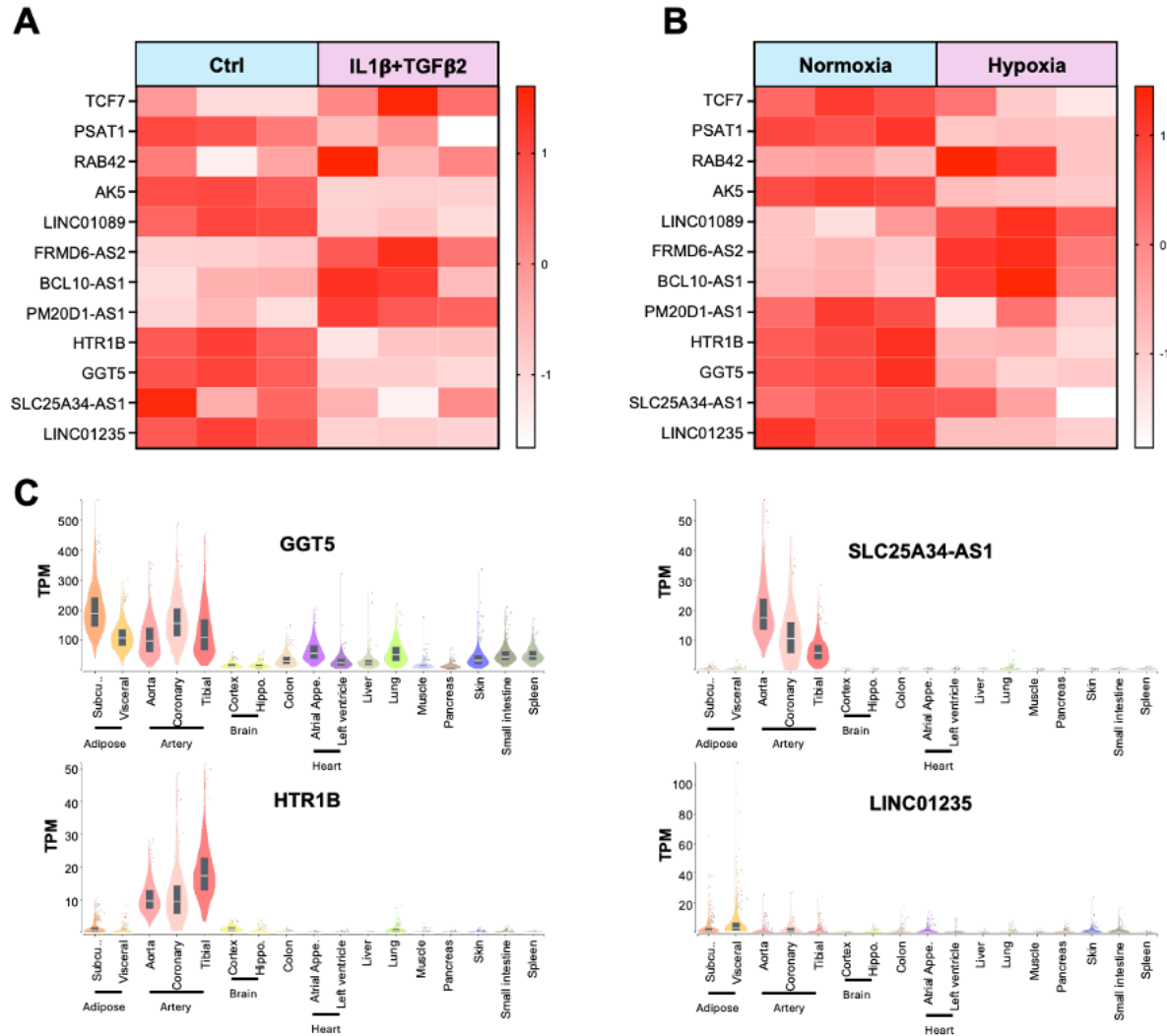




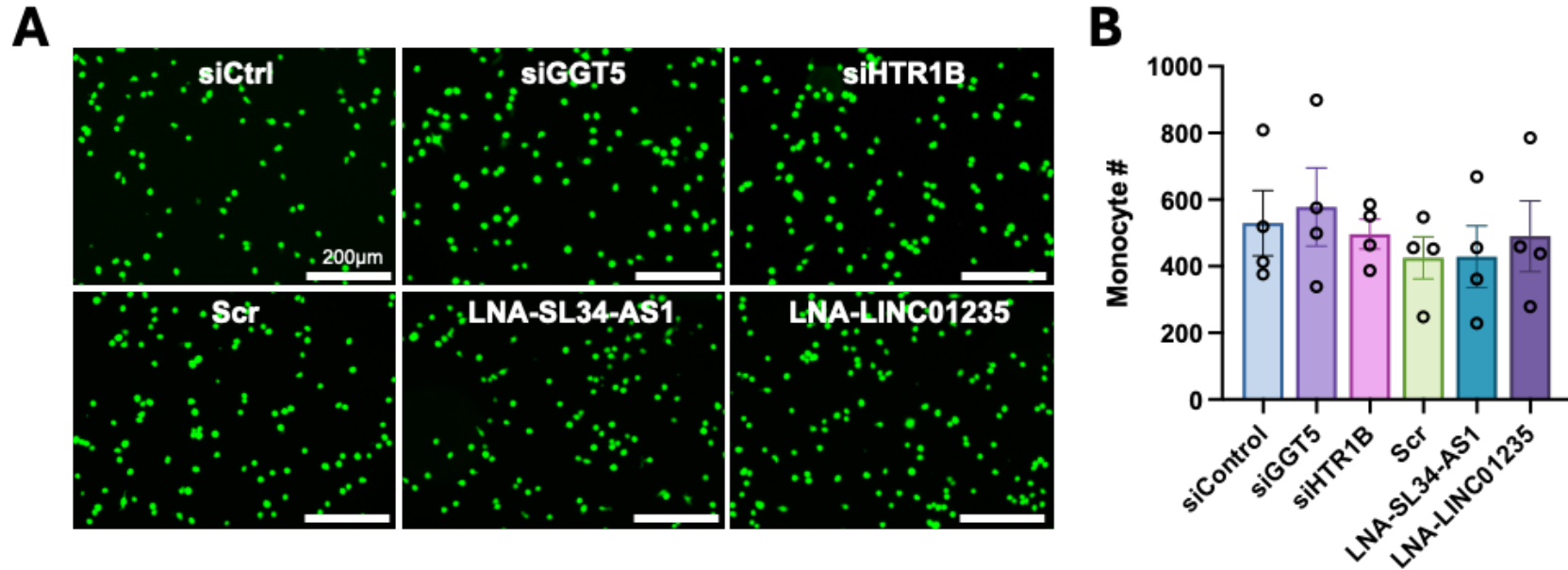
Supplementary Figure 1. Clinical characteristics of the human donor cohorts and analysis of the progressive diabetes-associated DEGs. (A) Age, BMI and HbA1c levels of human donors in this study. Data are represented as scatter plots with mean $\pm$ SEM * $P < 0.05$ based on one-way ANOVA followed by Dunnett's test. (B) Expression patterns of the 215 progressive DEGs identified by one-way ANOVA (164 progressively upregulated and 51 progressively downregulated), shown as median transcripts per million (TPM). (C) PLS-DA analysis of 22 human donor samples based on the 215 DEGs. (D) Gene categories of the 215 DEGs. (E) Enriched pathways of 215 DEGs, plotted with P values. (F) Heatmap of select EC markers and HT-responsive genes in human mesenteric arterial intima, plotted with z-scaled expression.



Supplementary Figure 2. Heatmap of ECs markers and HT-associated genes in 5 EC subtypes treated by NM or HT for 24 hours. The panel includes canonical EC marker genes and DEGs previously identified in HUVECs exposed to HT for 3 or 7 days. Expression values are plotted with z-scaled expression.



Supplementary Figure 3. Expression pattern and tissue distribution of candidate genes. Expression of candidate genes in HUVECs exposed to IL-1 β and TGF β 2 treatment (in **A**), expression of candidate genes in HUVECs under hypoxia (0.1-0.2% O₂, in **B**) based on RNA-seq (GSE118446 and 70330) and GTEx (in **C**). A and B are plotted with z-scaled expression.



Supplementary Figure 4. Effect of candidate gene knockdown in HT-treated ECs on monocyte adhesion. (A) Representative images of fluorescently labeled THP-1 cells adhering to HAECs transfected with the indicated siRNAs or LNA GapmeRs followed by HT treatment. **(B)** Quantification of adherent THP-1 cells. Data are represented as mean $\pm$ SEM from 4 independent experiments. $*P < 0.05$ based on one-way ANOVA followed by Dunnett's test relative to the corresponding controls. Scale bar = 200 μ m.

Supplementary Table 1. Human donor characteristics.

Donor	Non-diabetic (ND)		Pre-diabetic (PD)		T2D	
Sex	Male	Female	Male	Female	Male	Female
Number	7	0	4	2	6	3
Age, y Mean $\pm$ SEM	42.6 $\pm$ 5.7		37.7 $\pm$ 6.8		50.4 $\pm$ 2.8	
BMI, kg/m ² Mean $\pm$ SEM	25.4 $\pm$ 1.0		30.5 $\pm$ 2.8		33.7 $\pm$ 1.9	
HbA1c, % Mean $\pm$ SEM	5.3 $\pm$ 0.1		5.8 $\pm$ 0.0		8.0 $\pm$ 0.4	
Race	Asian 2, Hispanic 4, Caucasian 1		Hispanic 4, Caucasian 1, Black 1		Hispanic 4, Caucasian 4, Black 1	

Supplementary Table 2. List of DEGs shared by multiple EC subtypes.

Common in 5 EC subtypes	Common in HUVEC, HAEC, LMVEC, LSEC	Common in HUVEC, HMVEC, HAEC, LSEC	Common in HAEC, HMVEC, LMVEC, LSEC	Common in HUVEC, HMVEC, LMVEC, LSEC	Common in HUVEC, HAEC, HMVEC, LMVEC
BCL2A1	ARSG	CSF3	KIT	LIPG	ABCA8
CCL5	CALCRL	HTR1B	RASA4DP		ABTB2
CD74	FAT4				ACE
CSF2	MN1				ACHE
STARD10					ADGRG6
TNIP3					AK5
					ANO9
TLR2	PRKAR1B-AS1	MAMDC2	HAPLN3	CXCL10	APOL1
TMEM88	PROX1	MAP2K6	HLA-F	CXCL11	BIRC3
TNFAIP2	PSMB9	MGP	IFIH1	CXCL2	C15orf48
TNFAIP8	PSTPIP2	MIR99AHG	IKBKE	CXCL3	C1QTNF1
TNFRSF11B	RAB17	MPZL2	IL34	CXCL5	C2CD4A
TNFRSF4	RASA4	MSC	IL3RA	EBI3	C2CD4B
TNFRSF9	RCN3	MX1	IL4I1	EDNRB	CAVIN2-AS1
TNFSF15	RNF207	MYO7A	IL6	ENKUR	CBLN3
TRIL	ROBO1	NEURL3	IL7R	ENSG00000277117	CBR3
TRIM47	S100A3	NFKBIE	IRAK2	ENSG00000283265	CCL20
TYMP	SERPINE1	NIBAN1	IRF1	ENSG00000283541	CD69
UBD	SETBP1	NKX3-1	ITGA11	ENSG00000289423	CFB
VCAM1	SHISAL1	NOD2	JAK3	ENSG00000290429	CLDN1
VNN1	SLC15A3	NOS3	LAMB3	ENSG00000294658	CNTNAP3
WWC1	SLC2A6	NRCAM	LEISA1	ENSG00000296424	CNTNAP3B
ZNF71	SLC40A1	NUAK2	LIF	EPSTI1	CNTNAP3C
	SLC8A3	P2RY6	LINC02101	ETV7	CNTNAP3P2
	SLCO2B1	PARAIL	LRG1	GBP4	CRACR2B
	SP6	PDZD2	LTB	GGT5	CSF2RB
	TAPBP	PLA1A	LYPD6	GPR68	CXADR

Supplementary Table 3. List of 16 DEGs shared between human mesenteric arterial intima and cultured ECs exposed to HT.

Common DEGs	Category	Human intima	HUVEC and/or HAEC
ASIC1	Protein-coding	↑	↓ both
C6orf141	Protein-coding	↑	↓ both
LRRC71	Protein-coding	↓	↓ both
CREB3	Protein-coding	↓	↑ (HAEC)
EFCC1	Protein-coding	↑	↓ (HAEC)
RCN3	Protein-coding	↓	↑ both
RIPK2	Protein-coding	↓	↑ both
S100A3	Protein-coding	↓	↑ both
TCF7	Protein-coding	↑	↑ both
HTR1B	Protein-coding	↓	↓ both
PSAT1	Protein-coding	↓	↓ (HUVEC)
RAB42	Protein-coding	↑	↑ (HAEC)
PRKAR1B-AS1	LncRNA	↓	↑ both
ENSG00000276266	LncRNA	↑	↓ (HUVEC)
ENSG00000289029	LncRNA	↑	↑ both
ENSG00000289161	LncRNA	↑	↑ both

Supplementary Table 4. List of 54 DEGs shared between human mesenteric arterial intima and cultured ECs exposed to HT.

Common DEGs	Category	Human intima	HUVEC and/or HAEC
BCL2A1	Protein-coding	↓	↑ both
BIRC3	Protein-coding	↓	↑ both
CSF3	Protein-coding	↓	↑ both
IL34	Protein-coding	↓	↑ both
MSC	Protein-coding	↓	↑ both
RCN3	Protein-coding	↓	↑ both
S100A3	Protein-coding	↓	↑ both
SERPINE1	Protein-coding	↓	↑ both
TRIL	Protein-coding	↑	↓ both
TYMP	Protein-coding	↓	↑ both
AK5	Protein-coding	↓	↓ both
GGT5	Protein-coding	↓	↓ both
HTR1B	Protein-coding	↓	↓ both
BAALC-AS1	LncRNA	↓	↑ both
FAR2P2	LncRNA	↑	↓ (HAEC)
LIMASI	LncRNA	↓	↑ (HUVEC)
LINC00639	LncRNA	↑	↓ both
LINC03104	LncRNA	↓	↑ (HAEC)
PGM5P2	LncRNA	↑	↓ (HMVEC and LMVEC)
PRKAR1B-AS1	LncRNA	↓	↑ both
RRN3P2	LncRNA	↓	↑ both
MIR100HG	LncRNA	↓	↓ (HUVEC) ↑ (HMVEC)
MIR137HG	LncRNA	↓	↑ (HUVEC) ↓ (HAEC)
BCL10-AS1	LncRNA	↑	↑ both
FRMD6-AS2	LncRNA	↑	↑ (HUVEC)
LINC01089	LncRNA	↓	↓ both
LINC01235	LncRNA	↓	↓ both
PM20D1-AS1	LncRNA	↑	↑ (HUVEC)
SLC25A34-AS1	LncRNA	↓	↓ both
ENSG00000226197	LncRNA	↑	↓ (HMVEC and LMVEC)
ENSG00000243797	LncRNA	↓	↑ (HUVEC)
ENSG00000249631	LncRNA	↑	↓ both
ENSG00000253853	LncRNA	↑	↓ (HMVEC and LMVEC)
ENSG00000254943	LncRNA	↑	↑ (HUVEC)
ENSG00000269583	LncRNA	↓	↑ (HAEC)
ENSG00000273014	LncRNA	↓	↓ (HMVEC and LSEC)

ENSG00000273174	LncRNA	↑	↑ both
ENSG00000273312	LncRNA/antisense RNA	↑	↑ both
ENSG00000275496	LncRNA	↓	↑ (HAEC)
ENSG00000276266	LncRNA	↑	↓ (HUVEC)
ENSG00000286533	LncRNA	↓	↑ (HMVEC, LMVEC and LSEC)
ENSG00000286695	LncRNA	↑	↑ (HAEC)
ENSG00000287665	LncRNA	↓	↑ both
ENSG00000289029	LncRNA	↑	↑ both
ENSG00000289161	LncRNA	↑	↑ both
ENSG00000289357	LncRNA	↓	↓ both
ENSG00000289579	LncRNA	↓	↓ both
ENSG00000290579	LncRNA	↓	↓ both
ENSG00000290700	LncRNA	↑	↓ (HMVEC and LMVEC)
ENSG00000290970	LncRNA	↓	↓ both
ENSG00000296607	LncRNA	↑	↑ both
ENSG00000300971	LncRNA	↓	↑ (HUVEC)
ENSG00000305600	Non-coding RNA	↓	↓ both
ENSG00000308375	LncRNA	↓	↓ both

Supplementary Table 5. Sequences of qPCR primers, siRNAs and LNA GapmeRs.

Primer	Sequence
<i>GGT5</i> -F	CAGATGCTGGTGGAGGACATTG
<i>GGT5</i> -R	GTGGTGAGTACAGGGTATAGTCC
<i>HTR1B</i> -F	CACCACGCTCTCCAATGCCTTT
<i>HTR1B</i> -R	CATCACCAGGATGGACACAAGC
<i>SLC25A34-AS1</i> -F	GCGTAGAGCGAGAAGGATCC
<i>SLC25A34-AS1</i> -R	TGCAGATGCTGCTTTCTCTCT
<i>LINC01235</i> -F	GCTAAGAAGCAGCCTACCTTAC
<i>LINC01235</i> -R	GATGATGATGGAGTAGATCCTGC
<i>ACTB</i> -F	ACCTTCTACAATGAGCTGCG
<i>ACTB</i> -R	CCTGGATAGCAACGTACATGG
si <i>GGT5</i> -ss	CGGGGACCAGCUGGGCAGAUG
si <i>GGT5</i> -as	CAUCUGCCCAGCUGGUCCCCG
si <i>HTR1B</i> -ss	CCACGCUCUCCAAUGCCUU
si <i>HTR1B</i> -as	AAGGCAUUGGAGAGCGUGG
LNA <i>SLC25A34-AS1</i>	AAATGGCTCAGTTAGG
LNA <i>LINC01235</i>	GCTAGTGAAGATGATG