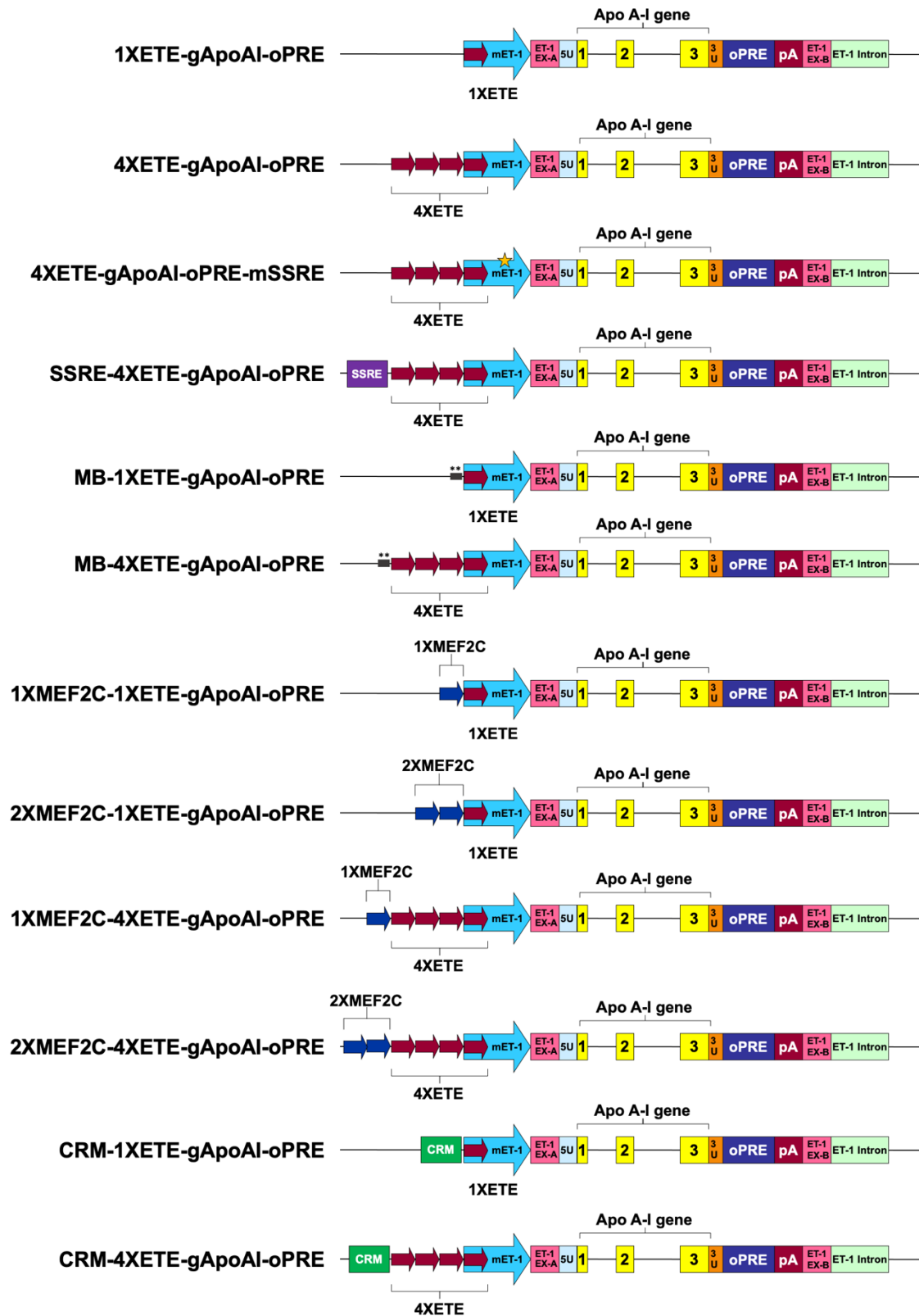
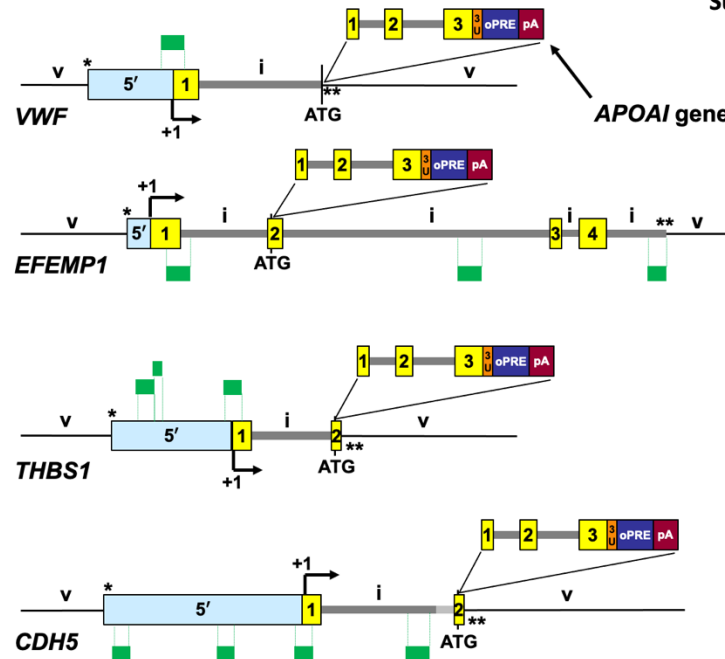


Supplementary Figure S1

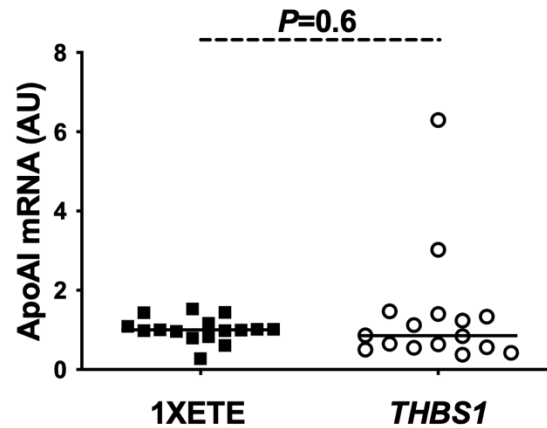


Supplementary Figure S1. Expression cassettes. All cassettes were tested in pBshuttle-based plasmids in vitro. Two of the cassettes, 4XETE-gApoAI-oPRE and SSRE-4XETE-gApoAI-oPRE were incorporated into helper-dependent adenoviral vectors and were also tested in vivo. Yellow blocks (1, 2, and 3), rabbit *APOA1* coding exons; large light-blue arrow (mET-1), murine endothelin-1 (*Edn1*) enhancer/promoter; red arrows, *Edn1* enhancer (1XETE), both in native position (within light-blue arrows) and added as 3 direct repeats (4XETE); yellow star, endogenous shear stress response element (SSRE) sequence; purple box, exogenous SSRE; ** introduced *MluI* and *BglII* restriction sites; small dark-blue arrow, mouse *Mef2c* enhancer element; green box, cis-regulatory module (CRM); 5U, 5'-untranslated region of rabbit *APOA1* gene, including exon 1 and intron 1; 3U, 3'-untranslated region of rabbit *APOA1* gene; ET-1 EX-A and ET-1 EX-B, 5' and 3' segments of mouse *Edn1* exon 1 (untranslated); ET-1 Intron, 5' segment of mouse *Edn1* intron 1; oPRE, optimized woodchuck hepatitis virus post-transcriptional regulatory element; pA, SV40 poly A signal. Drawing is not to scale. Six other cassettes (3X, 4X, and 5XMEF2C-1XETE-gApoAI-oPRE and 3X, 4X, and 5XMEF2C-4XETE-gApoAI-oPRE) are not shown.

Supplementary Figure S2



Supplementary Figure S2. Genomic knock-in expression cassettes. An engineered rabbit *APOAI* gene was inserted at the translation start sites (ATG) of genomic sequences cloned from the human *VWF*, *EFEMP1*, *THBS1*, and *CDH5* loci. The engineered *APOAI* gene includes the 3 *APOAI* coding exons (yellow boxes), beginning with the ATG in native exon 2, 2 *APOAI* introns (grey bars), a segment of *APOAI* 3' untranslated region (3U), the optimized woodchuck hepatitis virus post-transcriptional regulatory element (oPRE), and an SV40 poly A signal (pA). Cloned segments of human genomic DNA in the cassettes include: sequences 5' to the transcription start sites (blue boxes), the transcription start sites (+1), exons of *VWF*, *EFEMP1*, *THBS1*, and *CDH5* (yellow boxes numbered 1–4), introns (i), and the translation start sites (ATG). Green bars indicate positions of cis-regulatory modules identified in silico (see Materials and Methods). All cassettes were constructed in the pBshuttle plasmid vector (v). Junctions of the expression cassettes and pBshuttle are indicated (* and **). Drawing is not to scale.



Supplementary Figure S3. *APOA1* expression from pBshuttle-1XETE-gApoAI-oPRE (1XETE) and pBshuttle-THBS1-gApoAI-oPRE (*THBS1*). Bovine aortic endothelial cells were transfected and *APOA1* mRNA was measured by RT-qPCR 24 hours after transfection. Data points are from four independent experiments; bars are group medians. Median *APOA1* expression for 1XETE-gApoAI-oPRE is assigned a value of 1; all other points are measured relative to this value.

Supplementary Table S1. Relative transcript levels for 29 endothelial cell (EC)-associated genes, from ENCODE.

Gene Name	Cell Lines										
	Gene Symbol	A549	AG445	BJ	CD20-positive B cell line	GM12878	H1-hESC	HMEC cell line	HSMM cell line	HUVEC cell line	PMID
EGF Containing Fibulin Extracellular Matrix Protein 1	EFEMP1	14	100	320			6	67	225	2379	12963823
Thrombospondin 1	THBS1	15	277	1522			5	398	912	1903	12963823
Von Willebrand Factor	VWF									582	23990205
Cadherin 5	CDH5									371	24003143
Endothelin 1	EDN1	52	1	2	1	5		2	10	329	12963823
EGF Like Domain Multiple 7	EGFL7	3	0.7	5			18	2	0.9	320	15972971
Intercellular Adhesion Molecule 2	ICAM2	0	0	0.1	16	6	0.1	0	0.1	258	12963823
Platelet And Endothelial Cell Adhesion Molecule 1	PECAM1				8	7				216	23990205
Protein C Receptor	PROCR	43	33	14			24	40	3	193	9396465
Endothelial Cell-Specific Molecule 2	ECSCR						2			188	18394197
Sphingosine-1-Phosphate Receptor 1	S1PR1		15	5	25	2	3	6	19	176	12963823
Tyrosine Kinase With Immunoglobulin Like And EGF Like Domains 1	TIE1					0.8	0.7			166	12963823
Activin A Receptor Like Type 1	ACVRL1		3	3					5	130	21467543
Multimerin 1	MMRN1					3				81	18394197
Roundabout Guidance Receptor 4	ROBO4							1	1	78	24003143
Endothelial Cell Specific Molecule 1	ESM1			0.6						72	12963823
Hedgehog Interacting Protein	HHIP									55	18394197
Kinase Insert Domain Receptor	KDR						38			54	11076864
Adhesion G Protein-Coupled Receptor L4	ELTD1		8	1					3	45	12963823
Tissue Factor Pathway Inhibitor	TFPI	18	11	3		3	0.6		31	34	16165014
Histone Deacetylase 7	HDAC7	2	3	8	20	0.6	9	6	7	27	24003143
Nitric Oxide Synthase 3	NOS3						2			18	23990205
TEK Receptor Tyrosine Kinase	TEK		19				7		3	17	24003143
Endomucin	EMCN									16	18394197
Intercellular Adhesion Molecule 1	ICAM1	0.6	14	18	17	26	3	1	0.9	14	22723222
Thrombomodulin	THBD	15						2	8	13	16165014
Endothelial Cell-Specific Molecule 2	ECSCR*									1	18394197
E-Selectin	SELE									0.9	22723222
Vascular Cell Adhesion Molecule 1	VCAM1		11			5			10	0.7	22723222
P-Selectin	SELP				2					0.7	17272818
*paralog											

Supplementary Table S1 (continued).

Gene Name	Gene Symbol	Cell Lines									
		HeLa-S3	HepG2	IMR-90	K562	MCF-7	NHEK cell line	NHLF cell line	SK-N-SH	SK-N-SH_RA	PMID
EGF Containing Fibulin Extracellular Matrix Protein 1	EFEMP1	28		68	1	8	62	161	395	26	12963823
Thrombospondin 1	THBS1	0.6	16	458		61	322	440	47	24	12963823
Von Willebrand Factor	VWF										23990205
Cadherin 5	CDH5										24003143
Endothelin 1	EDN1	1	0.6	6		4	13	4	1	1	12963823
EGF Like Domain Multiple 7	EGFL7	0.7	2	2	50	1	1	0.6	12	15	15972971
Intercellular Adhesion Molecule 2	ICAM2	0	2	0	5	0	0	0.1	0	0.2	12963823
Platelet And Endothelial Cell Adhesion Molecule 1	PECAM1		1		3						23990205
Protein C Receptor	PROCR	10	1	28	3	1	34	13	18	11	9396465
Endothelial Cell-Specific Molecule 2	ECSCR			1					3	2	18394197
Sphingosine-1-Phosphate Receptor 1	S1PR1			8			2	3	4	27	12963823
Tyrosine Kinase With Immunoglobulin Like And EGF Like Domains 1	TIE1			2						1	12963823
Activin A Receptor Like Type 1	ACVRL1			2				4			21467543
Multimerin 1	MMRN1										18394197
Roundabout Guidance Receptor 4	ROBO4										24003143
Endothelial Cell Specific Molecule 1	ESM1			1					10		12963823
Hedgehog Interacting Protein	HHIP			1					0.8		18394197
Kinase Insert Domain Receptor	KDR										11076864
Adhesion G Protein-Coupled Receptor L4	ELTD1			3				5			12963823
Tissue Factor Pathway Inhibitor	TFPI	13	52	5	58	0.7		29		0.8	16165014
Histone Deacetylase 7	HDAC7	2	2	12	5	3	3	5	10	6	24003143
Nitric Oxide Synthase 3	NOS3		0.7		2						23990205
TEK Receptor Tyrosine Kinase	TEK			4							24003143
Endomucin	EMCN					1					18394197
Intercellular Adhesion Molecule 1	ICAM1	3	42	8	6	0.8		4	8	42	22723222
Thrombomodulin	THBD					4	3	2			16165014
Endothelial Cell-Specific Molecule 2	ECSCR*										18394197
E-Selectin	SELE										22723222
Vascular Cell Adhesion Molecule 1	VCAM1			3				2	2	9	22723222
P-Selectin	SELP										17272818
*paralog											

Relative transcript levels are listed for the 29 genes in the 18 ENCODE cell lines, including human umbilical vein EC (HUVEC). Expression Atlas ID: E-GEOD-26284. PMIDs identify reports of expression of each gene in EC.

Supplementary Table S2. Sequences of cis-regulatory modules (CRM).

Name	Gene	Length	Sequence
CRM1	<i>CDH5</i>	161	AGGCAGCCGCCACCGCAGGGCCTGCCTATCTGCAGCCAGCCCAGCCCTCACAA AGGAACAATAACAGGAAACCATCCCAGGGGGAAGTGGGCCAGGGCCAGCTGGAA AACCTGAAGGGGAGGCAGCCAGGCCCTCCCTCGCCAGCGGGGTGTGGCTCCCCCT
CRM2	<i>CDH5</i>	167	TTGCTTCCTCCTCTGCTACTAATCTGGTCTCACAGACCATCCCATTTCTGCTAGC CCACCAGCCGCTTCCTTGCTCCCAATGACACTTCCTGGCCTTGTGCCCTCCTGTT ACCTCCTTTGCCTCCAGAGAGGTTGGAGCAGAGGCTGGGCAGTGCCAGAAATCAG
CRM3	<i>CDH5</i>	268	CTGCCACACTGCCAGCTGAGGGCTGGTGCCAGAGCCGTGTCTGCTTGCCCCAT CAAGAGGTGGGAGGGATTGATCCACCTTCCTGCCCCACAGATGGTGCAGCCTCCA ACCTATTGTTTTCCAGGACGCTTCGGTGGAGAGCACAAGGAATGTAGGGTCTAGA AACAGGAAGCCCTGGCTTCGGCTGGACAAGGTTTCCTCCAGACTCAGGCCCTGCC TCCAGACAACAAGGCAGGGCCCTTGGTCCCACCCTGCCCTGCCTGGCTC
CRM4	<i>CDH5</i>	332	GCCTGGAAGGGGTTAAGCTGCCCGCCTGCAGCCTCAGCCTGAGCTATTGTGTTGC CAAACAAGGGCCGGACATGAGGGCAGGAAGCCAGCAGGGGCCACACATTTTCTG CAAAGTTGGATGATTCACTGCTGACTTGGGGACACCCAGGGGACAGAGGGGACA CCATCCCAGGAAGAATCTTAGGCTCATTTTGCCACATGGACCCATGACTGTTCCC TGTATCCTCTCTCTGCACCCCTCAGTCACACTGAAGCAACTATGAGAATTTCCAT TTGACAGATGGGACCATCGAGGCTGAGGGAAGCTGTGCAGCCAGTCCAAGGTCA CAC
CRM5	<i>EFEMP1</i>	352	ACCCTGCACAGTCCAGGGCAGTTCTCGGGTACTCAACACCCCTCAGCTCACCCCA CCTCACTCTCCCGCGCGCGGCCAGTGAGTACTGGGCTCGCTCGGGGCGACCCC CCGTTGGGGGCTCCTACCTGTGCGGCCGCGCTGCGCTCCGGGCCCCGGGCAGCG AGGGGAGTGCGCAGGGGAGGGCAGCCCCGTGGGTCTGATCTGGCGAAGTCCGG CAGCGGCCGCGCGGCAGGAGGAGGAGGAGAAAGGGAGGGAAAGGGGGAGGG CGAAGGGGGGCGGAGGAGAGAGCTGAGGGAGGCGGAGCGCTGAGCCCAGCGT TGCGAGCCCGGCGGTAGAGCGCGCAGCGCAGC
CRM6	<i>EFEMP1</i>	345	TTGAGAAATGTTGCTACAGGCGATAAGAGGCCCTCTGAAGAATTTTTAAGCTCAGGA AACAATCTGATCAGACGCTCATTTGAGAAAGTCACTGTAAGGAAGAAGCCCAAGGA AGGATTGAGCAAAAGTGGAGTAAACAAACAAATAAACTTAAATTTCTTTAATAAAC TGAGAGCTGCTTATGTACACAATGGATGCTTGACAAGGAAATAGCTGAATGGAAGC CCAGAGATCCATTTAGATATTTTACTGATGTCTGAACTTACTGGAGCGAGAATAA ATTCATTTGTCTCTCAGACTAATTTTTTTCTTGTTCCTCAACAGTGTTAAAGGTAC CACTA
CRM7	<i>EFEMP1</i>	272	AGTCTCCACACCAGGCTGCTCTGAAATGGTTTGCCAAGAAGAAAGGGAAACAATCT CATAGCACAGTTCAGTTAGCTAATATCCTACATGTCTTCAAAGCCCCAGATTCTTAT CACTTTGCTAATACGAGCCTACAGCTGTTTCTAGAATACACAGTGATGTGTATGCT CTGTGAAAATAAACAGAAAACCTAGGCAGATGATGCCATGGTGCAAGTGATATAA GTGAAACGTGCTCAAATGAGAGCTTAAAGAGATATAAACGTGAGTG
CRM8	<i>THBS1</i>	198	CCCGCCCCCTTCACTTTCTAGCTGGAAAGTTGCGCGCCAGGCAGCGGGGGCGG AGAGAGGAGCCCAGACTGGCCCCCACCTCCCGCTTCTGCCCCGCGCCGCCCA TTGGCCGGAGGAATCCCAGGAATGCGAGCGCCCCCTTTAAAGCGCGCGGCTCC TCCGCTTGCCAGCCGCTGCGCCCCGAGCTGGCCTGC
CRM9	<i>THBS1</i>	55	CCCTTGATGAGAATACGCACACCGCCCCCAAGCGGCCGCGGAGGGAGCGCCGC G
CRM10	<i>THBS1</i>	280	AATACAATAATAGGCAGAGAGTAATTTATTACTCTATGGGTCTGCTCTGTAAATAGC TGAAGACTCTGGAGCCAGATGGTTCTGCAAATTTCTCAAACAGGAGTCACGTTAAG AAGCACGAGTGGGCACAAAACTGTTTTTCAAGACACAATTTCAATTTGGCTTGTG GAACTGGATACGAGTAAGTTTCCTTAAATTCGAGTAGAAAGCAGCTGTCCTCCC CGGGCCCCCTTGATGAGAATACGCACACCGCCCCCAAGCGGCCGCGGAGGGAG CG
CRM11	<i>VWF</i>	237	ACTGTCTTGCTGTTATGTAGCCCAGGGGCTGTGGAGTCCCCACTGCTGGGGGAGA TAAAGCCCCAAGCTGTGACATCCACCAACCACCTCCCTTTCCACCACAATAGCTG TGAGCTGCCACAACAGGGGATTGGCCTCCTTTTAATTACCAAAGGAAACAATGAA AGGAAATGGTATTAGAAGTACCTCCAAGCTGATAAAGCTTTGTAGAGTTTGGAGGG AGACCTCCTGGCAG

Supplementary Table S3. Primer and probe sequences.

Primer Name	Primer Sequence
ApoAI F (BAEC)	5'-AGAATATGTGGCCCAGTTTGAAG-3'
ApoAI R (BAEC)	5'-TCCCAGTTGTCCAGGAGCTT-3'
ApoAI P (BAEC)	5'-56-FAM/CTCCGCCTT/ZEN/TGGAAAGCAACTCAACC/3IABkFQ-3'
ApoAI F (HAEC, HUVEC)	5'-ACCTTGGCTGTGCTCTTC-3'
ApoAI R (HAEC, HUVEC)	5'-CAGGCTGTCCCAGTTGTC-3'
ApoAI P (HAEC, HUVEC)	5'-56-FAM/CAGTCAAGG/ZEN/ACAGCGGCAGAGAAT/3IABkFQ-3'
GAPDH F (BAEC)	5'-TGACCCCTTCATTGACCTTCA-3'
GAPDH R (BAEC)	5'-GCCTTGACTGTGCCGTTGA-3'
GAPDH P (BAEC)	5'-56-FAM/TCCAGTATG/ZEN/ATTCCACCCACGGCAA/3IABkFQ-3'
GAPDH F (HAEC, HUVEC)	5'-GGTGTGAACCATGAGAAGTATGA-3'
GAPDH R (HAEC, HUVEC)	5'-GAGTCCTTCCACGATACCAAAG-3'
GAPDH P (HAEC, HUVEC)	5'-56-FAM/AGATCATCA/ZEN/GCAATGCCTCCTGCA/3IABkFQ-3'
oPRE F	5'-CAACTCCTTTCTGGGACTTTC-3'
oPRE R	5'-AGGCGGCGATGAGTTCTG-3'
oPRE P	5'-56-FAM/TTTCCCCCT/ZEN/CCCGATCGCCA/3IABkFQ-3'

Species-specific primers and probes were used for bovine aortic endothelial cells (BAEC), human aortic endothelial cells (HAEC), and human umbilical vein endothelial cells (HUVEC). ApoAI, apolipoprotein AI; F, forward; R, reverse; P, probe; GAPDH, glyceraldehyde phosphate dehydrogenase; oPRE, optimized woodchuck hepatitis virus post-transcriptional regulatory element.