

Supplementary table 1: Artery eQTL-GWAS Colocalization Analysis. CAD GWAS sample size, n =1157880. eQTL sample size: AOR (atherosclerotic aortic root), n=539; MAM (free internal mammary artery), n=553.													
SNP	e	other_allele	Chromosome	Position_hg19	P_value_GWAS	Beta_GWAS	SE_GWAS	P_value_eQTL	Beta_eQTL	Tissue_eQTL	PP.H4	Ensembl_ID	Gene_symbol
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	0.001502197	0.178581564	MAM	0.999999996	ENSG000000260832	CTD-325312.1
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	1.54197E-07	0.303741901	AOR	0.999999599	ENSG000000260832	CTD-325312.1
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	8.90791E-50	0.371012199	AOR	1	ENSG000000140945	CDH13
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	8.66212E-33	0.271866411	MAM	1	ENSG000000140945	CDH13
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	0.000765831	0.184700145	MAM	0.999998562	ENSG000000260788	CEDORA
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	2.11207E-05	0.24753787	AOR	0.999982865	ENSG000000260788	CEDORA
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	0.000964244	0.192767478	MAM	0.99999486	ENSG000000261410	CDH13-AS1
rs4783307	T	G	16	83076634	0.000000023	-0.02846679	0.0050945	0.001922826	0.149389834	AOR	0.991550906	ENSG000000261410	CDH13-AS1
rs7500448	A	G	16	83045790	1.108E-17	0.049992074	0.0058388	1.81243E-05	0.258910223	AOR	0.999999676	ENSG000000260228	CDH13-AS2

Supplementary table 2: Characteristics of Patient underwent carotid endarterectomy (CEA)		
Palque status	Early (57)	Advanced (145)
Gender	Male: 40	Male: 105
	Female: 17	Female: 40
Age (mean), years	72.3	72.4
BMI (Mean)	25.6	26.6
Smoking	Active smoker: 3	Active smoker:19
	Ex-smoker: 19	Ex-smoker: 44
	Non-smoker: 31	Non-smoker: 80
	Not Available (n/a): 4	Not Available (n/a): 2
Diabetes	Yes: 11	Yes: 29
	No: 43	No: 114
	Not Available (n/a): 3	Not Available (n/a): 2
Dialysis	No: 54	No:143
	Not Available (n/a): 3	Not Available (n/a): 2

Supplementary table 3: Characteristics of <i>CDH13</i> LoF carriers	
Characteristic	All <i>CDH13</i> LoF carriers (n = 272)
Age (years)	272 (54,69 ± 7,96)
Smoking	
Current	24 (9,05%)
Previous	54 (20,38%)
Never	187 (70,57%)
CAD	
No	249 (91,54%)
Yes	23 (8,46%)
Hypertension	
No	58 (21,32%)
Yes	214 (78,68%)
Heart failure	
No	258 (94,85%)
Yes	14 (5,15%)
Venous thromboembolism	
No	266 (97,79%)
Yes	6 (2,21%)
Stroke	
No	263 (96,69%)
Yes	9 (3,31%)
Peripheral vascular disease	
No	268 (98,53%)
Yes	4 (1,47%)
Adiponectin	23 (−0,34 ± 1,08)
Basophill count (10 ⁹ cells/Litre)	258 (0,04 ± 0,04)
Eosinophill count (10 ⁹ cells/Litre)	258 (0,19 ± 0,16)
Lymphocyte count (10 ⁹ cells/Litre)	258 (2,25 ± 1,33)
Monocyte count (10 ⁹ cells/Litre)	258 (0,47 ± 0,17)
Neutrophill count (10 ⁹ cells/Litre)	258 (4,35 ± 1,3)
Platelet count (10 ⁹ cells/Litre)	259 (260,03 ± 68,35)
Leukocyte count (10 ⁹ cells/Litre)	259 (7,31 ± 2,06)
C-reactive protein (mg/L)	252 (3,19 ± 4,65)

IL6 (count – olink Instance 0 NPX)	25 (0,38 ± 0,86)
TNF (count – olink Instance 0 NPX)	27 (0,12 ± 0,34)
Diastolic blood pressure, automated reading (mmHg)	252 (83,31 ± 10,12)
Systolic blood pressure, automated reading (mmHg)	252 (139,54 ± 19,23)
Pulse wave Arterial Stiffness index	150 (9,29 ± 4,33)

Supplementary table 4: Loss of function (LoF) variants of <i>CDH13</i> associated with CAD and detrimental cardiometabolic phenotypes in the UK biobank cohort											
CHROM	GENPOS	ID	Sample_size	Carriers	Non_carriers	Trait	BETA	SE	P_value	−log10_p_value	
16	82627058	CDH13(ENSG00000140945).M1.0.01	159397	150	159247	Arterial Stiffness index	2.44976	0.5957	3.91562E−05	4.4072	
16	82627058	CDH13(ENSG00000140945).M1.0.01	454886	258	454628	Lymphocyte count	0.281353	0.0693784	5.00622E−05	4.30049	
16	82627058	CDH13(ENSG00000140945).M1.0.01	455734	259	455475	Leukocyte count	0.427187	0.126259	0.000715863	3.14517	
16	82627058	CDH13(ENSG00000140945).M1.0.01	447020	252	446768	C−reactive protein	0.653885	0.271001	0.015828509	1.80056	
16	82627058	CDH13(ENSG00000140945).M1.0.01	42966	23	42943	Adiponectin	−0.349213	0.174423	0.045273076	1.34416	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	Heart failure	0.612363	0.345664	0.076468047	1.11652	
16	82627058	CDH13(ENSG00000140945).M1.0.01	439651	252	439399	Diastolic blood pressure automated reading	1.27591	0.737692	0.083702803	1.07726	
16	82627058	CDH13(ENSG00000140945).M1.0.01	454886	258	454628	Eosinophil count	0.0144654	0.00854796	0.090594118	1.0429	
16	82627058	CDH13(ENSG00000140945).M1.0.01	49082	25	49057	IL6	0.284918	0.17984	0.113129013	0.946426	
16	82627058	CDH13(ENSG00000140945).M1.0.01	455736	259	455477	Platelet count	5.12952	3.62915	0.157530989	0.802634	
16	82627058	CDH13(ENSG00000140945).M1.0.01	454886	258	454628	Neutrophil count	0.122694	0.0879529	0.163017414	0.787766	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	CAD	0.334942	0.251884	0.183602673	0.736121	
16	82627058	CDH13(ENSG00000140945).M1.0.01	439638	252	439386	Systolic blood pressure automated reading	1.58188	1.27998	0.216509521	0.664523	
16	82627058	CDH13(ENSG00000140945).M1.0.01	48349	27	48322	TNF	0.0987695	0.0835226	0.236987806	0.625274	
16	82627058	CDH13(ENSG00000140945).M1.0.01	454886	258	454628	Basophil count	0.00279139	0.00317487	0.37928529	0.421034	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	Venous thromboembolism	−0.231278	0.338985	0.495069305	0.305334	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	Stroke	0.242915	0.377069	0.519433553	0.28447	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	Hypertension	−0.0520642	0.155945	0.738483846	0.131659	
16	82627058	CDH13(ENSG00000140945).M1.0.01	469607	272	469335	Peripheral vascular disease	0.0863694	0.526279	0.869641988	0.0606595	
16	82627058	CDH13(ENSG00000140945).M1.0.01	454886	258	454628	Monocyte count	−0.00219256	0.0133738	0.869774759	0.0605932	

Supplementary table 5: Top 100 predicted binders of *CDH13-AS2* by LncRRlsearch

Sum of Energy	Min of Energy	Transcript ID	Transcript Name	Genomic Distance
-113.58	-113.58	ENST00000567109	CDH13-001	-1
-83.36	-17.75	ENST00000370447	<i>ZNF326-004</i>	10,000,000,000
-102.10	-17.83	ENST00000510439	<i>GOLGA6L4-001</i>	10,000,000,000
-83.01	-18.14	ENST00000531499	<i>GPR68-001</i>	10,000,000,000
-71.17	-18.27	ENST00000616356	<i>FCN1-201</i>	10,000,000,000
-68.93	-18.72	ENST00000624300	<i>CTD-2144E22.9-001</i>	48,853,355
-133.01	-19.70	ENST00000379751	<i>CENPB-001</i>	10,000,000,000
-194.16	-19.71	ENST00000627551	<i>RP11-573D15.8-018</i>	10,000,000,000
-87.78	-19.74	ENST00000261892	<i>SLC24A1-001</i>	10,000,000,000
-122.17	-19.76	ENST00000295910	<i>ERICH6-001</i>	10,000,000,000
-172.66	-19.97	ENST00000567390	<i>GOLGA6L7P-001</i>	10,000,000,000
-107.61	-20.05	ENST00000432442	<i>GS1-519E5.1-001</i>	10,000,000,000
-75.73	-20.26	ENST00000379380	<i>LYRM7-001</i>	10,000,000,000
-73.03	-20.30	ENST00000608477	<i>RP11-212P7.2-001</i>	10,000,000,000
-73.85	-20.32	ENST00000380433	<i>UCN3-001</i>	10,000,000,000
-72.54	-20.43	ENST00000232974	<i>ZBTB47-002</i>	10,000,000,000
-78.92	-20.50	ENST00000380243	<i>CCDC85C-001</i>	10,000,000,000
-406.55	-20.53	ENST00000222990	<i>SNX8-001</i>	10,000,000,000
-70.58	-20.87	ENST00000619213	<i>GOLGA6L6-001</i>	10,000,000,000
-74.67	-21.09	ENST00000626826	<i>HELLPAR-001</i>	10,000,000,000
-133.74	-21.55	ENST00000612859	<i>B3GALNT2-003</i>	10,000,000,000
-79.58	-21.70	ENST00000328654	<i>ZNF26-001</i>	10,000,000,000
-78.70	-21.77	ENST00000607778	<i>GTF2H5-001</i>	10,000,000,000
-102.31	-21.86	ENST00000439251	<i>PNMA5-201</i>	10,000,000,000
-811.27	-22.05	ENST00000378505	<i>RPGR-009</i>	10,000,000,000
-96.91	-22.47	ENST00000375712	<i>KIF3B-001</i>	10,000,000,000
-80.26	-22.89	ENST00000267889	<i>DISP2-001</i>	10,000,000,000
-84.28	-22.90	ENST00000366847	<i>FGFR1OP-001</i>	10,000,000,000
-86.18	-23.16	ENST00000248076	<i>F2RL3-001</i>	10,000,000,000
-78.27	-23.24	ENST00000527021	<i>AP006621.9-001</i>	10,000,000,000
-296.11	-23.53	ENST00000397609	<i>FAM98B-001</i>	10,000,000,000
-116.50	-23.66	ENST00000380167	<i>ATP6AP1L-001</i>	10,000,000,000
-107.99	-24.03	ENST00000614987	<i>RPS6KA5-001</i>	10,000,000,000
-83.87	-24.28	ENST00000624046	<i>RP11-361L15.5-001</i>	16,787,754
-106.56	-24.44	ENST00000355086	<i>SRGAP1-001</i>	10,000,000,000
-85.95	-24.61	ENST00000558190	<i>ATXN3-001</i>	10,000,000,000
-166.80	-24.66	ENST00000373191	<i>AGO3-003</i>	10,000,000,000
-175.42	-24.69	ENST00000623111	<i>MIR6820-001</i>	10,000,000,000
-86.85	-24.73	ENST00000623210	<i>RP11-463O12.5-001</i>	10,000,000,000
-108.74	-24.75	ENST00000428216	<i>MAVS-001</i>	10,000,000,000
-113.80	-24.90	ENST00000589281	<i>RP11-95O2.5-001</i>	10,000,000,000
-85.22	-25.05	ENST00000616371	<i>AP4S1-202</i>	10,000,000,000

-108.58	-25.29	ENST00000624919	<i>RP4-671O14.6-001</i>	10,000,000,000
-99.35	-25.31	ENST00000309893	<i>CA5A-001</i>	4,077,569
-68.76	-25.79	ENST00000374193	<i>WDR31-001</i>	10,000,000,000
-69.77	-26.00	ENST00000328963	<i>P2RX7-008</i>	10,000,000,000
-211.60	-26.14	ENST00000623959	<i>RP3-323A16.1-001</i>	10,000,000,000
-81.63	-26.17	ENST00000609923	<i>SLC25A16-002</i>	10,000,000,000
-96.50	-26.21	ENST00000623726	<i>RP5-1014D13.2-001</i>	10,000,000,000
-69.76	-26.23	ENST00000623543	<i>AC008079.10-001</i>	10,000,000,000
-122.06	-26.25	ENST00000307635	<i>ZNF556-001</i>	10,000,000,000
-70.90	-26.45	ENST00000498035	<i>HM13-013</i>	10,000,000,000
-70.70	-26.46	ENST00000561981	<i>FRRS1L-001</i>	10,000,000,000
-76.26	-26.66	ENST00000312814	<i>TMEM168-001</i>	10,000,000,000
-106.30	-26.73	ENST00000498286	<i>MTO1-001</i>	10,000,000,000
-73.35	-26.74	ENST00000555916	<i>RP5-1021I20.5-001</i>	10,000,000,000
-91.82	-26.94	ENST00000291439	<i>AP1M1-001</i>	10,000,000,000
-90.62	-27.18	ENST00000410105	<i>DACT3-003</i>	10,000,000,000
-84.44	-27.25	ENST00000536435	<i>ZNF268-001</i>	10,000,000,000
-71.98	-27.26	ENST00000401722	<i>SLC25A3-008</i>	10,000,000,000
-140.38	-27.68	ENST00000607772	<i>CNKSR3-001</i>	10,000,000,000
-68.93	-27.69	ENST00000377767	<i>DIS3-001</i>	10,000,000,000
-86.17	-27.74	ENST00000511313	<i>POLR2J3-005</i>	10,000,000,000
-102.52	-27.80	ENST00000428411	<i>SLC16A1-AS1-003</i>	10,000,000,000
-171.88	-27.82	ENST00000624072	<i>CTA-228A9.4-001</i>	10,000,000,000
-123.41	-27.87	ENST00000610020	<i>RPAP2-001</i>	10,000,000,000
-69.47	-28.08	ENST00000368990	<i>PLEKHA1-002</i>	10,000,000,000
-190.72	-28.09	ENST00000334976	<i>EMC10-001</i>	10,000,000,000
-120.68	-28.24	ENST00000238831	<i>YIPF4-001</i>	10,000,000,000
-73.13	-28.25	ENST00000561624	<i>CTD-2270L9.2-001</i>	60,349,953
-118.06	-28.26	ENST00000262160	<i>SMAD2-001</i>	10,000,000,000
-73.23	-28.27	ENST00000359591	<i>LRP10-001</i>	10,000,000,000
-72.33	-28.44	ENST00000380155	<i>SYAP1-001</i>	10,000,000,000
-88.36	-28.47	ENST00000270458	<i>CACNG8-001</i>	10,000,000,000
-70.20	-28.80	ENST00000336926	<i>HIP1-001</i>	10,000,000,000
-97.17	-29.12	ENST00000480046	<i>METTL2B-002</i>	10,000,000,000
-76.25	-29.44	ENST00000501122	<i>NEAT1-001</i>	10,000,000,000
-87.48	-29.66	ENST00000623130	<i>AC006548.28-001</i>	10,000,000,000
-113.98	-30.03	ENST00000258711	<i>CHST12-002</i>	10,000,000,000
-137.38	-30.24	ENST00000370132	<i>DBT-001</i>	10,000,000,000
-76.58	-30.36	ENST00000339077	<i>KLHL7-002</i>	10,000,000,000
-163.16	-30.81	ENST00000623789	<i>RP3-412A9.17-001</i>	10,000,000,000
-189.59	-30.91	ENST00000398004	<i>SLC35E3-001</i>	10,000,000,000
-94.50	-31.23	ENST00000293648	<i>ZNF562-001</i>	10,000,000,000
-151.03	-31.38	ENST00000377038	<i>DFFA-001</i>	10,000,000,000
-83.71	-31.41	ENST00000537226	<i>ZNF891-001</i>	10,000,000,000
-76.11	-31.48	ENST00000380455	<i>NQO2-001</i>	10,000,000,000

-136.28	-31.55	ENST00000624945	<i>RP3-394A18.1-001</i>	10,000,000,000
-68.99	-31.82	ENST00000624057	<i>AP000437.3-001</i>	10,000,000,000
-140.70	-32.56	ENST00000311048	<i>ZNF431-001</i>	10,000,000,000
-70.33	-32.77	ENST00000624878	<i>RP11-197N18.8-001</i>	10,000,000,000
-96.75	-33.76	ENST00000295461	<i>NIPAL1-001</i>	10,000,000,000
-119.38	-34.03	ENST00000356387	<i>Orai2-201</i>	10,000,000,000
-119.95	-34.08	ENST00000263275	<i>OPA3-002</i>	10,000,000,000
-85.29	-34.40	ENST00000371199	<i>XIAP-002</i>	10,000,000,000
-114.09	-35.25	ENST00000371608	<i>BCAS4-002</i>	10,000,000,000
-148.20	-35.46	ENST00000295851	<i>ABI2-001</i>	10,000,000,000
-77.55	-36.86	ENST00000624833	<i>CTC-351M12.1-001</i>	10,000,000,000
-228.05	-37.38	ENST00000396444	<i>USP8-001</i>	10,000,000,000
-115.05	-38.67	ENST00000499624	<i>GABPB1-AS1-001</i>	10,000,000,000
Note: Genomic Distance -1:Loci are overlapped. 10,000,000,000:Loci are located on different chromosomes, human: Energy threshold = -16kcal/mol.				

Supplementary table 6: RNA-targeting guide RNAs (rgRNAs) for dRfxCas13d-based RNA-immunoprecipitation

Oligo Name	Target	Oligo (5'-3')	Direction
CTR-rg1-O1	scrabble	AAACATCACCAGAAGCGTACCATACTCACGAACAG	Forward
CTR-rg2-O1	scrabble	AAACCTACCTGGTAGCCCTTGTATAATGATCAGGC	Forward
CTR-rg3-O1	scrabble	AAACTGCCACTACTGTTTCATGACTCAGGGCGATGG	Forward
CTR-rg4-O1	scrabble	AAACTGCGCCAGGCTTGTCTGCTCCCTCTTCGGGGGT	Forward
CTR-rg5-O1	scrabble	AAACTCACCAGAAGCGTACCATACTCACGAACAGT	Forward
CTR-rg1-O2	scrabble	AAAAGCTTCGTGAGTATGTACGCTTCTGGTGAT	Reverse
CTR-rg2-O2	scrabble	AAAAGCCTGATCATTATACAAGGGCTACCAGGTAG	Reverse
CTR-rg3-O2	scrabble	AAAACCATCGCCCTGAGTCATGAACAGTAGTGGCA	Reverse
CTR-rg4-O2	scrabble	AAAAACCCCCGAAGAGGGACGACAAGCCTGGCGCA	Reverse
CTR-rg5-O2	scrabble	AAAAACTGTTTCGTGAGTATGGTACGCTTCTGGTGA	Reverse
CDH13-rg1-O1	CDH13 mRNA	AAACCCAACCAGAGATGTACGACGGACCCCA	Forward
CDH13-rg2-O1	CDH13 mRNA	AAACGCACAGGCTTAGATTCCCCTGTCCCTG	Forward
CDH13-rg3-O1	CDH13 mRNA	AAACTTGGAGGGTGACTTCCTGATTGCCAGT	Forward
CDH13-rg4-O1	CDH13 mRNA	AAACGAGGAACAACATGACAGAAGTATCTCT	Forward
CDH13-rg5-O1	CDH13 mRNA	AAACGATTACAGGAAATGCTACCACTTTGGCC	Forward
CDH13-rg1-O2	CDH13 mRNA	AAAATGGGGTCCGTCGTACATCTCTGGTTGG	Reverse
CDH13-rg2-O2	CDH13 mRNA	AAAACAGGGACAGGGGAATCTAAGCCTGTGC	Reverse
CDH13-rg3-O2	CDH13 mRNA	AAAAACTGGCAATCAGGAAGTCACCCTCCAA	Reverse
CDH13-rg4-O2	CDH13 mRNA	AAAAAGAGATACTTCTGTCATGTTGTTCCCTC	Reverse
CDH13-rg5-O2	CDH13 mRNA	AAAAGGCCAAAGTGGTAGCATTTCCCTGAATC	Reverse
CDH13-AS2-rg1-O1	CDH13-AS2	AAACTAACTAAGACAATAAGTCCTTCCTTTC	Forward
CDH13-AS2-rg2-O1	CDH13-AS2	AAACCAGTAATATCCACCTGAGACCCTCTGC	Forward
CDH13-AS2-rg3-O1	CDH13-AS2	AAACTCGCAGGAGGATTGCTGGAGTCTGAGA	Forward
CDH13-AS2-rg4-O1	CDH13-AS2	AAACGGAGCCATGACTGCGCCACTGCACTCC	Forward
CDH13-AS2-rg5-O1	CDH13-AS2	AAACAAGGTCTGCGTATGAACTCTCTGTAT	Forward
CDH13-AS2-rg1-O2	CDH13-AS2	AAAAGAAAGGAAGGACTTATTGTCTTAGTTA	Reverse
CDH13-AS2-rg2-O2	CDH13-AS2	AAAAGCAGAGGGTCTCAGGTGGATATTACTG	Reverse
CDH13-AS2-rg3-O2	CDH13-AS2	AAAATCTCAGACTCCAGCAATCCTCCTGCGA	Reverse
CDH13-AS2-rg4-O2	CDH13-AS2	AAAAGGAGTGCAGTGGCGCAGTCATGGCTCC	Reverse
CDH13-AS2-rg5-O2	CDH13-AS2	AAAAATACAGAGAGTTTCATACGCAGACCTT	Reverse

Supplementary table 7: Single guide RNAs (sgRNAs) for CRISPR/Cas9 knockout system			
Oligo Name	Target	Oligo (5'-3')	Direction
CTR-sg1-O1	scrabble	CACCG CCACACCTGTCTAGCATGAC	Forward
CTR-sg2-O1	scrabble	CACCG CCAGTTGCTCTGGGGGAACA	Forward
CTR-sg3-O1	scrabble	CACCG ATTCAGCGCGCTCGCCCTGG	Forward
CTR-sg4-O1	scrabble	CACCG ATCTGCCATGGCGTCCTGGC	Forward
CTR-sg1-O2	scrabble	AAAC GTCATGCTAGACAGGTGTGGC	Reverse
CTR-sg2-O2	scrabble	AAAC TGTTCCCCCAGAGCAACTGGC	Reverse
CTR-sg3-O2	scrabble	AAAC CCAGGGCGAGCGCGCTGAATC	Reverse
CTR-sg4-O2	scrabble	AAAC GCCAGGACGCCATGGCAGATC	Reverse
<i>CDH13-AS2</i> -sg1-O1	<i>CDH13-AS2</i>	CACCG TGGTGCATACCTGTTCGCAGG	Forward
<i>CDH13-AS2</i> -sg2-O1	<i>CDH13-AS2</i>	CACCG TCTGAGAGGTTGAGGTTACA	Forward
<i>CDH13-AS2</i> -sg3-O1	<i>CDH13-AS2</i>	CACCG TAAAACTAGTGAATAGCCA	Forward
<i>CDH13-AS2</i> -sg4-O1	<i>CDH13-AS2</i>	CACCG GACTTTAGACCCCAATCCCT	Forward
<i>CDH13-AS2</i> -sg1-O2	<i>CDH13-AS2</i>	AAAC CCTGCGACAGGTATGCACCAC	Reverse
<i>CDH13-AS2</i> -sg2-O2	<i>CDH13-AS2</i>	AAAC TGTAACCTCAACCTCTCAGAC	Reverse
<i>CDH13-AS2</i> -sg3-O2	<i>CDH13-AS2</i>	AAAC TGGCTATTCACTAGTTTTTAC	Reverse
<i>CDH13-AS2</i> -sg4-O2	<i>CDH13-AS2</i>	AAAC AGGGATTGGGGTCTAAAGTCC	Reverse

Supplementary table 8: Guide RNAs (dgRNAs) for CRISPR-mediated transcriptional activation

Oligo Name	Target	Oligo (5'-3')	Direction
CTR-dg1-O1	scrabble	ACC CCTGTCTAGCATGAC	Forward
CTR-dg2-O1	scrabble	ACC GCTCTGGGGAACA	Forward
CTR-dg3-O1	scrabble	ACC GCGCGCTCGCCCTGG	Forward
CTR-dg4-O1	scrabble	ACC CATGGCGTCCTGGC	Forward
CTR-dg1-O2	scrabble	AAC GTCATGCTAGACAGG	Reverse
CTR-dg2-O2	scrabble	AAC TGTTCCCCCAGAGC	Reverse
CTR-dg3-O2	scrabble	AAC CCAGGGCGAGCGCGC	Reverse
CTR-dg4-O2	scrabble	AAC GCCAGGACGCCATG	Reverse
CDH13-AS2 -dg1-O1	CDH13-AS2	ACC GTGGAGGTTACCC	Forward
CDH13-AS2 -dg2-O1	CDH13-AS2	ACC AGCTACTGCTCATAG	Forward
CDH13-AS2 -dg3-O1	CDH13-AS2	ACC AAACCAGTCCAACC	Forward
CDH13-AS2 -dg4-O1	CDH13-AS2	ACC GGAATGATCCTAGCG	Forward
CDH13-AS2 -dg5-O1	CDH13-AS2	ACC GGCGGTGCCACAGC	Forward
CDH13-AS2 -dg1-O2	CDH13-AS2	AAC GGGGAACCTCCAC	Reverse
CDH13-AS2 -dg2-O2	CDH13-AS2	AAC CTATGAGCAGTAGCT	Reverse
CDH13-AS2 -dg3-O2	CDH13-AS2	AAC GGTTGGACTGGTTT	Reverse
CDH13-AS2 -dg4-O2	CDH13-AS2	AAC CGCTAGGATCATTCC	Reverse
CDH13-AS2 -dg5-O2	CDH13-AS2	AAC GCTGTGGCACC GCC	Reverse
CDH13 -dg1-O1	CDH13	ACC CTCCTCGTTTTGCA	Forward
CDH13 -dg2-O1	CDH13	ACC TCTTGTAAGCCAT	Forward
CDH13 -dg3-O1	CDH13	ACC TTTTCCGTGGGAGCC	Forward
CDH13 -dg4-O1	CDH13	ACC AGCATATTTTCCGT	Forward
CDH13 -dg5-O1	CDH13	ACC AAAACCGCGGCTCGT	Forward
CDH13 -dg6-O1	CDH13	ACC ACTCCAACGAGCCG	Forward
CDH13 -dg7-O1	CDH13	ACC TCGGGTCCGGATTGC	Forward
CDH13 -dg8-O1	CDH13	ACC CCTGCTAGCAAAA	Forward
CDH13 -dg1-O2	CDH13	AAC TGCAAAACGAGGGAG	Reverse
CDH13 -dg2-O2	CDH13	AAC ATGGCTTTACAAGA	Reverse
CDH13 -dg3-O2	CDH13	AAC GGCTCCCACGGAAAA	Reverse
CDH13 -dg4-O2	CDH13	AAC ACGGAAAATATGCT	Reverse
CDH13 -dg5-O2	CDH13	AAC ACGAGCCGCGGTTTT	Reverse
CDH13 -dg6-O2	CDH13	AAC CGGCTCGTTGGAGT	Reverse
CDH13 -dg7-O2	CDH13	AAC GCAATCCGGACCCGA	Reverse
CDH13 -dg8-O2	CDH13	AAC TTTTGCTAGCAGG	Reverse

Supplementary table 9: 63 microRNAs binding on 3'UTR of *CDH13* predicted by four databases (miRTarBase (PMID: 31647101), miRWalk (PMID: 30335862), scanMiRApp (PMID: 35188178), and TargetScan (PMID: 31806698, PMID: 26267216).). All are highly expressed in human umbilical vein endothelial cells (HUVECs), with reads per million >20. The expression of microRNAs in HUVECs were obtained from DIANA-miTED, a microRNA tissue expression database (PMID: 34469540).

1	hsa-miR-31-3p
2	hsa-miR-181a-5p
3	hsa-miR-155-5p
4	hsa-miR-181a-2-3p
5	hsa-miR-423-3p
6	hsa-miR-497-5p
7	hsa-miR-330-5p
8	hsa-miR-34a-5p
9	hsa-miR-99a-3p
10	hsa-miR-214-5p
11	hsa-miR-195-3p
12	hsa-miR-139-5p
13	hsa-miR-377-3p
14	hsa-miR-22-5p
15	hsa-miR-210-3p
16	hsa-miR-24-2-5p
17	hsa-miR-450b-5p
18	hsa-miR-433-3p
19	hsa-miR-125b-2-3p
20	hsa-miR-501-3p
21	hsa-miR-361-3p
22	hsa-miR-130b-5p
23	hsa-miR-188-5p
24	hsa-let-7b-3p
25	hsa-let-7f-1-3p
26	hsa-miR-10b-3p
27	hsa-miR-125a-3p
28	hsa-miR-125b-1-3p
29	hsa-miR-130a-3p
30	hsa-miR-130b-3p
31	hsa-miR-181b-5p
32	hsa-miR-181c-5p
33	hsa-miR-181d-5p
34	hsa-miR-185-5p
35	hsa-miR-186-5p
36	hsa-miR-19a-3p
37	hsa-miR-19b-3p

38	hsa-miR-24-3p
39	hsa-miR-27b-5p
40	hsa-miR-301a-3p
41	hsa-miR-301b-3p
42	hsa-miR-30a-5p
43	hsa-miR-30b-5p
44	hsa-miR-30c-1-3p
45	hsa-miR-30c-2-3p
46	hsa-miR-30c-5p
47	hsa-miR-30d-5p
48	hsa-miR-30e-5p
49	hsa-miR-370-3p
50	hsa-miR-376c-3p
51	hsa-miR-381-3p
52	hsa-miR-425-3p
53	hsa-miR-485-3p
54	hsa-miR-493-5p
55	hsa-miR-494-3p
56	hsa-miR-495-3p
57	hsa-miR-532-5p
58	hsa-miR-539-3p
59	hsa-miR-542-3p
60	hsa-miR-665
61	hsa-miR-935
62	hsa-miR-98-3p
63	hsa-miR-23a-5p

Supplementary table 10: The final 11 microRNAs selected for the RNA interference assay. * The expression of microRNAs in human umbilical vein endothelial cells (HUVEC) was obtained from DIANA-miTED, a microRNA tissue expression database (PMID: 34469540). The source information of the four prediction tools are miRTarBase (PMID: 31647101), miRWalk (PMID: 30335862), scanMiRApp (PMID: 35188178), and TargetScan (PMID: 31806698, PMID: 26267216).

Selected human microRNAs	Binding site conserved for mouse <i>Cdh13</i> -3'UTR	Prediction tool	Other rationale	HUVEC (Reads Per Million) *
hsa-miR-30a-5p	mmu-miR-30a-5p	TargScan and scanMiRApp		41257.25
hsa-miR-181a-5p	mmu-miR-181a-5p	miRTarBase and MirWalk and TargScan and scanMiRApp	Experimental hints indicated by miRTarBase	20529.66
hsa-miR-155-5p	mmu-miR-155-5p	miRTarBase and MirWalk and scanMiRApp	Experimental hints indicated by miRTarBase	2287.02
hsa-miR-19b-3p	mmu-miR-19b-3p	TargScan and scanMiRApp		1108.81
hsa-miR-125b-2-3p		MirWalk and TargScan and scanMiRApp		685.32
hsa-miR-34a-5p	mmu-miR-34a-5p	MirWalk and TargScan and scanMiRApp		296.18
hsa-let-7b-5p	mmu-let-7b-5p		RNAseq on pulldown sample of let-7b-5p in EC	1424.9
hsa-let-7b-3p	mmu-let-7b-3p	TargScan and scanMiRApp		58.58
hsa-miR-125a-3p	mmu-miR-125a-5p	TargScan and scanMiRApp		51.48
hsa-miR-485-3p	mmu-miR-485-3p	TargScan and scanMiRApp	Multiple binding sites	42.83
hsa-miR-433-3p	mmu-miR-433-3p	MirWalk and TargScan and scanMiRApp		23.82

Supplementary table 11: Sequence of miRNA mimics and scrambled control mimics	
Gene Name	Sequence
hsa-miR-30a-5p	UGUAAACAUCCUCGACUGGAAG
hsa-miR-181a-5p	AACAUUCAACGCUGUCGGUGAGU
hsa-miR-155-5p	UUAAUGCUAAUCGUGAUAGGGGUU
hsa-miR-19b-3p	UGUGCAAUCCAUGCAAAACUGA
hsa-miR-125b-2-3p	UCACAAGUCAGGCUCUUGGGAC
hsa-miR-34a-5p	UGGCAGUGUCUUAGCUGGUUGU
hsa-let-7b-3p	CUAUACAACCUACUGCCUUCCC
hsa-let-7b-5p	UGAGGUAGUAGGUUGUGUGGUU
hsa-miR-125a-3p	ACAGGUGAGGUUCUUGGGAGCC
hsa-miR-485-3p	GUCAUACACGGCUCUCCUCUCU
hsa-miR-433-3p	AUCAUGAUGGGCUCCUCGGUGU
Scrambled control siRNA	Qiagen SI03650318

Supplementary table 12: Experimental animals scoring criteria			
Maximum permissible level of stress according to animal testing approval: medium			
Scoring Parameters		Level	Special Measures
Behave	Normal behavior (lively, responds to touch, is curious and attentive, socially active)	0	
	Slowed movement, responds normally to touch and conspecifics	A	
	Reduced exploratory behavior or little interaction with conspecifics	B	
	No exploratory behavior	C	
	Isolation from the group, apathy	D	Immediate termination of the experiment
posture	Normal	0	
	Intermittent crouching	B	
	Curved back, clumsy gait, constant crouching	C	
	Convulsions, paralysis, tremors	D	Immediate termination of the experiment
Fur and Skin	Normal coat, shiny, no reddened skin, clean body openings	0	
	Slightly oily coat, slightly reddened skin, slight hair loss due to excessive grooming (barbering, Dalila effect) <20% of body surface	A	See below, consider separating the animals
	Bite or Scratch Wounds (max. 1 cm diameter)	B	Separate the animals, treat the wounds with healing clay, no improvement after 3 days = C
	Hair loss due to excessive grooming >20 to <50% of the body surface	B	See below, consider separating the animals
	Bite wounds (max. 1.5 cm diameter), hair loss 50%	C	Separate the animals, treat the wounds according to veterinary recommendations

	Dirty, raised coat, sticky eyes, dehydration (skin fold remains), bite wounds >1.5 cm diameter, hair loss >50%	D	Immediately stop the experiment
Body Weight	No reduction or weight gain	0	Weigh twice a week
	Weight reduction $\leq 2.5\%$	A	Weigh again within 48 hours twice as a result of A = B
	Weight reduction >2.5 to $\leq 10\%$	B	Weigh again within 24 hours, offer moist food, replace fluids if necessary, any weight loss directly as a result of = C
	Weight reduction >10 to $\leq 15\%$	C	Inform vet, weigh again within 24 hours, offer moist food, replace fluids if necessary, further weight loss > 2.5% (B-D) directly as a result of C = D
	Weight reduction >15%	D	Immediate termination of the test
Stool consistency	Formed	0	
	Mushroomy	B	
	Liquid	C	Twice as a result of C = D
	Bloody	D	

0	No stress, daily visual inspection by animal keepers, scoring frequency by scientific staff every 72 hours (AZ ROB-55.2-2532.Vet_02-20-075, Experiment 3: daily scoring control within the first week after irradiation)
A	Possible signs of developing stress: inform the responsible employee, scoring frequency increases to 48 hours; if necessary, application of healing clay, mashed food (wet food), separation from aggressive cage partners
	A in several scoring categories simultaneously = B

B	Low stress, inform the veterinarian, with scoring frequency increases to 24 hours, and therapeutic measures can be prescribed if needed
Several times as a result of B (same category)	Continue scoring daily in consultation with the veterinarian, monitor wound healing if necessary
C	Medium stress (maximum tolerated stress level), inform the veterinarian, scoring frequency increases to 24 hours, therapeutic measures can be ordered if necessary
Several times as a result of C (same category)	"Fur and skin": After consultation with the veterinarian and careful consideration, possibly tolerable, all other categories = D
D	High stress, intolerable level of stress, immediate termination of the experiment through painless euthanasia

Supplementary table 13: Antibodies for immunostaining and western blot			
catalogue	Reference number	Dilution	immunostaining
DAPI (1mg/ml)	Invitrogen,62248	1:1000	
CDH13(H cadherin/ T cadherin)	abcam,ab36905	1:200	
Cleaved Caspase-3 (Asp175) (5A1E)	Cell Signaling,9664S	1:100	
ZO-1(EPR19945-296)	abcam,ab221547	1:200	
Mac2(Galectin 3)	abcam,ab2785	1:500	
Alexa Fluor® 488 anti-mouse CD31	Biolegend	1:150	
NucView® 405 Caspase-3-Farbstoff	BioTracker	1:200	western blot
CDH13-EPR9621	abcam,ab167407	1:800	
b-actin(β -Actin Antibody #4967)	cell Signaling, 4967	1:1000	
Anti-rabbit IgG, HRP-linked Antibody	cell Signaling, 7074P2	1:100000	
Anti-mouse IgG, HRP-linked Antibody	cell Signaling, 77076P2	1:100000	

Supplementary table 14: List of cell lines			
Catalogue	Reference number	Medium	Seeding density
HUVEC, pooled donors, cryopreserved	PromoCell	Endothelial Cell Growth Medium 2(C-22011)	5,000 –10,000 cells per cm ²
	C-12203		
HCAEC, single donors.	PromoCell	Endothelial Cell Growth Medium MV (C-22020)	5000 - 10000 cells per cm ²
	C-12221		
HCSCMC	ATCC	Smooth Muscle Cell Growth Medium 2 (C-22062)	2,500 - 5,000 cells per cm ² .
	PCS-100-021		
HCF	PromoCell	Fibroblast Growth Medium 3 (C-23025)	3500 - 7000 cells per cm ²
	C-12375		
THP-1 monocyte	ATCC	RPMI-1640 Medium(Gibco™, 11875093)	1 - 4 x 10 ⁵ cells/mL
	TIB-202™		
Jurkat, Clone E6-1	ATCC	RPMI-1640 Medium(Gibco™, 11875093)	10 ⁵ - 10 ⁶ cells/mL
	TIB-152		
EA.hy926	ATCC	Dulbecco's Modified Eagle Medium (DMEM Gibco™)	2000 - 5000 cells per cm ²
	CRL-2922™		
HAOEC	PromoCell	Endothelial Cell Growth Medium MV (C-22020)	5000 - 10000 cells per cm ²
	C-12271		
HAOSMC	PromoCell	Smooth Muscle Cell Growth Medium 2 (C-22062)	5000 - 10000 cells per cm ²
	C-12533		
HAOAF	PromoCell	Fibroblast Growth Medium 2 (C-23020)	3500 - 7000 cells per cm ²
	C-12380		
HEK.293T	ATCC	Dulbecco's Modified Eagle Medium (DMEM Gibco™)	2,500 - 5,000 cells per cm ²
	CRL-3216™		

Supplementary table 15: List of plasmids		
Catalogue	Reference number	Application
psPAX2	addgene-12260	Packaging lentivirus
pCMV-VSV-G	addgene-8454	Packaging lentivirus
lentiSAMv2	addgene-75112	CRISPRa
lentiIMPHv2	addgene-89308	CRISPRa
lentiCRISPRv2	addgene-52961	CRISPR knockout
dCas13d-dsRBD-HA	addgene-154938	RNA-based pull-down
pXR003:CasRx gRNA cloning backbone	addgene-109053	RNA Guide(rg)-RNA backbone
psiCHECK(TM)-2	Promega-C8021	RNA interference assay

Supplementary table 16: List of PCR primers		
qPCR primers		
Gene Name	Forward Primer (5'-3')	Reverse Primer (5'-3')
<i>CDH13-AS2</i>	CAGAGAGTTTCATACGCAGACCT	GTCTGAGAGGTTGAGGTTACAGG
<i>CDH13-AS1</i>	AGACCAGTGCAGGCATTGAA	CCATCCCTCTGCTCTGTTGT
<i>CEDORA</i>	AACTGCAGGGGATCTGGTTG	TATAGGCCTGGTCGGGAGTT
<i>CTD3253/12.1</i>	CTAGAATGATTGGCAGTTGGC	CAGTCTATTCACAGAATTGTGC
<i>GAPDH</i>	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG

Amplification PCR primers for checking DNA editing		
Gene name	Forward primer (5'-3')	Reverse primer (5'-3')
<i>CDH13-AS2</i>	CGTTGGGCAGCATCTCTGACTTCTACC	GCCATAAGACAGGTTTGCTCAGAGATCC
<i>CDH13-AS2</i>	CAGAGAGTTTCATACGCAGACCT	GTAGATGGTTTGAGCCCAAGAG

Amplification PCR primers for CRISPR-KO and CRISPRa		
Gene name	Forward primer (5'-3')	Reverse primer (5'-3')
<i>CDH13</i>	GGGCTCCTTGACAGGATATATTTAAATTTGC	CCGTGTATATACATACAGATACTCATAC
<i>CDH13-AS2</i>	AGAAAGGAAGGACTTATTGTCTTAGTTACT	TGTAACTTCAGCCACATGCAGGGAGAAAC
<i>GAPDH</i>	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG

dCas13-HA pull-down amplification primer(300bp)		
Gene name	Forward primer (5'-3')	Reverse primer (5'-3')
<i>CDH13-AS2</i>	AAAGCCTGACTCACACGGTT	AGGCTCTCCTGCACTTTGTG
<i>CDH13</i>	GGTGGTTAAAACTGCTGGACA	TGGGACTGTTGACAGATGGC
<i>GAPDH</i>	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG

Supplementary table 17: *CDH13* 3'UTR sequence

CTCGAGTCCTGCTCCTCAGCCTCTTCAGCTTAGCTTGTCTGTGAGAACTCCTGACGTCTGAAGCTT
GACTCCCAAGTTTCCATAGCAACAGGAAAAAAAAAATCTATCCAAATCTGAAGATTGCGGTTTACA
GCTATCGAACTTCACAACTAGGCCTCAATTGTTCCGGTTTTTTATTTTCTTTACAATTTCACTTAGTCT
GTACTTCATCATTTTTGACAGCATCTTCCTCCCTCCTTTAATTAATGGAATCTTCTGAATTTTCCCTGA
ATGTTTAAAGATCATGACATATGACTTGATCTTCTGGGAGCAGGAACAATGACTACTTTTTCTGGTG
TGTTAACATGTCGCTAGCCAGTGCTCCAGGCACCCAGCTTTTGTCTGTGGGTTAGTATTGGTGTATG
TATGAGTATCTGTATGTATATATACACGGTATTTATAGAGAGAGACTATCCTGGAGAAGCCTCGTTT
TGATGCCATTCTTCCTTGCAAGGTTAAGCAAGGTGGGTGGAACTAAGACACCTGAACCTCCAGG
GCCTCCCGCATCAAGGTCAGCATGAGGACAGACCACAGAGCTGTCACCTTTTGCTCCGAAGCTACTT
CTCCACTGTCCCGTTCAGTCTGAATGCTGCCACAACCAGCCAGGCAGGTCCACAGAGAGGGAGAG
CAGAGAAAGAAGTCCTTTCTCTTTATTGAGTTCGAGGACTACAACCAATTTACACTGCCATCTGATG
CCGTGATCCTGAGCCAAGGAGGTGAGGAGCAGAGCAGGCAATTTACCACCAAATGCCAAGAAAA
GGGCTGACATTTTCTTTCATGGGCACCAACCTGCATTTGTATGTGTCCCGAATCCACAGTCGTACT
GATTCTAATGGGGACACAGATCATGGTAGAGAATCTCTCCCTCCTCAGTAAATGTACAACTGCACC
TGTCATCATGGAGGTCATACATGCATACAAAGAGGTGTACAGGTACCATCTTGTATACACATATATA
CCCACATGTACAGACATACATTTATGCACATTCACGCTGTTTGTTTCATATATACAGGCATAAAATAG
AGTAAATACAGGTAGTTTTTAAAGTACCCTTTTGTGTGAATTGACTACCGTTGTTTGCAAACCCGAA
AATAAAAGACGTTTATTATGTATGAAAAGTAACTGATTTGTATTCTGTGAGCATGTAAAAGCGGAAA
GTTAGTGCTTGTTCTAAGATTACCTTCTTGTTGATAAACCATAAATGAATCATCAAAGCTCACACCAA
ATTTTCTATCAAATAAACTAGTGACAGCTTGTGGCTTTTTATTAGAGCTCGCCACGAACGCGGCC
GC