Appendix: Supplementary methods

Small RNA sequencing

A total of 2 ml of pooled plasma derived from five or six patients per sample was used to perform exosome isolation using ultracentrifugation. miRNeasy Mini Kit (QIAGEN) was used to isolate total RNA from plasma exosomes following the manufacturer's instruction. Isolated RNA was loaded on 1.5% agarose gels to evaluate its degradation and contamination followed by quantitative determination in the NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific). A total of 2.5 ng RNA per sample was used to construct small RNA library. RNA librarys were sequenced on the platform of Illumina HiSeq2500. Clean reads filtered for ribosomal RNA (rRNA), transfer RNA (tRNA), small nuclear RNA (snRNA), small nucleolar RNA (snoRNA), other noncoding RNA (ncRNA) and repeats were compared with the miRBase database to assess miRNA expression.

Exosome isolation and identification

Exosomes were isolated from pooled plasma by ultracentrifugation for small RNA sequencing. Briefly, 2 ml of pooled plasma per sample was first centrifuged at 3,000 ×g and 4 ℃ for 15 min to obtain supernatant followed by dilution with PBS. The diluted supernatant was then centrifuged at 13,000 ×g and 4 ℃ for 30 min followed by filtration using a 0.22-μm filter. The filtered sample was loaded into the ultracentrifuge and ultracentrifuged at 100,000 ×g and 4 ℃ for 2 hours to collect exosomes. Exosome pellet was washed by resuspending it in PBS and was then ultracentrifuged at 100,000 g and 4 ℃ for 2 hours. Next, the obtained exosome pellet was dissolved in 100 μL PBS for RNA extraction.

For exosomes isolation from plasma in cohort 2, the Total Exosome Isolation (from plasma) Kit (Invitrogen) was applied according to the instructions, and the expression of plasma exosomal miRNA was validated.

To isolate exosomes from the cell culture supernatant, fresh culture medium (CM) supplying with 10% exosome-depleted fetal bovine serum (FBS) was added to cells and collected 48 hours later. The CM was processed for centrifugation at 500 ×g, 4 ℃ for 10 min, 2,000 ×g, 4 ℃ for 10 min successively to remove cells and dead cells, subsequently passed through a 0.22-μm Vacuum Filter System (Corning, cat. No. 431097) to remove large particles. The filtered supernatant was further concentrated by the Vivaflow 200 filtration system (Sartorius, cat. No. VF20P4) and then ultracentrifuged at 110,000 ×g and 4 ℃ for 70 min to precipitate exosomes. The exosome pellet was washed by dissolving it in PBS and ultracentrifuged once again, the final exosome sample was obtained by resuspending the second exosome precipitate in PBS and was stored at −80 ℃ for future use.

To characterize the isolated exosomes, transmission electron microscopy (JEOL-JEM1400, Tokyo, Japan) and ZetaView PMX 110 (Particle Metrix, Meerbusch, Germany) were used to capture the appearance and assess the diameter and number of exosomes, respectively. Western blotting was applied to identify exosome-related proteins, including CD9 and TSG101.

RNA isolation and qRT-PCR

TRIzol-based (Invitrogen, USA) traditional method was performed to isolate total RNA from cells, exosomes or serum. Specifically, for the isolation of RNA from exosomes or serum, cel-miR-39 was spiked in before adding chloroform to serve as the external reference gene, 0.1 mg/mL glycogen (Invitrogen) was added in the process of isopropanol precipitation to make the RNA pellet visible.

For miRNA, TransScript Green miRNA Two-Step qRT-PCR SuperMix (TransGen Biotech, Beijing, China) was used for the qRT-PCR of miRNA with a universal primer and a specific forward primer. RNU6 served as the internal reference gene in cell-miRNA PCR, while cel-miR-39 served as the external reference gene in exosome- or serum-miRNA PCR. For mRNA, TransScript II All-in-One First-Strand cDNA Synthesis SuperMix for qPCR and TransStart Top Green qPCR SuperMix (TransGen Biotech, Beijing, China) were used for mRNA RT-PCR and qRT-PCR, respectively. GAPDH served as the internal reference gene in mRNA PCR. All qRT-PCRs were conducted on an ABI 7900HT RT-PCR thermocycler (Life Technologies).

Western blotting

Proteins of exosomes or cells were harvested utilizing RIPA lysate buffer and protein concentrations were detected by the Bradford Protein Assay. Equivalent proteins from different samples were loaded for sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Separated proteins were then transferred to a polyvinylidene fluoride (PVDF) membrane followed by blocking with 5% milk for 1 hour at room temperature. After that, the diluted primary antibodies were added to incubate with the membranes

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overnight at 4 ℃. The next day, after incubation with HRP-conjugated secondary antibody for 1 hour at room temperature, the membranes were exposed and detected in an Amersham Imager 600. Antibodies used in this study were as follows: GAPDH (CST, #5174), claudin-11 (Abcam, ab175236), claudin-1 (CST, #13255), CD9 (Abcam, ab92726) and TSG101 (Abcam, ab83).

Cell Immunofluorescence

miR-375-3p mimic-transfected or exosome-treated HUVECs were plated on chamber slides (Biologix, Shandong, China) and cultured for 24–48 hours. Then, HUVECs were washed in PBS twice to remove dead cells and fixed in 4% paraformaldehyde solution for 10 min. After that, 0.2% Triton X-100/PBS was added to the chamber slides for 5 min to permeabilize the cell membranes. 5% BSA/PBS was used to block the non-specific binding sites of HUVECs and the primary antibodies (claudin-1, CST, #13995) were added to incubate overnight at 4 ℃. The next day, after incubation with secondary antibody (CST, #4412) in the dark, the slides were covered by ProLong™ Gold Antifade Mountant with DAPI (Invitrogen) and then photographed under a confocal microscope.

Liquid chromatography-mass spectrometry/mass spectrometry analysis (LC-MS/MS)

Proteins extracted from miR-375- or NC-transfected HUVECs (each group had three replicates) were processed for LC-MS/MS in Applied Protein Technology (Shanghai, China). Protein samples were digested to collect peptides by the filter-aided proteome preparation (FASP) method. A total of 100 µg peptides of each sample was used for tandem mass tag (TMT, Thermo Fisher Scientific) labeling following the instruction. TMT-labeled peptides of each sample were mixed in equal amounts followed by fractionation into 10 fractions by the High pH Reversed-Phase Peptide Fractionation Kit (Thermo Fisher Scientific). Each fraction was loaded onto a reversed-phase trap column (Thermo Scientific Acclaim PepMap100, 100 µm × 2 cm, nanoViper C18) and separated by a C18-reversed-phase analytical column (Thermo Scientific Easy Column, 10 cm long, 75 µm inner diameter, 3 µm resin) at a flow rate of 300 nL/min. A Q Exactive mass spectrometer (Thermo Scientific) was used to conduct LC-MS/MS in a data-dependent top10 manner with a survey scan of 300–1,800 m/z. MS/MS spectra data were searched in Proteome Discoverer 1.4 software for protein identification and quantitative analysis.

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Table S1 The clinical and pathological characteristics of the pooled samples in cohort 1

		SCLC patients		Healthy volunteers	
		Sample 1	Sample 2	Sample 3	Sample 4
Sex	Female	4	2	4	2
	Male	1	4	1	4
Age	<60	2	6	3	6
	≥60	3	0	2	0
T	T1-T2	2	3	-	-
	T3-T4	3	3	-	-
N	N0-N1	0	0	-	-
	N2-N3	5	6	-	-
M	M0	0	6	-	-
	M1	5	0	-	-
Stage	III	0	6	-	-
	IV	5	0	-	-

SCLC, small-cell lung cancer.

Table S2 The clinical and pathological characteristics of samples in cohort 2 and cohort 3

		Cohort 2 (82)		Cohort 3 (147)		
		SCLC (57)	Normal (25)	SCLC (69)	NSCLC (LUAD 20, LUSC 26)	Normal (32)
Sex	Female	22	13	14	18	10
	Male	35	12	55	28	22
Age	<60	29	22	28	25	14
	≥60	28	3	41	21	18
T	T1-T2	26	-	28	26	-
	T3-T4	31	-	41	20	-
N	N0-N1	19	-	10	12	-
	N2-N3	38	-	59	34	-
M	M0	45	-	40	29	-
	M1	12	-	29	17	-
Stage	I	9	-	4	1	-
	II	8	-	1	5	-
	III	28	-	35	23	-
	IV	12	-	29	17	-

SCLC, small-cell lung cancer; NSCLC, non-small-cell lung cancer; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma.

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Table S3 Sequences of primers used for PCR

Gene	Forward primer	Reverse primer
miR-375	CTTTGTTCGTTCGGCTCGC	-
Cel-miR-39	TCACCGGGTGTAAATCAGCTTG	-
RNU6	CTCGCTTCGGCAGCACA	-
Pri-miR-375	CGACGTGTCAGCCGCAGATG	CCTCGGTGATCTCCTGGTCCTG
Claudin-11	GGCTGGTGTTTTGCTCATTCTGC	AGCACCAATCCAGCCTGCATAC
Claudin-1	GTCTTTGACTCCTTGCTGAATCTG	CACCTCATCGTCTTCCAAGCAC
GAPDH	GTCTCCTCTGACTTCAACAGCG	ACCACCCTGTTGCTGTAGCCAA

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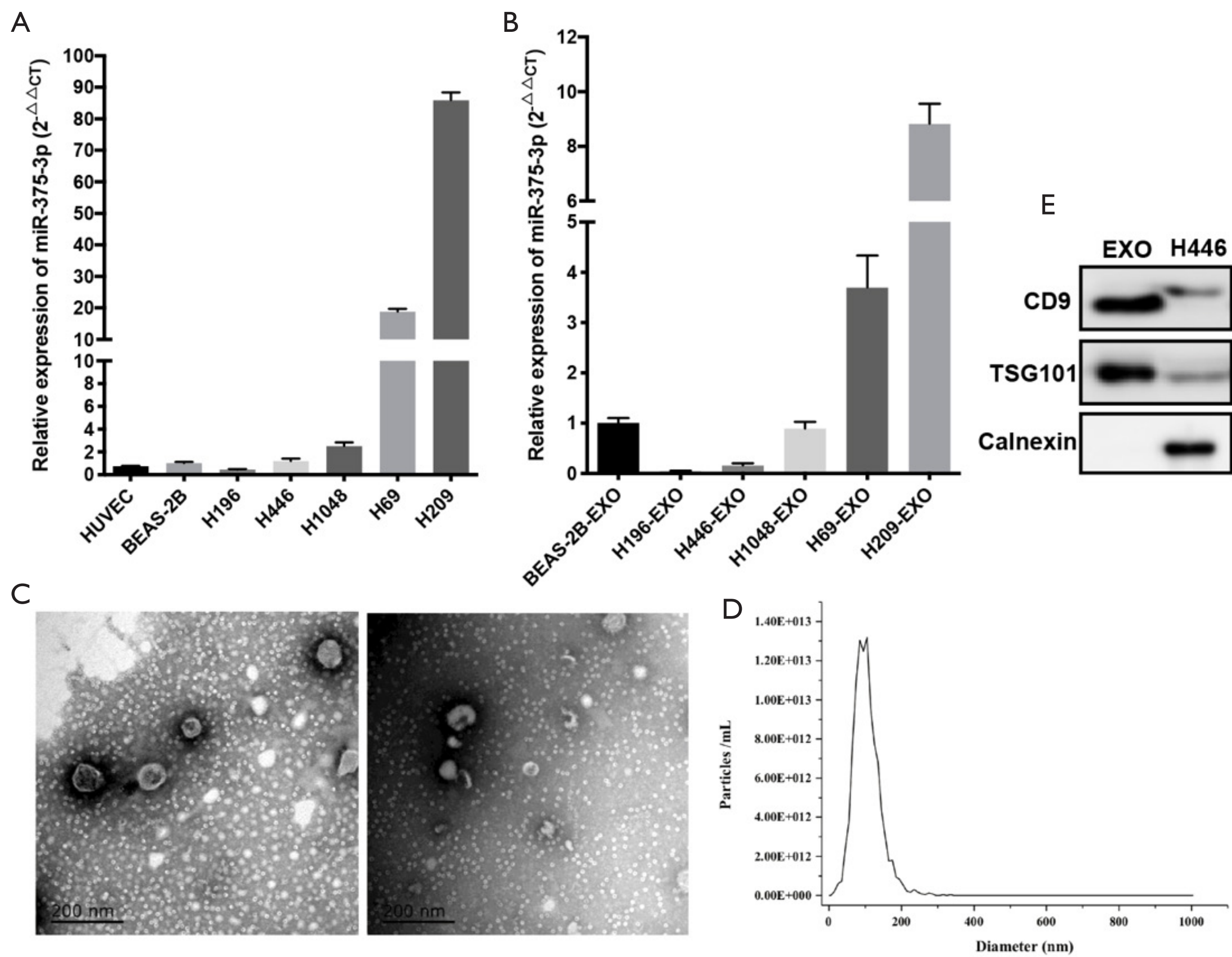

Figure S1 H446 and H1048 cells and their exosomes had low endogenous levels of miR-375-3p. (A,B) The level of miR-375-3p in HUVECs, BEAS-2B cells and SCLC cells (A) and SCLC-cell-secreted exosomes (B). (C) Representative images of H446-cell-secreted exosomes under TEM. (D) Distribution of the particle size of H446-cell-secreted exosomes. (E) Western blot analysis of TSG101, CD9 and Calnexin in H446 cell-secreted exosomes and H446 cells. TEM, transmission electron microscopy.

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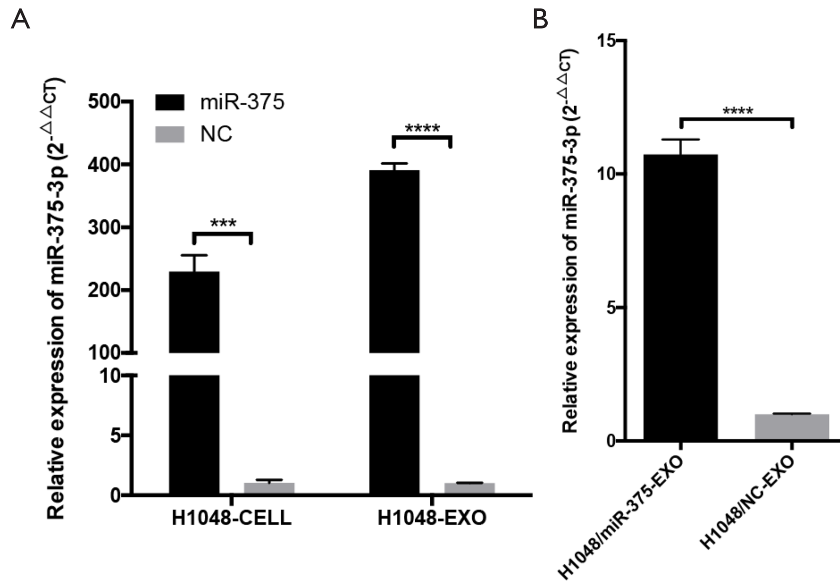

Figure S2 H1048-cell-secreted exosomal miR-375-3p was absorbed by HUVECs. (A) The level of miR-375-3p in H1048 cells or H1048-cell-secreted exosomes after transfection with miR-375-3p mimics (miR-375) or negative control mimics (NC). (B) The level of miR-375-3p in HUVECs after incubation with H1048/miR-375-EXO or H1048/NC-EXO for 12 hours. H1048/miR-375-EXO, exosomes derived from miR-375-transfected H1048 cells; H1048/NC-EXO, exosomes derived from NC-transfected H1048 cells. ***P<0.001; ****P<0.0001.

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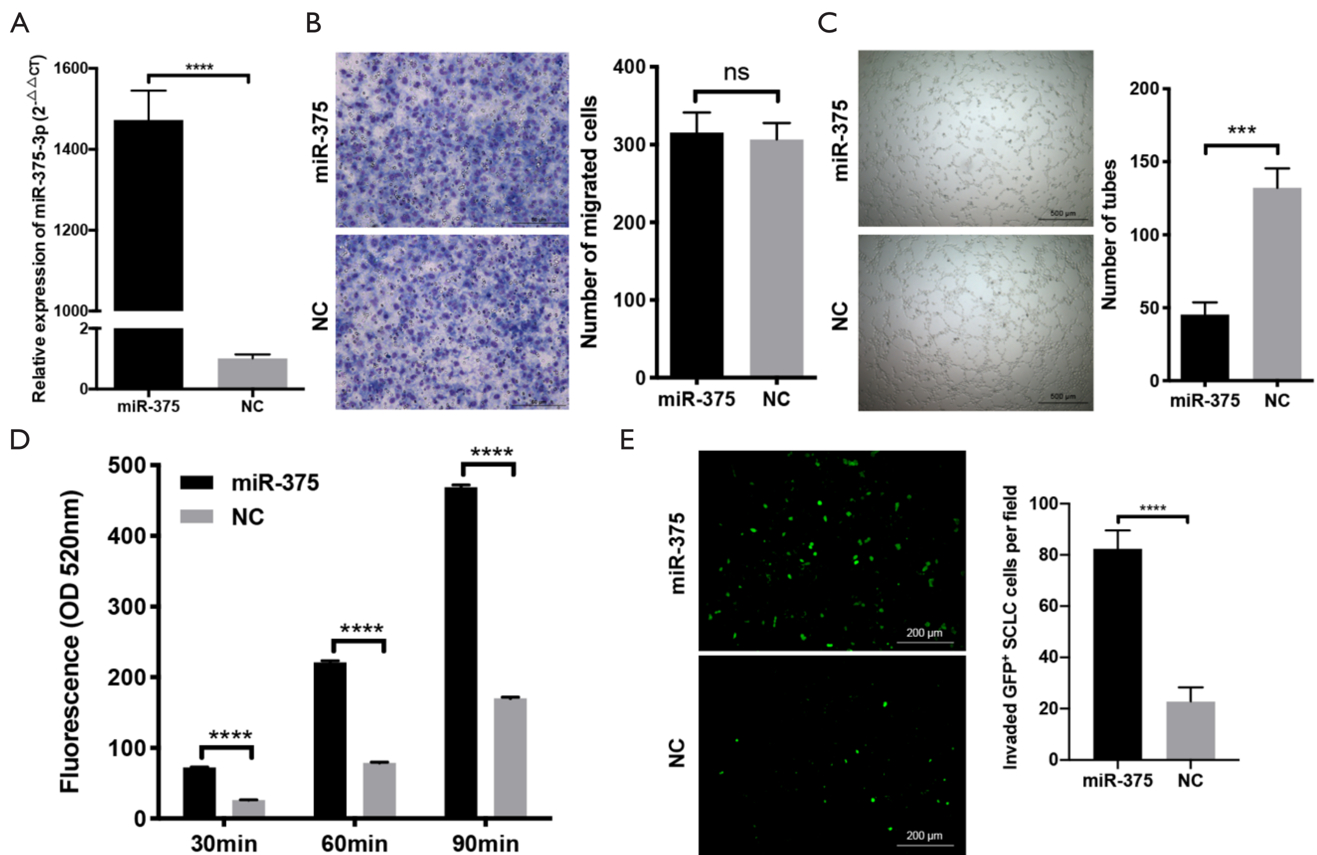

Figure S3 Mimics of miR-375-3p induced the permeability of HUVEC monolayers. (A) The level of miR-375-3p in miR-375-3p mimics (miR-375) or negative control mimics (NC) transfected HUVECs. (B) Representative images of migrated HUVECs after transfection with miR-375 or NC, with the right bar chart indicating the number of migrated cells. (C) Representative images of tubes formed by HUVECs after transfection with miR-375 or NC, with the right bar chart indicating the number of formed tubes. (D) Fluorescence intensity of FITC-dextran passing through HUVEC monolayers after transfection with miR-375 or NC. (E) Representative images of GFP+ SCLC cells migrated through miR-375- or NC-transfected HUVECs, with the right bar chart indicating the number of migrated cells. *, P<0.001; **, P<0.0001.

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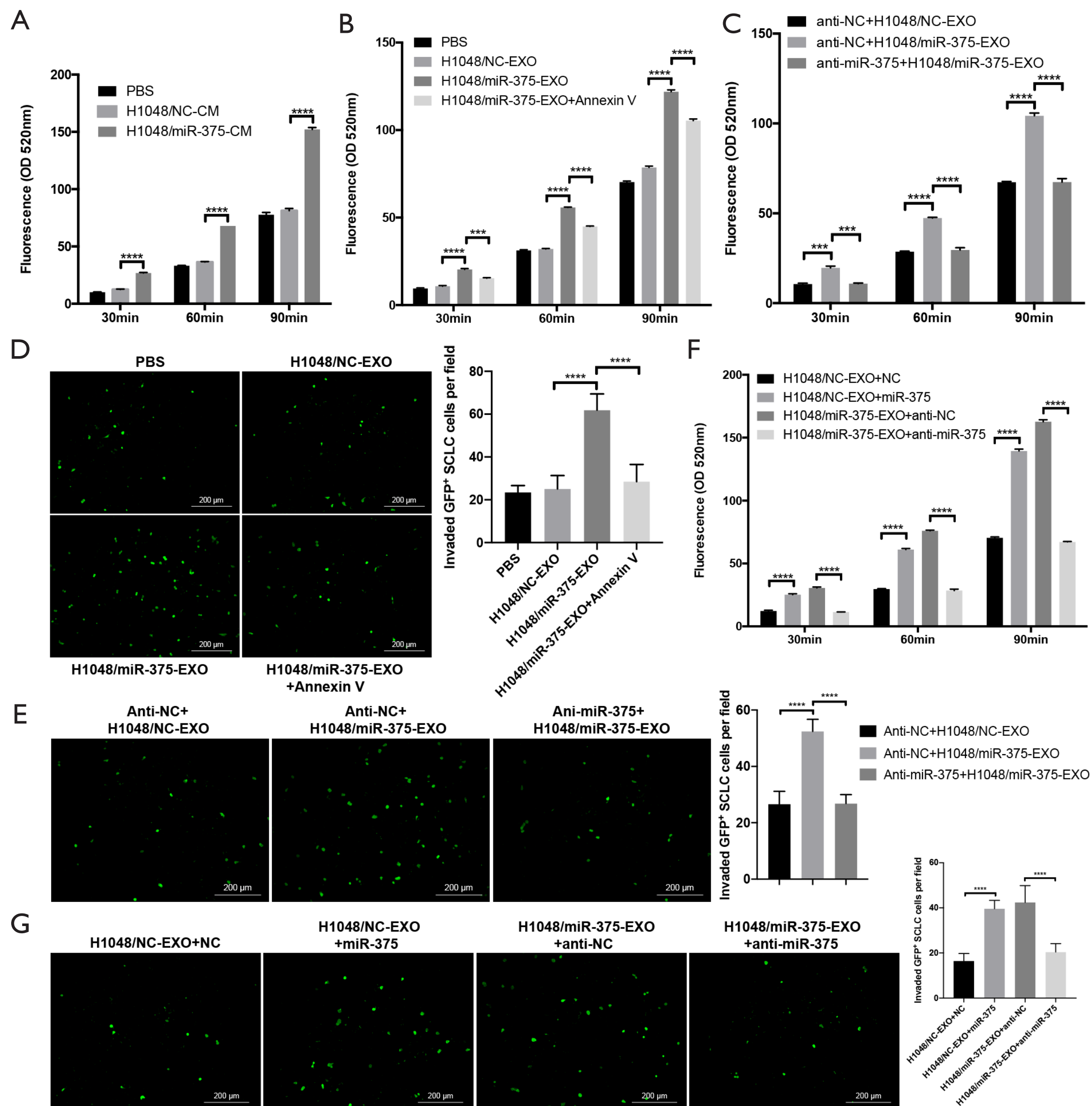

Figure S4 Exosomal miR-375-3p secreted by H1048 cells induced the permeability of HUVECs and promoted SCLC cell transendothelial migration in vitro. (A) Fluorescence intensity of FITC-dextran passing through HUVEC monolayers treated with H1048/miR-375-CM or H1048/NC-CM. (B) Fluorescence intensity of FITC-dextran passing through HUVEC monolayers treated with H1048/miR-375-EXO, H1048/NC-EXO or Annexin V-blocked H1048/miR-375-EXO. (C) Fluorescence intensity of FITC-dextran passing through H1048/miR-375-EXO- or H1048/NC-EXO-treated HUVEC monolayers pre-transfected with anti-miR-375 or anti-NC. (D) Representative images of GFP+ SCLC cells migrated through H1048/miR-375-EXO- or H1048/NC-EXO-treated HUVEC monolayers, the right bar chart indicated the number of migrated cells. (E) Representative images of GFP+ SCLC cells migrated through H1048/miR-375-EXO- or H1048/NC-EXO-treated HUVEC monolayers pre-transfected with anti-miR-375 or anti-NC; the right bar chart indicated the number of migrated cells. (F) Fluorescence intensity of FITC-dextran passing through HUVEC monolayers treated with miR-375-3p-mimic-loaded H1048/NC-EXO or miR-375-3p-inhibitor-loaded H1048/miR-375-EXO. (G) Representative images of GFP+ SCLC cells that migrated through HUVEC monolayers treated with miR-375-3p-mimic-loaded H1048/NC-EXO or miR-375-3p-inhibitor-loaded H1048/miR-375-EXO, the right bar chart indicated the number of migrated cells. H1048/miR-375-CM, culture medium derived from miR-375-transfected H1048 cells; H1048/NC-CM, culture medium derived from NC-transfected H1048 cells; H1048/miR-375-EXO, exosomes derived from miR-375-transfected H1048 cells; H1048/NC-EXO, exosomes derived from NC-transfected H1048 cells; anti-miR-375, miR-375-3p inhibitors; anti-NC, negative control inhibitors; ***P<0.001; ****P<0.0001.

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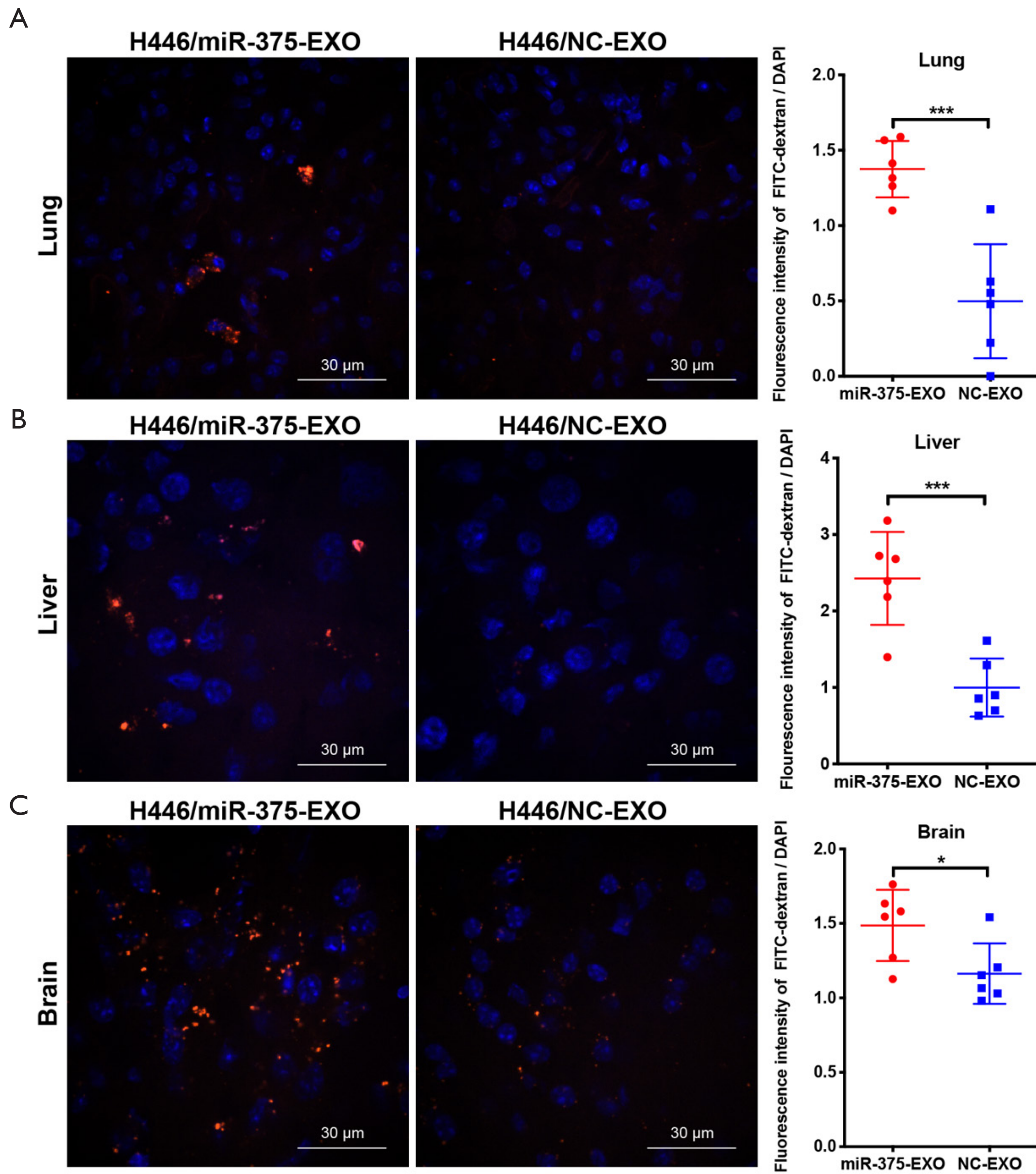

Figure S5 H446-cell-derived exosomal miR-375-3p induced the permeability of blood vessels *in vivo*. (A-C) Representative images of infiltrated FITC-dextran in the lung (A), liver (B) and brain (C) tissues of mice after treatment with H446/miR-375-EXO or H446/NC-EXO, with the red fluorescence indicating the infiltrated FITC-dextran, the blue fluorescence indicating the nucleus of cells and the right bar chart indicating the relative fluorescence intensity. H446/miR-375-EXO, exosomes derived from miR-375-transfected H446 cells; H446/NC-EXO, exosomes derived from NC-transfected H446 cells. *P<0.05; ***P<0.001.

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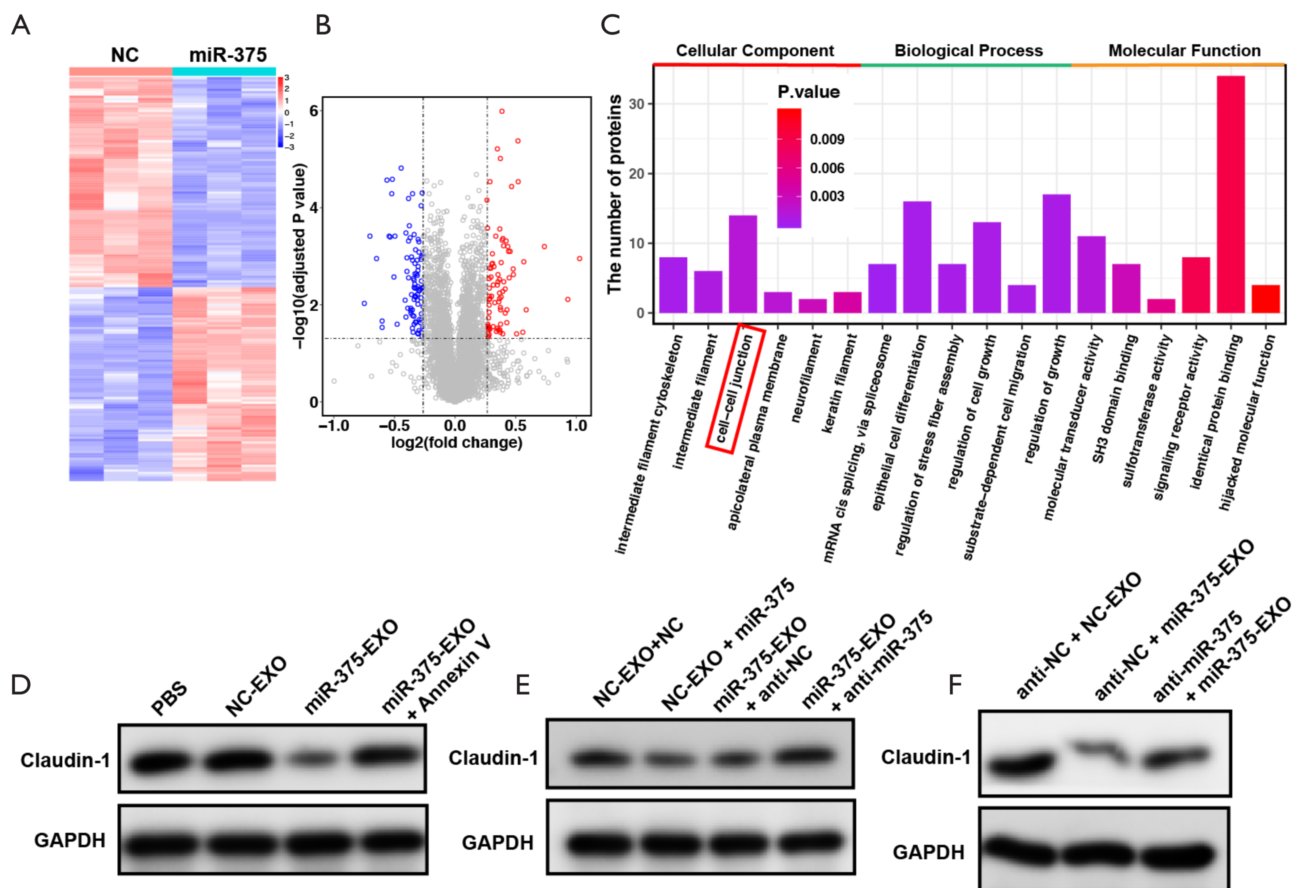

Figure S6 miR-375-3p inhibited the expression of tight junction protein claudin-1. (A,B) Heatmap (A) and volcano plot (B) of dysregulated proteins discovered by protein mass spectrometry analysis in miR-375-3p mimics (miR-375) or negative control mimics (NC) transfected HUVECs. (C) GO enrichment analysis in the dysregulated proteins discovered by protein mass spectrometry analysis. (D) Western blot analysis of claudin-1 in HUVECs that were incubated with PBS, NC-EXO, miR-375-EXO or Annexin V-pretreated miR-375-EXO. (E) Western blot analysis of claudin-1 in HUVECs after incubation with miR-375-3p-mimic-loaded NC-EXO (NC-EXO + miR-375) and its negative control (NC-EXO + NC), miR-375-3p-inhibitor-loaded miR-375-EXO (miR-375-EXO + anti-miR-375) and its negative control (miR-375-EXO + anti-NC). (F) Western blot analysis of claudin-1 in NC-EXO- or miR-375-EXO-treated HUVECs that were pre-transfected with anti-miR-375 or anti-NC.

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Table S4 Differentially expressed proteins identified by mass spectrometry analysis

Gene Name	Coverage	Unique Peptides	Peptides	PSMs	AAs	MW [kDa]	calc. pI	Group1-1/REF	Group1-2/REF	Group1-3/REF	average Group1	Group2-1/REF	Group2-2/REF	Group2-3/REF	average Group2	Group1/Group2	t test p value
MGAT4B	3.28	1	1	1	548	63.1587689	7.86962891	1.272983368	1.309962404	1.460677808	1.347874527	0.583875897	0.777477504	0.625299812	0.662217739	2.032335	0.00113
SDC1	5.48	1	1	2	310	32.441856	4.62744141	1.233001664	1.511600297	1.118344105	1.287648689	0.602955052	0.687027066	0.735941126	0.675307748	1.906756	0.007618
WBP4	2.66	1	1	1	376	42.4809435	5.56689453	1.185473155	1.275074544	1.305116799	1.255221499	0.826166152	0.703833906	0.730630703	0.753543587	1.665788	0.00063
NOLC1	24.46	21	21	40	699	73.5596396	9.46630859	1.36027985	1.039897395	1.204399253	1.2015255	0.812381554	0.806048562	0.783417857	0.800615991	1.500731	0.012498
HEXIM1	11.98	5	5	7	359	40.5984789	4.89404297	1.247062522	1.150649436	1.158272192	1.18532805	0.857620137	0.809779711	0.733281192	0.800227013	1.48124	0.001272
ADAM15	1.97	1	1	1	863	92.8991969	6.72705078	1.096115382	1.116268046	1.376712755	1.196365394	0.815564258	0.957759599	0.666308425	0.813210761	1.471155	0.036109
TOR4A	6.86	3	3	4	423	46.8849381	9.93505859	1.18939861	1.167990729	1.186556092	1.181315144	0.792916805	0.840085965	0.837895973	0.823632915	1.434274	2.86E-05
SETD7	2.19	1	1	3	366	40.6851182	4.62744141	1.172002531	1.197738307	1.174709515	1.181483451	0.818600652	0.838625329	0.821301452	0.826177468	1.43006	4.21E-06
PAN3	1.13	1	1	1	887	95.5521789	8.57275391	1.339954094	1.01971815	1.173432901	1.177701715	0.963606323	0.787562275	0.734474348	0.828547648	1.421405	0.039072
MFN1	1.75	1	1	1	741	84.1061655	6.32861328	1.08622832	1.171449845	1.250161077	1.169279747	0.838614455	0.85492205	0.821784519	0.838440341	1.394589	0.002376
ZCCHC3	2.23	1	1	1	403	43.5199085	8.52880859	1.204854927	1.19734775	1.103878466	1.168693714	0.813733321	0.901336781	0.803456479	0.83950886	1.392118	0.001848
OGFR	19.65	11	11	12	677	73.2801494	4.84326172	1.182310731	1.128654549	1.161281075	1.157415452	0.840269693	0.833081093	0.843118625	0.838823137	1.379839	3.65E-05
IFT27	4.84	1	1	1	186	20.4673311	5.41455078	1.159707317	1.208919791	1.113743522	1.16079021	0.807982926	0.878544838	0.854089007	0.846872257	1.371478	0.0008
BCL2L1	3.86	1	1	1	233	26.0327034	4.93212891	1.164658132	1.192829718	1.111394399	1.156294083	0.894045519	0.77048493	0.886298027	0.850276159	1.359904	0.002771
SDC4	11.11	2	2	3	198	21.6280324	4.50048828	1.088607336	1.199984124	1.161109771	1.14990041	0.83609875	0.854387064	0.849663061	0.846716292	1.35807	0.000788
CCDC9	4.14	3	3	3	531	59.6670617	5.40185547	1.217018967	1.128013926	1.149535119	1.164856014	0.870535925	0.883397734	0.830252985	0.861395548	1.352289	0.000628
SLFN11	5.44	3	4	4	901	102.769552	7.76708984	1.201865248	1.129043421	1.14465073	1.158526466	0.982034827	0.844107218	0.758176066	0.86143937	1.344913	0.012502
CANT1	6.23	2	2	3	401	44.8161609	6.08740234	1.099990236	1.133525189	1.187084305	1.14019991	0.923080005	0.928585951	0.695063463	0.848909807	1.343134	0.022847
G3BP2	29.67	9	11	23	482	54.0878091	5.55419922	1.144967578	1.157658588	1.128591858	1.143739341	0.859967582	0.897324563	0.80601763	0.854436591	1.338589	0.000482
MRPL54	7.25	1	1	3	138	15.8091817	9.59814453	1.093297885	1.107362117	1.248178635	1.149612879	0.846398467	0.880670376	0.864068802	0.863712545	1.331013	0.004775
CDK14	2.99	1	2	2	469	53.0233239	8.92431641	1.092577067	1.142672333	1.2021893	1.1458129	0.762326392	0.973572029	0.849151477	0.861804613	1.329551	0.014655
TRAPPC5	6.91	1	1	1	188	20.7701504	9.65673828	1.216492209	1.099941341	1.108810597	1.141748049	0.859123626	0.824594293	0.907112683	0.863610201	1.322064	0.003327
CXorf56	4.95	1	1	1	222	25.6079978	8.73388672	1.17096341	1.145661981	1.106450944	1.141025445	0.877317213	0.895777275	0.826413759	0.866502749	1.316817	0.000604
MESD	21.79	3	3	4	234	26.0603057	7.78173828	1.123007063	1.124732806	1.173787489	1.140509119	0.878411977	0.893237603	0.829113152	0.86692091	1.315596	0.000431
CWC25	2.82	1	1	1	425	49.6199925	10.184082	1.274379263	1.090182834	1.052126204	1.1388961	0.984630726	0.816166459	0.802500911	0.867766015	1.312446	0.039736
CEP152	0.47	1	1	3	1710	195.504004	5.60498047	1.064707998	1.153737489	1.197221137	1.138555541	0.810726018	0.885967587	0.90758189	0.868091832	1.311581	0.005187
DENR	32.32	6	6	9	198	22.0780714	5.30029297	1.17791784	1.092139115	1.139548606	1.136535187	0.881055316	0.865471024	0.861011077	0.869179139	1.307596	0.000471
HABP4	4.12	2	2	3	413	45.7575684	7.45947266	1.126064209	1.118808367	1.13292114	1.125931239	0.858609555	0.8596503	0.869455761	0.862571872	1.305319	1.01E-06
TPM4	57.66	7	23	77	248	28.5044925	4.69091797	1.164053497	1.160141718	1.15000218	1.158124465	0.850320504	0.854895853	0.887992183	0.864402847	1.301167	0.00135
KIAA1671	1.72	2	2	2	1806	196.590225	8.47021484	1.179053124	1.100366641	1.111374993	1.130264919	0.954325087	0.850843864	0.804949286	0.870039412	1.299098	0.006761
GALM	4.09	1	1	1	342	37.7421329	6.65380859	1.224781919	1.024204325	1.15118949	1.133391911	0.954285298	0.867332468	0.79720184	0.87293987	1.298362	0.0246
KDM2A	2.07	2	2	3	1162	132.707543	7.57666016	1.161798579	1.115592619	1.109008667	1.128799955	0.764287926	0.884182563	0.963104224	0.870524904	1.296669	0.012698
PFN2	27.14	4	4	9	140	15.0362664	6.99072266	1.1152044	1.117277908	1.129590617	1.120690975	0.851337506	0.878419955	0.867784431	0.865847297	1.294320	9.54E-06
EPHA8	2.09	1	2	2	1005	110.931575	8.06005859	1.034937446	1.119679001	1.239585583	1.131400677	0.762303476	0.899072336	0.961272243	0.874217685	1.294186	0.036977
RRBP1	62.06	76	78	175	1410	152.364688	8.60205078	1.191953892	1.027559936	1.166746135	1.128753321	0.837753873	0.925316341	0.855954549	0.873008254	1.292947	0.011374
SULT1B1	7.09	1	1	1	296	34.87664	7.06396484	1.139920454	1.127261736	1.130470298	1.132550829	0.906685148	0.996529031	0.727211619	0.876808599	1.291674	0.032076
CEP131	12.37	12	12	18	1083	122.075144	8.68994141	1.166106608	1.100687279	1.110342639	1.125712176	0.862542596	0.875567131	0.878765435	0.872291721	1.290523	0.00027
SLC4A1AP	9.8	5	5	5	796	88.7590173	5.18603516	1.180849881	1.066192234	1.136405148	1.127815755	0.915018759	0.86313448	0.84770726	0.875286833	1.28851	0.002958
CNTRL	0.77	1	3	4	2325	268.71966	5.55419922	1.204583265	1.066065457	1.117893797	1.129514173	0.903014881	0.897913782	0.830152536	0.877027066	1.28789	0.005683
TIMELESS	4.64	5	5	5	1208	138.571756	5.40185547	1.187566207	1.033708105	1.105418127	1.10889748	0.882647325	0.882748413	0.819655676	0.861683805	1.286908	0.007343
PPP1R18	13.87	5	5	10	613	67.9015087	5.40185547	1.052029004	1.166506212	1.166685803	1.128407006	0.927764633	0.812967432	0.899623924	0.880118663	1.282106	0.008513
PAFAH1B2	13.54	2	2	3	229	25.5533238	5.92236328	1.117471573	1.179064222	1.081386953	1.125974249	0.983214293	0.743767304	0.913839372	0.880273656	1.279118	0.032708
NSMCE2	4.45	1	1	1	247	27.914992	7.73779297	1.057768111	1.142488272	1.176302449	1.125519877	0.887564445	0.885173159	0.872202677	0.88164676	1.276611	0.002371
SIRT2	1.8	1	1	1	389	43.1544412	5.36376953	1.107211811	1.102229316	1.164730696	1.124723941	0.945745513	0.832990316	0.86642528	0.88172037	1.275602	0.003376
GOLGA2	17.17	13	13	13	1002	113.016648	5.02099609	1.122322011	1.10520855	1.116660428	1.114730329	0.8841694	0.864881697	0.878361028	0.87580408	1.272808	6.15E-06
TBC1D10B	4.83	4	4	4	808	87.1447384	9.18798828	1.15968084	1.046196857	1.134750565	1.113542754	0.852300039	0.915459477	0.85727499	0.875011502	1.272604	0.003956
ISCA1	24.03	2	2	3	129	14.1704382	9.07080078	1.248113106	1.036286924	1.10706886	1.13048963	0.920722519	0.935446556	0.811477931	0.889215668	1.271133	0.030451
BCAS3	1.51	1	1	1	928	101.172123	6.69775391	1.086025051	1.053117173	1.222946773	1.120696332	0.929936019	0.950747488	0.78038513	0.887022879	1.263436	0.035276
GDI1	53.02	11	18	48	447	50.5501449	5.13525391	1.092122102	1.143551139	1.10857959	1.114750944	0.855963156	0.891907859	0.903466435	0.88377915	1.261346	0.000377
ERO1A	26.07	12	12	21	468	54.3580549	5.68115234	1.040127592	1.174377194	1.133216307	1.115907031	0.869741578	0.860632612	0.941172324	0.890715505	1.252821	0.008886
IRAK2	3.52	2	2	3	625	69.3888199	5.71923828	1.108944392	1.118013208	1.113627562	1.113528387	0.899202127	0.9399653	0.840341276	0.893169568	1.246716	0.001617
WBP11	24.02	16	16	24	641	69.9539239	8.38232422	1.164914904	1.041655472	1.110145044	1.105571814	0.89772188	0.876589731	0.88902747	0.887779694	1.245322	0.003836
SPATA20	1.27	1	1	1	786	87.8431343	7.43017578	1.227176508	1.081922034	1.023855581	1.110984708	0.882109577	0.938010427	0.866259467	0.895459824	1.240656	0.028468
CETN3	7.19	1	1	1	167	19.5378917	4.74169922	1.074138059	1.122752367	1.13477736	1.110555928	0.885851647	0.866637939	0.933867689	0.895452425	1.240218	0.001396
CTTN	41.09	22	22	65	550	61.5485343	5.40185547	1.086599803	1.142963036	1.101675762	1.110412867	0.863409336	0.911708345	0.917549738	0.897555806	1.237152	0.000899
ZW10	15.53	8	9	12	779	88.7728734	6.26513672	1.06726586	1.100390068	1.122295523	1.096650484	0.883918615	0.927842267	0.856988512	0.889883131	1.232343	0.001423
ANKRD35	1.4	1	2	2	1001	109.898392	6.02392578	1.160167595	1.08503004	1.074999798	1.106732478	0.871450821	0.958609548	0.869880616	0.899980328	1.22973	0.006523
INPP1	4.26	1	1	1	399	43.9702493	5.26220703	1.063026791	1.091038968	1.164709974	1.106258577	0.889839649	0.910945925	0.899606237	0.900130604	1.228996	0.002634
SYP	3.19	1	1	1	313	33.8234389	4.80517578	1.101769191	1.129179879	1.085880776	1.105609949	0.851619258	0.926551373	0.924330942	0.900833837	1.227318	0.001779
EDC3	12.2	5	5	5	508	56.0423675	7.10791016	1.105575808	1.087458863	1.101999423	1.098344698	0.910938305	0.904591409	0.885887444	0.900465719	1.219732	2.94E-05
TMEM126B	6.09	1	1	1	230	25.9263658	8.80712891	1.145862325	1.035647045	1.125278366	1.102262579	0.908256882	0.936890074	0.866539191	0.903895382	1.219458	0.007389
CHST14	3.99	1	1	1	376	42.9694328	9.48095703	1.165921488	1.047197659	1.093699368	1.102272838	0.831661936	0.88082176	0.978825671	0.904050626	1.21926	0.031887
C9orf78	30.45	9	9	15	289	33.6671463	6.74169922	1.129815417	1.056142619	1.130739226	1.105565754	0.896939088	0.927913439	0.899458718	0.908103748	1.217444	0.001766
PPT1	18.63	5	5	7	306	34.1712526	6.52197266	1.056910051	1.154091703	1.121971409	1.110991054	0.954942515	0.867703057	0.916600994	0.913082189	1.216748	0.006564
SBF1	1.12	1	1	1	1868	208.31235	6.90283203	1.058356238	1.08765252	1.157333955	1.101114238	0.926024916	0.918750068	0.872413666	0.90572955	1.215721	0.004457
TDRKH	4.28	2	2	5	561	62.0074175	5.02099609	1.020812995	1.149811066	1.100683875	1.090435978	0.860998765	0.918858308	0.91294119	0.897599421	1.214836	0.009966
HDGFL2	12.22	6	7	11	671	74.2722336	7.48876953	1.093163909	1.048669983	1.10636946	1.08273415	0.930528815	0.849156782	0.89414605	0.891277216	1.214812	0.002834
CDK6	7.36	1	2	2	326	36.9150286	6.45556641	1.112223554	1.125266302	1.064665207	1.100718354	0.949780682	0.932764013	0.838487985	0.907010893	1.213587	0.007813
CARD9	1.87	1	1	1	536	62.2019217	6.07470703	1.157670706	0.986777881	1.153228818	1.099225802	0.893568352	0.936540269	0.887953188	0.906020603	1.213248	0.029536
RABL6	14.27	6	6	10	729	79.4995715	5.22412109	1.148181514	1.056918786	1.096785343	1.100628548	0.896278893	0.9789269	0.847530165	0.907578652	1.212709	0.01431
RPL26L1	33.79	1	9	21	145	17.2455538	10.550293	1.192182368	0.979255585	1.124641866	1.098693273	0.935716757	0.884643263	0.897710684	0.906023568	1.212654	0.040753
SLC1A5	17.19	9	9	22	541	56.5622546	5.47802734	1.179807928	1.033963722	1.059198096	1.090989915	0.941004663	0.875126222	0.883798832	0.899976572	1.212243	0.01819
SHTN1	23.45	13	14	17	631	71.5956955	5.32568359	1.064649991	1.087556614	1.124500609	1.092235838	0.941933747	0.776288034	0.987102084	0.901774622	1.211207	0.045569
TANC2	0.7	1	1	1	1990	219.512147	8.07470703	1.0254077	1.200342143	1.032706118	1.086157321	0.942076371	0.86129221	0.915430243	0.906266275	1.208471	0.031122
HIP1R	4.12	4	4	4	1068	119.314926	6.66845703	1.081838126	1.095818575	1.109163489	1.09560673	0.84903731	0.846267773	1.025717458	0.907007514	1.207336	0.034531
H3F3A	57.35	3	8	37	136	15.3185036	11.2680664	1.195226355	1.015997868	1.059488442	1.090237555	0.926944577	0.88986718	0.892572734	0.903128164	1.207179	0.027661
ARSA	3.35	1	1	3	507	53.5536789	6.07470703	1.012372788	1.114153215	1.166439376	1.097655126	0.875711802	0.886247548	0.967865059	0.90994147	1.206292	0.025139
PPP1R14B	17.01	2	2	4	147	15.9010464	4.85595703	1.008586803	1.14139628	1.136215914	1.095399665	0.939317114	0.828896305	0.957586401	0.90859994	1.205591	0.034301
GABARAPL1	12.82	1	2	4	117	14.0352394	8.73388672	0.975114501	1.187233249	1.12890041	1.09708272	0.893836976	0.927834455	0.910296211	0.910655881	1.204717	0.043597
GXYLT1	5.91	3	3	3	440	50.5335319	8.64599609	1.063298186	1.141373834	1.110484857	1.105052293	0.837282451	1.028256432	0.887011818	0.9175169	1.204394	0.038127
PBDC1	15.45	4	4	10	233	26.0406871	4.79248047	1.092863909	1.0848587	1.121736577	1.099819729	0.921384194	0.892862146	0.926533687	0.913593342	1.203839	0.000264
EVPL	2.21	4	5	5	2033	231.463005	6.96142578	1.165025225	1.008246282	1.078175343	1.083815617	0.956511673	0.866531091	0.883095706	0.902046156	1.201508	0.02672
TXLNA	45.97	23	24	53	546	61.8532498	6.52197266	1.106099942	1.079541547	1.085400682	1.090347391	0.897616134	0.921430296	0.906519711	0.908522047	1.200133	6.87E-05
LIMS1	6.15	2	2	2	325	37.2258444	8.04541016	0.917126607	0.892434635	0.918607693	0.909389645	1.078838259	1.149858521	1.047152477	1.091949752	0.832813	0.004422
CTPS1	39.26	18	21	46	591	66.6479928	6.45556641	0.885883955	0.923018091	0.9011351	0.903345715	1.057357445	1.118430388	1.079011932	1.084933255	0.832628	0.000961
FAU	25.68	1	1	1	74	7.75496421	4.34814453	0.929745078	0.884954358	0.912966357	0.909221931	1.12159048	1.016590201	1.142102899	1.09342786	0.831534	0.010891
SRSF4	22.67	7	12	35	494	56.6453333	11.5170898	0.872244007	0.954836334	0.906362726	0.911147689	1.015367777	1.185330898	1.089249993	1.096649556	0.830847	0.027542
EGFR	27.11	27	27	44	1210	134.190257	6.68310547	0.888872252	0.914896379	0.915785056	0.906517896	1.092516681	1.103142528	1.086623731	1.094094313	0.828556	4.88E-05
SNRNP27	17.42	3	3	4	155	18.8488754	11.6196289	0.868279541	0.959551715	0.892278293	0.906703183	1.004691031	1.207720685	1.076914312	1.096442009	0.82695	0.044057
APLP2	2.36	1	2	3	763	86.9001869	4.79248047	0.880296127	0.891701613	0.944520529	0.90550609	1.148550293	1.078971553	1.061288589	1.096270145	0.825988	0.004536
PTPN14	7.33	6	7	8	1187	135.17548	8.30908203	0.892659044	0.952615063	0.887690242	0.910988116	1.092399935	1.12157432	1.099406638	1.104460298	0.824826	0.001029
SRSF12	11.49	1	3	6	261	30.4936113	11.6928711	0.951158814	0.888309923	0.875309571	0.904926103	0.987957193	1.121946956	1.182779378	1.097561176	0.824488	0.036202
METTL2B	7.14	3	3	3	378	43.3983273	5.85888672	0.918160926	0.948883272	0.887535142	0.918193113	1.10193061	1.162757962	1.076843039	1.11384387	0.824346	0.003243
FZD6	1.56	1	1	1	706	79.2399516	7.95751953	0.991979268	0.894845533	0.828954058	0.90525962	1.104175324	1.104291177	1.087238397	1.098568299	0.824036	0.015428
SIRPA	22.82	9	9	15	504	54.9328262	6.97607422	0.945090086	0.912198759	0.865406122	0.907564989	1.109264599	1.099299501	1.09763656	1.102066887	0.823512	0.001145
TYMS	20.45	6	6	11	313	35.6931613	7.00537109	0.911637379	0.899062044	0.923100455	0.911266626	1.126534129	1.093025572	1.100560016	1.106706572	0.823404	9.16E-05
PSIP1	40.38	21	22	38	530	60.0666826	9.12939453	0.954145014	0.857326187	0.881234249	0.897568483	1.103283418	1.125448194	1.043835976	1.090855863	0.822811	0.007027
ZNF644	1.13	1	1	1	1327	149.471328	8.16259766	0.961392662	0.892051454	0.858919118	0.904121078	1.013482933	1.134550889	1.148829672	1.098954498	0.82271	0.020617
SLC16A7	2.3	1	1	1	478	52.1661611	9.30517578	0.897429483	0.916240128	0.896709797	0.903459803	1.004222557	1.193225643	1.105436579	1.100961593	0.82061	0.022915
MTDH	39.35	20	20	35	582	63.7988147	9.31982422	0.922692237	0.837604805	0.916892233	0.892396425	1.060825414	1.130949773	1.076400247	1.089391811	0.819169	0.004759
JPT1	33.77	3	3	3	154	16.0049121	5.60498047	0.90920371	0.839461819	0.94779446	0.898819997	1.149159193	1.007025107	1.137337687	1.097840662	0.818716	0.023023
ALMS1	0.17	1	1	1	4168	460.779856	6.27783203	0.902487798	0.935108132	0.86309725	0.90023106	1.154892127	1.051574486	1.105107264	1.103857959	0.815532	0.005
ZCCHC17	18.67	4	4	6	241	27.5522123	9.70068359	0.924380218	0.9173324	0.861331402	0.901014673	1.026367084	1.201391856	1.09124993	1.10633629	0.814413	0.020052
DPYSL3	34.21	11	13	22	570	61.9240981	6.49365234	0.890283976	0.927447229	0.879572875	0.89910136	1.07952669	1.107340613	1.12653917	1.104468824	0.814058	0.000499
COPE	2.92	1	1	1	308	34.460342	5.12255859	0.917378537	0.794500372	0.982561883	0.89814693	1.11180936	1.041285392	1.157161792	1.103418848	0.813967	0.033651
ENAH	18.27	11	11	15	591	66.4698978	6.93212891	0.911976569	0.907216256	0.862208354	0.893800393	1.122493	1.0683092	1.106826428	1.099209543	0.81313	0.000812
MMTAG2	21.67	5	5	7	263	29.3939418	10.0229492	0.862134287	0.906239261	0.918798133	0.895723894	1.067279694	1.170869204	1.076228841	1.10479258	0.810762	0.00499
MAT2B	23.05	6	6	6	334	37.5281776	7.35693359	0.927062672	0.871158461	0.89818236	0.898801164	1.131011679	1.107414232	1.090514979	1.109646963	0.809988	0.000454
KRT18	64.65	33	34	202	430	48.0285381	5.45263672	0.866115	0.917996691	0.890839394	0.891650362	1.05692247	1.114450411	1.135351761	1.102241547	0.808943	0.001634
KRT77	6.23	1	4	9	578	61.863513	5.98583984	0.80409357	0.985532179	0.900735659	0.896787136	1.033314546	1.193382698	1.099803836	1.108833694	0.808766	0.038842
SRSF11	27.07	10	11	30	484	53.5101801	10.5209961	0.898200148	0.904825481	0.868860292	0.890628641	0.972740131	1.207312819	1.127959258	1.102670736	0.807701	0.038428
GDF15	24.68	7	7	19	308	34.1187569	9.65673828	0.918674917	0.891149334	0.878874913	0.896233055	1.060792253	1.070777222	1.198796503	1.110121993	0.807328	0.009636
PARVB	11.81	2	4	6	364	41.6880756	6.72705078	0.870626489	0.925120413	0.905100341	0.900282414	1.065662596	1.146655883	1.133853243	1.115390574	0.807145	0.001941
PHLDA2	3.95	1	1	1	152	17.081849	9.17333984	0.834554348	0.935544593	0.914908805	0.895002582	1.122223727	1.070029838	1.134552707	1.108935424	0.807083	0.004275
PRDX1	67.34	11	14	76	199	22.0962799	8.13330078	0.842463604	0.936883295	0.895644333	0.891663744	1.118172289	1.074035961	1.124961067	1.105723106	0.806408	0.002493
AHNAK	69.58	247	251	803	5890	628.699422	6.15087891	0.861606872	0.899953488	0.910457774	0.890672711	1.135423144	1.030892882	1.150634482	1.105650169	0.805565	0.006032
GLUL	6.97	3	3	4	373	42.0373088	6.88818359	0.939432122	0.83798608	0.855122473	0.877513559	1.041572307	1.143712874	1.082675182	1.089320121	0.805561	0.008005
TSC22D2	5.38	4	5	7	780	79.1793571	5.02099609	0.926660543	0.886278588	0.867764101	0.893567744	1.150131684	1.093105616	1.088461187	1.110566162	0.804606	0.001189
FLCN	2.25	1	1	1	579	64.4320014	6.22705078	0.931937486	0.87736398	0.8675187	0.892273389	1.080774971	1.160129548	1.09426503	1.111723183	0.802604	0.002274
PPIG	13.79	11	11	13	754	88.5641255	10.2866211	0.869357197	0.924586332	0.888674029	0.894205852	1.09209939	1.18495147	1.07083321	1.115961357	0.801287	0.004547
SREK1	18.11	7	8	17	508	59.3450134	10.3891602	0.932511589	0.839854392	0.914060077	0.895475353	1.023363885	1.217407958	1.120121777	1.120297873	0.799319	0.023128
NT5E	11.5	5	6	9	574	63.3274882	7.03466797	0.856402293	0.896666319	0.897224747	0.88343112	1.069291021	1.132941885	1.123999656	1.108744187	0.796785	0.000723
HIGD1A	19.35	1	1	2	93	10.1362424	9.78857422	0.792435029	0.983229949	0.868555752	0.88140691	1.16039935	1.088719555	1.069941449	1.106353451	0.796678	0.022107
HMGCR	1.69	1	1	1	888	97.4126148	6.74169922	0.834705566	0.925860871	0.906189204	0.888918547	1.185162811	1.082297779	1.080013391	1.11582466	0.796647	0.006919
PTPN12	12.44	8	8	8	780	88.0514408	5.61767578	0.891291906	0.882023083	0.904417242	0.89257741	1.05152633	1.110720491	1.201622562	1.121289794	0.796027	0.006595
LSM12	23.59	3	3	4	195	21.6871303	7.73779297	0.916669499	0.917126753	0.834676323	0.889490858	1.102894318	1.136384593	1.115064691	1.118114534	0.795527	0.001419
MTRR	11.89	7	7	9	698	77.6250261	6.49365234	0.862307153	0.897104929	0.923584021	0.894332034	1.147289371	1.069375794	1.159448895	1.125371353	0.794699	0.002274
PNISR	9.44	9	9	11	805	92.5210779	10.0229492	0.867781688	0.914242479	0.874664536	0.885562901	1.062499127	1.186589479	1.095745774	1.114944793	0.794266	0.004502
MOB1B	25.93	6	6	17	216	25.0746393	6.72705078	0.845361993	0.918333163	0.886968417	0.883554524	1.152589212	1.051586789	1.141136382	1.115104128	0.792352	0.003773
OPHN1	1.25	1	1	1	802	91.5828915	7.95751953	0.830774627	0.905251392	0.922691705	0.886239241	1.074272018	1.187178671	1.09406364	1.118504777	0.792343	0.00658
ARL6IP4	14.49	5	5	7	421	44.8882055	10.9311523	0.86114946	0.918069306	0.880576912	0.886598559	1.026606749	1.242635017	1.088198663	1.119146809	0.792209	0.024833
TNRC6A	4.54	7	7	9	1962	210.16853	7.00537109	0.906652885	0.861388426	0.875459286	0.881166866	1.091537875	1.143193097	1.104016517	1.11291583	0.791764	0.00035
CD46	2.55	1	1	1	392	43.7186889	6.74169922	0.898146115	0.828050903	0.926869288	0.884355435	1.087638394	1.093626019	1.172016477	1.117760296	0.791185	0.0043
CNN3	42.86	10	12	24	329	36.3907858	6.04931641	0.814288026	0.925918495	0.903570016	0.881258846	1.089033055	1.127806412	1.125545329	1.114128265	0.790985	0.003047
PRPF40A	22.78	26	26	48	957	108.736581	7.56201172	0.883473357	0.904074525	0.866644468	0.884730783	1.102288356	1.205842188	1.048420087	1.11885021	0.79075	0.007846
TM4SF18	7.46	1	1	1	201	22.2624516	7.40087891	0.804721052	0.986979798	0.862451562	0.884717471	1.149593315	1.148660667	1.065790204	1.121348062	0.788977	0.017404
PNN	33.19	28	28	56	717	81.5789819	7.13720703	0.852974471	0.929905607	0.867254935	0.883378338	1.094525609	1.175486483	1.090367727	1.120126606	0.788642	0.002887
MOB3A	3.69	1	1	1	217	25.4478653	8.63134766	0.758285586	0.962873689	0.922673437	0.88127757	1.096805505	1.056859032	1.212518214	1.122060917	0.78541	0.036782
SMAD3	15.29	4	5	9	425	48.0497533	7.15185547	0.888816167	0.882736474	0.882626876	0.884726506	1.110088823	1.152499077	1.118610451	1.127066117	0.784982	5.04E-05
KRT8	82.61	34	44	347	483	53.6711355	5.59228516	0.85872528	0.885333326	0.885146524	0.87640171	1.06205374	1.137169725	1.152107399	1.117110288	0.784526	0.001186
RBPJ	1.4	1	1	1	500	55.6015347	7.18115234	0.849694576	0.879171309	0.915369132	0.881411672	1.115554624	1.228339664	1.028606232	1.12416684	0.784058	0.01628
SH3BP4	2.6	2	2	2	963	107.428058	7.70849609	1.024395121	0.807353586	0.80022274	0.877323816	1.099357514	1.136919834	1.125524636	1.120600662	0.782905	0.030794
RBMX2	6.21	2	2	3	322	37.3132165	9.83251953	0.881077777	0.880133571	0.877825182	0.879678844	1.07746011	1.239229206	1.05991114	1.125533485	0.781566	0.012575
CCDC59	8.3	2	2	3	241	28.6520367	9.87646484	0.893146596	0.884235046	0.863487272	0.880289638	1.206988468	1.133357701	1.046960242	1.129102137	0.779637	0.006146
UAP1	47.32	20	22	57	522	58.7318491	6.32861328	0.826415417	0.908154588	0.895560585	0.876710197	1.097134864	1.140280198	1.140181411	1.125865491	0.778699	0.001034
ZRANB2	20.61	6	6	8	330	37.3820233	10.0083008	0.90285986	0.85080453	0.862814234	0.872159541	1.087694342	1.23595056	1.040656122	1.121433675	0.777718	0.014948
CLDN11	14.98	3	3	6	207	21.9783852	7.89892578	0.905895995	0.896132089	0.833169716	0.878399266	1.239811051	1.074923496	1.085813597	1.133516048	0.774933	0.011644
SRSF6	30.81	8	13	32	344	39.563395	11.4291992	0.937835063	0.828336586	0.864822265	0.876997971	1.136104513	1.216741199	1.04285934	1.131901684	0.7748	0.012929
CBX3	43.72	9	10	30	183	20.7983504	5.32568359	0.907525072	0.855237017	0.857413991	0.873392027	1.160725477	1.114805431	1.109856197	1.128462368	0.773966	0.000411
TPM1	49.65	6	24	83	284	32.6886833	4.74169922	0.835912073	0.892581994	0.892328821	0.873607629	1.118441606	1.148824631	1.137069006	1.134778414	0.769849	0.000232
PARD6B	12.63	4	4	6	372	41.1570453	5.57958984	0.821024813	0.934051825	0.823762747	0.859613128	1.092386903	1.134772108	1.134621395	1.120593469	0.767105	0.0028
PDLIM2	5.97	2	2	4	352	37.4356833	8.71923828	0.899616394	0.81527021	0.872026325	0.862304309	1.115621872	1.130783959	1.127671611	1.124692481	0.766702	0.000485
PRPF4B	13.7	14	16	33	1007	116.915685	10.2573242	0.860101328	0.878422653	0.863626511	0.867383497	1.112307751	1.159277798	1.123986833	1.131857461	0.766336	6.39E-05
RAPGEF3	1.52	1	1	1	923	103.685569	7.56201172	0.817037864	0.910996099	0.871060638	0.866364867	1.053001308	1.115815999	1.239665296	1.136160868	0.762537	0.01163
SRRM1	14.49	11	11	24	904	102.274134	11.8393555	0.834252975	0.919485733	0.851669544	0.868469417	1.118861608	1.198371695	1.109840958	1.142358087	0.760243	0.002024
RBMS1	6.16	1	2	5	406	44.4768567	8.79248047	0.885205238	0.8842278	0.820143717	0.863192251	1.151877627	1.088763323	1.167687231	1.136109393	0.759779	0.001077
TTYH3	2.68	1	1	2	523	57.5078922	5.38916016	0.845644632	0.826882732	0.901177182	0.857901515	1.117638526	1.150371646	1.140349068	1.136119747	0.755115	0.000333
AKAP2	2.56	2	2	2	859	94.6027772	5.10986328	0.785208474	0.92720446	0.869639527	0.860684154	1.029412138	1.166127031	1.229272464	1.141603878	0.753925	0.017491
ZNF800	5.57	3	3	3	664	75.1887921	9.46630859	0.928090153	0.787490372	0.877287974	0.8642895	1.132411614	1.228401788	1.089269082	1.150027495	0.751538	0.00796
JAK1	12.82	12	13	19	1154	133.191257	7.54736328	0.84866261	0.848866421	0.853686412	0.850405148	1.143899628	1.148821394	1.182871556	1.15853086	0.734038	1.54E-05
QKI	6.74	1	2	3	341	37.6467284	8.55810547	0.825098559	0.802543178	0.877626462	0.8350894	1.122083915	1.03066032	1.340781482	1.164508573	0.717117	0.025346
ACSL3	15.69	8	9	14	720	80.3682999	8.38232422	0.818065896	0.857662308	0.823101596	0.832943267	1.119630195	1.185169304	1.215594692	1.17346473	0.709815	0.000387
ARGLU1	24.54	11	11	21	273	33.1968288	10.3452148	0.84388215	0.840670731	0.80409381	0.829548897	1.162449918	1.274193355	1.10038778	1.179010351	0.703598	0.002632
MSMO1	15.02	4	4	5	293	35.1925968	7.22509766	0.798717208	0.785483056	0.819005706	0.801068657	1.136886004	1.132350644	1.171473302	1.146903317	0.698462	2.54E-05
ARHGAP29	21.09	25	25	37	1261	141.974213	6.74169922	0.78614101	0.836154707	0.82878563	0.817027116	1.15088377	1.18365297	1.186221604	1.173586115	0.69618	5.05E-05
LDHB	49.1	18	21	87	334	36.6151447	6.04931641	0.830545154	0.819877938	0.791907629	0.81411024	1.243401952	1.141554907	1.158931768	1.181296209	0.689167	0.000394
UXS1	4.05	1	1	1	420	47.5466907	8.93896484	0.788076201	0.816172875	0.836396988	0.813548688	1.147077454	1.16883359	1.24934716	1.188419402	0.684564	0.00039
CXADR	6.85	2	2	2	365	40.0043764	7.56201172	0.790702376	0.785979609	0.833127576	0.803269854	1.169571017	1.18747051	1.202496218	1.186512582	0.677001	2.73E-05
SLC9A1	2.82	1	1	1	815	90.7050381	7.21044922	0.724929645	0.921332463	0.746941951	0.797734687	1.383294842	1.229904357	1.015439238	1.209546146	0.659532	0.028946
WNT5B	1.67	1	1	1	359	40.2965681	8.39697266	0.757493004	0.886118871	0.746203077	0.796604984	1.03742641	1.392742873	1.194287238	1.208152174	0.659358	0.021412
UBE2E2	16.92	1	3	4	201	22.2411398	7.70849609	0.792559576	0.783779012	0.765557193	0.780631927	1.309101291	1.232300089	1.12845793	1.223286437	0.638143	0.001119
HAS3	5.06	2	2	4	553	62.9572407	8.48486328	0.768691212	0.723248591	0.792630042	0.761523281	1.163620828	1.271765377	1.284305716	1.239897307	0.614183	0.000384
INA	3.81	1	2	10	499	55.3573958	5.40185547	0.919536772	0.547428638	0.768345964	0.745103791	1.24954256	1.252310418	1.260337686	1.254063555	0.594152	0.00925
CLDN1	7.11	1	1	3	211	22.7285833	8.08935547	0.959850312	0.890065026	0.995949452	0.948621597	1.053765057	1.033167572	1.023504107	1.036812245	0.914941	0.052576

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https://dx.doi.org/10.21037/tlcr-21-356

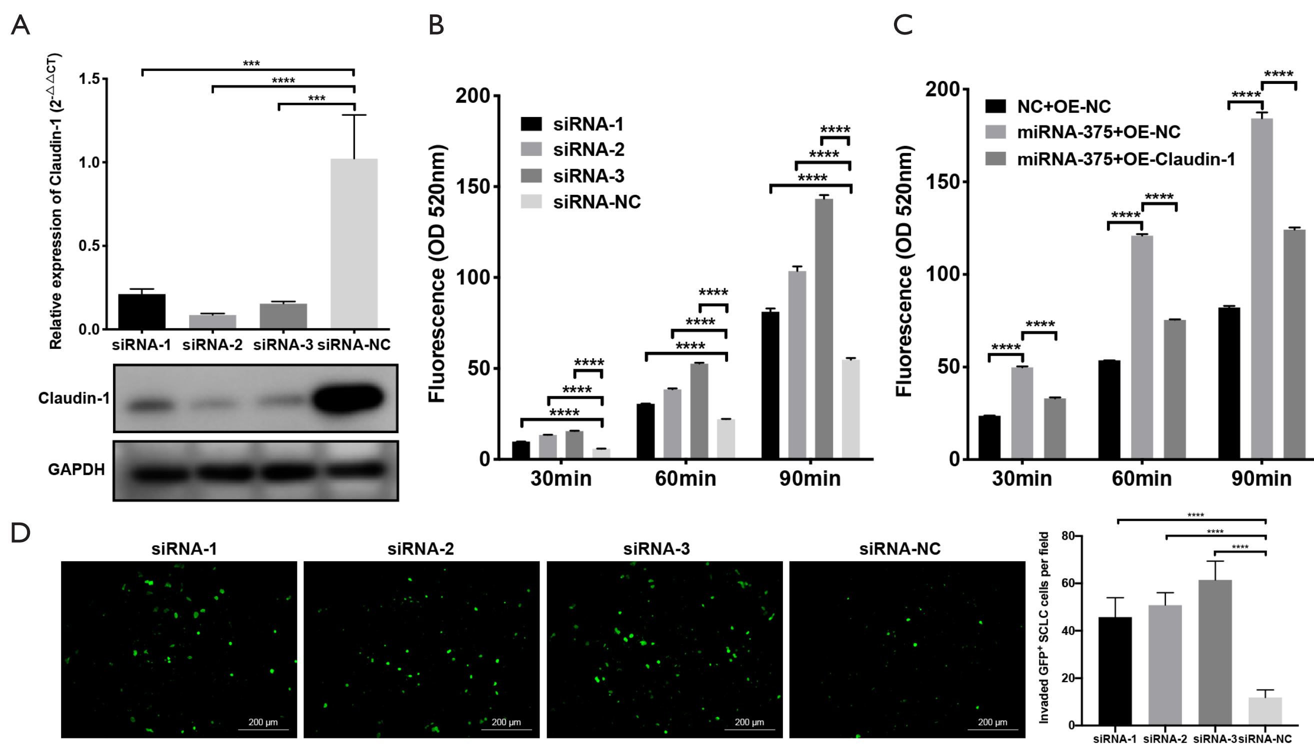

Figure S7 Knocking down the expression of claudin-1 increased the permeability of HUVECs monolayers. (A) Both the RNA and protein expression of claudin-1 in HUVECs were downregulated by three claudin-1-specific siRNAs. (B) The downregulation of claudin-1 in HUVECs induced the permeability of HUVEC monolayers. (C) The increased permeability of HUVEC monolayers induced by miR-375-3p was abrogated by the upregulation of claudin-1. (D) The downregulation of claudin-1 in HUVECs promoted the transendothelial migration of GFP + SCLC cells. *, P<0.001; **, P<0.0001.

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