

**Appendix files of Manuscript:**

**TFEB controls vascular development by regulating the proliferation of endothelial cells.**

**Table of content:**

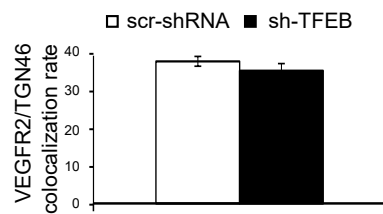
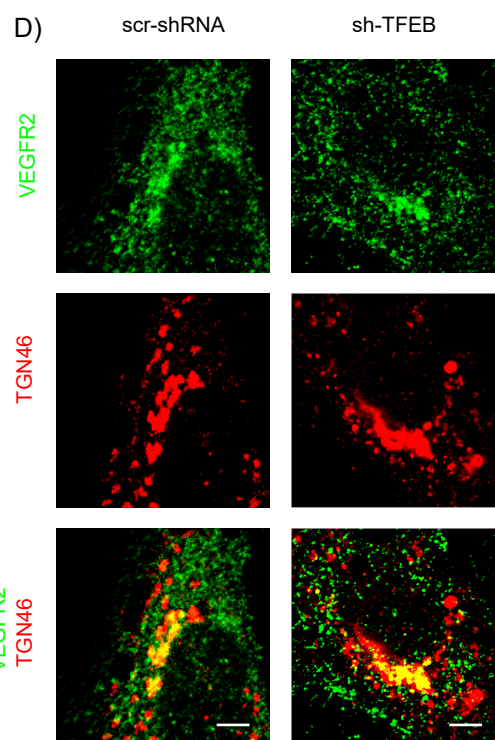
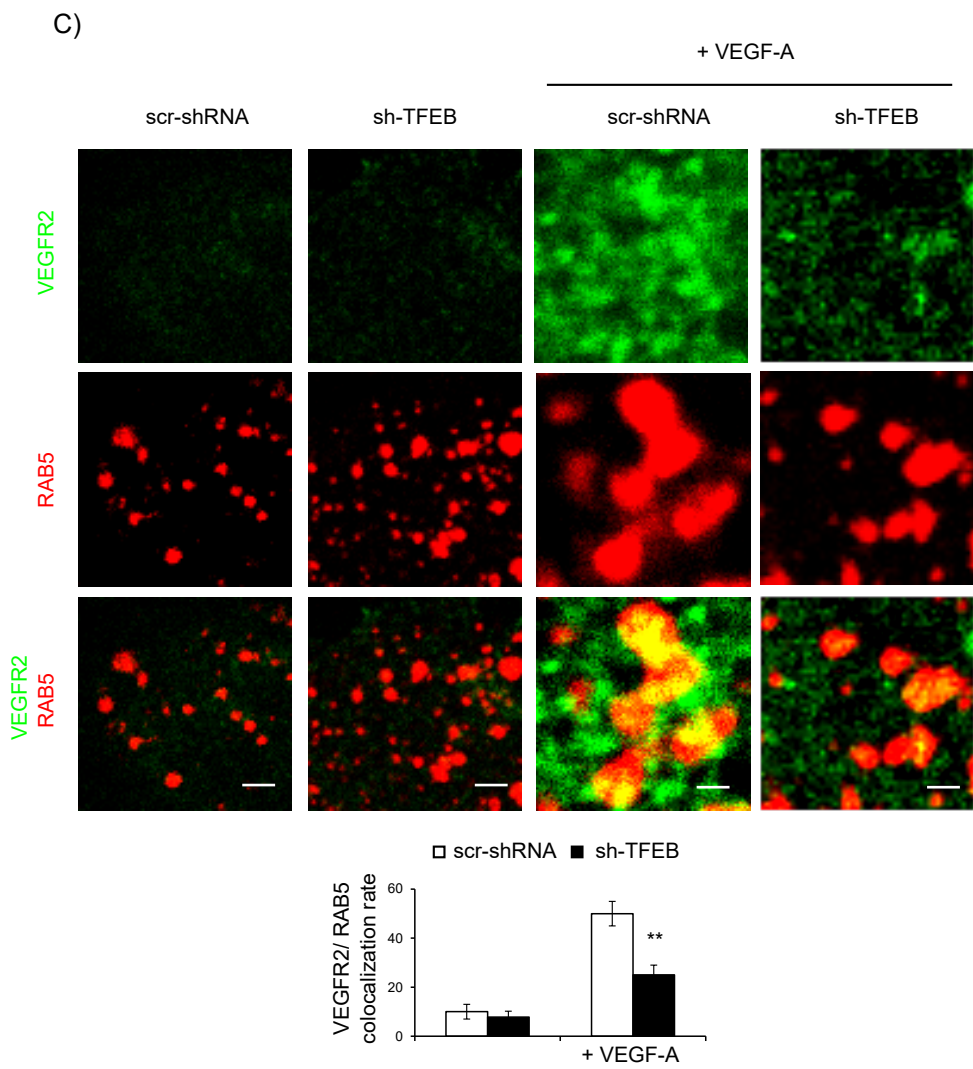
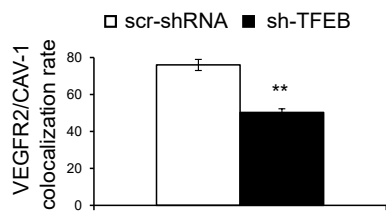
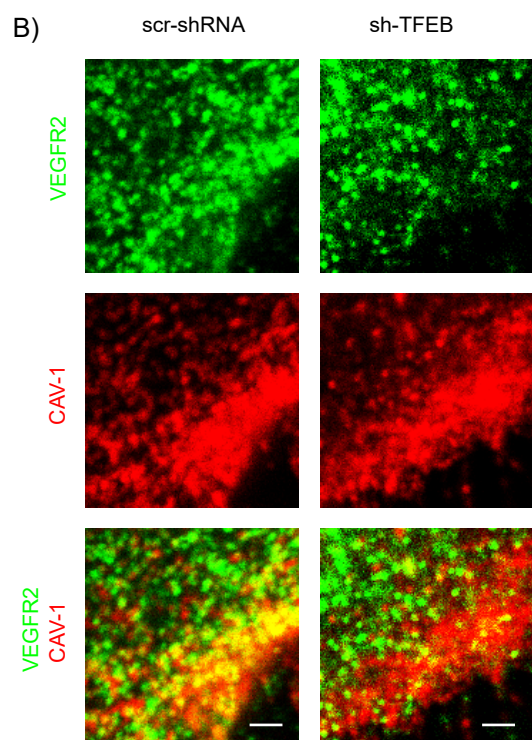
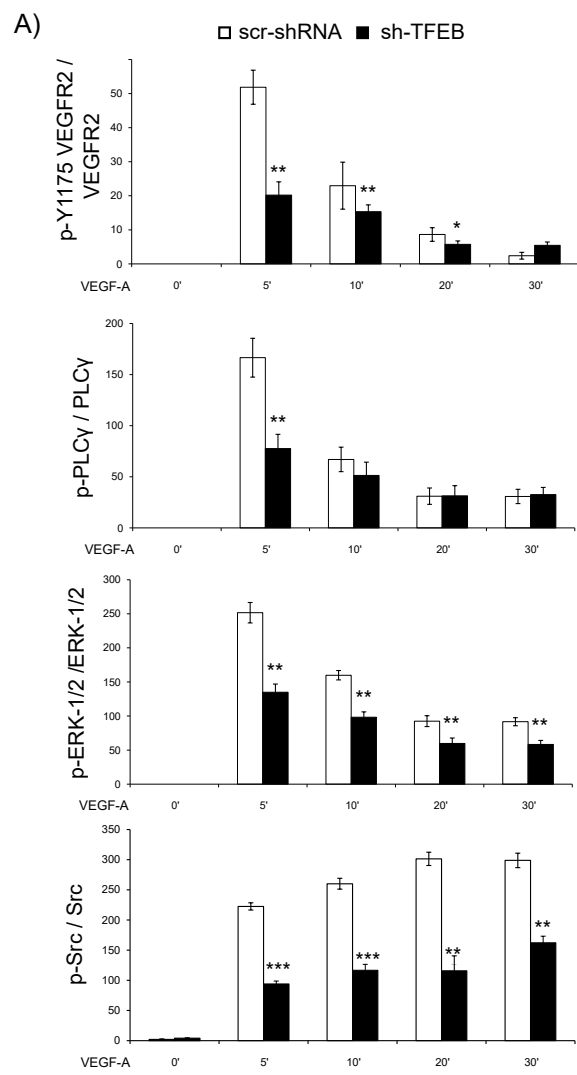
Appendix figure S1

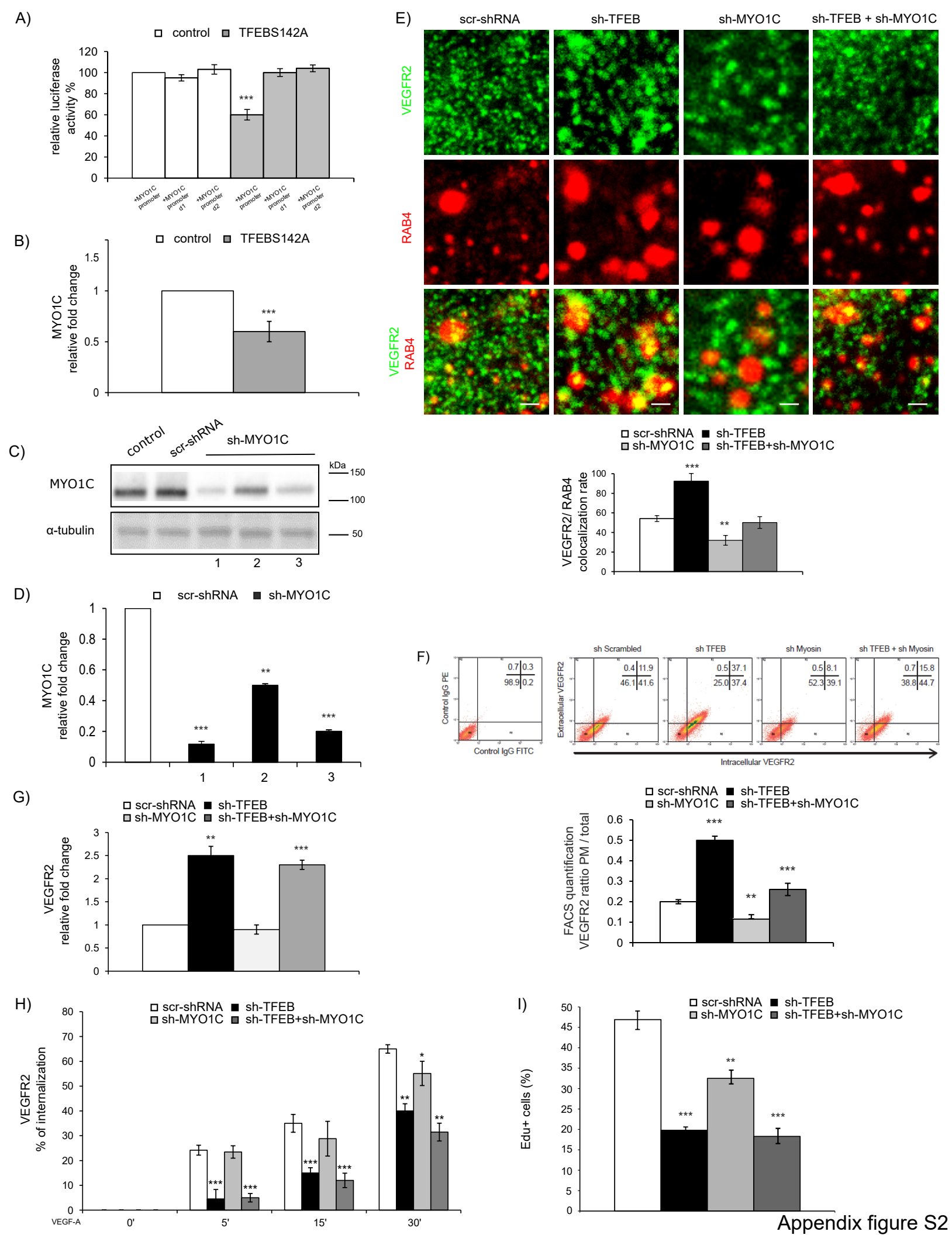
Appendix figure S2

Appendix figure S3

Appendix figure legends

Appendix material and methods

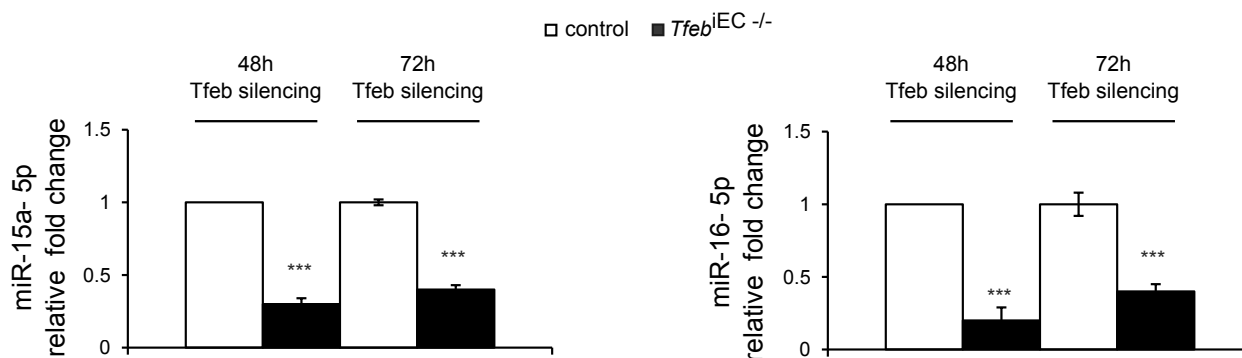




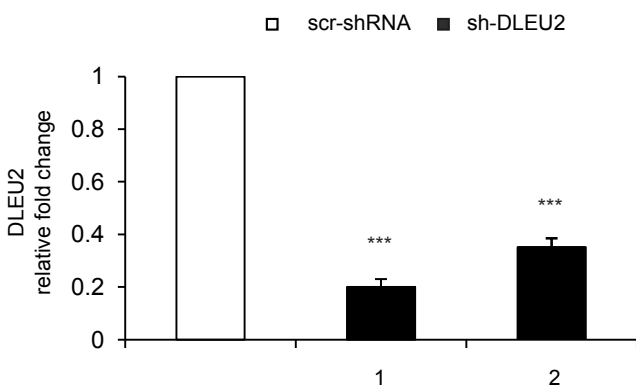
A)

microRNA name	Pre-miRNA considered	Function	Intragenic	Host gene	Same strand with respect to the host gene	VEGFR2 validated target	Significant TFEB binding peak(s) in the putative core promoter region of the host gene
miR-126	mir-126	ANGIOGENESIS	yes	ENSG00000172889, EGFL7	yes	no	
miR-218	mir-218-1	ANGIOGENESIS	yes	ENSG00000145147, SLIT2	yes	no	
	mir-218-2	ANGIOGENESIS	yes	ENSG00000184347, SLIT3	yes	no	
miR-17/18/20	MIR17HG (miR-17-92 cluster host gene)	ANGIOGENESIS	no				
	MIR18B / MIR20B cluster	ANGIOGENESIS	no				
	MIR18B / MIR20B cluster	ANGIOGENESIS	no				
miR-19a	MIR17HG (miR-17-92 cluster host gene)	ANGIOGENESIS	no				
miR-92a	MIR17HG (miR-17-92 cluster host gene)	ANGIOGENESIS	no				
miR-23/27	MIR23A / MIR27A / MIR24 cluster	ANGIOGENESIS	no				
	MIR23A / MIR27A / MIR24 cluster	ANGIOGENESIS	no				
miR-24	MIR23A / MIR27A / MIR24 cluster	ANGIOGENESIS	no				
	MIR3074 (MIR-24-1 precursor)	ANGIOGENESIS	no				
miR-16/424	MIR16-1	MICRORNA MODULATED BY ANGIOGENIC FACTORS	yes	ENSG00000231607, DLEU2	yes	yes	yes
	MIR15B / MIR16-2 cluster	MICRORNA MODULATED BY ANGIOGENIC FACTORS	yes	ENSG00000113810, SMC4	yes	yes	no
	MIR503HG / MIR450 / MIR542 cluster	MICRORNA MODULATED BY ANGIOGENIC FACTORS	no				
miR-132	MIR132	MICRORNA MODULATED BY ANGIOGENIC FACTORS	no				
miR-221/22	MIR221 / MIR222 cluster	MICRORNA MODULATED BY ANGIOGENIC FACTORS	yes	ENSG00000270069, RP6-99M1.2	yes	no	
miR-210	MIR210HG cluster	ISCHEMIA-INDUCED microRNAs	no				
miR-503	MIR503HG / MIR450 / MIR542 cluster	ISCHEMIA-INDUCED microRNAs	no				
miR-424	MIR503HG / MIR450 / MIR542 cluster	ISCHEMIA-INDUCED microRNAs	no				
miR-21	MIR21	microRNAs IN ENDOTHELIAL PROGENITOR CELLS	no				
miR-217	MIR217	microRNAs INVOLVED IN SENESCENCE	yes	ENSG00000226702, C011306.2	no		
miR-146a	MIR146A	microRNAs INVOLVED IN SENESCENCE	no				
miR-497	MIR497HG	Tu et al. 2015	yes	ENSG00000267047, RP11-589P10.7	yes	no	

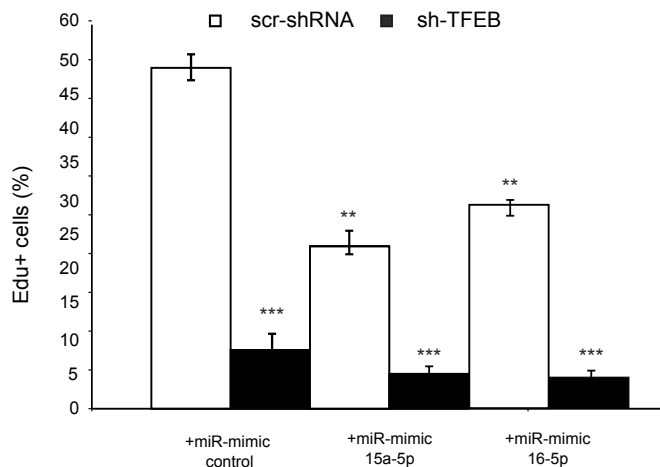
B)



C)



D)



## APPENDIX FIGURE LEGENDS

### Appendix figure S1. TFEB silencing and VEGFR2 activity and localization in human ECs.

(A) Densitometric analysis of immunoblot of total lysates from human scr-shRNA and sh-TFEB ECs (after VEGF-A stimulation, 30 ng/ml) probed with anti-pY1175 VEGFR2, anti-VEGFR2, anti-PLC $\gamma$ , anti-p-PLC $\gamma$ , anti-ERK-1/2, anti-p-ERK1/2, anti-p-Src, anti-Src and anti- $\alpha$ -tubulin Abs. The bar graphs show the densitometric analyses after normalization with  $\alpha$ -tubulin as ratio of p-Y1175 (n=3, mean $\pm$ SEM; ANOVA p<0.0001; \*p<0.001 and \*\*p<0.001 *versus* scr-shRNA by Bonferroni post-test), p-PLC $\gamma$  (n=3, mean $\pm$ SEM; ANOVA p<0.0001; \*\*p<0.001 *versus* scr-shRNA by Bonferroni post-test), p-ERK-1/2 (n=3, mean $\pm$ SEM; ANOVA p<0.0001; \*\*p<0.0001 *versus* scr-shRNA by Bonferroni post-test), p-Src (n=3, mean $\pm$ SEM; ANOVA p<0.0001; \*\*p<0.0001 and \*\*\*p<0.0001 *versus* scr-shRNA by Bonferroni post-test) *versus* total VEGFR2, PLC $\gamma$ , ERK-1/2 and Src.

(B) *TFEB* silencing alters VEGFR2 localization into caveolae in human ECs. Representative immunofluorescence images of human scr-shRNA and sh-TFEB ECs after staining with anti-VEGFR2 and anti-CAV-1 Abs (scale bar: 10  $\mu$ m). Bar graphs show the colocalization rate of VEGFR2 and CAV-1 (n=40, mean $\pm$ SEM; \*\*p<0.0001 *versus* scr-shRNA by Student's *t*-test).

(C) *TFEB* silencing alters VEGFR2 localization into Rab5+ endosomes in human ECs. Representative immunofluorescence images of antibody feeding assay with anti-VEGFR2 and anti-Rab5 Abs (scale bar: 10  $\mu$ m) in absence or presence of VEGF-A (30 ng/ml) stimulation. Bar graphs show the colocalization rate of VEGFR2 and Rab5 in human scr-shRNA and sh-TFEB ECs (n=15, mean $\pm$ SEM; \*\*p<0.0001 *versus* scr-shRNA by Student's *t*-test).

(D) *TFEB* silencing and VEGFR2 localization into Golgi in human ECs. Representative immunofluorescence images of VEGFR2 and Golgi colocalization in human scr-shRNA and sh-*TFEB* ECs obtained by staining with anti-VEGFR2 and anti-TGN46 Abs (scale bar: 10  $\mu$ m). Bar graphs show the colocalization rate of VEGFR2 and TGN46 (n=15, mean $\pm$ SEM; p=ns *versus* scr-shRNA by Student's *t*-test).

### **Appendix figure S2. Role of *MYO1C* silencing on *TFEB* effects in ECs.**

(A) Analysis of *TFEB* modulation of *MYO1C* promoter in human ECs. Bar graph shows the relative luciferase activity % evaluated in control and *TFEB*S142A human ECs after transfection of *MYO1C* promoter, *MYO1C* promoter d1 and *MYO1C* promoter d2 (n=3, mean $\pm$ SEM; \*\*\*p<0.0001 by Student's *t*-test).

(B) qPCR of *MYO1C* expression in control and *TFEB*S142A human ECs. Data are expressed as relative fold change compared with the expression in control ECs after normalization to the housekeeping gene TBP (n=3, mean $\pm$ SEM; \*\*\*p <0.0001 by Student's *t*-test).

(C,D) Characterization of *MYO1C* shRNA (n=3). (C) Western blot of *MYO1C* in human ECs carrying 3 different commercial sh-*MYO1C* RNAs (1-3) or the appropriate control (scr-shRNA) transduced by pLKO lentivirus vector. (D) *MYO1C* mRNA expression analyzed by qPCR in ECs carrying the different *MYO1C* shRNAs (1-3). Data are expressed as relative fold-change compared with scr-shRNA after normalization to the housekeeping gene TBP (n=3, mean $\pm$ SEM; \*\*p<0.001, \*\*\*p<0.0001 by Student's *t*-test).

(E) *TFEB* silencing and VEGFR2 localization into Rab4+ endosome in human ECs. Representative immunofluorescence images of VEGFR2 and Rab4 colocalization obtained by scr-shRNA, sh-*TFEB*, sh-*MYO1C* and sh-*TFEB*+sh-*MYO1C* human ECs staining with anti-VEGFR2 and anti-Rab4 Abs (scale bar: 10  $\mu$ m). Bar graphs show the colocalization

rate of VEGFR2 and Rab4 (n=15, mean±SEM; \*\*p <0.001, \*\*\*p <0.0001 *versus* scr-shRNA by Student's *t*-test).

(F) Cell distribution of VEGFR2. FACS analysis with anti-VEGFR2 antibody was performed in scr-shRNA, sh-TFEB, sh-MYO1C and sh-TFEB+sh-MYO1C human ECs. 1 representative experiment out of 3; % of the extracellular and intracellular protein is indicated). Data are expressed as ratio PM and total VEGFR2 (n=3, mean±SEM; \*\*p<0.001 and \*\*\*p<0.0001 by Student's *t*-test).

(G) qPCR of *VEGFR2* expression in scr-shRNA, sh-TFEB, sh-MYO1C and sh-TFEB+sh-MYO1C human ECs. Data are expressed as relative fold change compared with scr-shRNA ECs after normalization for housekeeping gene TBP (n=3, mean±SEM; \*\*p<0.001 and \*\*\*p<0.0001 by Student's *t*-test).

(H) *MYO1C* silencing does not modify VEGFR2 internalization. Bar graph of VEGFR2 internalization expressed as the percent of internalized VEGFR2 *versus* PM VEGFR2 after VEGF-A stimulation in scr-shRNA, sh-TFEB, sh-MYO1C and sh-TFEB+sh-MYO1C human ECs (n=6, mean±SEM, ANOVA p<0.0001; \*p<0.0001, \*\*p<0.0001 and \*\*\*p<0.0001 *versus* scr-shRNA by Bonferroni post-tests).

(I) *MYO1C* silencing does not modified EC proliferation. Representative graph of scr-shRNA, sh-TFEB, sh-MYO1C and sh-TFEB+sh-MYO1C human ECs treated for 24 hours with VEGF-A (30 ng/ml). DNA incorporation of EdU was detected by flow cytometry. The percentage of proliferating cells is indicated (n=4, mean±SEM; \*\*p<0.001, \*\*\*p<0.0001 *versus* scr-shRNA ECs by Student's *t*-test).

### **Appendix figure S3. *TFEB* indirectly regulates VEGFR2 expression**

(A) Table of angiogenesis-associated miRs and their correlation with TFEB in ECs.

(B) Expression of miR-15a and 16 isoforms in by qPCR (n=3, mean±SEM). *Tfeb* deletion in murine ECs down-regulates miR-15a-5p and miR-16-5p. qPCR of miR-15a-5p and miR-16-

5p in lung ECs obtained from control and *Tfeb*<sup>EC-/-</sup> mice in which *Tfeb* was silenced for 48h or 72h by in vitro treatment with 4-OH-tamoxifene (5  $\mu$ M for 48 or 72 h). Data are expressed as relative fold-change compared with the expression in ECs derived from control mice after normalization to the housekeeping gene U6 (n=3, mean $\pm$ SEM; \*\*\*p<0.0001 by Student's *t*-test).

(C) Characterization of DLEU2 shRNA (n=3). *DLEU2* mRNA expression analyzed by qPCR in human ECs carrying 2 different commercial sh-DLEU2 RNAs (1,2) or the appropriate control (scr-shRNA) transduced by pLKO lentivirus vector. Data are expressed as relative fold-change compared with scr-shRNA after normalization to the housekeeping gene TBP (n=3, mean $\pm$ SEM; \*\*\*p<0.0001 by Student's *t*-test).

(D) miR15a-5p and miR-16-5p not modified EC proliferation after TFEB silencing. Representative graph of human scr-shRNA, sh-TFEB ECs proliferation after transduction with miR-control, miR-15a-5p and miR-16-5p mimics and after stimulation with VEGF-A (30 ng/ml, 24h). DNA incorporation of EdU was detected by flow cytometry. The percentage of proliferating cells is indicated (n=4, mean $\pm$ SEM; \*\*p<0.0001, \*\*\*p<0.0001 *versus* scr-shRNA ECs



## Appendix Material and Methods

### *Reagents*

Wizard SV Genomic DNA Purification System, GoTaq G2 Hot Start Polymerase and The Dual-Luciferase® Reporter (DLR™) Assay System (Promega Corporation); Dynabeads Protein G, Power SYBR Green PCR Master Mix, Phusion Site-Directed Mutagenesis Kit, Lipofectamine® RNAiMAX Reagent, Click-iT® EdU Flow Cytometry Cell Proliferation Assay, Illumina TotalPrep RNA Amplification Kit, pMCS-CypridiLuc\_AC167\_MYO1C\_promoter, pMCS-CypridiLuc\_AC167\_MYO1C\_promoter\_d1 pMCS-CypridiLuc\_AC167\_MYO1C\_promoter\_d2, pMCV-GreenReLuc, Lipofectamine® RNAiMAX Reagent, Cypridina Luciferase Glow Assay Kit, Pierce Renilla Luciferase Glow Assay Kit, High Capacity cDNA Reverse Transcription kit, Taqman PCR Universal MasterMix, Taqman assays, SYBR GreenER kit, EZ-Link™ Sulfo-NHS-SS-Biotin, Maxisorp 96-well plates, phalloidin-555 and DAPI (Thermo Fisher Scientific); shRNA against *DLEU2* (Dharmacon); mirVana™ miRNA control and inhibitors or mimics (Ambion); hypoxyprobe-1-FITC-conjugated antibody (Chemicon); collagenase/dispase (Roche); miRNeasy Mini Kit and QIAquick PCR Purification Kit (Qiagen); NextSeq 500 Illumina sequencer and HumanHT-12 v4.0 Expression Bead Chip GenomeStudio software V2011.01 (Illumina); NEBNext® CHIP-Seq Library Prep Reagent Set for Illumina (New England Biolabs); CDK4-luciferase full length and CDK4-luciferase fragment A (Addgene); IntraPrep kit (Beckman Coulter); IgG (12-370, Millipore); human VEGF-A (R&D System); streptavidin-agarose beads (Upstate Biotechnology), Growth Factor Reduced Matrigel (Corning). Other reagents, if not indicated, were from Sigma Aldrich.

### *Mouse genotyping*

Mouse genotypes were analyzed by PCR with genomic DNA from yolk sacs, embryos and tail samples. DNA was extracted using the Wizard SV Genomic DNA Purification System. PCR reactions were performed using appropriate primers for specific PCR samples with a commercial kit (GoTaq G2 Hot Start Polymerase). The following primers used for genotyping:

Tfeb: 5'-CAGCCCCTTACCAGCGTCCC-3' and 5'-GGGTGCAATCTAATCAGGGGGC-3';

Tfeb delta allele: 5'-GTAGAACTGAGTCAAGGCATACTGG-3' and 5'-GGGTGCAATCTAATCAGGGGGC-3';

Cdh5-Cre-ER<sup>T2</sup>: 5'-GCCTGCATTACCGGTCGATGCAACGA-3' and 5'-GTGGCAGATGGCGCGGCAACACCATT-3';

Tie2-Cre: 5'-GCCTGCATTACCGGTCGATGCAACGA-3' and 5'-GTGGCAGATGGCGCGGCAACACCATT-3';

Tfeb-EGFP: 5'-CTGTATAGCACTGGCTCTGTAGACC-3' and 5'-GGTGGTGGGAATGGAAACC-3'.

### *Real-time PCR*

Extracted RNA was converted to cDNA using a High Capacity cDNA Reverse Transcription kit. Real-time PCR was performed on a CFX96 system (Bio-Rad) using Taqman PCR Universal MasterMix and specific Taqman assays. Experiments were performed in triplicate. TBP, RNU44 and U6 were used as reference genes.

The following Taqman assays were used: TFEB (human, Hs00292981\_m1, mouse, Mm00448968\_m1); CDK4 (human Hs00364847\_m1, mouse Mm00726334\_s1); E2F2 (human Hs00918090\_m1, mouse Mm01192124\_m1); E2F4 (human Hs00608098\_m1, mouse Mm01247763\_m1), E2F1 (human Hs00153451\_m1, mouse Mm00432939\_m1); CCNA1 (human Hs00171105\_m1); CCNA2 (human Hs00996788\_m1); CCNE2 (human

Hs00180319\_m1); CDCA4 (human Hs00937497\_s1); CDCA7 (human Hs00230589\_m1); CDT1 (human Hs00925491\_g1, mouse Mm00466006\_m1); CDC25B (human Hs01582335\_m1); CDCA5 (human Hs00969392\_g1); PCNA (human Hs00427214\_g1, mouse Mm00448100\_g1); VEGFR2 (human Hs00911700\_m1, mouse Mm01222421\_m1); DLEU2 (human Hs00863925\_m1, mouse Mm01319189\_m1); MYO1C (Hs00300761\_m1); miR-15a-3p (002419); miR-15a-5p (000389); miR-16-1-3p (002420); miR-16-5p (000391); TBP (human Hs00427620, mouse Mm\_00446971); RNU44 (001094); and U6 (001973).

For the ChIP experiments, immunoprecipitated DNA was analyzed by qPCR using a SYBR GreenER kit. The oligonucleotide sequences of the gene promoters were as follows: VEGFR2 5'- CCAACGAAGAGCCCTAGTGA-3' and 5'-ACCAGAAGGAACGAATGTGG-3'; DLEU2 5'-TTTGTGCAGTTTCAGCAAAG-3' and 5'-CTGTGTACTIONTAGGTCGTGTG-3'; and SMC4 5' CTGAAGAGGCGTTTCTGGAC-3' and 5'-GGAAGAGCGAGGGATTCTTT-3'; CDK4 5'- TGTGATAGCAACAGATCACG-3' and 5'- GTTCCTACGGCCCCATAC-3'.

## DEGs shTFEB vs scr-shRNA ECs

ID	logFC	P.Value	adj.P.Val
SRM	-2,048792018	3,43093E-08	0,000302239
SRP72	-1,798388784	3,86841E-08	0,000302239
APEX2	-1,635916211	5,81363E-08	0,000302813
TMEM123	-1,463902393	8,01245E-08	0,000313006
FAF2	-1,476758216	1,02001E-07	0,000318773
AES	-1,520757255	2,47114E-07	0,000643568
GRN	-1,389650848	4,73527E-07	0,000940215
DCXR	-1,556828299	4,81359E-07	0,000940215
MLLT6	-1,17956	7,55622E-07	0,001311928
LSM12	-1,193611561	8,85449E-07	0,001383603
ITGA5	-1,577157949	1,12944E-06	0,001452066
SLC25A22	-1,211121829	1,12981E-06	0,001452066
MKRN1	-1,169573453	1,22351E-06	0,001452066
KATNB1	-1,144669628	1,30097E-06	0,001452066
SAC3D1	-1,361511204	2,17313E-06	0,001987978
SLC7A5	-1,407839591	2,2019E-06	0,001987978
STK40	-1,191393782	2,20258E-06	0,001987978
AURKA	-1,421079127	2,3009E-06	0,001987978
NINJ1	-1,073818038	2,41723E-06	0,001987978
CCL2	2,1788295	2,70455E-06	0,002035279
CDK4	-1,114917257	2,73524E-06	0,002035279
DDX56	-1,055534286	2,94329E-06	0,002090537
HS.497591	-1,346550647	3,62869E-06	0,002465304
PIK3R2	-0,997017945	4,15448E-06	0,002689756
RAPGEF1	-1,019256046	4,30333E-06	0,002689756
SUV39H1	-1,458253426	4,58045E-06	0,002752851
NADK	-0,965808911	5,06905E-06	0,002874269
PABPC4	-1,034765446	5,15036E-06	0,002874269
SERBP1	-1,03870265	5,52742E-06	0,002978324
PI4KB	-1,031815092	5,97087E-06	0,003110026
MED16	-1,071761688	6,40902E-06	0,003230559
GTSE1	-1,419308994	7,00759E-06	0,003319763
CCM2	-0,910036894	7,09909E-06	0,003319763
SMPD1	-1,147274178	7,22334E-06	0,003319763
ADRBK1	-1,252214372	7,82215E-06	0,003362352
PPP1R14B	-1,186202359	7,83774E-06	0,003362352
GATAD2A	-0,97274953	7,96154E-06	0,003362352
ATP1B1	-1,300485223	8,31667E-06	0,003419903
CTDSP2	-1,212830248	8,9398E-06	0,003581881
SRPR	-1,326488384	9,28835E-06	0,003628492
RND1	1,087003757	1,01877E-05	0,003720105
DCP2	1,100967768	1,04244E-05	0,003720105
TBC1D13	-1,08278976	1,0444E-05	0,003720105
TK1	-1,68538161	1,04751E-05	0,003720105
CHMP1A	-1,063622295	1,21288E-05	0,004199097
PLAGL2	-0,97492323	1,23614E-05	0,004199097
PPIH	-1,64245125	1,30262E-05	0,004330786
CDCA7	-1,127405774	1,60971E-05	0,005240279
SMTN	-1,378699382	1,7533E-05	0,005591237
VCP	-0,974352274	1,90232E-05	0,005852942
TMED7	-0,836836862	2,0078E-05	0,005852942
PPRC1	-1,017780436	2,03406E-05	0,005852942
PNPLA2	-0,94727156	2,08495E-05	0,005852942
CDCA4	-1,164262677	2,09123E-05	0,005852942

## DEGs shTFEB vs scr-shRNA ECs

NFYC	-0,813214193	2,12859E-05	0,005852942
VIP	0,955743393	2,14998E-05	0,005852942
EIF1	-0,849085663	2,16226E-05	0,005852942
NCKIPSD	-0,944030878	2,20336E-05	0,005852942
C22ORF13	-0,912378449	2,20993E-05	0,005852942
HMG2	-1,13688005	2,30385E-05	0,005909145
EFNA1	1,141635859	2,30678E-05	0,005909145
CHAF1A	-0,945927579	2,39162E-05	0,006027656
DTL	-1,0689881	2,49134E-05	0,006151622
NDUFV1	-0,914701986	2,51954E-05	0,006151622
RPL28	-1,196885225	2,58268E-05	0,006162487
ALDH1A2	-1,418065819	2,64668E-05	0,006162487
AQP11	0,901604997	2,66898E-05	0,006162487
CCDC106	-0,936042892	2,68174E-05	0,006162487
MAP4K2	-0,991633393	2,9882E-05	0,006767191
ATG9A	-1,10103488	3,16352E-05	0,007021814
TRMT5	-1,187843246	3,19051E-05	0,007021814
CRKL	-0,814597117	3,29741E-05	0,007156304
MCM10	-1,048034148	3,36612E-05	0,00715909
FOX1	-1,624621026	3,40676E-05	0,00715909
CDC25B	-1,43870005	3,47582E-05	0,00715909
DCAF7	-0,791732291	3,55549E-05	0,00715909
HS.531457	-0,948127552	3,56949E-05	0,00715909
SF3A1	-0,899349565	3,57359E-05	0,00715909
FAM189B	-1,006805512	3,67331E-05	0,007181444
C19ORF56	-1,138452606	3,67666E-05	0,007181444
SCARB1	-0,951729627	3,84718E-05	0,007357934
MRPL4	-0,910678794	3,90271E-05	0,007357934
DDIT4	1,164906477	3,90828E-05	0,007357934
DPH2	-0,797545052	4,01061E-05	0,007460688
CKS1B	-1,183338624	4,11297E-05	0,007561093
CABLES2	-1,04765184	4,22455E-05	0,007675908
PDXP	-0,782004966	4,70595E-05	0,00845232
PMP22	-0,911630789	4,98439E-05	0,008771219
MCM3	-1,109383359	4,99577E-05	0,008771219
TP53INP1	1,19356065	5,42498E-05	0,009418967
LCOR	0,770870502	5,66489E-05	0,009727429
SNORA61	-1,074424416	6,21235E-05	0,010551537
YPEL5	0,929222233	6,36344E-05	0,010691945
C16ORF35	-0,908978561	6,68859E-05	0,011047487
TRABD	-0,826185464	6,71644E-05	0,011047487
NBL1	-1,114837899	6,79181E-05	0,011055087
TAF4	-0,869087058	6,98507E-05	0,011252441
PRMT2	-0,770355609	7,45548E-05	0,011724329
SORBS3	-0,87255715	7,47653E-05	0,011724329
FNBP1L	0,835082276	7,50309E-05	0,011724329
SHISA5	-0,73945235	7,60455E-05	0,011765218
C8ORF55	-0,877995206	7,83106E-05	0,011996871
NUAK1	0,869221521	8,06753E-05	0,012239145
SNORA24	-1,042036396	8,16722E-05	0,012271244
NECAP2	0,817437227	8,57232E-05	0,012654884
PAQR4	-1,035256163	8,58452E-05	0,012654884
POLM	-0,87467634	8,95771E-05	0,012977878
ETV4	-1,137847047	8,96974E-05	0,012977878
TOMM34	-0,82762865	9,09274E-05	0,013035152

## DEGs shTFEB vs scr-shRNA ECs

CDT1	-1,183425387	9,51937E-05	0,013418629
IL1A	0,968163888	9,53198E-05	0,013418629
NAT15	-0,869349459	9,73317E-05	0,013579509
CAMK2N1	-1,047499045	9,91743E-05	0,013600312
ZDHHC8	-0,700895549	9,92215E-05	0,013600312
C17ORF53	-1,024053807	0,000103552	0,014070489
IMPDH1	-0,72569461	0,000109437	0,014741945
NSUN4	-0,748967007	0,000111871	0,014940949
CRIP2	-0,67836923	0,000114246	0,0151289
SLC35A4	-0,820678074	0,000117008	0,015364468
CLDND1	-0,75987455	0,000121556	0,015828596
E2F4	-0,74085311	0,000132537	0,017013333
SEMA4D	-0,829990326	0,000132832	0,017013333
C2ORF34	-0,680801634	0,00013415	0,017042551
MAML1	-0,765076679	0,000135707	0,017101322
TCF3	-0,984123207	0,000140521	0,01743263
JOSD1	-0,79588689	0,000140568	0,01743263
HOXA9	0,82703235	0,000143308	0,017632508
ZNF323	0,888189599	0,000146483	0,017882365
BCL9L	-0,668732616	0,000151403	0,01833975
C15ORF52	0,902958545	0,000152718	0,018356705
UBE2L3	-0,889476863	0,000157714	0,018521701
PGM2L1	1,283633547	0,000157765	0,018521701
FKBP5	-0,703566758	0,000159114	0,018521701
THAP10	-1,045048606	0,000161149	0,018521701
BCL7C	-0,964819797	0,000163835	0,018521701
AMPH	-1,081372295	0,000163962	0,018521701
ATP1B3	-0,711173901	0,000164021	0,018521701
GOLPH4	-0,83544388	0,000164681	0,018521701
RARA	-0,793619866	0,00016497	0,018521701
RIC8A	-0,79015518	0,000165944	0,018521701
MMS19	-0,799418379	0,000177054	0,019621598
SLC39A14	-0,809326305	0,000180271	0,01983743
FURIN	-0,934750255	0,000189833	0,02074359
UHRF1	-1,251405683	0,000197252	0,021299082
STARD7	-0,676233055	0,000198311	0,021299082
RRS1	-0,680247713	0,000199006	0,021299082
GGA3	-0,784333634	0,000202623	0,021469636
ANGPTL4	0,675234502	0,000205221	0,021469636
PITPNM1	-0,953760006	0,000205587	0,021469636
EVI5L	-0,955332189	0,000206416	0,021469636
PIP5K1C	-0,84560007	0,000207469	0,021469636
N-PAC	-0,855251594	0,000211971	0,021791177
IQGAP1	-0,747262143	0,000224974	0,022976713
ARSD	0,938904433	0,000227048	0,023037977
FBXO32	1,002322379	0,000233124	0,023386411
CGNL1	-0,689521196	0,000235533	0,023386411
B3GALT6	-1,050678158	0,000235905	0,023386411
FANCE	-0,703920945	0,000236468	0,023386411
MIER2	-0,943332617	0,000241397	0,023614395
TMUB1	-0,731564914	0,000241796	0,023614395
FOSL1	-0,925512821	0,000243752	0,023657547
MBD6	-0,766739091	0,000250754	0,02418688
C16ORF62	-0,68563587	0,000259342	0,024861853
UBE3B	-0,877541711	0,000261021	0,024870162

## DEGs shTFEB vs scr-shRNA ECs

C8ORF4	1,233622599	0,000264237	0,025024
ATP2B4	-0,754716425	0,000266143	0,025052695
TBC1D24	-0,796386688	0,000274942	0,025590941
E2F2	-1,529487625	0,000276671	0,025590941
HS.12876	0,62202864	0,000278483	0,025590941
ATAD2	-0,772582644	0,000279662	0,025590941
DENND4B	-0,929900808	0,000280465	0,025590941
MCM2	-1,107721701	0,000283072	0,025590941
PABPN1	-0,764026637	0,000283736	0,025590941
STARD10	0,815160178	0,000284962	0,025590941
TROAP	-0,895352426	0,000290017	0,025895995
C20ORF117	-0,856538866	0,000293277	0,026038301
CDC42EP4	-0,637752489	0,000296411	0,026167871
CBFB	-0,735476492	0,000299438	0,026286626
CHMP7	-0,684665515	0,0003111	0,027077213
CLIP3	0,820975026	0,00031191	0,027077213
PLSCR4	1,073065886	0,000321	0,02771245
CCDC24	0,694605482	0,000332913	0,028527785
ITPR1	0,710729766	0,000335016	0,028527785
FAM65A	-0,639798005	0,000335922	0,028527785
DHX34	-0,624511601	0,00034	0,02857247
STEAP3	-0,931998761	0,000340105	0,02857247
FKBP9L	-0,914016636	0,000344886	0,02879173
CKAP5	-0,715885951	0,0003464	0,02879173
MGAT1	-0,824527113	0,000355974	0,029298374
HBP1	0,693615635	0,000356245	0,029298374
SLC25A39	-0,641872702	0,000360684	0,029447856
KPNA5	0,616296202	0,000363157	0,029447856
ADCY3	-0,819444123	0,000366521	0,029447856
PTGS2	0,653987691	0,000366522	0,029447856
ARHGAP23	-0,938474172	0,000367486	0,029447856
TRAF7	-0,760695051	0,000369437	0,029453202
SENP5	-0,625538502	0,000374767	0,029535321
MMS19L	-0,656348277	0,000375212	0,029535321
ANKRD46	0,814371375	0,000376174	0,029535321
MCM6	-0,83658405	0,000378028	0,029535321
RPAP1	-0,865939413	0,000383564	0,029818797
ZNF672	-0,728983318	0,000389911	0,030162113
SNHG1	-0,809035356	0,000393304	0,030201293
ECE2	-0,65352121	0,000394283	0,030201293
HS.154948	-0,64177816	0,00040076	0,030547693
GMNN	-0,754760547	0,00040309	0,0305761
USP1	-0,726981001	0,000406222	0,03066482
SLC40A1	0,803848478	0,000424054	0,031758236
KLHDC8B	0,761608329	0,000424771	0,031758236
RFC3	-0,82318453	0,00042952	0,031960365
BTBD2	-0,701349347	0,000438877	0,032501893
RPUSD3	-0,605781455	0,000444223	0,032742614
CCNA2	-0,780543298	0,000481009	0,035287528
LMNB2	-0,893208573	0,000486753	0,035355919
C16ORF59	-0,939073131	0,00048678	0,035355919
RAD51AP1	-0,633939371	0,000488729	0,035355919
TYRO3	-0,769766678	0,000493132	0,035510021
BLM	-0,775214512	0,000503305	0,036076358
ARHGDI1A	-0,662037311	0,000520057	0,037106914

## DEGs shTFEB vs scr-shRNA ECs

CDCA1	-0,700941462	0,00052414	0,037204848
MED22	-0,621066118	0,000526192	0,037204848
ERBB2	-0,753999774	0,000535353	0,037682124
CASP3	0,684048349	0,000548415	0,0384284
C7ORF49	-0,592978946	0,000555526	0,038752879
GABARAPL1	0,96587899	0,000562632	0,038979478
CYB561	-0,562828928	0,000565701	0,038979478
SLC35D2	0,645896975	0,000566258	0,038979478
HS.355933	-0,943410705	0,000572571	0,039081415
MSH6	-0,776341042	0,00057762	0,039081415
POLE2	-0,787709216	0,000583947	0,039081415
ULK1	-0,696346778	0,00058492	0,039081415
HOXD1	0,750602201	0,000587704	0,039081415
C14ORF124	-0,976155483	0,000591466	0,039081415
LACTB	0,808518754	0,000598794	0,039081415
GATA2	-0,557246422	0,000598926	0,039081415
ARL2	-0,641525518	0,000599315	0,039081415
HHEX	0,599360458	0,000600123	0,039081415
PFAS	-0,73538971	0,000600312	0,039081415
PRC1	-0,686294152	0,000602452	0,039081415
CLCN7	-0,612677939	0,000608427	0,039081415
RNF4	-0,564717448	0,000610052	0,039081415
STC1	-0,653940172	0,00061706	0,039081415
C9ORF140	-0,889000893	0,000618042	0,039081415
AP1B1	-0,886856406	0,000618324	0,039081415
BSDC1	0,624105685	0,000619661	0,039081415
SNORD99	-0,650369835	0,000621644	0,039081415
CTSB	-0,585711249	0,000622138	0,039081415
PLXNA1	-0,610262614	0,000622342	0,039081415
SLC10A3	-0,852604469	0,000625021	0,039081415
OAZ2	0,90427808	0,000625263	0,039081415
RRM2	-1,026962242	0,000632305	0,039364125
PPP3CB	0,568563238	0,000637251	0,039485458
OTUB1	-0,651396911	0,000639308	0,039485458
RMI1	-0,643515049	0,000650417	0,039717231
SEPT9	-0,727506539	0,00065081	0,039717231
SLC25A10	-0,66043994	0,000652454	0,039717231
SLC45A1	0,623747392	0,000653227	0,039717231
POMT2	-0,572662066	0,000660506	0,040004133
TNFAIP1	-0,649595802	0,000663347	0,040021063
EPOR	-0,587156742	0,000666478	0,040055301
C5ORF53	0,601465382	0,000681113	0,040706414
GBAS	-0,594006615	0,000682952	0,040706414
SLC24A6	-0,672552824	0,000685127	0,040706414
RWDD2B	-0,579144355	0,000690771	0,040853873
FAM53C	-0,61204753	0,000693245	0,040853873
MCM4	-1,026338252	0,000696398	0,040853873
CDC45L	-1,02548563	0,000700464	0,040853873
ATF3	0,838360806	0,000702312	0,040853873
TNFSF12	-0,760234854	0,000705857	0,040853873
ZSCAN2	0,604382445	0,00070591	0,040853873
C19ORF48	-0,75627673	0,000715288	0,04124387
FEN1	-0,85132479	0,000719661	0,041343479
PPP1R12A	0,542438546	0,00073003	0,041785532
TRIM25	0,648460113	0,000734664	0,041897303



## DEGs shTFEB vs scr-shRNA ECs

KRT18P13	0,574446969	0,000740973	0,042103408
MYO9B	-0,664768666	0,000751189	0,042529252
DENND1A	0,642329466	0,000759174	0,042826196
NFKBIA	0,809271061	0,000770599	0,043253576
NR2C2AP	-0,680765305	0,000772286	0,043253576
HS.513971	-0,661813275	0,000779658	0,043459195
VRK3	0,615248144	0,00078152	0,043459195
MAPRE3	0,559176034	0,000787621	0,043643168
OPN3	-0,650949256	0,000795692	0,04366015
PLK2	0,708205011	0,000795925	0,04366015
DDB1	-0,590045569	0,00079911	0,04366015
C11ORF75	-0,790475881	0,000802037	0,04366015
TGIF1	0,743077741	0,000805051	0,04366015
GINS2	-0,890979811	0,000807378	0,04366015
TYMS	-0,628165459	0,000807486	0,04366015
LYRM5	-0,582657381	0,000811411	0,043721077
TRIP13	-0,720551328	0,000822551	0,044169029
POLR2D	-0,689340758	0,000834364	0,044649895
HS.143408	-0,657213082	0,000838287	0,044706757
MYLIP	0,625236226	0,000874317	0,046469677
SDHAF2	-0,599202946	0,000879062	0,046537177
CD320	-0,567518072	0,000881544	0,046537177
NCLN	-0,594933433	0,000887042	0,046669761
FAM149B1	0,627467513	0,000895985	0,046919253
MARCH2	0,554602985	0,000897789	0,046919253
FAM124B	0,871646741	0,000910764	0,047438678
C1ORF135	-0,776815702	0,000914214	0,047460134
NEDD4	0,635532899	0,000919313	0,047566818
ENG	-0,734350999	0,000926558	0,047783501
DDX31	-0,595882634	0,000972934	0,049943622
PLCG2	0,569831261	0,000974837	0,049943622
ZNF702P	0,705863176	0,000989942	0,05055173
ATN1	-0,567702717	0,001019179	0,051875209
SNX4	0,636388254	0,001024319	0,051967547
RAB11FIP2	0,629332564	0,001030294	0,052101544
KIF24	-0,777040293	0,001039973	0,052157369
ARSJ	-0,53326363	0,00104128	0,052157369
CARD10	-0,632077181	0,001041412	0,052157369
TMEM173	0,608618645	0,001059423	0,052889899
TUBA3D	-0,529597066	0,001065612	0,053029452
SAMD14	0,533558793	0,001069924	0,053075046
TSPAN18	-0,704535283	0,001076252	0,053219962
FBXL18	-0,596184634	0,00108685	0,053574484
SCRIB	-0,5818955	0,001094871	0,053800177
HIP1	-0,587075682	0,001102329	0,053954753
CCNA1	-0,726748207	0,001104923	0,053954753
DEK	-0,546375742	0,001133544	0,055030774
LRP8	-0,574416219	0,001134002	0,055030774
HS.374278	0,609211577	0,001140805	0,055189514
HSDL1	0,784674188	0,00115006	0,05540536
DNMT1	-0,739635935	0,001152358	0,05540536
PCNA	-0,585464858	0,00116412	0,055799206
SHOC2	0,543816546	0,001168099	0,05581872
C9ORF100	-0,576954869	0,001181089	0,056267361
ANKRD52	-0,75980976	0,001194041	0,0567115

## DEGs shTFEB vs scr-shRNA ECs

ZWILCH	-0,608436764	0,0012037	0,056997018
ECSCR	-0,524080557	0,001211598	0,057197686
KCNK6	-0,693827336	0,001217189	0,057288553
RAVER1	-0,714099126	0,001233919	0,057825707
FRAT2	0,571590088	0,001236003	0,057825707
ITGB3BP	-0,564114578	0,001243193	0,057905796
TESK1	-0,532435973	0,001246505	0,057905796
SESN1	0,820759625	0,001249913	0,057905796
FLJ40504	0,547577647	0,001252538	0,057905796
RRP12	-0,63590328	0,001262763	0,058036525
TXNDC9	0,639929104	0,001262794	0,058036525
ELMOD1	-0,750877878	0,001282172	0,058754316
PRRG1	0,660657214	0,001288698	0,058814398
EYA3	-0,542202365	0,001291011	0,058814398
CENPM	-0,991589226	0,001302324	0,059157306
KLHL24	0,820444946	0,001313781	0,0594146
RIPK2	0,600182522	0,001315593	0,0594146
DKFZP761P0423	-0,666129196	0,001320073	0,059445113
FNDC3A	0,628230969	0,001331678	0,059795413
CENPA	-0,788489523	0,001342447	0,060106237
ASF1B	-0,826764072	0,001363925	0,06089339
MCM5	-0,71425852	0,001374453	0,061188601
DHX37	-0,613303344	0,001386304	0,061540851
SNHG8	-0,898435875	0,001392399	0,061636336
PLK1	-0,669370782	0,001406249	0,062073569
CCNE2	-0,599297968	0,001417678	0,06240181
DUT	-0,766667572	0,0014243	0,062517161
RNF38	0,637137718	0,001443031	0,063161925
CHAF1B	-0,957004253	0,001466102	0,063861634
AURKB	-0,754641123	0,001467191	0,063861634
CPEB3	0,638879382	0,001478632	0,064019665
SMARCD1	-0,542408503	0,001483895	0,064019665
NLF2	0,576887605	0,001484544	0,064019665
DHCR24	-0,601780793	0,00148721	0,064019665
ZNF697	0,555114305	0,00150412	0,064569704
GPR124	-0,710560142	0,001521239	0,065048426
TNS1	-0,568562299	0,001523597	0,065048426
GPR126	0,67670744	0,001547902	0,065789625
ATP6V0D1	-0,560664427	0,001549378	0,065789625
CENPJ	-0,650034482	0,001558272	0,065987955
ATP8B2	-0,638352784	0,001595581	0,06738526
JUND	-0,539468511	0,001611553	0,067693875
NDST1	-0,630732579	0,001620035	0,067867748
IL4I1	0,56338196	0,001663614	0,069507041
HEY2	-0,67529505	0,001691851	0,070498288
ZNF627	0,600112677	0,001703765	0,070805927
FBXO5	-0,635975974	0,001713242	0,070953087
FBXL6	-0,519437019	0,001716387	0,070953087
MRPL54	-1,094491931	0,001726048	0,0711642
C2CD4B	0,578294766	0,001735615	0,071311262
INPPL1	-0,554197896	0,001738743	0,071311262
NFIC	-0,654225224	0,001749321	0,071486194
CDCA5	-0,850675015	0,001752157	0,071486194
RWDD3	0,625012642	0,001765094	0,071795955
ABCA1	0,684971808	0,001770777	0,071795955

## DEGs shTFEB vs scr-shRNA ECs

SNORD104	-0,991282848	0,001775366	0,071795955
TJAP1	-0,633731692	0,001778128	0,071795955
C16ORF75	-0,997206071	0,001787025	0,071969188
SH2B3	-0,578337102	0,001812851	0,072821621
TNRC6B	0,648843474	0,001823872	0,073076456
PHF19	-0,599097905	0,001837705	0,073442383
RHOB	0,920793458	0,001845725	0,07357473
PRMT6	-0,526420261	0,001854645	0,073742188
BBS2	0,649643657	0,001872224	0,074011869
FCHO1	-0,509865211	0,0018776	0,074011869
SLC25A29	0,540454412	0,001889649	0,074011869
SIDT2	-0,587387229	0,001894225	0,074011869
GGCX	-0,512682261	0,001896429	0,074011869
BRCA1	-0,67563551	0,001896558	0,074011869
NOL6	-0,552213453	0,001909264	0,074011869
LRP5	-0,81598481	0,001911364	0,074011869
KIDINS220	0,518493476	0,00191233	0,074011869
FILIP1L	0,799333614	0,001923537	0,074011869
BAZ2B	0,539308371	0,001932117	0,074011869
EHD1	-0,535188277	0,001933219	0,074011869
DUSP5	-0,695211537	0,001933361	0,074011869
NME4	-0,729480101	0,001935137	0,074011869
LY6E	-0,680926564	0,001937211	0,074011869
SLFN11	-0,629159065	0,001953042	0,074434706
CCDC102A	0,52571578	0,001987219	0,075552992
RRAGC	0,5654234	0,002020881	0,07664634
SLC2A3	0,766809636	0,002047648	0,07732387
SORBS2	0,901805437	0,002050592	0,07732387
H2AFZ	-0,615243037	0,002053591	0,07732387
EED	-0,533312146	0,002065292	0,077575755
TDRD7	0,655226898	0,002070209	0,077575755
KPNA4	-0,518091824	0,002084536	0,077925736
NFKBIE	0,583080055	0,002093485	0,077969403
OGDH	-0,615432461	0,002102269	0,077969403
NCOR2	-0,749129693	0,002102589	0,077969403
DCUN1D3	0,505723974	0,002112354	0,078020765
POLA1	-0,648179027	0,002117036	0,078020765
EXOSC2	-0,598130043	0,002171197	0,079641143
HS1BP3	0,671267961	0,002194572	0,080310041
RAG1AP1	0,537395715	0,002207748	0,080439802
DDX11	-0,569903014	0,002210485	0,080439802
TMEM201	-0,81059031	0,002221106	0,080439802
KLHL36	0,530067597	0,002223857	0,080439802
RAD54L2	-0,504206773	0,002256684	0,081086037
NRM	-0,5759694	0,002257291	0,081086037
CENPN	-0,623072349	0,002275242	0,081543419
TMEM187	0,591786285	0,002289472	0,081824208
AXUD1	-0,534144093	0,002310613	0,082115485
FIGNL1	-0,561483268	0,002317479	0,082115485
RAB5B	0,54734411	0,002332877	0,082317865
MLL4	-0,558196079	0,002340917	0,082317865
H2AFX	-0,826710628	0,002349073	0,082317865
ANKRD9	-0,525732032	0,002357331	0,082317865
SLC2A4RG	-0,506168503	0,002360412	0,082317865
FAM117B	0,593156217	0,002362209	0,082317865

## DEGs shTFEB vs scr-shRNA ECs

RHOD	0,59803265	0,00236353	0,082317865
ARMCX1	0,665529213	0,002365335	0,082317865
C15ORF39	-0,642745284	0,00237779	0,082567432
NPR1	-0,696132612	0,002398054	0,083086464
HNRNPL	-0,732508586	0,002483109	0,085679037
TBC1D9	0,637126719	0,002501104	0,086084251
RALGAPB	0,52217734	0,002518744	0,086324321
C5ORF41	0,544638086	0,002521034	0,086324321
BTBD11	-0,628436579	0,002524652	0,086324321
UBFD1	0,506156551	0,002540974	0,08669271
SCAP	-0,512743709	0,002569367	0,08747044
BEXL1	0,546664174	0,002598089	0,088255943
RNF144A	-0,617031449	0,002607845	0,088395197
ANKRD57	-0,53378899	0,002628005	0,088885717
CSNK1D	0,542070431	0,002636184	0,08896978
IFRD2	-0,53701988	0,002656866	0,089474542
MTHFD1	-0,510814368	0,002664181	0,089527946
SUPT6H	-0,510211418	0,002671654	0,089586409
KCNMB1	-0,644236411	0,002677917	0,089604152
SNN	0,506508366	0,00269058	0,089737785
HS.126108	-0,503559676	0,002693397	0,089737785
SLC37A4	-0,578631683	0,002703914	0,089745815
FANCB	-0,537456891	0,002718965	0,090013869
HJURP	-0,620285712	0,002765072	0,090730655
CHMP5	0,508860573	0,002774851	0,090730655
PPM1D	0,552197715	0,002775261	0,090730655
PDXK	-0,559238997	0,002775455	0,090730655
C14ORF179	0,515920064	0,002802289	0,091140872
XPO6	-0,60784541	0,00280695	0,091140872
DNAJC9	-0,611801636	0,002812802	0,091140872
SLC7A2	0,702840044	0,002817535	0,091140872
PTGR1	0,585370738	0,002821363	0,091140872
ZNF217	0,570902239	0,002822999	0,091140872
RNF41	-0,536968538	0,002846395	0,091518049
GAS2L3	-0,547541373	0,002893431	0,092802035
NNMT	0,625455512	0,002902454	0,092802035
GINS4	-0,585720753	0,002904147	0,092802035
HIST2H2BE	0,514699545	0,002911203	0,092837673
C1QTNF6	-0,5225129	0,002924146	0,093060506
PPIC	0,54294821	0,002956582	0,093363538
PGP	-0,544060543	0,002960999	0,093363538
BEX2	0,679599437	0,002967813	0,093363538
OIP5	-0,613538523	0,002969517	0,093363538
MTMR4	-0,540230745	0,002983728	0,093574138
COPG	-0,626065304	0,003020516	0,094397159
RIPK5	0,607526743	0,003045934	0,095001538
SERPINH1	-0,777607398	0,003059672	0,095143032
EXO1	-0,751789007	0,003062648	0,095143032
ZNF598	-0,503503693	0,003125305	0,096484478
CXORF38	0,599360305	0,003126567	0,096484478
CC2D1A	-0,505943597	0,003130159	0,096484478
MAP1LC3B	0,565380941	0,003130528	0,096484478
TTF2	-0,510394489	0,003160749	0,09722414
HMGCL	0,570359819	0,003189922	0,097928739
DDAH1	0,500665959	0,003204342	0,098178535

DEGs shTFEB vs scr-shRNA ECs

LYPLA2P1	-0,536534109	0,003224278	0,098596013
HS.258266	-0,577238222	0,003243391	0,098986777
RPL13A	-0,508812214	0,003255697	0,099168653
PGRMC2	0,576821942	0,003269842	0,09940573
ESPL1	-0,654244947	0,00329985	0,099552444
UBE2T	-0,754845713	0,003300723	0,099552444
TNFRSF1B	-0,555331893	0,00330634	0,099552444
MAMLD1	-0,60431816	0,003306522	0,099552444