Supplementary Information

Figure Legends

Figure S1. Direct reprogramming of human fibroblasts to functional iECs. (A) FACs plot data (obtained using CD31+ antibody) of iECs derived from fibroblasts (*left panel*) compared to HMVECs (*right panel*). (B) Representative bright field image of iECs depicting a typical "cobblestone" monolayer. (C-F) Real-Time RT-PCR of iECs for endothelial markers CD144, KDR, vWF and eNOS. (G) Immunofluorescent staining of the iECs for endothelial markers CD144 and vWF. (H) iECs incorporate acetylated LDL compared to fibroblasts. (I) iECs form capillary-like network compared to fibroblasts when seeded on matrigel (J) L-NAME inhibits the NO production in iECs. (K) iECs formed vascular structures in matrigel which contained red blood cells; a larger vessel is shown in this view. (L) Capillary density in the matrigel plug, normalized to total number of cells in the field.

Figure S2. iECs are heterogeneous. (A) Quantitative gene expression analysis of arterial, venous and lymphatic markers in iECs when compared to parental fibroblasts. Data represented as mean \pm S.E.M., n = 3. (B) *Gene expression data* of cells that have undergone the transdifferentiation protocol at day 28 immediately prior to FAC sorting. At this time point, there is no increase in endodermal and ectodermal markers, nor is there expression of pluripotency markers such as Nanog and Oct4. Only the mesodermal (endothelial) markers PECAM1 and DES are increased.

Figure S3. Histone modifications during direct reprogramming to iECs.

ChIP analysis to assess H3K4me3 and H3K27me3 of the CD31 promoters on iECs and HMVEC. Quantitative RT-PCR showed an (A) increase in histone H3K4 and (B) decrease in

histone H3K27 trimethylation levels in iECs as also observed in HMVEC. Data represented as mean \pm S.D, n = 2.

Figure S4. Improvement in blood perfusion in the ischemic hindlimb after iEC transplantation. (A) Perfusion ratios of ischemic limbs at day 0, 4, 7, 11, 14 and 18 after iEC treatment. The perfusion ratio (value of the ischemic limb divided by that of the nonischemic limb) was greater in mice that received iEC transplantation compared to those that received control EGM-2 medium on day 7 and 14 (n=5 each group, *P<0.05). (B) Effect of injection of fibroblasts on blood perfusion in the ischemic hindlimb is similar to that obtained with injection of EGM2 media.

Figure S5. Characterization of iECs derived from TLR3-KD cells. (A-E) Quantitative RT-PCR of iECs derived from Scramble and TLR3-KD fibroblasts for endothelial markers CD31, CD144, KDR, vWF and eNOS. (F) Immunofluorescent staining of the iECs derived from Scramble and TLR3-KD fibroblasts for endothelial markers CD31, CD144 and vWF. (G&H) Heat map of genes differentially expressed in iECs generated from scramble or TLR3KD fibroblasts. RNA-seq data shows that most of upregulated genes observed in scramble-iECs associated with endothelial biology are reversed in the TLR3KD-iECs. A variety of genes whose expression was activated in iEC was prevented by anti-TLR3 but unaffected by the scrambled vector. For example, angiogenesis essential genes GJA4, HOXA1, HOXA3, HOXB3, HEY2, GBX2, and SEMA3A were all prevented from being activated in iEC treated with TLR3 KD but not so in the scrambled-treated iEC. For the assessment gene expression similarities between iEC and HMVEC, we identified genes from the ANOVA performed in Figure 3 that were more strongly expressed in both iEC and HMVEC as compared to parental fibroblasts Subsequently, using Toppgene (http://toppgene.cchmc.org/), we used its Fisher's Exact test function to assess the enrichment of that set of genes for its enrichment for genes known to be associated with endothelial and angiogenic biology.

Figure S6. Direct reprogramming of TLR3 knockout tail-tip fibroblasts to iECs. FACs plot data obtained using CD144+ antibody to quantify iECs. (*left panel*) - WT tail-tip fibroblasts treated with vehicle control, then transdifferentiation medium; (*middle panel*) - WT tail-tip fibroblasts treated with Poly I:C then transdifferentiation medium; and (*right panel*) – TLR3KO tail-tip fibroblasts treated with Poly I:C then transdifferentiation medium.

Fig S7. No changes in gene expression of markers for mesoderm, endoderm and ectoderm; nor endothelial progenitor markers including c-kit and CD34 during transdifferentiation of fibroblasts to iECs.

Fig. S8. Changes in gene expression of KDR, CD144, CD31 and eNOS during the transdifferentiation of fibroblasts to iECs.



Fig. S1





Κ











F





Ε eNOS Relative fold change 10₇ 8-6-4-2-0 Scram-iECs TLR3KD-iECs Fibroblast

CD144/DAPI

vWF/DAPI









50.0 30.0 20.0

15.0 10.0

7.5

5.0

4.0

3.0

2.5

2.0

1.5 1.0



CD144





Supplemental Table 1: List of 172 upregulated genes with known endothelial biology

| Symbol | Description | FPKM_fibroblast | FPKM_iEC (1) | FPKM_iEC (2) | FPKM_HMVEC |
|-------------|---|-----------------|--------------|--------------|--------------|
| ECSCR | endothelial cell surface expressed chemotaxis and apoptosis regulator | 0.0 | 47.9 | 37.9 | 1082.8 |
| ARHGEF15 | Rho guanine nucleotide exchange factor (GEF) 15 | 0.1 | 40.2 | 57.7 | 52.2 |
| LMO2 | LIM domain only 2 (rhombotin-like 1) | 0.0 | 10.7 | 11.4 | 8.6 |
| EFNA5 | ephrin-A5 | 0.0 | 8.8 | 3.1 | 4.4 |
| FABP5P1 | fatty acid binding protein 5 pseudogene 1 | 0.0 | 8.3 | 8.2 | 7.5 |
| SHE | Src homology 2 domain containing E | 0.1 | 8.9 | 6.9 | 14.5 |
| C20orf160 | chromosome 20 open reading frame 160 | 0.0 | 4.9 | 4.7 | 9.5 |
| APLN | apelin | 1.0 | 120.0 | 111.9 | 173.9 |
| FLT4 | fms-related tyrosine kinase 4 | 0.0 | 4.9 | 6.1 | 46.2 |
| EMCN | endomucin | 0.7 | 81.3 | 80.3 | 59.6 |
| KDR | kinase insert domain receptor (a type III receptor tyrosine kinase) | 1.0 | 120.2 | 118.5 | 79.0 |
| CLDN5 | claudin 5 | 0.0 | 3.5 | 5.6 | 38.2 |
| ERG | v-ets erythroblastosis virus E26 oncogene homolog (avian) | 0.5 | 41.5 | 37.6 | 92.3 |
| HOXB3 | homeobox B3 | 0.2 | 18.7 | 20.9 | 11.7 |
| CXADR | coxsackie virus and adenovirus receptor | 0.1 | 6.5 | 4.5 | 3.8 |
| FGF12 | fibroblast growth factor 12 | 0.3 | 20.5 | 23.9 | 3.1 |
| NRARP | NOTCH-regulated ankyrin repeat protein | 0.1 | 10.4 | 10.7 | 22.8 |
| ESAM | endothelial cell adhesion molecule | 0.4 | 32.6 | 43.6 | 100.8 |
| TIE1 | tyrosine kinase with immunoglobulin-like and EGF-like domains 1 | 2.0 | 149.3 | 147.1 | 392.5 |
| INPP5D | inositol polyphosphate-5-phosphatase, 145kDa | 0.1 | 6.4 | 4.4 | 30.6 |
| LIPG | lipase, endothelial | 0.1 | 9.2 | 7.6 | 83.9 |
| HOXD3 | homeobox D3 | 0.2 | 12.3 | 11.7 | 6.0 |
| CHD7 | chromodomain helicase DNA binding protein 7 | 0.8 | 48.2 | 47.7 | 6.8 |
| NOS3 | nitric oxide synthase 3 (endothelial cell) | 1.3 | 70.1 | 55.9 | 45.1 |
| PLVAP | plasmalemma vesicle associated protein | 0.2 | 8.8 | 8.8 | 14.1 |
| THBD | thrombomodulin | 0.5 | 23.1 | 20.5 | 41.1 |
| THSD/A | thrombospondin, type I, domain containing /A | 0.1 | 5.4 | 5.5 | 3.8 |
| GJA4 | gap junction protein, alpha 4, 37kDa | 0.2 | 7.7 | 7.1 | 35.4 |
| AKR1C3 | aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II) | 0.6 | 28.4 | 28.8 | 22.3 |
| GRB14 | growth factor receptor-bound protein 14 | 0.8 | 36.7 | 25.4 | 4.7 |
| RASIP1 | Ras interacting protein 1 | 0.5 | 21.7 | 18.8 | 44.6 |
| IEK | IEK tyrosine kinase, endothelial | 1.1 | 45.6 | 45.6 | 58.8 |
| BMP6 | bone morphogenetic protein 6 | 0.4 | 16.3 | 15.8 | /2.3 |
| GBX2 | gastrulation brain nomeobox 2 | 0.2 | 8.7 | 8.5 | 9.2 |
| SUX18 | SKY (sex determining region Y)-box 18 | 0.2 | 6.6 | 7.2 | 47.3 |
| IBXI | | 0.3 | 10.9 | 9.9 | 49.6 |
| | phosphodiesterase 4D, cAMP-specific | 0.5 | 18.5 | 21.8 | 3.1 12.2 |
| | | 0.3 | 9.0 | 8.3 | 12.3 |
| PNP SOV7 | purine nucleoside prospriorylase | 3.0 | 119.4 | 119.7 | 202.3 |
| | shi (sex determining region i)-box / | 0.5 | 0.0 52.0 | 7.0 | 40.5 |
| | multimorin 2 | 1.5 | 10.0 | 12.0 | 133.3 |
| E2E9 | E2E transcription factor 9 | 0.4 | 10.5 | 0.1 | 27 |
| | roundabout avon guidance recenter, homolog 4 (Drosophila) | 1.0 | 24.6 | 21.2 | 3.7 197 7 |
| | nodocalyzin-like | 14.5 | 24.0 | 363.6 | 270.7 |
| CDH5 | cadherin 5, type 2 (vascular endothelium) | 0.8 | 19.1 | 20.8 | 315.8 |
| | alkaline nhosnhatase liver/hone/kidney | 0.4 | 95 | 7.2 | 5 7 |
| PDGFB | platelet-derived growth factor beta polypentide | 0.4 | 8.4 | 9.1 | 163.9 |
| ANGPT2 | angionoietin 2 | 0.2 | 5.8 | 4.0 | 83.3 |
| ANKRD1 | ankyrin repeat domain 1 (cardiac muscle) | 2.5 | 56.5 | 53.8 | 581.3 |
| FGFR3 | fibroblast growth factor receptor 3 | 1.5 | 35.3 | 32.6 | 5.6 |
| HES1 | hairy and enhancer of split 1. (Drosophila) | 1.1 | 25.1 | 21.2 | 27.7 |
| FABP5 | fatty acid binding protein 5 (psoriasis-associated) | 5.1 | 109.9 | 115.4 | 183.9 |
| GRAP | GRB2-related adaptor protein | 0.2 | 4.0 | 4.6 | 47.9 |
| CASP10 | caspase 10, apoptosis-related cysteine peptidase | 0.8 | 15.9 | 17.0 | 15.1 |
| LYL1 | lymphoblastic leukemia derived sequence 1 | 0.4 | 7.4 | 7.6 | 31.0 |
| EXOC3L1 | exocyst complex component 3-like 1 | 1.1 | 20.2 | 16.1 | 11.1 |
| JAG1 | jagged 1 | 2.2 | 38.2 | 41.2 | 93.8 |
| NRCAM | neuronal cell adhesion molecule | 6.8 | 116.7 | 116.8 | 18.6 |
| MDK | midkine (neurite growth-promoting factor 2) | 37.0 | 620.2 | 603.2 | 333.2 |
| PTPRB | protein tyrosine phosphatase, receptor type, B | 2.5 | 41.5 | 41.3 | 43.5 |
| TNFRSF1B | tumor necrosis factor receptor superfamily, member 1B | 0.5 | 7.6 | 8.7 | 8.3 |
| CCNB1 | cyclin B1 | 10.5 | 168.0 | 179.1 | 67.1 |
| NOTCH4 | notch 4 | 0.5 | 7.3 | 3.7 | 22.1 |
| F11R | F11 receptor | 1.2 | 18.6 | 18.3 | 94.2 |
| CEACAM1 | carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein) | 0.3 | 4.3 | 4.2 | 47.2 |
| CENPA | centromere protein A | 1.4 | 19.2 | 17.9 | 8.4 |
| SPRY1 | sprouty homolog 1, antagonist of FGF signaling (Drosophila) | 2.0 | 27.1 | 26.7 | 63.0 |
| ICAM2 | intercellular adhesion molecule 2 | 1.2 | 15.5 | 20.1 | 212.2 |
| RAMP2 | receptor (G protein-coupled) activity modifying protein 2 | 1.7 | 21.8 | 20.2 | 32.5 |
| ESCO2 | establishment of cohesion 1 homolog 2 (S. cerevisiae) | 1.5 | 18.6 | 19.1 | 6.2 |
| ITGA6 | integrin, alpha 6 | 14.0 | 173.8 | 167.9 | 115.4 |
| TNFRSF21 | tumor necrosis factor receptor superfamily, member 21 | 3.4 | 40.8 | 37.0 | 23.6 |
| HEY1 | hairy/enhancer-of-split related with YRPW motif 1 | 0.5 | 5.4 | 4.2 | 5.4 |

| Symbol | Description | FPKM_fibroblast | FPKM_iEC (1) | FPKM_iEC (2) | FPKM_HMVEC |
|----------|---|-----------------|--------------|--------------|--------------|
| EZH2 | enhancer of zeste homolog 2 (Drosophila) | 2.4 | 28.5 | 23.0 | 6.9 |
| LFNG | LFNG O-fucosylpeptide 3-beta-N-acetylglucosaminyltransferase | 2.5 | 29.2 | 30.4 | 8.1 |
| RAPGEF3 | Rap guanine nucleotide exchange factor (GEF) 3 | 2.3 | 25.9 | 22.4 | 17.0 |
| CD34 | CD34 molecule | 1.0 | 11.3 | 9.0 | 23.0 |
| PIK3R3 | phosphoinositide-3-kinase, regulatory subunit 3 (gamma) | 0.9 | 10.0 | 12.1 | 10.5 |
| TBXA2R | thromboxane A2 receptor | 1.1 | 11.6 | 10.6 | 3.7 |
| BIRC5 | baculoviral IAP repeat containing 5 | 3.3 | 36.1 | 32.8 | 13.9 |
| CCNE2 | cyclin E2 | 1.7 | 17.9 | 12.6 | 7.0 |
| JAG2 | jagged 2 | 0.3 | 3.3 | 5.6 | 43.7 |
| HOXA3 | homeobox A3 | 1.3 | 13.7 | 14.1 | 3.9 |
| CCNF | cyclin F | 1.1 | 10.9 | 11.4 | 5.7 |
| STIL | SCL/TAL1 interrupting locus | 1.1 | 10.5 | 11.0 | 4.0 |
| EGFL7 | EGF-like-domain, multiple 7 | 14.1 | 134.6 | 126.1 | 599.7 |
| KDM8 | lysine (K)-specific demethylase 8 | 0.8 | 6.7 | 4.4 | 3.9 |
| ZFPM2 | zinc finger protein, multitype 2 | 1.6 | 13.8 | 11.1 | 6.1 |
| SIPRI | spningosine-1-phosphate receptor 1 | 4.5 | 39.5 | 32.8 | 110.5 |
| MILLI4 | myelold/lymphold or mixed-lineage leukemia (trithorax homolog, Drosophila) | 10.7 | 90.3 | 86.3 | 34.7 |
| KIF11 | kinesin family member 11 | 2.2 | 18.6 | 18.3 | 5.9 |
| NRP2 | neuropiin 2 aatiaa idaatifiad kuusaa adaad aatika kuKi C7 | 18.2 | 152.8 | 1/2.2 | 96.3 |
| | anugen luenuneu by monocional anubouy Ki-67 | 3.7 | 31.2 | 30.8 | 17.1 |
| FLII | Friend leukemia virus integration 1 | 3.5 | 28.6 | 28.5 | 68.1 |
| PLAZG4A | phospholipase A2, group IVA (cytosolic, calcium-dependent) | 0.8 | 0.0 | 0.4 | 22.8 |
| | eluctoria | 8.8 | 71.4 | 70.4 | 99.2 |
| RECOLA | Rec0 protein like 4 | 40.0 | 321.9 | 299.9 | 12.2 |
| | necų protein-likė 4 | 4.0 | 51.7 | 55.9 | 15.5 |
| | prexiti Az | 1.5 | 0.2 | 7.5 | 74.0 |
| | AT rich interactive domain 3B (BRIGHT-like) | 1.2 | 10.3 | 9.0 | 28.5 |
| | | 2.4 | 61.2 | 5.0 | 65.7 |
| | homeodomain interacting protein kinace 2 | 8.3 1.6 | 11 5 | 12.8 | 53 |
| DUSP6 | dual specificity phosphatase 6 | 29.1 | 213.9 | 195.9 | 108 7 |
| | nlasminogen activator, urokinase | 14.4 | 103.0 | 103.6 | 62.0 |
| FOXM1 | forkhead hox M1 | 4.7 | 33.5 | 33.1 | 12.6 |
| MYC | v-myc myelocytomatosis viral oncogene homolog (avian) | 21.8 | 150.7 | 147.8 | 70.7 |
| MCAM | melanoma cell adhesion molecule | 95 | 64.8 | 65.2 | 786.2 |
| FFS | feline sarcoma oncogene | 3.0 | 20.0 | 22.9 | 20.4 |
| NES | nestin | 27.7 | 184.1 | 179.3 | 64.4 |
| PLEKHG5 | pleckstrin homology domain containing, family G (with RhoGef domain) member 5 | 5.0 | 33.1 | 32.1 | 21.7 |
| LDLR | low density lipoprotein receptor | 10.2 | 66.7 | 50.5 | 47.2 |
| GIT1 | G protein-coupled receptor kinase interacting ArfGAP 1 | 17.5 | 111.6 | 99.8 | 76.7 |
| TK1 | thymidine kinase 1. soluble | 7.6 | 48.2 | 48.7 | 27.4 |
| STEAP3 | STEAP family member 3, metalloreductase | 0.9 | 5.4 | 5.5 | 13.6 |
| FURIN | furin (paired basic amino acid cleaving enzyme) | 21.5 | 135.2 | 123.2 | 70.7 |
| EPHB2 | EPH receptor B2 | 1.1 | 7.0 | 4.8 | 19.1 |
| MERTK | c-mer proto-oncogene tyrosine kinase | 0.5 | 3.0 | 4.1 | 4.3 |
| EPHB4 | EPH receptor B4 | 14.6 | 88.3 | 80.8 | 106.3 |
| FDPS | farnesyl diphosphate synthase | 47.7 | 277.8 | 290.3 | 384.1 |
| DCHS1 | dachsous 1 (Drosophila) | 3.2 | 18.4 | 17.9 | 17.5 |
| TMEM231 | transmembrane protein 231 | 2.4 | 13.9 | 12.1 | 5.5 |
| ARAP3 | ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 3 | 5.0 | 27.8 | 26.4 | 28.9 |
| HMGB2 | high mobility group box 2 | 29.6 | 162.3 | 186.7 | 101.1 |
| VASH1 | vasohibin 1 | 4.7 | 25.5 | 29.0 | 14.1 |
| PRKCH | protein kinase C, eta | 0.9 | 5.0 | 6.4 | 46.2 |
| FLNB | filamin B, beta | 33.2 | 172.9 | 171.7 | 163.0 |
| NFATC1 | nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1 | 1.1 | 5.4 | 4.8 | 7.0 |
| SGK1 | serum/glucocorticoid regulated kinase 1 | 32.9 | 155.8 | 187.5 | 203.7 |
| SH3PXD2B | SH3 and PX domains 2B | 4.9 | 23.0 | 31.2 | 15.1 |
| NEDD4L | neural precursor cell expressed, developmentally down-regulated 4-like, E3 ubiquitin protein ligase | 1.5 | 6.9 | 7.3 | 8.4 |
| HSP90AB1 | heat shock protein 90kDa alpha (cytosolic), class B member 1 | 216.7 | 961.2 | 926.6 | 542.4 |
| GOLM1 | golgi membrane protein 1 | 19.5 | 85.9 | 82.0 | 69.8 |
| RAC3 | ras-related C3 botulinum toxin substrate 3 (rho family, small GTP binding protein Rac3) | 4.6 | 20.3 | 19.7 | 14.4 |
| DHCR7 | 7-dehydrocholesterol reductase | 16.3 | 71.7 | 74.0 | 69.9 |
| ACVRL1 | activin A receptor type II-like 1 | 6.5 | 28.6 | 26.9 | 153.2 |
| HMGA1 | high mobility group AT-hook 1 | 97.1 | 411.6 | 401.9 | 567.9 |
| ADAM15 | ADAM metallopeptidase domain 15 | 36.2 | 153.0 | 117.1 | 208.1 |
| HOXA5 | nomeobox A5 | 3.0 | 12.6 | 11.6 | 13.4 |
| SNAI1 | snall nomolog 1 (Drosophila) | 3.4 | 14.1 | 14.4 | 17.9 |
| KCE1 | KUEL nomolog, prenyl protein protease (S. cerevisiae) | 4.5 | 18.5 | 19.5 | 13.4 |
| RGCC | regulator of cell cycle | 4.3 | 17.5 | 15.4 | 101.1 |
| IEAD2 | IEA domain tamily member 2 | 10.6 | 43.4 | 43.3 | 26.2 |
| PIK3CB | priospriaticylinositol-4,5-dispriosprate 3-kinase, catalytic subunit beta | 4.7 | 18.7 | 13.6 | 17.0 |
| | 24-denydrocholesterol reductase | 14.0 | 55.9 | 58.5 | 54.9 |
| AKAP12 | A KINASE (PKKA) ANCHOF PROTEIN 12 | 16.5 | 65.2 | 64.6 | 118.7 |
| | movelonate kinase | 3.9 | 12.3 | 11.5 | 49.8 |
| | nevalunale Nindse | 5.4 2.6 | 10.0 | 11.8 | 11./ 25.2 |
| NUICHI | | 2.0 | 10.0 | 9.7 | 20.3 |

| Symbol | Description | FPKM_fibroblast | FPKM_iEC (1) | FPKM_iEC (2) | FPKM_HMVEC |
|---------|---|-----------------|--------------|--------------|------------|
| PLCG1 | phospholipase C, gamma 1 | 25.5 | 92.5 | 87.5 | 80.0 |
| TNFAIP3 | tumor necrosis factor, alpha-induced protein 3 | 3.4 | 12.1 | 14.5 | 17.3 |
| ABCA3 | ATP-binding cassette, sub-family A (ABC1), member 3 | 1.9 | 6.6 | 7.7 | 12.4 |
| LAMA5 | laminin, alpha 5 | 9.1 | 31.8 | 26.7 | 86.4 |
| E2F7 | E2F transcription factor 7 | 1.7 | 5.9 | 5.3 | 9.3 |
| POLG | polymerase (DNA directed), gamma | 18.2 | 61.9 | 62.2 | 45.7 |
| NSDHL | NAD(P) dependent steroid dehydrogenase-like | 7.1 | 24.2 | 27.1 | 23.1 |
| MKS1 | Meckel syndrome, type 1 | 4.2 | 14.3 | 18.3 | 13.1 |
| NT5E | 5'-nucleotidase, ecto (CD73) | 34.4 | 112.3 | 112.5 | 262.4 |
| CSK | c-src tyrosine kinase | 17.4 | 56.0 | 56.7 | 51.3 |
| MAP1S | microtubule-associated protein 1S | 6.0 | 19.1 | 19.1 | 20.9 |
| SPTBN1 | spectrin, beta, non-erythrocytic 1 | 26.6 | 85.3 | 86.7 | 78.5 |
| WRN | Werner syndrome, RecQ helicase-like | 4.2 | 13.3 | 12.5 | 11.6 |
| EPHA2 | EPH receptor A2 | 16.1 | 50.7 | 51.3 | 77.4 |
| PGF | placental growth factor | 4.7 | 14.4 | 17.1 | 59.9 |
| EFNB1 | ephrin-B1 | 13.8 | 41.5 | 40.4 | 44.3 |
| PDE2A | phosphodiesterase 2A, cGMP-stimulated | 1.5 | 4.6 | 6.2 | 45.1 |
| USF1 | upstream transcription factor 1 | 13.4 | 38.6 | 48.8 | 50.9 |
| GATAD2A | GATA zinc finger domain containing 2A | 19.2 | 54.8 | 57.8 | 46.3 |
| PLD1 | phospholipase D1, phosphatidylcholine-specific | 4.6 | 12.6 | 15.3 | 36.0 |
| COL4A5 | collagen, type IV, alpha 5 | 5.4 | 14.3 | 14.9 | 51.6 |
| CBFB | core-binding factor, beta subunit | 24.4 | 64.0 | 78.9 | 57.2 |

Supplemental Table 2: Bioinformatic and Pathway Analysis of iECs

1085 iEC and HMVEC- high, EC up-regulated

| | | | 58 |
|------------------------|--|----------|-----------|
| atesory | Name | onlen. | Benesin , |
| GO: Biological Process | mitotic cell cycle | 1.65E-50 | 154 |
| GO: Biological Process | M phase | 4.38E-37 | 110 |
| Coexpression Atlas | DevelopingKidney e15.5 Endothelial cells top1000 | 8.63E-32 | 139 |
| GO: Cellular Component | chromosome | 1.11E-23 | 98 |
| GO: Cellular Component | microtubule cvtoskeleton | 2.27E-20 | 110 |
| GO: Biological Process | blood vessel development | 8.62E-11 | 63 |
| GO: Biological Process | angiogenesis | 1.21E-10 | 51 |
| GO: Biological Process | S phase of mitotic cell cycle | 1.44E-09 | 27 |
| GO: Biological Process | circulatory system development | 6.05E-08 | 76 |
| GO: Biological Process | cholesterol biosynthetic process | 1.04E-07 | 13 |
| Mouse Phenotype | abnormal vascular development | 1.37E-07 | 57 |
| GO: Biological Process | sprouting angiogenesis | 2.32E-06 | 12 |
| GO: Biological Process | chromatin remodeling | 3.01E-06 | 18 |
| GO: Biological Process | hemopoiesis | 3.07E-06 | 55 |
| Mouse Phenotype | abnormal blood vessel morphology | 3.57E-06 | 88 |
| GO: Biological Process | endothelium development | 6.06E-06 | 13 |
| GO: Biological Process | cell junction organization | 4.41E-05 | 24 |
| Mouse Phenotype | abnormal artery development | 6.45E-05 | 19 |
| GO: Molecular Function | cytoskeletal protein binding | 7.87E-05 | 56 |
| Mouse Phenotype | abnormal vein development | 3.37E-04 | 8 |
| GO: Cellular Component | cell junction | 3.94E-04 | 59 |
| Mouse Phenotype | decreased angiogenesis | 4.35E-04 | 13 |
| Pathway | Angiogenesis | 5.29E-04 | 21 |

1270 fibroblasts-high, EC down-regulated

| | | | 200 |
|------------------------|---|----------|--------------|
| (Jule of the second | Name | onlend | # Benes in 1 |
| GO: Cellular Component | extracellular matrix | 6.37E-27 | 87 |
| GO: Biological Process | muscle structure development | 3.05E-20 | 87 |
| GO: Biological Process | extracellular structure organization | 1.31E-16 | 48 |
| GO: Biological Process | vasculature development | 4.76E-16 | 80 |
| GO: Biological Process | cell adhesion | 1.80E-13 | 110 |
| GO: Biological Process | biological adhesion | 2.67E-13 | 110 |
| Mouse Phenotype | muscle phenotype | 4.61E-13 | 140 |
| GO: Molecular Function | extracellular matrix structural constituent | 7.45E-11 | 22 |
| GO: Biological Process | angiogenesis | 8.01E-10 | 52 |
| GO: Molecular Function | growth factor binding | 1.13E-09 | 25 |
| GO: Molecular Function | fibronectin binding | 5.68E-09 | 11 |
| Human Phenotype | Aneurysm | 1.10E-07 | 12 |
| Pubmed | Transforming growth factor-fl signaling in myogenic cells regulates vascular morphogenesis, differentiation. | 1.48E-07 | 12 |
| Mouse Phenotype | abnormal blood vessel morphology | 7.17E-07 | 107 |
| Pathway | Focal Adhesion | 1.36E-06 | 29 |
| Pubmed | GPR124, an orphan G protein-coupled receptor, is required for CNS-specific vascularization and establishment of | 1.91E-06 | 17 |
| Pathway | Genes involved in Regulation of Insulin-like Growth Factor (IGF) Activity by Insulin-like Growth Factor Binding Pro | 2.11E-06 | 8 |
| Pathway | HIF-1-alpha transcription factor network | 1.94E-05 | 14 |
| Pathway | Genes involved in Smooth Muscle Contraction | 4.42E-05 | 8 |
| GO: Cellular Component | Golgi apparatus | 1.02E-04 | 94 |
| Pathway | Angiogenesis | 2.87E-04 | 21 |
| GO: Cellular Component | anchoring junction | 7.34E-04 | 24 |