

Supplementary Figures

Supplementary Figure 1

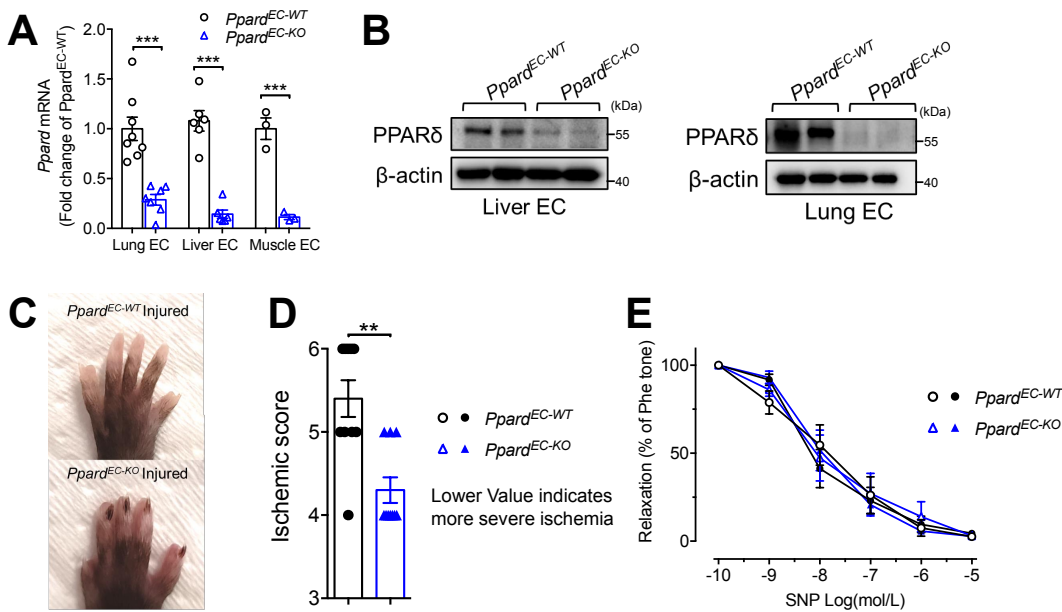


Figure S1. PPAR δ expression Endothelial cells were isolated from lung, liver and skeletal muscle measured at mRNA level by qRT-PCR (A) (n = 8 for lung group, n = 6 for liver group, n = 3 for skeletal muscle group) and at protein level by Western blotting (B). C, Representative pictures of the foot color and nails at days 7 after HLI. D, Ischemic score as described (n = 10, each group). E, Concentration-response curves to SNP in femoral arteries at days 28 after HLI (n = 6, each group). Results are means \pm SEM. Student's t test was used for comparison between two samples, and one-way ANOVA and multiple comparison test was used for more than two samples. * p < 0.05, ** p < 0.01, *** p < 0.001 between groups.

Supplementary Figure 2

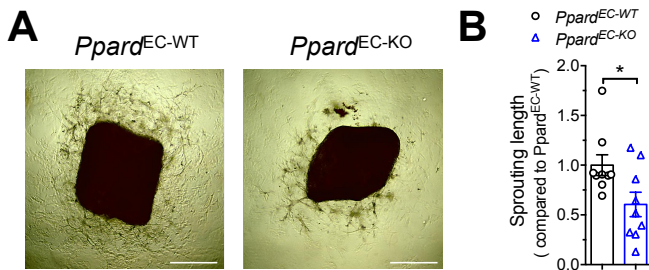


Figure S2. A (representative images) and B (summarized analysis) of sprouting length from mouse aortic ring in *Ppard*^{EC-KO} mice compared to *Ppard*^{EC-WT} (n = 9, each group). Scale bar: 200 μ m. Student's t test was used for comparison between two samples, and one-way ANOVA and multiple comparison test was used for more than two samples. * p < 0.05, ** p < 0.01, *** p < 0.001 between groups.

Supplementary Figure 3

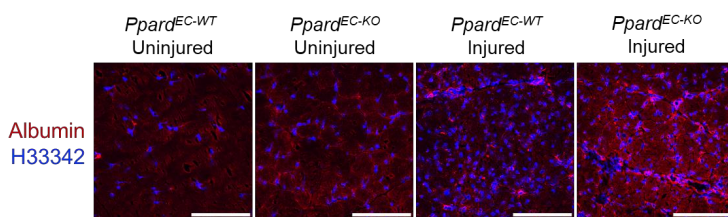


Figure S3. Representative images of immunostaining of albumin (red) in frozen sections of GA muscle 14 days after HLI (n = 6, each group). Scale bar: 200 μ m.

Supplementary Figure 4

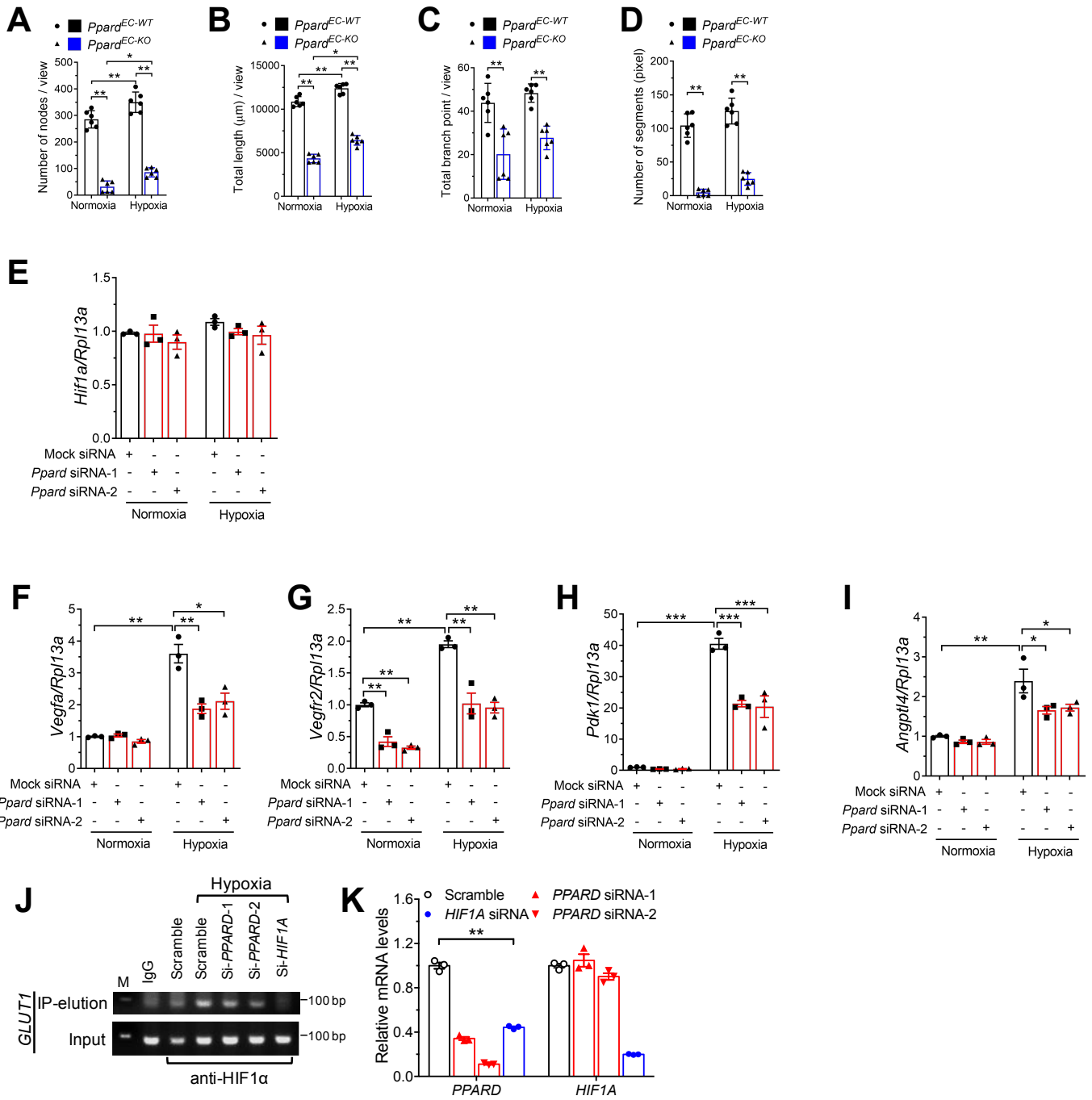


Figure S4. A-D, summarized analysis of tube formation in **Figure 5A** analyzed using the Angiogenesis Analyzer of Image J (n = 6, each group). E-I, qPCR analysis of *Hif1a*, *Vegfa*, *Vegfr2*, *Pdk1*, and *Angptl4* mRNA levels in mBMECs under hypoxia for 12 h after transfection with siRNA, from 3 biological replicates. J, Representative gel showing ChIP of anti-HIF1α immunoprecipitates from HeLa cells after *HIF1A* or *PPARD* silencing, followed by hypoxia for 12 h to show HIF1α enrichment on the *GLUT1* promoter. K, mRNA expression of HIF1α or PPARδ under hypoxia for 12 h, in HeLa cells. Results are means ± SEM. * p < 0.05, ** p < 0.01 between groups by one-way ANOVA and multiple comparison test.

Supplementary Figure 5

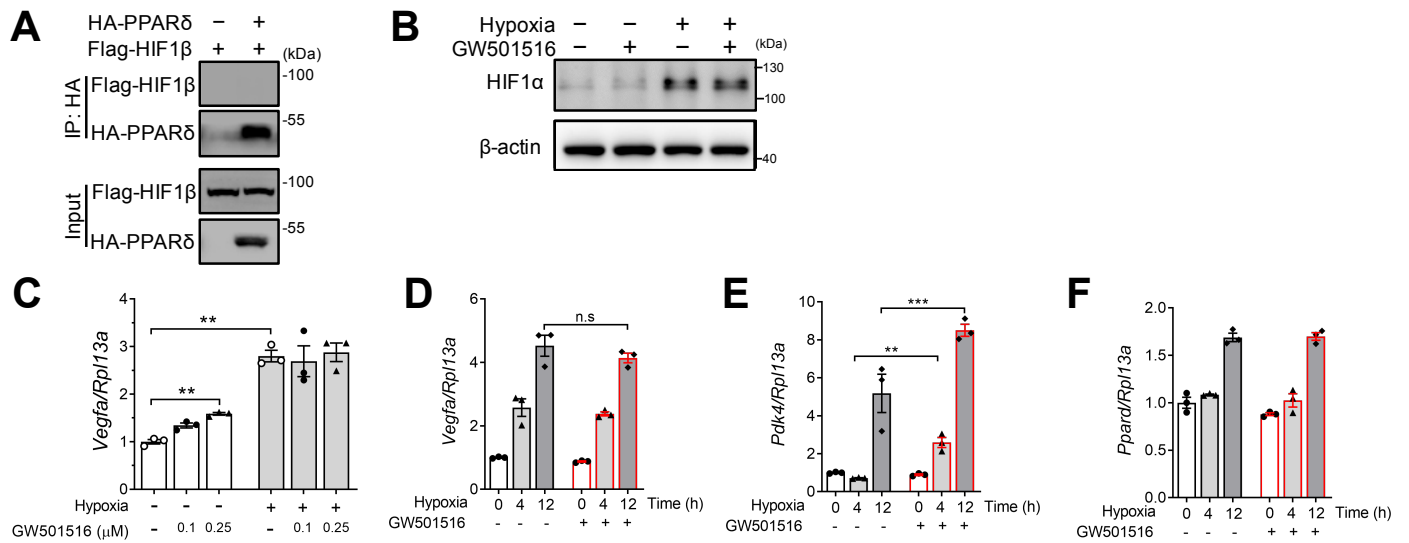


Figure S5. **A**, Immunoblots showing the anti-HA immunoprecipitates in HEK293T cells with indicated plasmids transfected, indicating the no interaction of PPAR δ and HIF1 β in HEK293T cells. **B**, Immunoblots showing HIF1 α under indicated conditions in BMECs (Hypoxia: 12 hours) with or without GW501516 (100 nmol/L). Results are representative data with at least three replicates. **C-F**, qPCR analysis of *Vegfa*, *Pdk4*, and *Ppard* in mBMECs under hypoxia for 12 h after treated with GW501516 at the indicated concentration and duration. Results are biological replicates expressed in means \pm SEM. * $p < 0.05$, ** $p < 0.01$ between groups by one-way ANOVA and multiple comparison test.

Supplementary Figure 6

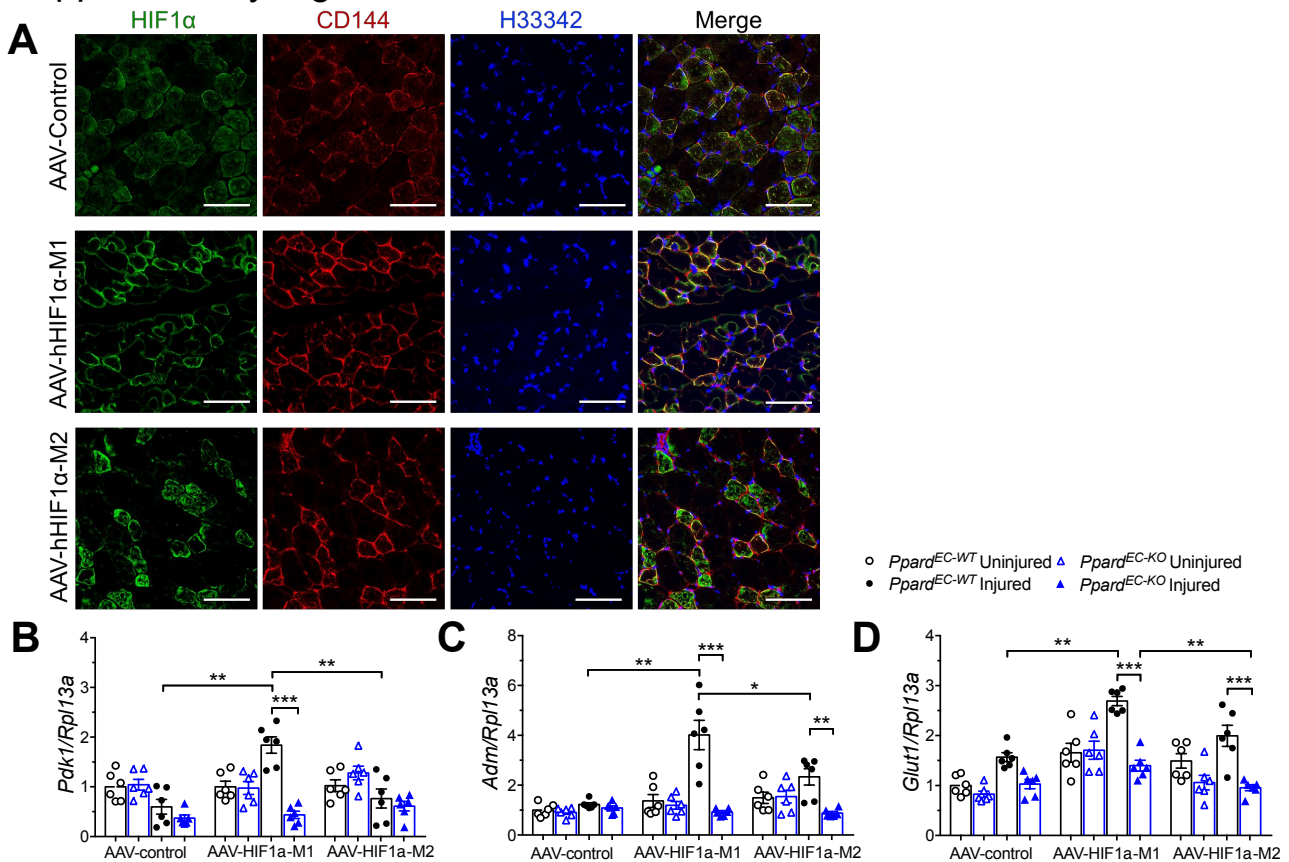


Figure S6. **A**, Representative images of immunofluorescence of HIF1 α (green) expression to co-localized with CD144 (red) in muscle at day 7 after HLI (n = 3, each group). Scale bar: 200 μ m. **B-D**, qPCR analysis for HIF1 α downstream gene mRNA expression in muscles collected 7 days after HLI (n = 6, each group). Results are means \pm SEM. * $p < 0.05$, ** $p < 0.01$, between groups by one-way ANOVA and multiple comparison test.

Table S1: List of primers

Genes	Primer sequence (5' to 3')
Mouse <i>18sRNA</i>	GCAATTATTCCCATGAACG GGCCTCACTAAACCATCCAA
Mouse <i>Gapdh</i>	ATGGTGAAGGTCGGTGTGAA GAGGTCAATGAAGGGGTCGT
Mouse <i>Pax3</i>	GCGTCTCTAAGATCCTGTGCAG GATTTCCAGCTAAACATGCCCG
Mouse <i>Pax7</i>	GTTCGGGAAGAAAGAGGACGAC GGTTCTGATTCCACATCTGAGCC
Mouse <i>Myf5</i>	GGTGGAGAACTATTACAGCCTGC ACAGTAGATGCTGTCAAAGCTGC
Mouse <i>MyoD</i>	GCACTACAGTGGCGACTCAGAT TAGTAGGCGGTGTCGTAGCCAT
Mouse <i>Myogenin</i>	CCATCCAGTACATTGAGCGCCT CTGTGGGAGTTGCATTCCTGG
Mouse α -SMA (<i>Acta2</i>)	TGCTGACAGAGGCACCACTGAA CAGTTGTACGTCCAGAGGCATAG
Mouse <i>CD31(Pecam1)</i>	AGTCAGAGTCTTCCTTGCCC CTCCACGGGTTTCTGTTTGG
Mouse <i>Cxcl12</i>	GCCAACGTCAAGCATCTGAA TTCGGGTCAATGCACACTTG
Mouse <i>Aqp1</i>	CTTGCCATTGGCTTGTCTGTGG CCAGTGGTTTGAGAAGTTGCGG
Mouse <i>Klf2</i>	CACCTAAAGGCGCATCTGCGTA GTGACCTGTGTGCTTTCGGTAG
Mouse <i>Fabp4</i>	AAGGTGAAGAGCATCATAACCCT TCACGCCTTTCATAACACATTCC
Mouse <i>Egfr</i>	CTGAGCATGTCTACAGACCCAG TCTGTGTCCGTCGCAAGTGGTG
Mouse <i>Afn</i>	TGCCAGCCTTTCTGGATGATCC CTGGATGGTCAAGGCAGCATTG
Mouse <i>Jam-2</i>	CAGACTGGAGTGAAGAAGGTG GCTGACTTCACAGCGATACTCTC
Mouse <i>Jam-3</i>	GCATTGCTTCCAATGACGCAGG GATGAAGCAGCCTCGTCTGTAC
Mouse <i>Nectin-2</i>	GCCATACTGACCTGTGATGTACG TCCACAGAGTGGACAAGCAGCT
Mouse <i>Gja5</i>	GTGCCAAACCAGGAGCAGATTC CGCCGTTTGTCACTATGGTAGC
Mouse <i>Tie2</i>	GAAGTGAAGGACGCTTCCACATTC TCAGAAACGCCAACAGCACGGT
Mouse <i>Vegfa</i>	GCTGTAACGATGAAGCCCTG CCTATGTGCTGGCTTTGGTG
Mouse <i>Apelin</i>	ATGAATCTGAGGCTCTGCGT GTCCTCGAAGTTCTGGGCTT
Mouse <i>Vegfr2</i>	TTTGGCAAATACAACCCTTCAGA GCAGAAGATACTGTCACCACC
Mouse <i>Angiop-1</i>	AGGCTTGGTTTCTCGTCAGA TGCCATGAGCTCCAGTTGT
Mouse <i>IL-8</i>	GGTATATTCGAGACCATTTACTG GCCAACAGTAGCCTTCACCCAT
Mouse <i>Fgf2</i>	AAGCGGCTCTACTGCAAGAACG

	CCTTGATAGACACAACCTCCTCTC
Mouse <i>Hgf</i>	GCAGTACCCTCACAAAGCATG ACTCGGATGTTTGGGTCAGT
Mouse <i>Cldn5</i>	GCAAGGTGTATGAATCTGTGCT GTCAAGGTAACAAAGAGTGCCA
Mouse <i>Zo-1</i>	GTTGGTACGGTGCCCTGAAAGA GCTGACAGGTAGGACAGACGAT
Mouse <i>Occludin-1</i>	TGGCAAGCGATCATACCCAGAG CTGCCTGAAGTCATCCACACTC
Mouse <i>Nectin-1</i>	AGCGGACAGATGTGAAGCTCAC TTCTGCCAGGCTGTAGGTGAT
Mouse <i>Icam1</i>	AAACCAGACCCTGGAAGTGCAC GCCTGGCATTTCAGAGTCTGCT
Mouse <i>Vcam1</i>	ACAGACAGTCCCCTCAATGG TCCTCAAACCCACAGAGCT
Mouse <i>E-selectin</i>	AGTTGTGAGTTCTCCTGCGA CACTCCATGACGCCATTCTG
Mouse <i>Ccl2</i>	CATCCACGTGTTGGCTCA GATCATCTTGCTGGTGAATGAGT
Mouse <i>Ccr2</i>	ACCAGAAGAGGGCATTGGAT GCCGTGGATGAACTGAGGTA
Mouse <i>Cx3cl1</i>	GTGCGACAAGATGACCTCAC GCGTCTTGGACCCATTTCTC
Mouse <i>IL-1β</i>	GAAATGCCACCTTTTGACAGTG TGGATGCTCTCATCAGGACAG
Mouse <i>IL-6</i>	TCTATACCACTTCACAAGTCGGA GAATTGCCATTGCACAACTCTTT
Mouse <i>IFNγ (IFNG)</i>	CAGCAACAGCAAGGCGAAAAAGG TTTCCGCTTCCTGAGGCTGGAT
Mouse <i>Hif1α</i>	ACTTTTGGGCCGCTCAATTT ACTTTTGGGCCGCTCAATTT
Mouse <i>Glut1</i>	GCTTCTCCAAGTGGACCTCAAAC ACGAGGAGCACCGTGAAGATGA
Mouse <i>Angptl4</i>	CTGGACAGTGATTCAGAGACGC GATGCTGTGCATCTTTTCCAGGC
Mouse <i>Rpl13a</i>	AGTATCTGGCCTTTCTCCGG CCGAACAACCTTGAGAGCAG
Mouse <i>Pdk1</i>	CTGAGCATGTCTACAGACCCAG TCTGTGTCCGTGCAAGTGGTG
Mouse <i>Ppard</i>	AGGAGAAAGAGGAAGTGGCC GGGAGGAATTCTGGGAGAGG
Mouse <i>Adm</i>	GCCAGATACTCCTTCGCAGTTC AGGAACTGTCGTCTCATCAGCG
Human <i>Hif1α</i>	GCCACATCATCACCATATAGAG GACTCAAAGCGACAGATAACAC
Human <i>Ppard</i>	GGCTTCCAAGTACGGTGTTCATG CTGGCACTTGTGCGGTTCTTC
Human <i>Glut1</i> (For ChIP)	TAGCAACAGCGAGCGTGCCG CCCCGTCGTTTGGTCTCCT
<i>PPARδ-DBD</i>	ATTCATCGATAGATCTGATGGAGCAGCCACAGGAGGAAGC CC ATGCCACCCGGGATCCTTACAGCCCTGCCACCAGCTTCTC CTTC

PPAR δ -LBD	ATTCATCGATAGATCTGCAGGTGGCCGACCTGAAGGCCTTC TC ATGCCACCCGGGATCCTTAGTACATGTCCTTGTAGATCTCC T
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Table S2: List of antibodies

Target antigen	Source	Catalog	Working concentration
Anti-alpha smooth muscle Actin	Abcam	ab32575	1:500
AF647 Rat Anti-Mouse CD144	BD biosciences	562242	1:100
Alexa Fluor® 488 anti-mouse CD31	MEC13.3	Biologend	1:200
PE-Cy TM 7 Rat Anti-CD11b	BD biosciences	552850	1:100
Anti-Albumin	Abcam	ab207327	1:500
CD144 (VE-cadherin) Monoclonal Antibody	Invitrogen	14-1441-82	1:500
Brilliant Violet 605 TM anti-mouse CD45 Antibody	Biologend	103140	1:200
BV605 Rat Anti-Mouse CD144	BD Biosciences	748261	1:100
PE/Cy7 anti-mouse F4/80	Biologend	123114	1:100
Anti-CD68 antibody	Abcam	ab31630	1:250
PerCP/Cy5.5 anti-mouse Ly-6C Antibody	Biologend	128012	1:100
VEGFR1 antibody	Affbiotech	AF6204	1:250
CD81 antibody-internal	Affbiotech	DF2306	1:250
CD63 antibody-internal	Affbiotech	DF2305	1:250
Claudin 5 antibody-C-terminal	Affbiotech	AF5216	1:250
HIF1A antibody	Affbiotech	BF0593	1:500
LIVE/DEAD TM Fixable Aqua Dead Cell Stain Kit	Invitrogen TM	L34966	1:500
Goat anti-Rabbit IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 488	Invitrogen	A-11034	1:500
Anti-PPAR delta antibody (ab23673)	Abcam	ab23673	1:1000
Goat Anti-Rabbit IgG (H + L)-HRP Conjugate	Bio-rad	1706515	1:2000
Goat Anti-Mouse IgG (H + L)-HRP Conjugate	Bio-rad	1706516	1:2000
Brilliant Violet 605 TM anti-mouse CD64 (Fc γ RI) Antibody	Biologend	139323	1:100
Alexa Fluor® 647 anti-mouse/human Ki-67 Antibody	Biologend	151206	1:100
PE anti-mouse CD106 Antibody	Biologend	105713	1:100
mouse anti-beta-actin loading control antibody	Thermofisher	MA5-15739	1:1000
mouse anti-GAPDH loading control antibody	Thermofisher	MA5-15738	1:1000
PE anti-mouse Ly-6G Antibody	Biologend	127608	1:100
AF488 anti-mouse CD4 antibody	Biologend	100529	1:100
Recombinant Anti-VCAM1 antibody	Abcam	ab134047	1:250
Purified Rat Anti-Mouse CD16/CD32 (Mouse BD Fc Block TM)	BD Pharmingen TM	553142	1:1000
ZO-1 Monoclonal Antibody (ZO1-1A12)	Invitrogen	33-9100	1:100

HIF-1 α (D1S7W) XP [®] Rabbit mAb #36169	CST	36169S	1:100
Goat anti-Mouse IgG (H+L) Highly Cross- Adsorbed Secondary Antibody, Alexa Fluor Plus 488	Invitrogen	A32723	1:500
Goat anti-Rat IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 568	Invitrogen	A-11077	1:500
PE/Cy7 anti-mouse CD133 Antibody	Biolegend	315-2C11	1:100
Mouse VEGFR2/KDR/Flk-1 Antibody	R&D	Af644	1:100
Anti-CD31 antibody	Abcam	ab28364	1:500
Fluorescein labeled Griffonia (Bandeiraea) Simplicifolia Lectin I (GSL I, BSL I)	Vectorlabs	FL-1101-5	