Supplementary Table S1: Primers used for gene expression analysis, genotyping, and sex determination.

Gene	NCBI number	Primer sequence (5'→3')	Product length (bp)
Genotyping			
hsFLT1	NM_001159920.2	for: CAAGGACGTAACTGAAGAGG rev: TTTCTTCCCACAGTCCCAAC	465
Col1a1	/	for: CCATCCCAACAATACATCACA rev: TGGTTTCTTTGGGCTAGAGG	200
tTA	/	for: AAGGGAGCTGCAGTGGAGTA rev-wt: CCGAAAATCTGTGGGAAGTC	297
Sex determination			
IL-3	NM_010556.4	for: GGGACTCCAAGCTTCAATCA rev: TGGAGGAGGAAGAAAAGCAA	544
Sry	NM_011564.1	for: TGGGACTGGTGACAATTGTC rev: GAGTACAGGTGTGCAGCTCT	402
Reference/Housekeeping gene			
Gapdh	XM_011241214.1	for: ACAACTCACTCAAGATTGTCAGCA rev: ATGGCATGGACTGTGGTCAT	121
Glucose and glycogen metabolism			
Glut-1	NM_011400.3	for: GCTGTGCTTATGGGCTTCTC rev: ACACCTGGGCAATAAGGATG	202
Glut-3	NM_011401.4	for: GGAGGAGAACCCTGCATATGATA rev: TGGCTTCATAGTCATCCTTTAGTAAC	96
Gyg	NM_001355261.1	for: TATACTCCTACCTCCCGGCA rev: TTGACAAGGCCATGGTGTTG	223
Gys1	NM_030678.3	for: CTGGCCGCTATGAGTTTTCC rev: TGGGGTGTCCCATAGTTGT	194
Cx26	NM_008125.3	for: ATGCTACGACCACCACTTCC rev: TACGGACCTTCTGGGTTTTG	194
Fatty acid transporters			
Cd36	NM_001159558.1	for: CAGTGCAGAAACAATGGTTGTCT rev: TGACATTTGCAGGTCTATCTACG	137
Fabp	NM_010174.2	for: TTTGTCGGTACCTGGAAGCT rev: CTGTCACCTCGTCGAACTCT	214
Abca1	NM_013454.3	for: CGACCATGAAAGTGACACGC rev: AGCACATAGGTCAGCTCGTG	117
Amino acid transporter			
Snat-1	NM_001166458.1	for: AGCACAGGGCGACATTCTCATC rev: ACAGGTGGAACTTTGTCTTCTTG	134
Snat-2	NM_175121.4	for: ACAAATGGGTTGTGGTA rev: CCTAGATTTCTCAGCAGTGACAATG	92
Angiogenesis			
Flk-1	NM_001363216.1	for: GGCGGTGGTGACAGTATCTT rev: GTCACTGACAGAGGCGATGA	162

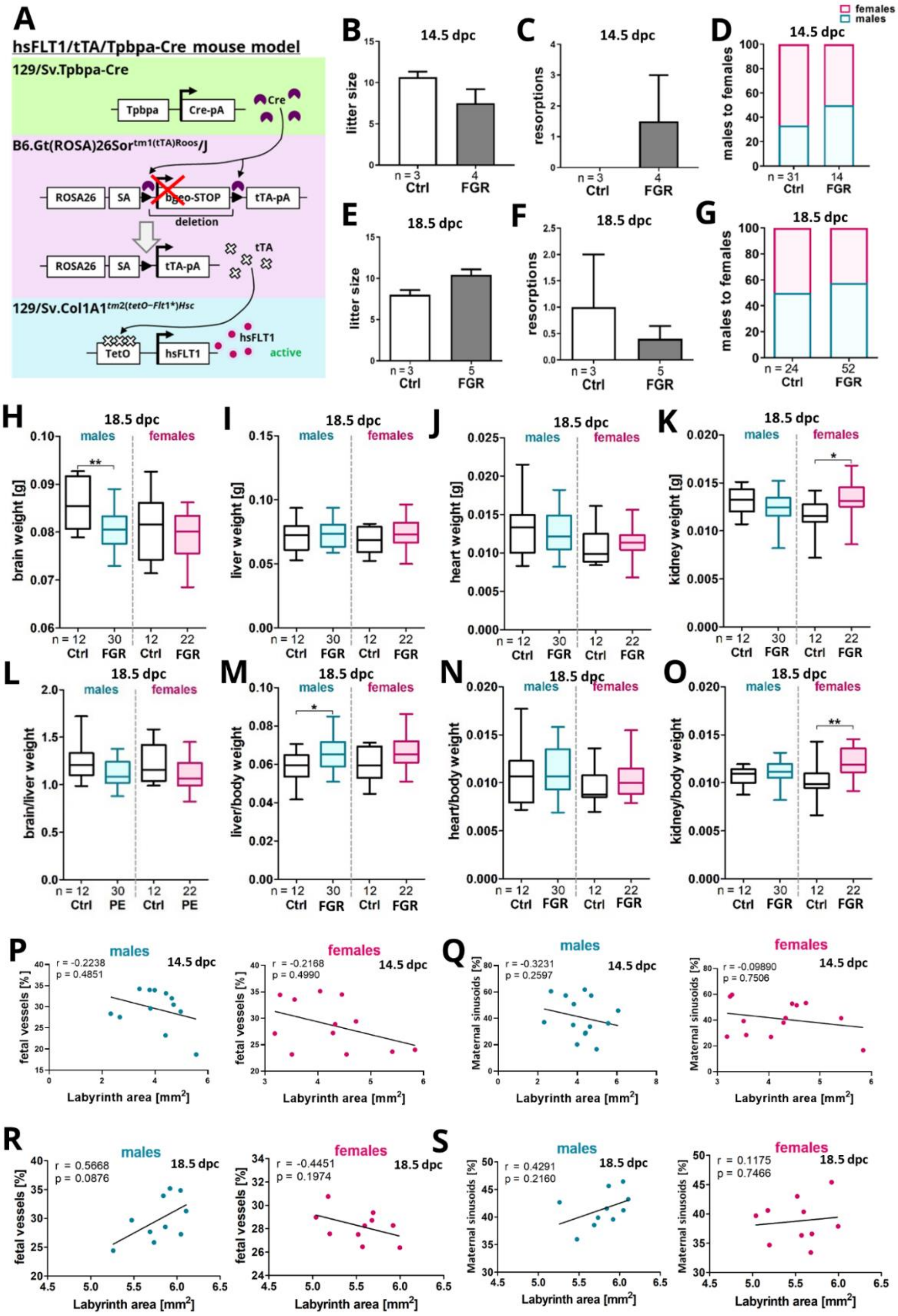
Flt-4	NM_008029.3	for: GTGGCTGTGAAGATGCTGAA rev: TGACACGCAAGAAGTTGGAG	199
Plgf	XM_011244016.1	for: CGTCCTGTGTCCTTCTGAGT rev: CCTCTTCCTCTTCCCCTTGG	200
Vegfa	NM_001025257.3	for: CAGGCTGCTGTAACGATGAA rev: GCATTCACATCTGCTGTGCT	140
Vegfb	NM_011697.3	for: AACACAGCCAATGTGAATGC rev: GGAGTGGGATGGATGATGTC	157
Vegfc	NM_009506.2	for: CAAGGCTTTTGAAGGCAAAG rev: TCCCCTGTCCTGGTATTGAG	159
Cd31	NM_001032378.2	for: ATGACCCAGCAACATTCACA rev: CACAGAGCACCGAAGTACCA	200
hsFLT1	XM_017020485.1	for: AATCATTCCGAAGCAAGGTG rev: TTTCTTCCCACAGTCCCAAC	219
Hypoxia markers			
HO-1	NM_010442.2	for: CACGCATATACCCGCTACCT rev: CCAGAGTGTTCATTCGAGCA	175
Hif1α	NM_001313920.1	for: TCAAGTCAGCAACGTGGAAG rev: TATCGAGGCTGTGTCGACTG	198
Hif2α	NM_010137.3	for: GCAAGCCTTCCAAGACACAA rev: CCTGAGCTCCTGGTAGATGG	228
Phd1	NM_001357767.1	for: TGCATCAAGTGGAGGAGGAG rev: GATGCTCCTGGACGGTGATA	246
Phd2	NM_001363475.1	for: AGGTGAGAAAGGTGTGAGGC rev: CACAGTACAGTCCAGCAGA	228
Trophoblast and glycogen cell marker			
Plap	NM_007431.3	for: TCAGGGCAATGAGGTCACAT rev: CCTCTGGTGGCATCTCCTTA	161
Igf-2	NM_001315489.1	for: ACCTTCCAGCCTTTTCCTGTC rev: GTAGACACGTCCCTCTCGGA	357
Igf-2R	NM_010515.2	for: TATGTGAACGGCTCTGCTTG rev: GAGCAAGCCTGGTCTGTTTC	200
Pcdh12	NM_017378.2	for: CTTCACCTCATCACGCTCAA rev: TGCCCTCTGTCCTCTGCTAT	197
Gcm1	NM_008103.3	for: TGCTCACCTATGGCTCTCCT rev: AAAATTCTGCCAAGCCCTTT	201
Cytokine marker			
Tnfα	NM_001278601.1	for: CGTCAGCCGATTTGCTATCT rev: CGGACTCCGCAAAGTCTAAG	206

Supplementary Table S2: Antibodies used for Immunoblot and immunohistochemistry.

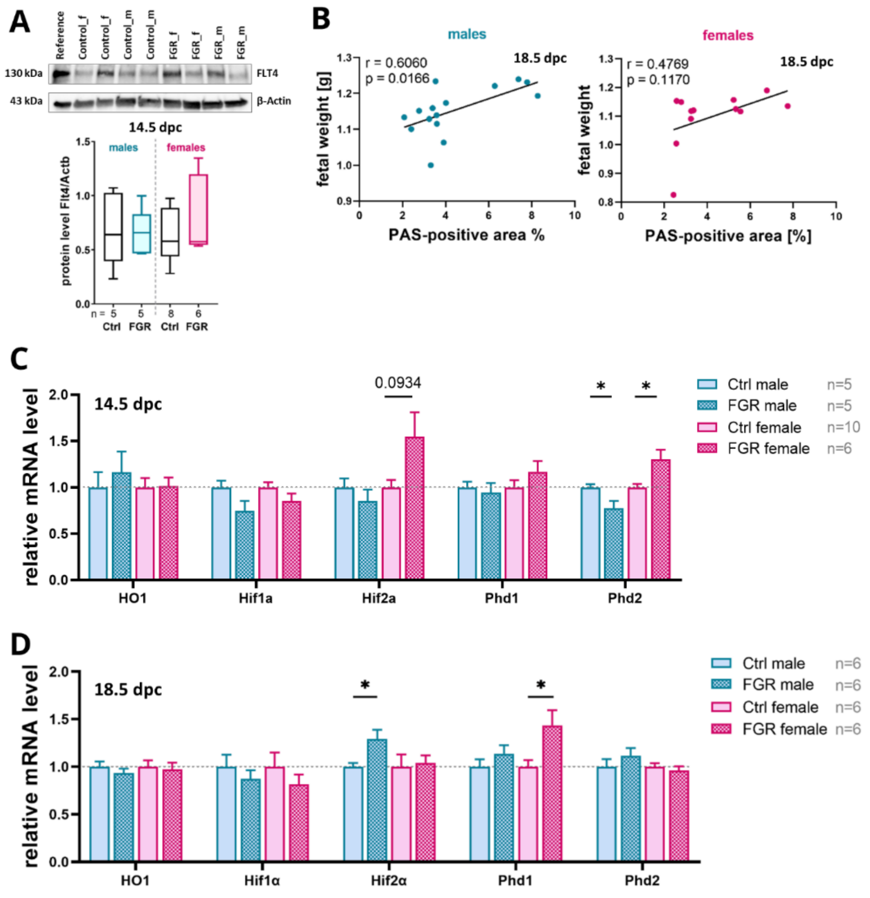
Primary antibody	Dilution	Host	Company	Reference number
Anti-CD31[a]	1:200 in PBS/BSA (0.5 %)	Rat	Dianova (Hamburg, Germany)	DIA-310
Anti-CD31[b]	1:5000 in 2 % milk powder	Rat	Dianova (Hamburg, Germany)	DIA-310
Anti-CX26[b]	1:350 in 2 % milk powder	Rabbit	Santa Cruz Biotechnology (Dallas, USA)	#710500
Anti-FLK1[b]	1:1000 in 5 % milk powder	Rabbit	Cell Signaling Technology (Danvers, USA)	#2479
Anti-FLT4[b]	1:200 in 0.5 % milk powder	Goat	R&D Systems (Minneapolis, USA)	AF743
Anti-GLUT1[b]	1:3000 in 2 % milk powder	Rabbit	Novus Biologicals (Centennial, USA)	NB110-39113
Anti-TNFα[b]	1:1000 in 2 % milk powder	Rabbit	Abcam (Cambridge, GB)	ab183218
Peroxidase anti-ß-actin[b]	1:20000 in TBS-T	Mouse	Sigma-Aldrich (St. Louis, USA)	A3854
Secondary antibody	Dilution	Host	Company	Reference number
Anti-goat IgG-HRP[b]	1:5000 in 0.5 % milk powder	Donkey	Invitrogen (Karlsruhe, Germany)	AB_10990162
Anti-rabbit IgG-HRP[b]	1:5000 in 0.5 % milk powder	Goat	Dako (California, USA)	p0448
Anti-rat IgG-HRP[b]	1:5000 in 0.5 % milk powder	Goat	Invitrogen (Karlsruhe, Germany)	AB_10965062
Anti-rat IgG-Biotin[a]	1:100 in 0.5 % PBS/BSA	Donkey	Invitrogen (Karlsruhe, Germany)	A18743

[a] used for Immunohistochemistry

[b] used for Immunoblot analysis.



Supplementary Figure S1. Impact of placenta-specific hsFLT1 overexpression on phenotype of dams and fetuses at 14.5 and 18.5 dpc. A) Schematic depiction of the interaction between all three transgenes necessary to induce hsFLT1 overexpression in the hsFLT1/tTA/Tpbpa-Cre mouse model. **B/C**) At 14.5 dpc the litter size was higher in the control group (**B**), and resorptions were only observed in the FGR group (**C**). **D**) More females were born in the control group whereas the sex ratio in the FGR group was equal. **E/F**) At 18.5 dpc the litter size was higher in the FGR group (**E**), and resorptions were only observed in both groups (**F**). **G**) No change in sex ratio was observed at 18.5 dpc. **H-O**) Organ weights and organ/bodyweight ratios at 18.5 dpc: The brain weight (**H**) was significantly reduced in the FGR male group and the kidney weight was significantly increased in the female FGR group (**K**) wherease the liver and heart weights did not change between the groups (**I, J**). The liver to body weight was significantly increased in males in the FGR group (**M**) and the kidney/body ratio was significantly increased in the females in the FGR group (**O**). The brain/liver weight and the heart/body weight did not change between the groups (**L, N**). µm **P/Q**) No Correlation of the percentage of fetal vessels (**P**) and maternal sinusoids (**Q**) with the labyrinth area was observed at 14.5 dpc **R**) At 18.5 dpc the percentage of fetal vessels correlated by trend (p=0.0876) to the labyrinth area in male FGR placentas but not in females. **S**) Whereas the percentage of maternal sinusoids did not correlate to the labyrinthine area in male and female FGR group at 18.5 dpc. Data is presented in a box plot with median, interquartile range and lower/upper extreme or in a bar graph with standard error. n=number of dams (**B/C, E/F**), fetuses (**D,G**) or fetal organs (**H-O**). * p ≤ 0.05 and ** ≤0.01 as determined by the Mann-Whitney test. Scale bar = 400 .



Supplementary Figure S2: Impact of placenta-specific hsFLT1 overexpression on the lymphangiogenic marker Flt4 and hypoxia-induced gene expression at 14.5 and 18.5 dpc. A) FLT4 protein level at 14.5 dpc was not changed upon placenta-specific hsFLT1 expression as shown by Western Blot analysis. **B**) The fetal weight significantly correlate to the percentage of PAS-stained area (glycogen containing cells) in the spongiotrophoblast area of male placentas but not in female placentas. **C**) Transcript levels of hypoxia/oxidative stress markers in placentas at 14.5 dpc. Only *Hif2α* was increased by trend in the female FGR groups and *Phd2* was significantly decreased in male FGR and increased in female FGR group compared to controls. **D**) At 18.5 dpc *Hif2α* mRNA was significantly increased in male FGR and *Phd1* mRNA in female FGR group. The mRNA levels were determined by qPCR and normalized to the housekeeping gene *Gapdh*. Data is presented in a box plot with median, interquartile range and lower/upper extreme or in a bar graph with standard error. n=number of placentas. * p ≤ 0.05 as determined by the Mann-Whitney test. Statistical analysis of correlation were calculated by Spearman r test.