Supplemental Information
Supplemental Tables 1 and 2
Supplemental Figures 1-4

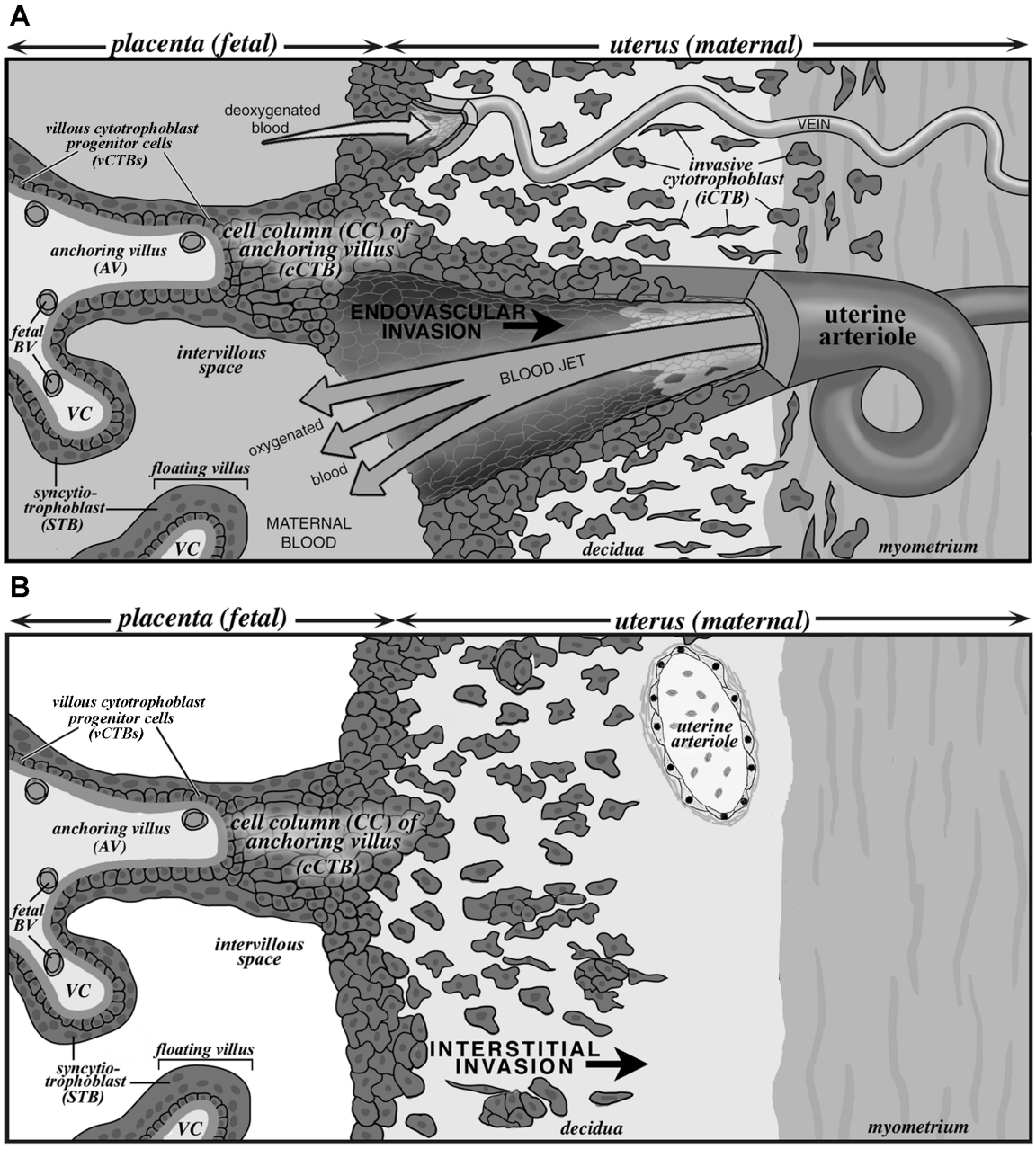
Supplemental Table 1. Maternal and infant characteristics

	PE (*n* = 5)	nPTL (*n* = 5)	*P* value
Maternal age, yr	29.0 (5.9)*	25.6 (6.3)	0.40
BMI, kg/m^2	27.4 (4.2)	26.0 (5.0)	0.68
Systolic blood pressure, mmHg	148 (11)	112 (7)	< 0.001
Diastolic blood pressure, mmHg	88 (5)	65 (13)	< 0.01
Proteinuria, designation	+1 to +3	0	NA
Gestational age at delivery, week	31.2 (2.5)	29.5 (3.7)	0.45
Birth weight, g	1365 (528)	1572 (694)	0.61

*__mean ± SD, 2-tailed Student's t-test.__

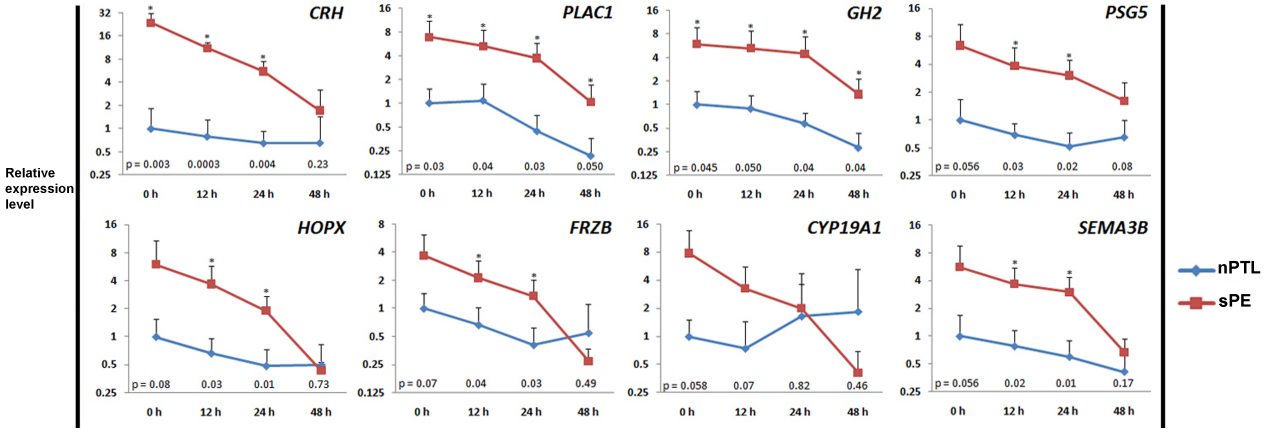
Supplemental Table 2. Reagents, sources and concentrations

Reagent	Source	Concentration
Polyclonal anti-SEMA3B	Novus Biologicals	Diluted 1:1000
Polyclonal anti-NRP-1 (C-19) and NRP-2 (C-9)	Santa Cruz Biotechnology Inc. (Santa Cruz, CA)	2 μg/ml (IB)
Monoclonal anti-VEGF R2	Dr. K. Chwalisz (Scherring AG, Berlin, Germany)	1:500
Polyclonal anti-PI3K p85	Upstate USA Inc (Charlottesville, VA)	1:100
Polyclonal anti-PI3K p100α	Epitomics (Burlingame, CA), Becton Dickinson (San Jose, CA)	1:2000 250 ng/ml
Polyclonal anti-Akt, anti-p-Akt (Ser473) and anti-p-GSK3α/β (Ser21/Ser9)	Cell Signaling Technology (Danvers, MA)	1:1000 1:1000 1:1000
Monoclonal anti-GSK3 (4G-IE)	Upstate Cell Signaling Solutions (Billerica, MA)	1 μg/ml
Monoclonal anti-V5	Invitrogen Corp (Carlsbad, CA)	160 ng/ml
Monoclonal anti-α-actin (AC-40)	Sigma-Aldrich Corp (Saint Louis, MO)	1:500
(rat) monoclonal anti-cytokeratin (7D3)	Generated in collaboration with Dr. C. Damsky (Damsky *et al.*, 1992)	1:200
NRP1-Fc, NRP2-Fc and CD6-Fc fusion proteins	R&D Systems (Minneapolis, MN)	400 ng/ml
Monoclonal anti-VEGF (A4.6.1)	Dr. Napoleone Ferrara (Genentech, South San Francisco, CA)	400 ng/ml
Wortmannin	Calbiochem Signal Transduction (San Diego, CA)	2 μM
Complete EDTA-free Protease inhibitor cocktail	Roche Applied Science (Indianapolis, IN)	_
LiCL	Sigma-Alrich Corp	20 mM
SEMA3B	Produced in house	50-100 ng/ml (COS-1 cells), 2 μg/ml (*E. coli*)
$VEGF_{165}$	R&D Systems	40 ng/ml medium; 60 pg/filter

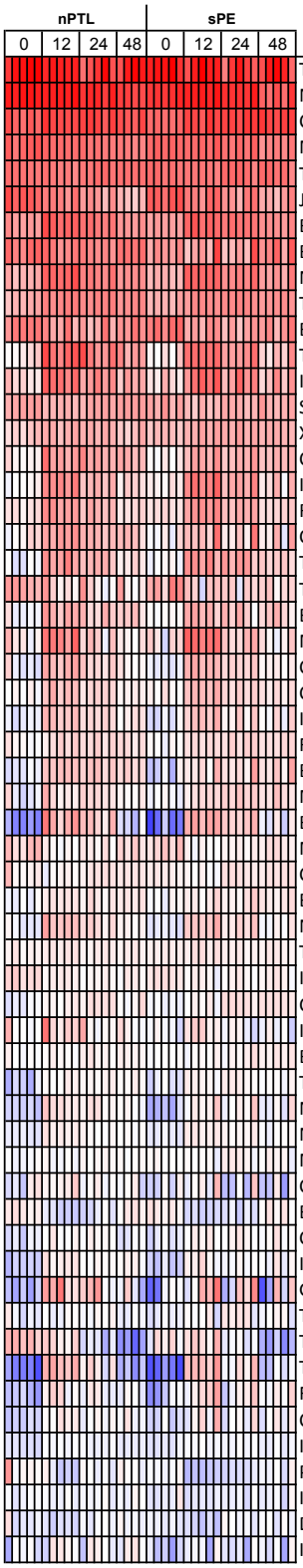


Supplemental Figure 1. Diagram of the cellular organization of the human maternal-fetal interface in normal pregnancy and in preeclampsia. (A) Villous cytotrophoblasts (vCTBs) progenitors, the specialized (fetal) epithelial cells of the placenta, differentiate and invade the uterine wall (interstitial invasion; iCTBs), where they also breach maternal blood vessels (endovascular invasion). The basic structural units of the placenta are the chorionic villi, composed of a stromal villous core (VC) with fetal blood vessels, surrounded by a basement membrane and overlain by vCTBs. During differentiation, these cells detach from the basement membrane and adopt one of two fates. They either fuse to form the multinuclear syncytiotrophoblasts (STBs) that cover floating villi or join a column of cytotrophoblasts (cCTBs) at the tips of anchoring villi (AV). The syncytial covering of floating villi mediates the nutrient, gas and waste exchange between fetal and maternal blood. The anchoring villi, through the attachment of cCTBs, establish physical connections between the fetus and the mother. iCTBs penetrate the uterine wall through the first third of the myometrium. A subset of these cells home to uterine spiral arterioles and remodel these vessels by replacing the

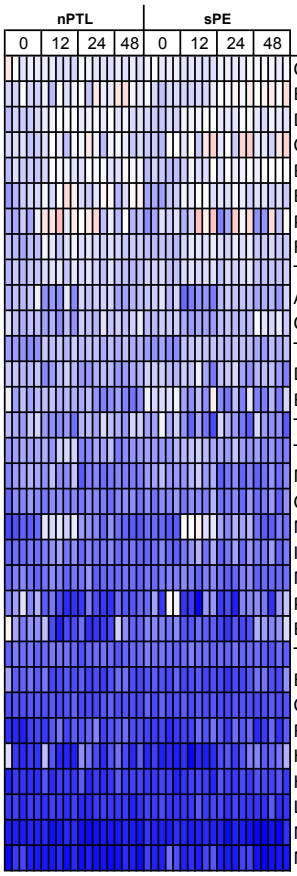
endothelial lining and intercalating within the muscular walls. To a lesser extent, they also remodel uterine veins. (B) In PE, the interstitial and the endovascular components of CTB invasion are restricted. As a result, interstitial invasion is shallow and many uterine arterioles retain their original structures.



Supplemental Figure 2. Confirmation of the expression patterns of selected genes that were misexpressed in sPE. Taqman qRT-PCR was performed using cDNA samples prepared from CTBs that were isolated from the placentas of women whose pregnancies were complicated by preterm labor with no sign of infection (nPTL) or severe preeclampsia (sPE). The analyses were done on cells immediately after isolation (0 h) and after 12, 24, or 48 h of culture. The reactions were done in triplicate. The relative gene expression levels of each transcript were plotted on the y-axis. Data points are the mean ± standard deviation. Fold change differences between the sPE and nPTL samples at each time point were assessed using a Student's t-test. The values shown are the mean ± SD. p values are displayed at bottom of each panel.

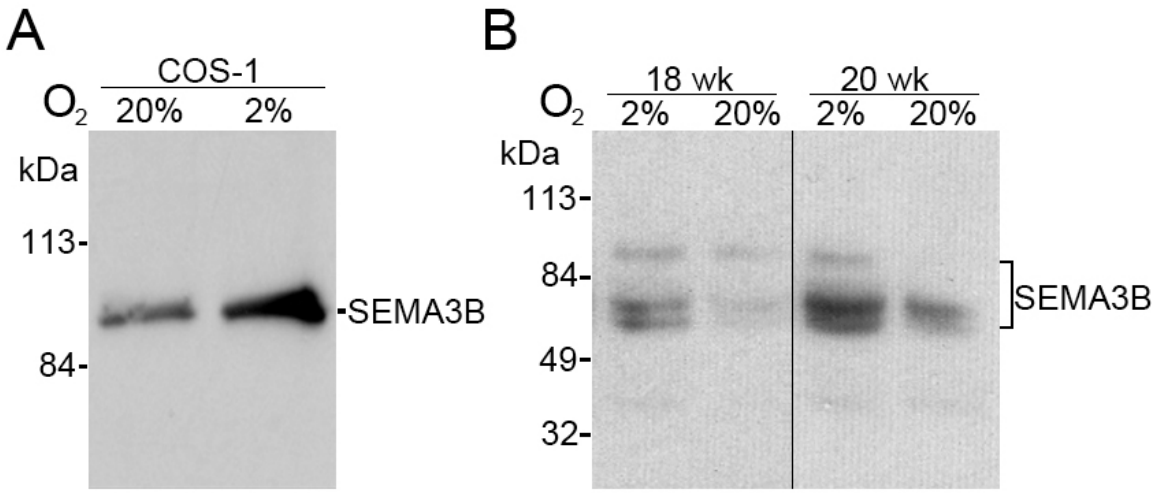


Symbol	Title
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha
CYCS	cytochrome c, somatic
MCL1	myeloid cell leukemia sequence 1 (BCL2-related)
TFG	TRK-fused gene
JUN	jun oncogene
BIRC2	baculoviral IAP repeat-containing 2
BCL2A1	BCL2-related protein A1
NR3C1	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)
TNFRSF1A	tumor necrosis factor receptor superfamily, member 1A
BNIP3L	BCL2/adenovirus E1B 19kDa interacting protein 3-like
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B
IRF1	interferon regulatory factor 1
SFRS2IP	splicing factor, arginine/serine-rich 2, interacting protein
XIAP	X-linked inhibitor of apoptosis
CASP4	caspase 4, apoptosis-related cysteine peptidase
IRF7	interferon regulatory factor 7
RELA	v-rel reticuloendotheliosis viral oncogene homolog A (avian)
CASP1	caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)
TNFRSF10B	tumor necrosis factor receptor superfamily, member 10b
TNFRSF21	tumor necrosis factor receptor superfamily, member 21
BCL2L11	BCL2-like 11 (apoptosis facilitator)
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)
CASP3	caspase 3, apoptosis-related cysteine peptidase
CASP7	caspase 7, apoptosis-related cysteine peptidase
IRF2	interferon regulatory factor 2
FADD	Fas (TNFRSF6)-associated via death domain
BID	BH3 interacting domain death agonist
MDM2	Mdm2 p53 binding protein homolog (mouse)
BIRC3	baculoviral IAP repeat-containing 3
MAP3K1	mitogen-activated protein kinase kinase kinase 1
CASP2	caspase 2, apoptosis-related cysteine peptidase
BCL2L2	BCL2-like 2
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
TRADD	TNFRSF1A-associated via death domain
IRF3	interferon regulatory factor 3
CHUK	conserved helix-loop-helix ubiquitous kinase
IRF6	interferon regulatory factor 6
BCL2L1	BCL2-like 1
TRAF3	TNF receptor-associated factor 3
NFKBIE	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, epsilon
NFKBIB	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta
MAP2K4	mitogen-activated protein kinase kinase 4
CARD16	caspase recruitment domain family, member 16
BAD	BCL2-associated agonist of cell death
CASP8	caspase 8, apoptosis-related cysteine peptidase
IKBKE	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase epsilon
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)
TP53	tumor protein p53
TNF	tumor necrosis factor
TRAF1	TNF receptor-associated factor 1
FAS	Fas (TNF receptor superfamily, member 6)
CD40	CD40 molecule, TNF receptor superfamily member 5
IKBKG	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma
PARP1	poly (ADP-ribose) polymerase 1
IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta
DFFA	DNA fragmentation factor, 45kDa, alpha polypeptide
IRF5	interferon regulatory factor 5



Symbol	Title
CASP9	caspase 9, apoptosis-related cysteine peptidase
BAX	BCL2-associated X protein
DAXX	death-domain associated protein
CRADD	CASP2 and RIPK1 domain containing adaptor with death domain
BAK1	BCL2-antagonist/killer 1
BOK	BCL2-related ovarian killer
PRF1	perforin 1 (pore forming protein)
RIPK1	receptor (TNFRSF)-interacting serine-threonine kinase 1
TRAF6	TNF receptor-associated factor 6
APAF1	apoptotic peptidase activating factor 1
CASP6	caspase 6, apoptosis-related cysteine peptidase
TRAF2	TNF receptor-associated factor 2
DFFB	DNA fragmentation factor, 40kDa, beta polypeptide (caspase-activated DNase)
BCL2	B-cell CLL/lymphoma 2
TPR	translocated promoter region (to activated MET oncogene)
TNFRSF25	tumor necrosis factor receptor superfamily, member 25
MAP3K14	mitogen-activated protein kinase kinase kinase 14
CASP10	caspase 10, apoptosis-related cysteine peptidase
NGF	nerve growth factor (beta polypeptide)
IRF4	interferon regulatory factor 4
MAPK10	mitogen-activated protein kinase 10
PTPN13	protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase)
BIRC5	baculoviral IAP repeat-containing 5
TP73	tumor protein p73
EPR1	effector cell peptidase receptor 1 (non-protein coding)
CD40LG	CD40 ligand
FASLG	Fas ligand (TNF superfamily, member 6)
HELLS	helicase, lymphoid-specific
HRK	harakiri, BCL2 interacting protein (contains only BH3 domain)
LTA	lymphotoxin alpha (TNF superfamily, member 1)
NGFR	nerve growth factor receptor
NTRK1	neurotrophic tyrosine kinase, receptor, type 1

Supplemental Figure 3. CTBs isolated from the placentas of nPTL and sPE patients did not upregulate genes that are associated with apoptosis over 48 h of culture.



Supplemental Figure 4. Hypoxia upregulated SEMA3B expression after 48 h in culture. Transfected COS-1 cells (A) and chorionic villus explants established from normal (18 and 20 wk) second trimester placentas (B) were cultured for 48 h in standard conditions (20% O_2) or in a hypoxia chamber (2% O_2). Vertical lines denote noncontiguous lanes from the same gel. The entire experiment was done a total of three times. SEMA3B expression was quantified by immunoblot analysis.