



Supplementary Figure 1. Trophoblast side-population marker gene expression in placentas from single complication pregnancies (only preeclampsia or only fetal growth restriction) or pregnancies with concurrent preeclampsia/fetal growth restriction. mRNA expression of side-population-enriched genes in placentas from participants with only fetal growth restriction (FGR, n=13, blue circle), concurrent fetal growth restriction and preeclampsia (FGR/PE, n=17, yellow circle), or only preeclampsia (PE, n=61, green circle) compared to gestation-matched preterm (<34-week) controls (n=18, grey square). *CXCL8* was upregulated in FGR-only (p=0.0003) and concurrent cases (p=0.0033) **(A)**. *ELL2* was upregulated in concurrent cases (p=0.0023) and preeclampsia-only placentas (p=0.0004) **(B)**. *GATA6* was downregulated in concurrent (p=0.015) and preeclampsia-only placentas (p=0.0014) **(C)**. *HK2* was elevated in all conditions (p=0.015 FGR-only, p<0.0001 concurrent and preeclampsia-only) **(D)**. *HLA-DPB1* was unaltered under all conditions **(E)**. *INTS6* was reduced exclusively in placentas with only FGR (p<0.0001) **(F)**. *SERPINE3* **(G)** and *UPP1* **(H)** had no changes in mRNA expression between groups. mRNA expression was normalised to the geometric mean of housekeeper genes. Individual symbols represent individual participants. Data is expressed as mean ± SEM. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Supplementary Table I. Whole slide multiplexed immunofluorescence (mIF) analysis for trophoblast side-population markers in human placental villous cross sections. Performed on n=3 biological replicates of preterm controls, preeclampsia and fetal growth restriction (2 panels of 3 markers each completed on serial section). Panel 1 consisted of HLA-DPB1, UPP1 and SERPINE3. Panel 2 consisted of CXCL8, INTS6, and HK2. Analysis conducted using HALO® Image Analysis Platform's Highplex FL module v4.1.3, with percentage (%) of total cells shown for each biological replicate, and mean \pm SEM for each category.

Category	Biological replicate	Panel 1 (% total cells)				Panel 2 (% total cells)			
		HLA-DPB1	UPP1	SERPINE3	Co-localisation	CXCL8	INTS6	HK2	Co-localisation
Preterm control	1	6.44	57.42	50.98	1.06	59.53	96.66	97.22	57.90
	2	9.24	46.71	24.31	5.07	9.16	36.68	18.66	5.66
	3	0.78	44.42	44.11	0.28	16.77	90.01	93.99	15.44
<i>Mean \pm SEM</i>		<i>5.49 \pm 2.49</i>	<i>49.52 \pm 4.01</i>	<i>39.80 \pm 8.00</i>	<i>2.14 \pm 1.48</i>	<i>28.49 \pm 15.68</i>	<i>74.45 \pm 18.98</i>	<i>69.96 \pm 25.67</i>	<i>26.33 \pm 16.03</i>
Preeclampsia	1	0.45	38.37	37.82	0.18	38.82	89.26	92.68	37.08
	2	4.29	61.32	51.29	3.35	36.06	46.24	61.87	22.28
	3	0.05	91.59	95.36	0.04	65.22	44.13	77.99	34.95
<i>Mean \pm SEM</i>		<i>1.60 \pm 1.35</i>	<i>63.76 \pm 15.41</i>	<i>61.49 \pm 17.38</i>	<i>1.19 \pm 1.08</i>	<i>46.70 \pm 9.29</i>	<i>59.88 \pm 14.70</i>	<i>77.51 \pm 8.90</i>	<i>31.4 \pm 4.62</i>
Fetal growth restriction	1	5.19	67.00	40.14	3.57	84.28	86.65	76.64	67.57
	2	0.85	36.78	30.15	0.30	52.17	97.52	69.57	39.20
	3	1.14	68.72	68.55	0.59	85.13	93.60	96.57	78.75
<i>Mean \pm SEM</i>		<i>2.39 \pm 1.40</i>	<i>57.50 \pm 10.37</i>	<i>46.28 \pm 11.50</i>	<i>1.49 \pm 1.05</i>	<i>73.86 \pm 10.85</i>	<i>92.59 \pm 3.18</i>	<i>80.93 \pm 8.08</i>	<i>61.84 \pm 11.77</i>

Supplementary Table II. Participant clinical characteristics <34-week gestation placental samples for preeclampsia, fetal growth restriction and gestation-matched controls. BMI = body mass index, SBP = systolic blood pressure and DBP = diastolic blood pressure. Mann-Whitney U tests used for comparison of medians. Chi-square tests used for categorical variables. BMI data missing for 4/18 control, 1/17 fetal growth restriction/preeclampsia (FGR/PE) and 8/61 PE samples. Smoking status data missing for 1/17 FGR/PE and 6/81 PE samples.

	Controls (n=18)	Fetal Growth Restriction (n=12)	Fetal Growth Restriction/ Preeclampsia (n=18)	Preeclampsia (n=61)	P-value
Birth Parent Age (years) Median (IQR)	32.5 (25.8 – 36.3)	30.5 (24.3 – 36.0)	31.0 (25.0 – 32.3)	31.0 (28.0 – 35.0)	$p_{FGR} = 0.569$ $p_{FGR/PE} = 0.246$ $p_{PE} = 0.865$
Gestation at Delivery (weeks) Median (IQR)	30.4 (29.2 – 32.0)	31.4 (30.1 – 32.1)	29.9 (26.5 – 30.8)	30.0 (28.1 – 31.7)	$p_{FGR} = 0.225$ $p_{FGR/PE} = 0.175$ $p_{PE} = 0.505$
BMI (kg/m²) Median (IQR)	28.2 (24.8 – 35.1)	23.6 (19.3 – 30.5)	28.6 (25.6 – 35.5)	27.0 (24.0 – 36.1)	$p_{FGR} = 0.115$ $p_{FGR/PE} = 0.688$ $p_{PE} = 0.677$
Parity no. (%) 0 1 ≥2	4 (22.2) 9 (50.0) 5 (27.8)	9 (75.0) 1 (8.3) 2 (16.7)	15 (83.3) 2 (11.1) 1 (5.6)	39 (63.9) 15 (24.6) 7 (11.5)	$p_{FGR} = 0.013$ $p_{FGR/PE} = 0.001$ $p_{PE} = 0.007$
SBP at Delivery (mmHg) Median (IQR)	125.0 (117.3 – 130.0)	122.5 (116.3 – 132.3)	170.0 (155.0 – 180.0)	175.0 (165.0 – 181.5)	$p_{FGR} = 0.875$ $p_{FGR/PE} < 0.0001$ $p_{PE} < 0.0001$
DBP at Delivery (mmHg) Median (IQR)	75.0 (70.0 – 80.0)	80.0 (71.3 – 84.5)	102.5 (93.8 – 110.0)	102.5 (100.0 – 110.0)	$p_{FGR} = 0.078$ $p_{FGR/PE} < 0.0001$ $p_{PE} < 0.0001$
Birth weight (g) Median (IQR)	1587 (1298 – 2011)	993.5 (861.0 – 1110)	882.0 (581.0 – 1156)	1201 (887.0 – 1466)	$p_{FGR} = 0.0007$ $p_{FGR/PE} < 0.0001$ $p_{PE} = 0.0055$
Assigned female at birth no. (%)	8 (44.4)	5 (41.7)	11 (61.1)	28 (45.9)	$p_{FGR} = 0.880$ $p_{FGR/PE} = 0.317$ $p_{PE} = 0.913$
Smoking status no. (%) Never Quit Current Unanswered	13 (72.2) 4 (22.2) 1 (5.6) 0 (0.0)	6 (50.0) 4 (33.3) 2 (16.7) 0 (0.0)	15 (83.2) 1 (5.6) 1 (5.6) 1 (5.6)	50 (82.0) 2 (3.3) 3 (4.9) 6 (9.8)	$p_{FGR} = 0.410$ $p_{FGR/PE} = 0.384$ $p_{PE} = 0.044$