Supplementary Figures & Tables for:

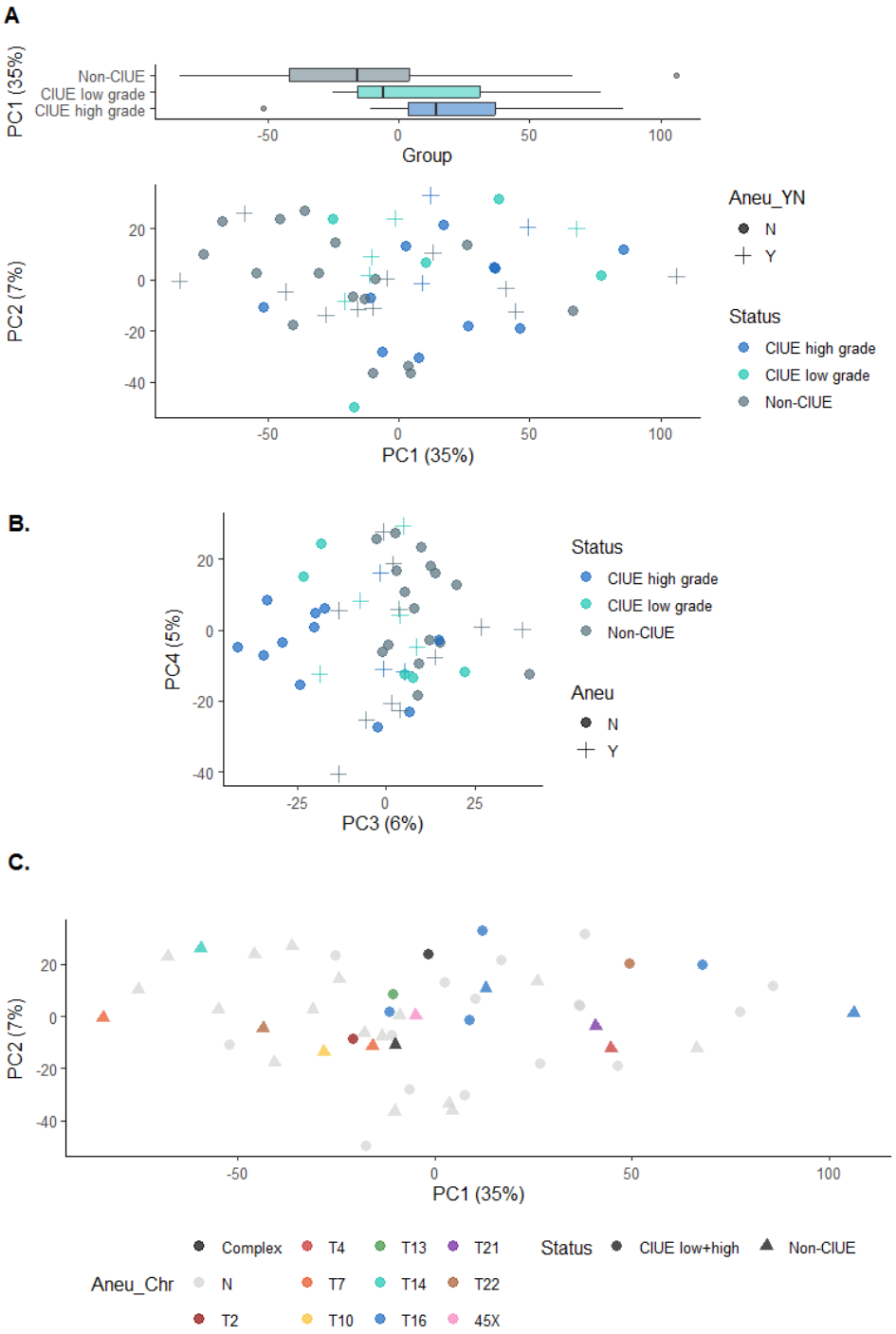
The Role of Placental DNA Methylation in the Pathogenesis of Chronic Intervillositis of Unknown Etiology

Amy M Inkster[1,2], Maria S Peñaherrera[1,2], Wendy P Robinson[1,2], Jefferson Terry[3]

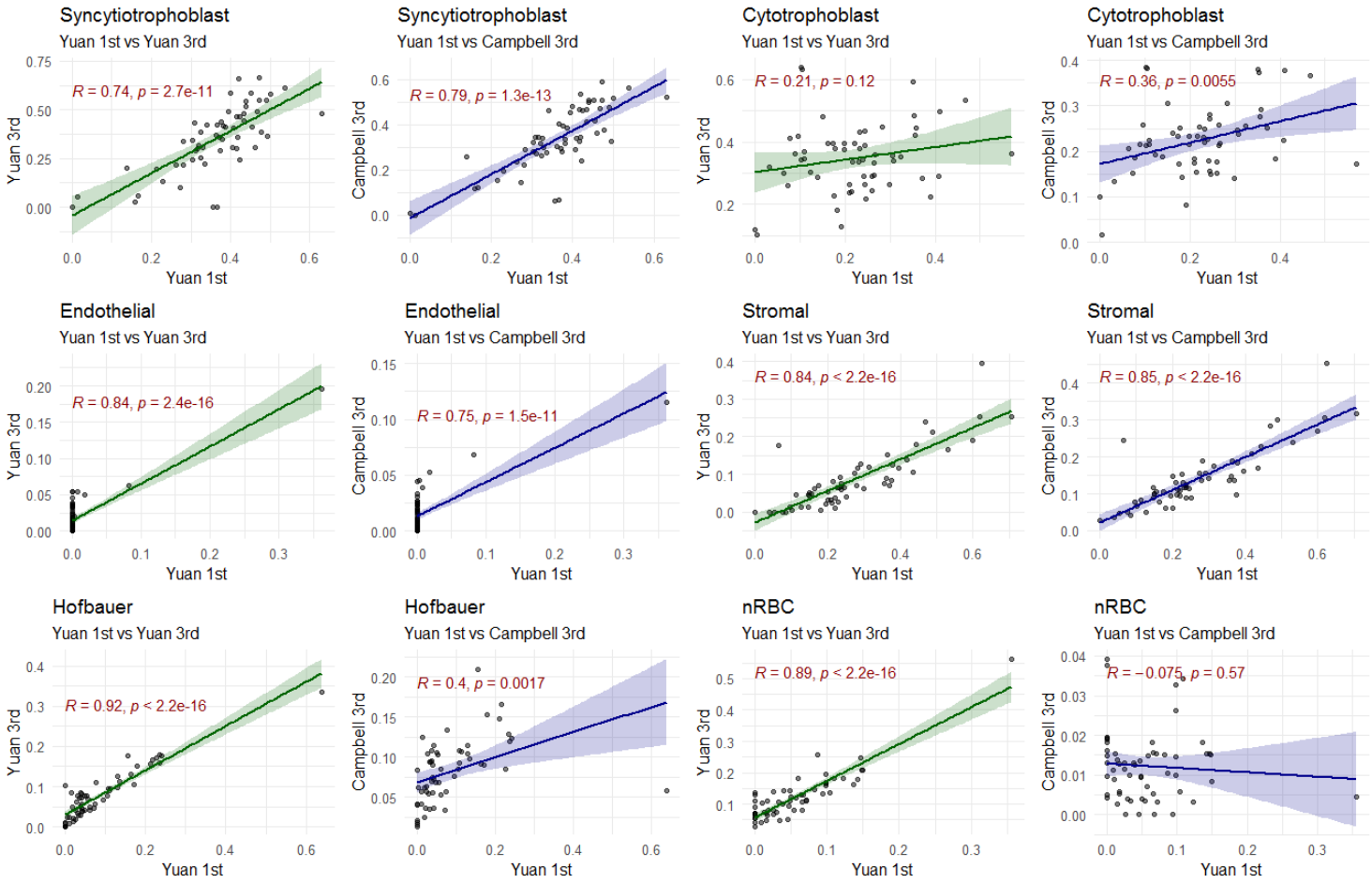
1. BC Children's Hospital Research Institute, 950 W 28th St Vancouver, British Columbia, Canada V5Z 4H4
2. Department of Medical Genetics, Faculty of Medicine, University of British Columbia, 4500 Oak Street, Room C234, Vancouver, British Columbia, Canada V6H 3N1
3. Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of British Columbia, #G-227 2211 Wesbrook Mall, Vancouver, British Columbia, Canada V6T 2B5

Correspondence:
Jefferson Terry
Department of Pathology
British Columbia Children's and Women's Hospitals
4480 Oak Street
Vancouver, British Columbia, V6H 3V4
jefferson.terry@cw.bc.ca

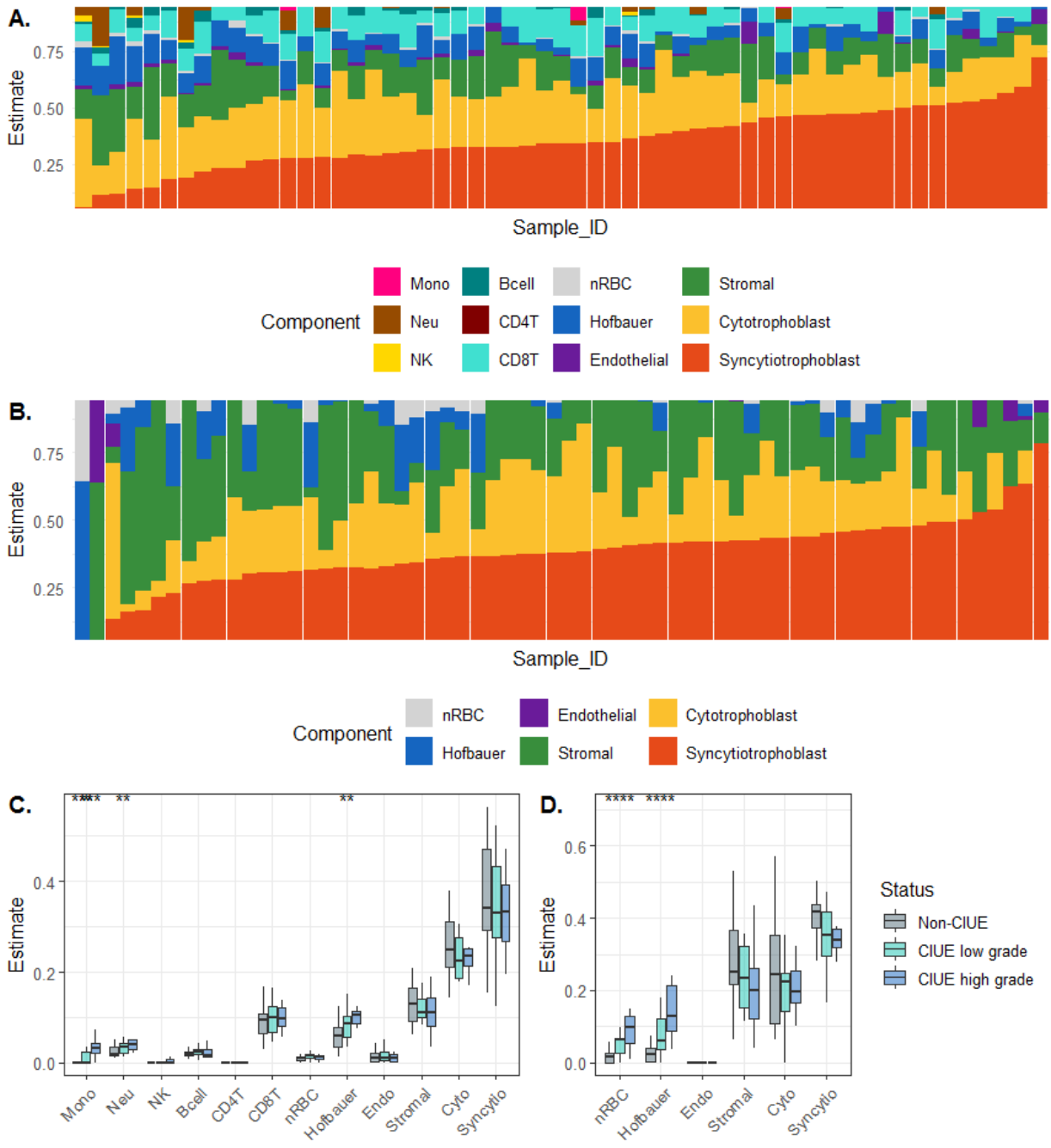
Supplementary Table 1 – see attached file.



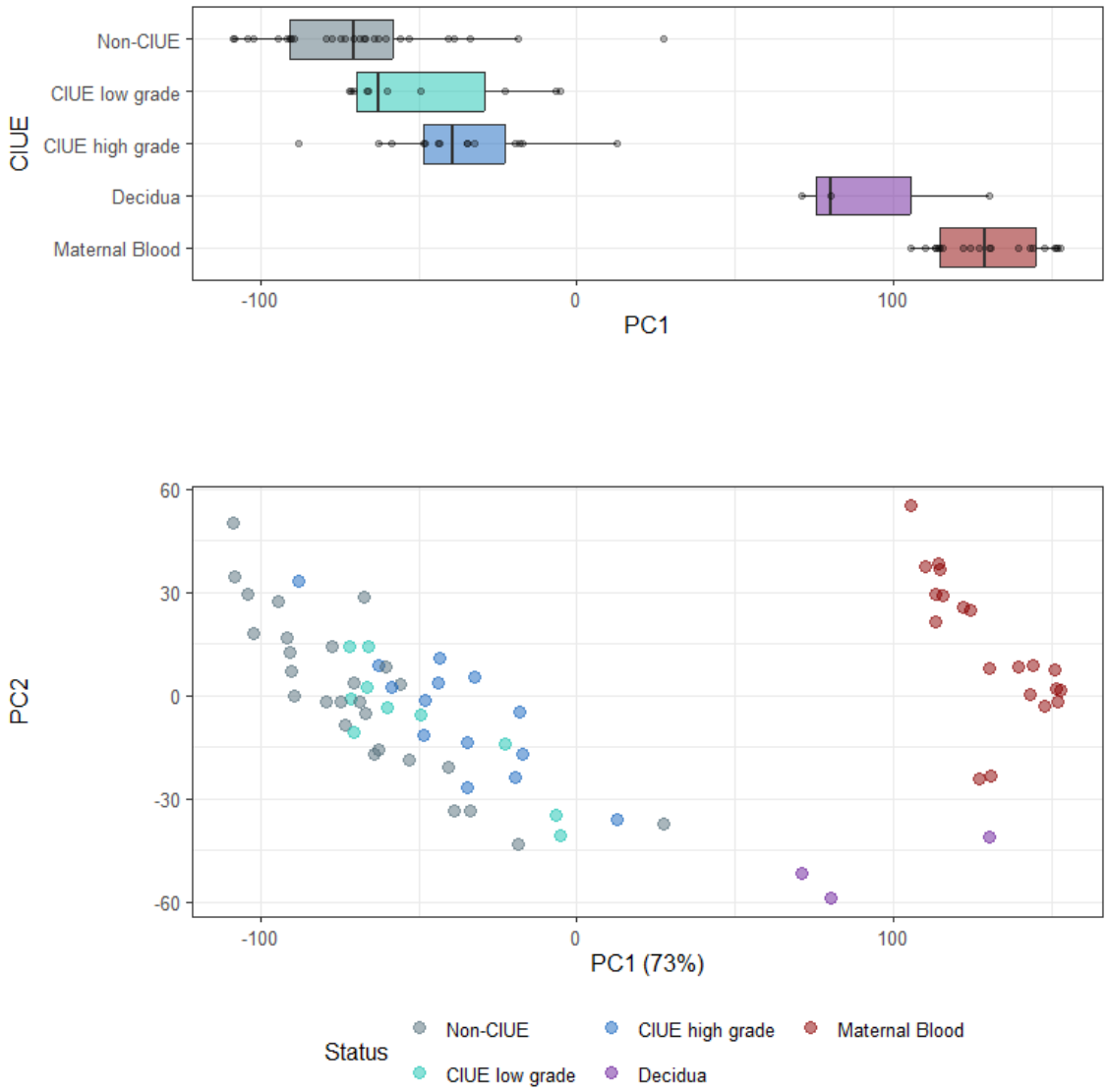
Supplementary Figure 1. PCA on placental samples only. **(A)** Top panel is a boxplot showing diagnosis group positions along PC1 (X Axis). Bottom panel shows a scatterplot of PC1 (X) versus PC2, with each point reflecting a sample, and samples colored by CIUE status, point shape represents aneuploidy (yes/no). **(B)** PC3 versus PC4 scatterplot, colored by CIUE status and with point shape representing aneuploidy (yes/no). **(C)** PC1 versus PC2 colored by aneuploid chromosome. Complex indicates the partial T1 with t(1;10) and compound T13, T16.



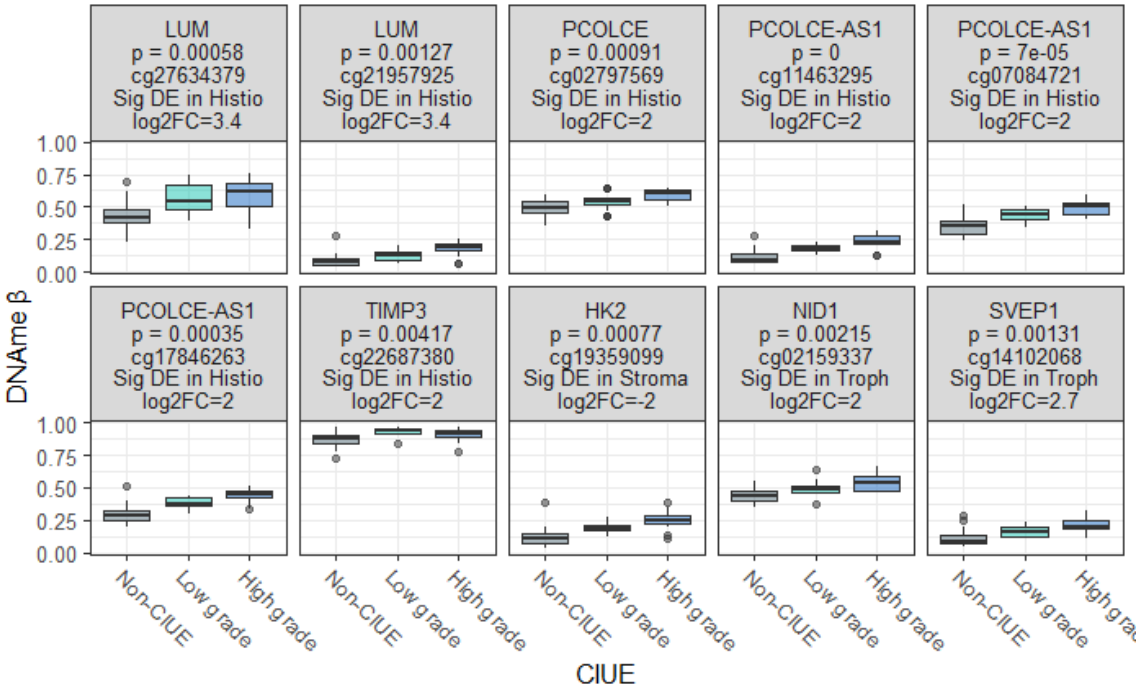
Supplementary Figure 2. Comparison of Campbell and Yuan placental cell composition estimations. In all samples, estimated cell types using the Yuan 3rd trimester reference versus the Yuan 1st trimester reference, and Yuan 1st trimester reference versus Campbell 3rd trimester reference. Estimates shown in all placental samples regardless of CIUE status.



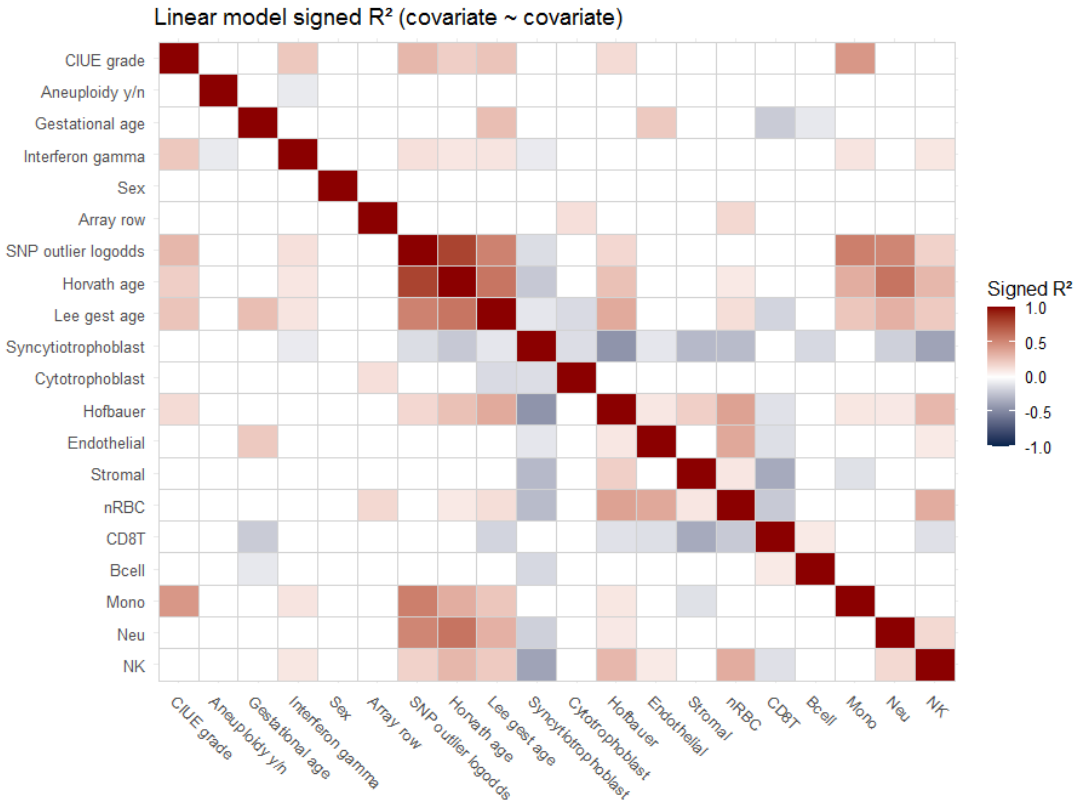
Supplementary Figure 3. Comparison of Campbell and Yuan (1st trimester) placental cell composition tools. (A) Campbell et al. cell composition estimates per sample. **(B)** Yuan et al. first trimester cell composition estimates per sample. **(C)** Campbell et al. estimated cell composition boxplots, separated by CIUE status. **(D)** Yuan et al. first trimester estimated cell composition boxplots, separated by CIUE status. For C and D, the reference level is non-CIUE and significance of t-tests for mean differences by CIUE group are indicated by stars at the top of the plot (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$).



Supplementary Figure 4. **Expanded principal components analysis on CIUE data set with additional maternal blood samples**. Top panel is a boxplot showing diagnosis group positions along PC1 (X Axis). Bottom panel shows a scatterplot of PC1 (X) versus PC2, with each point reflecting a sample, and samples colored by CIUE status, or by tissue for maternal blood and decidua.



Supplementary Figure 5. Candidate gene analysis for differential DNAme associated with CIUE, in genes known to be differentially expression in CIUE tissues. In each plot, the gene is indicated at the top of the panel title, with the CpG that reaches nominal significance indicated below. A summary of the differential expression (DE) analysis is provided in the final two lines of each panel title, indicating the tissue in which the gene was DE, and the direction of the DE result (positive = higher in non-CIUE, negative = higher in CIUE).



Supplementary Figure 6. Signed R^2 heatmap of covariate ~ covariate relationships between all relevant sample variables (unadjusted). Significant relationships at $p < 0.05$ are shaded in red (positive R^2) or blue (negative R^2). Non-significant relationships are indicated in white.