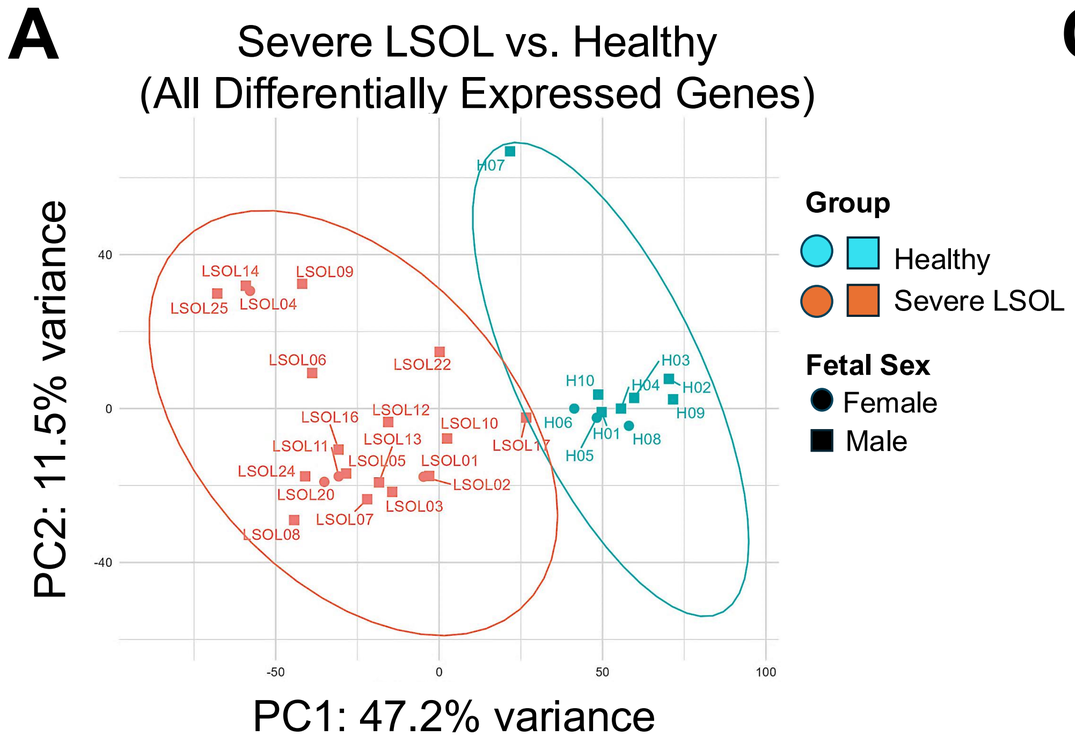
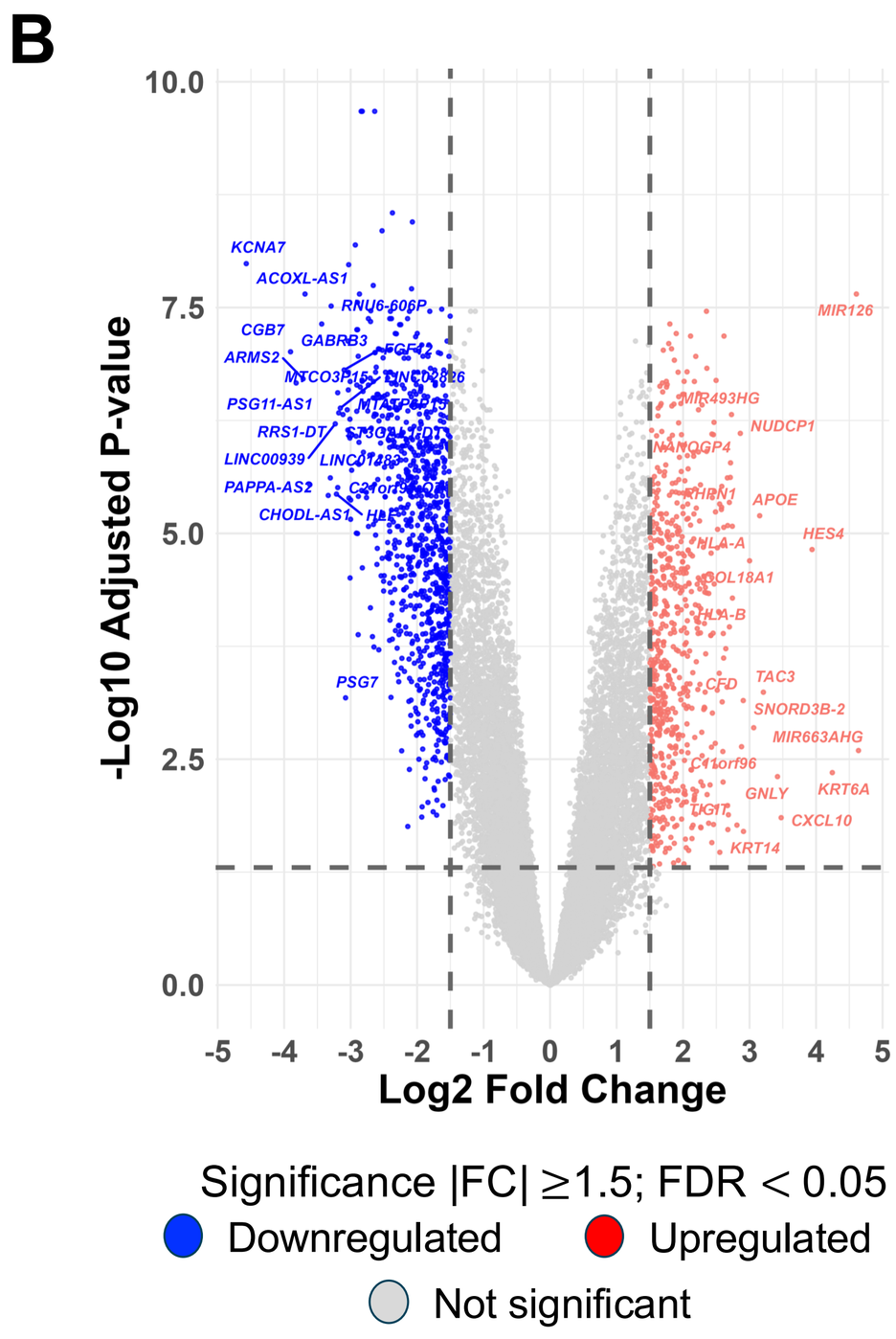
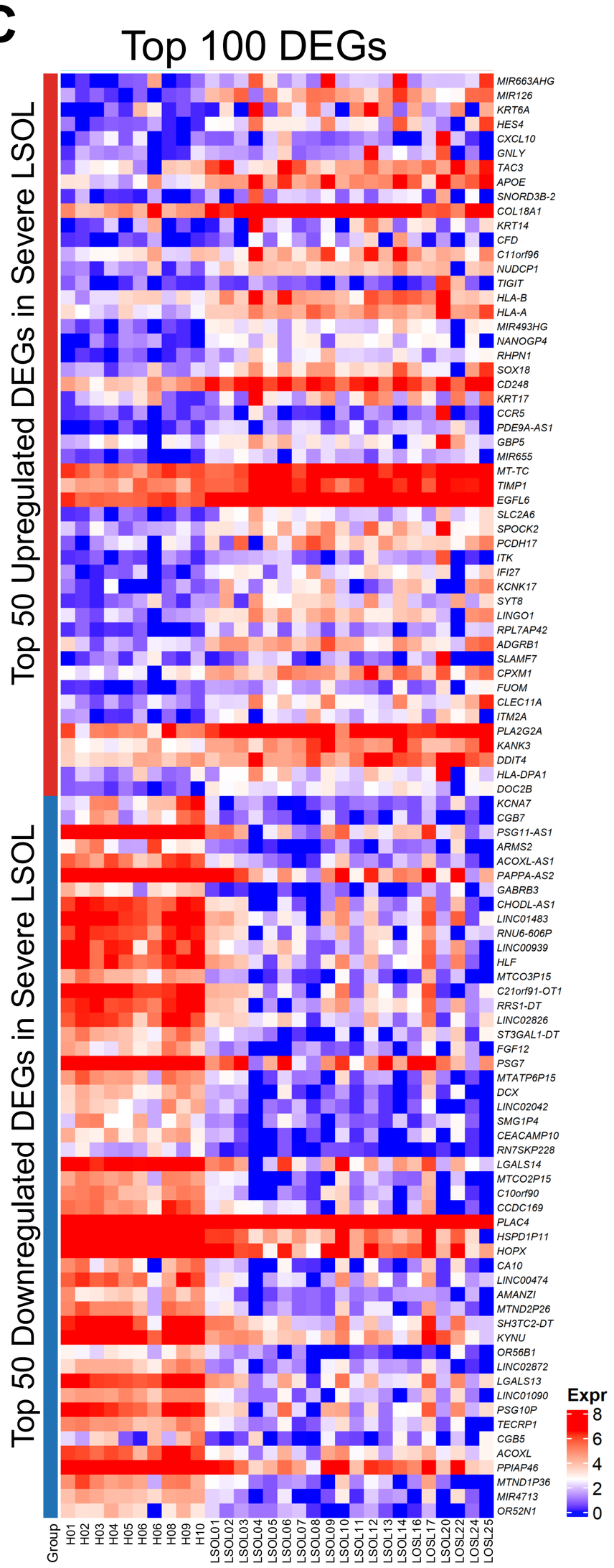


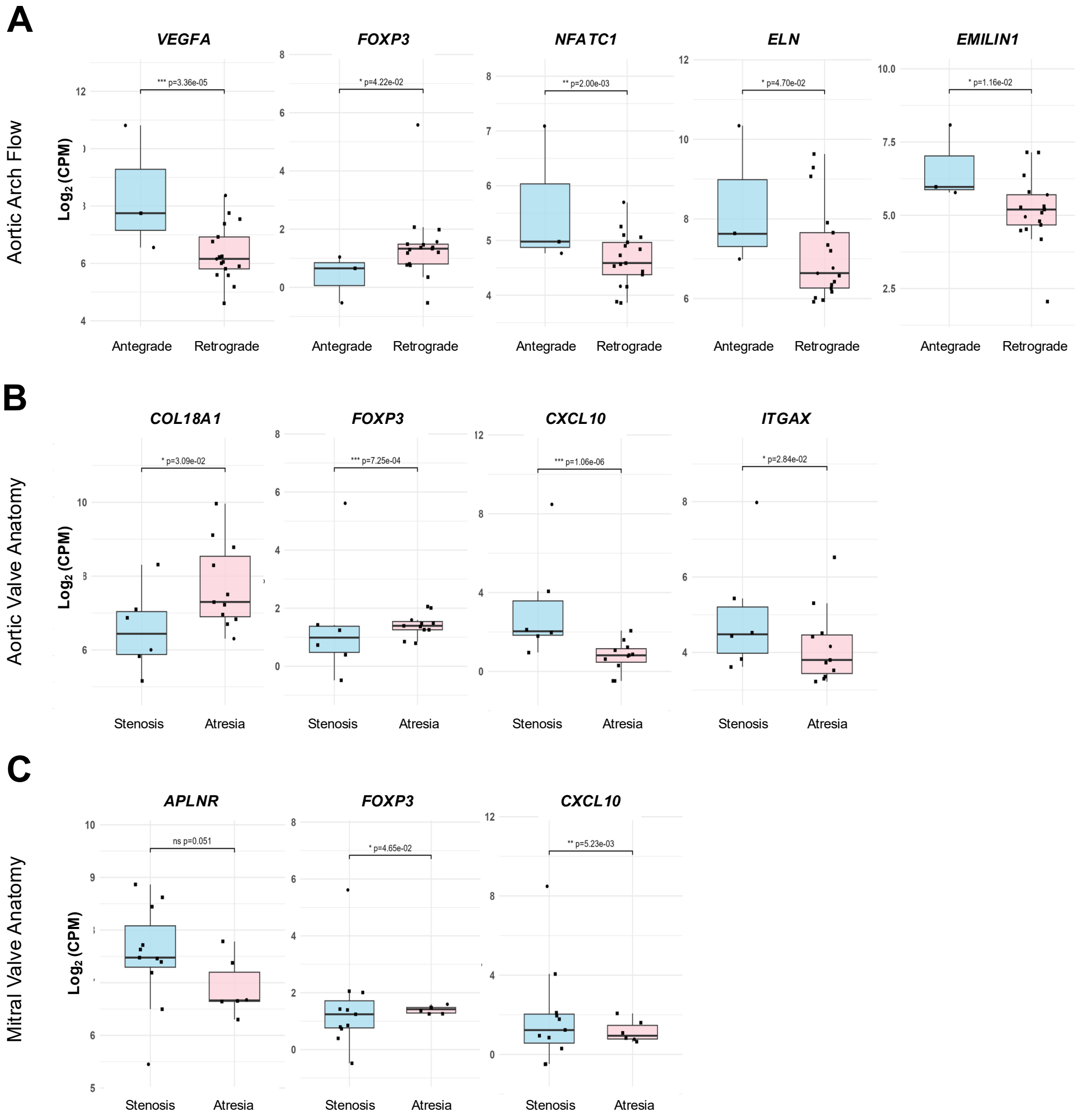




Supplemental Figure 1. Global transcriptomic differences between Severe LSOL and healthy placentas.
(A) Principal component analysis (PCA) of all differentially expression genes (DEGs) shows clear separation between Severe LSOL placentas (orange) and healthy controls (cyan), accounting for 47.2% and 13.5% of the variance along PC1 and PC2, respectively. Individual samples are annotated, with ellipses representing 95% confidence intervals. (B) Volcano plot of differential expression analysis comparing Severe LSOL vs. healthy placentas. Significantly upregulated (red) and downregulated (blue) genes are highlighted (FDR < 0.05, log2 fold change > 1.5). (C) Heatmap of the top 50 upregulated and downregulated DEGs separated by placental subgroups (Healthy and Severe LSOL). Rows represent genes and columns represent samples, with expression levels scaled by Z-score.



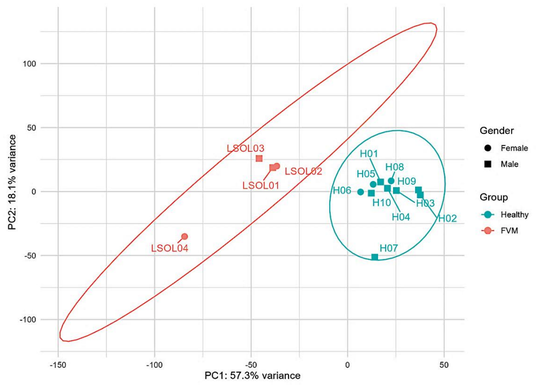
Supplemental Figure 2. Gene Ontology (GO) biological process enrichment analysis of the top 50 upregulated pathways in placental tissue from severe left-sided obstructive lesions (LSOL) compared with healthy controls (left), and severe LSOL without placental pathology (LSOL_NoPP) compared with healthy controls (right). Dot plots display enriched GO terms ranked by enrichment ratio. Dot size represents the number of genes associated with each pathway, and color intensity indicates statistical significance (−log10[FDR]).



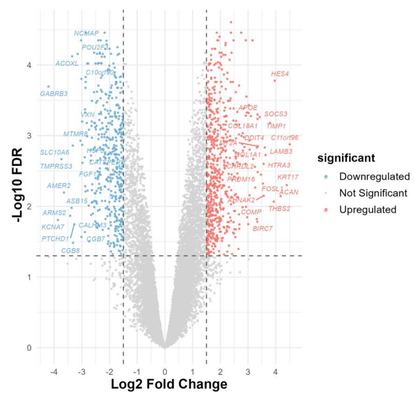
Supplemental Figure 3. Box plots of normalized expression (Log2(CPM)) for top higher- and lower-expressing genes in severe fetal LSOL placentas comparing patients with **(A)** antegrade versus retrograde aortic arch flow, **(B)** stenotic versus atretic aortic valve anatomy, and **(C)** stenotic versus atretic mitral valve anatomy. Boxes represent the interquartile range with a median line; points indicate individual samples where circles indicate female and squares represent male patients. Differential expression was determined using normalized counts and edgeR with thresholds of |logFC| ≥ 1.5 and nominal p-value ≤ 0.05 considered significant. Exact p-values are as indicated in the plots.

LSOL_FVM (N=4)

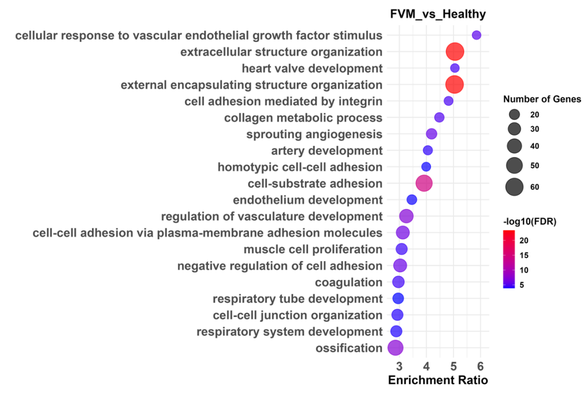
A PCA plot for protein coding genes



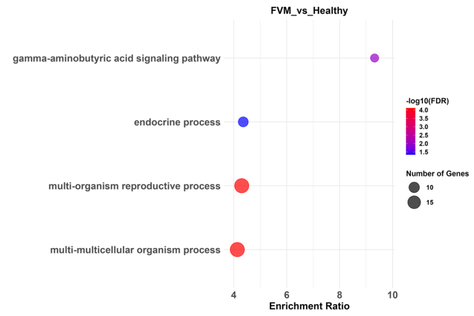
B Volcano plot for protein coding genes (edgeR)



C GO enriched Pathway for Upregulated genes

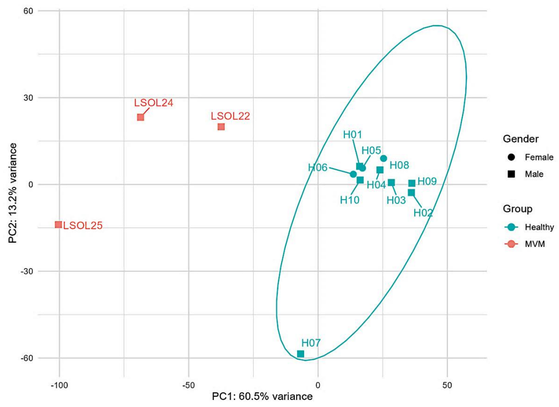


D GO enriched Pathway for downregulated genes

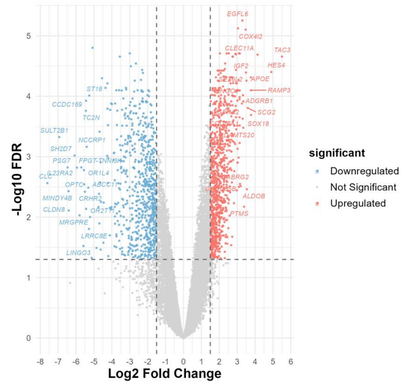


LSOL_MVM (N=3)

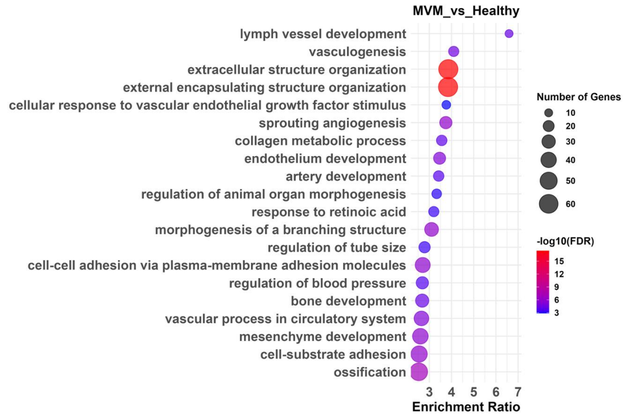
E PCA plot for protein coding genes



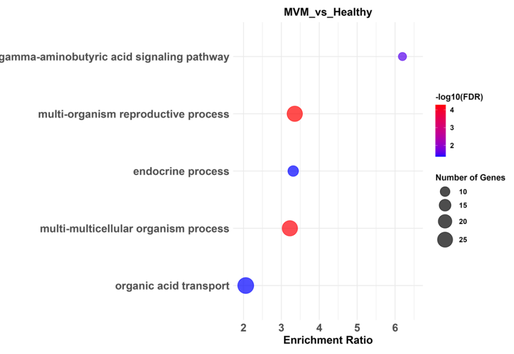
F Volcano plot for protein coding genes (edgeR)



G GO enriched Pathway for Upregulated genes

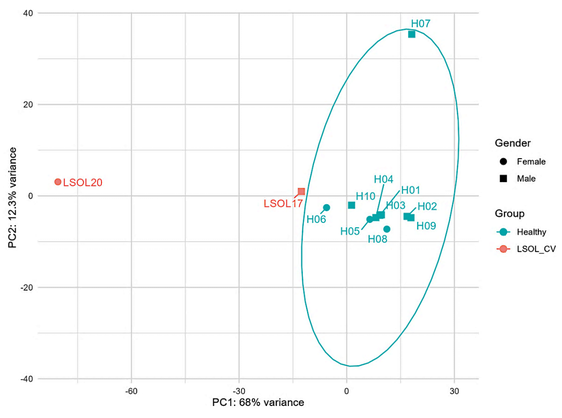


H GO enriched Pathway for downregulated genes

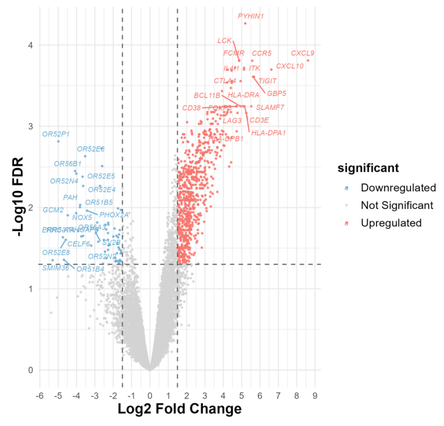


LSOL_CV (N=2)

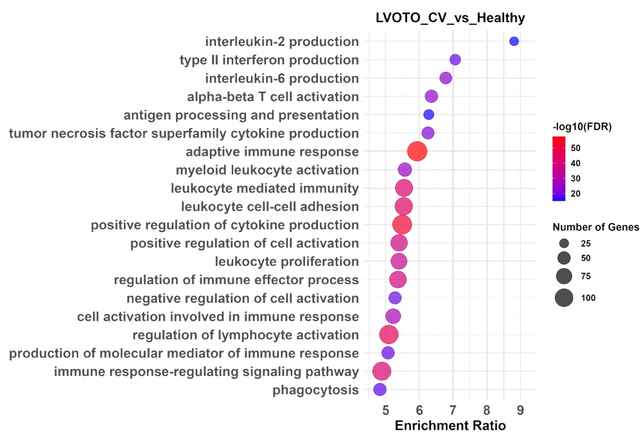
I PCA plot for protein coding genes



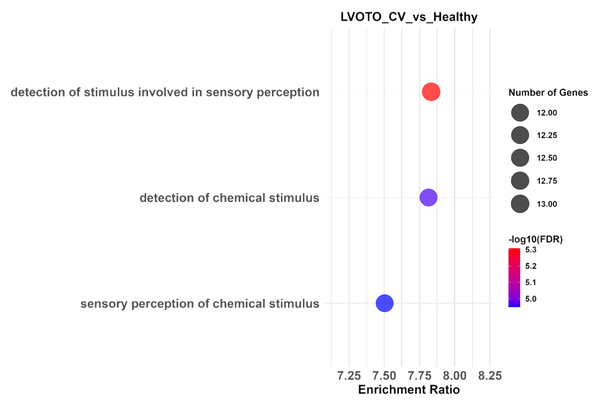
J Volcano plot for protein coding genes (edgeR)



K GO enriched Pathway for Upregulated genes

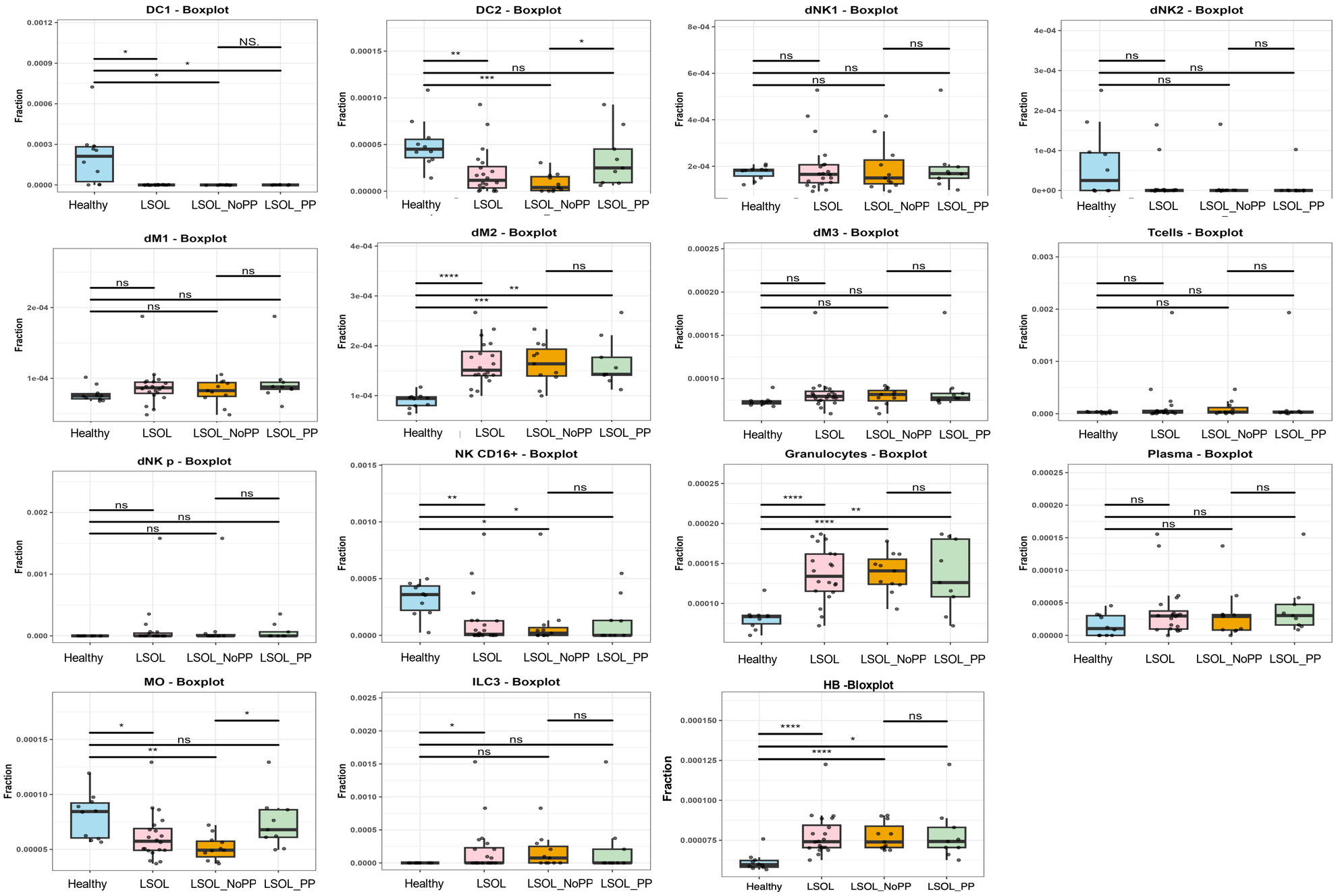


L GO enriched Pathway for downregulated genes

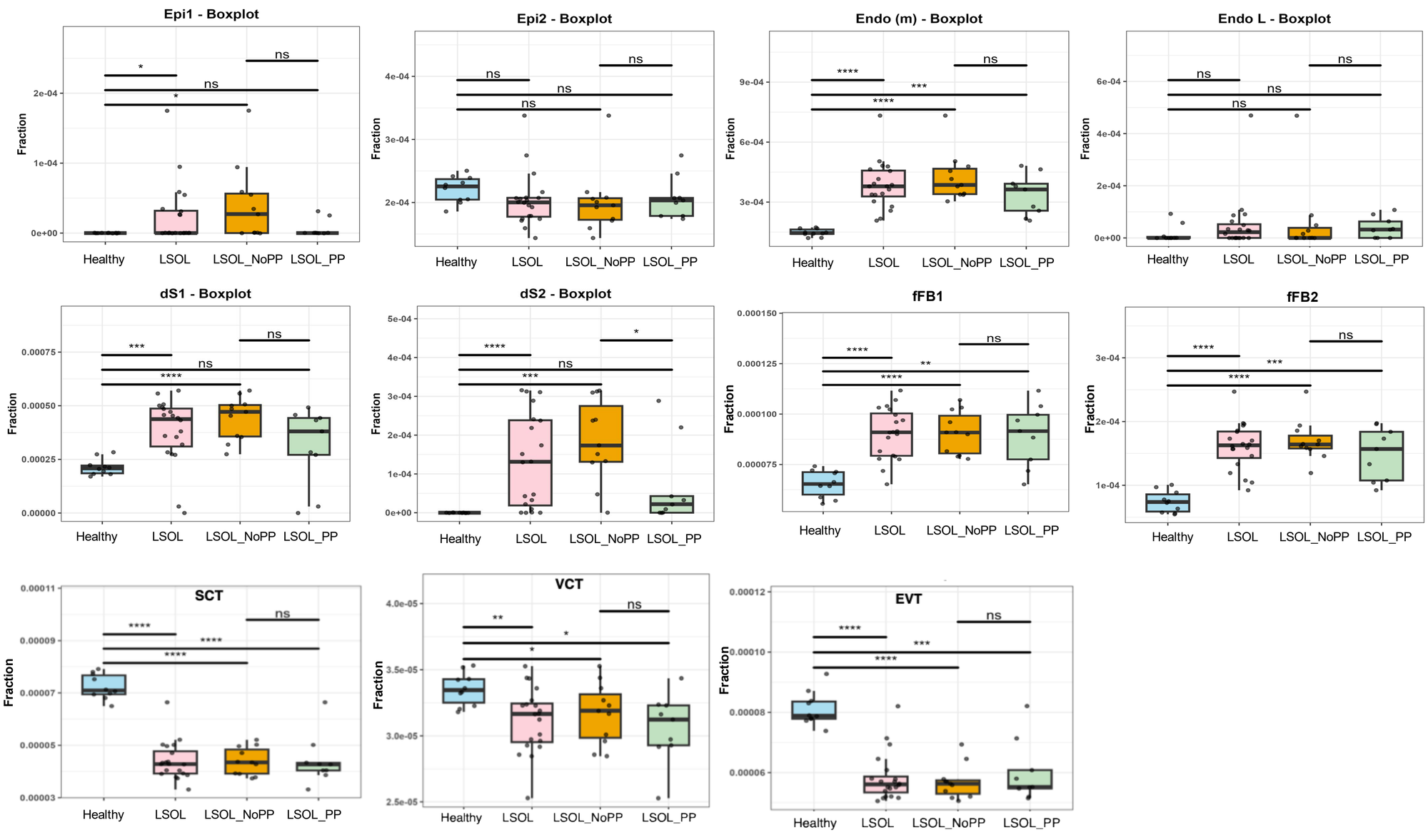


Supplemental Figure 4. Transcriptomic profiling and Gene Ontology (GO) enrichment analysis of placental severe LSOL subgroups compared with healthy controls.
(A,E,I) PCA plots demonstrating separation of protein-coding gene expression profiles between healthy placentas and LSOL groups, including LSOL_FVM, LSOL_MVM, and LSOL_CV. Each point represents an individual sample, and ellipses indicate group clustering.
(B,F,G) Volcano plots showing differentially expressed protein-coding genes identified by edgeR analysis for each LSOL subtype compared with healthy controls. Red dots indicate significantly upregulated genes (FC>1.5), blue dots indicate significantly downregulated genes (FC> -1.5) with FDR<0.05, and gray dots represent non-significant genes.
(C,G,K) GO enrichment analysis of significantly upregulated genes (GO enrichment pathway FDR<0.05). LSOL_FVM and LSOL_MVM demonstrated enrichment of pathways related to extracellular structure and matrix organization, cell adhesion, vasculogenesis and developmental pathways. In contrast, LSOL_CV showed predominant enrichment of immune and inflammatory pathways.
(D,H,L) GO enrichment analysis of significantly downregulated genes (GO enrichment pathway FDR<0.05). Downregulated pathways across LSOL subgroups MVM, and FVM included endocrine processes, reproductive processes, and gamma-aminobutyric acid (GABA) signaling pathways. LSOL subgroup CV included sensory perception–related signaling. Dot size represents the number of genes within each pathway, and color intensity corresponds to enrichment significance (-log10 FDR).

Immune cell types

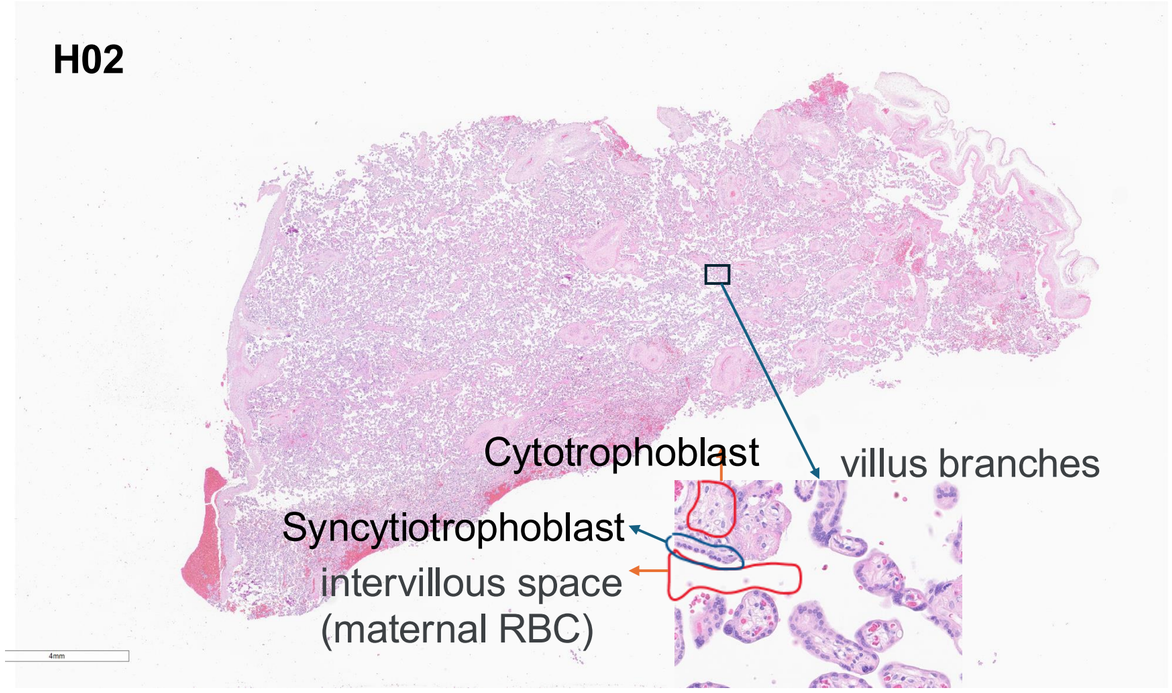


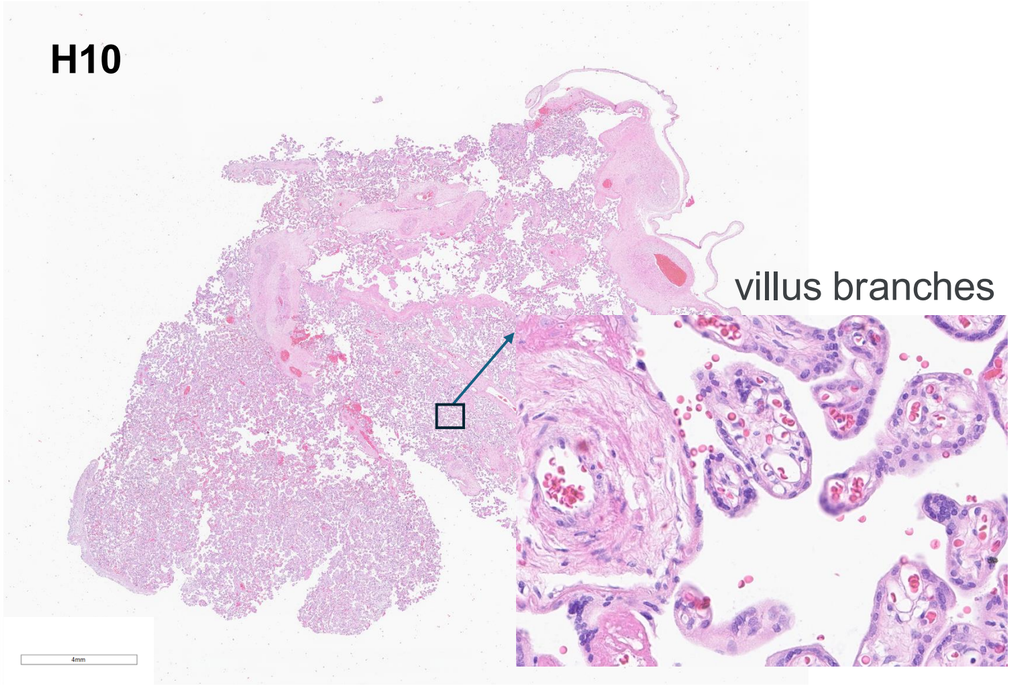
Nonimmune cell types



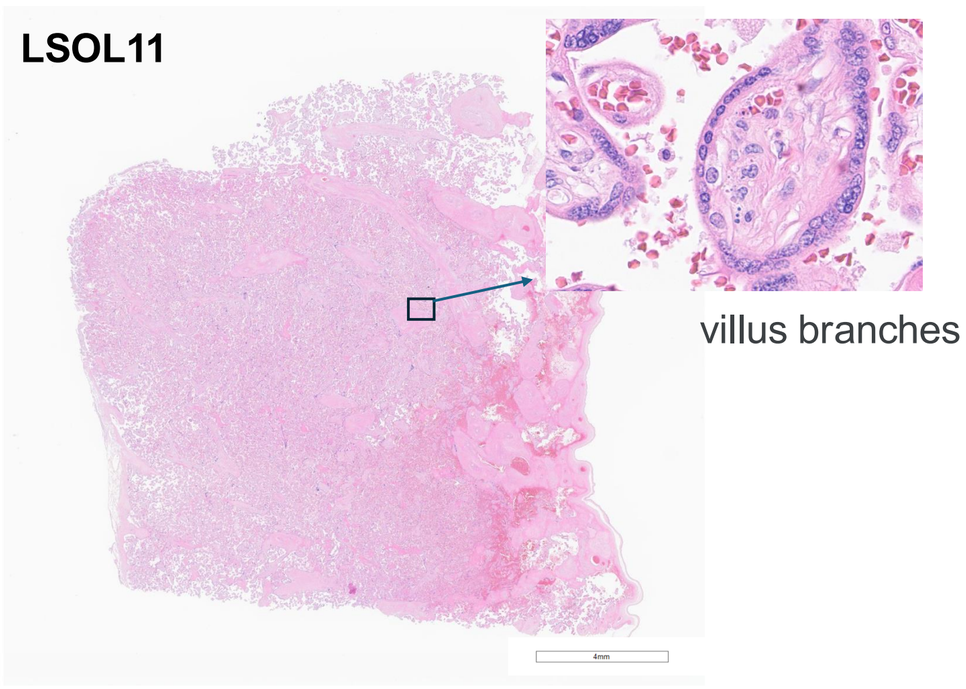
Supplemental Figure 5. Differences in maternal-fetal interface cell types across placental subgroups.
Boxplots shows the deconvolution derived cell type compositions across the indicated placental subgroups. Group-wise differences were assessed using pairwise comparisons with adjusted P-values indicated as follows: $p < 0.05$ (*), $p < 0.01$ (**), $p < 0.001$ (***), $p < 0.0001$ (****), and ns, not significant.

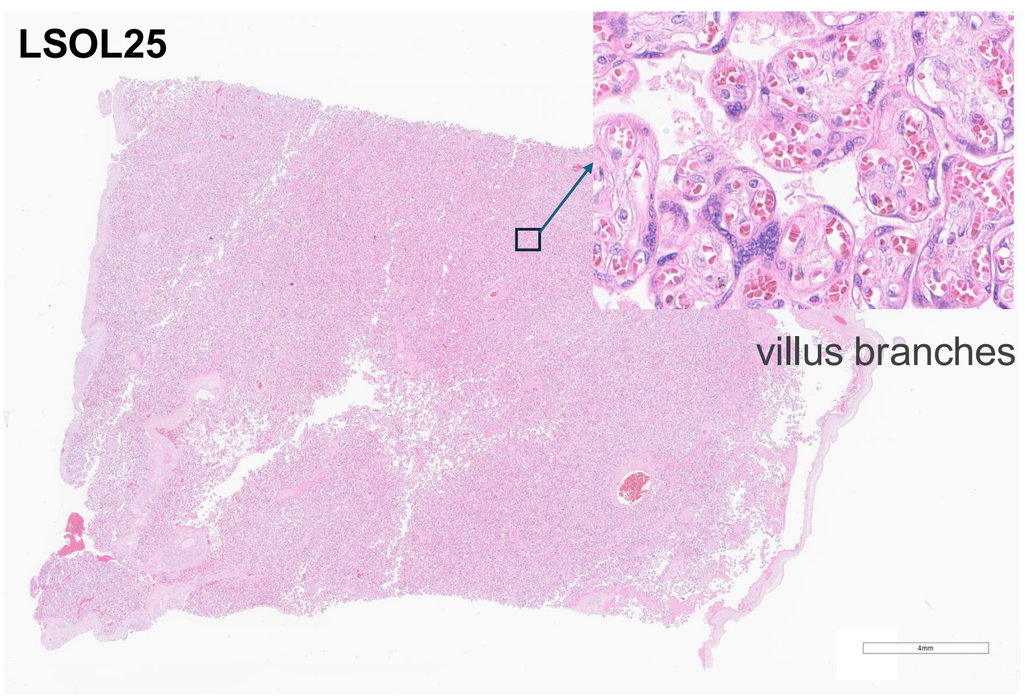
Healthy placenta whole slide scans





Severe LSOL Placenta whole slide scans





Supplemental Figure 6. Representative whole-slide scanned hematoxylin and eosin (H&E)-stained FFPE placental tissue sections used in entirety for RNA extraction from healthy control placentas (H02, H10) and severe left-sided obstructive lesion (LSOL) placentas (LSOL11, LSOL25). Insets highlight representative chorionic villous architecture at higher magnification, including villus branching patterns, syncytiotrophoblast and cytotrophoblast layers, and intervillous spaces containing maternal red blood cells.