Developing a Single-Cell Atlas of the Macaque Placenta and Fetal Brain to Characterize Zika Infection Dynamics in Pregnancy

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I characterized placenta and fetal brain tissues on the cellular level by leveraging single-cell (sc)RNA-seq data from pregnant pigtail macaques (Macaca nemestrina). My hypothesis was that the transcriptional profiles of the pigtail macaque placenta closely align with those of the human, and that the downregulation of genes specific to the fetal immune response and fetal organ development were targeted by Zika virus infection. scRNA-Seq data from the decidua of fifteen pregnant pigtail macaques were used in this study and derived from cDNA libraries that were created using the 10X Genomics platform. Data was aggregated, normalized, and visualized on a UMAP plot. Annotation of cell clusters was performed by comparison of highly expressed genes with published human placental scRNA-Seq atlases. I identified one cluster of decidual NK cells that expressed classic markers for cytotoxic granules (GZMA, GZMB, GNLY, PRF1), four decidual M1 and M2 macrophage populations expressing IL1B and CCL17, respectively, and at least five clusters analogous to human decidual stromal cells present between glands in the decidua spongiosa. Cell populations within Zika-infected animals revealed high expression of MZB1, which has contributed to the pathogenesis of autoimmune diseases. The fetal brain of Zika-infected animals saw increased frequencies of cell populations that downregulated ENPP2, which controls cell proliferation and differentiation. The preliminary analysis of the nonhuman primate placenta reveals a striking similarity to the human placenta with analogous activation states and expression profiles within single cell clusters, and provides a novel technique with which to characterize cell-specific responses to congenital Zika virus infection that manifest in fetal brain injury.

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