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A Novel Single Nuclei Sequencing Approach to Examine Effects of Oxycodone on Parietal Trophoblast Giant Cells in the Mouse Placenta

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The placenta is the primary communication organ with the mother and is vulnerable to pharmaceutical agents, including opioid drugs, consumed by pregnant women. Parietal trophoblast giant cells (pTGC) of the mouse placenta are analogous to human extravillous trophoblast (EVT) as both are at the interface of maternal and fetal tissues. The large nuclei of pTGC have precluded attempts at characterizing their transcriptome profile with conventional approaches beyond embryonic age 8.5 (E 8.5). We used a sequencing method that does not rely on filtration to characterize the pTGC transcriptome profile at E 9.5 and 12.5. We tested the hypothesis that pTGC are susceptible to maternal OXY treatment. This method successfully identified the pTGC transcriptome profile at both stages of gestation. Classic markers of pTGC, including *Prl2c2*, other *Prl* forms, and *Hand1*, were evident at E 12.5 in Clusters 0 and 5. Top 100 transcripts in these clusters closely align with those identified in human EVT. Maternal OXY treatment increased expression of *Afp* and *Apob* in both clusters. Within Cluster 0, *Maob* was upregulated, but *Prl4a1* was downregulated by OXY treatment. Pathways likely affected include those involved mRNA splicing and metabolism of RNA and retinoids. Diseases associated with differentially expressed genes in Cluster 0 include ventricular septal defect and abnormal extraembryonic tissue morphology. This sequencing method delineated the pTGC transcriptome profile and how maternal OXY treatment impacts genetic machinery within these cells. A better understanding of trophoblast cell populations susceptible to opioids may result in early detection biomarkers and potential remediation strategies.