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Effects of Oxycodone on Trophoblast Stem Cells

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Many drugs are abused during pregnancy, including opioids. Due to the on-going opioid crisis, it is important to test how such drugs, specifically oxycodone, might affect offspring development in utero and contribute to offspring's long-term behavioral pathologies. Earlier work shows significant reduction in the area of the mouse placenta occupied by trophoblast giant cells and subsequent profound changes in offspring behavior in response to developmental exposure during pregnancy. We hypothesized that maternal treatment of human placental trophoblast cells with oxycodone (OXY) would deleteriously affect the development and gene expression patterns of the placenta in humans and mice. We have used a well-established model for human placental trophoblast development in vitro, in which pluripotent human stem cells are exposed to BMP4 (bone morphogenetic protein 4) and inhibitors of FGF2 and ACIVIN signaling. I tested two concentrations of oxycodone (250 nM and 50 nM) on H1 human embryonic stem cells (hESC) which were driven along the trophoblast lineage described above. All cell colonies were imaged daily to determine whether there were visible differences in morphology. Medium from each well was collected daily to allow measurements of the concentrations of the human pregnancy hormone (human gonadotropin, hCG) by ELISA. These assays were used to assess whether the cells were developing normally over time. At d7, the cells were lysed to measure DNA content, which allowed normalization of data. Each experimental condition was in duplicate and repeated X3 to provide a robust statistical assessment. My experiments indicate that neither concentration of oxycodone influenced the production of hCG or changes in colony size or morphology. These negative effects so far with these in vitro approaches suggest potential differences between the mouse and human trophoblast in response to oxycodone, although the human equivalent of mouse trophoblast giant cells may not be represented in our cultures.