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The Impact of Prenatal Opioid Exposure on Placental Opioid Receptors

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Illicit opioid use by pregnant people have substantially increased over the past decades, leading to pregnancy complications such as fetal growth restriction. While the placenta is essential to support fetal growth and development, whether prenatal opioid exposure (POE) has a direct impact on the function of placental trophoblasts remains unknown. As POE triggers cellular responses that depend on opioid receptors (OPRs), we first interrogated the expression of three main OPRs, including OPRM1, OPRD1, and OPRK1, in trophoblasts. Specifically, we focused on the two main villous trophoblast subtypes, mononuclear cytotrophoblast (CTB) and multinuclear syncytiotrophoblast (STB). We hypothesized that OPRs differ their expression in CTB when compared to STB, leading to distinct responses to POE. To test our hypothesis, we employed three models, including term placental specimens, trophoblast stem (TS) cells from first-trimester CTB, and primary human trophoblast (PHT) cells isolated from healthy term placentas. We found that OPRM1 and OPRD1 proteins were expressed in the STB layer of healthy term placentas in a distinct spatial distribution. While our initial results indicated that the OPR mRNA expression declined in STB vs CTB, we recently found that the expression of OPRM1 protein significantly increased in STB vs CTB derived from PHT cells, suggesting a discordant regulation of OPRM1's mRNA and protein expression. Assessment of OPR activation in STB vs CTB, and the effect of POE on OPR protein expression are currently underway. Together, our results suggest that STB and CTB may show differential vulnerability to POE, culminating in placental dysfunction.