Research Week 2023

Development of a 3-dimensional trophoblast organoid model system

Brady Wessel

Keywords

Trophoblasts, Organoids, Pregnancy, Female, Placenta, Macaca mulatta, Humans, Three Dimensional Cell Culture Techniques, Fetal Blood, Nutrients

Abstract

Access to early gestational placental tissue in humans is constrained by a host of ethical challenges. As a result, early events of placentation and fetal development are poorly understood. The need for superior modelling capabilities has sparked interest in tissue-derived organoids in a translational animal model. Using tissue derived from rhesus macaque (Macaca mulatta) as a model system is favorable due to their structural and developmental similarities to the human placenta, and their ability to alleviate ethical concerns. Organoids are 3-dimensional cell cultures that assemble into miniature versions of their parent tissue. This makes them an invaluable tool for in vitro studies. Placental organoids can be generated by collecting proliferative cytotrophoblast cells from early gestational timepoints. These cells retain their stemness and can organize into organoids expressing cytotrophoblast (CTB) and syncytiotrophoblast (SYN) cell types. Crucially, placental organoids can be induced to differentiate into extravillous trophoblast (EVT), which are the cell phenotype responsible for anchoring the placenta to the maternal decidua. One caveat of trophoblast organoids is the inversion between their SYN and CTB cell layers. As the maternal/fetal blood barrier, SYN reside outside CTB in normal placentae, whereas in organoids they are found in the innermost layers. SYN are responsible for oxygen, nutrient, and waste exchange between the mother and fetus. Proper exterior presentation of SYN will allow manipulation of in vitro conditions and facilitate effective functional studies. Developing trophoblast organoid models from the Rhesus macaque which are meticulously characterized and validated will be important for discovery and innovation. Correcting polarity alongside characterization will offer an incredibly powerful tool for researchers to examine questions around early placental development, as well as assaying what external stimuli (e.g., drugs, virus) can cross or impact the function of the maternal/fetal barrier, and yield insight into the mechanisms of placentation and maternal blood supply.