Placenta barrier-on-a-chip could lead to better understanding of premature births

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More than one in 10 babies worldwide are born prematurely, according to the World Health Organization. Now scientists report in *ACS Biomaterials Science & Engineering* that they have developed an organ-on-a-chip that could help explain why. The device, which replicates the functions of a key membrane in the placenta, could lead to a better understanding of how bacterial infections can promote preterm delivery. It could also lead to new treatments for this condition.

Bacterial infections, a common trigger of premature births, can cause inflammation of the placenta or the placental barrier, a membrane that regulates the flow of nutrients and other substances between mother and child. As a result, the amniotic sac can rupture, producing early-onset labor. Studying this problem has proven tricky, in part because it's not feasible to run clinical trials including pregnant women, and human placentas donated after birth can only survive a few hours. However, researchers recently created a placenta-on-a chip—a promising new microfluidic device that allows placental cells to grow and function as if they were still in the body. Delving deeper, Jianhua Qin and colleagues sought to create a similar device that would specifically replicate the functions of placental barrier and how it responds to bacterial infection.

The researchers implanted human trophoblasts (representing the mother's cells) and endothelial cells (representing the fetus) from a human umbilical cord vein onto opposite sides of a three-layer microfluidic device. A porous membrane between the two cell layers allowed the tissues to form a placental barrier between them. After

determining that the barrier was functioning much as it would in the body, the researchers added E. coli bacteria to the maternal layer. The bacteria proliferated rapidly, breached the placental barrier, and subsequently triggered inflammation and cell death in both of the adjoining maternal and fetal layers. The researchers concluded that placental barriers-on-a-chip could help explain inflammatory responses in human placenta and possibly lead to better ways to treat or prevent preterm birth caused by infections.

More information: Jianhua Qin et al. Placental barrier-on-a-chip: modeling placental inflammatory responses to bacterial infection, *ACS Biomaterials Science & Engineering* (2018). DOI: 10.1021/acsbiomaterials.8b00653

Abstract

Placental inflammation, as a recognized cause of preterm birth and neonatal mortality, displays extensive placental involvement or damage with the presence of organisms. The inflammatory processes are complicated and tightly associated with increased inflammatory cytokine levels and innate immune activation. However, the deep study of the underlying mechanisms was limited by conventional cell and animal models due to great variations in the architecture and function of placenta. Here, we established a microengineered model of human placental barrier on the chip and investigated the associated inflammatory responses to bacterial infection. The multilayered design of the microdevice mimicked the microscopic structure in the fetal-maternal interfaces of human placenta, and the flow resembled the dynamic environment in the mother's body. Escherichia coli (E. coli), one of the predominant organisms found in fetal organs, were applied to the maternal side, modeling acute placental inflammation. The data demonstrated the complex responses including the increased secretion of inflammatory cytokines by trophoblasts and the adhesion of maternal macrophages following bacterial infection. Particularly, transplacental

communication was observed between two placental cells, and implied the potential role of trophoblast in fetal inflammatory response syndrome in clinic. These complex responses are of potential significance to placental dysfunctions, even abnormal fetal development and preterm birth. Collectively, placental barrier-on-a-chip microdevice presents a simple platform to explore the complicated inflammatory responses in human placenta, and might help our understanding of the mechanisms underlying reproductive diseases.

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