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New placenta model could reveal how birth defect-causing infections cross from mom to baby

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Researchers at the University of Pittsburgh and Magee-Womens Research Institute (MWRI) have devised a cell-based model of the human placenta that could help explain how pathogens that cause birth defects, such as Zika virus, cross from mother to unborn child. The findings were published today in *Science Advances*.

The placenta is a complex and poorly understood organ that anchors the developing fetus to the uterus, nourishes the baby, and provides a barrier to the spread of microorganisms from an infected mother to the fetus, explained senior investigator Carolyn Coyne, Ph.D., associate professor of microbiology and molecular genetics at Pitt School of Medicine and a member of the MWRI.

"The human placenta is unique and unlike that of other many other placental mammals," she said. "With our new model in the research toolkit, we and other scientists hope to advance our knowledge of the placenta, examine its function , and learn how it can prevent most, but not all, maternal infections from causing problems for the baby.

Researchers currently can obtain and study placental cell lines, but such cells do not fuse spontaneously to form the characteristic structure of the human organ. Some scientists study cells, called primary human trophoblasts, that are isolated from placentas obtained after childbirth, but such cells do not divide, can be more difficult to obtain, and are

more difficult to genetically manipulate to learn about biochemical pathways that have a role in placental function, Dr. Coyne said.

Dr. Coyne's team took a different approach: They cultured a human placental trophoblast cell line in a microgravity bioreactor system developed by NASA. The trophoblasts along with blood vessel cells were added to small dextran beads that were then spun around in a container filled with cell culture fluid, creating shear stress and rotational forces to better mimic the environment at the maternal-fetal interface than static cell-culture systems.

As a result, the cells fused to form syncytiotrophoblasts, and thus more closely resemble the primary cells lining the outermost layer of the tree-like or villous structure of the human placental tissue. Next, the researchers tested the functional properties of their model by exposing it to a virus and to *Toxoplasma gondii*, a parasite found in cat feces that can lead to fetal infection, causing miscarriage, congenital disease and/or disability later in life.

"We found that the syncytiotrophoblasts formed in our system recapitulated the barrier properties of the naturally occurring cells and they resisted infection by a model virus and three genetically different strains of Toxoplasma," said co-investigator Jon P. Boyle, Ph.D., associate professor of biological sciences at Pitt. "With this model, we can experiment with different biological factors to see what might allow an infectious agent to get through the placental barrier to the fetus."

Understanding the placenta might one day lead to ways to prevent fetal damage from the so-called TORCH infections: toxoplasmosis, rubella, cytomegalovirus, herpes and HIV, he added.

The researchers are beginning to use their model to test whether Zika virus, and other pathogens associated with congenital disease, can infect

placental cells and/or cross the placental barrier.

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