Placental cells may prevent viruses from passing from mother to baby

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Cells of the placenta may have a unique ability to prevent viruses from crossing from an expectant mother to her growing baby and can transfer that trait to other kinds of cells, according to researchers at Magee-Womens Research Institute (MWRI) and the University of Pittsburgh School of Medicine. Their findings, published in the early online version of the *Proceedings of the National Academy of Sciences*, shed new light on the workings of the placenta and could point to new approaches to combat viral infections during pregnancy.

It is imperative that the fetus be protected from infections of its mother in order to develop properly, said co-senior investigator Yoel Sadovsky, M.D., Elsie Hilliard Hillman Chair of Women's Health Research, professor of obstetrics, gynecology and reproductive medicine, Pitt School of Medicine, and MWRI director. But how the placenta, long thought to be just a passive barrier between mother and child, accomplishes this feat has not been clear.

"Our findings reveal some of the complex and elegant mechanisms human placental cells, called trophoblasts, have evolved to keep viruses from infecting cells," Dr. Sadovsky said. "We hope that we can learn from this to devise new therapies against viral infections."

Led by Dr. Sadovsky and co-senior investigator Carolyn Coyne, Ph.D., associate professor, Department of Microbiology and Molecular Genetics at Pitt and MWRI member, the research team studied human trophoblast cells in the lab, exposing them to a panel of viruses. Unlike

non-placental cells, trophoblasts were resistant to viral infection, but that trait was not a result of an inability of viruses to bind or enter the cells.

The researchers noted that when the medium, or fluid environment, in which the trophoblasts were cultured was transferred to non-placental cells, such as those that line blood vessels, they became resistant to viral infection, too.

The team noted that when the medium was exposed to sonication, which involves exposure to sound waves, viral resistance was no longer transferred to non-placental cells. This finding led them to take a closer look at exosomes, which are tiny spheres called nanovesicles that are secreted by trophoblasts and are sensitive to sonication. They found that fragments of genetic material called microRNAs contained within the exosomes, as well as lab-synthesized mimics of them, were able to induce autophagy, a mechanism of prolonged cellular recycling and survival. Blocking autophagy at least partially restored the cells' vulnerability to viral infections.

"Our results suggest this pathway could be a powerful evolutionary adaptation to protect the fetus and mother from viral invaders," Dr. Coyne said. "We might be able to use these microRNAs to reduce the risk of viral infection in other cells outside of pregnancy, or perhaps to treat diseases where enhancing autophagy would be beneficial."

More information: Human placental trophoblasts confer viral resistance to recipient cells, www.pnas.org/cgi/doi/10.1073/pnas.1304718110

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