High-risk pregnancy: The interferon effect

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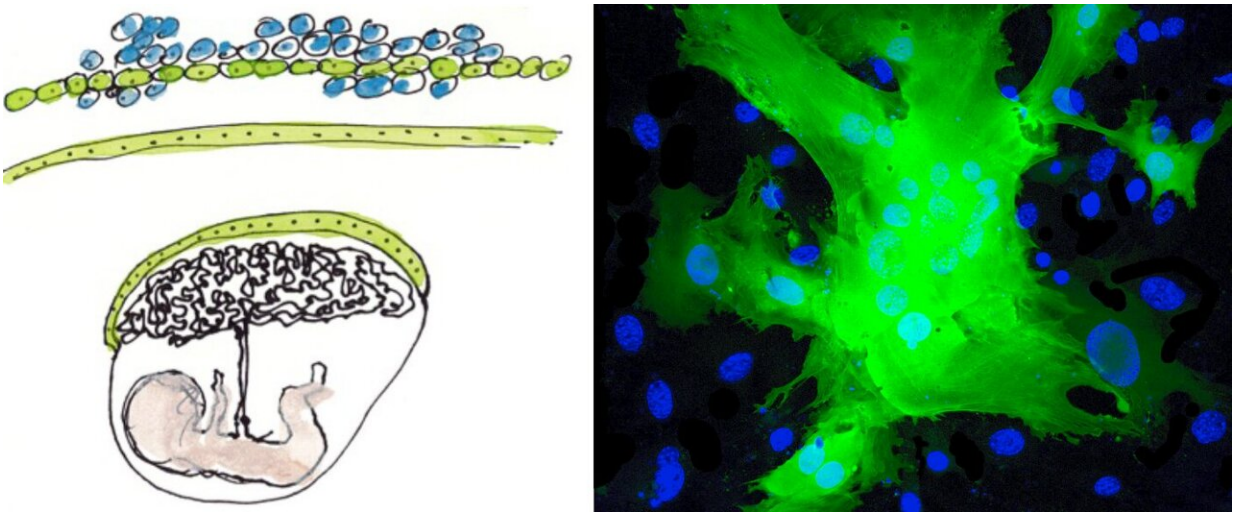

Fluorescence microscopy of fused cells (in green) and nucleus (in blue). Credit: © Fabrice Hyber -- Organoïde-Institut Pasteur/Fluorescence microscopy of fused cells (in green) and nucleus (in blue).

High-risk pregnancies occur frequently, and have multiple causes. It is estimated that 10 to 20 percent of pregnant women miscarry during their first trimester of pregnancy. Slow fetal growth may also arise as a result of maternal infection with certain microbes, parasites or viruses (such as toxoplasmosis or infection with rubella virus, cytomegalovirus, herpes or Zika) or because of genetic or autoimmune diseases. Teams from the Institut Pasteur, the CNRS, Inserm, Necker-Enfants Malades Hospital (AP-HP) and Université de Paris have identified a new cellular mechanism that alters placental development, potentially causing serious

complications during pregnancy. The mechanism is linked with the production of interferon, a molecule produced in response to infection, especially viral infection. The findings are published in *Science* on July 11, 2019.

The placenta is both a surface for exchange and a barrier between mother and fetus—it delivers nutrients needed for fetal growth, produces hormones and protects the fetus from microbes and the maternal immune system. The external layer of the placenta, known as the syncytiotrophoblast, is composed of cells which fuse together, forming giant cells that are optimized for the placenta's barrier and exchange functions. Cell fusion is mediated by a protein known as syncytin. If the syncytiotrophoblast fails to form correctly, it can cause placental insufficiency and hinder fetal development. An abnormal syncytiotrophoblast can be observed in conditions such as slow intrauterine growth, the lupus and in women whose fetus has Down syndrome.

Interferon is a substance produced by immune cells during infection to combat viruses and other intracellular microbes. High levels of interferon are observed in autoimmune or inflammatory diseases such as lupus, and also in some infections. In this study, the scientists demonstrated that interferon is responsible for placental abnormality and that it acts by preventing syncytiotrophoblast formation. Specifically, interferon induces the production of a family of cellular proteins known as IFITMs (interferon-induced transmembrane proteins), which block the fusion activity of syncytin.

IFITM proteins are beneficial since they prevent viral fusion with cellular membrane, thereby stopping viruses from entering and multiplying within cells. The scientists used experimental models and human cells to demonstrate that this beneficial effect can nevertheless be harmful if IFITM proteins are produced in an important level in the

placenta.

"Identifying the role of IFITMs gives us a better understanding of the mechanisms involved in placental development and how it may be disrupted during infections and other diseases," comments Olivier Schwartz, Head of the Virus and Immunity Unit at the Institut Pasteur and joint last author of the paper. The scientists want to investigate whether placental pathologies of unknown etiology, such as some early spontaneous abortions and occurrences of preeclampsia, also involve IFITM proteins. In the longer term, blocking the effects of IFITMs could represent a new therapeutic strategy to prevent interferon-related placental abnormality.

More information: "IFITM proteins inhibit placental syncytiotrophoblast formation and promote fetal demise" *Science* (2019). science.sciencemag.org/cgi/doi … 1126/science.aaw7733

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