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## Placenta-on-a-chip developed to test drug transport

The pendrive-sized device contains two layers of human cells that model the interface between mother and fetus. | Photo Credit: <u>University of Pennsylvania</u>

Scientists have developed an "organ-on-a-chip" platform to study how drugs are transported across the human placental barrier. Some maternally-administered medications can enter the fetal bloodstream, but how the placenta determines which molecules can get through is still poorly understood.

The new placenta-on-a-chip developed by researchers at the University of Pennsylvania in the US is a small block of silicone that houses two microfluidic channels separated by a porous membrane. The researchers grow human trophoblast cells on one side of the membrane and endothelial cells on the other.

The layers of those two cell types mimic the placental barrier, which determines what passes from the maternal to the foetal circulatory systems. By adding different molecules to the blood-like fluid flowing through the "maternal" microfluidic channel, the researchers can measure the rate at which they transfer to the "foetal" channel and how much they accumulate in the barrier itself.

The ability to test this process on human placentas is in high demand, researchers said. Pregnant women are excluded from clinical drug trials, and animal models have severe limitations. Those limitations were tragically demonstrated in the case of thalidomide, where a morning sickness drug able to transport across the human placental barrier led to tens of thousands of birth defects and deaths.

To validate their placenta-on-a-chip as a testing platform, Dan Huh, assistant professor at University of Pennsylvania and his colleagues compared the transport of two drugs that have been studied via ex vivo placental perfusion: heparin, an anticoagulant, and glyburide, used in the treatment of gestational diabetes.

Heparin is understood to be too large a molecule to pass through the placental barrier, and the team's placenta-on-a-chip also bore out that result.

Glyburide is considered safe to use during pregnancy, thanks to specialised efflux transporters expressed by the placental tissue that prevent maternally administered drug molecules from reaching the foetus. The placenta-on-a-chip was able to emulate this protective mechanism. .

"We're getting close. This study has given us confidence that the placenta-on-a-chip has tremendous potential as a screening platform to assess and predict drug transport in the human placenta," Huh said.

Further research and validation studies will be necessary before the placenta-on-a-chip sufficiently replicates its in vivo counterpart for the purposes of clinical testing, researchers said.

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