The Washington Post

Democracy Dies in Darkness

Scientists create synthetic mouse embryos, a potential key to healing humans

The embryo developed for eight days, with a beating heart, a rudimentary brain and a gut tube

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August 1, 2022 at 5:10 p.m. EDT

Stem cell researchers in Israel have created synthetic mouse embryos without using a sperm or egg, then grown them in an <u>artificial womb</u> for eight days, a development that opens a window into a fascinating, potentially fraught realm of science that could one day be used to create replacement organs for humans.

The objective, scientists involved with the research said, is not to create mice or babies outside the womb, but to jump-start the understanding of how organs develop in embryos and to use that knowledge to develop new ways to heal people.

From a clump of embryonic stem cells, scientists at the Weizmann Institute of Science created synthetic embryos that closely resembled real mouse embryos, with rudimentary beating hearts, blood circulation, folded brain tissue and intestinal tracts. The mouse embryos grew in an artificial womb and stopped developing after eight days, about a third of a mouse pregnancy.

The advance, a decade in the making, arrives in a field crowded with efforts to develop embryo models from human and mouse cells. Scientists can use such models to peer into the earliest stages of embryonic development and to study how organs form.

But as the models grow closer in resemblance to the real thing, they also open ethically murky territory. At what point do synthetic embryos become so similar to the real thing that they are subject to protections akin to those applied to real embryos?

"This is an important landmark in our understanding of how embryos build themselves," Alfonso Martinez Arias, a developmental biologist at Pompeu Fabra University in Barcelona who is not involved in the research, said in an email. He called the experiment a "game changer."

The research, published Monday in the <u>journal Cell</u>, is far from growing a mouse, much less a human, outside the womb. It was a proof of concept that a complete synthetic embryo could be assembled from embryonic stem cells, and while the researchers were successful, it was a highly error-prone process, with only a small fraction of embryos going on to develop the beginnings of a beating heart and other organs.

Although the synthetic mouse embryos bore a close resemblance to natural mouse embryos, they were not exactly the same and did not implant or result in pregnancies in real mice, according to Jacob Hanna, the stem cell scientist at the Weizmann Institute of Science who led the work.

"It's an interesting next step, not shocking, but one that makes more plausible in the long run a proposition with broad implications: the possibility of turning any mouse cell into a living mouse," said Henry T. Greely, a bioethicist at Stanford Law School.

The research, like other recent studies, puts the possibility of a complete human synthetic embryo on the horizon, several researchers said, making it necessary to continue a societal discussion about how these entities should be handled. Last year, the International Society for Stem Cell Research relaxed a historical "14-day rule" that said researchers could grow natural embryos for only 14 days in the laboratory, allowing researchers to seek approval for longer studies. Human embryo models are banned from being implanted into a uterus.

"The mouse is a starting point for thinking about how one wants to approach this in humans," said Alex Meissner, a stem cell biologist at Max Planck Institute for Molecular Genetics. "It's not necessary to be alarmed or raise any panic, but ... as we learn, it's important to have in parallel the discussion: How far do we want to take it?"

Hanna said his hope is that the technology could be used not as a replacement for reproduction but as a way to create synthetic human embryo models that could result in precursors of organs that could be studied and potentially used therapeutically.

For decades, the major hope for stem cell therapy has been as a repair for the body's own tissues. Stem cells can develop into any tissue or organ, so the potential to use those cells to fix spinal cord injuries, patch damaged hearts or cure diabetes has been alluring. But turning those cells into complex, functioning tissue has been a challenge. Hanna's hope is that watching this process unfold during early development will provide important clues.

"Our goal is not making pregnancy outside the uterus, whether it's mice or any species," Hanna said. "We are really facing difficulties making organs — and in order to make stem cells become organs, we need to learn how the embryo does that. We started with this because the uterus is a black box — it is not transparent."

Hanna has founded a company, Renewal Bio, that plans to use the technology therapeutically. One possible use would be to take skin cells from a woman with fertility problems, reprogram those cells to create stem cells and then grow synthetic embryo models that could be used to produce eggs.