

A more womb-like chip for IVF was born in Japan

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Since the birth of Louise Brown, the first test-tube baby in 1978, *in vitro* fertilization (IVF) has produced approximately three million infants worldwide. Although success rates continue to improve, the technology is still far from reliable enough for infertile couples, many of whom attempt IVF multiple times. Many researchers are focusing on developing technologies that try to mimic the womb in order to improve IVF.

According to Popular Science, Teruo Fujii at the University of Tokyo's Institute of Industrial Science and his colleagues (Yasuyuki Sakai at the University of Tokyo's Center for Disease Biology and Integrative Medicine and the Inui Maternity Clinic) have invented a plastic chip-like incubator that nurtures early embryos like a real womb does. Their research was presented at a meeting of the European Society for Human Reproduction and Embryology in Lyon, France, August 2007. (October 30, 2007, Sharon Guynup Popular Science. <http://www.popsci.com/popsci/science/250216b8ff0f5110vgnvcm1000004eeebccdrd.html>).

Fujii's team has created a novel "lab on a chip" that is 2 millimeters across and 0.5 millimeters high in which up to 20 eggs can be fertilized. Currently, IVF eggs mature while resting on the top floor of a two-tiered silicone microchip, a very womb-like environment (see Figure 1 and the cover of this issue). "We wanted to culture embryos in an environment that is closer to what happens inside the body," Fujii said.

To test the device, Fujii and his team carried out several experiments on mice, comparing resulting embryos with those produced using conventional IVF. First, 10 mouse eggs were carefully placed individually inside a "cage" on the top floor of a two-tiered silicone microchip. Next, sperm cells were added to fertilize the eggs. Over the next 48 to 72 hours, a pulsing micro-pump washed the early embryos with rhythmic waves of a culture fluid that helped them grow in an attempt to simulate what happens in the womb. Then, the embryos were removed, and the healthy ones were implanted into the actual wombs of mother mice (26 July, 2007, Linda Geddes, New Scientist. <http://www.newscientist.com/channel/sex/mg19526146.200-wombonachip-may-boost-ivf-successes.html>).

Currently, test-tube human embryos are kept in "microdroplets" -- a mixture of mineral oil and culture fluid -- to keep them from drying out. However, the artificially fertilized embryos tend to grow considerably slower in microdroplets because during IVF eggs or embryos were often moved or washed with culture fluid, causing changes in temperature and pH.

In another advanced experiment in mice, Fujii's team suggested the chip was more successful than traditional microdroplets in improving the success rate of IVF. Fertilized eggs grew much faster on the chip than in traditional microdroplets. After 2 days, the chips contained around 77-119 cells, compared to 58-94 cells in microdrops. The faster-growing embryos are believed to stand a better chance of survival after being reinserted back into the mother's womb. At the time for implantation into a real womb, 80% of embryos held inside the chips were ready for implantation, while only 20% in microdroplets grew to that stage in the same amount of time.

"It's a large difference between the conventional method and our device," Fujii said. He and his colleagues believe that their "womb-on-a-chip" is superior to the conventional system.

First, endometrial cells, which line real wombs, are also grown on the chip. These cells release chemicals tailored to the changing needs of a growing embryo, delivering the amino acids, proteins, and growth

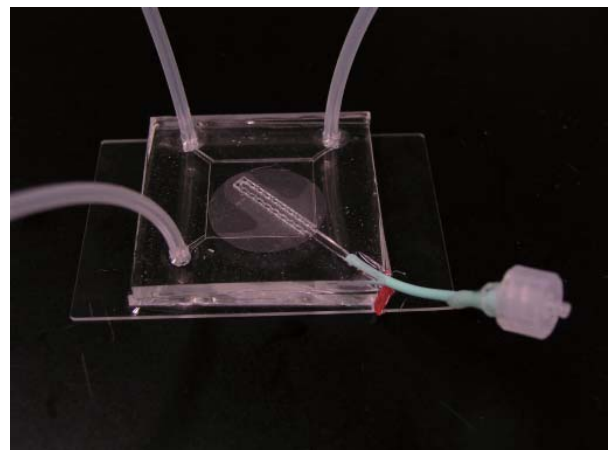


Figure 1. The newly developed IVF device (photo by Prof. Fujii).

factors that help the embryo develop. Second, the chip functions a bit like a gentle car wash, using pumps to periodically bathe the cells in the fluid needed to keep them alive. It can be programmed to infuse the inside of the device with as little as one trillionth of a liter of liquid and employs tiny chambers to contain the eggs and prevent nutrients from becoming too diluted. Another benefit is reduced stress to an embryo since it is not sucked into a pipette, which can cause physical damage or fatal changes in pH or temperature.

Following these successful experiments in mice, Fujii's team was granted permission to begin trials on human embryos. There is, however, always a level of uncertainty when research moves from animals to humans, which is not limited to reproductive technologies.

Until recently, IVF was only for those with fertility problems. The strong ethical stance against assisted reproduction, especially that involving human embryos, often puzzles scientists. Some people are worried by

increasingly artificial means of reproduction. One concern is that some people are resorting to IVF-pre-implantation genetic diagnosis (PGD) so they can choose their child's most basic characteristic: sex. Another concern is that "assisted reproduction" will help and encourage women to have children ever-later in life (*October 22, 2007, Sharon Guynup, Boston Globe. http://www.boston.com/yourlife/health/articles/2007/10/22/scientists_try_to_build_a_better_womb_for_ivf/*), which is worthy of concern given the increased risks for mother and infant when an older mother gives birth.

Such concerns have not deterred Fujii and his team, who are now "working towards translating this technology for humans." He is, however, aware that fertility treatment is still an invasive, psychologically challenging procedure and that it could take at least five years for the technology to reach clinics.

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