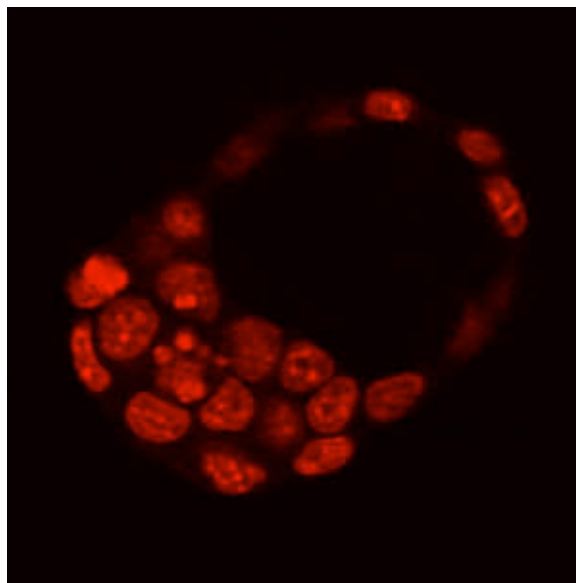




## Test Tube Mice Don't Behave Normally

Reproduction technologies such as in vitro fertilization (IVF) may not be as risk-free as once thought. That's the implication of a controversial study that for the first time finds behavioral oddities in adult mice that were cultured in petri dishes as embryos.



**Seeds of change.** Culturing embryos in vitro to this stage could affect later development.

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To test this assumption, a team led by Richard Schultz, a cell biologist at the University of Pennsylvania in Philadelphia, implanted mouse embryos into a mouse 2 days after fertilization. Into the same womb they implanted fertilized embryos that were cultured in a petri dish for an additional 3 days. Marker genes were inserted into the genomes of the mice to tell the offspring apart after birth.

As has been shown before, embryo culture seemed to have no effect on the birth or early development of mice. But differences did crop up once the grownup mice were put through a series of standard behavioral tests. Culture-derived mice performed slightly worse on memory tests. And male culture-derived mice explored a maze more boldly than did the other mice, the team reports online this week in

The ability to manipulate human embryos has provided doctors with a powerful toolkit, from the implantation of IVF embryos in surrogate mothers to promising therapies based on stem cells. All of these technologies require embryos to be maintained outside of the human body. Only about 20% of such cultured embryos are ultimately viable, and an extended stay in culture medium helps weed out the duds. This step has been assumed to have no long-term effect on development.

the *Proceedings of the National Academy of Sciences*. Schultz speculates that this difference is due to subtle changes in gene expression that occurred during culturing. Whether or not such effects are caused in humans depends in part on whether the culture medium is "optimal" for the embryos, which Schultz says is "unlikely."

But other researchers point to possible flaws in the experiment. Michael Summers, a reproductive biologist at the Reproductive Science Center in Boston says that the standard media used by Schultz's team "are known to be suboptimal" for culturing mouse embryos. New and improved media might lead to more normal mice, he says. "However, it shows that we should probably exercise more caution and try to limit the amount of time human embryos are cultured until these uncertainties are resolved," says Summers.

**--JOHN BOHANNON**

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