Identifying the source of stem cells

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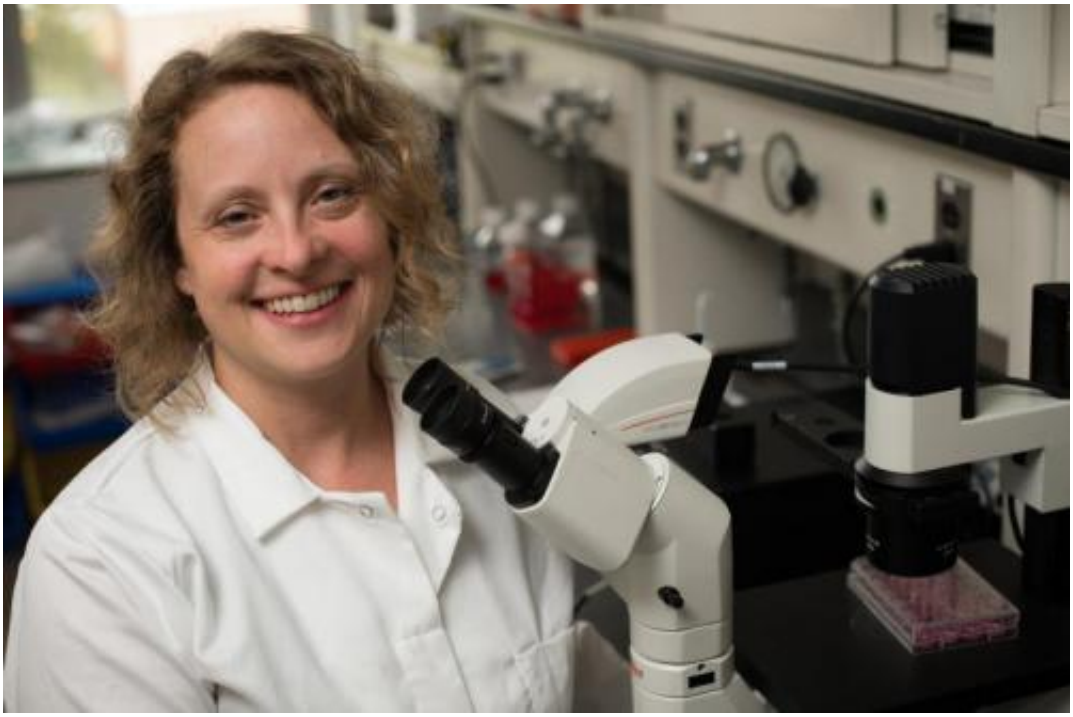


Amy Ralston, MSU biochemist and molecular biologist, has identified a possible source of stem cells, which can advance regenerative and fertility research. Credit: G.L. Kohuth

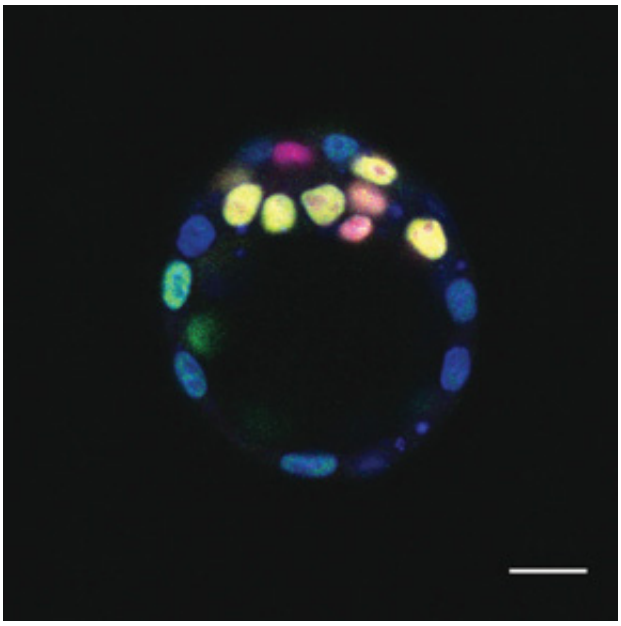
When most animals begin life, cells immediately begin accepting assignments to become a head, tail or a vital organ. However, mammals, including humans, are special. The cells of mammalian embryos get to make a different first choice – to become the protective placenta or to commit to forming the baby.

It's during this critical first step that research from Michigan State University has revealed key discoveries. The results, published in the current issue of *PLOS Genetics*, provide insights into where stem cells come from, and could advance research in regenerative medicine. And since these events occur during the first four or five days of human pregnancy, the stage in which the highest percentage of pregnancies are lost, the study also has significant implications for fertility research.

Pluripotent stem cells can become any cell in the body and can be created in two ways. First, they can be produced when scientists reprogram mature adult cells. Second, they are created by embryos during this crucial four-day window of a mammalian pregnancy. In fact, this window is uniquely mammalian, said Amy Ralston, MSU assistant professor of biochemistry and molecular biology, and lead author on the study.

"Embryos make pluripotent stem cells with 100 percent efficiency," she said. "The process of reprogramming cells, manipulating our own cells to become stem cells, is merely 1 percent efficient. Embryos have it figured out, and we need to learn how they're doing it."

The researchers' first discovery is that in mouse embryos, the gene, Sox2, appears to be acting ahead of other genes traditionally identified as playing crucial roles in stem cell formation. Simply put, this gene could determine the source of stem cells in mammals. Now researchers are trying to decipher why Sox2 is taking the lead role.



Amy Ralston has identified a possible source of stem cells, which can advance regenerative and fertility research. Credit: Courtesy of MSU

"Now we know Sox2 is the first indicator that a cell is pluripotent," Ralston said. "In fact, Sox2 may be the pre-pluripotent gene. We show that Sox2 is detectable in just one or two cells of the embryo earlier than previously thought, and earlier than other known stem cell genes."

The second discovery is that Sox2 has broader influence than initially thought. The gene appears to help coordinate the cells that make the fetus and the other cells that establish the pregnancy and nurture the fetus.

Future research will focus on studying exactly why Sox2 is playing this role. The team has strong insights, but they want to go deeper, Ralston said.

"Reprogramming is amazing, but it's inefficient," she said. "What we've

learned from the embryo is how to improve efficiency, a process that could someday lead to generating stem cells for clinical purposes with a much higher success rate."

More information: *PLOS Genetics*, www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1004618

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