Team IDs mechanism for multiplying adult stem cells

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While research on human embryonic stem cells gets most of the press, scientists are also investigating the potential therapeutic uses of adult stem cells. Although less controversial, this research faces other difficulties. Adult stem cells are extremely difficult to isolate and multiply in the lab.

Now, as reported in the May 6 issue of *Cell*, researchers led by Rudolf Jaenisch of the Whitehead Institute have discovered a mechanism that might enable scientists to multiply adult stem cells quickly and efficiently.

"These findings provide us with a new way of looking at adult stem cells and for possibly exploiting their therapeutic potential," says Jaenisch, who also is a professor of biology at MIT.

This research focuses on a gene called Oct4, a molecule that is known to be active in the early embryonic stage of an organism. Oct4's primary function is to keep an embryo in an immature state. It acts as a gatekeeper, preventing the cells in the embryo from differentiating into tissue-specific cells. While Oct4 is operating, all the cells in the embryo remain identical, but when Oct4 shuts off, the cells begin growing into, say, heart or liver tissue.

Konrad Hochedlinger, a postdoctoral researcher in Jaenisch's lab, was experimenting with the Oct4 gene, curious to see what would happen in laboratory mice when the gene was reactivated in adult tissue in which it had long been dormant. Hochedlinger found that when he switched the gene on, the mice immediately formed tumors in the gut and in the skin where the gene was active. When he switched the gene off, the tumors subsided, demonstrating that the process is reversible.

Discovering that simply flipping a single gene on and off had such an immediate effect on a tumor was unexpected, even though Oct4 is known to be active in certain forms of testicular and ovarian cancer. Still, the most provocative finding was that "Oct4 causes tumors by preventing adult stem cells in these tissues from differentiating," says Hochedlinger. In other words, with Oct4 active, the stem cells could replicate themselves indefinitely, but could not produce mature tissue.

One of the main obstacles with adult stem cell research is that, in order for these cells to be therapeutically useful, researchers need to multiply them in the lab. But when adult stem cells are isolated, they immediately start growing into their designated tissue type, which limits their replication. If scientists could take a liver adult stem cell and multiply it in a dish, without having it form mature liver tissue, more tissue could be made.

This experiment showed that when Oct4 was reactivated, the adult stem cells in those tissues continued to replicate without forming mature tissue. In a mammal's body, this type of cell behavior causes tumors. But under the right laboratory conditions, it could be a powerful tool.

"This may allow you to expand adult stem cells for therapy," Hochedlinger said. "For instance, you could remove a person's skin tissue, put it in a dish, isolate the skin stem cells, then subject it to an environment that activates Oct4. This would cause the cells to multiply yet remain in their stem cell state. And because this process is reversible, after you have a critical mass of these cells, you can then place them back into the person where they would grow into healthy tissue."

"This could be very beneficial for burn victims," Jaenisch said.

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Source: MIT