

Stem cell transplant can grow new immune system in certain mice

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Researchers at the Stanford University School of Medicine have taken a small but significant step, in mouse studies, toward the goal of transplanting adult stem cells to create a new immune system for people with autoimmune or genetic blood diseases.

The researchers found a way to transplant new blood-forming stem cells into the bone marrow of mice, effectively replacing their immune systems. Many aspects of the technique would need to be adapted before it can be tested in humans, said Irving Weissman, MD, a co-senior author of the study and director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. The work was done on a particular group of mice that are a poor mimic for the human immune system. Still, Weissman suggested the remaining hurdles could eventually be overcome.

When those barriers are surmounted, the benefits are potentially big. The study will be published in the Nov. 23 issue of *Science*.

A person with an autoimmune disease such as multiple sclerosis has a defective immune system in which immune cells attack the person's own body. An immune system transplant, much like a liver or heart transplant, would give the person a new system that might not attack the body.

The way to get a new immune system is to transplant new blood-forming stem cells into the bone marrow, where they generate all the cells of the

blood. But before transplanting new stem cells, the old ones first must be removed, which is currently done by intensive chemotherapy or radiation. Those processes eliminate the cells of the bone marrow, but also damage other tissue and can cause lasting effects including infertility, brain damage and an increased risk of cancer. A treatment for M.S. at the expense of brain function is hardly an ideal therapy.

Weissman and co-first author Deepta Bhattacharya, PhD, a postdoctoral scholar in Weissman's lab, thought one way around this problem would be to eliminate only the blood-forming stem cells without affecting bone marrow cells or other tissues. They worked with Agnieszka Czechowicz, first author and medical student, to accomplish that feat by injecting the mice with molecules that latch on to specific proteins on the surface of the blood-forming stem cells, effectively destroying the cells. That technique eliminated the blood-forming stem cells without otherwise harming the mice.

"It is essentially a surgical strike against the blood-forming stem cells," said Weissman, the Virginia & D.K. Ludwig Professor for Clinical Investigation in Cancer Research. When they transplanted new blood-forming stem cells into the mice, those cells took up residence in the bone marrow and established a new blood and immune system.

In a person with autoimmune disease, that new immune system would likely no longer attack tissues of the body. Likewise, in people with a genetic disorder such as sickle cell anemia, the new blood system would not have the sickle-cell mutation, eliminating the cause of disease. However, the barriers are still significant.

First, the researchers don't know whether the same molecule on human blood-forming stem cells would be the right one to target with a therapy. Also, the mice they used in the study lack a functioning immune system. They'll need to get the therapy working in mice with a normal immune

system before they can begin testing the technique in humans.

Although these steps will take time to overcome, Weissman said he considered this work to be the beginning of research that could lead to human studies.

Source: Stanford University

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