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ANTIBODY COULD INCREASE CURE RATE FOR BLOOD, IMMUNE DISORDERS

An antibody to a protein on blood-forming stem cells may enable bone marrow transplants without the need for chemotherapy and radiation

February 15, 2019, NEW YORK— A study led by Ludwig Stanford investigator Judith Shizuru shows that an antibody-based treatment can gently and effectively eliminate diseased, blood-forming stem cells in the bone marrow to prepare for the transplantation of healthy stem cells. The researchers believe the potential treatment, which was tested in mice, could circumvent the need to use harsh, potentially life-threatening chemotherapy or radiation to prepare people for transplantation, vastly expanding the number of people who could benefit from the procedure. The study was published online Feb. 11 in *Blood.*

Shizuru and her colleagues have previously shown that an antibody targeting a protein called CD117 on the surface of blood-forming (hematopoietic) stem cells can efficiently and safely eliminate the cells in mice and non-human primates. The antibody, called SR1, binds and inhibits CD117's ability to regulate hematopoietic stem cell growth and function.

The use of antibodies against CD117 for that purpose is based on studies conducted in the laboratory of study co-author Irving Weissman, who is director of both Ludwig Stanford and of Stanford's Institute for Stem Cell Biology and Regenerative Medicine.

Blood cancers, such as leukemia, arise when hematopoietic stem cells or their progeny begin dividing uncontrollably. Often the best chance for a cure for these and other diseases originating in the bone marrow is to eliminate the patient's defective hematopoietic stem cells and replace them with healthy ones from a closely matched donor. For this to be an option, the patient must be able to withstand a combination of chemotherapy and radiation in doses high enough to kill stem cells in the marrow.

Shizuru has long explored gentler approaches to bone marrow transplantation, including the creation of space for transplanted hematopoietic stem cells to take hold. (To learn more about Shizuru and her research, read the Ludwig profile of her work here.)

In the current study, Shizuru and her colleagues studied a mouse model of a class of human diseases called myelodysplastic syndromes (MDS), which are considered a type of cancer. People with MDS are unable to make mature, properly functioning blood cells and the only cure is a stem cell transplant.

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Shizuru and her colleagues found that SR1 blocked the growth of both healthy and diseased stem cells in culture. They then investigated its effect on mice engineered to have both human and mouse hematopoietic stem cells and found that it efficiently eliminated both healthy human hematopoietic stem cells and cells isolated from low-risk MDS patients. In animals with diseased hematopoietic human stem cells, SR1 pretreatment significantly improved the ability of healthy stem cells to engraft.

Although SR1 could significantly reduce the number of high-risk MDS cells from the mice, the effect was transient: The diseased cells eventually returned even after transplant. In such cases, the researchers suggest, it may be necessary to combine anti-CD117 treatment with other therapies to eliminate the diseased cells.

“Based on the results of this study and others, we have received approval from the Food and Drug Administration to move forward with a clinical trial for MDS patients using a version of SR1 appropriate for a trial in humans,” Shizuru said. “We are very hopeful that this body of research is going to have a positive impact on patients by allowing better depletion of diseased cells and engraftment of healthy cells.”

The Stanford release from which this summary is derived can be found here.

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About Ludwig Cancer Research

Ludwig Cancer Research is an international collaborative network of acclaimed scientists that has pioneered cancer research and landmark discovery for more than 40 years. Ludwig combines basic science with the ability to translate its discoveries and conduct clinical trials to accelerate the development of new cancer diagnostics and therapies. Since 1971, Ludwig has invested $2.7 billion in life-changing science through the not-for-profit Ludwig Institute for Cancer Research and the six U.S.-based Ludwig Centers. To learn more, visit www.ludwigcancerresearch.org.

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