Gene therapy restores immunity in children and young adults with rare immunodeficiency

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Gene therapy can safely rebuild the immune systems of older children and young adults with X-linked severe combined immunodeficiency (SCID-X1), a rare inherited disorder that primarily affects males, scientists from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, have found. NIAID's Suk See De Ravin, M.D., Ph.D., is scheduled to describe the findings at the 57th American Society of Hematology Annual Meeting in Orlando, Florida.

SCID-X1 is caused by mutations in the *IL2RG* gene that prevent infection-fighting immune cells from developing and functioning normally, leaving affected infants highly susceptible to life-threatening infections. Transplantation of blood-forming stem cells, ideally from a genetically matched sibling donor, is a lifesaving treatment for infants with SCID-X1. Those without a matched sibling often receive stem cells from a parent, which only partially restores immunity. Such patients require lifelong treatment and may continue to experience complex medical problems, including chronic infections.

In the current study, researchers tested the safety and effectiveness of gene therapy combined with low-dose chemotherapy in five SCID-X1 patients aged 7 to 24 with worsening immune systems despite one or more previous transplants from a parent. The investigators removed stem cells from the patient's bone marrow and used a lentiviral vector, which

was developed in collaboration with St. Jude Children's Research Hospital, to deliver a normal *IL2RG* gene to the cells. The corrected cells were infused back into the patient after a low dose of chemotherapy to help the stem cells establish themselves and begin producing new blood cells.

The first two patients to receive the therapy showed substantial improvements in immunity and clinical status, with one patient continuing to improve three years after therapy. Despite improvements in immunity, the second patient died of pre-existing, infection-induced lung damage two years after receiving gene therapy, suggesting the importance of early treatment before organ damage becomes irreversible. The three other patients received the therapy three to six months ago and are beginning to show improvements in immune function. Researchers are continuing to monitor the surviving patients.

More information: SS De Ravin et al. Lentiviral hematopoietic stem cell gene therapy for older patients with X-linked severe combined immunodeficiency. Program number 261, session 801. ash.confex.com/ash/2015/webprogram/Paper85517.html

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