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Gene therapy shows promise for severe combined immunodeficiency

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Researchers have found that gene therapy using a modified delivery system, or vector, can restore the immune systems of children with X-linked severe combined immunodeficiency (SCID-X1), a rare, life-threatening inherited condition that primarily affects boys. Previous efforts to treat SCID-X1 with gene therapy were initially successful, but approximately one-quarter of the children developed leukemia two to five years after treatment. Results from a study partially funded by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), suggest that the new vector is equally effective at restoring immunity and may be safer than previous approaches.

In SCID-X1, mutations in a specific gene prevent the development of infection-fighting T cells. The standard therapy for SCID is transplantation of blood-forming stem cells, but some patients lack a suitable donor. In gene therapy, doctors remove stem cells from the patient's bone marrow, use a vector to insert a corrected gene and then return the corrected cells to the patient. Scientists suspect that the vectors used in earlier studies may have activated genes that control cell growth, contributing to leukemia.

In the current study, nine boys with SCID-X1 underwent gene therapy using a vector engineered by the study researchers. Seven boys developed functional T cells at levels comparable to those seen in previous studies and have remained healthy for one to three years after treatment. Analyses of the children's T cells suggest that the new vector

causes fewer genomic changes that could be linked to leukemia. Researchers will continue to monitor the boys for leukemia development. Of the two other boys, one died of a pre-existing viral infection shortly after receiving the therapy, and one failed to develop corrected T cells and was given a stem cell transplant from an unrelated donor.

More information: S Hacein-Bey-Abina, S-Y Pai et al. A modified y-retrovirus vector for X-linked severe combined immunodeficiency. *New England Journal of Medicine* DOI: 10.1056/NEJMoa1404588 (2014).

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