Engineered version of HIV is used to cure genetic blood disorder

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For the second time, researchers have used the HIV virus in gene therapy to cure a severe genetic disease, this time the blood disorder beta-thalassemia, which causes life-threatening anemia.

French researchers had previously used a "defanged" version of the virus that causes AIDS to cure two boys with the rare disorder adrenoleukodystrophy, which was at the heart of the popular movie "Lorenzo's Oil." Beta-thalassemia is a much more common disease, and although the new research involved only one patient, it suggests that this approach could have wide applicability.

"This work represents a major step forward for the gene therapy of hemoglobin disorders," wrote Dr. Derek A. Persons of St. Jude Children's Research Hospital in Memphis, Tenn., in an editorial accompanying the report in the journal *Nature*.

The feat marks at least the sixth disease for which gene therapy has recently been shown to be beneficial.

Beta-thalassemia is caused by defects in the production of the beta-globin chain, a key component of hemoglobin, the molecule that carries oxygen in red blood cells. It affects primarily people of Mediterranean, Middle Eastern, South Asian, Southeast Asian and Chinese descent, with about 60,000 children being diagnosed with it worldwide each year.

Treatment generally involves frequent blood transfusions -- typically

monthly -- but that leads to a buildup of iron that can damage organs. As a result, patients must also undergo chelation therapy to remove as much of the iron as possible. The disease can be cured by bone marrow transplants, but only if a suitable donor is found.

The researchers in the new study used an HIV virus that had been engineered to carry the correct version of the hemoglobin gene. Most previous research on gene therapy has used other retroviruses, such as the mouse leukemia virus, to carry the desired gene into cells. But those so-called vectors had a tendency to insert genes in the wrong locations, leading in some cases to cancer. Attempts to try gene therapy in patients were put on hold until scientists could overcome the problem.

Dr. Philippe Leboulch of the University of Paris and his colleagues used the HIV-based vector -- produced by Bluebird Bio of Cambridge, Mass., and Paris -- to treat an 18-year-old French boy who had been diagnosed with beta-thalassemia at age 3. Before the treatment, he was receiving three packs of red blood cells monthly and chelation therapy to remove iron, but was still ill. No suitable bone marrow donor was available.

The team removed blood-forming stem cells from the patient's bone marrow and treated them in a test tube to add the working gene. The boy was given chemotherapy to destroy as many of the remaining stem cells as possible, then the treated cells were injected.

Within a year, the boy was able to stop receiving transfusions, and he has remained stable for 22 months since then.

"He is happy to have a normal life back, and for the first time has a full-time job in a main restaurant in Paris," Dr. Francoise Bernaudin, the clinical hematologist who has been monitoring his condition, said in a statement. The team has also been able to remove excess iron that has built up over the years by bleeding him regularly, she said.

The researchers are planning to enroll another 10 patients for more studies.