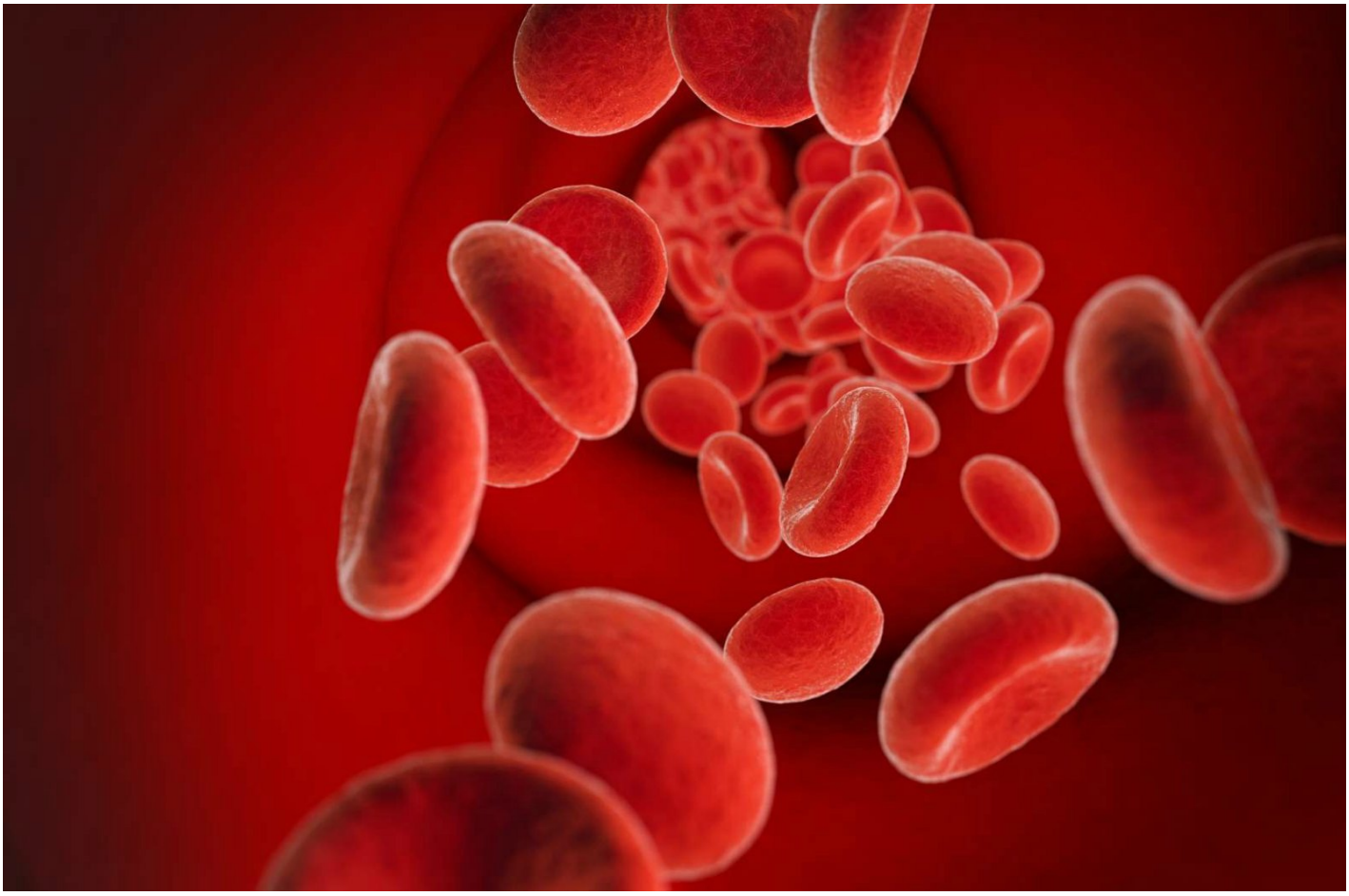
Hemophilia B Treated With Gene Therapy Vector From St. Jude

St Jude Children's Research Hospital



Hemophilia B, a disease in which the patient's blood fails to clot properly, affects about one in 30,000 individuals, mainly males. It is caused by a mutation in the gene coding for Factor IX (FIX), a factor involved in blood clotting. People with hemophilia B suffer from lower than normal levels of Factor IX.

Hemophilia B is well suited for gene therapy replacement because the lack of a single protein is responsible for the disease and achieving even a modest rise in FIX levels is enough to alleviate a subject's clotting deficiency. Several groups of researchers have conducted research with gene therapy vectors designed to express FIX, but have not been able to achieve stable production of therapeutic levels in humans.

Drs. John Gray, Andrew Davidoff and Amit Nathwani jointly designed a FIX expression vector that may finally reach this goal. It includes two significant improvements for which St. Jude sought patent protection. The first is a specific coding sequence designed for optimal expression of FIX. The second is a transcriptional regulatory control region that regulates the expression of FIX in liver cells. This transcriptional regulatory control region consists essentially of a

smaller version of a known liver specific enhancer and promoter, both of which are reduced in size but still retain their function.

> *By reducing the size of this control region, the chimeric FIX gene was able to fit into a self-complementary virus vector which is more efficiently transduced into cells than standard virus vectors.*

Standard treatment is directed toward stopping the bleeding associated with the disease by infusion of factor IX concentrates to replace the defective clotting factor. Current recombinant protein treatment causes peaks and troughs; whereas, gene therapy replaces the defective gene and yields stable FIX levels. It is hoped hemophilia B gene therapy will be successful enough to replace all recombinant FIX products.

The University College London, in collaboration with Drs. Arthur Nienhuis and Andy Davidoff, initiated a Phase I/II study in adults using the St. Jude vector. Six patients with severe hemophilia B have been treated with vector produced at St. Jude in the Children's GMP. To date, all six patients have demonstrated increased circulating factor IX levels for the duration of the trial, which has been over a year in some of these cases. Four of the six have been able to discontinue their previously necessary prophylactic factor IX protein injections.

St. Jude filed a patent application claiming the aforementioned improvements to this expression vector, which was recently granted on October 4, 2011 as U.S. Patent No. 8,030,965.

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