Gene therapy, the future in hemophilia treatment?

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Hemophilia A and B are attractive target diseases for gene therapy, as stable expression of coagulation factor VIII and IX may correct the bleeding diathesis. Hepatic gene delivery using vectors derived from adeno-associated virus (AAV) resulted in therapeutic functional clotting factor IX (FIX) expression levels in severe hemophilia B patients. Although T-cell-mediated immune responses eliminated the transduced hepatocytes, transient immunosuppression may potentially overcome this limitation. Alternatively, vectors are being developed that result in higher FIX expression levels at lower vector doses. Lentiviral vectors are being explored for in-vivo hepatic gene delivery and for ex-vivo transduction of hematopoietic stem cells. This resulted in stable correction of the bleeding diathesis in hemophilic mice. Finally, nonviral vectors derived from transposons result in sustained clotting-factor expression in rodent models. Translational studies in large animal models are required to move these new approaches forward into the clinic. New insights from clinical trials and advances in preclinical studies may ultimately pave the way toward a cure in patients suffering from hemophilia.

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