Promising results of gene therapy to treat diseases of the eye

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The easy accessibility of the eye and the established link between specific genetic defects and ocular disorders offer hope for using gene therapy to provide long-term therapeutic benefit. Two reports in the current issue of Human Gene Therapy, a peer-reviewed journal published by Mary Ann Liebert, Inc., describe the effective replacement of a human gene to preserve photoreceptor function in a mouse model of severe retinal degeneration.

Basil Pawlyk and colleagues from Harvard Medical School and Massachusetts Eye and Ear Infirmary (Boston, MA) delivered the human gene for RGPR-interacting protein-1 to mice affected with Leber congenital amaurosis (LCA), a condition linked to a mutated form of RPGRIP1 that causes degeneration of photoreceptors in the eye. The researchers packaged the gene in an adeno-associated virus (AAV) vector and injected the vector under the retinas of the affected mice. They demonstrated expression of the human gene in the photoreceptors, with correct localization to the cilia. Further evaluation revealed improved function and survival of the photoreceptors in the treated eyes.

The authors conclude that the results of this study, presented in the paper entitled, "Replacement Gene Therapy with a Human RPGRIP1 Sequence Slows Photoreceptor Degeneration in Murine Model of Leber Congenital Amaurosis," validate a gene therapy design that could serve as the basis for a future clinical trial in patients affected by this form of LCA.

In the same issue, Kamolika Roy, Linda Stein, and Shalesh Kaushal from University of Massachusetts Medical School (Worcester) review the use of recombinant AAV vectors for gene therapy to treat ocular diseases. Based on the success of three early-stage clinical trials in LCA, they conclude that this approach appears "to be a safe, effective, and long-term treatment for LCA, a previously untreatable disorder." In the article, "Ocular Gene Therapy: An Evaluation of Recombinant Adeno-Associated Virus-Mediated Gene Therapy Interventions for the Treatment of Ocular Disease," they conclude that rAAV-mediated gene therapy is "the most suitable gene therapy treatment approach for ocular diseases."

"The successful correction of this photoreceptor defect in a relevant mouse model of LCA should usher in a new wave of translational research in retinal degeneration syndromes," says James M. Wilson, MD, PhD, Editor-in-Chief of Human Gene Therapy, and Head of the Gene Therapy Program, Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, in Philadelphia.

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