Gene therapy cures canines of inherited form of day blindness

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Veterinary ophthalmology researchers from the University of Pennsylvania have used gene therapy to restore retinal cone function and day vision in two canine models of congenital achromatopsia, also called rod monochromacy or total color blindness.

Achromatopsia is a rare autosomal recessive disorder with an estimated prevalence in human beings of about 1 in 30,000 to 50,000. It primarily affects the function of the cone photoreceptors in the retina and serves as a representative model for other more common inherited retinal disorders affecting cones. Cone function is essential for color vision, central visual acuity and most daily visual activities, which underlines the importance of the newly developed treatment.

The treatment cured younger canines regardless of the mutation that caused their achromatopsia. It was effective for the 33 months of the study and most likely is permanent; however, researchers also observed a reproducible reduction in the cone therapy success rate in dogs treated at 54 weeks of age or older.

The successful therapy in dogs was documented by the restoration of the cone function using electroretinography and by objective measure of day vision behavior. The behavioral results suggest that inner retinal cells and central visual pathways were able to usefully process the input from the recovered cones.

The results represent the second successful cone-directed gene

replacement therapy in achromatopsia animal models and the first outside of mouse models. The gene therapy targets mutations of the CNGB3 gene, the most common cause of achromatopsia in humans. Achromatopsia-affected dogs represent the only natural large animal model of CNGB3-achromatopsia.

The results hold promise for future clinical trials of cone-directed gene therapy in achromatopsia and other cone-specific disorders.

"The successful restoration of visual function with recombinant adeno-associated virus-mediated gene replacement therapy has ushered in a new era of retinal therapeutics," said András M. Komáromy, assistant professor of ophthalmology at the Penn School of Veterinary Medicine and lead author of the study.

Many vision-impairing disorders in humans result from genetic defects, and, to date, mutations have been identified in ~150 genes out of ~200 mapped retinal disease loci. This wealth of genetic information has provided fundamental understanding of the multiple and specialized roles played by photoreceptors and the retinal pigment epithelium in the visual process and how mutations in these genes result in disease. Together with the development of gene-transfer technologies, it is now possible to realistically consider the use of gene therapy to treat these previously untreatable disorders.

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