Delivering large genes to the retina is problematic

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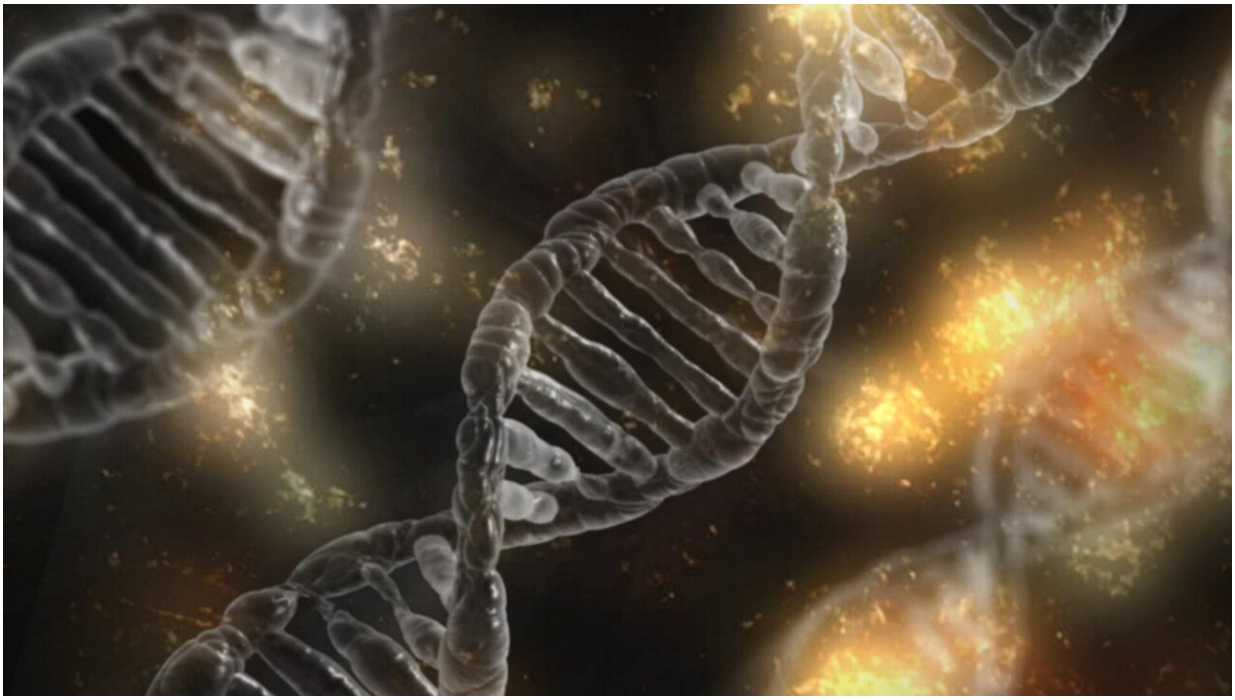

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A new study has shown that a commonly used vector for large gene transfer can successfully deliver genes to retinal cells in the laboratory, but when injected subretinally into rats it provokes a robust and acute inflammatory response. A detailed description of this study and the implications of its results are published in *Human Gene Therapy*.

Luke Wiley and colleagues from University of Iowa, Iowa City, coauthored the article entitled "Helper-Dependent Adenovirus Tranduces the Human and Rat Retina but Elicits an Inflammatory Reaction When Delivered Subretinally in Rats." Many of the genes that cause inherited retinal degeneration are too large to deliver using more conventional approaches, such as adeno-associated viruses. The researchers showed that the vector known as helper-dependent adenovirus serotype 5 (HDAd5) was able to deliver genetic material to rod and cone photoreceptors in human retinal organ cultures. However, when they used the same vector for gene delivery to a live rat model, they reported a strong immune reaction. The researchers conclude that further work is needed to understand the inflammatory pathways involved and to identify ways to modulate the immune response to enable safe delivery of large genes to the retina using HDAd5.

"The work by Dr. Wiley and his group at the University of Iowa opens up the possibility of gene therapy for genetic retinal disease patients whose defects are in genes that are too large to fit into adeno-associated virus (AAV) particles," says Editor-in-Chief Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and Executive Deputy Chancellor, University of Massachusetts Medical School, Worcester, MA.

More information: Ian C. Han et al, Helper-Dependent Adenovirus Transduces the Human and Rat Retina but Elicits an Inflammatory Reaction When Delivered Subretinally in Rats, *Human Gene Therapy* (2019). DOI: 10.1089/hum.2019.159