CRISPR genome editing technology can correct alpha-1 antitrypsin deficiency

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Groundbreaking research demonstrates proof-of-concept for using CRISPR-Cas9 genome editing technology to correct the gene mutation responsible for alpha-1 antitrypsin (AAT) deficiency, successfully making a targeted gene correction in the livers of affected mice that restored at least low levels of normal AAT. In the studies, both published in Human Gene Therapy.

The article entitled "In vivo Genome Editing Partially Restores Alpha1-Antitrypsin in a Murine Model of AAT Deficiency " was coauthored by Terence Flotte, Editor-in-Chief of Human Gene Therapy, and Wen Xue, both from the University of Massachusetts Medical School (Worcester), together with a team of researchers from UMass Medical School, Tongji University (Shanghai, China), and Wuhan University (China). The researchers co-injected two adeno-associated viral (AAV) vectors: one to deliver the Cas9 component of the CRISPR-Cas9 system; and the second encoding an AAT gene-targeted guide RNA and carrying a homology-dependent repair template.

Shen Shen, Editas Medicine, together with researchers from Editas and St. Louis University School of Medicine (MO) coauthored the article "Amelioration of Alpha-1 Antitrypsin Deficiency Diseases with Genome Editing in Transgenic Mice." They demonstrated both a gene knockdown approach, in which they reduced the expression of the toxic mutated AAT in liver cells by more than 98%, and the use of a dual-vector system capable of achieving a 4-5% nucleotide correction at the site of the target mutation.

"Those two back-to-back papers published in Human Gene Therapy represent an important milestone in AATD gene therapy, demonstrating for the first time that in vivo genome editing by rAAV-mediated delivery of CRISPR-Cas9 holds the potential for a novel therapeutic modality to treat AATD," says Human Gene Therapy Editor Guangping Gao, Ph.D., Gene Therapy Center & Department of Microbiology and Physiological Systems, University of Massachusetts Medical School.


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