CRISPR genome editing technology can correct alpha-1 antitrypsin deficiency

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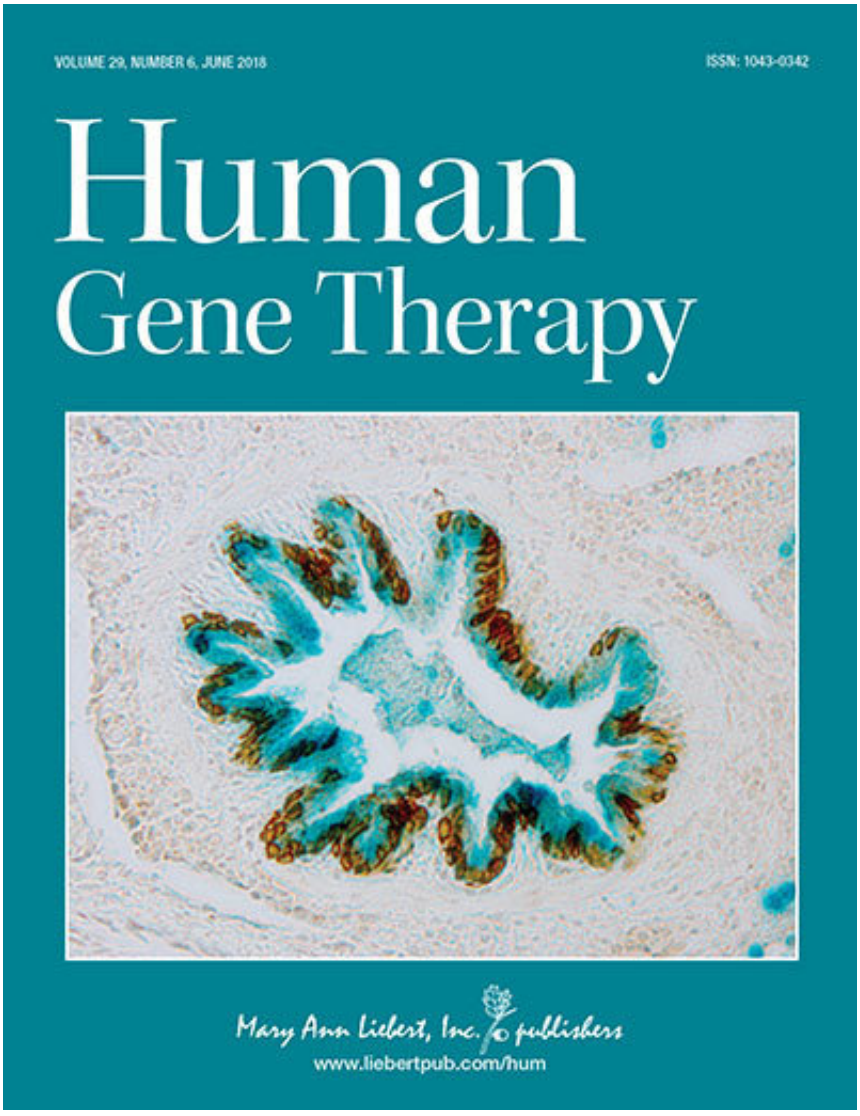

Credit: Mary Ann Liebert, Inc., publishers

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 re-searchers 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 Uni-versity School of Medicine (MO) coauthored the article "Amelioration of Alpha-1 An-titrypsin Deficiency Diseases with Genome Editing in Transgenic Mice." They demon-strated 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 im-portant milestone in AATD gene therapy, demonstrating for the first time that in vivo ge-nome editing by rAAV-mediated delivery of CRISPR-Cas9 holds the potential for a novel therapeutic modality to treat AATD," says *Human Gene Therapy Editor* Guang-ping Gao, Ph.D., Gene Therapy Center & Department of Microbiology and

Physiological Systems, University of Massachusetts Medical School.

More information: Chun-Qing Song et al, In vivo Genome Editing Partially Restores Alpha1-Antitrypsin in a Murine Model of AAT Deficiency, *Human Gene Therapy* (2018). DOI: 10.1089/hum.2017.225