Novel CRISPR Gene Therapy for Haploinsufficiency
Tech ID: 30127 / UC Case 2017-040-0

INVENTION NOVELTY

This technology presents a way to treat human genetic disease caused by haploinsufficiency and reduced protein production. The method employs the use of adeno-associated viral (AAV) vectors for the in vivo delivery of a CRISPR-based gene expression activator (CRISPRa) that boosts transcription from the existing functional copy of the affected gene.

VALUE PROPOSITION

Haploinsufficiency – having only one functional copy of a gene due to gene deletion or other gene-inactivating mutations, is the basis of many human genetic disorders caused by the insufficient amounts of product generated by the affected gene. Attempts to treat such developmentally-predetermined conditions have relied on gene therapy and the re-introduction of a second functioning gene copy. However, this therapeutic approach has been hampered by a series of confounding factors including gene size, mutations caused by gene or vector insertion, and inability to target specific cells or deliver specific doses of the gene. A unique merit of this novel technology is the use of non-pathogenic and non-integrating AAV vector to deliver a CRISPRa, which is targeted to the enhancer or promoter region of a gene. In the case of low gene dosage-based conditions, this allows for inducing transcription from the existing copy of the gene without creating any changes in the patient’s DNA. Furthermore, as the AAV vector will not be carrying the actual missing gene copy, this method circumvents common limitations to using AAV for effective delivery in patients.

TECHNOLOGY DESCRIPTION

Gene transcription is increased by a nuclease defective Cas9 (dCas9) fused to a transcriptional activation domain combined with a unique guide RNA construct targeted to the regulatory (promoter and/or enhancer) regions of a gene. Thus, this CRISPRa complex does not cause nicks or breaks in the DNA, can be easily packaged in an AAV vector for in vivo delivery, and cell/tissue-specificity is determined by the targeted cis-regulatory regions. The inventors have demonstrated successful in vivo use of the technology by curing obesity in Sim1 and Mc4r mouse haploinsufficiency models, which as is the case in humans, results in defects in the leptin pathway and hyperphagic obesity.

LOOKING FOR PARTNERS

To develop & commercialize the technology as a gene therapy tool for the treatment of human disease based on genetic haploinsufficiency.

STAGE OF DEVELOPMENT

Pre-clinical / Proof of concept

RELATED MATERIALS


OTHER INFORMATION

## DATA AVAILABILITY

Under CDA / NDA

## PATENT STATUS

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## ADDRESS

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