GENE-EDITING OF FMR1 USING CRISPR/CAS9

Published date: Feb. 27, 2018

Technology description

Market Need

Fragile X syndrome is an X-chromosome-linked disease that affects males more severely than females and is the most common cause of inherited intellectual disability, often co-occurring with Autism spectrum disorder. According to the CDC, around 1 in every 6000 males and 7000 females are born with the condition. Patients usually present with delay in reaching early language and communication milestones, lower than average intelligence quotient that declines with age, attention problems, anxiety, self-injury, hypersensitivity, and aggressiveness. Genetically, the disease is caused by an expansion of the CGG triplet repeat within the fragile X mental retardation 1 (FMR1) gene. The normal range for CGG repeats is 5 to 40, with a pre-mutation range being above 40 and up to 200 repeats, which is the threshold for FXS. The result of excessive repeats is that not enough FMR1 protein is produced and it is important for the normal development of the connection between neurons. Currently, there is no cure for this disease and treatment is limited to speech therapy, behavioral therapy, sensory integration occupational therapy, special education, or individualized educational plans, and, when necessary, treatment of physical abnormalities. Medications such as antidepressants, antipsychotics, and stimulants can be prescribed for symptoms. Thus, there is a need for a therapy that addresses the cause of FXS.

Technology Overview

The Davidson lab focuses on gene therapy approaches for inherited genetic diseases, specifically those childhood-onset neurodegenerative diseases for which there are no current treatments. For FXS, the group has developed a CRISPR/Cas9-based gene therapy approach to target and induce deletion of the excessive CGG trinucleotide repeat regions in the 5’ untranslated region of the FMR1 gene that is responsible for pathological effects. The CRISPR/Cas9 system is able to cause precise breaks in DNA that are able to be specifically directed by a short RNA guide sequence. Herein, many guide RNAs have been designed to target the CGG repeat regions and adjacent sequences in order to induce deletion of some or all of the CGG repeats. Thus far, group has shown that this approach is effective in deleting the CGG repeats in-vitro in human embryonic kidney cells and human fibroblasts that harbor either pre-mutation or a full mutation allele. With further development, this could be the first curative treatment for FXS.

Advantages

- Treats cause of FXS
- Targeted delivery with minimal off target effects

Institution

The Children's Hospital of Philadelphia

Inventors

Beverly Davidson
CSSO and Center Director
Path
Alejandro Mas Monteys
Instructor
Pathology and Laboratory Medicine
Carolyn Yrigollen

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com