Genetic Correction of Mutant Huntingtin in Vivo

https://www.neurodegenerationresearch.eu/survey/genetic-correction-of-mutant-huntingtin-in-vivo/

Principal Investigators

ELLERBY, LISA M

Institution

BUCK INSTITUTE FOR RESEARCH ON AGING

Contact information of lead PI
Country

USA

Title of project or programme

Genetic Correction of Mutant Huntingtin in Vivo

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,946,674.31

Start date of award

01/09/2016

Total duration of award in years

5

The project/programme is most relevant to:

Huntington's disease

Keywords
Research Abstract

The proposed research is intended to determine if a monogenetic disease such as Huntington’s disease (HD) can be treated by using homologous recombination (HR) to genetically correct the disease containing allele in vivo. The approach will utilize a genome engineering system, CRISPR (Clustered Regulatory Interspaced Short Palindromic Repeats) delivered in vivo. In recent work in HD-iPSCs (induced pluripotent stem cells), we utilized homologous recombination to genetically correct the disease containing cells and found this completely reverses HD disease phenotypes. We have adapted the CRISPR technology to carry out

genetic correction/expansion and have found very high levels of homologous recombination in human cells (Preliminary Results). The overall goal is to use this technology in vivo and carry out genetic correction of disease-containing mutations such as the CAG expansion in huntingtin (HTT). This work will serve as a proof of concept to demonstrate utility not only for monogenic neurodegenerative diseases but also for other types of genetic diseases. To achieve our goals we will carry out the following aims: Specific Aim 1. To demonstrate robust CRISPR-mediated recombination of the mutant HTT in human HD patient-derived neural cells using lentivirus; Specific Aim 2. To demonstrate robust CRISPR-mediated recombination in mouse models of HD expressing the human HTT protein using viral delivery; Specific Aim 3. To develop a protein-mediated delivery system using the nickase Cas9 D10A protein, gRNA and DNA to mediate homologous recombination in human-patient HD neural stem cells and HD mouse models. These studies will advance our understanding of how to perform genetic correction in cells derived from the brain. The successful demonstration of in vivo genetic correction of the disease allele in the brain would be a major leap forward in neuroscience.

Lay Summary
The proposed research is intended to determine if monogenetic disease such as Huntington’s disease can be treated repairing the disease causing mutation using a novel enzyme system-CRISPR/Cas9. This could represent a new treatment for the disease.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Huntington's disease

Years:
2016

Database Categories:
N/A

Database Tags:
N/A