Technology Offer

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GENE-EDITING FOR THE TREATMENT OF HUNTINGTON'S DISEASE

Huntington's disease (HD) is an orphan disease caused by brain-destroying mutant proteins which ends in dementia and death. Genetic mutation is due to a repetition of DNA triplet and affects around 1/10'000 people worldwide. Currently, no curative treatment is available.

DESCRIPTION

The invention provides a kit for the treatment of Huntington's disease using CRISPR system for blocking the expression of the mutant huntingtin (*mHTT*) or repairing the CAG expansion causing the disease. The kit (or therapeutic cassette) comprises a gene delivery vector, a human codon-optimized Cas9, one artificial single guide RNA (sgRNA) recognizing the *HTT* gene, and a system ensuring transient editing activity.

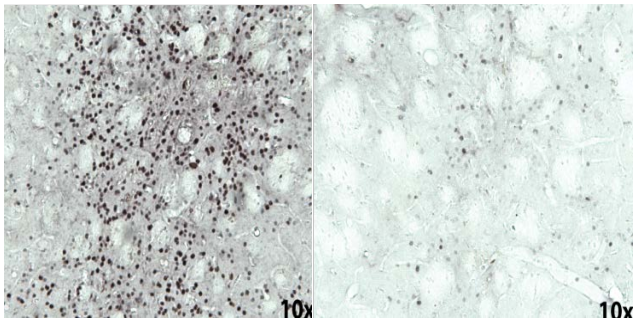
INTELLECTUAL PROPERTY

Patent application: PCT/EP2015/067986
extended in national phases, pending
Publication N°: WO2016020399
Priority date: August 04, 2014
Applicant: Lausanne University hospital
Inventors: N. Déglon and N. Merienne

ADVANTAGES

- Novel therapeutic strategy for an orphan disease with a high unmet medical need
- Single treatment of mutant code for a permanent benefice
- High safety due to DNA targeting and self inactivation
- Use of one kit/delivery system including all components
- Gene delivery vector targeting neuronal and glial cells

TYPICAL RESULTS



Left: brain of untreated mouse, showing huntingtin protein aggregation. Right, the brain of a mouse treated with CRISPR-Cas9 editing, showing the strong reduction of misfolded huntingtin, after 3 weeks of treatment.

PROOF OF CONCEPT

In mouse primary affected HD neurons/astrocytes, and in human neurons derived fom iPS cells up to fifty percent gene disruption was achieved.

In adult mice expressing a *mHTT* gene, the group treated with the "therapeutic cassette" containing the gene-editing enzyme Cas9 and the RNA targeting the *HTT* gene showed an extremely efficient gene disruption and up to 90% reduction of *mHTT* aggregation compared to control group (without CRISPR treatment).

STAGE OF DEVELOPMENT

Pre-clinical stage: *in vitro* and *in vivo* using cells and mouse models of Huntington's disease.

KEY PUBLICATION: Merienne et al. (2017) Cell Reports 20: 2980-2991

COLLABORATION OFFER

PACTT is looking for industrial partners for further development and offers to grant exclusive or non exclusive patent licenses.

REFERENCE

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