Alzheimer treatment based on the editing of the Amyloid Precursor Protein gene

https://www.neurodegenerationresearch.eu/survey/alzheimer-treatment-based-on-the-editing-of-the-amyloid-precursor-protein-gene/

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Country

Canada

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Alzheimer treatment based on the editing of the Amyloid Precursor Protein gene

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CIHR

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1

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Research Abstract
Alzheimer disease is due to an accumulation of beta-Amyloïd plaques in the brain. These plaques are produced by the abnormal degradation of the Amyloïd Precursor Protein (APP). This protein in normally cut by the alpha-Secretase enzyme. However, its abnormal digestion by the beta-Secretase leads to the formation of an abnormal protein fragment, which aggregates and accumulates as plaques in the brain. Many mutations of the APP gene favor the formation of these plaques by favorizing the cutting of APP by the beta-Secretase. However, Jonnson et al. (Nature, 2012) have identified in a population of elderly healthy persons a modification of the APP gene, which reduces the digestion of the APP protein by the beta-Secretase and thus

prevents Alzheimer. We have recently been able to produce in human cells this specific modification of the APP gene by homologous recombination with a fragment of the APP gene containing this modification. To induce this recombination, the APP gene was cut with a short sequence of RNA (called a gRNA) using the recently developed CRISPR technology. We have also inserted a sequence in the APP gene a sequence of nucleotides, which produce a modification of the APP protein, which was detected with an antibody. I have deposited a patent on this therapeutic approach. The present project aims to improve the specificity and the frequency of the homologous recombination by using simultaneously several pairs of gRNA and a nuclease (the enzyme that cuts the DNA). The project also aims to demonstrate that the production of beta-Amyloid peptide is reduced in 293 T cells and in neurons containing this favorable mutation compared to cells that contain a mutation causing Alzheimer, which favors the formation of Amyloid peptides. We will also produce an Adeno Associated Virus containing all the necessary components to mutate the APP gene in the brain of mouse models of Alzheimer that contains a humanized sequence of the APP gene.

Further information available at:

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