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The use of CRISPR/Cas9 to treat hereditary diseases: Duchenne muscular dystrophy, Friedreich's ataxia and Alzheimer disease

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The new CRISPR/Cas9 technology permits to induce double strands breaks (DSBs) in the DNA at a specific sequence in the human genome selected by a guide RNA complementary to a 20 nucleotides sequence. These DSBs may be repaired by different process that either permits to knockout a gene or to repair a mutated gene responsible for a hereditary disease. This technique is used in our laboratory to develop therapies for 3 different diseases: duchenne muscular dystrophy (DMD), Friedreich ataxia (FRDA) and Alzheimer disease (AD). DMD is due to the deletion of one or several exons in the DMD gene that leads to a frame shift, a premature stop codon and the absence of the dystrophin protein. By inducing DSBs in the exons that precede and follow the patient deletion, we have been able to delete an additional segment of the gene leading to the formation of a hybrid exon that not only restores the normal reading frame but also restores the normal structure of the internally truncated dystrophin protein. This should thus permit to transform a DMD patient in a mild Becker muscular dystrophy patient. FRDA is due to an increased number of the trinucleotide GAA in intron 1 of the frataxin gene. This leads to a reduced transcription and a reduced production of the frataxin protein. We have used the CRISPR/Cas9 technology to induce DSB before and after the repeat to remove it. This treatment has led to a doubling of the frataxin mRNA and protein and this should be therapeutic in the patients. Hereditary AD is to point mutations in the amyloid precursor protein (APP) gene. Using the CRISPR/Cas9 system, have induced a DSB in that gene and replaced the mutated nucleotides. This could also lead to a potential therapy.

Biography

Jacques P Tremblay has received PhD in Neuroscience from the University of California at San Diego in 1974. Since that time, he has been at Laval University as a Post-doctoral Researcher, Professor and Director of the Department of Anatomy. He is currently a Full Professor in the Department of Molecular Medicine. He has published over 250 scientific articles on hereditary diseases. He has worked specifically on myoblast transplantation as a treatment for Duchenne muscular dystrophy. For the last 3 years, he also worked on gene correction with the CRISPR/Cas9 technology for Duchenne muscular dystrophy, Friedreich's ataxia and Alzheimer's disease.

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