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# DEVELOPMENT OF THERAPIES FOR HEREDITARY DISEASES BY MODIFYING GENES WITH THE CRISPR/CAS9 TECHNOLOGY

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**The CRISPR/Cas9 technology permits to induce double strand breaks (DSBs) at a precise site in the genome by targeting a 18 to 20 nucleotides sequence followed by a Protospacer Adjacent Sequence (PAM). Our research group is using this technology to develop treatments for several hereditary diseases. We have modified a mutated dystrophin gene responsible for Duchenne Muscular Dystrophy (DMD) by cutting in an exon that precedes and in an exon follows the patient deletion. This permitted to form an hybrid exon that not only restored the correct reading frame but which also coded for a dystrophin protein with a correct spectrin-like repeat. A Cas9 protein fused with VP64 and 2 sgRNA targeting the promoter of alpha-1 chain of laminin were also use to induce the expression of that gene. This protein formed a complex with beta-1 and gamma-1 laminin chains and made links with the alpha-7 beta-1 integrin to reduce the severity of DMD. The CRISPR technology was also use to remove the long GAA repeat in intron 1 of the frataxin gene responsible for Friedreich ataxia. This was done by inducing DSBs before and after the repeats. This increased the expression of the frataxin protein. Finally, we have also modified the Amyloïd Precursor Protein (APP) gene to insert in exon 16 the threonine codon in position 673, a mutation that reduces the cutting of the APP protein by the beta-secretase and thus reduces the formation of amyloid peptides responsible for Alzheimer disease.**

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