Developing an AAV-Based CRISPR Strategy for SOD mRNA knockdown for ALS Treatment

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative, and ultimately fatal disease whose rate of progression can be influenced by several different genetic factors. One genetic cause of ALS has been found to be a mutation of the SOD1 gene. Gene therapy using an adeno-associated virus (AAV) vector, a type of non-enveloped virus, is a new therapy for several genetic diseases. However, no gene therapy has been developed for ALS. The purpose of this study will be to possibly develop an AAV vector that targets SOD mRNA in order to alleviate or stop the progression of ALS symptoms. 4-8 week old SOD1 transgenic mice will be injected with AAV-vector containing CRISPR-SOD guide RNA to induce SOD mRNA degradation. After injection, the mice will then be examined every week for changes in body weight, motor activity, and survival time. Based on previous studies, it can be expected that injection of the AAV-CRISPR-SOD vector will reduce the levels of SOD mRNA and increase survival of the motor neurons and the SOD mice. : Developing an AAV that targets SOD mRNA provides a new potential gene therapy option for ALS. By down regulating the SOD gene using CRISPR-CasRx, motor neuron survival can be maintained, thus at least partially maintaining motor functions, and potentially extending survival time. Supported by R25ES020721 and ORED.