AAV Modification for Improved Gene Therapy of Eye and Brain Tissue

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Technology description

Mutation for Decreased Heparin Binding Provides Significantly Improved Eye and Brain Transduction for Gene Therapies

This adeno-associated virus (AAV) vector contains mutations in AAV2 capsid amino acids that are defective for heparin binding and have been found to increase transduction efficiency and biodistribution of gene therapy in the eyes and brain. Gene therapy has become increasingly popular among researchers in the medical field for treatment of diseases and disorders in the eyes and brain such as retinitis pigmentosa, diabetic retinopathy, glaucoma, spinal cord injury, and motor neuron diseases. However, there are few AAV vectors that provide widespread distribution to the brain and the retina, because many of these vectors interact with heparin and are unable to achieve wide distribution. Researchers at the University of Florida have developed a modification to AAV that enables widespread distribution of transgenes in brain and retina tissue by decreasing the ability of AAV to bind to heparin in these tissues. The modified AAV vectors are competitive with or superior to existing serotypes or mutants available with regards to efficacy and safety. The heparin mutants also could be combined with mutations in lysine, serine, threonine and tyrosine, allowing incorporation of multiple modifications to AAV in order to achieve desired levels of viral transduction and immune system neutralization during gene therapy treatments.

Technology

The AAV vector has been modified to improve eye and brain transduction by weakening AAV cell surface receptor binding. AAV utilizes heparin sulfate proteoglycan (HSPG) as its primary receptor. The affinity of AAV to bind with HSPG decreases transduction efficiency and biodistribution of the gene therapy, particularly in the treatment of eye and brain tissue. University of Florida researchers introduced mutations in AAV2 capsid amino acids that are defective for heparin binding. The mutations developed improved the ability of the AAV to introduce genes into eye and brain cells, which in turn increases the ability of gene therapy to combat diseases and disorders in the eyes and brain.

Application area

Gene therapy AAV vector for widespread distribution of transgenes in brain and retina tissue

Advantages

Provides superior transduction of genes to brain and retina tissue, allowing gene therapy to more effectively combat diseases and disorders of the brain and eye
Heparin mutants could be combined with other mutations, allowing gene therapy to be customized to achieve desired levels of viral transduction and immune system neutralization

Institution

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