TPF

Proof of Concept Program / EN

A novel, highly cell-specific AAV vector for gene delivery to the Central Nervous System

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What is the problem?

Diseases of the Central Nervous System (CNS) are the major cause of disability worldwide, and a major economic burden. Gene therapies designed to treat these diseases are a promising solution, and many are in clinical trials. However, almost all gene therapy products in clinical trials require invasive and risky procedures to deliver gene therapy. Therefore, there is an urgent need for easily deliverable, highly specific gene therapy vectors that can deliver genetic cargo to neurons in the CNS.

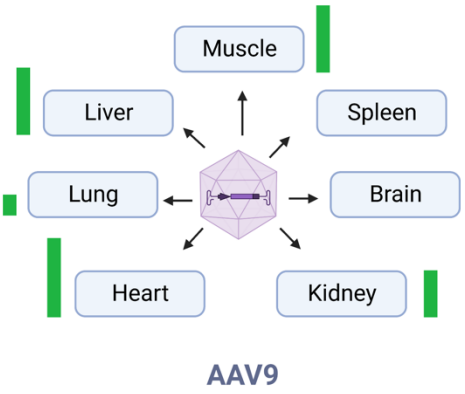

Figure 1. Typical AAV9 vectors used for delivery of genetic cargo to neurons suffer from off-target effects, like a high immune response and requiring high doses.

What is your solution?

The solution is to develop a novel adeno-associated virus (AAV) viral vector to deliver gene therapy cargo exclusively to neurons in the Central Nervous System (CNS).

The project aims to develop modified AAV9 vectors, a type of AAV that has some ability to cross the blood-brain barrier to deliver gene therapy to the CNS. However, AAV9 is unable to specifically target neurons, and also induces off-target expression of genes in the heart, liver, and other organs (Fig 1). By modifying the AAV9 capsid, the outer shell of the virus, with small peptides that specifically bind to receptors that are only expressed in neurons in the CNS, the project aims to dramatically improve specific delivery of gene therapy cargo (Fig 2). This will reduce off-target effects such as liver toxicity, that are common with currently available AAV vectors. This will also allow the viral vector to be administered via systemic injection, removing the need for invasive and risky injection techniques.

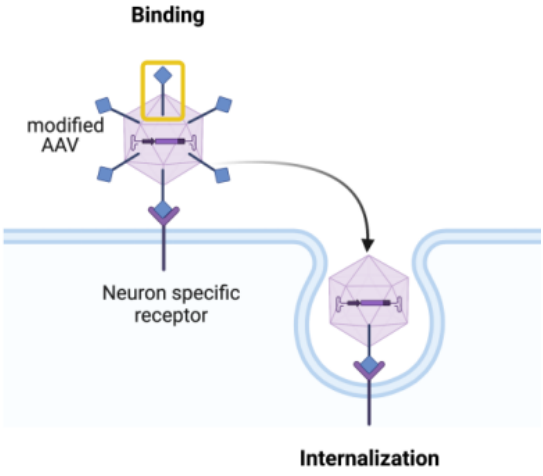

Figure 2. Our strategy is to target AAV particles to receptors specifically expressed on Central Nervous System neurons, and deliver their genetic cargo.

Keywords: Gene therapy, Gene delivery, cell-specific targeting, viral vectors

Contribution to SDGs

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