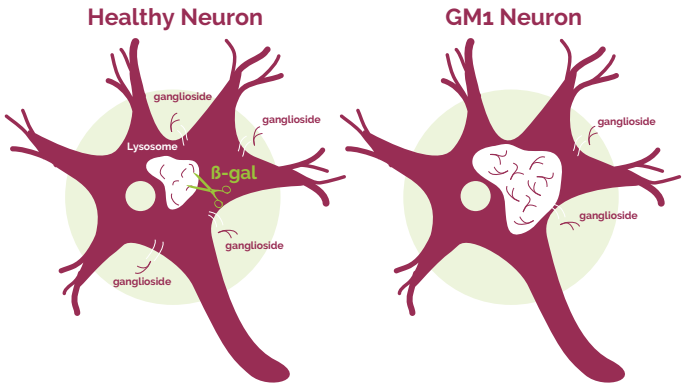
What is Gene Therapy for GM1 Gangliosidosis?

GM1 gangliosidosis (GM1) is a **rare genetic** disease

Genetic mutations lower the level of ß-galactosidase (ß-gal) activity in the body - an enzyme needed to break down GM1 ganglioside and keratan sulfate. Low levels of ß-gal cause waste products to accumulate. Neurons are particularly affected.

affects 1 in 100,000



RESIDUAL ß-gal ACTIVITY CORRELATES WITH DISEASE SEVERITY

Type 1 GM1 Gangliosidosis — **Type 2 GM1 Gangliosidosis** — **Type 3 GM1 Gangliosidosis** — **MPS IVB**

Neurologic Symptoms & Seizures → **Bone & Joint Problems**

CURRENTLY THERE IS NO TREATMENT

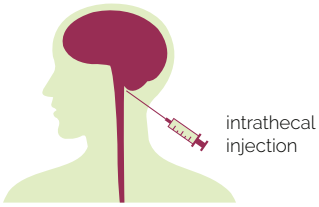
HOW CAN GENE THERAPY HELP?

Gene therapy represents a promising new experimental therapy with the potential to improve cognitive deficits after a one-time treatment. While several approaches to GM1 gene therapy are being developed, intrathecal gene therapy strives to deliver a functional copy of the ß-gal gene to the brain via the cerebrospinal fluid.

1. a normal healthy copy of the ß-gal gene is produced

2. gene is inserted into a harmless Adeno-Associated Virus (AAV) to create a viral vector

3. AAV vector is injected into the cerebrospinal fluid (CSF) that flows around the brain and spinal cord



4. some cells take up AAV vector and begin to make functional ß-gal, which is released into the CSF

5. secreted ß-gal can be used by other cells throughout the brain and spinal cord which may improve cognitive function

Safety First

Safety is being evaluated in animal models

What's next?

early clinical trials for GM1 evaluating safety in human subjects are on the horizon

the orphan disease center

Penn Medicine