Understanding Gene Therapy for Canavan Disease

Targeting the Cells Responsible for Making White Matter

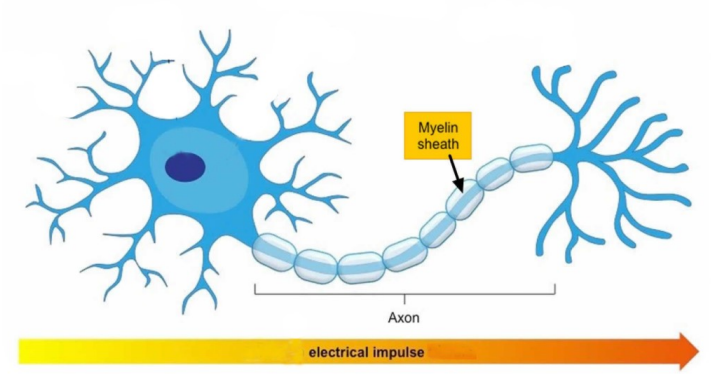
What is Canavan disease?

Canavan is a rare neurological genetic disease that prevents the normal growth of white matter (myelin) in the brain and affects children at birth.

What causes Canavan disease?

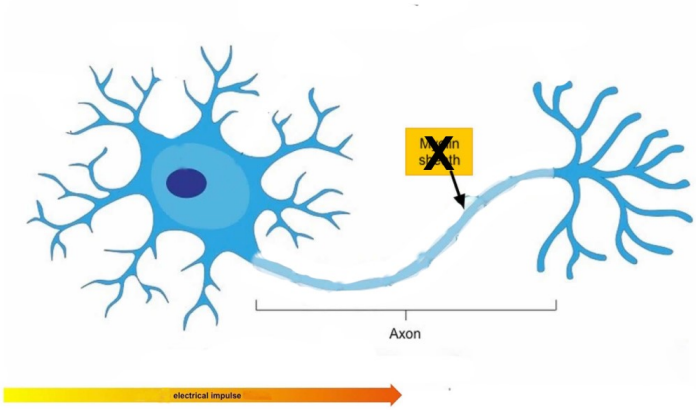
The disease is caused by a defect in the ASPA gene and is autosomal recessive, meaning both parents carry one mutation. When both parents are carriers, there is a 1 in 4 or 25% chance that their child will be affected.

Why is the ASPA gene important?



The ASPA gene provides instructions for making an enzyme called Aspartoacylase (ASPA).

In the brain this enzyme breaks down N-Acetylaspartate (NAA).

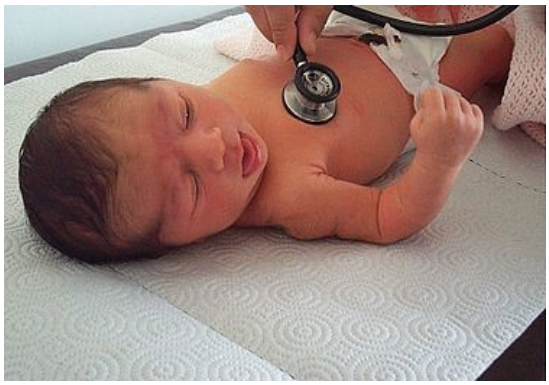


When not broken down, NAA accumulates in the brain and prevents the normal growth of myelin.

Without myelin and the insulated covering it provides, neurons are unable to fire off messages from the brain.

What are some of the symptoms related to Canavan disease?

Patients are affected at birth, but may appear normal until three months of age when symptoms begin to develop, some of which include:



- Poor head control
- Large head size
- Eye tracking difficulty
- Excessive irritability
- Diminished muscle tone
- Delays in motor and developmental milestones

What is Myrtelle's gene therapy for Canavan disease and how is it designed to work?

Myrtelle is developing a vector, called rAAV-Olig001-ASPA, to deliver a therapeutic ASPA gene directly to the oligodendrocyte cells that are responsible for producing myelin to restore the ability of oligodendrocytes to make the ASPA enzyme on their own.

1. The ASPA gene is delivered directly into the fluid that surrounds the brain and spinal cord (cerebrospinal fluid), allowing the gene therapy to reach many cells.
2. To help the gene reach the targeted oligodendrocytes it is packaged using a unique adeno-associated virus (AAV) vector. This virus is inactive and cannot cause disease.
3. Once the ASPA gene is inside the cells, researchers believe it may help the cells make and release Aspartoacylase (ASPA), the enzyme needed to breakdown N-Acetylaspartate (NAA).
4. Gene therapy is **not** meant to change your child's genetic makeup.

How is gene therapy given?

The gene therapy is given as a single dose, one time injection into the affected regions of the brain. The neurosurgical procedure directly targets the oligodendrocytes of the brain where the ASPA gene therapy needs to be delivered. Injecting into this area helps direct the therapy to regions most intimately involved with disease initiation and progression.

For more information on the Myrtelle gene therapy clinical study for Canavan disease:

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