LYSOGENE

Understanding Gene Therapy for GM1 Gangliosidosis

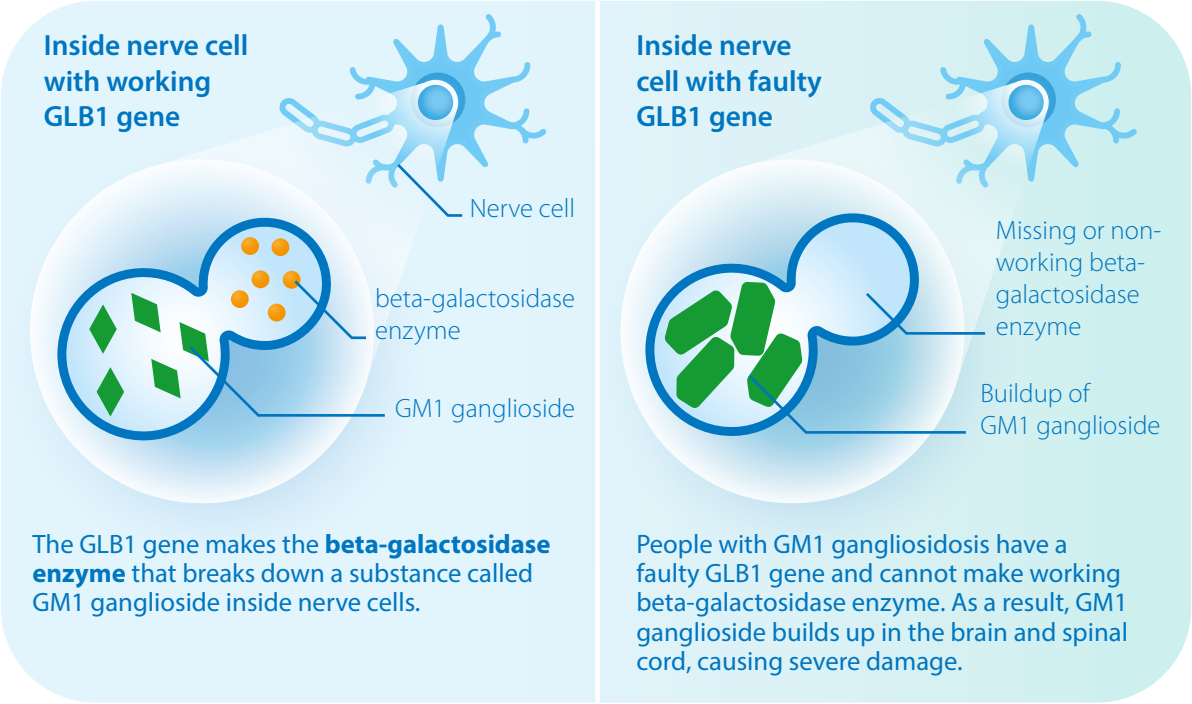
Targeting the genetic cause of disease

What is GM1 gangliosidosis?

GM1 gangliosidosis is a rare genetic condition that results in severe and life-threatening damage to the brain and spinal cord.

What causes GM1 gangliosidosis?

GM1 gangliosidosis is caused by a defect, or mutation, in the GLB1 gene.



The GLB1 gene makes the **beta-galactosidase enzyme** that breaks down a substance called GM1 ganglioside inside nerve cells.

People with GM1 gangliosidosis have a faulty GLB1 gene and cannot make working beta-galactosidase enzyme. As a result, GM1 ganglioside builds up in the brain and spinal cord, causing severe damage.

There are different types of GM1 gangliosidosis based on age when symptoms first appear and severity of disease progression.

Early infantile (Type 1): most severe; symptoms usually first appear before 12 months of age.

Late infantile (Type 2a): symptoms usually first appear between 1 and 2 years of age

Juvenile (Type 2b): symptoms usually first appear between 2 and 3 years of age.

Adult (Type 3): symptoms usually first appear in the teenage years.

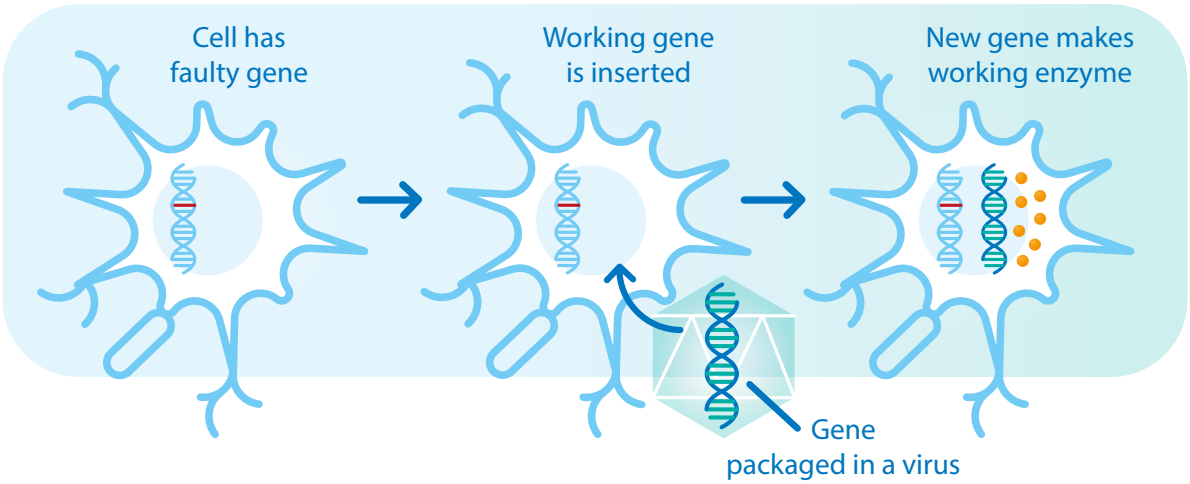
gangliosidosis = *"gang-lee-oh-sigh-DOH-sis"* / ***galactosidase*** = *"guh-lak-TOE-si-days"*

What is the goal of gene therapy?

The goal of gene therapy is to deliver a working gene into the cells of the body to enable them to make the enzyme they are missing. Gene therapy may be able to slow or stop disease progression but cannot reverse damage already caused by the disease.

Gene therapy for GM1 gangliosidosis

There are currently no disease-modifying treatments for GM1 gangliosidosis. The Lysogene clinical study is testing an investigational gene therapy that aims to insert a working GLB1 gene into the cells of the brain and spinal cord.



How it is thought to work:

1. The working GLB1 gene is delivered directly into the fluid that surrounds the brain and spinal cord (cerebrospinal fluid). This allows the gene therapy to reach many cells in the brain and spinal cord.
   - To help the gene get into the cells easily, it is packaged inside a specific type of virus. This virus is inactive and cannot cause diseases.
2. Once the GLB1 gene is inside the cells, researchers believe it may help the cells make and release beta-galactosidase enzyme, which is needed to break down GM1 ganglioside.
3. Only one treatment may be needed.
4. Gene therapy is **not** meant to change your child's genetic makeup.

How is the therapy given?

The gene therapy is given as a single, one-time injection into a fluid-filled space in the back of the head called the cisterna magna. During the procedure, your child will be asleep and the surgical team will use imaging of your child's brain to guide the needle. The actual injection takes 5 to 15 minutes.

Injecting into this area helps to get as much therapy as possible to the brain and spinal cord.

For more information on the Lysogene gene therapy clinical study for GM1 gangliosidosis:

Contact	Visit	Visit
patientadvocacy@lysogene.com	**www.lysogene.com**	**clinicaltrials.gov** (NCT04273269)