Gene Therapy Approaches for Treatment of Fabry Disease

About Fabry Disease

Fabry disease is a rare, genetic condition which is estimated to affect around 1 in 100,000 people.

In Fabry, an enzyme called α-galactosidase A (α-Gal A) is missing or there is a reduced amount. This means that the body cannot break down a certain type of fat called globotriaosylceramide (Gb3). Gb3 continues to build-up in body cells causing damage to tissues and organs. Gradually, this leads to a range of physical symptoms and complications, which vary from one person to another.[1]

There is no cure for Fabry disease. Current treatments can provide an enzyme to break down Gb3 on an ongoing basis. These include Enzyme Replacement Therapy (ERT) which requires frequent burdensome infusions and, for eligible patients, chaperone therapy, a daily oral pill. New treatments are being studied that may prevent organ damage or slow the progression of disease, resulting in improved quality of life for patients.

What is Gene Therapy?

Gene therapy is a way of altering the genetic instructions inside the body's cells to treat or stop disease.

To get the correct copy into the cells, a new healthy gene is created in a laboratory, and placed in a modified (harmless) version of a virus called a "vector," to carry the altered genes into targeted cells.

The new working gene instructs cells to start producing a missing protein or enzyme, and slow or stop the progression of disease.

***In vivo* and *ex vivo* approaches can be used to deliver the working gene into the cells with new instructions. *In vivo* means that the treatment is delivered directly into the body. *Ex vivo* means the person's own cells are modified outside the body, and then returned.[2]**

Gene Therapy Approaches for Fabry Disease

Multiple gene therapy approaches are being studied as a one-time treatment that may provide stable, continuous production of α-Gal A to slow or stop the progression of Fabry disease.

These include:

- Liver-Targeted Adeno-Associated Virus (AAV) Gene Therapy
- Cardiomyocyte-Targeted Adeno-Associated Virus (AAV) Gene Therapy
- Hematopoietic Stem Cell Therapy

Liver-Targeted Adeno-Associated Virus (AAV) Gene Therapy

- *In vivo*
- Using a vector called an AAV, a healthy copy of the gene responsible for the production of the α-Gal A enzyme is delivered into the body
- The AAV is administered through an intravenous infusion and targets cells in the liver

- Once inside the liver, the new working gene is expected to instruct liver cells to make the α-Gal A enzyme
- Liver cells are then expected to secrete the α-Gal A enzyme via the bloodstream for delivery to other organs
- No conditioning is administered
- The patient is monitored for a minimum of 5 years

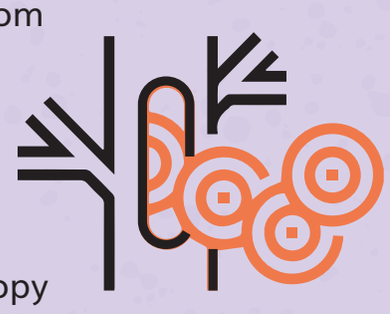
Cardiomyocyte-Targeted Adeno-Associated Virus (AAV) Gene Therapy

- *In vivo*
- Using a vector called an AAV, a healthy copy of the gene responsible for the production of the α-Gal A enzyme is delivered into the body
- The AAV is administered through an intravenous infusion and targets cells in the heart

- Once inside the heart, the new working gene is expected to instruct heart cells to make the α-Gal A enzyme
- Heart cells are then expected to secrete the α-Gal A enzyme via the bloodstream for delivery to other organs
- No conditioning is administered
- The patient is monitored for a minimum of 5 years

Hematopoietic Stem Cell Therapy

- *Ex vivo*
- Hematopoietic stem cells are collected from the patient
- In a laboratory, the patient's stem cells are modified with a lentivirus, a vector carrying a healthy copy of the gene responsible for the production of the α-Gal A enzyme
- Modified stem cells are administered back to the patient



- Once inside the body, modified stem cells are expected to produce the α-Gal A enzyme
- The α-Gal A enzyme is delivered via the bloodstream to other organs
- Before the cells are injected, a chemotherapy agent is required to avoid rejection
- The patient is monitored for 15 years

New approaches to the treatment of Fabry disease are ongoing. Visit this resource to learn more about clinical trials or support for people living with Fabry disease:

Fabry International Network | fabrynetwork.org

References

1. **Fabry International Network. What is Fabry? Retrieved from** https://www.fabrynetwork.org/what-is-fabry/
2. **American Society of Gene & Cell Therapy. Fabry Disease and Gene Therapy. Retrieved from** https://asgct.org/global/documents/patient-ed-infographics/sept-launch-websit e-material/fabry-disease-and-gene-therapy.aspx