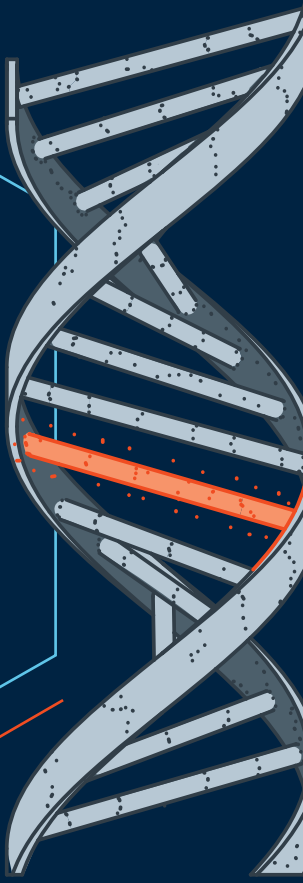
AN OVERVIEW OF GENE THERAPY

A resource for patients about gene therapy using blood stem cells



Blood stem cells play an important role in the body. Stem cells are located in the bone marrow, where they develop into the different types of blood cells, including red blood cells, white blood cells, and platelets.

This guide can help you learn about gene therapy. The goal of gene therapy is to treat disease at the genetic level by adding new genes (gene addition) or editing existing genes.

In this guide, we'll be taking a look at how gene addition can be used to modify blood stem cells to treat certain genetic diseases.

genehome
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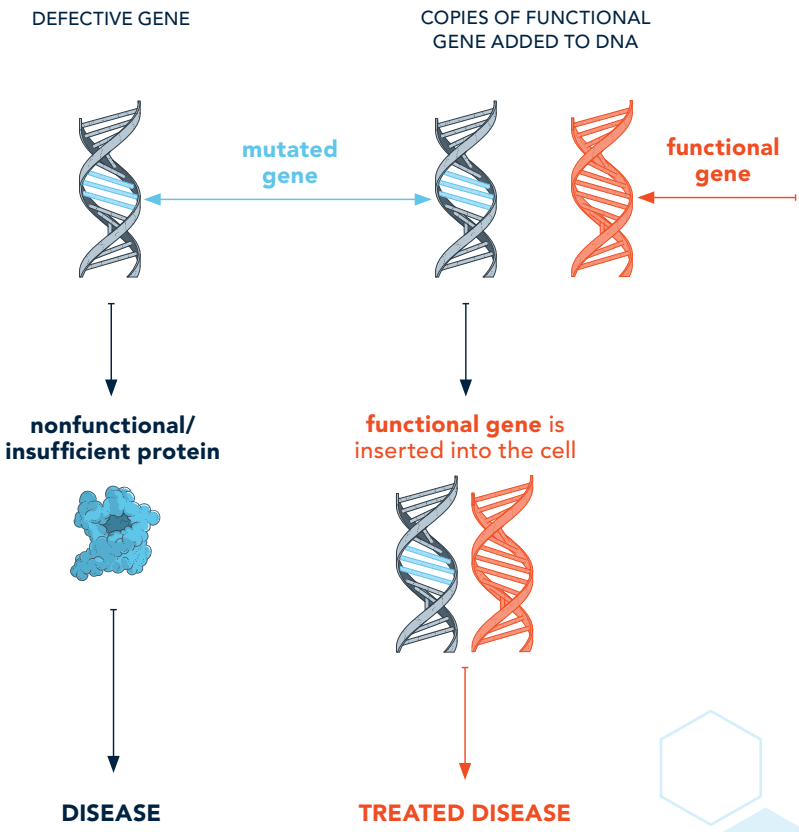
WHAT IS **GENE THERAPY**?

Gene therapy is a type of treatment that uses genetic material with the goal of changing the course of a disease. It is a therapeutic approach that is being investigated for the treatment of multiple diseases.

Here we focus on an approach called gene addition. In this approach, copies of functional genes are added to a cell to help do the work of a defective gene. The addition of functional genes can take place either inside (*in vivo*) or outside of the body (*ex vivo*).

This brochure provides an introduction to *ex vivo* gene addition using blood stem cells.



WHAT IS THE GOAL OF **GENE THERAPY**?

The goal of gene therapy is to treat disease at the genetic level (the source). Gene therapy is a promising treatment option that is being studied for a number of diseases, including inherited diseases and cancers.

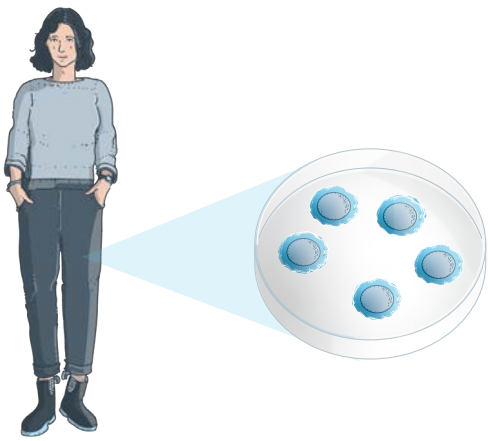
WHAT HAPPENS DURING BLOOD STEM CELL **GENE THERAPY**?

There are **4 KEY STEPS** in gene therapy

The following are the general steps involved in *ex vivo* gene addition therapy using blood stem cells. Experiences may be different based on the individual and the gene therapy used.

1 BLOOD STEM CELLS ARE COLLECTED FROM THE PATIENT

- The patient will first receive medicine to get their blood stem cells to release from their bone marrow into their circulating blood for collection (**mobilization**)
- Blood stem cells are collected from a vein in the patient's arm using a special machine (**apheresis**)
- After the collection process is complete, the patient is discharged from the hospital
- There are risks associated with cell collection and the medicines received during this process; the patient should discuss these and all risks with their doctor



PATIENT BLOOD STEM CELLS

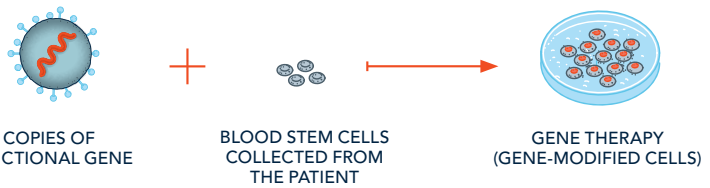
A KEY TAKEAWAY:
The patient's own blood stem cells play a major part in creating the gene therapy

Hospital that provides gene therapy

Lab that manufactures gene therapy

2 CREATION OF GENE THERAPY

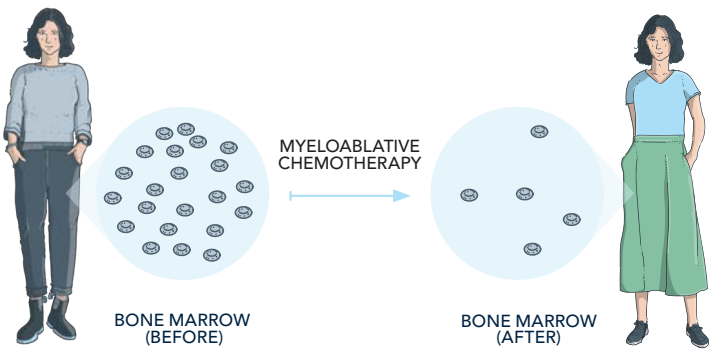
- After the patient's blood stem cells are collected, they are sent to a lab where copies of a functional gene are added
- The cells that have functional copies of the gene are referred to as **gene-modified cells**; these cells are the **gene therapy**



A KEY TAKEAWAY:
Each dose is made specifically for each individual patient

3 PATIENT PREPARATION FOR GENE THERAPY INFUSION

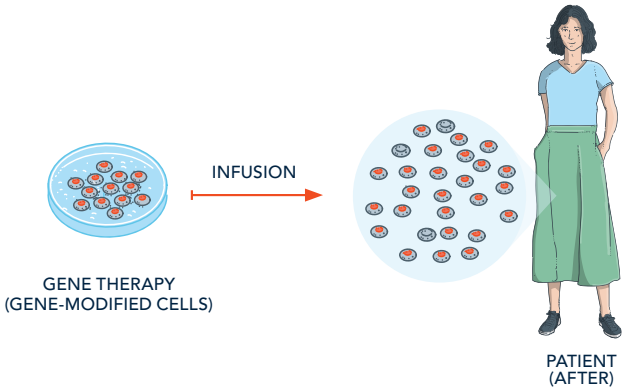
- The patient's body is prepared to receive gene therapy; chemotherapy is used to clear out faulty stem cells in the bone marrow
- This type of chemotherapy may also be referred to as **myeloablative conditioning** (or **myeloablation**)



A KEY TAKEAWAY:
Myeloablative chemotherapy affects the immune system and may cause some serious side effects. The patient should share any questions they have and discuss all risks with their doctor.

4 GENE THERAPY INFUSION AND ENGRAFTMENT

- After chemotherapy is complete and the patient is ready, the gene therapy is usually delivered by intravenous (IV, or into a vein) infusion
- After the gene therapy has been infused, the gene-modified cells will need time to multiply and produce new cells so that the patient's body has enough cells with the functional gene (**engraftment**)
- The patient remains in the hospital until
  - — Their key immune cells have returned to adequate levels
  - — Their doctor determines that it is okay for them to be discharged
- Until the patient's cells have recovered, they will have increased risk for bleeding and serious infections; the patient should discuss these and all risks with their doctor
- The goal is for the patient to have functional copies of the modified gene



A KEY TAKEAWAY:

After the patient is ready to be discharged from the hospital, they will require follow-up monitoring, which may extend over a period of years.

The extent and length of follow-up required for each patient will be determined by the patient's healthcare team. Follow-up monitoring may capture:

- Gene therapy safety
- How well the gene therapy is working

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GLOSSARY

Apheresis: in gene therapy, this is the process separating stem cells from blood cells using a machine

Blood stem cell: specific stem cells found in the bone marrow and circulating blood that can develop into blood cells, such as red blood cells, white blood cells, and platelets

Engraftment: the process of transplanted cells being accepted by the patient's body and producing enough new cells to reach an adequate level

Gene: instructions made of DNA used to create the proteins the body needs to function

Gene-modified cells: stem cells in which functional copies of a defective gene have been added to help correct the function of the cell

Gene therapy: a method of treating genetic diseases at the genetic level (the source) with the goal of changing the course of a disease

Mobilization: process where a medicine is used to get blood stem cells to move into the circulating bloodstream

Myeloablative conditioning: a process that clears out the patient's faulty bone marrow cells to make room for gene therapy

Protein: class of molecules composed of one or more chains of amino acids that perform different functions the body needs including structure, function, and regulation of tissues and organs

Stem cell: cells in the body which can form all the different cell types with specific functions, such as blood cells, brain cells, muscle cells, or bone cells

References: 1. Definition of hematopoietic stem cell – NCI dictionary of cancer terms. National Cancer Institute website. Accessed September 21, 2020. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/hematopoietic-stem-cell **2.** What is gene therapy? How does it work? FDA website. Accessed September 21, 2020. https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm589197.htm **3.** Use of genetically modified stem cells in experimental gene therapies. National Institutes of Health website. Accessed September 21, 2020. https://stemcells.nih.gov/info/Regenerative_medicine/2006Chapter4.htm **4.** Definition of stem cell mobilization – NCI dictionary of cancer terms. National Cancer Institute website. Accessed September 21, 2020. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/stem-cell-mobilization **5.** Harvesting blood stem cells for transplantation. PubMed Health website. Accessed September 21, 2020. https://www.ncbi.nlm.nih.gov/books/NBK279428/ **6.** Bone marrow transplant. Mayo Clinic website. Accessed September 21, 2020. https://www.mayoclinic.org/tests-procedures/bone-marrow-transplant/about/pac-20384854 **7.** Definition of myeloablation. Taber's Medical Dictionary Online. Accessed September 21, 2020. https://www.tabers.com/tabersonline/view/Tabers-Dictionary/753860/0/myeloablation?q=myeloablation **8.** Blood and bone marrow transplant. National Heart, Lung, and Blood Institute website. Accessed September 21, 2020. https://www.nhlbi.nih.gov/health-topics/blood-and-bone-marrow-transplant

This brochure was developed by bluebird bio with input provided by patients and families living with genetic diseases.

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