

# Gene Transfer Therapy

## Questions and Answers About Gene Transfer Therapy for Sickle Cell Disease

### Introduction

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Doctors at Cincinnati Children's Hospital Medical Center are exploring improved ways to treat genetic diseases, including sickle cell disease. One method currently being studied is called "gene transfer." The hope is that we will be able to begin human clinical trials using gene transfer sometime in the next one to two years. The following is information about sickle cell disease and about how gene transfer works. Since this is a relatively new modality, we hope that this information will help you learn more about what gene transfer is, and also help us in finding out what questions or concerns you might have.

### Sickle Cell Disease Basics

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#### What is sickle cell disease?

It is a hereditary blood disease caused by Hemoglobin S or sickle hemoglobin (Hb S). Hb S causes red blood cells to become sickle-shaped, resulting in blocked blood vessels and many other medical problems.

#### What is hemoglobin?

Hemoglobin gives blood its red color. Hemoglobin is very important, because it carries oxygen from your lungs throughout your body.

#### What is hemoglobin S?

Healthy red blood cells contain adult hemoglobin (Hb A). A person with sickle cell disease makes red blood cells that contain *sickle* hemoglobin (Hb S).

#### Is hemoglobin S dangerous?

Yes, because Hb S containing red blood cells change their shape to a sickle (hook) shape and actually can block blood vessels. Blocked blood vessels cannot deliver enough oxygen to the body. This damages tissue and organs, and causes pain.

#### What is hemoglobin F?

Hemoglobin F is fetal hemoglobin (Hb F). It is the type that an unborn baby has. After birth, the baby's Hb F levels start dropping. Hb F normally disappears by six to nine months, and Hb A or Hb S replaces the Hb F. The baby without sickle cell disease makes healthy Hb A, but the baby with sickle cell disease makes unhealthy Hb S.

#### Why is hemoglobin F important?

Hb F can fight the effects of Hb S and prevent sickling of red blood cells. When Hb F levels are higher, the number of sickle cell problems can be lower. A drug called Hydroxyurea works to treat sickle cell disease by increasing Hb F levels and decreasing sickling episodes.

### Gene Transfer Therapy Basics

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#### What are genes?

Genes are bits of information found inside the cells of your body that you inherit from your parents. Genes tell your body how to work and make you... you.

#### Is hemoglobin an actual gene?

Everyone has two hemoglobin genes (one inherited from each parent) that provide genetic information to make the hemoglobin protein. A person who has one hemoglobin S gene and one hemoglobin A has sickle cell trait. A person with two hemoglobin S genes has sickle cell disease.

## What is gene transfer therapy? How would it work for sickle cell disease?

Gene transfer therapy is the process of adding a healthy gene to help fight the effects of an unhealthy gene. For sickle cell disease, one would want to transfer an anti-sickling gene, like Hb F permanently into blood cells. As these blood cells divide and grow into red blood cells, the red blood cells would no longer sickle.

## Is gene transfer therapy being conducted on patients with sickle cell disease?

No, it is not currently being conducted in the United States. We can fix sickle cells in mice that have sickle cell disease, and human sickle cells in the test tube. However, we do not know whether gene transfer will work in people with sickle cell disease until we do a research study to ensure that gene transfer is safe and efficient. We can promise that if and when we do this study, we will be committed to keeping you as safe as possible while learning more about whether gene transfer therapy can treat your sickle cell disease.

## What would a gene transfer therapy in sickle cell disease involve?

To treat your sickle cell disease with gene transfer therapy, we would need to add a healthy hemoglobin gene (Hb F) or a corrective gene to stop the Hb S from sickling your red blood cells.

- First, we would collect a small amount of your bone marrow. Bone marrow is found inside of your bones, and is the source of your red blood cells, white cells and platelets.
- Second, we would add the corrective gene to your bone marrow stem cells in the laboratory. To get the corrective gene into the cell, we use shells of viruses as a vehicle to deliver the gene. These viruses are emptied of all their disease causing components. They cannot cause illness, but are very good at getting the material we want – in this case a new gene- into the cell.
- Third, we transfuse the cells with the corrected gene into your body via a vein in hope that you can make healthy red blood cells for the remainder of your life.

## What else should I know about gene transfer therapy for sickle cell disease?

The hope of gene transfer therapy is to fix your body through this process so that you can make healthy red blood cells. What we know so far is that we have been successful with gene transfer in mice with sickle cell disease, but it has not been tried in people. So there are two major questions investigators studying gene transfer therapy must answer:

- 1) Is gene transfer in people safe?
- 2) Does it work?

These are the questions that a clinical research trial will try to answer before gene transfer therapy can be a cure for sickle cell disease.

## How is gene transfer therapy different from a bone marrow transplant?

Bone marrow transplant involves transfer of bone marrow stem cells from a matched normal donor into a patient with sickle cell disease. If done from a matched sibling, it can be curative. Matched siblings are available to 10-15 percent of patients. Unrelated donor transplant is currently being studied as a research study, to determine if it is safe and efficient at correcting sickle cell disease. Bone marrow from another individual results in immunological side effects (rejection of the bone marrow by the patient's cells, or the new bone marrow reacting to the patient's cells). Gene transfer therapy involves using the patient's own bone marrow. So a matched donor is not necessary. Second, it causes no immune side effects, since one is getting one's own cells back.

## For More Information

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### To learn more about the gene transfer therapy study, contact:

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