A Closer Look at Gene Therapy

Our genes make us unique. Inherited from our parents, genes help determine physical features and traits like height, eye and hair color. Genes are made up of DNA, which are genetic instructions to build enzymes and proteins. Enzymes and proteins make muscles, bones, and blood, among many other things in the body, which support most of the body's functions, such as digestion and transporting oxygen through the blood.

Genes that are missing from birth, or don't work properly, can cause disease because the proteins built from the genes are missing or defective. Scientists have been working for decades on ways to modify genes or replace faulty genes with healthy ones to treat, cure or prevent a disease or medical condition.

What is Gene Therapy?

Gene therapy is a way of altering the genetic instructions inside the body's cells to treat or stop disease. Gene therapy goes further than just treating some of the symptoms of a disorder.

By introducing a healthy gene into a person who has a disease caused by a defective gene, this treatment addresses the underlying cause of the disorder, helping the body better fight disease by tackling it at the source.

Once researchers first understand which gene is causing the disorder, they can insert a healthy version of the gene into cells to help the body fight or treat disease.

In the type of gene therapy that is currently being studied, only somatic cells are targeted for treatment. Somatic cells are all cells in the body excluding reproductive cells. Therefore, any changes to the genes through gene therapy will only impact the cells of the individual's body who has received the treatment. Consequently, it is still possible for the defective gene to be passed along to future children.

Gene Delivery

One of the biggest challenges to gene therapy is successfully getting the new gene into the cells. To accomplish this, scientists create a new healthy gene in a laboratory, then use a delivery vehicle called a vector to carry the new gene into the cells.

Viruses are commonly used as vectors. Viruses are made harmless by removing all disease-causing genetic information, creating a shell to insert the healthy gene.

Viruses aren't the only vectors that can be used to carry altered genes into the body's cells. Other vectors being studied in clinical trials include liposomes or fatty particles that can carry the new genes into the target cells.

Genes delivered into the bloodstream by a vector do not know where to go automatically, so different techniques are used by medical researchers to direct the healthy genes to the right cells. Gene delivery is an important area of study and researchers continue to look for new ways to reach cells containing defective genes that could be successfully treated with gene therapy.

Gene therapy is a complex science and researchers must first understand the link between the defective gene and the disorder, then customize a vector. For gene therapy to be effective the vector carrying the new gene must do several things successfully.

TARGET. A gene must be correctly delivered into the targeted cells with an appropriate vector.

LOCALIZE. Once delivered into the targeted cells, the new gene must find its intended new "home" in the cell nucleus, adjacent to but separate from the cell's existing DNA.

ACTIVATE. Once in the cell's nucleus, the new or fixed gene must "turn on" to instruct the protein to function properly – by producing a normal protein or knocking down production of a bad protein.

AVOID. Care must be taken to avoid harmful side effects like infection, activation in cells which are not the target in the disease, unintentional damage to other healthy genes or the possibility of the body's own immune system attacking the vector.

Candidates for Gene Therapy

Gene therapy has potential to provide treatments for many disorders that currently have limited or no available treatments. People with genetic disorders caused by mutations in single genes tend to be good candidates for gene therapy. Genetic testing can help individuals and families identify disease-causing gene variants. Other tests can determine if a person has pre-existing antibodies that would make gene therapy unsuccessful because of the body's immunity to certain types of vectors used in the treatment.

While there is much excitement around gene therapy to treat or stop disease, the clinical trials required to show the safety and effectiveness are complex. Other drug treatments typically leave the body fairly quickly, but gene therapies are specifically designed to stay in the body for a long time. This means full testing and monitoring after administration of gene therapy may take more time than for standard therapies, such as pills.

Because of this commitment, it is important to remember that in most clinical trials, a patient can still access the current standard of care, if needed. For example, successful gene therapy would enable the liver to produce functional blood clotting factor VIII in a patient with hemophilia A. However, if the therapy didn't work or didn't work right away, the patient could still receive factor VIII during clinical trial participation.

Gene therapy offers the unique potential to provide a cure for a disease instead of simply treating the symptoms. The future of gene therapy research has given hope to people with genetic diseases that currently have no other cures. Visit these websites to learn more learn more about gene therapy.

American Society of Gene & Cell Therapy | asgct.org
ARM Foundation for Cell & Gene Medicine | thearmfoundation.org

Clinical Trials for Gene Therapy

There are hundreds of clinical trials for gene therapy in progress. The National Institutes of Health website ClinicalTrials.gov can help identify active and recruiting clinical trials around the world including:

- **Genetic disorders like MPS I, hemophilia and hereditary blindness**
- **Blood disorders including beta thalassemia**
- **Nervous system diseases like Parkinson's Disease, spinal and muscular atrophy**