

What is Gene Editing?

Sometimes, cell and gene medicine terms become confusing. Specialists need distinctive words in order to communicate accurately and effectively with each other, yet as a patient or caregiver who isn't a healthcare professional, these words can seem overly complex.

This brochure is part of our "Quick Overview" Series, designed to make sense of terms you may see or hear as you learn about cell and gene medicine options.

Gene Editing

Gene Editing is a laboratory technique that corrects defective genetic code. The goal of gene editing is to correct an error in DNA, the body's instruction code. Gene editing is very precise. In fact, corrections are made inside cells. Healthcare professionals who specialize in gene editing perform various gene editing functions based on a patient's healthcare needs.

What can they do to the genetic code?

They can:

1. Repair
2. Regulate
3. Pause
4. Disable
5. Reprogram

REFERENCES

¹<https://ghr.nlm.nih.gov/primer/genomicresearch/genomeediting>

² Osborn M, Webber B, Knipping F, et al. Evaluation of TCR Gene Editing Achieved by TALENs, CRISPR/Cas9, and megaTAL Nucleases. Mol. Therapy 2016 - DOI 10.1038/mt.2015.197

For more information:

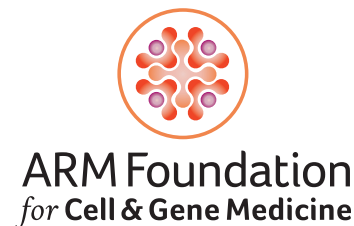
What is Gene Editing? by the Royal Society

<https://youtu.be/XPDb8tqgfjY>

Healing Genes Website

<http://healinggenes.org/cell-gene-medicine/learning-zone/beginner-zone/gene-editing/>

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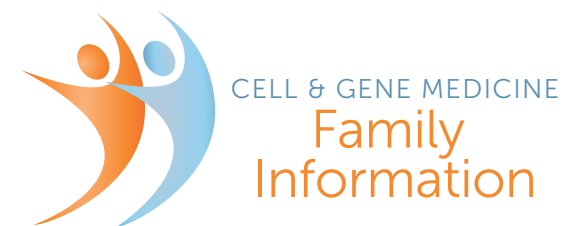


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A Quick Overview of Gene Editing



Gene Editing Allows Scientists to Remove, Disrupt, or Correct Defective DNA

The goal of gene editing is to change DNA inside selected cells to help treat disease. This can involve **repairing** a genetic defect, **inserting** a working copy of the gene into a strand of a patient's genetic code, or **disabling** a faulty gene linked to a patient's health problem.

Gene editing is also called genome editing. Gene editing directly edits or changes faulty DNA to correct or remove a defect.

Many gene editing treatments are in clinical trials.

Researchers believe gene editing may be especially useful in treating disorders linked to single genes, such as [cystic fibrosis](#), [hemophilia](#), and [sickle cell disease](#).¹

Gene editing also holds promise for the treatment and prevention of [complex diseases](#), including cancer, heart disease, Hepatitis B, some mental health illnesses, and even human immunodeficiency virus (HIV) infection.

To succeed in such precise work, scientists use “molecular scissors” to cut a segment of DNA at a very specific point.

After cutting the DNA, the cell naturally begins to repair the cut. That gives scientists a number of gene editing options because they can aid the body's natural DNA healing process. For example, a scientist can introduce a healthy gene or even insert a section of repaired genetic code, which the cell then readily accepts and

incorporates into its natural repair process. The scientist also can make sure a gene is silenced or “knocked out.”

Commonly Used Terms

Non-homologous end joining (NHEJ)

In this process, random pieces of DNA are inserted into or deleted from the temporary gap that's left after a precision cut. When the cell begins to heal itself, the body recognizes that the genetic code doesn't make any sense, and, as a result, no longer makes the protein associated with that gene.

Homology-directed repair (HDR)

In this process, scientists insert a segment of corrected DNA. This can replace the genes that don't function correctly.

What “molecular scissors” do scientists use to make these precision cuts?

- **Meganucleases** are also called homing endonucleases. They are naturally occurring enzymes that recognize and cut long DNA sequences precisely. MegaTALs, fusions of a meganuclease to a protein that recognizes and binds DNA sequences, have been reported to function better than meganucleases alone.²

- **ZFN** is short for zinc finger nuclease, which is the combination of a special protein that can be used to target a desired DNA sequence and a nuclease (enzyme) to cut DNA. Among their many critical roles in the body, zinc finger proteins are important in DNA recognition, turning genes on and off, regulation of cell death, as well as protein folding and assembly.

Scientists can engineer them to target specific DNA locations and then add a nuclease domain to create double-strand breaks in the DNA at the targeted location.

- **TALEN** is short for transcription activator-like effector nuclease. As with ZFNs, scientists combine a protein that recognizes the targeted (broken) gene with an enzyme that will cut DNA. TALENs are built so they can target nearly any sequence.

- **CRISPR-Cas9** is short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9.

CRISPR-Cas9 can cut DNA at a desired location in a DNA sequence. This activates the cell's own DNA repair machinery to add or delete pieces of genetic material or to replace an existing segment of damaged genetic material with a laboratory-customized segment. But unlike other types of nucleases that use protein sequence to target DNA, CRISPR-Cas9 uses a short RNA sequence referred to as a guide RNA to target desired DNA sequences. This makes CRISPR-Cas9 extremely easy to reprogram to target different sites. Other aspects of Cas9 make it hard to get into certain types of cells, which makes it less well suited to treat certain types of diseases.

Homologous Recombination

Scientists have a mechanism for gene editing that can be performed by exchanging a healthy strand of DNA with similar or identical damaged molecules of DNA. This is called homologous recombination. Scientists use a bioengineered harmless virus to transport the healthy segment of DNA into a tissue or even a cell. The healthy genetic material then issues new (correct) instructions to the tissue or cell.