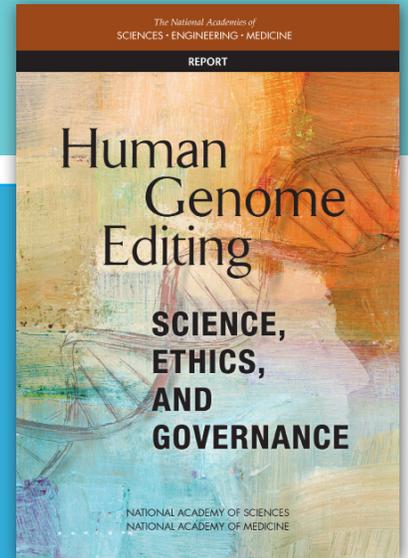


New Developments in Human Genome Editing

A Guide for Patients and Families Affected by Inherited Diseases and Disabilities



Background

Genome editing is a powerful new way to make precise changes to the human genome, a person's complete set of genetic material. These new methods have made the process of editing the human genome more precise, efficient, flexible, and less expensive than previous approaches. Interest in the possible uses for human genome editing has rapidly increased, including how it might be used to treat people with inherited diseases and disabilities. Examples of health conditions with a genetic basis that might be addressed by future human genome editing therapies include cancer, sickle-cell disease, Huntington's disease, muscular dystrophy, and cystic fibrosis.

As with many other scientific advances that hold promise for addressing important health problems, human genome editing also raises some ethical concerns, as well as questions about its potential risks and impact on society. These questions must be fully addressed before we move forward at full steam to develop and use these technologies in humans. To help examine these complex issues, the National Academy of Sciences and National Academy of Medicine convened the Committee on Human Gene Editing to carry out a study on how human genome editing can and should be used in people. The committee outlined its findings in a report called *Human Genome Editing: Science, Ethics, and Governance*. Important information from the report that pertains to people affected by inherited disease and disabilities is summarized below.

New Genome Editing Techniques

In recent years, new genome editing techniques have been developed, and a technique called CRISPR/Cas9 has received significant attention from scientists who see great potential for this tool to benefit human health. The reason for this excitement is that CRISPR/Cas9 makes genome editing much cheaper, easier, and more efficient than it was in the past. These advances have removed important barriers that previously presented serious challenges to using genome editing to solve health problems in humans.

Why Now?

With the new techniques that are now available, genome editing is beginning to transition from the realm of laboratory research—which doesn't involve work with human subjects—to clinical research—studies that do involve people. This period of transition is significant, and it requires that we take time to thoroughly examine a

number of important issues that are related to how human genome editing is used now, and how it should be used in the future.

Somatic Genome Editing (Editing of Non-Reproductive Cells)

Genome editing of somatic cells focuses on tissues that are not related to reproduction. Examples of somatic cells include lung, heart, skin, and other tissues besides sperm and egg cells. The distinction between reproductive and non-reproductive cells is important because if a person's somatic cells are changed with a genome editing therapy, their offspring will not inherit those changes—only the treated person will be affected. Methods to use somatic cell genome editing to address human health problems are in the early stages of development, and clinical trials that use these techniques are already underway for studies of certain cancers and for HIV. The U.S. National Institutes of Health (NIH) approved a project using several new genome editing technologies to help

Glossary

Below are common terms used when discussing human genome editing.

- **Human Genome:** A person's complete set of genetic material
- **Human Genome Editing:** The process of making precise additions, deletions, or alterations to a person's genome
- **Somatic Cells:** All the cells present in the human body, except for sperm, eggs, and the cells from which these develop
- **Somatic Genome Editing:** The process of editing a person's somatic cells, which affects only the individual receiving treatment
- **Germline Cells:** Reproductive cells like sperm and eggs, and the cells from which they develop
- **Heritable (Germline) Genome Editing:** The process of editing a person's reproductive (germline) cells, which could impact the children as well as future descendants of the individual receiving treatment
- **CRISPR/Cas9:** A new technique for genome editing that has made it easier, cheaper, and more efficient compared to previous methods

increase the impact of existing treatments by programming patients' immune cells to target cancer cells. The first trial will test whether CRISPR/Cas9 is safe for use in people. If it's successful, future trials would involve even larger groups of people. As somatic genome editing continues to develop, it is likely that clinical trials targeting additional health conditions will be conducted.

What Diseases Could Be Treated With Somatic Genome Editing?

Genome editing of somatic cells is likely to be more effective for treating some inherited conditions than it is for others. For example, somatic genome editing is more likely to be an effective therapy for inherited conditions that are caused by a single gene than those caused by multiple genes. Cystic fibrosis and sickle-cell disease are examples of diseases that are caused by mutations to a single gene. In these and other conditions in *Table 1*, there is a direct link between a mutation to a single gene and development of the condition, thereby making the condition a good target for a genome editing intervention. In contrast, conditions such as type 2 diabetes, hypertension, and heart disease are thought to be associated with mutations in multiple genes, each of which makes a relatively small contribution to developing the disease. These small contributions are "mixed in" with the effects of environmental factors such as obesity, physical

activity, and smoking. Because the genetic component of these common conditions is less directly linked to development of disease, these conditions are less likely to be good targets for genome editing therapies in the future. The committee recognizes the value of ongoing efforts to develop somatic genome editing to treat disease. However, it makes a clear distinction that clinical trials should be limited to studies that target treatment or prevention of disease and disability, and not for less compelling purposes such as cosmetic or other enhancements that do not address a health condition.

Heritable Genome Editing (Editing Reproductive Cells)

Genome editing of heritable (germline) cells involves the cells associated with human reproduction—human sperm, eggs, and the cells from which they develop, as well as, possibly, human embryos. Unlike somatic genome editing, heritable genome editing could impact future generations because any changes that are made to sperm and eggs could be passed down to the treated person's offspring. This type of genome editing has been done in animals, but not yet in humans. However, the medical and scientific communities are interested in heritable genome editing because it has the potential to help parents avoid passing down certain genetic diseases to their children.

Table 1 - Examples of Potential Therapeutic Applications of Somatic Cell Genome Editing*

Disease	Stage of Development
Sickle-Cell Disease	Clinical development
Sickle-Cell Disease/ β -Thalassemia	Preclinical
Severe Combined Immunodeficiency X-linked (SCID-X1)	Clinical development
X-Linked Hyper IgM Syndrome	Preclinical-clinical development
Hemophilia B	Clinical trial**
Cystic Fibrosis	Discovery
HIV	Clinical trial
HIV	Discovery
Cancer Immunotherapy	Conceptual through clinical trial
Duchenne's Muscular Dystrophy (DMD)	Preclinical
Huntington's Disease	Discovery
Neurodegenerative Diseases	Conceptual

*This table contains select examples of research and clinical trials for human genome editing interventions to treat disease and disability as of February 2017. Please note that this list is not meant to be comprehensive, and for some diseases there are multiple genome editing strategies at different stages of development. The goal of clinical trials is to determine whether these interventions are safe and effective, and the status of such trials often changes quickly.

**Current information on clinical trials is available at clinicaltrials.gov.

Although the potential benefits of heritable genome editing are clear, this type of editing is more controversial than editing somatic cells because the genetic changes could be inherited by future generations, so they affect more than just the person who chooses to receive the treatment. In addition to this ethical concern, it is possible that unintended and unwanted changes could be passed down to future generations as well as intended ones. There are also concerns about the potential impact heritable genome editing could have on the way society accepts children born with disabilities, and that these methods reflect a failure to appreciate the natural world. In light of these concerns, the committee recommends that although heritable genome editing could be done in humans in the future, it would only make sense to apply it to very serious diseases that meet strict criteria, and more research and public debate are needed before it would be appropriate to move forward with this type of work.

Engage in the Discussion

If you are affected by an inherited disease or disability, the most important thing you can do now is to engage in the conversation about human genome editing. Public engagement is an important part of how new technologies like genome editing will ultimately be regulated, so it is critical for people who are impacted by conditions that could eventually be treated with these techniques to be active

participants in the public debate about their use. Opportunities to get involved in public discussions on human genome editing include:

- Attend public meetings held by U.S. state and federal bioethics commissions. These often involve open meetings, public testimony, and transcripts of commission discussions.
- Pay attention to activities held by the [NIH Recombinant DNA Advisory Committee \(RAC\)](#), which offers periodic opportunities for public discussion of genome editing. This committee provides advance notice of meetings that are open to the public where time is made available for public comment. The RAC sometimes makes its meetings available by webcast, and the NIH Office of Biotechnology Activities has created an email alert to which the public can subscribe to stay informed of upcoming RAC meetings and activities.
- Visit [ClinicalTrials.gov](#), a database containing information on clinical studies that are being conducted around the world.
- Attend public discussions and informational meetings held by the Food and Drug Administration related to [therapies that use genome editing technology](#).

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For more information, visit: www.national-academies.org/gene-editing

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