# Human genome editing offers tantalizing possibilities—but without clear guidelines, many ethical questions remain

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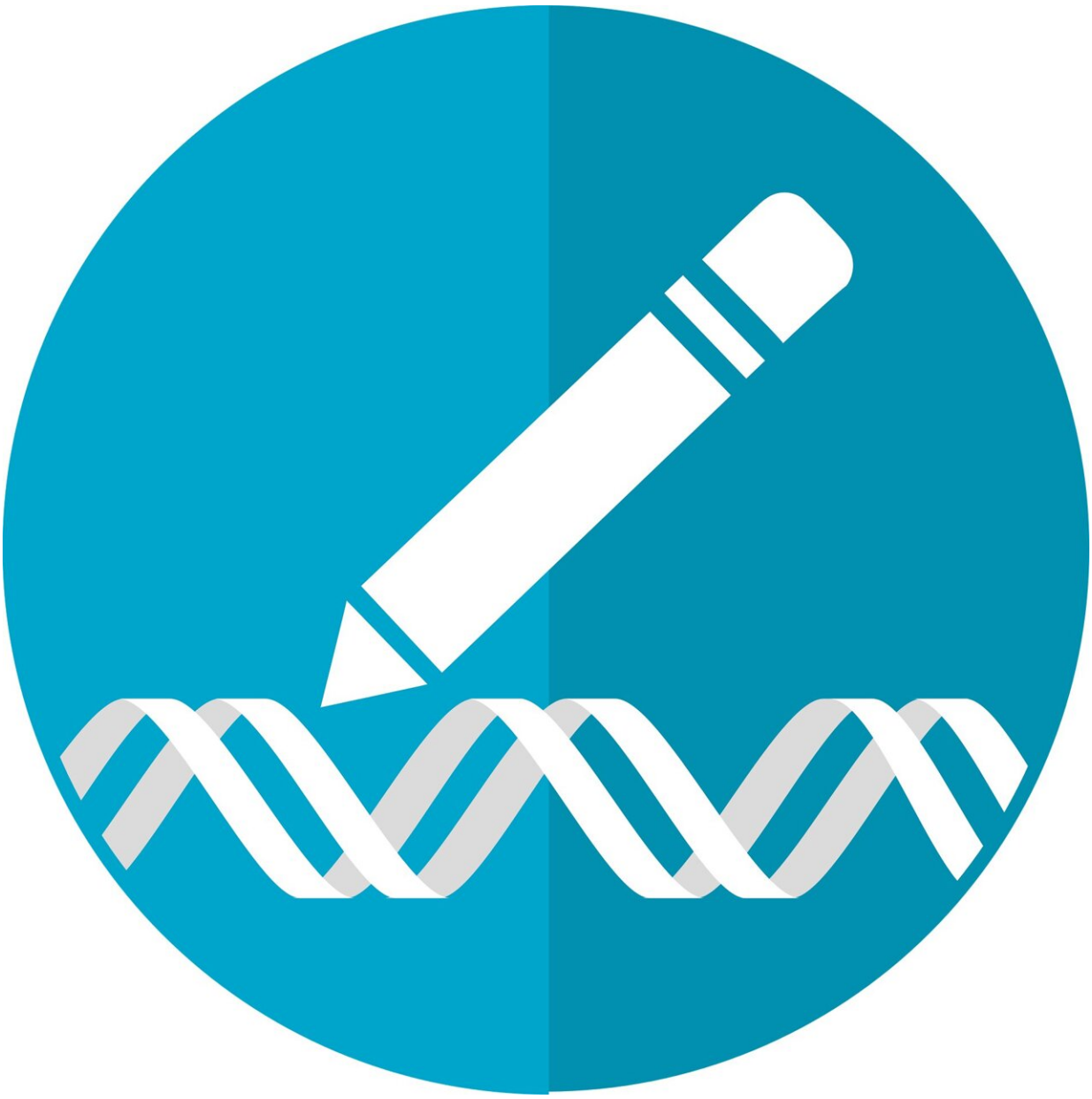

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The Third International Summit on Human Genome Editing, a three-day conference organized by the Royal Society, the U.K. Academy of Medical Sciences, the U.S. National Academies of Sciences and Medicine and The World Academy of Sciences, was held this week in March 2023 at the Francis Crick Institute in London. Scientists, bioethicists, physicians, patients and others gathered to discuss the latest developments on this technology that lets researchers modify DNA with precision. And a major topic at the summit was how to enforce research policies and ethical principles for human genome editing.

One of the first agenda items was how to regulate human genome editing in China in light of its misuse in 2018, when scientists modified the DNA of two human embryos before birth to have resistance against HIV infection. The controversy stems from the fact that because the technology is relatively early in its development, and its potential risks have not been reduced or eliminated, editing human embryos in ways they could pass on to their own offspring could lead to a variety of known and unknown adverse complications. The summit speakers noted that while China has updated its guidelines and laws on human genome editing, it failed to address privately funded research—an issue other countries also face. Many countries, including the U.S., do not have sufficiently robust regulatory frameworks to prevent a repeat of the 2018 scandal.

We are a biochemist and a geneticist who teach and conduct research in genomics and ethics at the Rochester Institute of Technology. As in our classrooms, debate about genome editing continues in the field.

## What is genome editing?

The human genome typically consists of 23 pairs of chromosomes made of approximately 3.2 billion nucleotides—the building blocks of DNA. There are four nucleotides that make up DNA: adenine (A), thymine (T), guanine (G) and cytosine (C). If the genome were a book, each chromosome would be a chapter, each gene on a particular chromosome would be a paragraph and each paragraph would be made of individual letters (A, T, G or C).

One can imagine a book with over 3 billion characters might need editing to correct mistakes that occurred during the writing or copying processes.

Genome editing is a way for scientists to make specific changes to the DNA in a cell or in an entire organism by adding, removing or swapping in or out one or more nucleotides. In people, these changes can be done in somatic cells, those with DNA that cannot be inherited by offspring, or in gamete cells, those containing DNA that can be passed on to offspring. Genome editing of gamete cells, which includes egg or sperm, is controversial, as any changes would be passed on to descendants. Most existing guidelines and policies prohibit its use at this time.

## How CRISPR works

In 2012, scientists published a groundbreaking study demonstrating how CRISPR, or Clustered Regularly Interspaced Short Palindromic Repeats, can be used to accurately change specific DNA sequences.

CRISPR's natural origins are as a kind of immune response for bacteria. Bacteria that can be infected with viruses have evolved mechanisms to combat them. When a bacterium is infected with a particular virus, it

keeps a small piece of the viral DNA sequence called a "spacer" in its own genome. This spacer is an exact match to the viral DNA. Upon subsequent infection, the bacterium is able to use the spacer to recruit a scissorlike protein called Cas9 that can sever new viral DNA attempting to integrate into the bacterium's genome. This cut to the genetic material prevents the virus from replicating and killing its bacterial host.

After this discovery, scientists were able to fine-tune the system in the lab to be highly precise. They can sever DNA from a variety of cells, including human cells, at a specific location in the genome and subsequently edit it by adding, removing or swapping nucleotides. This is similar to adding or removing letters and words from a book.

This technology has the potential to treat diseases that have genetic origins. One of the summit's sessions covered CRISPR's ongoing experimental use to treat patients with sickle cell anemia and beta-thalassemia, two blood disorders caused by mutations in the genes. Notably, genetic modification to treat sickle cell anemia and beta-thalassemia involves editing somatic cells, not germline cells. But as the summit speakers noted, whether these likely expensive therapies will be accessible to the people who need them most, especially in low- and middle-income countries, is a problem that requires changes to how treatments are sold.

## Ethics of human genome editing

Many questions remain concerning the safety of genome editing, along with its potential to promote eugenics and exacerbate inequities and inequality.

A number of the summit's sessions involved discussion on the ethics and regulation of the use of this tool. While the landmark 1979 Belmont Report outlined several ethical pillars to guide human research in the

U.S., it was published before human genome editing was developed. In 2021, the World Health Organization issued recommendations on human genome editing as a tool to advance public health. There is no current international law governing human genome editing.

There is still a debate regarding how to use this technology. Some people equate genome editing to interfering with the work of God and argue that it shouldn't be used at all, while others recognize its potential value and weigh that against its potential risks. The latter focuses on the fundamental question of where to draw the line between which applications are considered acceptable and which are not. For example, some people will agree that using genome editing to modify a defective gene that may lead to an infant's death if untreated is acceptable. But these same people may frown upon the use of genome editing to ensure that an unborn child has specific physical features such as blue eyes or blond hair.

Nor is there consensus about what diseases are desirable targets. For example, it may be acceptable to modify a gene to prevent an infant's death but not acceptable to modify one that prevents a disease later in life, such as the gene responsible for Huntington's disease.

The potential for positive applications of human genome editing is both numerous and tantalizing. But establishing informed regulatory legislation everyone can agree on is and will continue to be a challenge. Conferences such as the human genome editing summit are one way to continue important discussions and educate the scientific community and the public on the benefits and risks of genome editing.

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