EDUCATION

Genetic Technology

Humans have been altering the genes of plants and animals for thousands of years, but advances in technology now enable the direct manipulation of genes. Genetic technology has implications for food, research, medicine, conservation and more.

GRADES

8 - 12+

SUBJECTS

Genetics, Biology, Health



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PHOTOGRAPH

Matej Vucić Collecting eDNA Samples

Matej Vucić conducting electrofishing sampling in Neretva, Bosnia and Hercegovina.

PHOTOGRAPH BY KARMELA ADŽIĆ

BACKGROUND INFO VOCABULARY

Learning materials

VIDEO

- Nature: CRISPR: Gene editing and beyond

REFERENCE

- Stanford News: What is CRISPR? A bioengineer explains
- Technology Networks: Genetic Modification Techniques and Applications

Genetic technologies have reshaped many aspects of science and society, including agriculture, health and even conservation. Underlying modern genetic technology—from genetic testing to gene editing—is the ability to figure out where genes are located in part of an organism's DNA sequence

or the whole genome, which is the organism's entire DNA sequence. This is called sequencing.

Genome sequencing began with simple microbial organisms that used single-stranded RNA, rather than double-stranded DNA, as their genetic material. DNA tends to be much longer and more complex than RNA. But in 1977, English scientist Frederick Sanger developed the Sanger sequencing method, which uses a chemical reaction for DNA sequencing. This breakthrough accelerated the use of DNA sequencing. Scientists used this technique throughout the rest of the 20th century, including for the Human Genome Project, which resulted in the first sequence of the human genome, completed in 2003.

Since then, new sequencing technologies referred to as next-generation sequencing (NGS) have dramatically sped up sequencing and lowered costs, enabling more advanced genetic research and development. These newer sequencing technologies can simultaneously "read" multiple segments of DNA or RNA that are more than 10,000 base pairs long. This is a much faster process than the Sanger method of reading segments of just a few hundred base pairs, one at a time.

Genetic Testing

After the development of gene sequencing came genetic testing. With genetic testing, people can find out if they have a genetic disorder, determine their likelihood of developing various diseases and assess their risk of passing on an inherited condition to their children. Genetic tests allow people to be proactive about their disease risk and take steps to prevent disease or make plans for what to expect when a disease does

develop. For example, genetic testing can tell someone if they have a mutation in their BRCA genes that may increase their likelihood of developing breast and ovarian cancers.

However, there can be negative consequences to genetic testing. There ar laws in countries around the world to prevent health insurance companies from discriminating against people based on their genetics, such as charging them more for their policy or denying them coverage altogether. South Korea's Bioethics and Safety Act, for instance, prevents genetic discrimination in insurance coverage as well as in other areas, like educatio and employment. But such laws don't always apply to all types of insurance For example, in the United States, the Genetic Information Nondiscrimination Act does prevent U.S. health insurance companies from discriminating based on genetic information, but it does not apply to life insurance companies, although some states do have laws to protect agains genetic discrimination by life insurance as well as other types of insurance companies.

Gene Editing

Gene editing refers to making changes to the genes in an organism's DNA. Gene editing technologies work like molecular scissors. They use enzymes called nucleases to break apart DNA strands, allowing scientists to modify DNA at specific locations. The major gene-editing technologies are zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs) and CRISPR-Cas9, which stands for clustered regularly interspaced short palindromic repeats (CRISPR), and CRISPR-associated protein 9 (Cas9).

ZFNs and TALENs work similarly, using proteins that bind to and cut specific parts of the DNA, though the two methods use different proteins. Scientist have been using ZFNs in research since the late 1980s. TALEN technology, which was introduced around 2010, improved on ZFNs and is considered easier to use.

In 2012, U.S. and French scientists Jennifer Doudna and Emmanuelle Charpentier announced the development of CRISPR-Cas9 gene editing, a tool derived from bacterial immune systems. When a bacterium is infected with a virus, it can extract pieces of the virus' DNA and insert it into its own DNA, creating a CRISPR sequence. The next time the bacterium encounters the virus, the bacterium's immune system can recognize it. The bacterium can then use the CRISPR sequence to produce RNA that attaches to the attacking virus' DNA. This RNA tells the bacterium's Cas9 enzyme where to cut the virus' DNA, disabling the virus.

Researchers adapted this technique to edit DNA in cells of other organisms using RNA "guides" attached to a Cas9 enzyme that can bind to a targeted DNA sequence. Cas9 can then cut the DNA at the desired location. Researchers can add or remove genes at the cut or replace part of the DNA with a new sequence. CRISPR systems allow scientists to edit genomes more efficiently and accurately than other methods, and at lower costs.

Gene Editing in Medicine

Gene editing has transformed medicine, leading to effective treatments fo serious health conditions. One example is chimeric antigen receptor (CAR) T-cell therapy, first approved in 2017. CAR T-cell therapy is a cancer treatment that changes the genes in a person's T-cells, a type of white

blood cell that is an element of the immune system, to make them attack cancer cells. Scientists extract a person's T-cells from their blood, and then take the cells to a lab where they use TALEN technology to alter the cells' genes so the cells can better recognize and destroy cancer cells. CAR T-cell therapy has been approved to treat certain lymphomas (cancers of part of the immune system) and blood cancers.

Gene therapies that use CRISPR-Cas9 gene editing are more recent. A gene therapy for two blood disorders, sickle cell anemia and beta thalassemia, is the first approved therapy that uses CRISPR-Cas9 technology. The United Kingdom's Medicines and Healthcare Products Regulatory Agency approved the treatment, Casgevy, in 2023, followed by several other countries, including the United States, European Union countries, Saudi Arabia and Bahrain.

People with sickle cell anemia have two copies of a genetic variant for hemoglobin, resulting in sickle-shaped red blood cells that clump together and block blood vessels, which causes severe pain. People with beta thalassemia also have a gene mutation that affects hemoglobin, causing low red blood cell levels that may require a lifetime of regular blood transfusions.

To create a patient's Casgevy gene therapy, a sampling of their red blood cells are collected and taken to a lab where CRISPR-Cas9 edits the hemoglobin genes in the cells to promote proper red blood cell production. The patient must then receive chemotherapy to ready their bone marrow to accept an infusion of the new cells.

Despite the promising results from clinical trials, few patients received the new treatment following its approval. This is for a number of reasons. One reason is the treatment is very expensive, particularly for people who do not have access to health insurance or whose health insurance does not cover the treatment. It is also very time-consuming, with treatment taking up to a year. And Casgevy is not without risks. People must receive chemotherapy as part of the treatment, which can raise the risk of infertility and damage healthy cells. There's also the risk of off-target effects, in which CRISPR might change genes other than the ones intended.

Gene editing has not been without controversy. In 2018, Chinese researche He Jiankui announced his work had produced the first genetically edited babies, a set of twins. He and his colleagues used CRISPR-Cas9 to modify a gene called CCR5 in the twins' embryos to make them immune to human immunodeficiency virus (HIV).

But He did not have legal permission to conduct this work. Further, the babies were not at risk of being born with the virus, leading to accusations that He was unethically experimenting on the babies rather than treating them for a disease. The babies appeared healthy at birth, but the gene CCR5 does more than help regulate immunity to HIV. It also helps the brain and immune system function, and editing this gene could have unintended effects. Since He's work was made public, experts have agreed that we nee to know more about the long-term consequences of gene editing before modifying human embryos, as any changes made to an embryo's DNA coul affect the baby and their future offspring.

Genetic Engineering in Food and Agriculture

Genetically modifying crops or livestock is not a new idea; humans have been selectively breeding plants and animals to express certain traits for millennia. While selective breeding does not involve humans directly modifying an organism's DNA, with genetic engineering, now people can introduce desirable traits faster and more accurately.

Genetic engineering refers to altering an organism's genome through gene editing and other techniques. Before targeted gene-editing tools were widely available, researchers had recombinant DNA technology. To create recombinant DNA, researchers isolate segments of DNA from two different species and combine them. Using this process, scientists created a type of genetically modified corn called Bt corn, available since 1996. A type of soil bacteria (*Bacillus thuringiensis*) secretes Bt toxin, which is toxic to the caterpillars that eat corn but not humans. Scientists inserted the Bt gene into a corn variety, allowing the corn to produce this environmentally friendly insect repellent, reducing the use of pesticides. However, in the decades since Bt corn was introduced, scientists have found evidence that pests are becoming resistant to Bt due to overplanting of Bt corn, limiting its effectiveness.

As with medicine, targeted gene editing is relatively new to agriculture. It was in 2019 when the first gene-edited plant—a soybean designed to produce oleic acid, a relatively healthy oil—came to market. It was created by a U.S. company, Calyxt, using TALENs.

Scientists are also exploring gene-editing tools to create plants that can better resist climate change. The cacao tree (*Theobroma cacao*), which is native to the tropical rainforests of Central and South America but grown throughout the tropics in western Africa and Asia, produces the cocoa

beans used to make chocolate. The tree faces many pests and disease takes over 30% of the harvest every year. Several research groups are trying to use CRISPR-Cas9 to improve cacao tree immunity.

Genetically modified organisms, or GMOs, have sparked debate despite the benefits they offer. GMOs have been on the market since 1994, and ever since, misconceptions about their safety have been a top concern. However, researchers who have explored safety and health issues regarding GMOs have not found evidence that eating GMOs is any more harmful than eating non-GMOs. Still, researchers continue to monitor the safety of GMOs.

GMOs do come with one potential risk, though it is not from GMOs themselves. Some crops are engineered to resist herbicides like weed killers. This means farmers may use more herbicide than they would otherwise, since it won't harm their crops. To limit exposure to herbicides, people should wash and scrub fruits and vegetables under running water prior to eating them.

Genetic Technology in Conservation

Modern genetic technology has also significantly changed the way scientists think about wildlife conservation. For example, National Geographic Explorer Christopher Schmitt uses gene sequencing technology to learn about the genetics of woolly monkeys (*Lagothrix spp.*), particularly how they adapt to extreme environments.

Another conservation approach called "genomic selection" allows scientists to predict which traits an endangered species will have. Similar to selective breeding in agriculture, this could allow conservationists to promote breeding strategies that better adapt wildlife to the environment.

Conservation has also borrowed another approach from agriculture: recombinant DNA. American chestnut trees (*Castanea dentata*) nearly went extinct at the end of the 19th century in North America. The Asian Chestnut Blight fungus (*Cryphonectria parasitica*) made its way to the continent through imports of Asian chestnut species, and the American chestnut had no natural genetic resistance to the fungus. Fortunately, wheat did. A team of scientists at the State University of New York College of Environmental Science and Forestry copied the gene from wheat and combined it with American chestnut DNA to produce trees tolerant to the blight. The team is seeking regulatory approval from U.S. agencies before the public can access the genetically modified seeds.

Another useful conservation tool is environmental DNA (eDNA). eDNA refers to bits of genetic material shed by species in their environment. eDNA can come from skin, scales and mucus in water, soil or air. Tracking eDNA allows scientists to monitor biodiversity throughout an ecosystem without having to find and track individual organisms. It can also help scientists identify and track invasive species at the start of their invasion, which could potentially reduce the harm they cause to the ecosystem. But eDNA can't tell scientists everything. Some species do not shed DNA easily, and eDNA can't tell scientists how many members of a species exist in an area.

Genetic Technology Around the Globe

While genetic technologies have much to offer humanity and the environment, the resources and benefits of this technology are not equally distributed. Low- and middle-income countries, and disadvantaged communities within high-income countries, have not participated in genetic

research as much as high-income countries or wealthy communities due to limited resources and discriminatory practices. For instance, genomic research is popular in the United States and United Kingdom. As a result, most medical genomic research involves a disproportionately high number of people of European ancestry, despite those nations growing populations of people from other parts of the world. Low-income countries also have not had the resources to build infrastructure that genetic technology and research requires.

This is starting to change, as scientists from a variety of countries are forming partnerships and investing in genetics in low- and middle-income countries. For example, Human Heredity and Health in Africa (H3Africa) was a 10-year initiative with international support aimed at funding African researchers and supporting them in leading genetics research. H3Africa's accomplishments include creating the computing infrastructure needed for

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