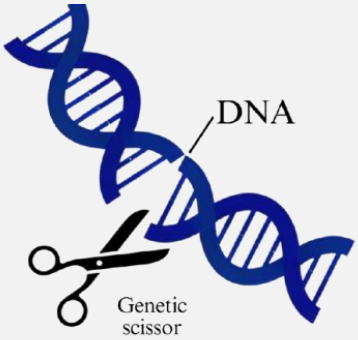
Science & Technology Policy Brief

Gene Editing



Gene Editing has enabled targeted modification of DNA within living organisms. It has potential uses in medical research, disease treatment, and agriculture. This brief outlines the techniques, potential applications, and associated concerns with these technologies.

Summary

- Gene editing uses enzymes to add, remove or alter genetic material at particular locations in the genome.
- Different methods are used for gene editing. CRISPR-Cas9 is the most commonly used method. It was adapted from a naturally occurring defence mechanism of bacteria.
- Gene editing has various applications such as disease treatment, control of infectious diseases, and crop improvement.
- Potential concerns include safety risk from unintended edits made to DNA, use for designer babies, ecological risk, and regulatory challenges in identifying genetically edited organisms.

Background

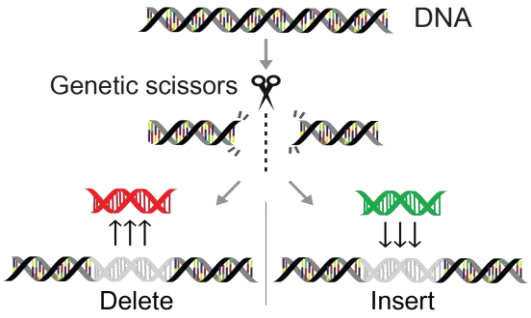
Cells are the basic building block of all living organisms.[1] Nearly all cells contain DNA (Deoxyribonucleic acid).[1] DNA carries the instructions needed for a living organism to develop, survive, and reproduce.[2] A gene is a segment of DNA.[1] It is passed from parents to offspring and carries instructions that determine traits such as eye colour or hair type (often in combination with other genes).[1] It is estimated that humans have between 20,000 and 25,000 genes.[1] In most sexually reproducing species (including humans), individuals carry two copies of most genes, one inherited from each parent.[1] The complete set of DNA is called a genome.[3]

For thousands of years, humans have selectively bred plants as well as animals to pass on desirable traits.[4] For example, cabbage, broccoli, and cauliflower were selectively bred from their wild relatives by choosing plants with preferred leaf or flower structures.[4,5] Advancements in sciences have made it possible to directly manipulate genes of an organism in a lab. These may involve inserting a new gene, removing or deactivating an existing gene, or altering the sequence of a gene.[6] These laboratory-based techniques are referred to as genetic engineering.[6] The plant, animal or microbe whose genes are modified through these methods are called Genetically Modified Organisms (GMOs).[7] A common example is Bt-Cotton. It is a cotton variety that has been engineered to resist bollworm, a major cotton pest.[8] As of 2024, it occupied more than 96% of the total cotton cultivated in India.[9]

Gene Editing

Gene Editing is a technique that allows changing DNA at targeted locations.[10] It uses enzymes to manipulate DNA sequences at one or more selected sites.[11] These technologies act like scissors, cutting DNA at a specific spot.[12] DNA can then be removed, added or replaced at the target location.[12] Gene editing is being explored for a range of applications. Some of these include developing gene-edited tomatoes that may help lower blood pressure and treating conditions such as sickle cell disease by editing a patient's stem cells.[13,14]

Figure 1: Gene editing



Several approaches to gene editing have been developed over the past three decades (see Box 1). A well-known one is called CRISPR-Cas9.[11] It is adapted from a naturally occurring defence mechanism that bacteria uses against viruses.[15] When a virus infects a bacterial cell, a fragment of the viruses' genetic material is stored in a region in bacterial genome called the CRISPR locus.[15] This helps bacteria to "remember the virus". If the virus infects again, bacteria use stored genetic material to

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produce guide RNAs (Ribonucleic acid).[15] These guide RNAs bind to specific sites of the invading viruses' genetic material.[15] The Cas9 protein produced by bacteria then cuts the genetic material at those sites.[15] Thus, the guide RNA and Cas9 protein are the key components of CRISPR-Cas9.

The same "cutting" ability of Cas9 is used on DNA of other organisms. Once a cut is made, cells naturally attempt to repair the break.[16] This repair can happen in multiple ways.[16] In one of these pathways, the cell simply joins broken DNA ends.[17] This process often introduces small deletions that can disrupt the function of a gene.[17] In another pathway, the cell repairs the break by copying from a DNA template.[18] Scientists use this mechanism in gene editing by supplying an external DNA template at the cut site.[18] The cell then uses this template to repair the break.[18] This allows specific sequences to be added or replaced.[18]

Box 1: Different types of gene editing techniques

Apart from CRISPR- Cas9, the most common types of gene editing techniques used are Zinc-Finger Nucleases (ZFNs) and TALE Nucleases (TALENs).[11] They all use enzymes to make genetic modifications at one or more selected sites within the genome.[11] However, unlike CRISPR–Cas9, which uses a guide RNA to recognise a target DNA sequence, ZFNs and TALENs rely on custom-designed proteins i.e., zinc-finger protein and TALE protein.[11]

ZFNs were first applied for gene editing around 2002-03, followed by the development of TALENs in 2010 and CRISPR-Cas9 in 2013.[19] Several other variants of Cas proteins were also developed later.[19] Compared to TALENs and CRISPR–Cas9, constructing zinc-finger proteins used in ZFNs is complex, limiting its ability to target different DNA sites.[11] CRISPR-Cas9 systems has been revolutionary because it is cheap and easier to use.[11] However, all three techniques can produce unintended edits (see off-target effects on the next page).[11]

Applications of Gene Editing

Biomedical research: Cellular and animal models are widely used to study human diseases, and test novel vaccines or therapies.[20,21] Gene editing technologies have enabled the creation of precise cellular and animal models and expanded the types of animals that can be used as models.[22] For example, mouse models for cystic fibrosis (a genetic disorder) do not develop symptoms such as bacterial infection which are seen in humans.[23] However, they were used largely because their genetics were relatively easy to modify compared to those of large animals.[24] Due to CRISPR, large animals models that more closely resemble human biological systems (such as those of pigs) can also be used.[22] The integration of CRISPR with organ chips (systems that simulate functions of human organs) is also rapidly advancing and may offer enhanced disease modelling tools in the future.[25]

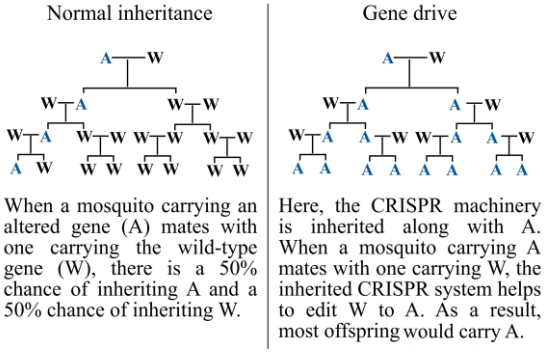
Treatment of diseases: Gene editing technologies are used to treat genetic disorders such as sickle cell disease (see Box 2), and β-thalassemia.[26] They are also being used to enhance the natural ability of human immune cells to fight cancer.[27] This is being done by strengthening T-cells (a type of immune cell that kills cancerous cells) by removing genes that limit their activity or by adding genes that help them better identify cancer cells.[28,29] Advances in CRISPR-based precise editing tools are also enabling correction of point mutations (small changes in DNA sequence).[30] This may expand the range of treatable diseases.

Box 2: Gene editing for treating sickle cell disease

Sickle cell disease (SCD) is an inherited genetic disorder that affects haemoglobin, the major protein that carries oxygen in red blood cells (RBCs).[31] Normally, RBCs are disc-shaped so they can move easily through blood vessels.[31] In SCD, gene mutation causes most RBCs to be "sickle-shaped", which can block blood flow.[31] Blood and bone marrow transplant has been the only cure.[31] However, its use is constrained by limited donors and risk of complications such as the donor cells attacking recipient's body.[32] In December 2023, US FDA (Food and Drug Administration) approved Casgevy, the first cell-based gene therapy for specific patient groups.[33] In this treatment, patient's stem cells are modified using CRISPR to increase production of a type of haemoglobin that prevents sickling.[33] Thus, gene editing is being used to shift from managing such chronic diseases to providing a cure.

Control of vector borne diseases: CRISPR-Cas9 offers potential to reduce the prevalence of diseases spread by mosquitoes and other insects.[34] For example, genes of *Anopheles* mosquitoes can be modified to prevent malaria parasite to develop inside them.[35] However, under normal circumstances, only around half of the next generation would carry the modified gene.[34] To spread the trait through a population, gene drives are used. Gene drives refer to systems that increase the likelihood of a gene being inherited across generations.[34] In CRISPR-Cas9 based gene drives, guide RNA, Cas9 and possibly a desired gene is placed in the reproductive cells of *Anopheles* mosquitoes.[36] This system helps spread the desired genes. For example, when an offspring inherits one edited gene and one normal gene, Cas9 cuts the normal copy, and the cell repairs it by copying the edited version.[37] This process makes the offspring carry two copies of the edited gene, so almost all of its offspring inherit the modification.[37]

Figure 2: Gene drives increase likelihood of inheritance of select genes



When a mosquito carrying an altered gene (A) mates with one carrying the wild-type gene (W), there is a 50% chance of inheriting A and a 50% chance of inheriting W.

Here, the CRISPR machinery is inherited along with A. When a mosquito carrying A mates with one carrying W, the inherited CRISPR system helps to edit W to A. As a result, most offspring would carry A.

Gene-edited crops: Gene editing is used in crops to introduce various traits such as higher yield (more food from same land area), resistance to diseases and pests, and greater tolerance to environmental factors such as drought. For example, wheat plants are edited to be resistant to fungi and tomato plants are edited to produce vitamin D.[38,39] Similarly, rice is being edited to remove genes that make it sensitive to higher salt levels in soil.[40] Higher salinity normally stunts rice growth and lowers yields.[40] (see PRS brief on Genetically Modified Crops for more information on genetically modified crops).

Usage in livestock: Gene editing is used to make livestock resistant to diseases and environmental factors. For example, CRISPR-Cas9 has been used to produce pigs resistant to Porcine Reproductive and Respiratory Syndrome, which causes pneumonia and higher mortality.[41] Similarly, it has been used to improve heat tolerance of cattle.[42,43] Dairy cattle have also been gene-edited to be hornless, as an alternative to manual dehorning.[44]

Box 3: Some recent developments in India

- **Treatment of sickle cell disease:** In November 2025, the central government announced development of BIRSA 101, India's first indigenous CRISPR-based gene therapy for sickle cell disease.[45] A technology transfer agreement was also signed with the Serum Institute of India to enable production.[45]
- **Indigenous alternative for CRISPR-Cas9:** In November 2025, the Central Rice Research Institute developed a new indigenous genome editing technology.[46] It is aimed to offer a compact, low-cost and IP-free alternative to CRISPR-Cas system.[46]
- **Gene-edited rice varieties:** In May 2025, the Indian Council of Agricultural Research developed two gene-edited rice varieties with higher yield, lower water use, and greater tolerance to salinity and drought.[47]
- **Disabling genes in buffalo:** In June 2024, the National Dairy Research Institute used CRISPR-Cas9 to disable a gene in reproductive cells of a buffalo.[48,49] This gene produces a common allergen found in milk.[49]

Concerns regarding Gene Editing

Safety concerns

Off-target effects

Gene editing techniques can produce unintended editing at sites other than the target DNA sequences known as off-target effects.[50] For instance, CRISPR-Cas9 induced unintended off-target edits can interfere with how genes are expressed ("turned on or off"), potentially causing harmful outcomes such as cancer.[50] Off-target effects can occur in any organism where gene editing is used such as plants, animals, and humans.[51] Several factors influence where off-targets may arise, such as the target site or the cell type.[50] Genetic variations among individuals also impact off-target activity.[52] The study of patient-specific off-target effect is limited by cost and logistical feasibility.[52] Even when effects are identified, it is hard to predict the health impact.[52] Although advances in precise editing tools have reduced off-target effects, they can still have some limitations.[53]

Immune response

Cas proteins such as Cas9 are derived from bacterial species that infect humans at high frequencies.[54] The use of these proteins for gene editing may trigger an immune response.[54] Immune response refers to the body's defence reaction against what it perceives as a foreign substance, in this case a Cas9 protein.[55] Some studies have tried to engineer Cas variants to minimise the pre-existing immunity.[56] Currently, most CRISPR-based therapies rely on editing patient-derived cells outside the body.[52,57] This approach may address risk of immune rejection in some cases.[52] However, not all cell types may be safely isolated, modified, and transplanted back into the patient.[52] Multiple studies are done to deliver the gene-editing component to modify cells directly where they reside.[52] Effective delivery and editing still remains difficult for many tissues of the human body.[58]

Germline editing

Genes in reproductive cells such as eggs, sperms or embryos may also be edited.[59] These cells pass their DNA to future generations so any edits made to them are inherited. The aim of editing may also be to propagate the desired change to all cells. However, embryo editing may result in mosaicism, which means that the embryos would have some edited and non-edited cells.[59] Mosaicism may occur if gene editing happened after division of the initial single-cell embryo into two cells.[60] For example, at the two-cell stage, one of the cells acquires one type of edit while the other cell has a different edit or no edit.[60] Mosaicism may result in severe health conditions.[59] It may be difficult to predict the consequences in one individual and to foresee the effects in future generations.[59] Similar challenges are observed in plants and animals where reproductive cells are edited.[61,62]

Box 4: Gene editing in human embryos

Editing reproductive cells may lead to changes across the population. Therefore, many countries either do not allow research or have strict regulations for research.[19] However, in 2018, a scientist named He Jiankui in China announced that he had used CRISPR-Cas9 to edit the genomes of two human embryos.[19] The attempt was made to edit CCR5 gene, which encodes a protein used by HIV.[19] These embryos were carried to term, producing the first babies with heritable genome edits.[19] He revealed that one of the twins will be resistant to HIV because both copies of her CCR5 gene were removed.[63] The other could still develop infection as gene editing inadvertently left one copy of her CCR5 gene intact.[63] The experiment was heavily criticised for its lack of transparency, clarity, and justification given that little is known of the risks of removing this gene.[19]

Human enhancement

Human enhancement refers to an intervention aimed at improving human abilities and well-being, even when there is no illness to treat.[64] For example, future applications may include modifying cognitive capacity or physical endurance in humans. The possibility of using gene editing techniques such as CRISPR to edit embryos ("designer babies") for socially desired characteristics raises several ethical questions. These include whether permanent genetic changes should be made on the basis of social preferences.[65,66] Similar concerns may arise when considering the use of gene editing in other types of cells for "enhancement" rather than only for treating or preventing disease.[67]

Informed consent

In research and clinical settings, informed consent is typically required and can be withdrawn at any time.[66,68] ICMR has released guidelines mandating such consent and re-consent in a research requiring long term follow-up.[66,69] The irreversible nature of gene editing and particularly of gene editing in reproductive cells raise certain concerns. These include: (i) whether participants can truly withdraw from a study given that the possibility of undoing the edits is challenging, and (ii) how consent should be handled for long-term monitoring in cases where edits may affect future generations.[68]

Effect of gene drives on ecosystems

Modern gene-editing tools such as CRISPR-Cas9 can create gene drives to spread human-designed traits. This can have unintended implications. Gene drives to reduce or eliminate harmful species in agriculture could have adverse effects if the genetic changes spreads to related species that are not meant to be targeted.[70] For example, Palmer amaranth is a damaging weed in USA that gene drives could help supress.[70] However related *Amaranthus* species are cultivated for food in Mexico, India, and China raising concerns about gene drives unintentionally affecting these non-target species.[70] Given such risks, it becomes essential to monitor such effects through methods such as genetic tracking.[37]

Gene drives have mostly been developed and tested in controlled settings.[70] The release of gene drives into the environment could affect local ecosystems.[37] For example, using a gene drive to prevent the spread of disease in a particular plant species could unintentionally alter the ecological balance (it may change which species become more dominant in an environment).[37] There are also concerns that it may not be possible to fully predict all such ecological effects before any intervention.[37] To address ecological risks, some recent gene drives are being designed to be self-limiting i.e. to spread only for a few generations.[71]

Box 5: Regulations on gene editing

In USA, UK, Brazil and India, gene editing is regulated under a national legislation or guidelines by regulatory bodies. Several countries allow gene editing in plants and animals subject to certain regulations.[72,73,74,75] Among humans, editing in non-reproductive cells is generally permitted, but editing in reproductive cells is widely prohibited across countries.[19,76,77,78,79,80] In UK, editing reproductive cells is permitted for research.[81] In USA, gene editing of reproductive cells for research is not prohibited but federal funding cannot support research that creates or destroys human embryos.[82]

In India, gene editing in plants and animals is primarily governed by the Environment Protection Act, 1986 and the associated 1989 Rules.[83] The Rules establish a multi-tier regulatory system, such as the Review Committee on Genetic Manipulation (RCGM) to monitor biosafety in ongoing research, and the Genetic Engineering Appraisal Committee (GEAC) to approve environmental release of genetically edited plants and animals.[83] Certain gene edited plants that do not contain foreign DNA are exempt from the GMO approval process.[84] For humans, the research and use of gene editing is governed by ICMR's guidelines.[66,69] These guidelines specify framework related to safety, consent, and use of gene therapy in humans.

Distinguishing gene editing for regulation

Traditional genetic engineering techniques alter genomes by inserting (or deleting) DNA combinations that do not occur naturally.[85] These changes can usually be identified because the inserted foreign DNA is known, points of insertion (or deletion) are traceable, and standard detection tests exist.[85,86] In contrast, newer gene editing techniques can alter genes without integrating foreign DNA.[85] This makes it harder to distinguish the edited change from naturally occurring ones.[85] This creates challenges for detection of gene-edited organisms that may fall under the biosafety regulatory provisions.[87]

Intellectual property rights

There are two main concerns: (i) whether human gene is patentable and (ii) whether overlapping patents across a genome may slow research and hinder healthcare application.[88,89] The question of gene patentability is contested internationally. In Europe, isolation of a naturally occurring gene may be patentable provided certain conditions are met such as if the gene has a defined technical application.[90] In US and India, isolation of naturally occurring gene sequences is not considered patentable.[91,92]

Patents on multiple DNA sequences owned by many parties have also raised concerns about "patent thickets".[89] Patent thickets can make it difficult to accumulate all the permissions needed to conduct research, testing or treatment.[87,89] This is particularly relevant for conditions caused by multiple genes such as heart disease.[93]

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