# CRISPR

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**Manifest Pedagogy:**

Over the last 3 years, the gene-editing technology with near unlimited potential has produced flawless results in clinical trials. CRISPR is a revolutionary technology that can solve many problems of humanity.India has approved a 5-year project to develop CRISPR to cure sickle cell anaemia.Many countries and laws have already been put forward to bring the best outcome. With proper laws and control over its usage, it will definitely be a huge gift for humankind.

**In News:** The gene-editing technology which has led to innovations in medicine, evolution and agriculture has completed 10 years of innovation.

**Placing it in the Syllabus:** Science and Technology

**Static Dimensions**

- Background
- What is genome editing?
- About CRISPR technology
- Technology in action

**Current Dimensions**

- Applications of CRISPR Technology
- The advantages of this technology
- Issues associated with this Technology

**Content**

***Background***

- Over the last two and a half years, as the coronavirus pandemic ravaged the world and exposed the vulnerabilities of humans to new diseases, scientists

continued to push ahead with significant progress in utilising an exciting recent technology for permanent cures to some of the most intractable health disorders.

- In the 10 years since it was developed, the genome-editing technology called CRISPR has begun to deliver on the near unlimited potential that scientists say it has to improve the quality of human life.
- The technology enables a simple but remarkably efficient way to 'edit' the genetic codes of living organisms, thus opening up the possibility of 'correcting' genetic information to cure diseases, prevent physical deformities, or to even produce cosmetic enhancements.
- Over the last three years especially, several therapeutic interventions using CRISPR for diseases like thalassaemia or sickle cell anaemia have gone into clinical trials, mainly in the United States, and the initial results have been flawless.
- Last year, the Indian government approved a five-year project to develop this technology to cure sickle cell anaemia that mainly afflicts the tribal populations of the country.
- Hundreds of research groups and companies around the world are working to develop a range of specific solutions using CRISPR.
- The developers of the technology, **Jennifer Doudna and Emmanuelle Charpentier, won the Nobel Prize for Chemistry in 2020,** one of the fastest recognitions accorded by the Nobel committee following a breakthrough.

## What is genome editing?

- Genome editing or gene editing is a group of technologies that give scientists the ability to change an organism's DNA.
- Through these technologies, a genetic material can be added, removed or altered at any particular location in

the genome.

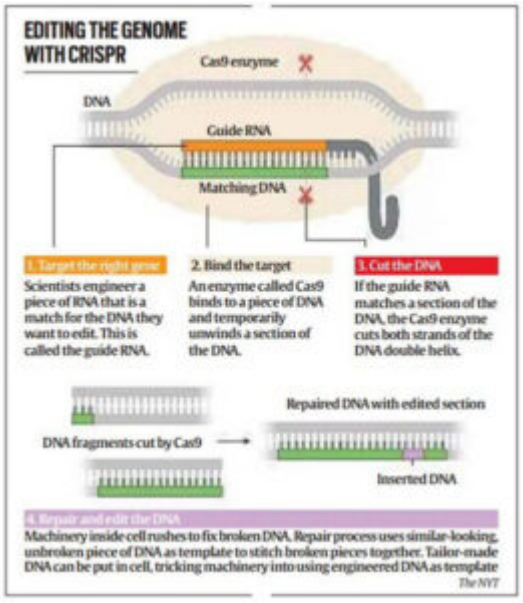
- Among the many approaches to genetic editing, **CRISPR-CAS9** is one of them.
- The CRISPR-Cas9 system has generated a lot of buzz in the scientific community because it is faster, cheaper, more accurate, and more efficient than previous techniques of editing DNA and has a wide range of potential applications.

***About CRISPR technology***

- CRISPR is short for **Clustered Regularly Interspaced Short Palindromic Repeats,** which is a reference to the clustered and repetitive sequences of DNA found in bacteria, whose natural mechanism to fight some viral diseases is replicated in this gene-editing tool.
- Editing, or modification, of gene sequences to eliminate – or introduce – specific properties in an organism is not a new development.
    - It has been happening for several decades now, particularly in the field of agriculture, where genetically modified variants, with specific desirable traits, are regularly developed.
    - It usually involves the introduction of a new gene, or suppression of an existing gene, through a process described as genetic engineering.
- CRISPR technology is different. It is simple, and still far more accurate – and it does not involve the introduction of any new gene from the outside.
    - Its mechanism is often compared to the 'cut-copy-paste', or 'find-replace' functionalities in common computer programmes.
    - A bad stretch in the DNA sequence, which is the cause of disease or disorder, is located, cut, and removed – and then replaced with a 'correct' sequence.
    - And the tools used to achieve this are not

mechanical, but biochemical – specific protein and RNA molecules.

- The technology replicates a natural defence mechanism in some bacteria that uses a similar method to protect itself from virus attacks.
- The CRISPR-Cas9 system consists of two key molecules that introduce a change mutation into the DNA.
    - **Cas9**– An enzyme that acts as a pair of 'molecular scissors' that can cut the two strands of DNA at a specific location in the genome.
    - **Guide RNA (gRNA)-** The gRNA is designed to find and bind to a specific sequence in the DNA.
- Depending on the nature of the edit that is carried out, the process is divided into three categories – **SDN 1, SDN 2 and SDN 3**.
    - **SDN1** introduces changes in the host genome's DNA through small insertions/deletions without introduction of foreign genetic material.
    - In the case of **SDN 2,** the edit involves using a small DNA template to generate specific changes.
    - Both these processes do not involve alien genetic material and the end result is indistinguishable from conventionally bred crop varieties.
    - The **SDN3** process involves larger DNA elements or full length genes of foreign origin which makes it similar to genetically modified organisms (GMO) development.




## ***Technology in action***

- The first task is to identify the particular sequence of genes that is the cause of the trouble.
    - Once that is done, an RNA molecule is programmed to locate this sequence on the DNA strand, just like the 'find' or 'search' function on a computer.
    - After this, a special protein called Cas9, which is often described as 'genetic scissors', is used to break the DNA strand at specific points, and remove the bad sequence.
- A DNA strand, when broken, has a natural tendency to re-attach and heal itself.
    - But if the auto-repair mechanism is allowed to continue, the bad sequence can regrow.
    - So, scientists intervene during the auto-repair process by supplying the correct sequence of genetic codes, which attaches to the broken DNA strand.
    - It is like cutting out the damaged part of a long zipper, and replacing it with a normally functioning part.
- The entire process is programmable, and has remarkable efficiency, though chances of error are not entirely

ruled out.

## ***Applications of CRISPR Technology***

- **Health**-A vast number of diseases and disorders are genetic in nature that is, they are caused by unwanted changes or mutations in genes.
    - These include common blood disorders like sickle cell anaemia, eye diseases including colour blindness, several types of cancer, diabetes, HIV, and liver and heart diseases.
    - Many of these are hereditary as well. This technology opens up the possibility of finding a permanent cure to many of these diseases.
    - In India **CSIR's Institute of Genomics and Integrative Biology** have indigenously developed a CRISPR-based therapeutic solution for sickle cell anaemia, which is now being readied for clinical trials.
- **Gene abnormalities** -This is also true for the deformities arising out of abnormalities in gene sequences, like stunted or slow growth, speech disorders, or inability to stand or walk.
    - Also, CRISPR is just a platform; a tool to edit gene sequences. What is to be edited, and where, is different in different cases.
    - Therefore, a specific solution needs to be devised for every disease or disorder that is to be corrected.
    - The solutions could be specific to particular population or racial groups, since these are also dependent on genes.
- **CRISPR-based therapeutic solutions** are not in the form of a pill or drug.
    - Instead, some cells of every patient are extracted, the genes are edited in the laboratory, and the corrected genes are then re-injected into

the patients.
    - These mainly pertain to blood disorders, diabetes, inherited eye diseases, and some kinds of cancers.
    - The case of Victoria Gray, suffering from sickle cell anaemia, who was in the first batch of patients who were treated using CRISPR-based solutions, has been widely tracked.
        - Gray is now considered cured of the disease. Several others who volunteered with her for the trials too have responded positively to the treatment.
- **Agriculture –**Japan has already approved the commercial cultivation of a tomato variety that has been improved using CRISPR-based intervention.
- **Performance** -Increasing the tolerance of soldiers against biological or chemical warfare. This technology has the potential to influence human performance optimization.
- **Create animal models** to mimic human diseases and to understand disease development by mutating or silencing genes.
- **Commercial:**CRISPR was first used for commercial purposes to make bacterial cultures used in cheese and yoghurt production resistant to viral infections.

***The advantages of this technology***

- **Faster and Cheaper**– It is faster and cheaper than previous techniques of editing DNA.
- **High accuracy**– Genetic engineering has made the work more accurate by allowing scientists to have greater control on trait development.
- **Viable compared to GMO**– CRISPR technology proves viable against the criticisms of Genetically Modified Organisms (GMO).

***Issues associated with this Technology***

- **Misuse**-Because of CRISPR's power to induce dramatic changes in an individual, scientists, including the main developer Doudna, have been warning of the potential for misuse of the technology.
- **Designer Baby**-In 2018, a Chinese researcher disclosed that he had altered the genes of a human embryo to prevent the infection of HIV.
    - This was the first documented case of creating a 'designer baby', and it caused widespread concern in the scientific community.
- Preventive interventions to obtain special traits is not something that scientists currently want the technology to be used for.
    - Also, because the changes were made in the embryo itself, the new acquired traits were likely to be passed to future generations.
    - Though the technology is fairly accurate, it is not 100 per cent precise, and could induce a few errors as well, making changes in other genes.
    - This has the possibility of being inherited by successive generations.
- **Impact Diversity**– Diversity in all species of animals is a key to evolution on earth. Genetically engineering our species will have a detrimental effect on our genetic diversity- as in something like cloning would.

***WayForward***

- Investment in Research and development along with global collaboration to utilise this technology for solving some of the pressing issues faced by mankind like hunger, malnutrition, diseases etc.
- Evolving a code of ethics and conduct for the scientist working with the technology to ensure it is used responsibly and in the right spirit.
- India must evolve a robust legal and regulatory framework to prevent its possible misuse.

## Mould your thoughts

1. Discuss the working mechanism of CRISPR Technology. Also enumerate its possible applications and ethical issues involved with its use. (250 words)

## Approach to the answer

- About CRISPR
- Working mechanism
- Possible applications
- Ethical issues involved
- Wayforward and Conclusion