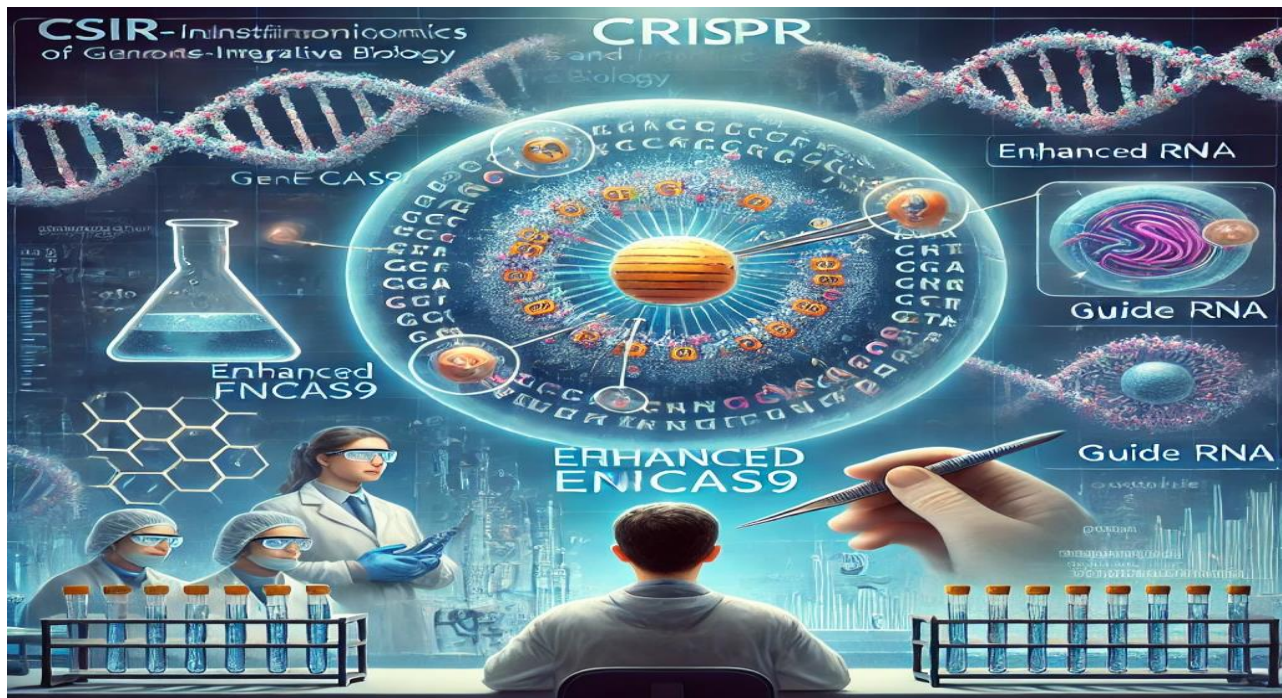


# UNDERSTANDING CRISPR: AN INDIAN BREAKTHROUGH IN GENE EDITING – PAPER - III



## The scientific advancements in gene editing with the enhanced FnCas9 CRISPR tool

### What is CRISPR?

CRISPR is a revolutionary tool in the field of genetics and biotechnology. The term stands for "Clustered Regularly Interspaced Short Palindromic Repeats," which refers to a natural defense mechanism found in some bacteria. Bacteria use CRISPR to defend themselves against viruses by storing snippets of viral DNA and using them to recognize and destroy these viruses in the future.

In recent years, scientists have adapted this bacterial system to edit genes in other organisms, including plants, animals, and humans. This adaptation has been groundbreaking because it allows for precise modifications to DNA, potentially fixing genetic disorders and improving various aspects of biology and medicine.

### How CRISPR Works

CRISPR works like a pair of molecular scissors that can cut DNA at specific locations. Here's a simplified explanation of its process:

- **Guide RNA (gRNA):** This is a short piece of RNA designed to match a specific sequence in the target DNA. It serves as a guide for the CRISPR system, directing it to the exact location where editing is needed.
- **Cas9 Enzyme:** Cas9 is a protein that acts like a pair of scissors. It follows the guide RNA to the target DNA sequence and makes a cut in the DNA.
- **PAM Sequence:** This is a short DNA sequence next to the target DNA sequence that helps the Cas9 enzyme to locate and bind to the correct part of the DNA.
- **DNA Repair:** After the DNA is cut, the cell's natural repair mechanisms kick in. Scientists can use this repair process to introduce new genetic material or correct mutations in the DNA.

By using this process, researchers can add, remove, or alter specific genes in the genome, which has tremendous applications in medicine, agriculture, and more.

## Problems with CRISPR

While CRISPR has many advantages, it also has some significant problems:

- **Off-Target Effects:** One major issue is that CRISPR can sometimes cut the DNA at unintended locations. These "off-target" effects can lead to unintended changes in the genome, which can potentially cause problems or side effects.
- **Efficiency vs. Precision:** Older versions of CRISPR, such as those using the SpCas9 enzyme, are either precise but less efficient or efficient but prone to off-target effects. Balancing these two factors has been a challenge.

## How Indian Innovation Resolved the Problems

In recent developments, scientists from the CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB) in New Delhi have made significant strides in improving CRISPR technology. Here's how they addressed the problems:

- **Switching Enzymes:** The team explored a different enzyme, called FnCas9, derived from the *Francisella novicida* bacteria. FnCas9 is known for its high precision but was less efficient.
- **Enhancing Precision and Efficiency:** Researchers, led by Debojyoti Chakraborty and Souvik Maiti, modified the FnCas9 enzyme to improve its efficiency without compromising its precision. They adjusted the enzyme's interaction with the PAM sequence, increasing its binding strength and making the gene editing process more effective.

- **Improved Performance:** The enhanced FnCas9, or enFnCas9, showed improved cutting rates and precision compared to both the original FnCas9 and other CRISPR systems. This new version can target almost twice as many genetic changes as previous versions, reducing the likelihood of off-target effects.

## Who Are Involved in This Innovation

The key figures in this Indian innovation include:

- **Debojyoti Chakraborty and Souvik Maiti:** Scientists from CSIR-IGIB who led the research to enhance the FnCas9 enzyme.
- **Indumathi Mariappan:** A researcher from the L.V. Prasad Eye Institute in Hyderabad, who tested the new enzyme's effectiveness in treating genetic disorders.
- **Shailja Singh:** A researcher at Jawaharlal Nehru University, who emphasizes the importance of precise CRISPR tools in genetic disease research.

These scientists and their teams have played a crucial role in advancing gene-editing technology and making it more reliable.

## Benefits of Enhanced CRISPR Technology

The improved CRISPR technology offers several benefits:

- **Higher Precision:** The enhanced FnCas9 enzyme makes gene editing more accurate, reducing the risk of unintended changes to the genome.
- **Increased Efficiency:** The new version of CRISPR can make edits more effectively, increasing its usefulness for various applications.
- **Better Diagnostics:** The improved system can identify and correct genetic mutations more efficiently, which is crucial for diagnosing and treating genetic disorders.
- **Potential for Therapies:** The new CRISPR technology holds promise for developing treatments for genetic diseases, such as inherited blindness, by correcting mutations in patients' cells.

## Significance to India

The development of this enhanced CRISPR technology has significant implications for India:

- **Affordable Therapeutics:** By developing this technology locally, India can create more affordable treatments for genetic disorders, which is crucial for a country with a large population and significant healthcare needs.
- **Reducing Dependence:** With indigenous technology, India can reduce its dependence on foreign licenses and technology, which can be expensive.
- **Advancing Research:** This breakthrough positions India as a leader in gene-editing research and could attract international collaborations and investments in biotechnology.

- **Improving Healthcare:** The new technology has the potential to improve healthcare outcomes in India by providing more precise and effective treatments for genetic diseases, ultimately benefiting millions of people.

In conclusion, the recent advancements in CRISPR technology by Indian scientists represent a significant leap forward in genetic engineering. By enhancing precision and efficiency, this new tool has the potential to transform medical research and treatment, making it a valuable asset for both India and the global scientific community.

## MAIN PRACTICE QUESTIONS

### Question 1:

**Describe the enhanced CRISPR technology developed by Indian scientists and explain how it addresses the limitations of previous CRISPR systems.**

### Answer Outline:

#### 1. Introduction

- Brief overview of CRISPR technology and its significance.

#### 2. Limitations of Previous CRISPR Systems

- **Off-Target Effects:** Explanation of unintended cuts in DNA.
- **Efficiency vs. Precision:** Trade-offs in older CRISPR versions like SpCas9.

#### 3. Indian Innovation

- **New Enzyme:** Introduction to FnCas9 from *Francisella novicida*.
- **Enhancements Made:** Modifications to FnCas9 by CSIR-IGIB scientists.
  - Increased binding affinity with PAM sequence.
  - Enhanced flexibility and access to hard-to-reach genome regions.

#### 4. Impact of Enhanced FnCas9

- **Precision Improvements:** Reduction in off-target effects.
- **Increased Efficiency:** Higher rate of successful gene edits.
- **Applications in Diagnostics and Therapeutics:** Broader scope for detecting and treating genetic mutations.

#### 5. Conclusion

- Summary of the significance of the enhanced CRISPR technology and its implications for future research and applications.

## Question 2:

**Discuss the significance of the enhanced CRISPR technology for India, particularly in terms of its impact on healthcare and biotechnology.**

### Answer Outline:

#### 1. Introduction

- Overview of CRISPR technology and its general applications.

#### 2. Significance for Indian Healthcare

- **Affordable Therapeutics:** Potential to reduce costs of genetic disease treatments.
- **Improved Treatment Options:** Enhanced precision for treating genetic disorders like inherited blindness.

#### 3. Impact on Indian Biotechnology

- **Reducing Dependence:** Local development of technology reduces reliance on expensive foreign licenses.
- **Advancing Research:** Positions India as a leader in cutting-edge genetic research.

#### 4. Economic and Social Benefits

- **Cost-Effective Solutions:** Benefits for low- and middle-income populations.
- **Research and Development:** Encouragement of international collaborations and investments.

#### 5. Conclusion

- Summary of how the enhanced CRISPR technology benefits India's healthcare system, biotechnology sector, and overall scientific advancement.