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CURRENT AFFAIRS

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"A CRISPR TECHNOLOGY BUILT TO USE THE FNCAS9 ENZYME"

This article covers "Daily Current Affairs" and details the topic of CRISPR technology and its new version based on the FnCas9 enzyme.

Syllabus mapping: GS-3-Science and Technology-Biotechnology: Awareness in the fields of biotechnology.

For Prelims:

What are the terms related to the CRISPR technology?

For Mains:

What is the mechanism of CRISPR technology, the application of this technology in various fields, and issues related to the technology?

Why In the News?

A CRISPR technology built to use the **FnCas9** enzyme was found to edit genomes more efficiently and with less unintended damage than existing technologies.

What is the CRISPR technology: (Clustered Regularly Interspaced Short Palindromic Repeats)

Origin: CRISPR was first discovered in bacteria, where it functions as an adaptive immune system to protect against viruses. Bacteria and archaea use CRISPR to store segments of viral DNA (called spacers) and use them to recognize and cut the DNA of invading viruses during subsequent infections.

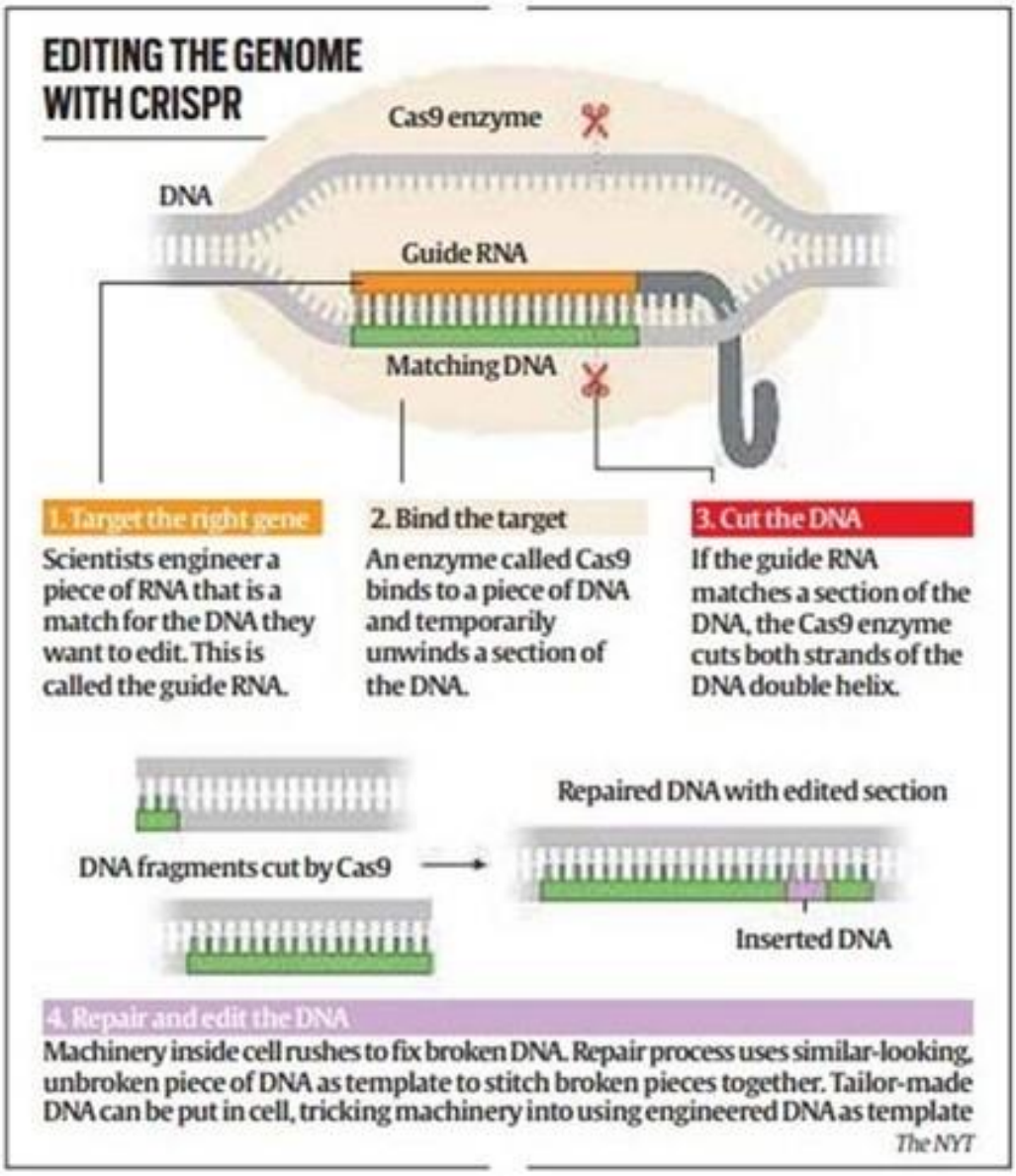
This technology does not involve introducing new genes from external sources, a method that has been utilized for many years, especially in agriculture. For instance, genetically modified crops like BT Cotton in India are an example of this technique.

Components:

1. **CRISPR Arrays**: These are sequences of DNA containing short, repeated sequences interspersed with "spacer" sequences derived from previous viral infections.
2. **CRISPR-associated (Cas) Proteins:** These are endonucleases that are guided by the CRISPR RNA to target and cut specific DNA sequences. The most well-known Cas protein is Cas9.

The working mechanism of CRISPR:

1. **Guide RNA (gRNA):** A synthetic RNA molecule that directs the Cas protein to the specific location in the target DNA sequence.
2. **Cas Protein:** The Cas9 protein (or other Cas variants) is guided by the gRNA to the target DNA where it makes a double-strand break.
3. **DNA Repair:** The cell's natural repair mechanisms then attempt to repair the break. This can lead to gene knockouts or insertions if a new piece of DNA is provided.



Recent Advancement: "Switching SpCas9 with FnCas9"

CRISPR-Cas9: Cas9: Acts as a molecular scissor, cutting DNA at the target site. The main function of CRISPR-Cas 9 is to **add, remove, or alter DNA sequences in genomes.**

Issue with SpCas9:

1. **Off-Target Effects:** SpCas9 can cut unintended parts of the genome, leading to potential off-target effects.
2. **High Fidelity vs. Efficiency:** Engineering SpCas9 for higher specificity often reduces its editing efficiency.

Exploring FnCas9: The Cas9 enzyme from Francisella novicida bacteria (FnCas9) is highly precise in targeting specific DNA sequences. However, Initial FnCas9 has low efficiency compared to SpCas9. So the following enhancements have been made:

1. **Amino Acid Modifications**: Altered amino acids in FnCas9 that interact with the PAM sequence to increase binding affinity.
2. **Increased Binding Affinity:** Stronger configuration of Cas9 on DNA improves gene editing effectiveness.
3. **Flexibility:** Enhanced FnCas9 is more adaptable and capable of accessing harder-to-reach regions of the genome.

Impact:

1. **Improved Specificity**: Reduced off-target effects.
2. **Increased Efficiency:** Enhanced ability to edit specific DNA regions effectively.
3. **Expanded Editing Potential:** Opens new avenues for gene editing applications.

Variants and Innovations

Cas9 Variants:

SpCas9: Derived from *Streptococcus pyogenes*, the most commonly used Cas9 protein.

FnCas9: From *Francisella novicida*, smaller and potentially more versatile.

AsCas12a: A smaller Cas protein with different properties and applications.

Other CRISPR Systems:

CRISPR/Cas12 (Cpf1): An alternative system with different cutting mechanisms and potential advantages for certain applications.

CRISPR/Cas13: Targets RNA instead of DNA, useful for applications involving RNA viruses and gene regulation.

Base Editing: A technique that allows for precise changes to individual DNA bases without causing double-strand breaks.

Prime Editing: A newer technique that enables highly accurate edits and insertions with fewer off-target effects.

Applications of the CRISPR:

1. **Gene Editing:** This system involves the editing of genetic material which has vast potential in various fields.
2. **Genetic Disorders:** Correcting mutations associated with diseases such as cystic fibrosis, sickle cell anemia, and muscular dystrophy.
3. **Cancer:** Editing immune cells to better target and destroy cancer cells.
4. **Crop Improvement:** Creating crops with desirable traits such as pest resistance, drought tolerance, or improved nutritional content.
5. **Livestock:** Developing genetically modified animals with enhanced traits or disease resistance.
6. **Functional Genomics:** Studying gene function and interactions by creating precise genetic modifications.
7. **Model Organisms:** Generating animal models with specific genetic traits for research purposes.

Ethical and Safety Considerations

1. **Off-Target Effects:** Unintended edits in the genome that could lead to unintended consequences.
2. **Germline Editing:** Editing the genomes of embryos or germ cells raises ethical concerns and potential long-term effects on future generations.
3. **Regulations:** Different countries have varying regulations and guidelines regarding the use of CRISPR technology, especially in human germline editing.

Regulatory Framework

Regulatory Framework in India:

1. **Genetic Engineering Appraisal Committee (GEAC)**: The GEAC, under the Ministry of Environment, Forest and Climate Change, is responsible for assessing and approving genetically modified organisms (GMOs) and products. It oversees the regulatory processes for new biotechnologies, **including CRISPR-edited crops.**
2. **Department of Biotechnology (DBT)**: The DBT, part of the Ministry of Science and Technology, supports and regulates biotechnological research and development in India. It provides guidelines for the use of genetic engineering techniques, including CRISPR.

International framework:

1. **World Health Organization (WHO):** Provides international guidelines and recommendations for the use of genetic engineering technologies, including CRISPR, focusing on safety and ethical issues.

2. **International Society for Stem Cell Research (ISSCR):** Provides ethical guidelines and best practices for stem cell research and gene editing, including CRISPR technologies.

Ways to make proper and efficient use of CRISPR technology:

1. **Off-Target Effects:** Implement strategies to minimize off-target effects, such as using advanced CRISPR variants or optimizing guide RNAs.

2. **Biosafety:** Adhere to biosafety protocols to prevent accidental release or misuse of CRISPR-edited organisms.

3. **Collaboration:** Foster interdisciplinary collaboration to leverage expertise in genomics, molecular biology, and bioinformatics.

4. **Standardization**: Develop and adhere to standard protocols for CRISPR experiments to ensure reproducibility and consistency.

5. **Regulation:** Comply with national and international regulations governing CRISPR technology, including those related to gene editing, GMOs, and clinical trials.

6. **Regulatory Harmony:** Work towards harmonizing regulations and guidelines across countries to facilitate international research and commercialization of CRISPR technologies

7. **Ethical Considerations:** Address ethical concerns, especially in sensitive areas like germline editing and human genetic modifications.

Conclusion:

CRISPR represents a powerful tool with vast potential across numerous fields. Its development continues to evolve, offering new possibilities and presenting ongoing challenges and ethical considerations.

PRELIMS QUESTION:

Q. In which of the following is CRISPR technology used?

1. Genetic disease treatments such as cystic fibrosis, sickle cell anemia, and muscular dystrophy.

2. Introduction of the new genes in the maize crop.

3. To improve the nutritional value of plants and increase their yield.

How many of the statements given above are correct?

(a) Only one

(b) Only two

(c) All three

(d) None

ANSWER: b

MAINS QUESTION

The need is to balance the rapid advancements in CRISPR technology with stringent ethical and safety regulations to ensure responsible use and prevent potential misuse. Discuss?

(150 words 10 marks)

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