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Genetics and Society

Gene Editing

Factsheet

All About Gene Editing

What is gene editing?

Gene editing or genome editing is a process where the DNA sequence of living organisms like plants, animals or microorganisms is altered in a precise, controlled manner using DNA editing technologies. Through this process, genetic material can be inserted into, replaced or deleted from a DNA sequence. Such alterations allow scientists to obtain desired outcomes in the expression of genes or traits.

Tools for gene editing

Gene editing can be performed with a variety of engineered nucleases such as transcription activator-like effector nucleases (TALENs), zinc-finger nucleases (ZFNs), and homing endonucleases or meganucleases (MNs). But the recently developed clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated protein 9 (Cas9) has been a game changer.

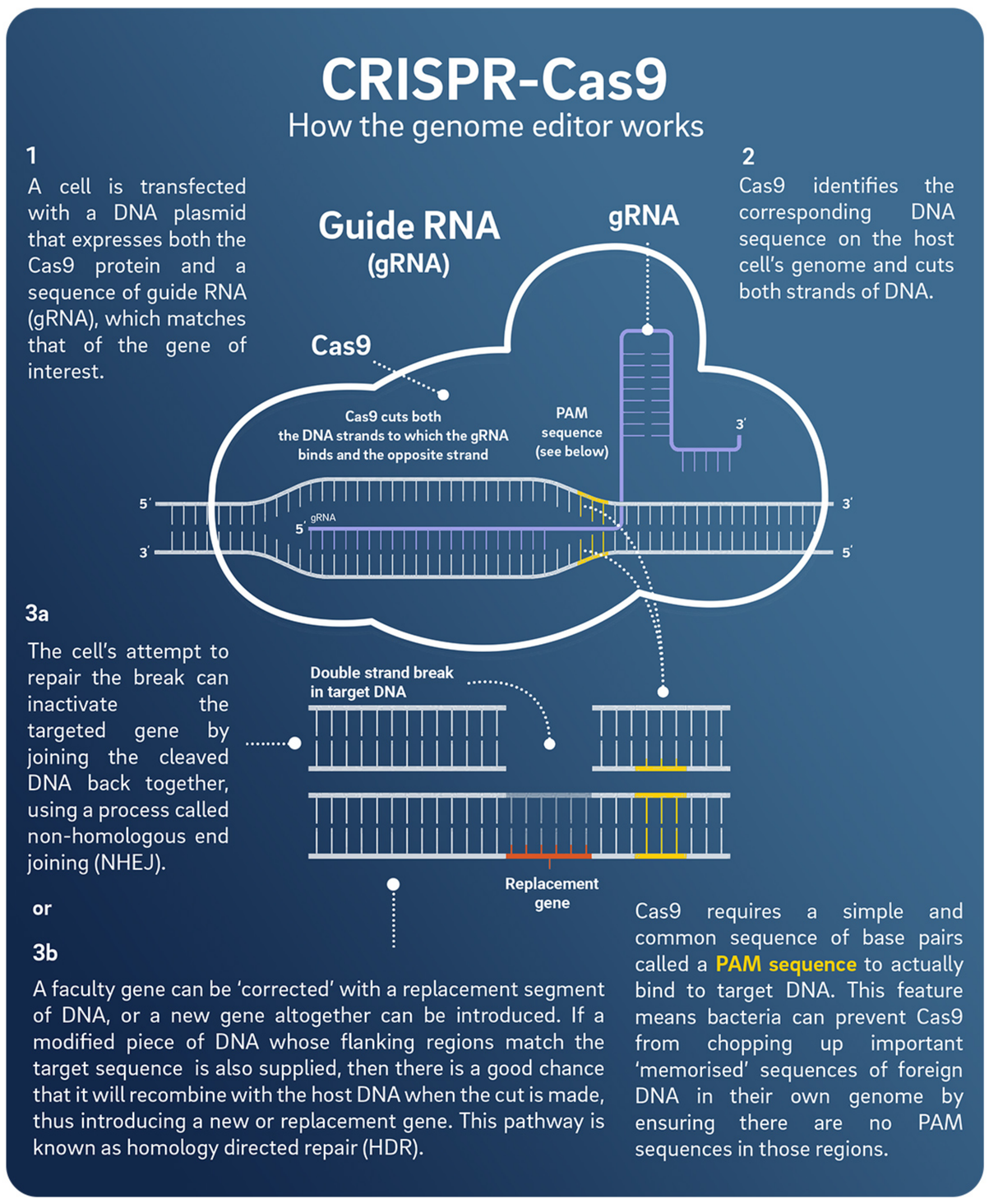
Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR):

Credit: Alexander Heinel/Picture Alliance/DPA

Emmanuelle Charpentier and Jennifer Doudna revolutionized the gene editing space with their CRISPR/Cas9 discovery. They won the Nobel Prize in Chemistry 2020 for their contributions. CRISPR-Cas is a big leap from earlier gene editing technologies because it is faster, easier, cheaper and more precise.

The CRISPR-Cas9 system, which is a natural component of the bacterial immune system employed to fight off viruses, consists of two parts. The first is the Cas9 enzyme, an endonuclease, which functions as a pair of "molecular scissors". This pair of scissors can cleave DNA strands in the genome.

The second component, the guide RNA (gRNA), is a very specific RNA sequence that identifies the DNA sequence of interest, binds with it and thereby guides the Cas9 enzyme to the specific site for making cuts to both strands of the DNA double helix at a precise location. When this happens, the living cell has the capacity to identify the damaged DNA strands and initiate their repair. By using this DNA repair mechanism, scientists can introduce changes to the DNA sequence at the target site.

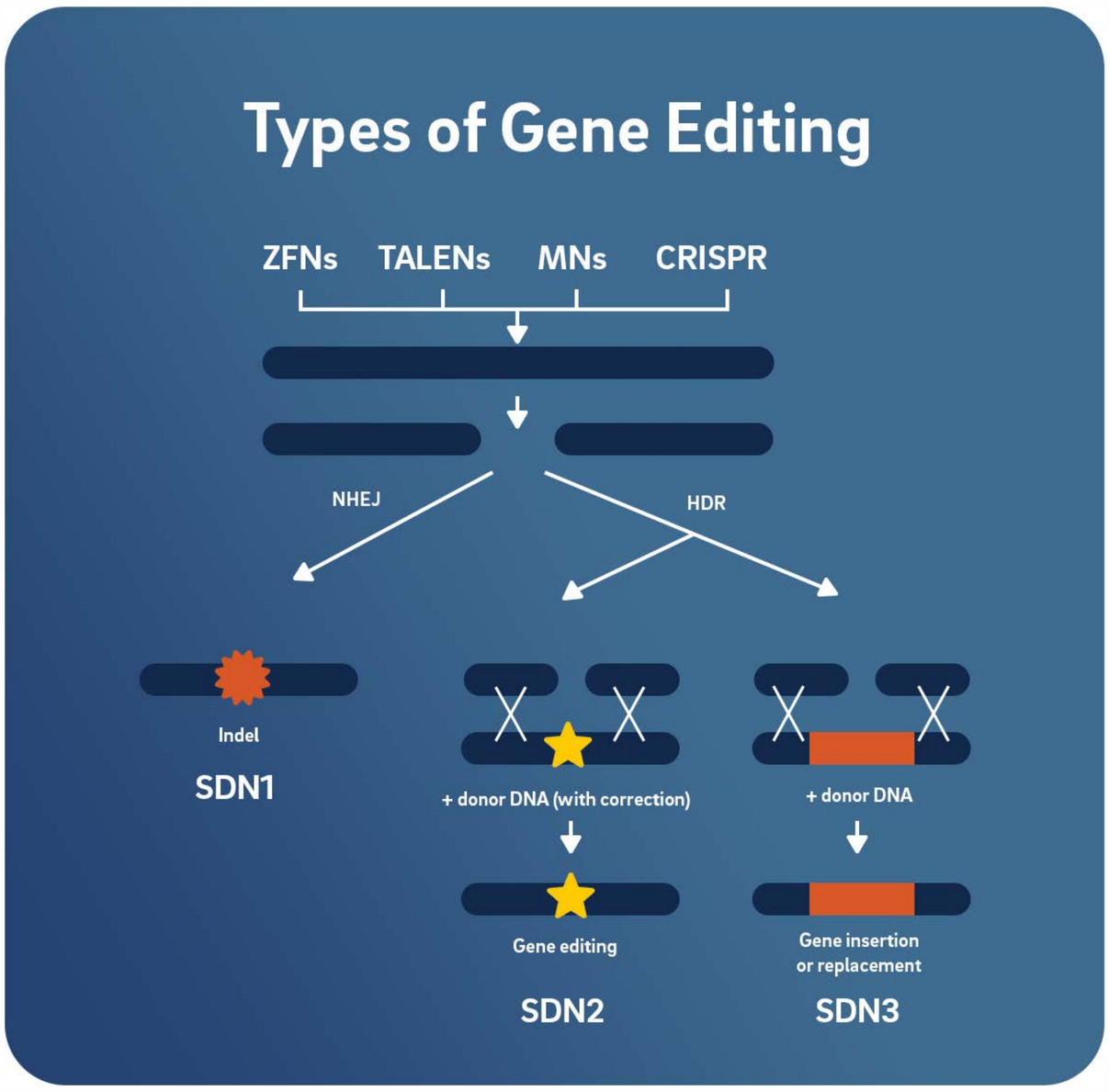


Adapted from https://commons.wikimedia.org/wiki/File:CRISPR-Cas9-biologist.jpg

Genome editing can be done using three different approaches:

Site-Directed Nuclease (SDN) 1
a double-stranded break is made in the DNA. Spontaneous repair of this break by the cell's own mechanism through non-homologous end joining (NHEJ) can lead to insertion or deletion (indel) of a few nucleotides causing gene silencing, gene knock-out or a change in the activity of a gene.

Site-Directed Nuclease (SDN) 2
produces a double-stranded break, and while the break is repaired by the cell, a small nucleotide template, which is complementary to the area of the break, with small sequence changes in the genomic code is supplied. While this is used by the cell to repair the break by homology directed repair (HDR), the changes in the supplied template cause mutation/s of the target gene.



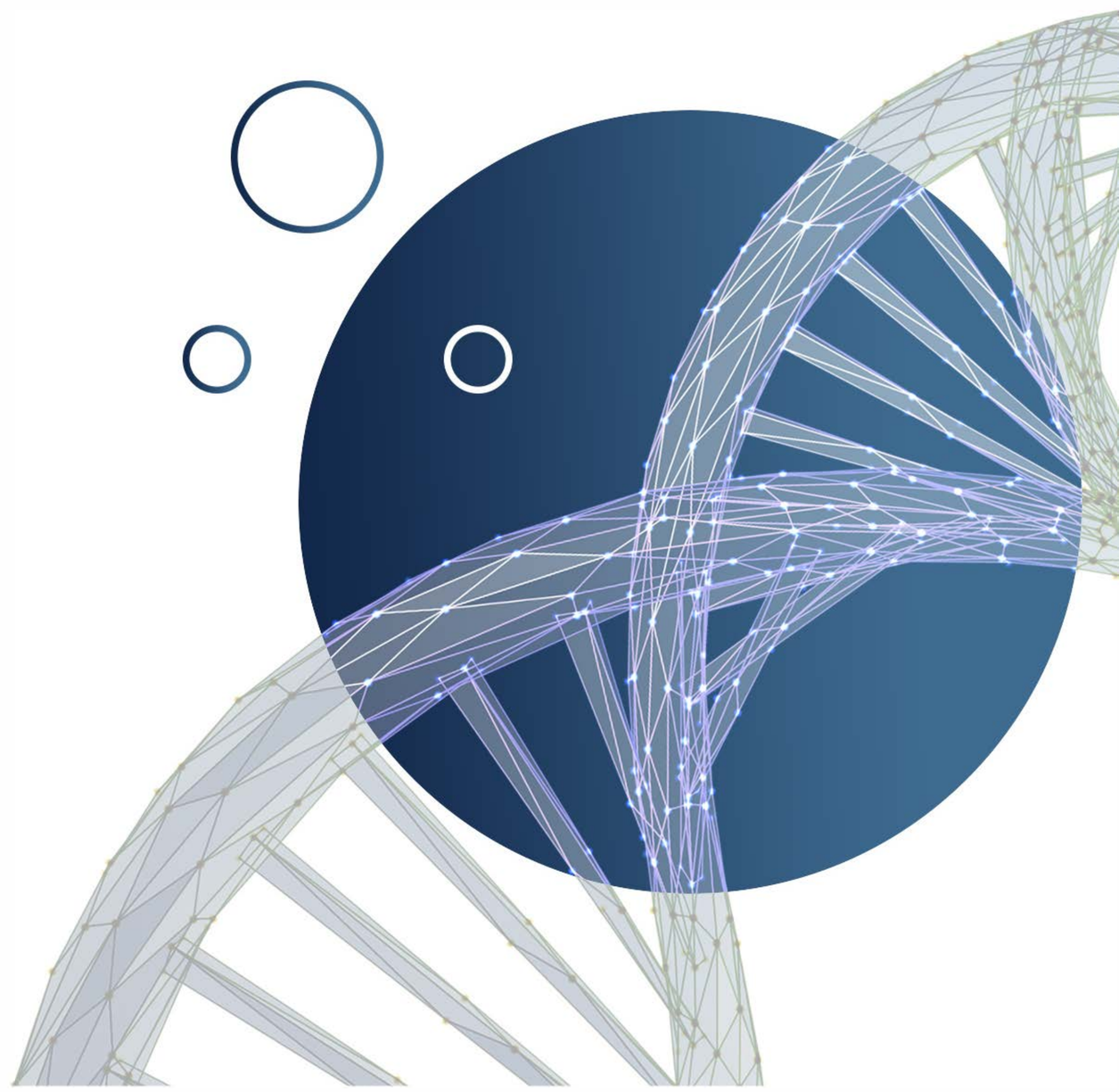
Site-Directed Nuclease (SDN) 3 - also induces a double-stranded break in the DNA, but is accompanied by a template containing a foreign gene. The cell's natural repair process then utilizes this template to repair the break through HDR resulting in the introduction of the foreign DNA fragment with a new trait of interest.

When SDN1 and SDN2 approaches are used, the CRISPR components that have been used to edit the selected native genes for obtaining desirable traits can easily be removed by segregation in the next and subsequent generations. Therefore, these approaches can be used to develop gene edited organisms free from any foreign DNA and indistinguishable from the organism already existing in the environment.

Gene edited organisms are different from genetically modified organisms.

The outcomes of gene editing and gene modification are often mistakenly understood to be synonymous. However, there is a clear difference between both these terms. 'Gene edited' organisms are those whose genomes have been altered at a precise site using tools like CRISPR, to knock out or replace specific genes to obtain desired outcomes that are very similar to those occurring naturally in nature.

'Genetically engineered' organisms (loosely termed as Genetically Modified Organisms – GMO) are those which have been created by the insertion of a foreign gene, known as a 'transgene', to get a desired outcome. Some examples are the pest resistance genes from *Bacillus thuringienis* (bacteria) in the case of Bt cotton and corn, and a growth hormone-regulating gene in the case of AquAdvantage® salmon.



Since genetically modified organisms contain transgenes, they require stringent risk assessment studies before they can be put to actual use. But in the case of certain categories of gene editing, which do not include the insertion of any foreign gene, a gene edited organism is indistinguishable from organisms that exist in nature, and therefore has lesser requirements for regulatory oversight in certain countries.

The Future of Gene Editing

Applications of gene editing technologies

Improvement of climate resilient crop varieties

Treatment of monogenic human disorders

Fitter, healthier, and more productive farmed animals

New diagnostic methodologies

Biodiversity conservation

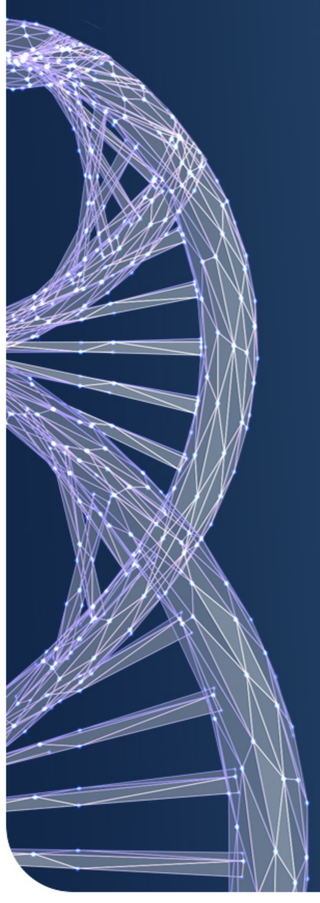
Drug and vaccine development

Development of animal models to understand diseases

Manufacturing biopharmaceuticals and nutraceuticals

Creation of gene drives to fight vector borne diseases

Upcoming promising developments



Disease modeling: To understand the intricacies of how a disease develops for exploring various management and treatment approaches

Gene Therapy: For therapeutic delivery of specific nucleic acids to treat inherited diseases, some types of cancer and viral infections. E.g., cancer immunotherapies

Advanced diagnostic tools: For assessing predisposition to develop certain diseases and explore predictive medicine pathways

Gene Editing in India

Recent achievements & the way forward

Indian scientists are making great progress in using gene-editing to develop pest resistant or nutritionally improved food crop varieties like banana, tomato, rice, millets, pulses and oilseeds.

The revolutionary CRISPR based FELUDA test was developed by a research team at the CSIR-Institute of Genomics and Integrative Biology and was approved by the Drug Controller General of India (DCGI) for commercial launch as it was a more accurate, cheaper and faster alternative to RT-PCR tests for detecting COVID-19 positive cases. The same lab has recently developed a similar paper test known as RAY to rapidly detect a COVID19 variant, which was first detected in the UK.

These are just a few examples of applications of gene editing from the Indian research community. There are a host of other areas in agriculture and human health where work with this new technology has been initiated. The Indian government is developing an enabling environment with newer facilities and guidelines to provide directions.

The COVID-19 pandemic has shifted focus towards the use of fast, cost effective and innovative technologies for the betterment of humanity, and the years to come look promising for leveraging gene editing technologies to safeguard public health and food security in India.

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