

# Novas Técnicas Genómicas

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## **BIOTECNOLOGIA**

“Qualquer tecnologia que utilize sistemas biológicos, organismos vivos, ou seus derivados, para fabricar ou modificar produtos ou processos para uma utilização específica.”

(ONU, Convenção de Biodiversidade 1992, Art. 2)

BIOTECHNOLOGY TIMELINE CELEBRATING INNOVATION IN BIOTECHNOLOGY

The Evolution of the Revolution

**8,000 BC**  
Biotechnology begins, as humans begin choosing or altering plants and livestock so they can be domesticated. Potatoes become the first cultivated food.

**300 BC**  
Greeks develop grafting techniques for plant breeding.

**1663**  
English physicist, mathematician and inventor Robert Hooke discovers the existence of the cell.

**1796**  
First small pox vaccine is discovered. Edward Jenner discovered the process of vaccination by inoculating a small boy with cowpox and then trying to re-infect him with smallpox. The boy recovered from the weaker cowpox infection and thus became immune to smallpox. The cowpox virus was called 'Vaccinia', from the Latin word for cow, 'Vacca'. This is how the word 'Vaccine' came into use.

**1839-1855**  
German scientists Matthias Schleiden and Theodor Schwann propose that all organisms are composed of cells. Prussian physician Rudolf Virchow declares: "Every cell originates from another cell."

**1861**  
French chemist Louis Pasteur develops pasteurization, a process that protects food by heating it to kill dangerous microbes.

**1865**  
After seven years of cultivating and testing thousands of pea plants, Gregor Mendel publishes a description of rules governing how hereditary traits pass between generations, the foundation of modern genetics.

**1870-1910**  
Father of modern plant breeding Luther Burbank develops over 800 new strains of fruits, vegetables and flowers. His blight-resistant Burbank potato is heavily planted across Ireland, ending the potato famine. Botanist William James Beal produces the first experimental corn hybrid in the laboratory.

**1885**  
Vaccine for Babi's disease discovered. Pasteur vaccinated a young boy who had been bitten by a rabid dog. This vaccine was made from the extract of the spinal column of a rabies infected rabbit. A modified version of this vaccination is still used today, and has saved thousands of lives.

**1859**  
Charles Darwin's landmark book, The Origin of Species is published.

**1838**  
Swedish chemist Anns Jakob Berzelius discovers proteins.

**1855**  
The Escherichia coli bacterium is discovered. It later becomes a major research, development and production tool for biotechnology.

**1833**  
First enzyme discovered and isolated.

**1590**  
Dutch spectacle-maker Jansen invents the microscope. Dutch student of natural history and microscope-maker Antoni van Leeuwenhoek discovers bacteria.

**2,000 BC**  
Egyptians and Sumerians learn brewing and cheese making.

**4,000 BC**  
Egyptians master the art of winemaking. In China, moldy soybean curds become the first antibiotic to treat infections and ailments.

**1919**  
The word **biotechnology** is used in print for the first time.

**1922**  
In Toronto, Dr. Frederick Banting and his assistant Charles Best discover insulin as a treatment for diabetes.

**1941**  
Danish microbiologist A. Justin coins the term **genetic engineering** a technique involving the transfer of a select piece of genetic material from one organism to another.

**1943**  
Canadian scientist Oswald Theodore Avery isolates pure DNA.

**1945**  
DNA is produced in a test tube for the first time.

**1946**  
Nobel Prize for the discovery of the 'Double Helix' structure of DNA. The Nobel Prize in Physiology or Medicine 1962 was awarded jointly to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".

**1953**  
James Watson and Francis Crick are the first to describe the double helix structure of DNA.

**1958**  
Nobel Prize for the discovery of the genetic codes of the 20 amino acids, leading researchers to later conclude that the genetic code is universal among all living things.

**1962**  
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**1966**  
Marshall W. Nirenberg and Har Gobind Khorana win the Nobel Prize for deciphering the genetic codes of the 20 amino acids, leading researchers to later conclude that the genetic code is universal among all living things.

**1970**  
Norman Borlaug becomes the first plant breeder to win a Nobel Prize, for his work on new wheat varieties that increase yields by 70 per cent. This marks the beginning of the Green Revolution in world agriculture.

**1970**  
American microbiologist Daniel Nathans discovers the first restriction enzyme that can cut DNA into pieces for various studies and applications. The restriction enzyme technique becomes a fundamental tool in modern genetic research, helping to create the biotechnology industry and providing the basis for the Human Genome Project.

**1971**  
First complete synthesis of a gene. First gene spliced DNA from different organisms.

**1973**  
Stanley Cohen and Herbert Boyer develop recombinant DNA technology. Considered to be the birth of modern biotechnology, they complete the first successful genetic engineering experiment by inserting a gene from an African clawed toad into bacterial DNA.

**1976**  
The sequence of nucleic acid base pairs that combine to make DNA is determined for the first time for a specific gene.

**1977**  
Herbert Boyer, founder of the pioneer biotechnology firm Genentech, uses E. coli bacteria to produce human insulin. The technique represents a significant improvement in the efficiency and long term viability of producing this vital medical therapy, formerly extracted from limited supplies of animal tissues that could lead to allergic reactions. The vast majority of insulin used in the today is now produced through this recombinant method.

**1984**  
Genetic fingerprinting is discovered, which is used today to establish family relationships and to identify criminal suspects.

**1985**  
Chymosin, an enzyme used in cheese-making, becomes one of the first food products in Canada to be manufactured with recombinant techniques. Normally extracted from rennet, an enzyme complex found in the lining of a cow's stomach, chymosin is now produced directly in agents such as an escholi bacteria.

**1986**  
The first genetically engineered plants are grown outside in fields for the first time in the USA. They are genetically altered tobacco plants.

**1988**  
The first recombinant DNA vaccine for livestock is developed.

**1989**  
Discovery of defective gene for cystic fibrosis by Dr. Lap-Chee Tsui at Toronto's Hospital for Sick Children. Similar discoveries later link specific genes to other disorders, such as sickle cell, Huntington's Disease, and a rare heart problem known as Right Ventricular Cardiomyopathy. Each has added to a growing knowledge of the complex relationship between gene function and disease.

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**1990**  
The Human Genome Project is launched. This international, 13-year effort to determine the sequences of the three billion chemical base pairs that make up the DNA of a person, eventually identifies 20,000-25,000 genes.

**1997**  
The world meets Dolly the sheep, the first cloned mammal. UNESCO adopts the Universal Declaration on the Human Genome and Human Rights, recognizing the human genome as a common heritage that must be safeguarded from inappropriate manipulation.

**1998**  
The roundworm C. elegans becomes the first multi-cellular organism to have its genome completely sequenced.

**1999**  
German and Swiss scientists develop golden rice, fortified with beta-carotene, which stimulates production of Vitamin A, thus preventing forms of blindness.

**2005**  
The billionth biotech acre is planted by one of 8.5 million farmers in one of 21 countries.

**2007**  
First Vaccine against human papillomavirus for use by women and girls in more than 80 countries.

**2009**  
A Canadian team of scientists and engineers from the University of Toronto develop a microchip with nanoscale components to detect chemical markers for cancer, a technique that could make diagnosis much faster. The international Potato Genome Sequencing Consortium, releases a draft of the full sequence of genome of the potato, the world's third most important crop.

**2009**  
Winnipeg's National Microbiology Laboratory completes the first genetic sequencing of the H1N1 flu virus, just as the disease is reaching international pandemic proportions. Quebec-based firm Medicago grows H5N1 (bird flu) vaccine in tobacco leaves. The product becomes the first plant-based influenza vaccine to undergo human trials in Canada.

**2010**  
First synthetic cell. In May 2010, J. Craig Venter Institute created the first fully synthetic, self-replicating bacterial cell, which was named Synthia. While the U.S. government has plugged \$430 million into synthetic biology since 2005, most of it has gone toward developing alternative fuels. Some firms are now starting to leverage the technology for medical purposes.

**2011**  
Access to treatment for HIV/AIDS. The United Nations adopts a political declaration adopted committed to expanding access to treatment for AIDS for 15 million people by 2015. In Europe, measures are already in place to achieve this goal. European biotechnology scientists launched a clinical trial of an anti-HIV biotech medicine produced using genetically modified tobacco. A first of its kind study in the EU. If the Phase I study is successful, larger trials will follow and researchers foresee a new antibody which will be combined with other medication to offer better protection against HIV/AIDS at a far cheaper price, thus allowing wider access to treatment in poorer countries.

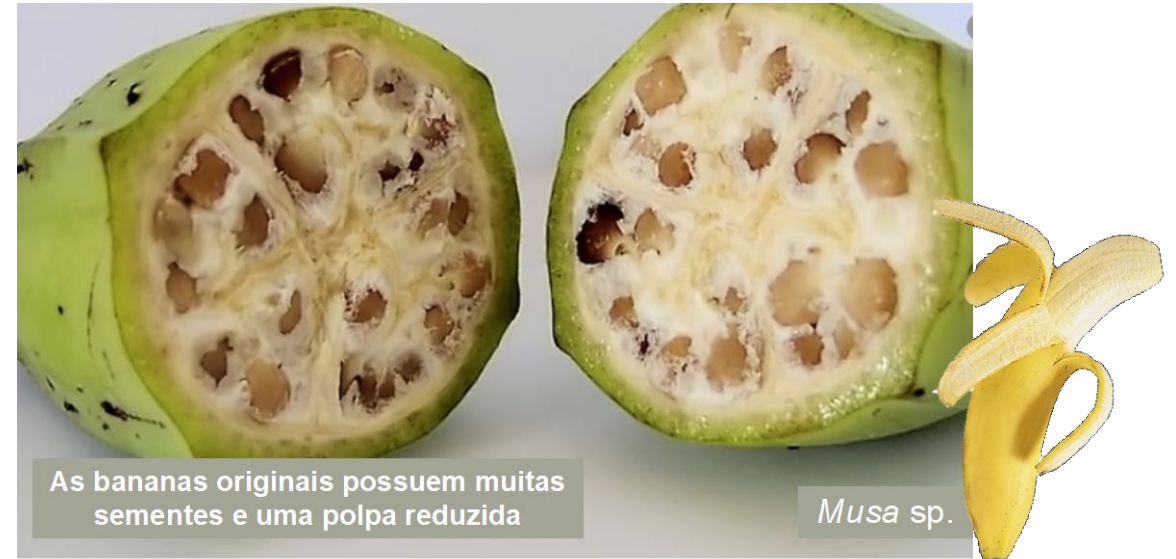
**2013**  
The first biotech eye has seen the light of day in the United States, giving hope to the blind around the world. Developed by Second Sight Medical Products, the Argus II Retinal Prosthesis System has helped more than 60 people recover partial sight, with some experiencing better results than others.

**2013**  
The world celebrates the 60th anniversary of Watson and Crick's discovery of the double helix.

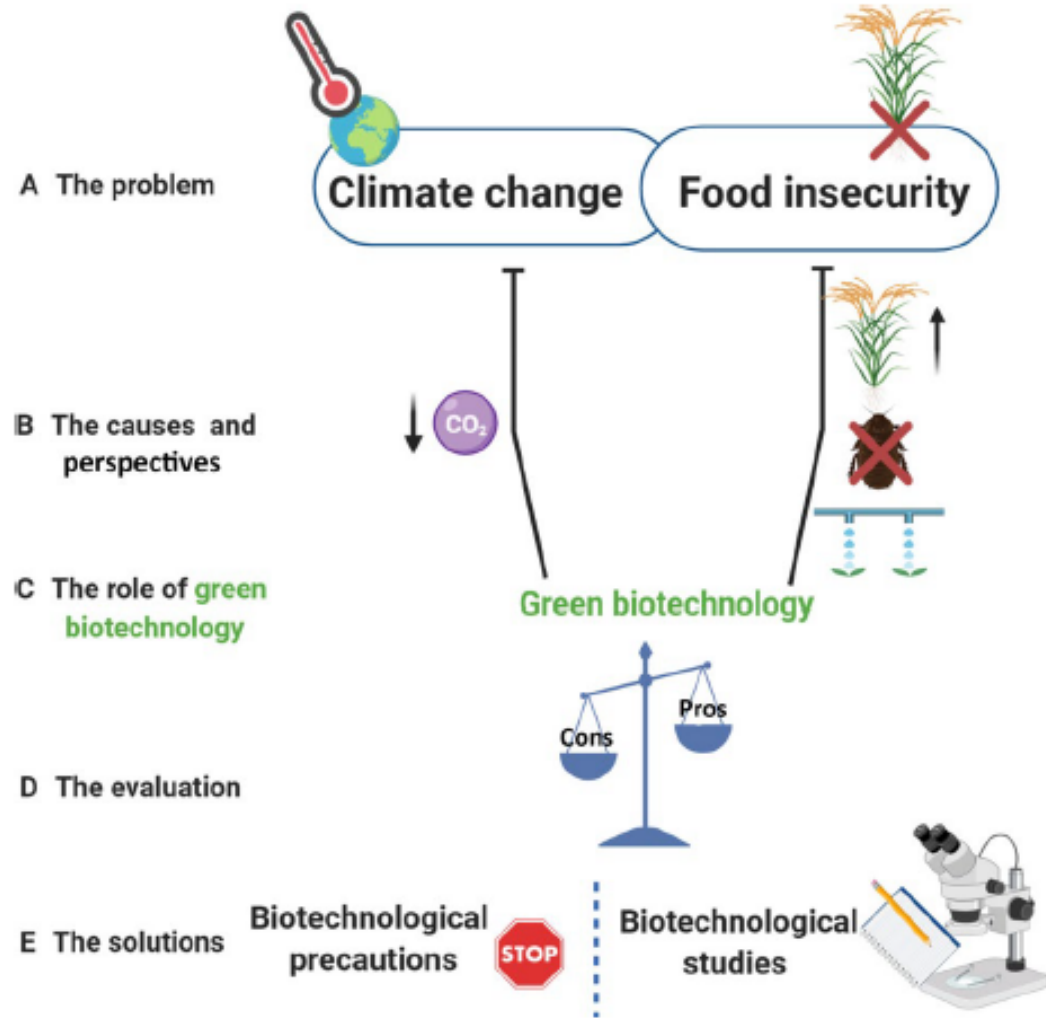
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Biotecnologia Verde pode ser definida como a aplicação de técnicas biotecnológicas em plantas, com o objetivo de modificar características das mesmas e contribuindo para uma agricultura mais eficiente e sustentável.

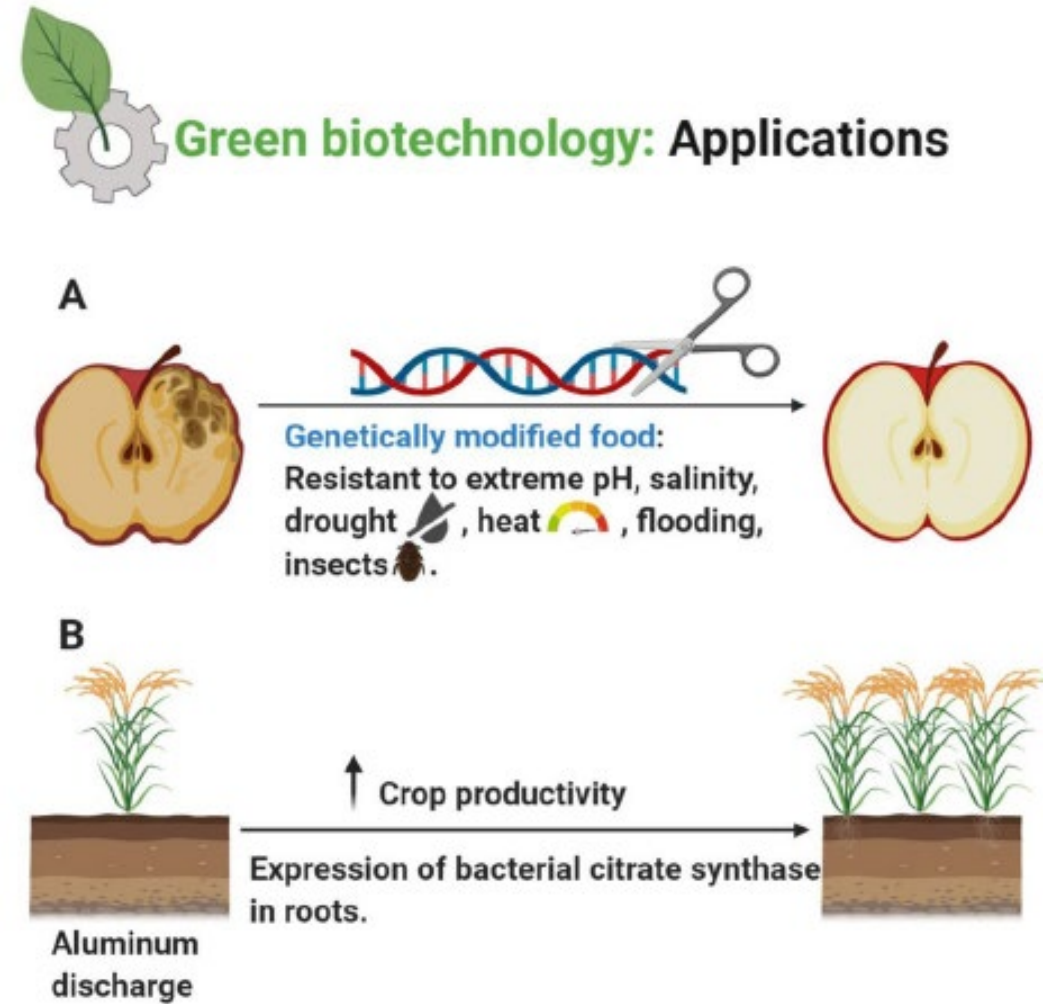
# A domesticação provocou alterações nas plantas

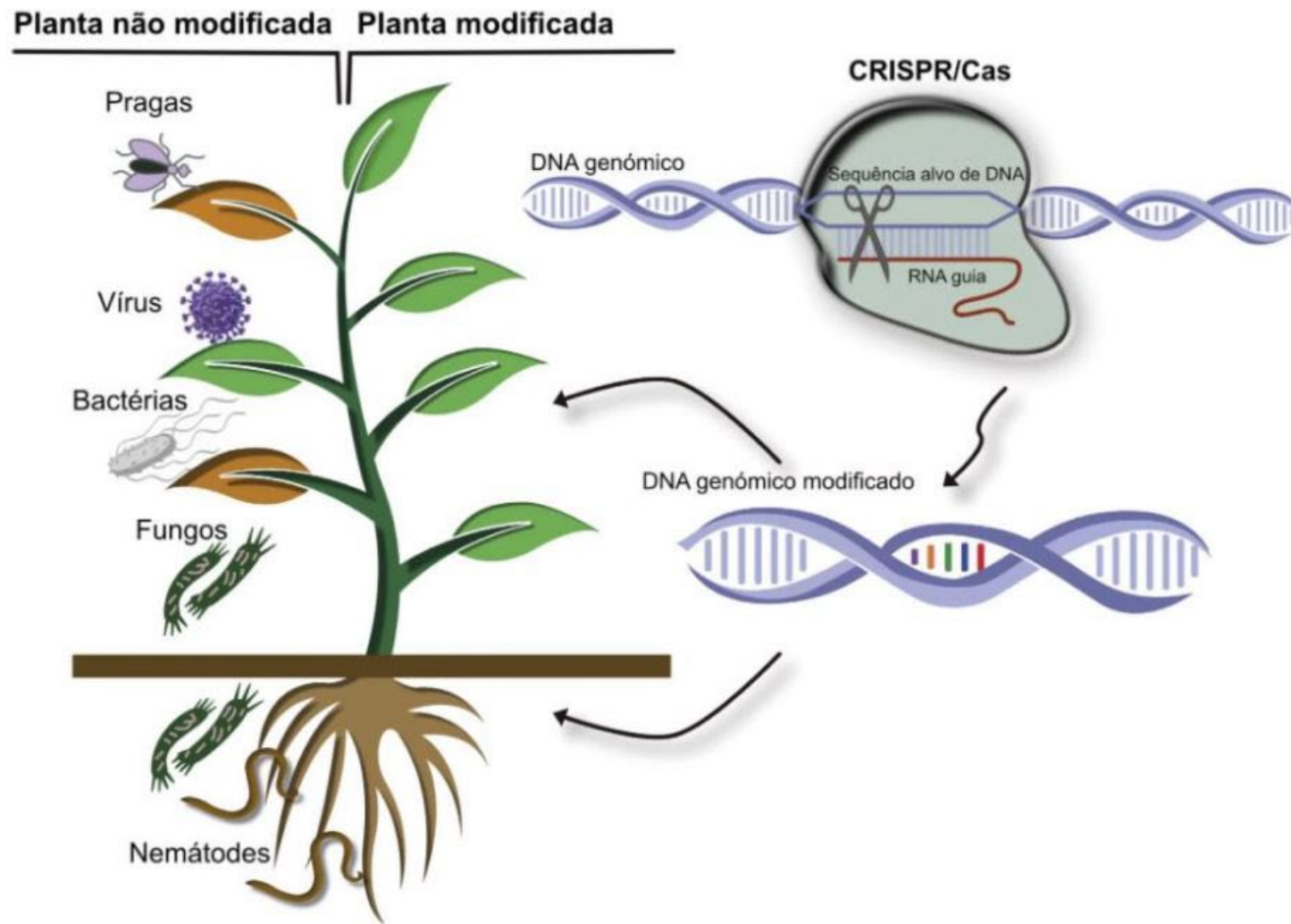


# Desafios



# Aplicações





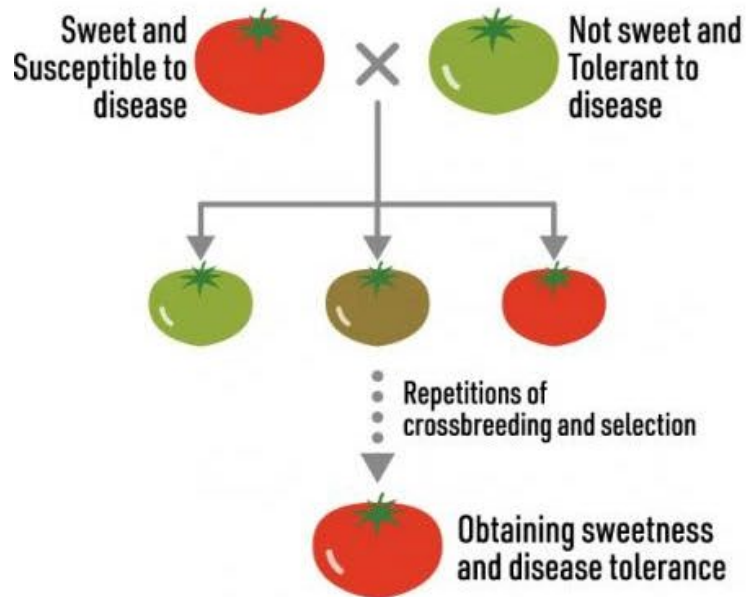
As culturas estão invariavelmente expostas a **pragas e doenças**.

No sentido de acelerar o processo de melhoramento de plantas, as **NOVAS TÉCNICAS GENÔMICAS**, como as tecnologias de edição de genoma, permitem introduzir mecanismos de resistência ou remover suscetibilidade de forma rápida e precisa.

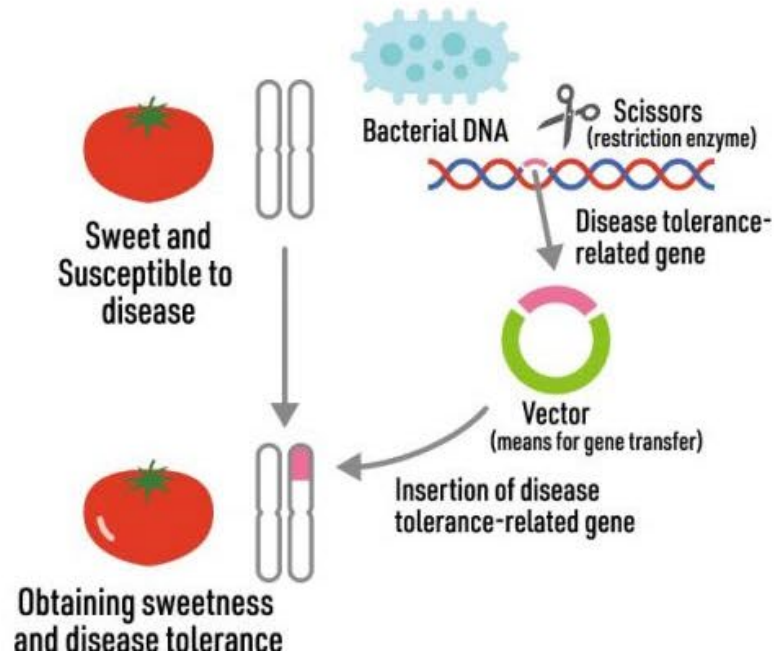
Fonte: InPP

# Como obter uma planta melhorada?

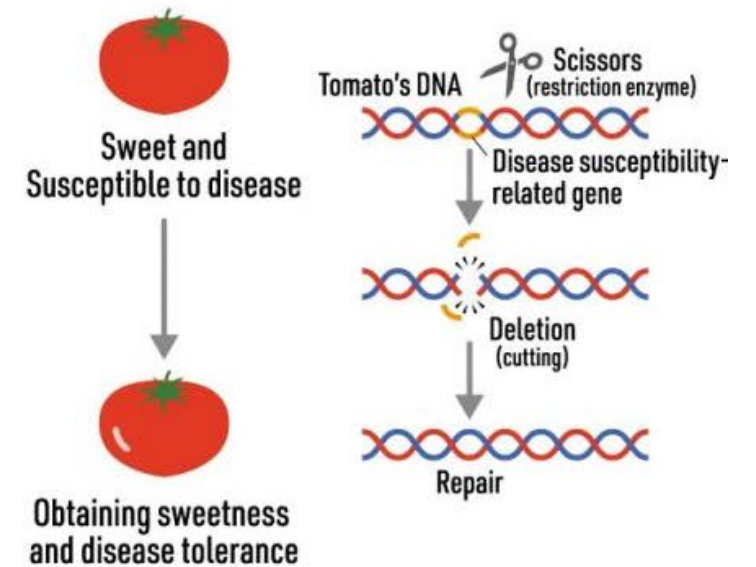
## Melhoramento convencional



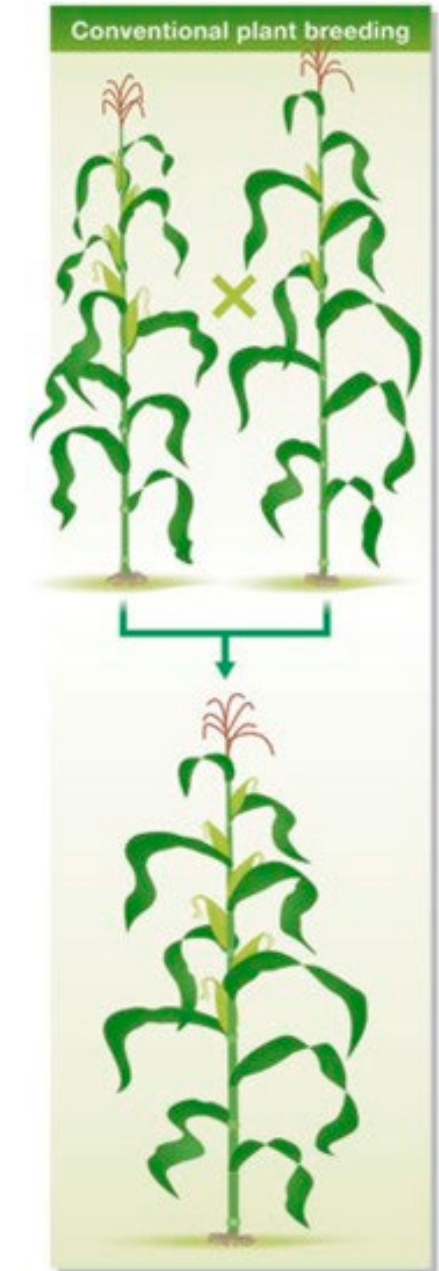
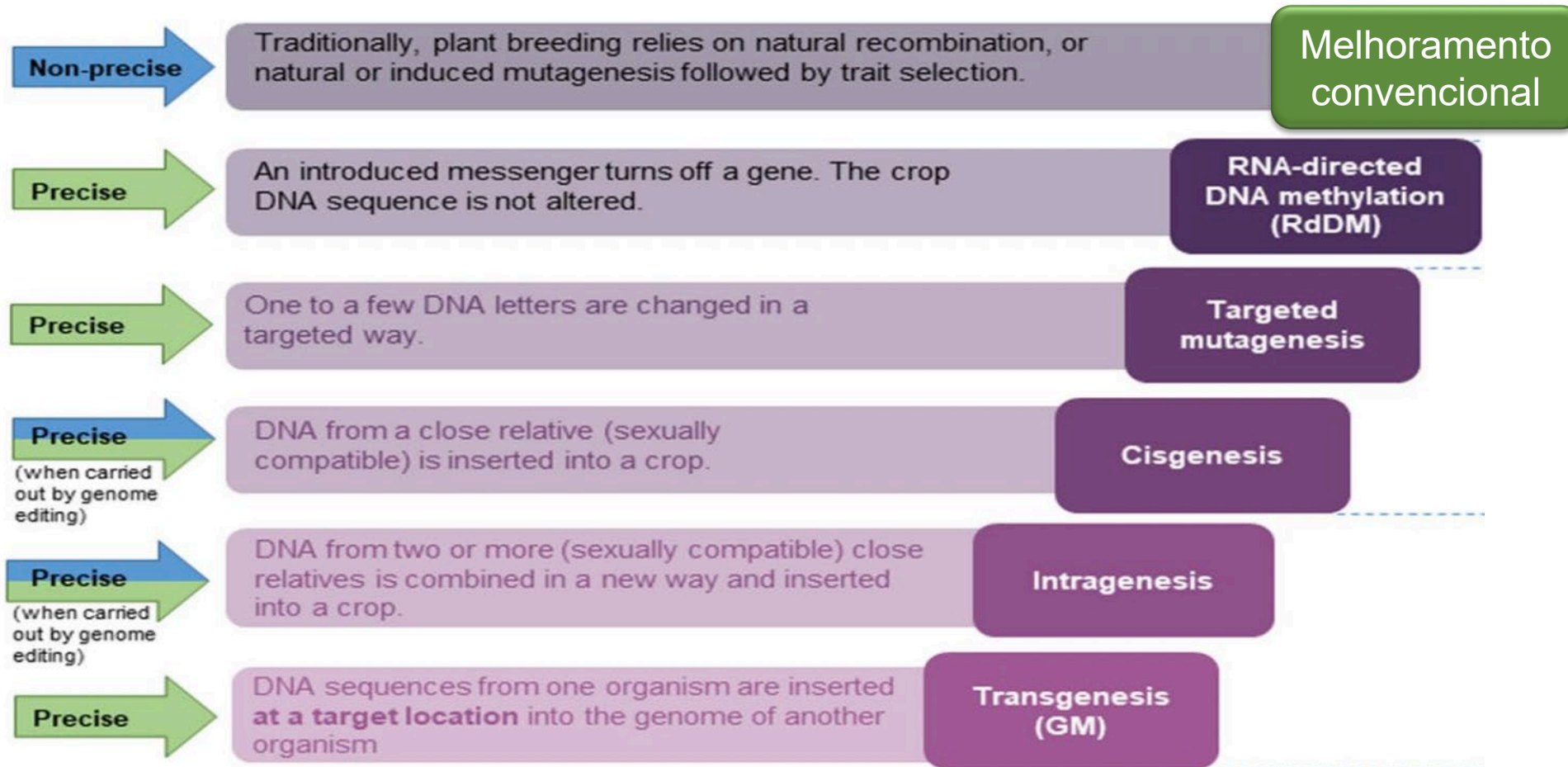
## Modificação genética



## Edição genética

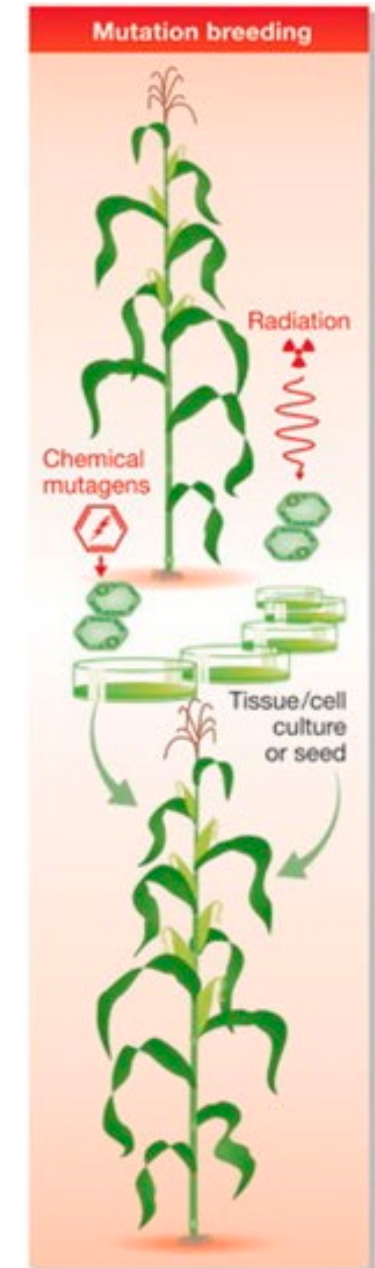
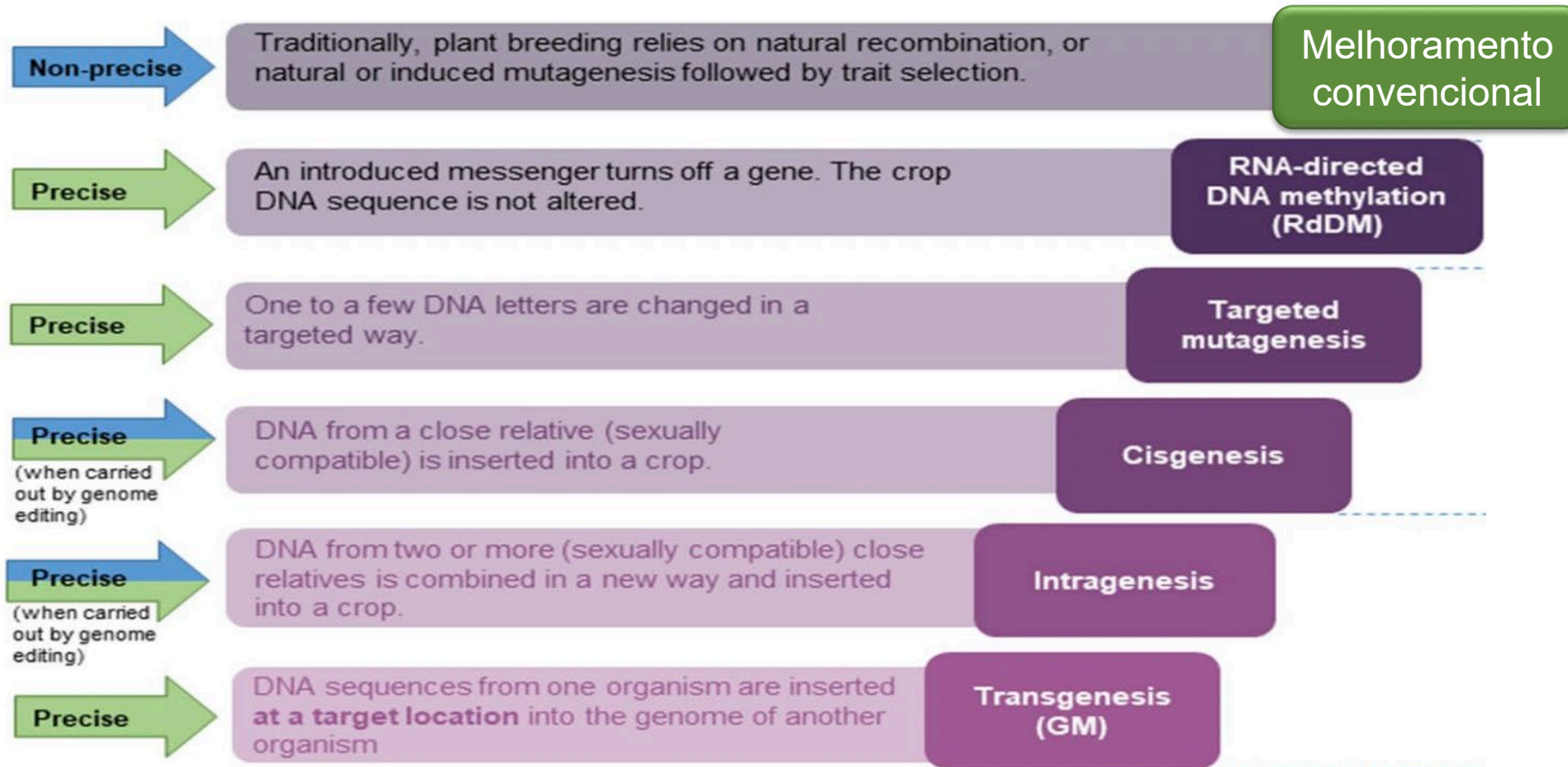


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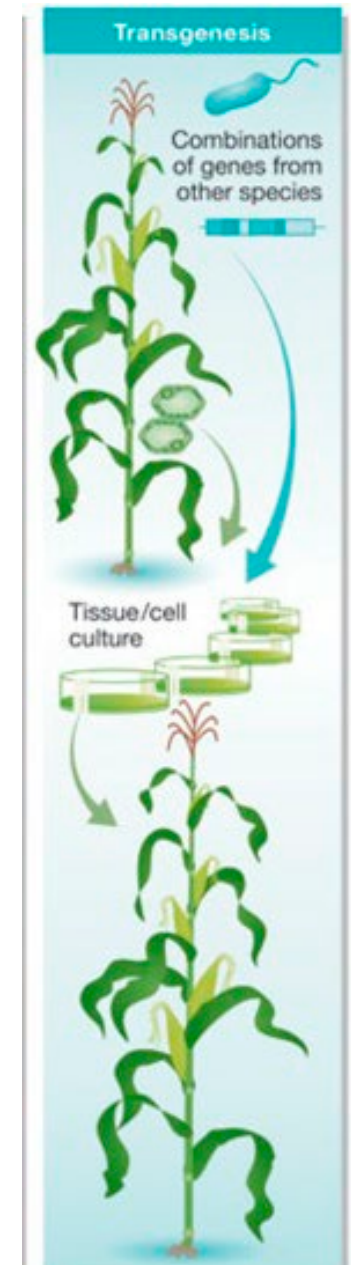
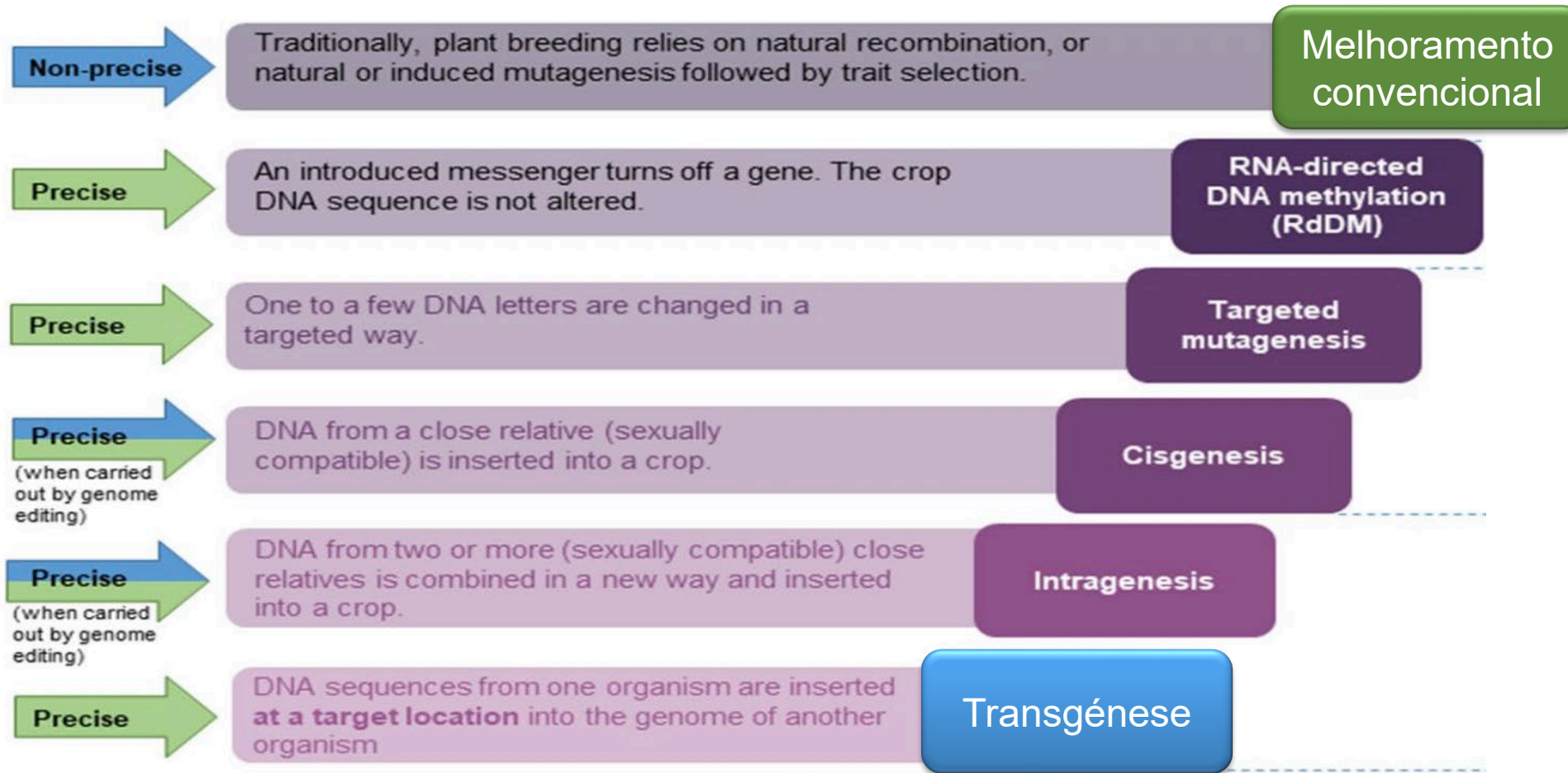




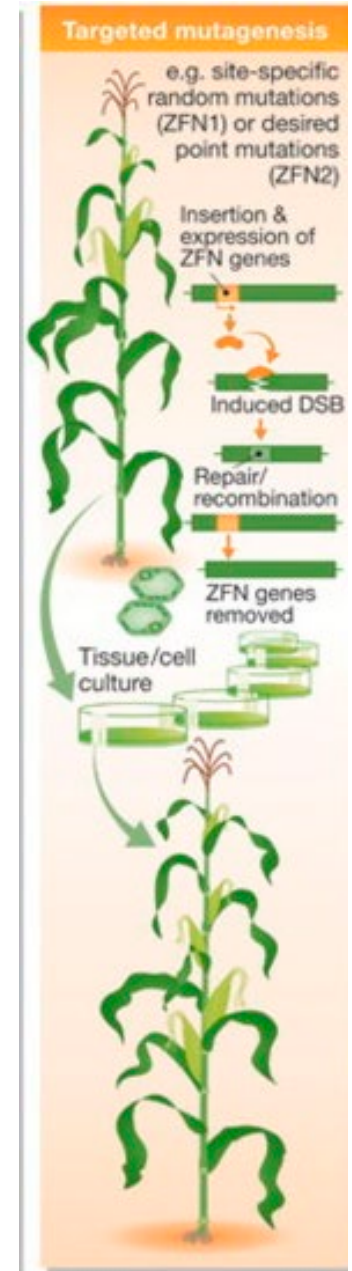
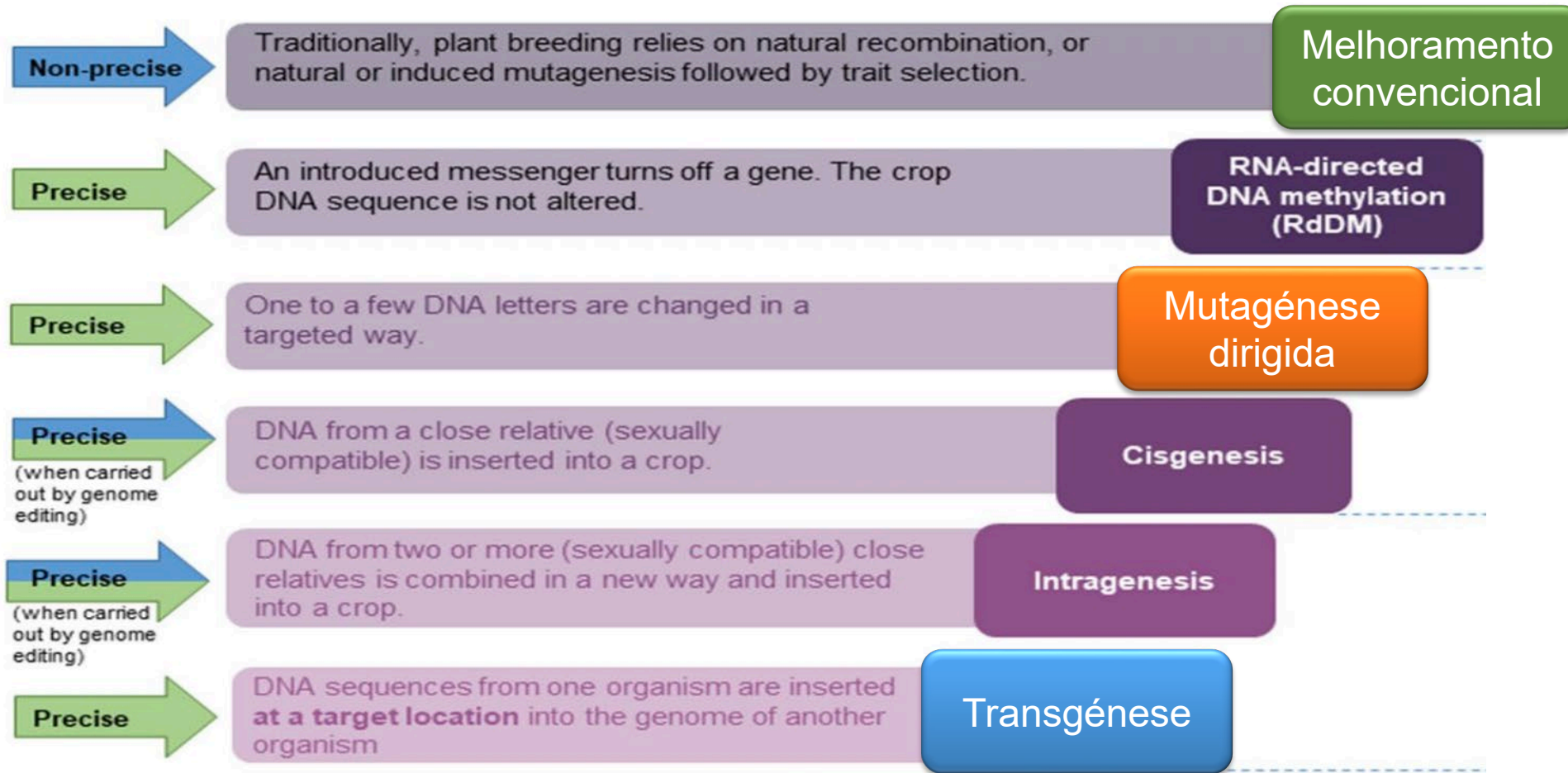
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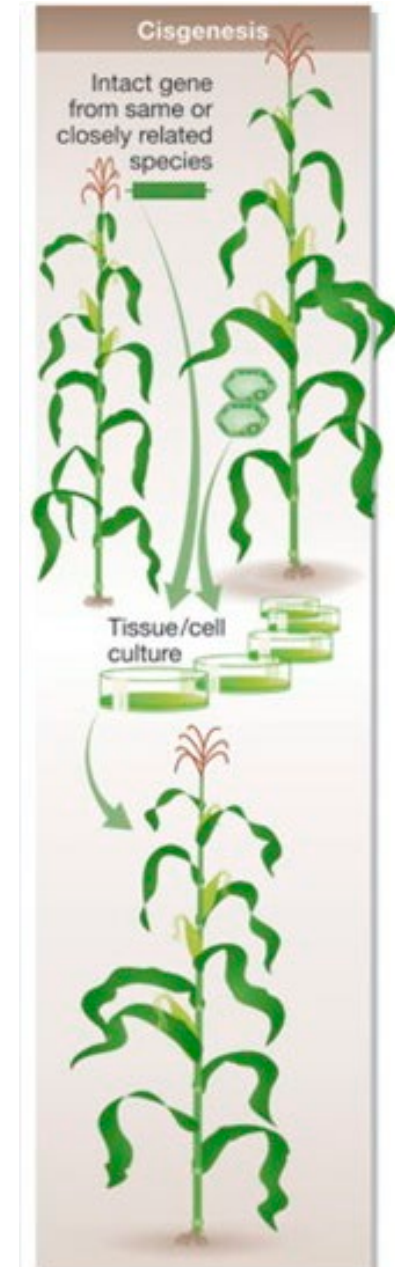
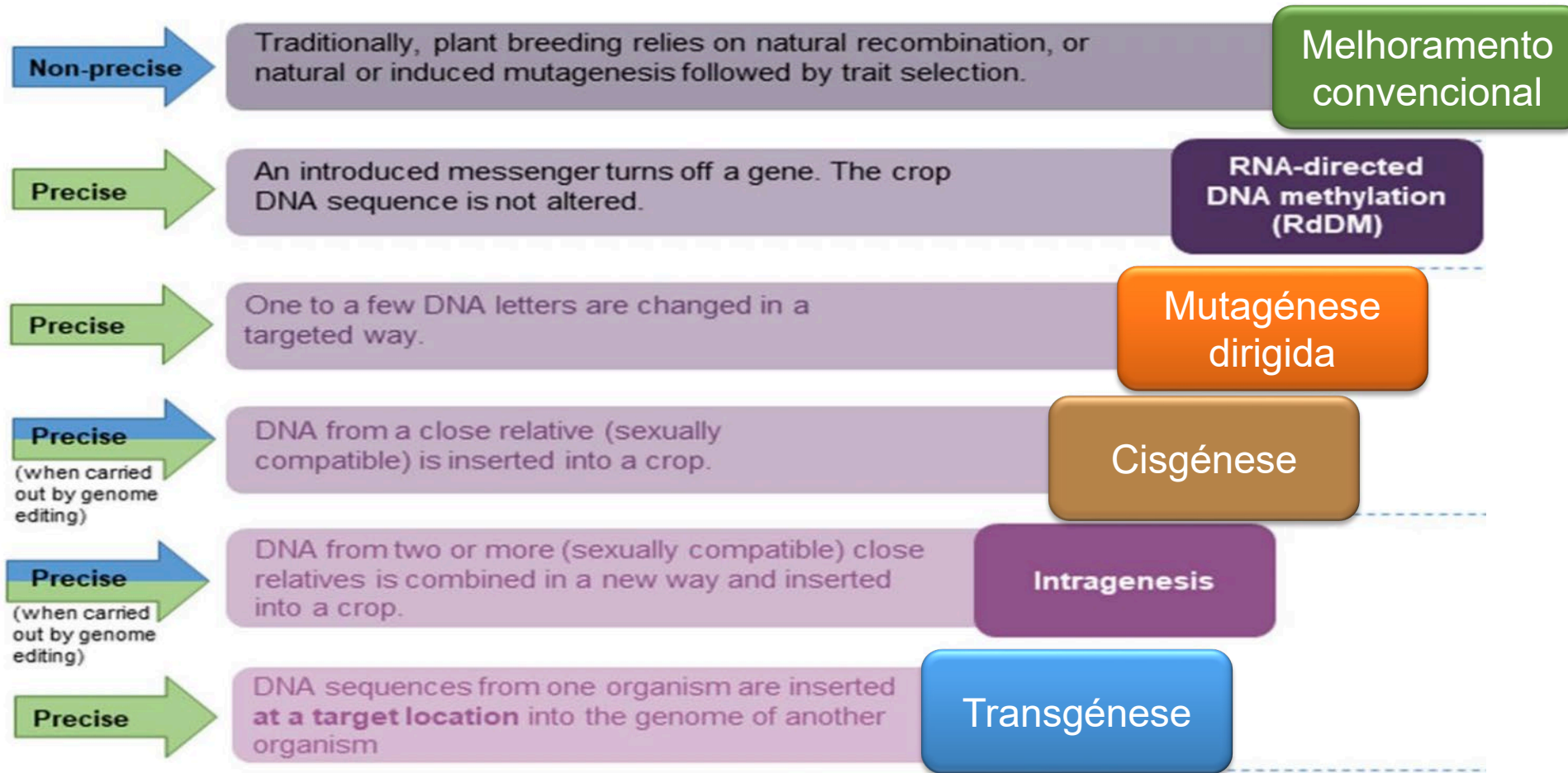
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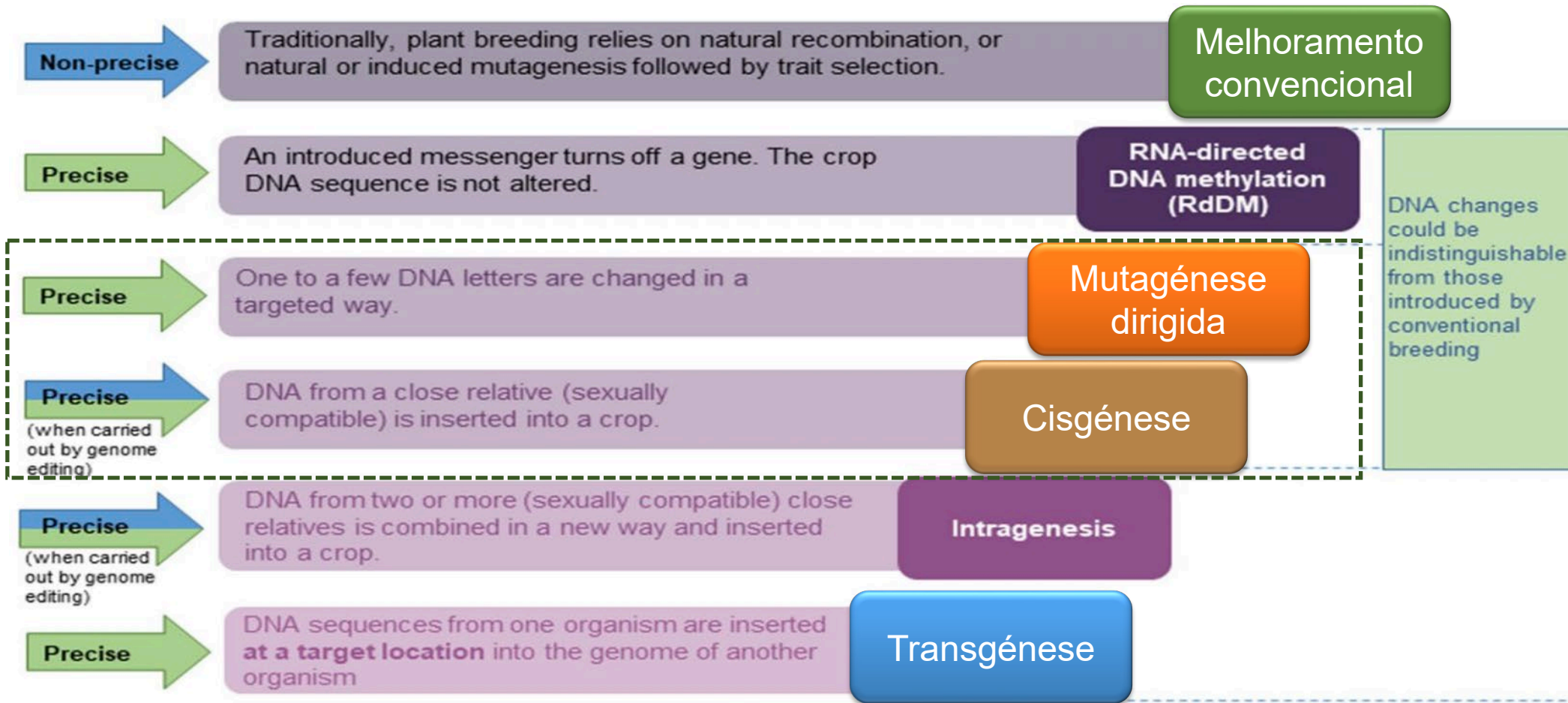
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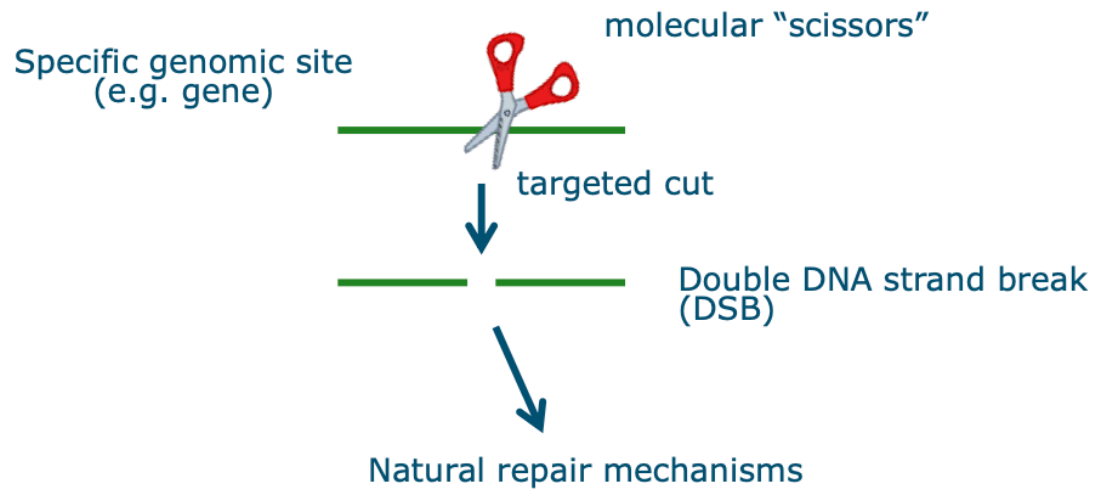
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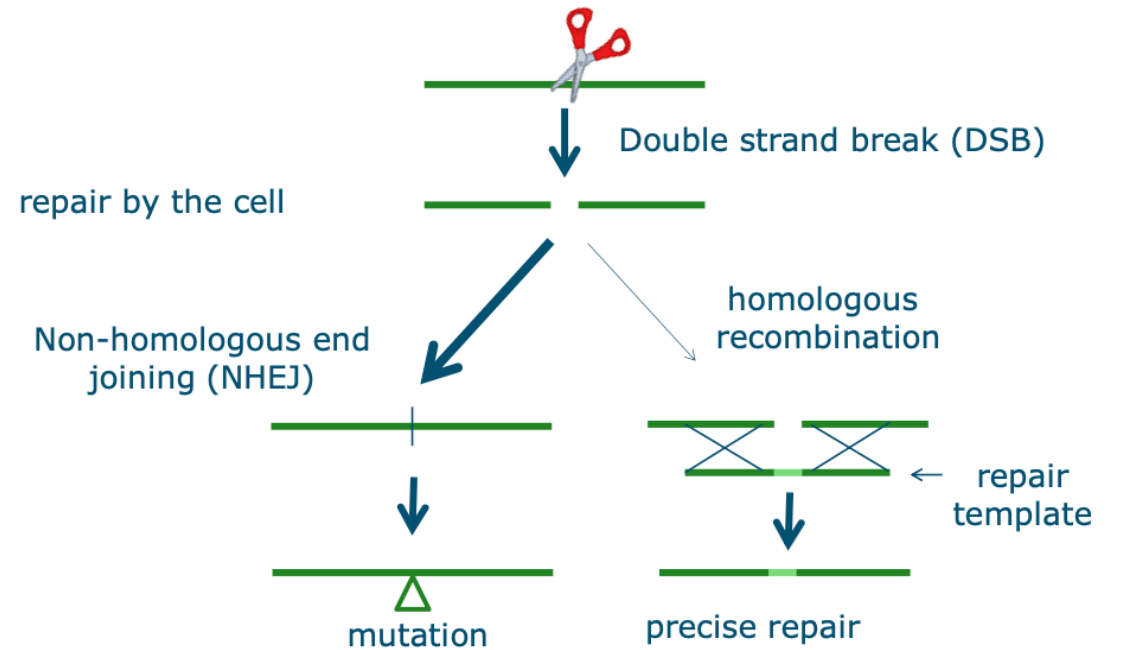
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# Mutagénesis dirigida



## Natural repair mechanisms

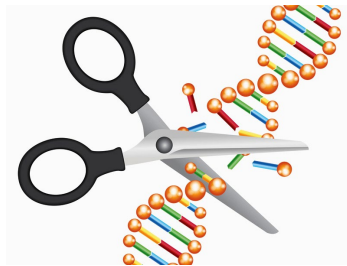


# Mutagénesis dirigida

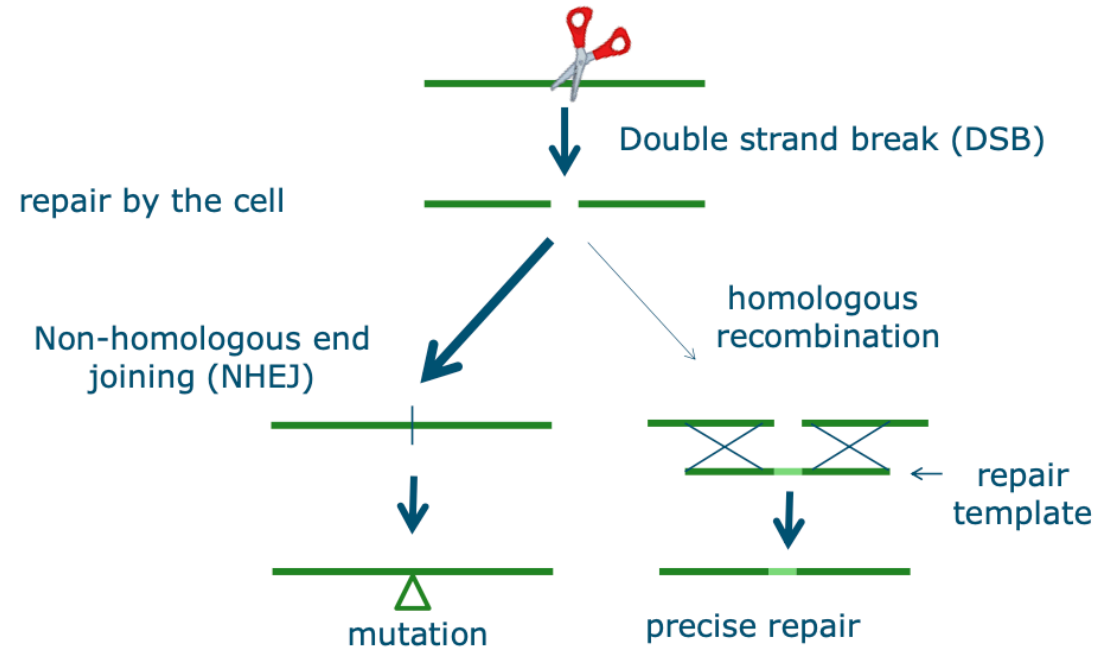
## Site-Directed Nucleases (SDN):

- ✓ **Zinc Finger**
- ✓ **TALENs** (transcription activator-like effector nucleases)
- ✓ **CRISPR/Cas9 systems** (Clustered Regularly Interspaced Short Palindromic Repeats - associated protein-9 nuclease (Cas9))

✓ ...



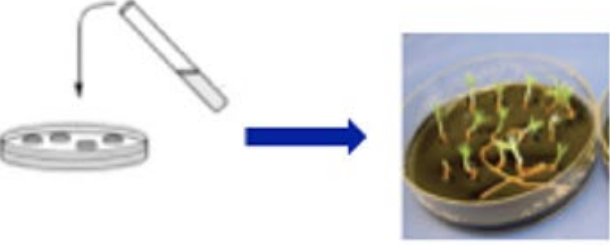
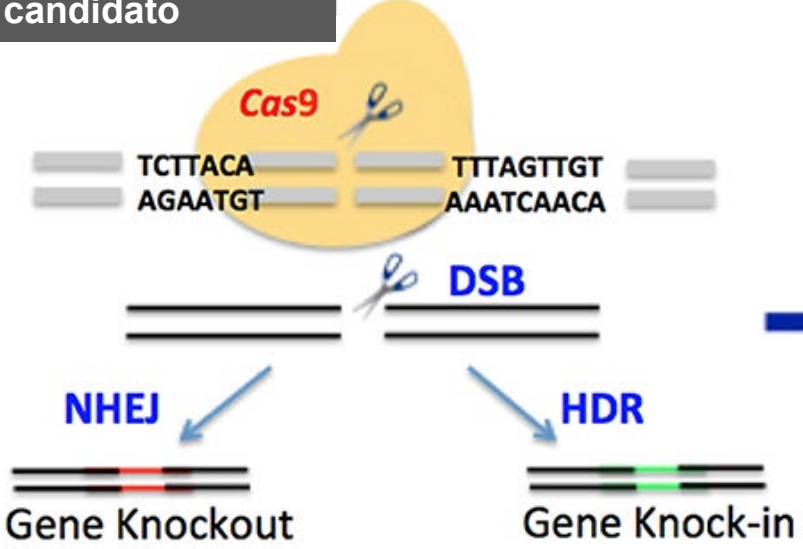
## Natural repair mechanisms



Edição do gene candidato

Transformação

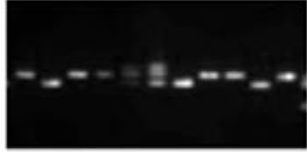
Cultura de tecidos



Genotipagem

Fenotipagem (expressão do gene)

Regeneração









Estudos evolutivos

Testes em campo  
Avaliação da estabilidade



Fonte: Ferramentas de edição genética  
New Breeding Technologies (NBTs)



Crop	Trait	Edited genes	Stage
 Banana	Disease resistance (BXW, Fusarium wilt, BSV)	<i>DMR6</i> , BSV sequences	3,1
 Cassava	Disease resistance (BB)	<i>SWEET</i> gene promoters	3
	Food safety (cyanide-free)	Linamarin synthase	3
	Quality (waxy starch)	<i>GBSS1</i>	3
 Maize	Disease resistance (MLN)	<i>C6 QTL</i>	1
	Weed resistance ( <i>Striga</i> )	Strigolactone	3
 Potato	Disease resistance (PVY <sup>a</sup> , late blight)	<i>eIF-4E</i> , <i>StDMR6-1</i> , <i>StCHL1</i>	2
 Rice	Disease resistance (BLB, RHB)	<i>SWEET</i> gene promoters, <i>AGO4</i> , <i>STV11</i>	4,3
	Food safety (low arsenic and cadmium)	<i>OsNRAMP5</i> , <i>OsPT8</i> , <i>LS1</i> , <i>LS2</i>	3
	Nitrogen remobilization, and methane emission reduction	Unpublished	3
	Insect resistance <sup>a</sup> (BPH)	BPH resistance alleles	2
 Wheat	Disease resistance (rusts, mildew) <sup>a</sup>	<i>Lr67</i> and others	3

Fonte: Pixley et al. Nat Genet 54, 364–367 (2022).  
<https://doi.org/10.1038/s41588-022-01046-7>



**OBRIGADA!**