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Diversity of breeding technologies and impact for plant variety protection

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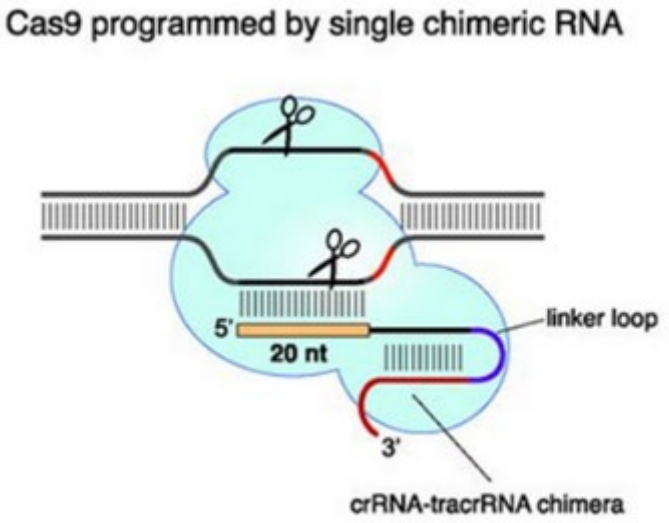
Key message

- The Essentially Derived Variety (EDV) issue is likely to be modified by the New Genomic Techniques (NGTs), their future use in breeding over a range of crops and the intellectual property regimes that are relevant in the domain

CRISPR/Cas method is today the dominant NGT technology

« Clustered Regularly Interspaced Palindromic Repeats » / « CRISPR Associated Protein 9 »



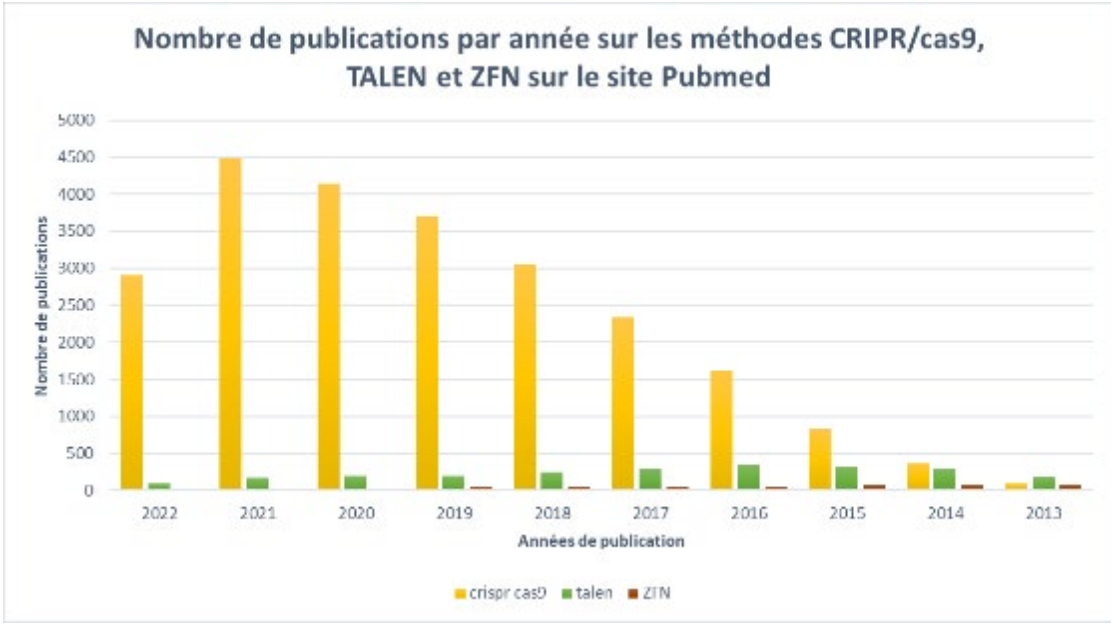
<u>Major recent progresses</u>

Technical and financial accessibility

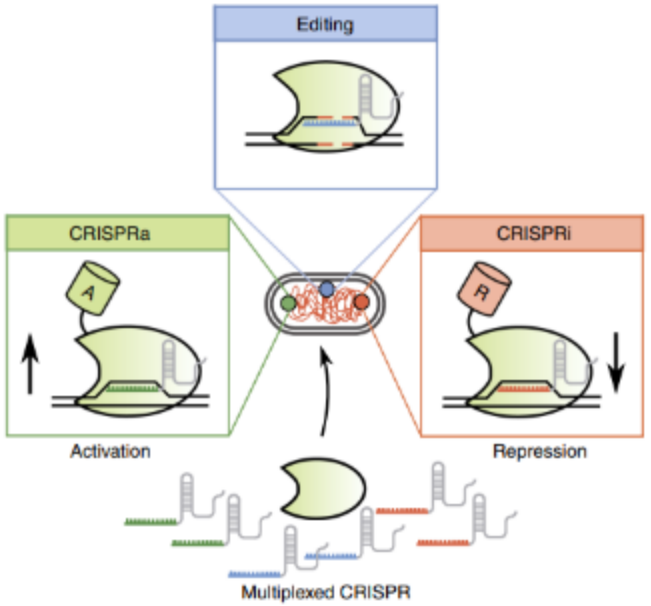
Tool affordable to an increasing number of laboratories

Possibilities of multiple targets editions

Cas 9: nuclease with the highest number of studies and uses (fundamental and applied research)



CRISPR/cas : recent technical progresses and use of this technology



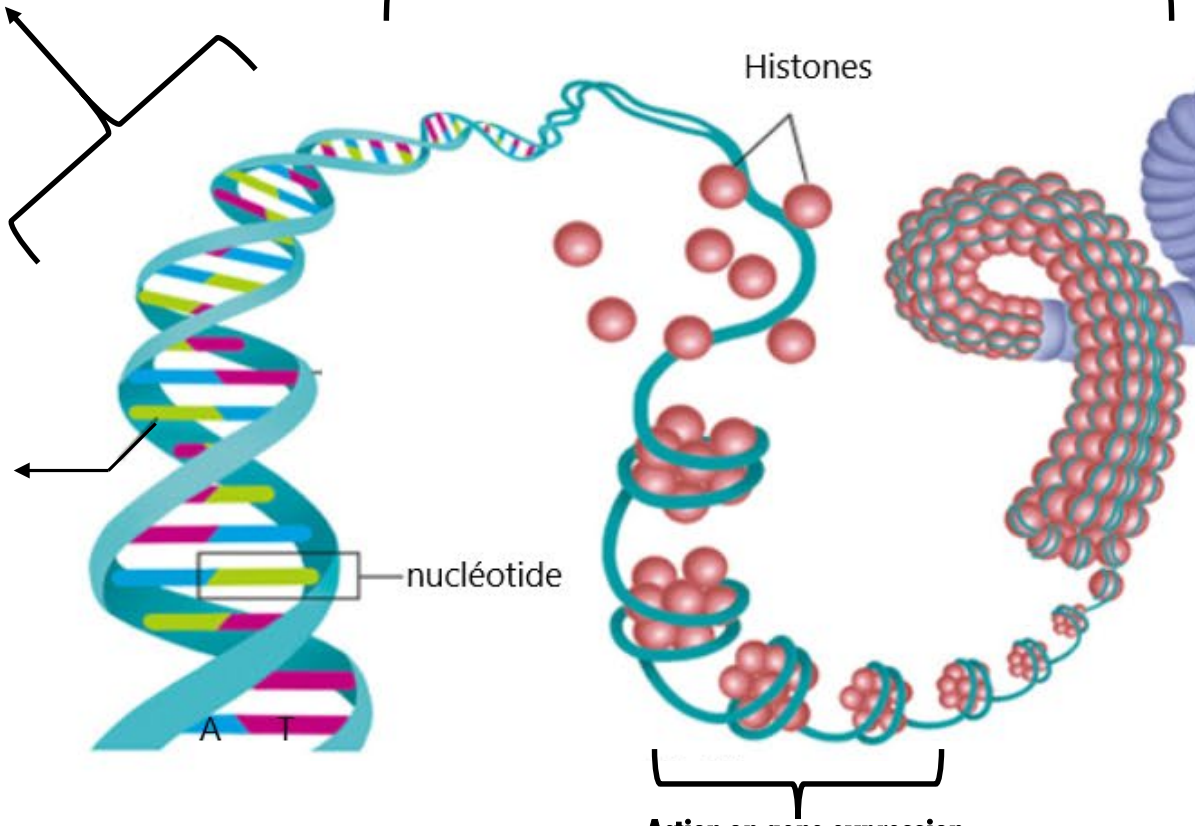
(McCarty et al., 2020)

Technical advances

Multiplex modifications
To simultaneously target several DNA sequences. To modify expression of several genes of of multigenic families.

More variability in PAMs motives + « PAMless »

Base Editing and Prime Editing methods to induce modification of 1 or more bases.

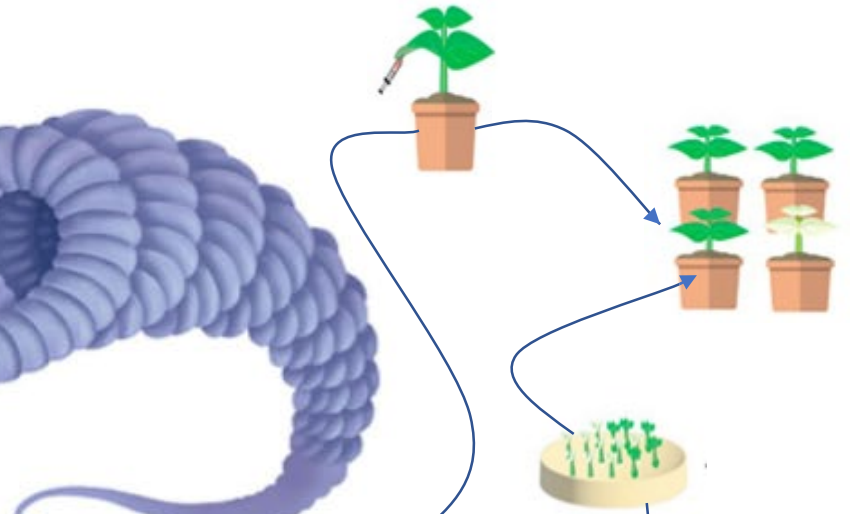


Action on gene expression

Cas recruting effectors

Action on epigenome by modification of epigenetic marks
➔ condensation/decondensation of DNA

To avoid *in vitro* step
De novo induction of the mzristem
« Virus-induced heritable gene editing »



Production of edited plants without intermediary phases of transgenesis

Chromosom reorganisation
induction of inversion and Translocation of chromosoms.

- **Promising tool whose all possibilities for plant breeding have not yet been documented**
  - **Accelerating innovation to foster agriculture sustainability**
  - **More accessible traits**
  - **New variation available**

- Many proofs of concept of the ability to modify agroecological traits

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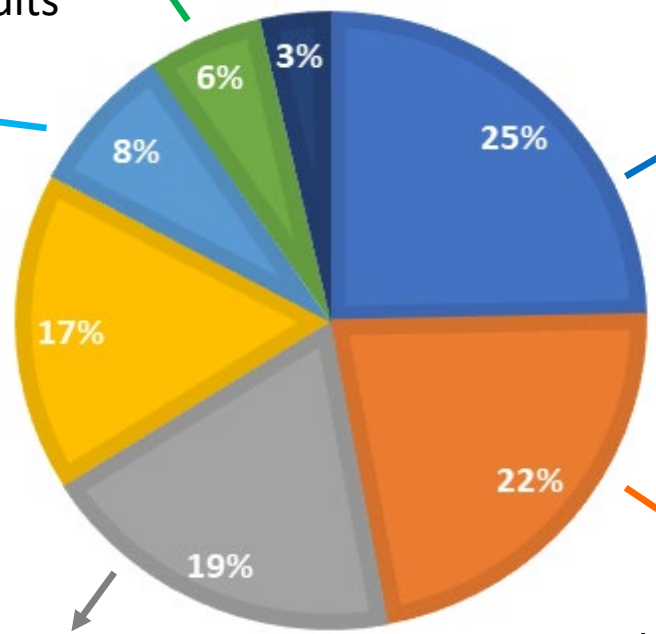
According to scientific literature (WOS): use of genome editing techniques for plant breeding objectives



Aroma / coulor
Flowers
Fruits

Tolerance to herbicides

Yield
Plant architecture
Number of grains
Grain weight

Resistance to abiotic stresses
Resistance to drought stress
Cropping on polluted soils
Tolerance to high temperature

Industry and processing
Shelf life duration
Browning

Nutritional and product quality
Increasing content of nutritious compounds
Decreasing antinutritional factors

Resistance to biotic stresses
bacteria, fungi, viruses,
insects

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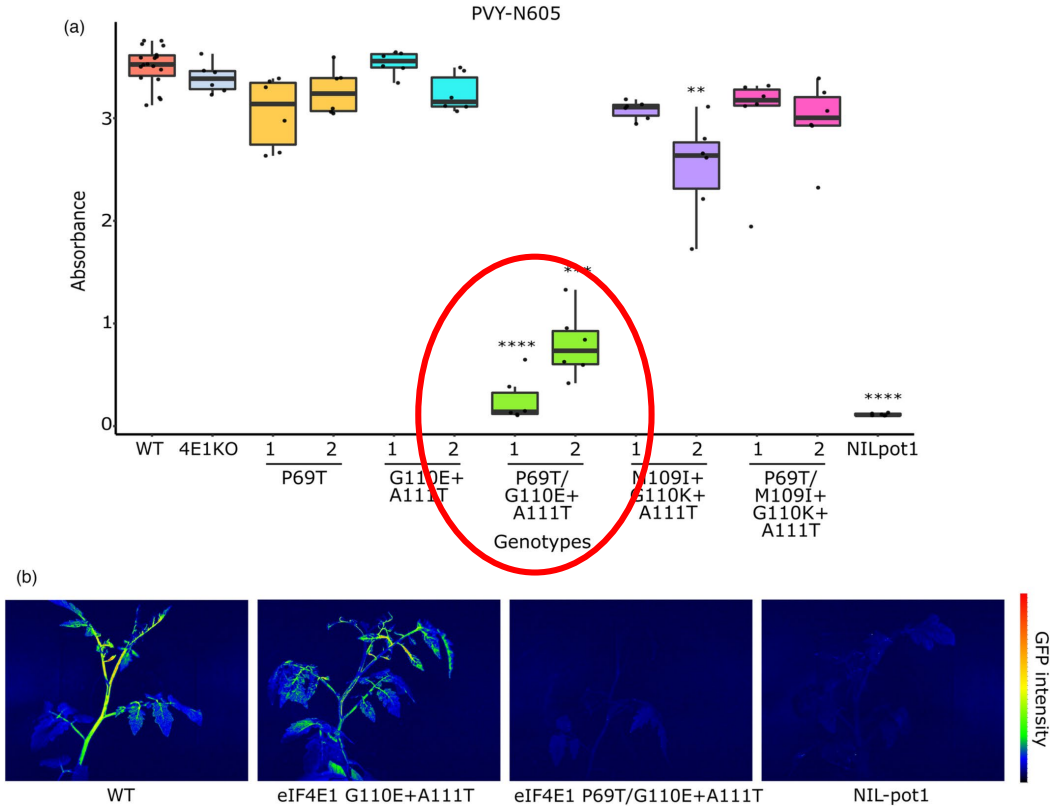
Example of gene-editing of tomato, copying eiF4E1 pepper allele. Inrae Avignon, France

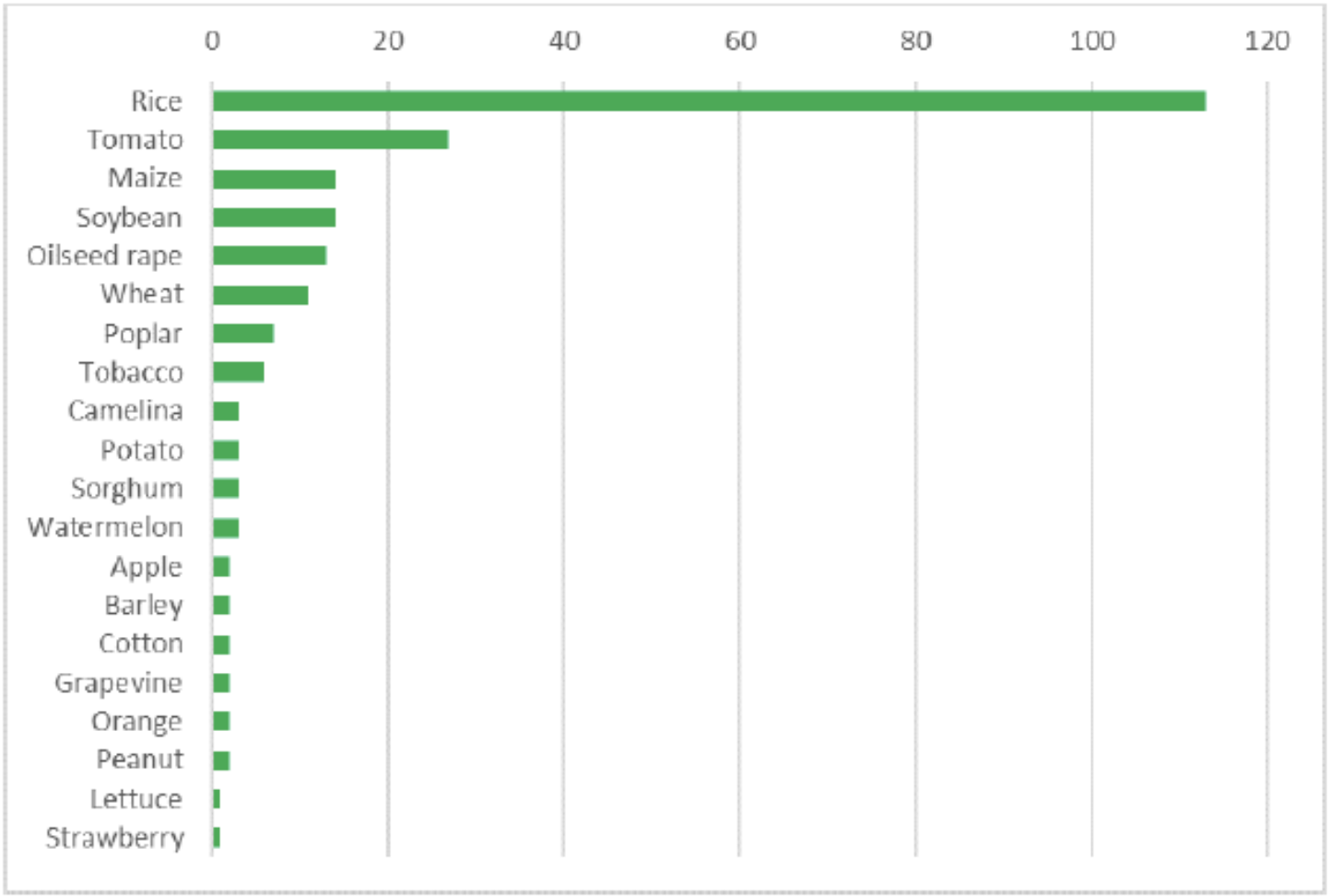
An iterative gene-editing strategy broadens eIF4E1 genetic diversity in Solanum lycopersicum and generates resistance to multiple potyvirus isolates



Kuroiwa K, et al, Plant Biotechnology Journal, First published: 30 January 2023, DOI: (10.1111/pbi.14003)

A limited number of species concentrates most efforts:

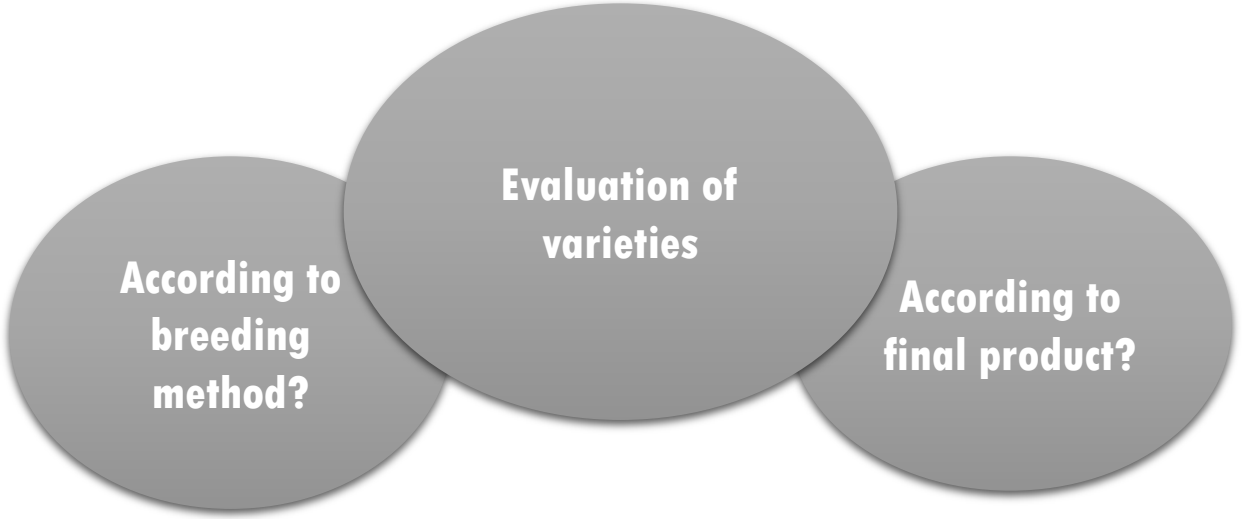
- Market size
- High-quality genome sequencing required
- Efficient *in vitro* regeneration



Number of scientific publications, with proofs of concept (in 2022)

Evaluating edited varieties

Evaluating edited varieties for their registration



Demand for access to market (2001/18/CE directive)

Detail on breeding method and on modification

Risk evaluation

Monitoring plan

Classical breeding method

GMO

NGT

Determining risks associated to method:

Ex : Off-target; mutation occuring during *vitro* culture

Traits already variable within the species

Agronomic traits with a variability already existing within the species, corresponding to a continuous breeding

New variation

Can generate new effects/services never observed and evaluated in classical breeding

Evaluating services and disservices and integrating them explicitely in the decision rules

Risk evaluation?

Survey plan?

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Intellectual property issues and EDV

Access to genetic diversity

- Concerns regarding the accessibility to the genetic diversity, existing either in the current varieties under Plant Breeders Rights or in the genetic resource
    - Patents on edited traits are a key issue
    - The coexistence of the various intellectual property regimes is really at stake

Intellectual property

	Patent/technology	Patent/trait	P.B.R.
Technology	✓	✗	✗
Gene	✗	✓	✗
Variety	✗	✗	✓
Breeder exemption	✗	✓	✓
Farmer priviledge	✗	✓	✓
Crossed licence	✗	✓ ⇄	✓

NGT variety could be under P.B.R. and patent

For breeders

For the use of a variety carrying a patented gene/allele, the breeder must:

-Pay a licence right if the gene is preserved in the final variety

-Withdraw the gene and not to pay a licence right

Multiplicity of patented genes would create a minefield for breeders

Full transparency required on PI on varieties

<u>More challenging work for breeders</u>

Survey of patents databases (OEB, PINTO, ACLP, ILP, …)

Patents on traits could be a source of rejection by the society

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Essentially Derived Varieties

- EDV key issues (according to B. Kiewiet, 2006)
  - Retaining the expression of the essential characteristics of the initial variety
  - It conforms (essentially in the Basic Regulation) to the initial variety
  - EDV must be related to phenotypical characteristics and must be genetically heritable
  - EDV are determined as
    - Originating from an act of derivation
    - Phenotypically similar to the initial varieties except for the difference due to the derivation
- How does this fit with NGT?
  - The genome editing may go far beyond a simple/single modification
    - Regulation genes
    - Deep physiology
    - Multiplex possibility
  - **With NGTs progresses → high-throughput editing by a specialized operator on a variety protected by a PBR (*delivered to another owner*).**

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- Integration of NGTs in breeding programs
  - Creating new genetic diversity to be used in breeding programs (*the induced genetic diversity may require the adaptation of many other physiological traits*). This is likely to be the situation for most edited traits (phenology, resistance to abiotic stresses, architecture).
    - In that case, the technology will be used early in the breeding programs and no EDV will be relevant
  - Providing extra traits in optimum genetic backgrounds.
    - In that case, EDV is relevant. This is likely to be the case for pest and disease resistance traits/genes

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- **NGT: large possibilities**
  - Precision, multiple targets
  - Today, mainly proofs of concept
  - Importance of technological sovereignty

- **NGT: some hurdles as not all species can be edited**
  - Need of high-density genome sequencing
  - In vitro regeneration

- **Variety evaluation**
  - Variable traits : no need of modification of the evaluation pathway
  - Disruptive traits : characterization of services and disservices at the scale of the crops and cropping systems

- **Traceability and transparency required for coexistence**

- **Intellectual property**
  - Different possible regimes
  - An important issue on patenting edited traits

- **Concerns**
  - Acceptability: sharing benefits, access to technology, focussing on traits of societal relevance (climate change, agroecological transition)
  - Genetic resources and diversity of cultivated species
  - Boosting effort of public research

Conclusions

- **Technologies (cost, accessibility) that could speed up concentration of breeding companies**
  - Today 6 companies= 50% of variety markets

- **Possible weakening of the PBR system** (which showed a tremendous efficiency since 1961 to foster genetic gains in all cultivated species)

- **Essentially Derived Varieties**
  - Varieties carrying edited traits could be EDV, but…
  - Edited traits or multiplex edition could modify expression of essential characteristics
  - High-throughput edition could become a reality for some 'important' species


Thank you for your attention …