Controverse scientifique UMT SI Bio

# *NGT, nouvelles techniques d'édition du génome : des questions pour les productions agricoles et pour l'Agriculture Biologique ?*

## *Une introduction*

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# Cet exposé introductif :

1) Que sont les « nouvelles » techniques de modification du génome ?
2) Pourquoi une attention particulière aujourd'hui sur ces techniques ?
3) Quelques bases techniques pour comprendre
4) Edition de génomes et transition agroécologique :
   - ✓aspects scientifiques et techniques
   - ✓aspects économiques et sociaux de l'innovation

# Les techniques de modification du génome visées par la directive 2001/18/EC

- Le droit européen **définit** l'OGM …

  *« Organisme dont le matériel génétique a été modifié d'une manière qui ne s'effectue pas naturellement par multiplication et/ou par recombinaison naturelle »*

- … et **distingue** les techniques qui :

| | | |
|---|---|---|
| … ne **résultent <u>pas</u> en une modification génétique**. | Annexe IA, Partie 2 | Induction polyploïde, conjugaison, fécondation in vitro, etc. |
| … résultent en **modification génétique sous le coup de la directive.** | Annexe IA, Partie 1 | Utilisation d'**ADN recombinant**, fusion cellulaire entre espèces sexuellement incompatibles, etc. |
| … résultent en **modification génétique hors du champ de la directive.** | Annexe IB | **Mutagenèse (si pas utilisation de rDNA)**, fusion cellulaire entre espèces sexuellement compatibles, etc. |

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# Les « nouvelles » techniques sont celles … auxquelles on n'avait pas pensé dans la Directive 2001/18/EC !

***New breeding techniques :***

mutagenèse dirigée par oligonucléotides (ODM), **nucléases à doigt de zinc** (ZFN), **cis-/ intragenèse**, greffe entre plantes GM et non GM, agroinfiltration, modifications épigénétiques par *RNA-dependent DNA methylation* (RdDM), *Reverse Breeding*

(liste de techniques identifiées par les Pays-Bas en 2006),

auxquelles se sont ajoutées la **mutagenèse ciblée par nucléases de type TALEN et CRISPR/Ca9**

cf. rapport du HCB, 2017 :

Haut Conseil des Biotechnologies

**COMITE SCIENTIFIQUE**

**AVIS SUR LES NOUVELLES TECHNIQUES D'OBTENTION DE PLANTES (*NEW PLANT BREEDING TECHNIQUES*-NPBT)**

Paris le 2 novembre 2017
*(adopté par le CS le 26 avril 2017)*

# Une attention particulière sur la mutagenèse ciblée par nucléases : pourquoi ?

**CRISPR/Cas9** rend la mutagenèse ciblée par nucléases extrêmement puissante et versatile.

**Le génome peut être modifié de façon ciblée sans ajout de matériel génétique exogène dans la plante finale.**

PS : ceci est également vrai pour la **cis-/intragenèse**, où l'ADN introduit provient de la même espèce ou d'une espèce du *gene pool* (i.e. sexuellement compatible).

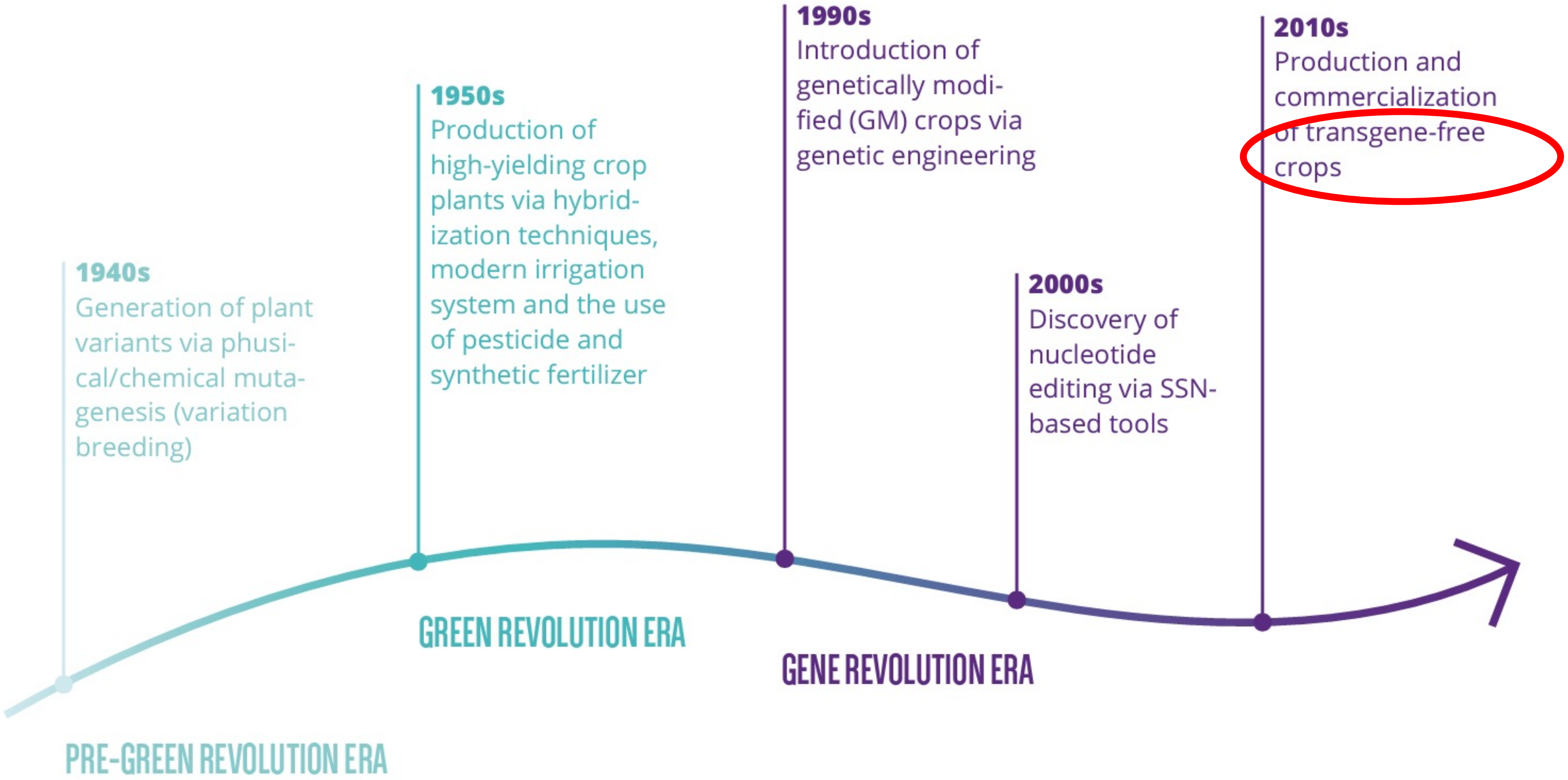


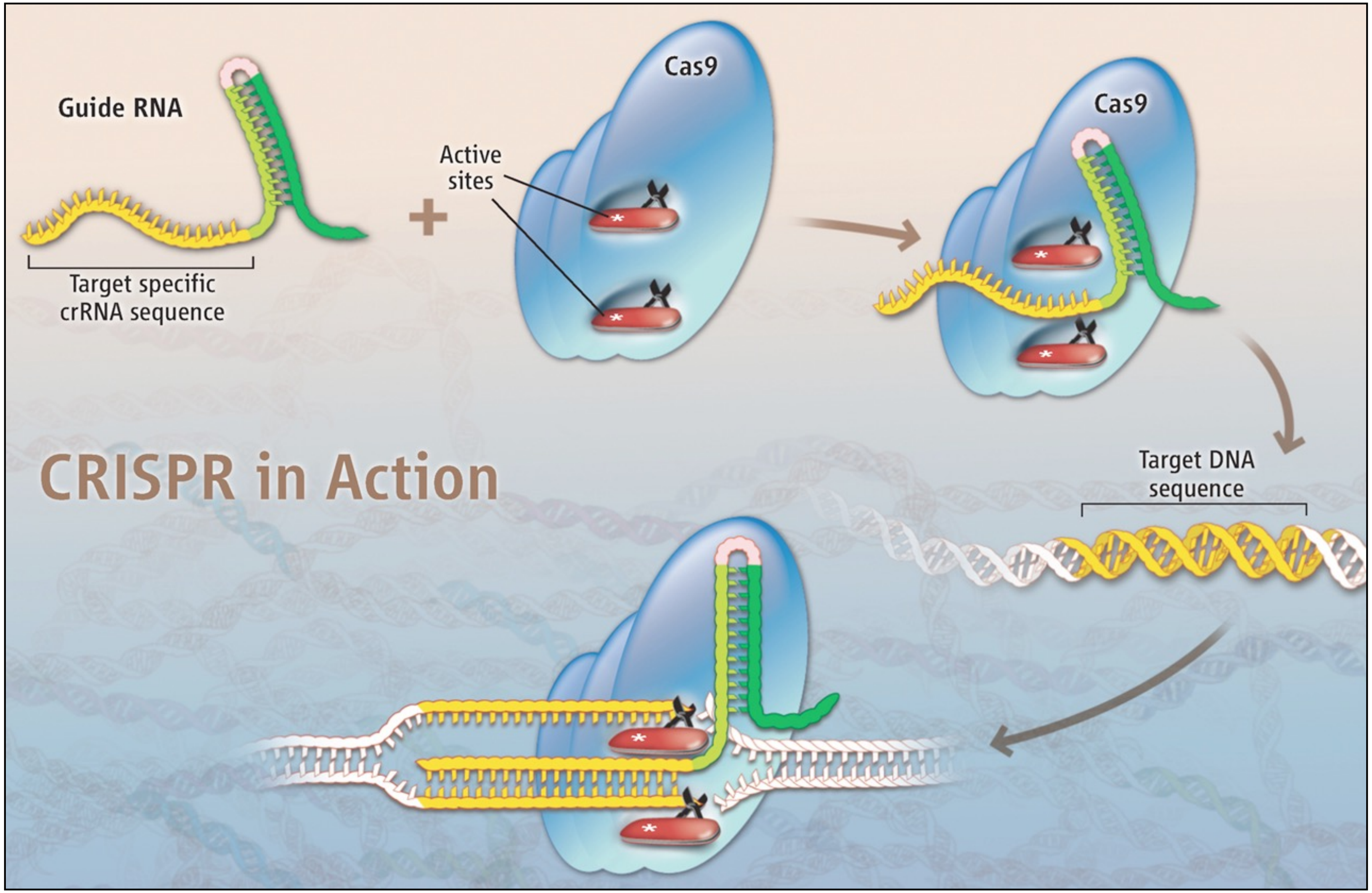

**FIGURE 2** *The shift from the Green Revolution to the Gene Revolution era with an indication of important events*

*Figure copied from Hamdan et al, Green revolution to Gene revolution: technological advances to feed the world, Plants, 2022*

https://www.sojdrova.cz/blog/zastavme-diskriminaci-evropskych-zemedelcu-a-umozneme-jim-pestovat-nove-odrudy-plodin-zajistime-tim-potravinovou-bezpecnost

# Prix Nobel de Chimie 2020 pour l'invention de la technique de modification des génomes CRISPR*/Cas9

(* CRISPR = *clustered regularly interspaced short palindromic repeats*)

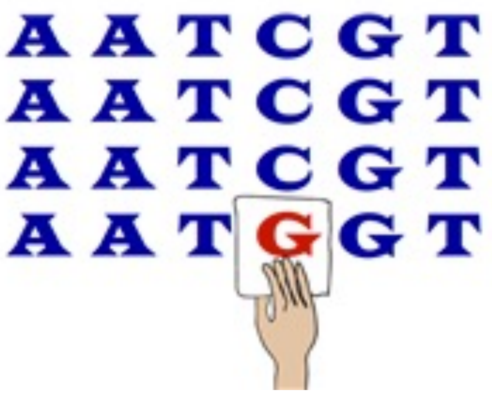


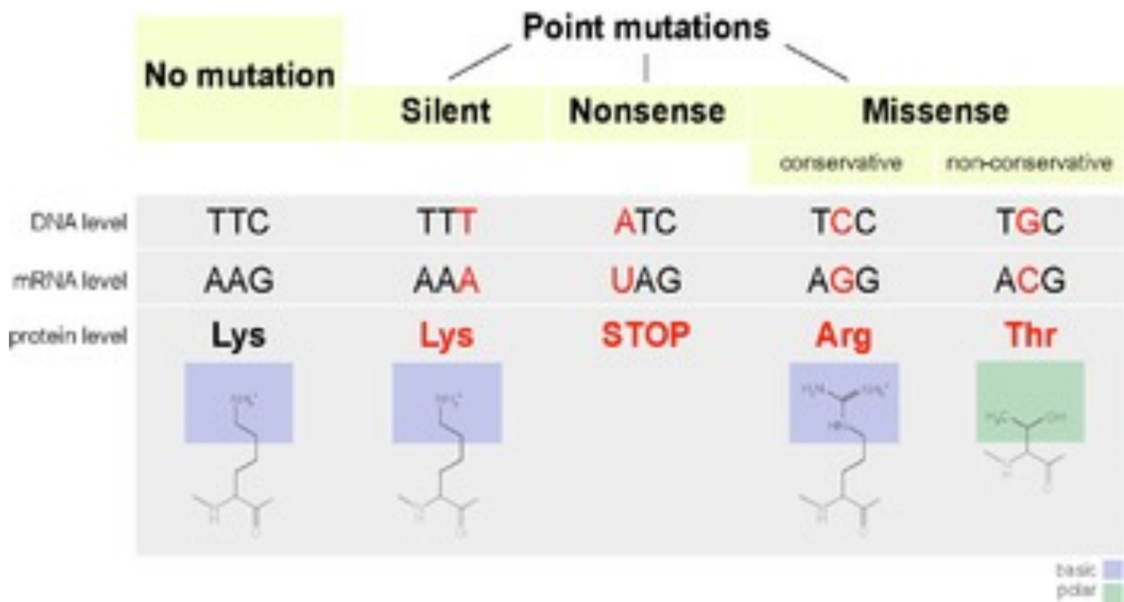


**Emmanuelle Charpentier, née en 1968 à Juvisy-sur-Orge (Essonne), est généticienne, microbiologiste et biochimiste.**


**Jennifer Doudna, née en 1964, est professeure de biochimie et de biologie moléculaire à l'Université de Californie à Berkeley.**

# « Editer » un génome, c’est quoi ?




L’édition d’ADN est une <u>modification ponctuelle et ciblée</u> de sa séquence nucléotidique - substitution, délétion ou addition de nucléotides - résultant en une altération de sa fonction (généralement le codage d’une protéine).
C’est une <u>mutation génique ciblée.</u>

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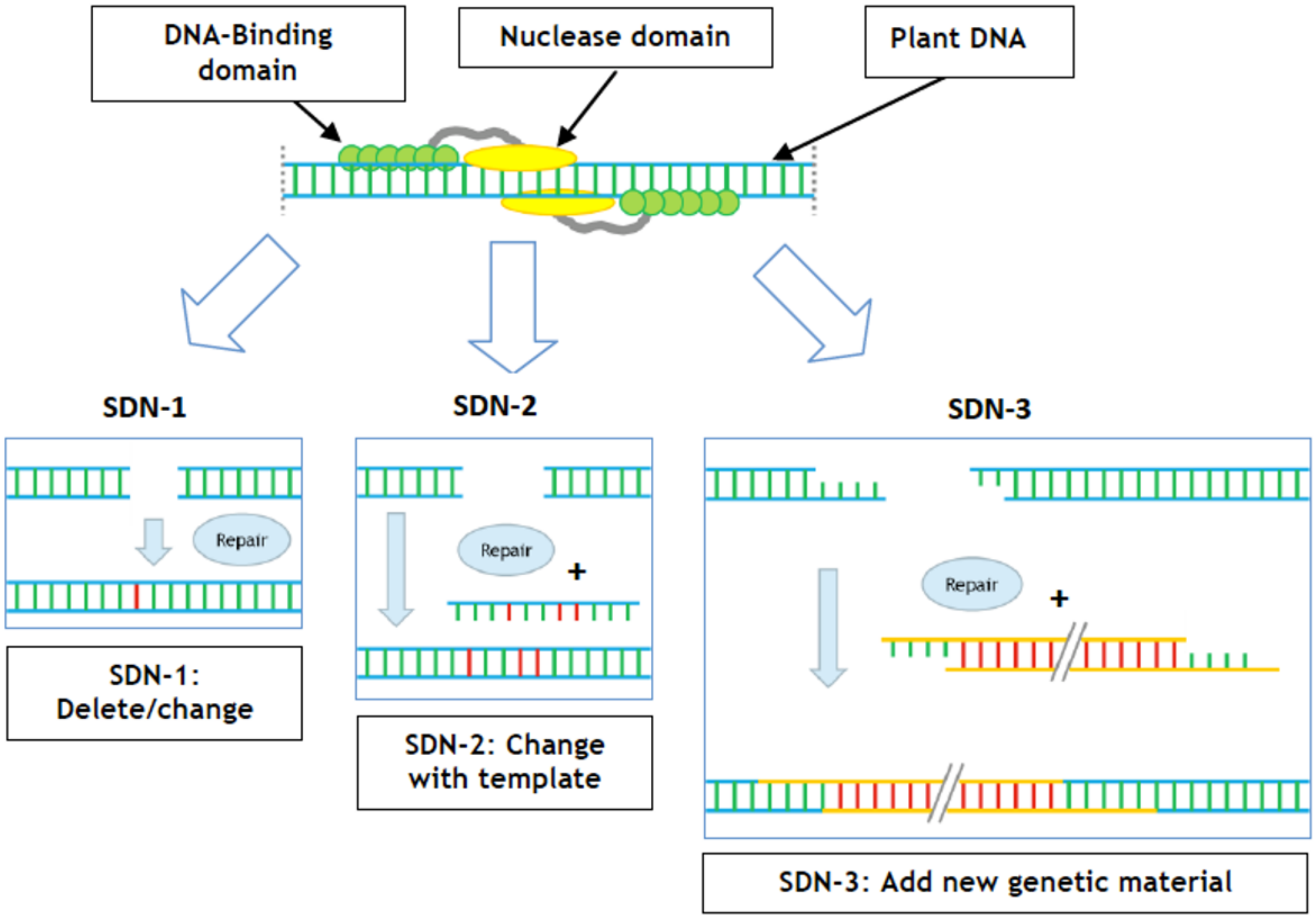
SDN technology:
different applications for different genome modifications



# Une attention particulière sur la mutagenèse ciblée par nucléases : pourquoi ?

En clair : on produit des plantes qu'on aurait pu produire par les approches conventionnelles de l'amélioration variétale (exploitation de la variation allélique du *gene pool* et augmentation de la variation allélique par mutagenèse aléatoire).

→Faut-il **réguler les mutants ciblés et les plantes cis- / intragéniques** comme les OGM régulés de la directive ou comme les mutants aléatoires exclus de celle-ci ?

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# Dans l'UE, les organismes à génomes édités par CRISPR/Cas9 sont des OGM.

CVRIA

Press and Information

**Court of Justice of the European Union**
**PRESS RELEASE No 111/18**
Luxembourg, 25 July 2018

Judgment in Case C-528/16
Confédération paysanne and Others v Premier ministre and Ministre de l'Agriculture, de l'Agroalimentaire et de la Forêt

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Décision de la Cour de Justice de l'UE  (25 Juillet 2018)

« *The Court of Justice takes the view, first of all, that organisms obtained by mutagenesis are GMOs within the meaning of the GMO Directive, in so far as the techniques and methods of mutagenesis alter the genetic material of an organism in a way that does not occur naturally. It follows that those organisms come, in principle, within the scope of the GMO Directive and are subject to the obligations laid down by that directive.* »

https://doi.org/10.1093/plphys/kiac359 PLANT PHYSIOLOGY 2022: 190: 1579–1587

Plant Physiology®

Update

# Genome editing around the globe: An update on policies and perceptions

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T.S., R.W., and F.H. wrote the manuscript.
The author responsible for distribution of materials integral to the findings presented in this article in accordance with the policy described in the Instructions for Authors (https://academic.oup.com/pphys/pages/General-Instructions) is Thorben Sprink.

## Abstract

A decade ago, the CRISPR/Cas system has been adapted for genome editing. Since then, hundreds of organisms have been altered using genome editing and discussions were raised on the regulatory status of genome edited organisms esp. crops. To date, many countries have made decisions on the regulatory status of products of genome editing, by exempting some kinds of edits from the classical GMO regulation. However, the guidance differs between countries even in the same region. Several countries are still debating the issue or are in the progress of updating guidance and regulatory systems to cover products of genome editing. The current global situation of different regulatory systems is putting a harmonized framework on genome-edited crops in the far future. In this update, we summarize the current developments in the field of regulation concerning edited crops and present a short insight into perception of genome editing in the society.

eu-sage.eu/index.php/genome-search

eusage

European Sustainable Agriculture Through Genome Editing

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**TRAITS CATEGORIES**

- ☐ Traits related to increased plant yield and growth (144)
- ☐ Traits related to improved food/feed quality (142)
- ☐ Traits related to biotic stress tolerance (118)
- ☐ Traits related to industrial utilization (93)
- ☐ Traits related to herbicide tolerance (49)
- ☐ Traits related to abiotic stress tolerance (48)
- ☐ Traits related to product color/flavour (38)
- ☐ Traits related to storage performance (13)

**GENOME EDITING TECHNIQUE**

- ☐ CRISPR/Cas (576)
- ☐ TALENs (30)
- ☐ BE (22)
- ☐ ZFN (7)
- ☐ ODM (6)

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# Traits related to industrial utilization

| | | | |
|---|---|---|---|
| Male sterility. Important genetic resources for commercial hybrid seed production. ( Zhang et al., 2021 ) | SDN1 CRISPR/Cas | Chinese Academy of Agricultural Sciences, | READ MORE |
| Manipulation of flowering time to develop cultivars with desired maturity dates. Stabilization of flowering time and period supports efficient mechanised harvesting. ( Ahmar et al., 2021 ) | SDN1 CRISPR/Cas | Huazhong Agricultural University, China | READ MORE |
| Generating male sterility lines (MLS). Using MLS in hybrid seed production for monoclinous crops reduces costs and ensures high purity of the varieties because it does not produce pollen and has exserted stigmas. ( Xie et al., 2018 ) | SDN1 CRISPR/Cas | University of Science and Technology Beijing, China Beijing Solidwill Sci-Tech Co. Ltd, China | READ MORE |
| Generating male sterility lines (MLS). Using MLS in hybrid seed production for monoclinous crops reduces costs and ensures high purity of the varieties because it does not produce pollen and has exserted stigmas | SDN1 CRISPR/Cas | Chinese Academy of Sciences, China | READ MORE |

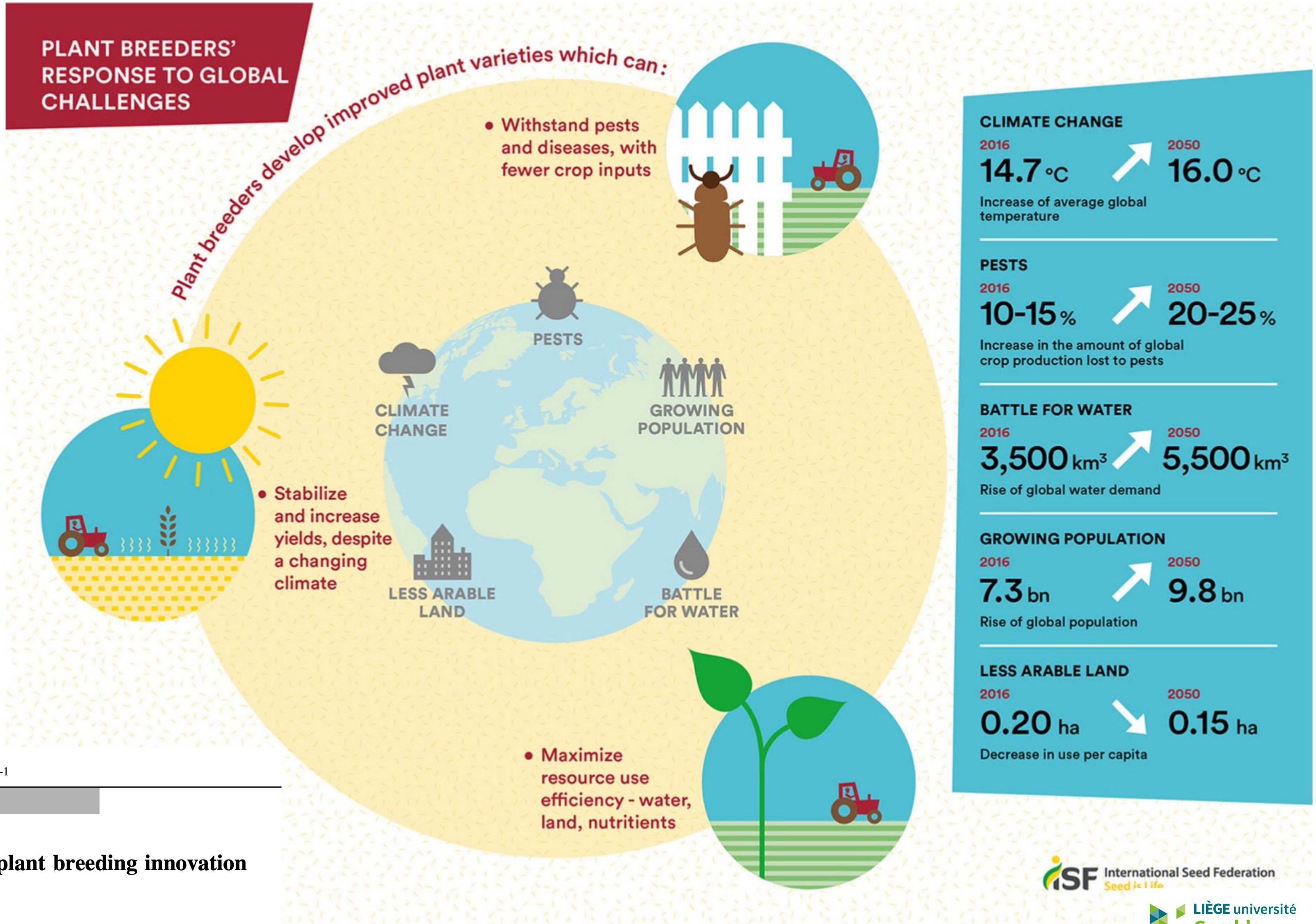
# Field trials of gene-edited and intragenic plants in the EU

(Source: JRC register, consulted on December 5th 2022, https://webgate.ec.europa.eu/fip/GMO_Registers/GMO_Part_B_Plants.php)

| Country | Plant | Trait (mutated gene) | Technology* |
|---|---|---|---|
| Belgium | Maize | Drought tolerance (histone-linker protein gene) | CRISPR/Cas9 |
| Belgium | Maize | Improved growth under UV-induced DNA damage (DNA-repair gene) | CRISPR/Cas9 |
| Belgium | Maize | Lowered lignin, higher forage digestiblity (lignin biosynthetic genes) | CRISPR/Cas9 |
| Belgium | Maize | Growth characteristics (cytochrome P450 monooxygenase gene) | CRISPR/Cas9 |
| Spain | Tobacco | Juvenility and impaired flowering (SPL gene) | CRISPR/Cas9 |
| Spain | Tobacco | Alkaloid composition (alkaloid biosynthetic genes) | CRISPR/Cas9 |
| Sweden | Poplar | Lignin content and composition (lignin biosynthetic genes) | CRISPR/Cas9 |
| Sweden | Potato | Amylose-free starch (granule-bound starch syntase gene) | CRISPR/Cas9 |
| UK | Cabbage | Lower glucosinolate (transcription factor) | CRISPR/Cas9 |
| Spain | Tobacco | Higher squalene content (squalene biosynthetic genes) | Intragenesis |

* gene-edited plants containing transgenes as selection markers are not included in the table.

# Pourquoi il faut « améliorer » les plantes cultivées




Transgenic Res (2019) 28:81–86
https://doi.org/10.1007/s11248-019-00138-1

PROCEEDINGS PAPER

**The global need for plant breeding innovation**

Petra Jorasch


HLPE. 2019. Agroecological and other innovative approaches for sustainable agriculture and food systems that enhance food security and nutrition. A report by the High Level Panel of Experts on Food Security and Nutrition of the Committee on World Food Security, Rome.

*(available at www.fao.org/cfs/cfs-hlpe)*

**Table 1 Consolidated set of 13 agroecological principles**

| Principle | FAO's ten elements | Scale application* |
|---|---|---|
| ***Improve resource efficiency*** | | |
| **1. Recycling.** Prefer~~entially use local renew~~able resources and close as far as possible resource cycles of nutrients and biomass. | Recycling | FI, FA |
| **2. Input reduction.** Reduce or eliminate dependency on purchased inputs and increase self-sufficiency | Efficiency | FA, FO |
| ***Strengthen resilience*** | | |
| **3. Soil health.** Secure and enhance soil health and functioning for ~~improved plant growth, particularly~~ by managing organic matter and enhancing soil biological activity. | | FI |
| **4. Animal health.** Ensure animal health and welfare. | | FI, FA |
| **5. Biodiversity.** Maintain and enhance diversity of species, functional ~~diversity and genetic resources and thereby maintain overall~~ agroecosystem biodiversity in time and space at field, farm and landscape scales. | Part of diversity | FI, FA |
| **6. Synergy.** Enhance positive ecological interaction, synergy, integration and ~~complementarity among the elements of~~ agroecosystems (animals, crops, trees, soil and water). | Synergy | FI, FA |
| **7. Economic diversification.** Diversify on-farm incomes by ensuring that small-scale farmers have greater financial independence and value addition opportunities while enabling them to respond to demand from consumers. | Part of diversity | FA, FO |
| ***Secure social equity/responsibility*** | | |
| **8.Co-creation of knowledge.** Enhance co-creation and horizontal sharing of knowledge including local and scientific innovation, especially through farmer-to-farmer exchange. | Co-creation and sharing of knowledge | FA, FO |
| **9. Social values and diets.** Build food systems based on the culture, identity, tradition, social and gender equity of local communities that provide healthy, diversified, seasonally and culturally appropriate diets. | Parts of human and social values and culture and food traditions | FA, FO |
| **10. Fairness.** Support dignified and robust livelihoods for all actors engaged in food systems, especially small-scale food producers, based on fair trade, fair employment and fair treatment of intellectual property rights. | | FA, FO |
| **11. Connectivity.** Ensure proximity and confidence between producers and consumers through promotion of fair and short distribution networks and by re-embedding food systems into local economies. | Circular and solidarity economy | FA |
| **12. Land and natural resource governance.** Strengthen institutional arrangements to improve, including the recognition and support of family farmers, smallholders and peasant food producers as sustainable managers of natural and genetic resources. | Responsible governance | FA, FO |
| **13. Participation.** Encourage social organization and greater participation in decision-making by food producers and consumers to support decentralized governance and local adaptive management of agricultural and food systems. | | FO |

*Scale application: FI = field; FA = farm, agroecosystem; FO = food system
*Source:* derived from from Nicholls *et al.*, 2016; CIDSE, 2018; FAO, 2018c.

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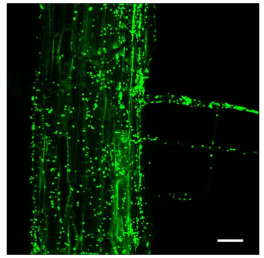
# Domaines à fort potentiel d'amélioration variétale par édition de génomes (exploitation de la variation allélique sans transfert de gènes)

| | |
|---|---|
| **Biologie des interfaces** | Interaction avec les bioagresseurs<br>- Gènes de résistance, confusion chimique<br>- Recrutement d'antagonistes<br>Interaction avec les (micro)organismes bénéfiques<br>- Immunité, effet *priming*<br>- Biostimulation<br>- Symbioses mutualistes |
| **Résilience des cultures et atténuation du changement climatique** | Tolérance aux stress abiotiques<br>Productivité photosynthétique et puits de carbone |
| **Qualité des produits végétaux** | Suppression de composés antinutritionnels<br>Ingénierie métabolique (métabolismes primaire et secondaires)<br>Conservation des aliments |



AGENCE NATIONALE DE LA RECHERCHE
ANR

# LES APPORTS DE LA GÉNOMIQUE À L'AGROÉCOLOGIE

**Bilan des projets financés sur la période 2005–2019 et perspectives pour la recherche**

LES CAHIERS DE L'ANR **N° 12** - SEPTEMBRE 2020

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HLPE. 2019. Agroecological and other innovative approaches for sustainable agriculture and food systems that enhance food security and nutrition. A report by the High Level Panel of Experts on Food Security and Nutrition of the Committee on World Food Security, Rome.

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# L'édition des génomes : un contexte d'innovation problématique

- Traçabilité de la technologie :

  **Comment distinguer un allèle obtenu par mutagenèse ciblée du même allèle « natif » ou obtenu par mutagenèse aléatoire ?** Comment étiqueter et informer le consommateur sans pouvoir tracer ? Comment contrôler les marchés ? Comment organiser la co-existence entre cultures GM et non GM ?

- Accès à la technologie :

  Propriété intellectuelle par brevet sur la technologie (sur le nouveau trait, donc sur l'allèle, donc sur le matériel biologique qui l'exprime …).

- Insécurité juridique sur les semences :

  Comment éviter les procès en contrefaçon contre les allèles « natifs », identiques aux allèles mutés par SDN et brevetés ?

Coordination européenne Via Campesina Bruxelles, le 9 novembre 2022

# IMPACTS DE L'INITIATIVE DE LA COMMISSION VISANT À MODIFIER LA RÉGLEMENTATION DE CERTAINS OGM VÉGÉTAUX SUR L'APPLICATION DU DROIT EUROPÉEN DES BREVETS

# Pour nourrir le débat …

Le chercheur en biotechnologie n'est-il pas ambivalent lorsqu'il revendique la maîtrise des génomes et en même temps des pratiques similaires à l'amélioration des plantes « classique »?

Grâce à l'édition des génomes, l'agriculture conventionnelle deviendra-t-elle plus vertueuse que l'AB du point de vue environnemental ?

A-t-on des raisons de penser que le consommateur réservera un meilleur accueil aux « nouveaux OGM » qu'aux premiers mis sur le marché ?

Merci pour votre attention !

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