Genome-Edited Foods

Yiping Qi, PhD
Professor of Plant Science and Landscape Architecture
University of Maryland, College Park

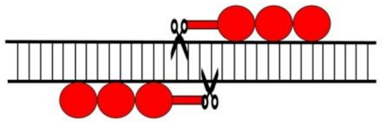
Maximizing Agriculture to Enhance Nutrient Composition to Better Fulfill Dietary Recommendations

NASEM Workshop, Jan 30, 2024

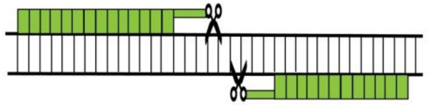
Rapid Evolution of Sequence Specific Nucleases (SSNs) for Plant Genome Editing

Image source: Greenhouse Grower

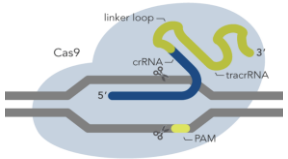
1st demo in Plants



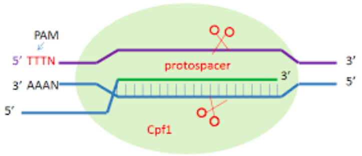
Zinc-Finger Nucleases (ZFNs) — **2005**



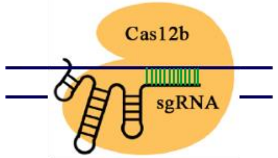
TALENs — **2011**



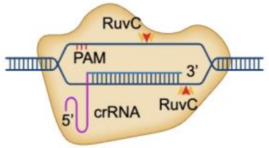
CRISPR-Cas9 — **2013**



CRISPR-Cas12a (Cpf1) — **2016**

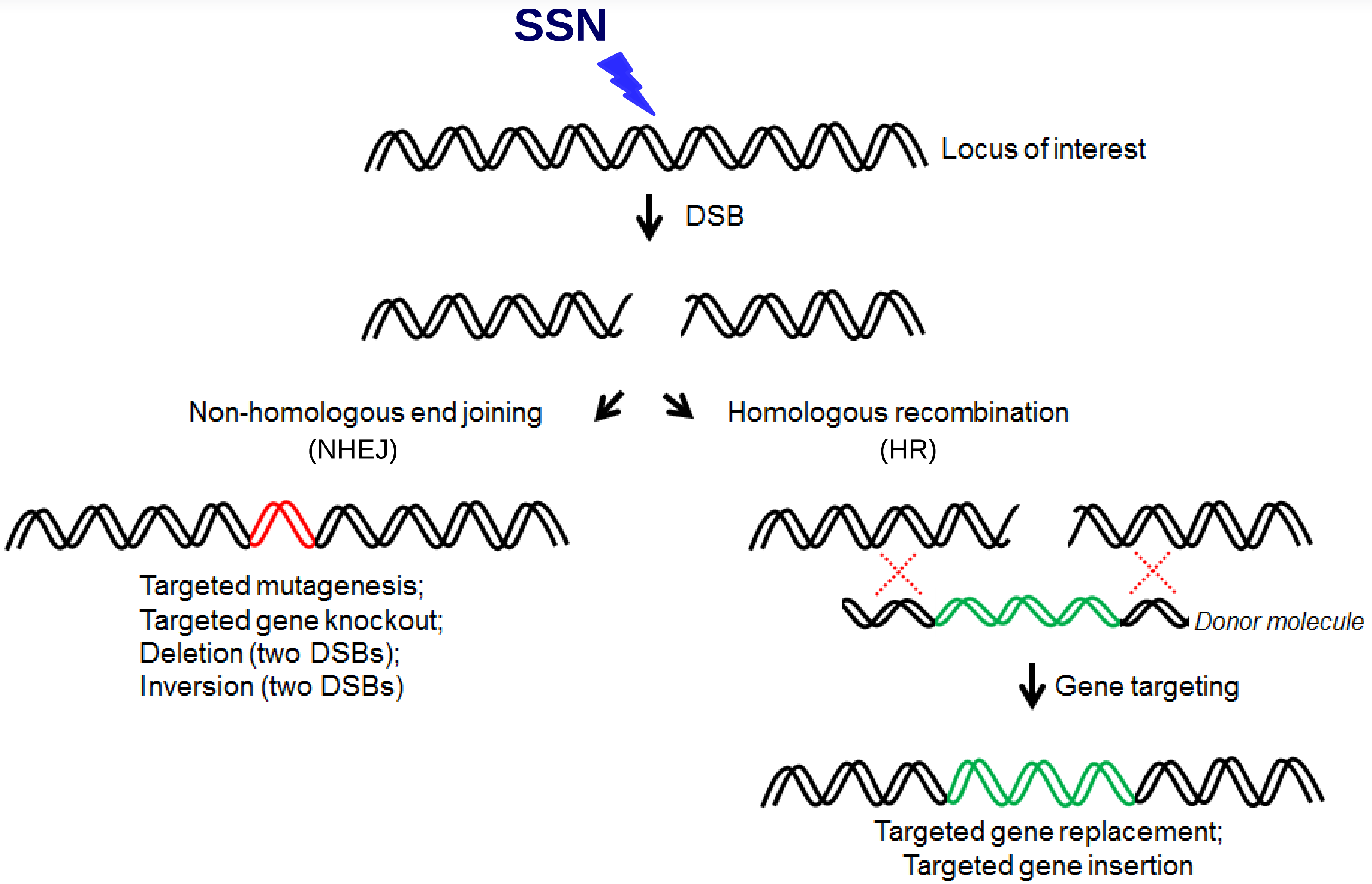


CRISPR-Cas12b — **2020**

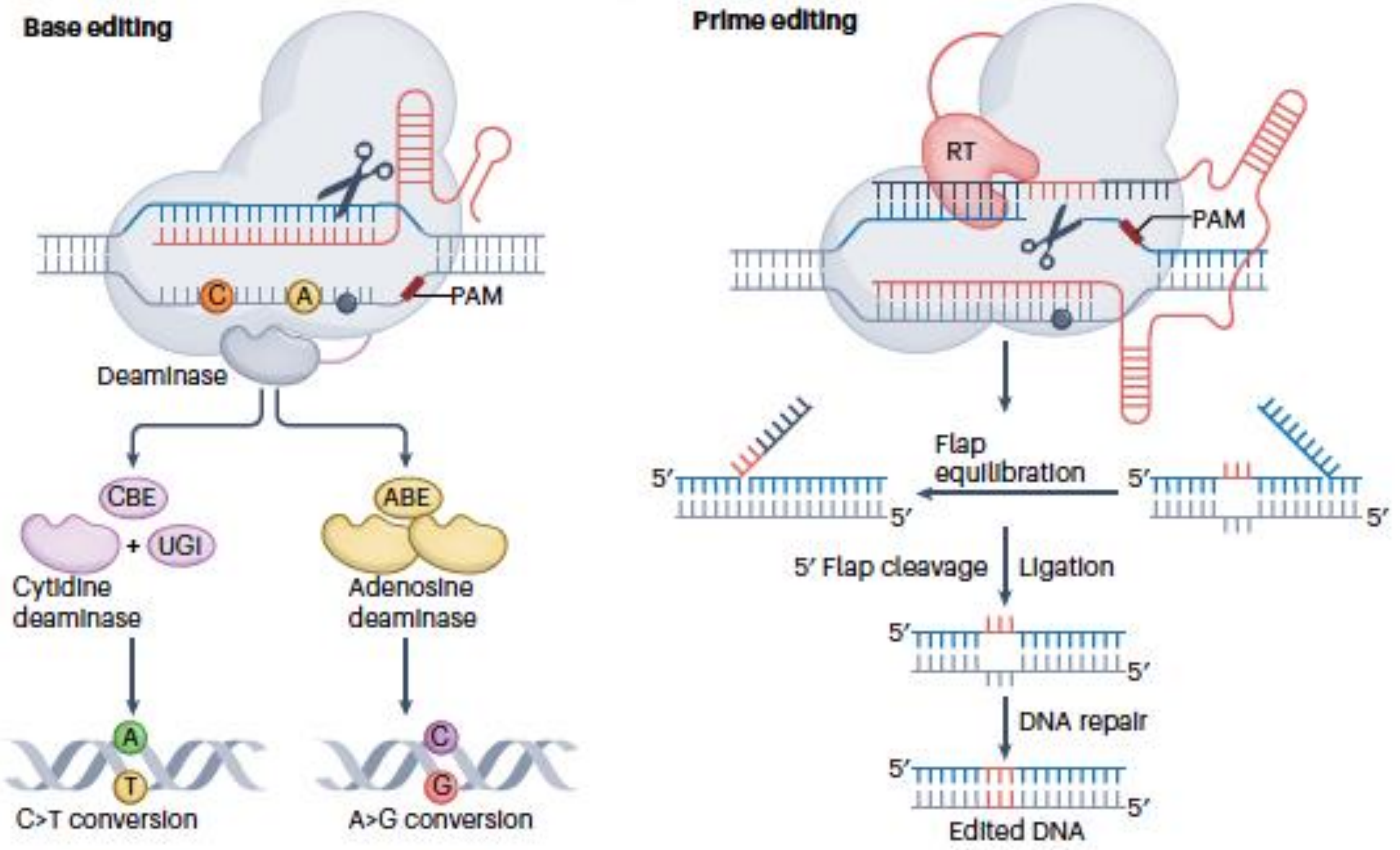


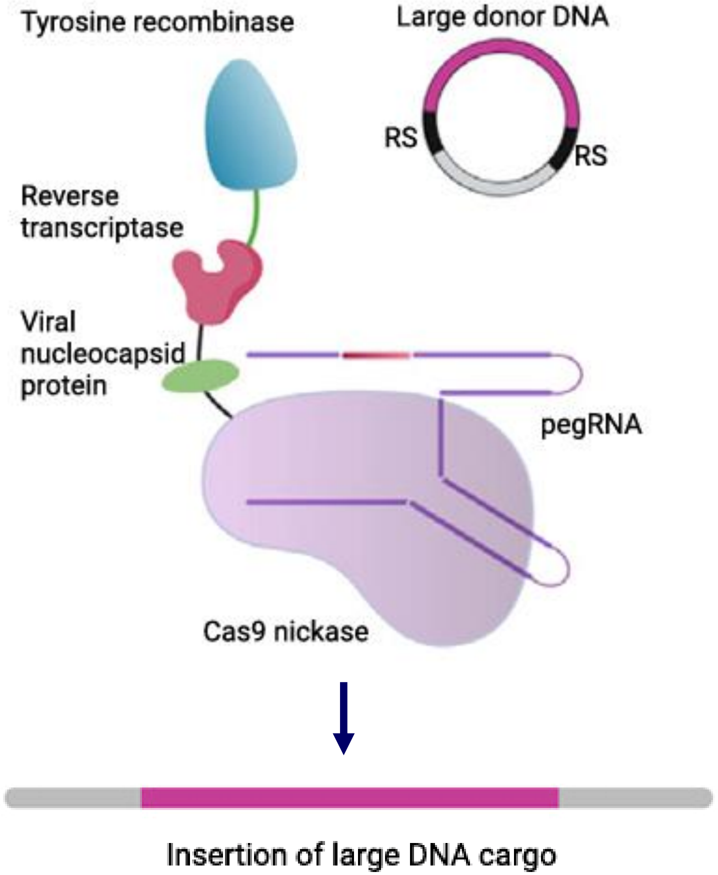
CRISPR-Cas12j (CasΦ) — **2022**

Genome Editing Requires Sequence-Specific Nucleases (SSNs)



Precise Base Changes, Gene Replacement, and Gene Insertion by CRISPR Derived Technologies





Tuncel et. al, Nature Review Bioeng, 2023
Pan and Qi, Trends in Plant Sci, 2023

Genome Editing is Set to Revolutionize Crop Breeding

Metrics	GM	Genome editing
Regulation	Heavy, currently only permitted in about ~30 countries	Potentially light regulation, not regulated in some countries
Timeline to develop a new trait*	~13 years	~ 5 years
Cost to develop a new trait	~$136 Million	~$10 Million or To be determined
Applicable crops	Corn, soybean, cotton, canola, papaya	Almost all crops if an editing system is available

*From gene discovery to commercialization
Reference: Phillips McDougall AgriFutura Newsletter No. 222

Safety Assessment of Two Top CRISPR Genome Editing Systems

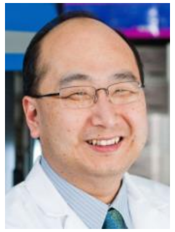
Plant Biotechnology Journal

Plant Biotechnology Journal (2018), pp. 1–11 doi: 10.1111/pbi.12982

Activities and specificities of CRISPR/Cas9 and Cas12a nucleases for targeted mutagenesis in maize

Keunsub Lee[1,2], Yingxiao Zhang[3], Benjamin P. Kleinstiver[4,5], Jimmy A. Guo[4], Martin J. Aryee[5,6], Jonah Miller[1], Aimee Malzahn[3], Scott Zarecor[1,7], Carolyn J. Lawrence-Dill[1,2,7,8], J. Keith Joung[4,5], Yiping Qi[3,9,*] and Kan Wang[1,2,*]

Kan Wang
(ISU)



Keith Joung
(Harvard)

Tang *et al. Genome Biology* (2018) 19:84
https://doi.org/10.1186/s13059-018-1458-5

Genome Biology

RESEARCH Open Access

A large-scale whole-genome sequencing analysis reveals highly specific genome editing by both Cas9 and Cpf1 (Cas12a) nucleases in rice

Xu Tang[1†], Guanqing Liu[2,3†], Jianping Zhou[1†], Qiurong Ren[1], Qi You[2,3], Li Tian[1], Xuhui Xin[1], Zhaohui Zhong[1], Binglin Liu[1], Xuelian Zheng[1], Dengwei Zhang[1], Aimee Malzahn[4], Zhiyun Gong[2], Yiping Qi[4,5*], Tao Zhang[2,3*] and Yong Zhang[1*]

Yong Zhang
(UESTC)

Tao Zhang
(Yangzhou U)

The SECURE Rule by USDA-APHIS

AUTHENTICATED U.S. GOVERNMENT INFORMATION GPO

29790 **Federal Register** / Vol. 85, No. 96 / Monday, May 18, 2020 / Rules and Regulations

DEPARTMENT OF AGRICULTURE

Animal and Plant Health Inspection Service

7 CFR Parts 330, 340, and 372

[Docket No. APHIS–2018–0034]

RIN 0579–AE47

Coordinated Framework for Regulation of Biotechnology (Coordinated Framework) [1] was published by the Office of Science and Technology Policy. It describes the comprehensive Federal regulatory policy for ensuring the safety of biotechnology research and products and explains how Federal agencies use existing Federal statutes to ensure public health and environmental

On January 19, 2017, we published in the **Federal Register** (82 FR 7008–7039, Docket No. APHIS–2015–0057) a proposed rule [2] intended to revise our regulatory approach from ''regulate first before analyzing risks'' to ''analyze plant pest and noxious weed risks of GE organisms prior to imposing regulatory restrictions.''

Under the January 2017 proposed

APHIS

Lee, K., Y. Zhang, B.P. Kleinstiver, *et al.* (2018). Activities and specificities of CRISPR/Cas9 and Cas12a nucleases for targeted mutagenesis in maize. Plant Biotechnol J. *https://onlinelibrary.wiley.com/doi/10.1111/pbi.12982.*

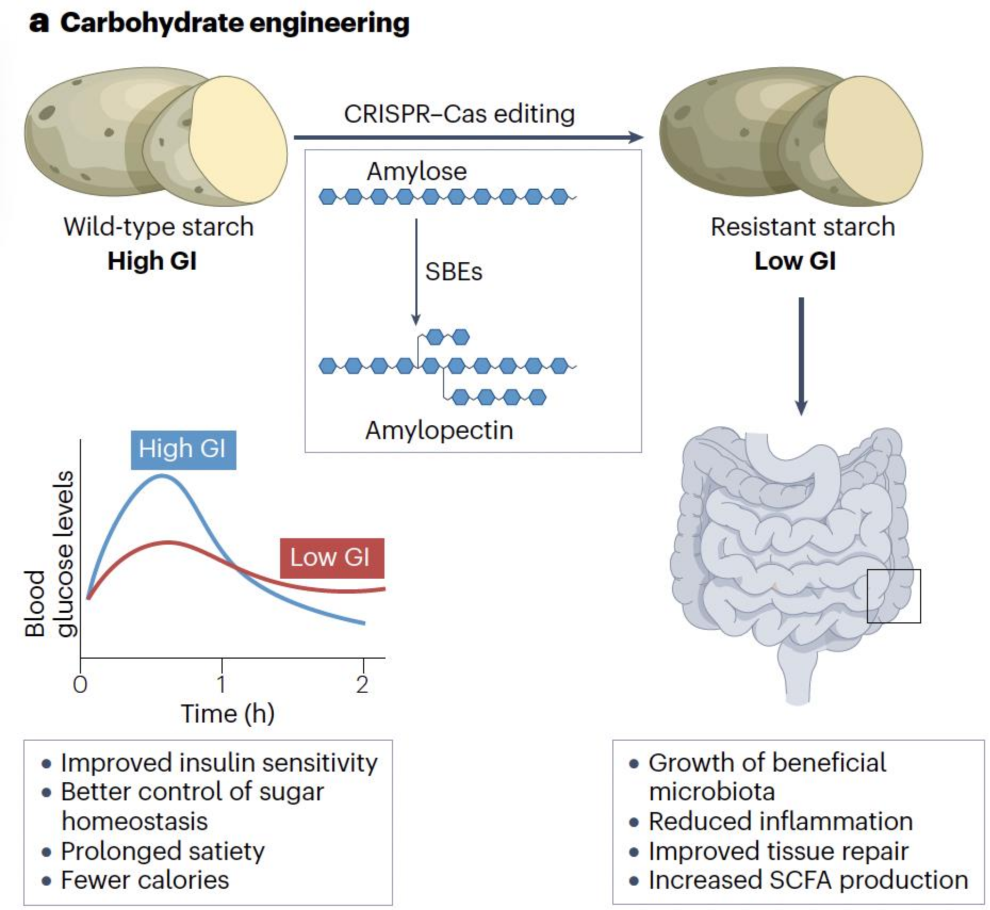
Tang, X, G. Liu, J. Zhou, *et al.* (2018) A large-scale whole-genome sequencing analysis reveals highly specific genome editing by both Cas9 and Cpf1 (Cas12a) nucleases in rice. Genome Biol 19:84. *https://genomebiology.biomedcentral.com/articles/10.1186/s13059-018-1458-5.*

De-regulate:

- **Single SSN-induced small insertions and deletions (indels)**
- **Singe base change**

Engineering the Nutritional Value of Crops by Genome Editing

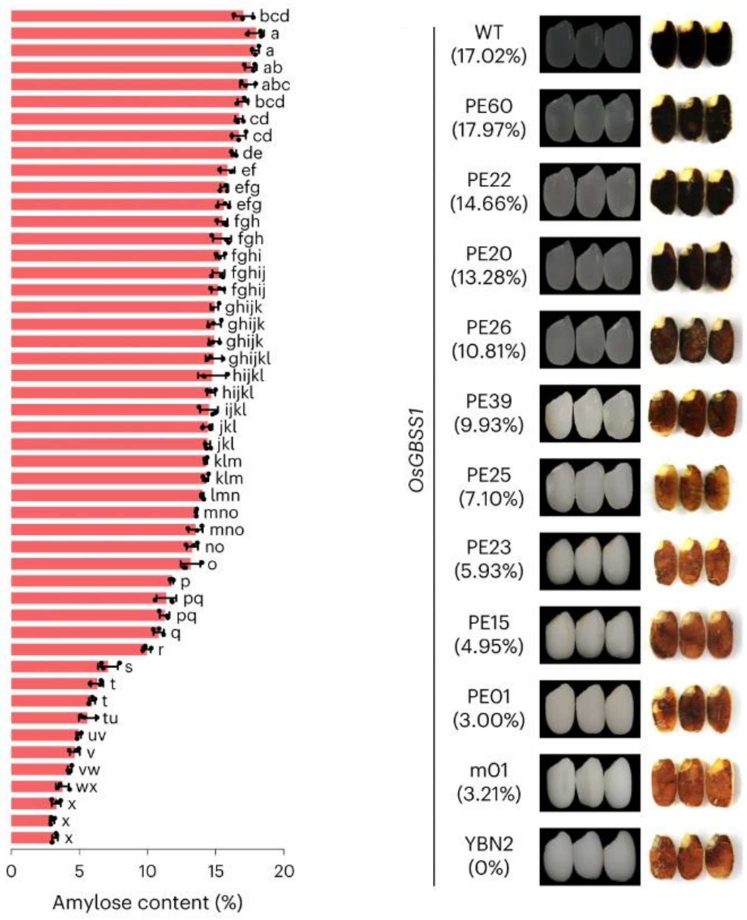
❖ Macronutrient



GI: glycaemic index

Tuncel et. al, Nature Review Bioeng, 2023

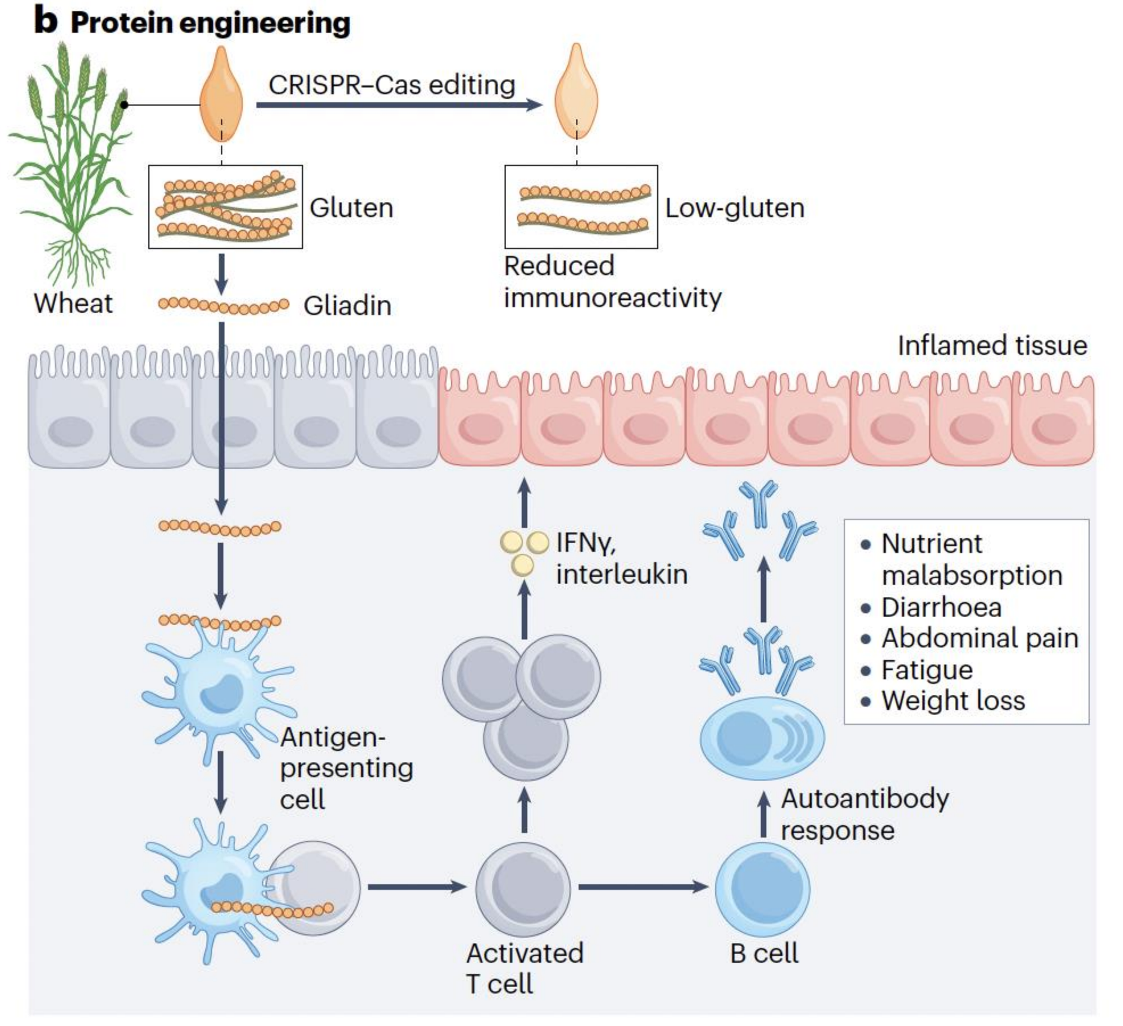
Promoter editing of GBSS1



Zhou et. al, Nature Plants, 2023

Engineering the Nutritional Value of Crops by Genome Editing

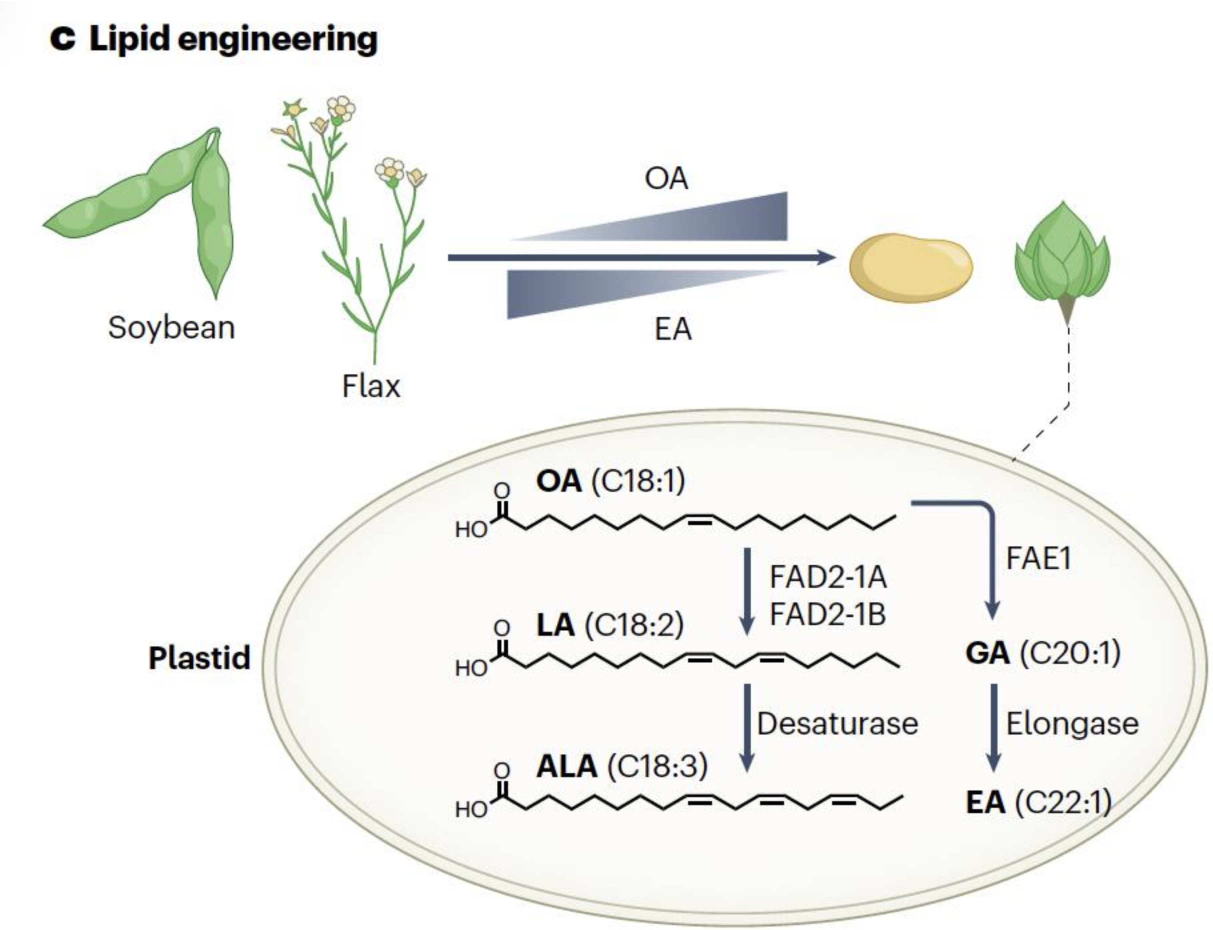
- ❖ **Macronutrient**



Tuncel et. al, Nature Review Bioeng, 2023

Engineering the Nutritional Value of Crops by Genome Editing

❖ Macronutrient

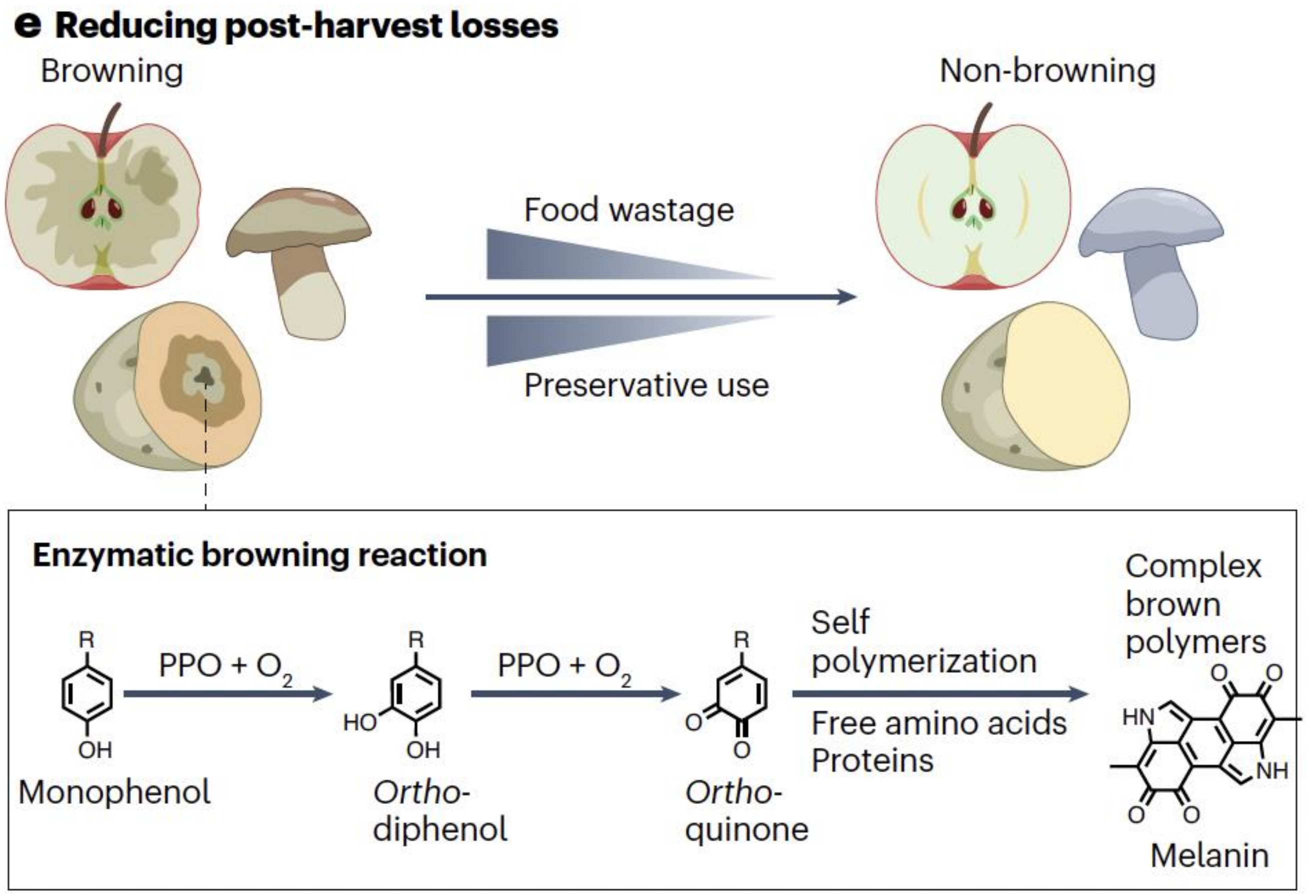


OA: Oleic acid

Tuncel et. al, Nature Review Bioeng, 2023

Engineering the Nutritional Value of Crops by Genome Editing

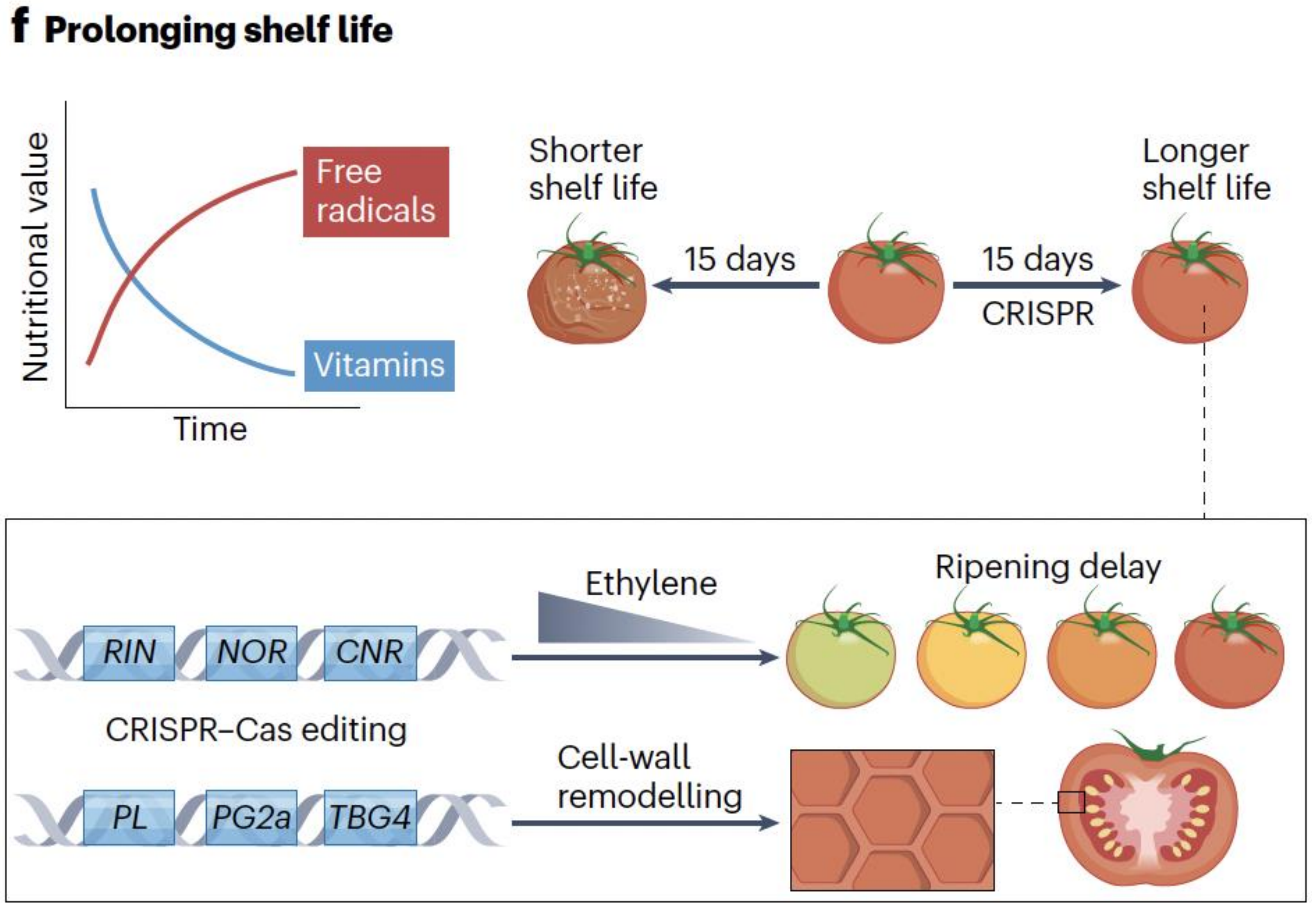
❑ Preserve nutrition



Tuncel et. al, Nature Review Bioeng, 2023

Engineering the Nutritional Value of Crops by Genome Editing

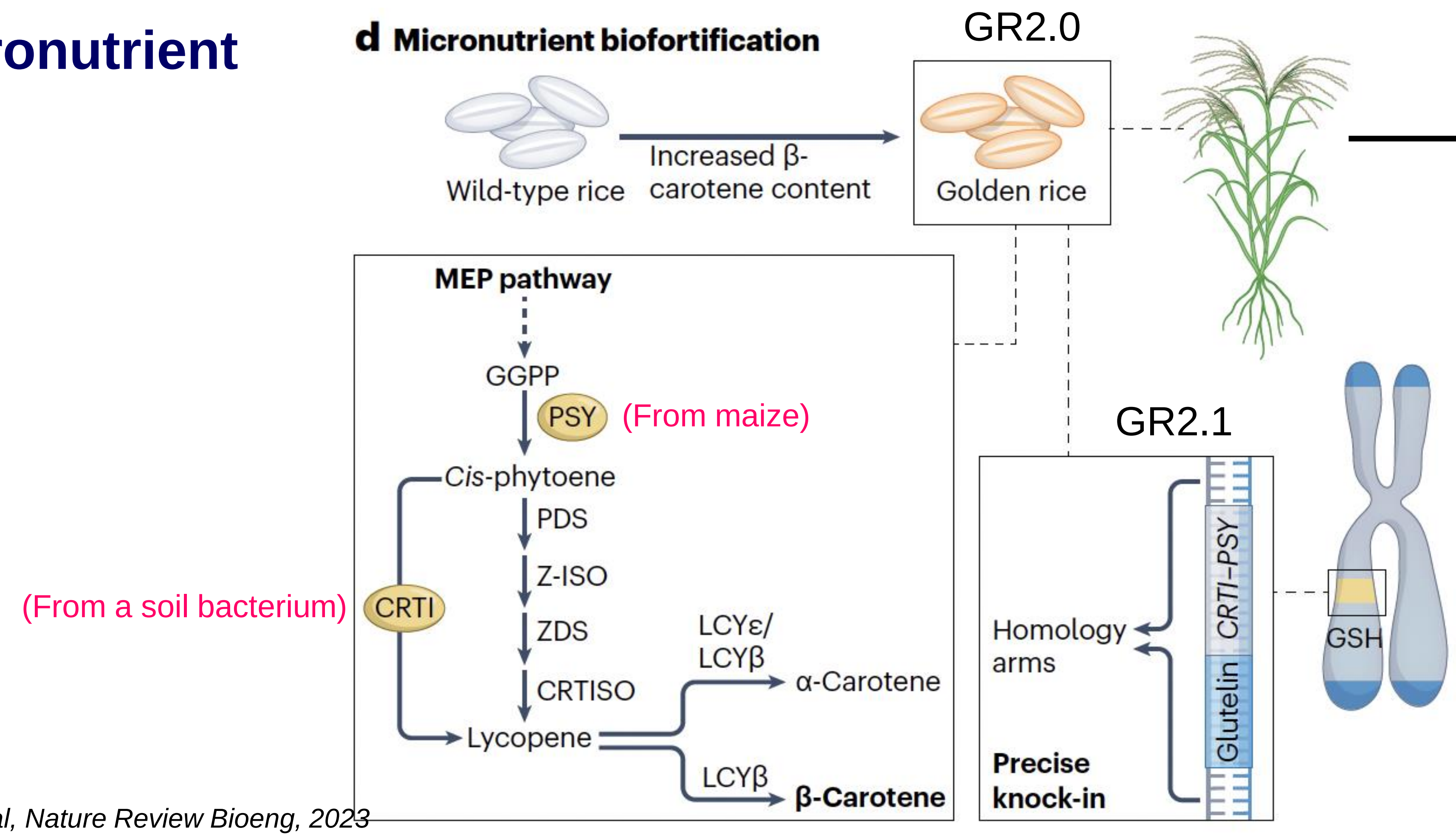
❑ Preserve nutrition



Tuncel et. al, Nature Review Bioeng, 2023

Engineering the Nutritional Value of Crops by Genome Editing

- **Micronutrient**



Fight Vitamin A deficiency

- Low beta-carotene
- Still a GMO

Next-generation Golden Rice

USDA NIFA

Tuncel et. al, Nature Review Bioeng, 2023

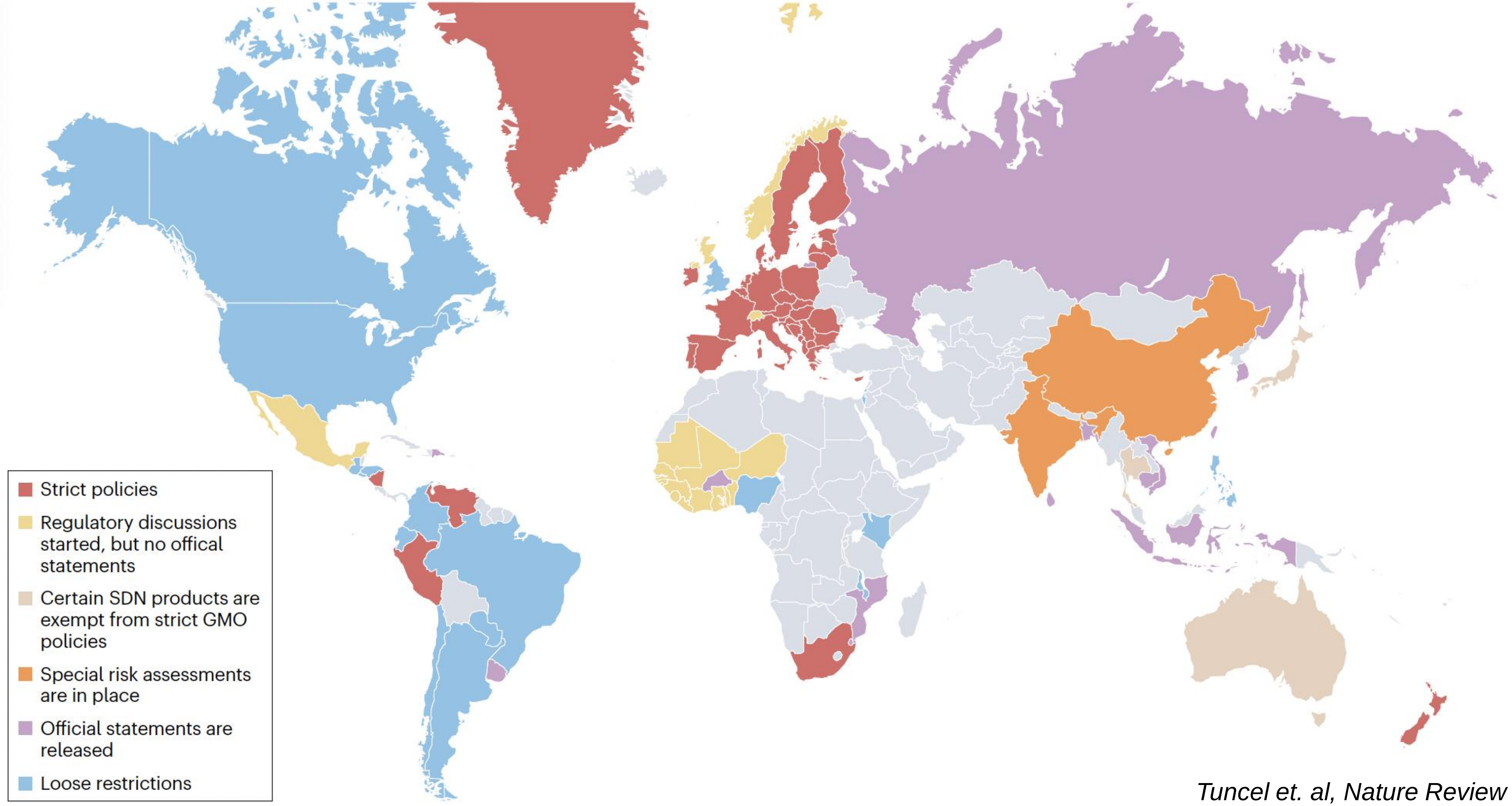
Genome-Edited Products Available in the Market or Awaiting Approval

Product	Target genes	Method	Phenotype	Market status	Company
Maize[35,189]	*GBSSI*	CRISPR–Cas	High-yield waxy	Pre-commercial	Corteva
Tomato[52]	*GAD3*	CRISPR–Cas	High GABA	Released, 2021	Sanatech Seed
Soybean[54,190]	*FAD2-1A*, *FAD2-1B*	TALEN	High oleic acid	Released, 2019	Calyxt
Red sea bream[157]	Myostatin	CRISPR–Cas	More muscle mass	Released, 2021	Regional Fish Institute
Tiger puffer fish[157]	Leptin receptor	CRISPR–Cas	Increased appetite	Released, 2021	Regional Fish Institute
Cattle[183]	Prolactin receptor	CRISPR–Cas	Heat-tolerant slick coat	FDA-approved	Recombinatics
Pennycress[191]	NA	CRISPR–Cas	Reduced erucic acid and fibre	Pre-commercial FDA-approved	CoverCress
Lettuce (GreenVenus)[192]	NA	CRISPR–Cas	Non-browning	Pre-commercial, expected release, 2023	Intrexon
Mustard greens[193]	Myrosinase	CRISPR–Cas	Reduced pungency	FDA-approved, expected release, 2023	Pairwise

FDA, US Food and Drug Administration; NA, not available; TALEN, transcription activator-like effector nuclease.

Tuncel et. al, Nature Review Bioeng, 2023

Global Regulation of Genome Edited Crops



Tuncel et. al, Nature Review Bioeng, 2023

Summary

1. There has been very rapid development of genome editing technologies.
2. These technologies can speed up crop breeding and promote innovations in crop improvements on **nutrition** and other traits (e.g., yield, climate resilience, etc.)
3. Global regulations, currently falling behind, play key roles on commercialization of genome edited foods.

nature reviews bioengineering

https://doi.org/10.1038/s44222-023-00115-8

Review article

Check for updates

Genome-edited foods

Aytug Tuncel[1], Changtian Pan[2], Thorben Sprink[3], Ralf Wilhelm[3], Rodolphe Barrangou[4,5], Li Li[6,7], Patrick M. Shih[8,9,10,11], Rajeev K. Varshney[12], Leena Tripathi[13], Joyce Van Eck[7,14], Kranthi Mandadi[15,16,17] & Yiping Qi[1,18]