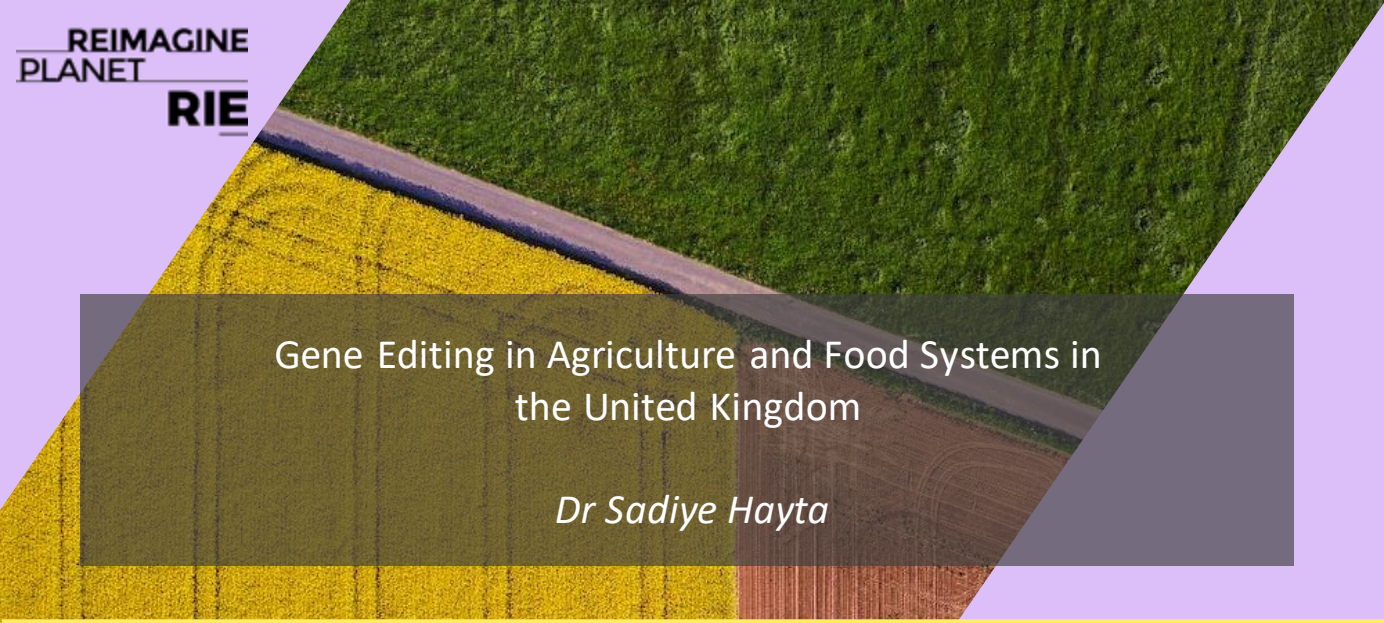
REIMAGINE PLANET RIE



Gene Editing in Agriculture and Food Systems in the United Kingdom

Dr Sadiye Hayta

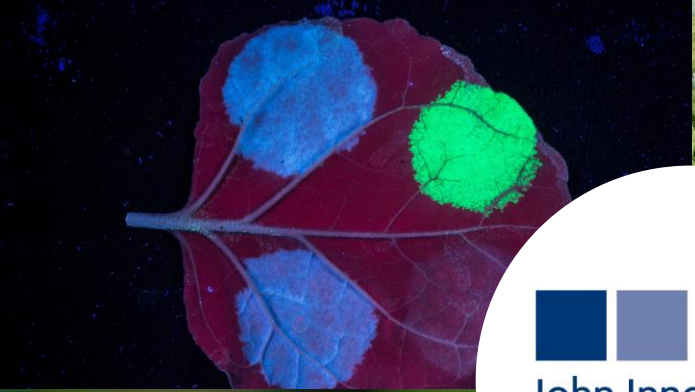
Sponsored by:
The OECD Co-operative Research Programme: Sustainable Agricultural and Food Systems

OECD
BETTER POLICIES FOR BETTER LIVES

Global Conference on
Sustainability in Agriculture & Food Systems
Innovation, Indicators & Implementation

Norwich Research Park

A unique cluster of world class institutions all located within 1km



John Innes Centre

Unlocking Nature's Diversity

Advancing Plant Health

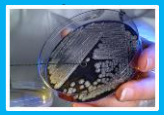
- Reduce chemical inputs
- Burden of disease/pests
- Promote plant health
- In the context of global challenges

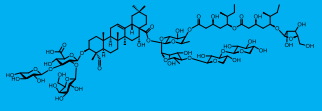
Building Robustness in Crops

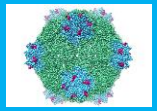
- Identify how to improve yield
- Optimise plant architecture
- Predict & manipulate plant response
- Deliver climate-resilient crops

Harnessing Biosynthesis for Sustainable Food & Health

- Plant-based food with enhanced nutrition
- Crops that require low inputs of chemicals
- Sustainable routes to valuable molecules
- Address emerging diseases & antimicrobial







Delivering Sustainable Wheat

- Increased wheat yield with improved nutrition
- Pest management and climate adaption
- Adaption to changing agriculture methods
- Delivery throughout the supply chain

WHAT IS DSW?

A multi-institute collaborative effort that addresses challenges in future global wheat production, focusing on increasing productivity and human nutrition while minimizing agricultural inputs.

RESOURCES

Watkins sequence

Germplasm

Long Range Haplotype

DELIVERY

WISP DFW

Breeders Toolkit

Providing pre-breading traits to wheat breeding companies

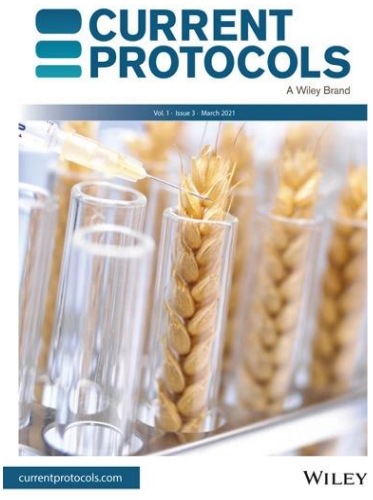
DSW

Breeders Toolkit

Gene Edited

JIC WHEAT TRANSFORMATION

John Innes Centre
Unlocking Nature's Diversity



Current Protocols / Volume 1, Issue 3 / e65
PROTOCOL | Open Access

CRISPR-Cas9 Based Genome Editing in Wheat

Mark A. Smedley, Sadiye Hayta, Martha Clarke, Wendy A. Harwood

First published: 09 March 2021
https://doi.org/10.1002/cpz1.65

Current Protocols / Volume 1, Issue 3 / e58
PROTOCOL | Open Access

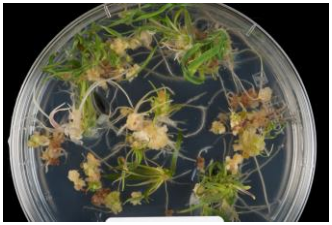
An Efficient *Agrobacterium*-Mediated Transformation Protocol for Hexaploid and Tetraploid Wheat

Sadiye Hayta, Mark A. Smedley, Martha Clarke, Macarena Forner, Wendy A. Harwood

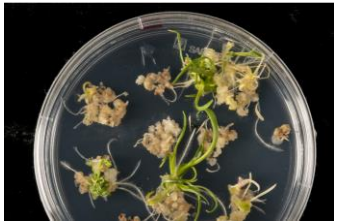
First published: 03 March 2021
https://doi.org/10.1002/cpz1.58

addgene
A better way to share plasmids

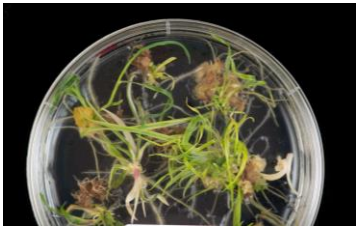
Transformation has become more genotype independent



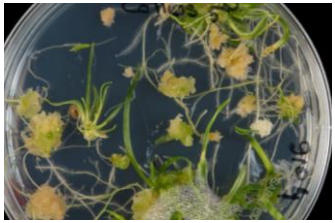
Paragon



Cadenza



Skyfall



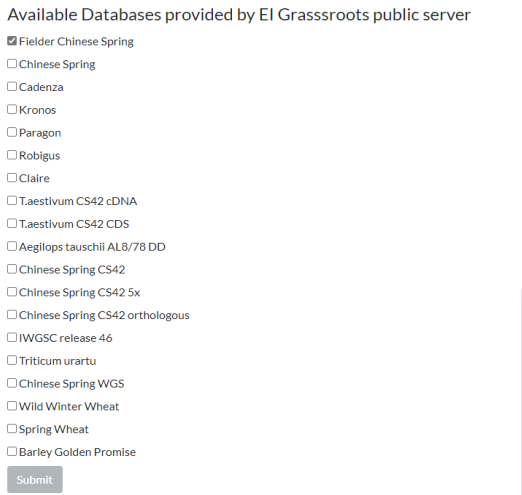
Borlaug100 (AKA Reedling)

CRISPR in wheat

The wheat varieties we transform

- Fielder
- Kronos
- Cadenza and mutant lines
- Paragon and mutant lines
- Chinese Spring
- Winter wheat
- Elite and commercial varieties

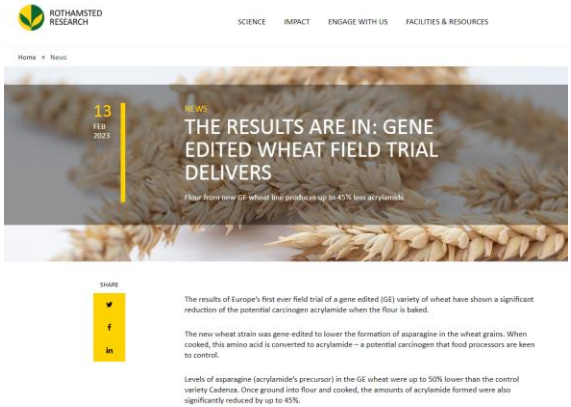
More sequences are available



CRISPR-Cas9 based gene editing in wheat

- We can use CRISPR-Cas based genome editing regularly in different wheat varieties.

Wheat gene editing in UK



May 2021

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Chile and Mexico-CIMMYT

CRISPR Brassica field trial -2019

John Innes Centre
Unlocking Nature's Diversity

Large documentation to DEFRA and reviewed by ACRE.

Several local authority bodies and public also required notification.

90 days review.

First CRISPR Brassica field trial 2019 at JIC aiming to better characterise the role of Myb28 in regulating sulphur metabolism, specifically the accumulation of aliphatic glucosinolates, in field-grown *Brassica oleracea*.
Mikhaela Neequaye, Lars Ostergaard JIC

New Genetic Technology (Precision Breeding Bill)

- Apply to NBT where end product could have been achieved through traditional breeding methods

Step 1: **To unlock research** in plants by making it easier to carry out research field trials. Requiring a notification to Defra but will not have the burden of GMO approval process. **April 2022**

Step 2: Bring forward primary legislation to amend the definition of a **GMO to exclude organisms** that have genetic changes that could have been **achieved through traditional breeding methods.**

Gene-edited tomatoes to produce vitamin D

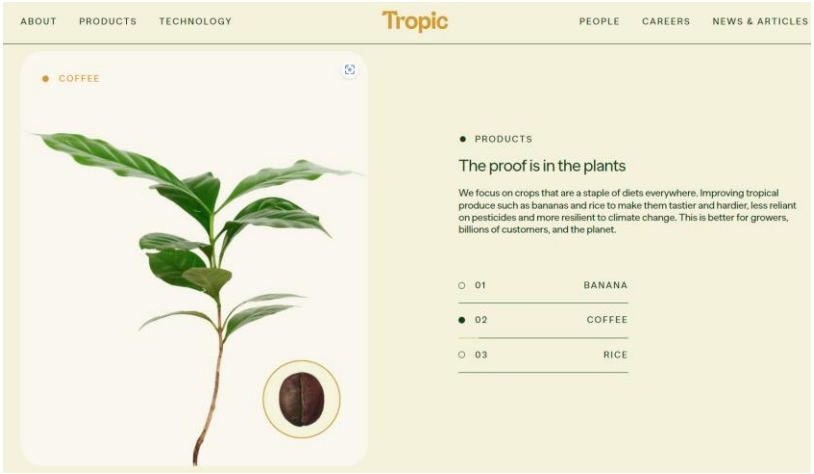
John Innes Centre
Unlocking Nature's Diversity

June 2022-This GE tomato with extra vitamin D

Prof Cathie Martin

The plants started to grow outside within 20 days of submitting the notification

Tropic Bioscience (Norwich Research Park)



- Non browning banana
- Virus resistant bananas
- Naturally decaffeinated coffee

May-2023

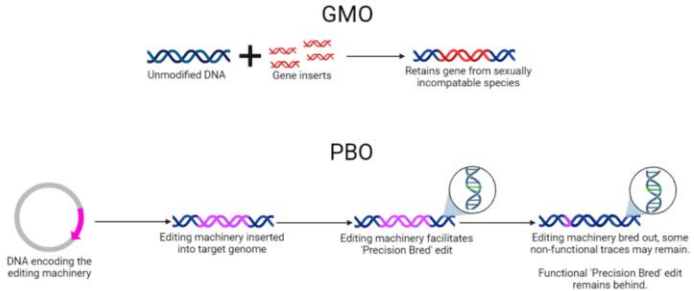
Tropic's Non-Browning Gene-Edited Banana Cleared for Production in the Philippines

From policy proposal to an Act...

The Genetic Technology (Precision Breeding) Bill received Royal Assent from the King on Thursday 23rd March 2023, becoming an Act.

What is Precision Breeding?

- Precision breeding (PB) describes a range of technologies, such as **gene editing**, that enables DNA to be edited **much more efficiently and precisely** than current breeding techniques. **This is different to GM**.
- We are defining as organisms produced by **modern biotechnology,** but which could have also been **produced through traditional processes**.
- Scientific advice is that there is **no greater risk to the environment** than organisms developed through traditional breeding.



Key policy changes

The Act will bring about the following policy changes:

Removal of precision bred plants and animals from regulatory requirements applicable to GMOs

Organisms whose genomes have been altered using modern biotechnology

Genetically modified organisms (GMOs): produces organisms **containing genes from a sexually incompatible species** and that **could not occur through traditional breeding.**

Precision bred organisms (PBOs): where the genetic changes could have occurred **naturally or through traditional breeding** methods.

Key policy changes

The implementation of the associated delegated powers will deliver a more proportionate and science based regulatory system:

Introduction of two notification systems:

- **For research purposes**, developers will need to notify precision bred organisms to Defra before trials can take place.
- **For marketing,** developers will need to notify Defra and receive a confirmation from Defra SoS on the status of the organism.
- The information collected will be published on a public register.

Establishment of a proportionate regulatory system for precision bred animals that ensures animal welfare is safeguarded. Defra will not be introducing changes to the regulations for animals until this system is in place.

Establishment of a new science-based authorisation process for food and feed products developed using precision bred organisms.

Advisory Committee on Releases to the Environment

Qualifying higher plants (QHPs)

Unlocking research in plants

Research and analysis

Technical guidance on using genetic technologies (such as gene-editing) for making 'qualifying higher plants' for research trials

Published 11 April 2022

Applies to England

https://www.gov.uk/government/publications/acre-guidance-on-genetic-technologies-that-result-in-qualifying-higher-plants/technical-guidance-on-using-genetic-technologies-such-as-gene-editing-for-making-qualifying-higher-plants-for-research-trials

Qualifying higher plants (QHPs)

The Genetically Modified Organisms (Deliberate Release) (Amendment) (England) Regulations 2022 concern field trials of genetically modified (GM) plants that could have been produced by traditional breeding techniques or could have arisen through natural processes.

The statutory instrument describes these plants as 'qualifying higher plants' (QHPs).

This guidance is to assist researchers and developers in this area to understand whether the plants they wish to grow outside in research trials are QHPs and can therefore be notified and grown as such.

Qualifying higher plants (QHPs)

1. QHP notifications

Defra has established a system for notifying QHPs for research trials. You may 'self-determine' whether your plants are QHPs, having considered the guidance provided here. Such a determination should be based on an assessment of detailed experimental data generated and recorded during the development and molecular analysis of the plants.

No formal confirmation of QHP status from Defra is required. However, you must notify Defra that you intend to grow QHPs outside for research trials by completing and submitting a notification form to Defra's GM and Genetic Resources team.

SDN1s are Qualifying higher plants (QHPs)

3.1 SDN1-type changes to genetic material

QHPs may be developed using bacterially derived site directed nucleases (SDNs). These gene-editing systems (such as CrisprCas9) can create DNA strand breaks at locations within a genome that are known to be related to a specific trait. Breeders and scientists rely on small errors commonly made by the cell's own DNA repair mechanism to produce changes to the DNA sequence that result in useful characteristics.

The DNA repair mechanism usually exploited during SDN1 editing is called non-homologous end joining (NHEJ). Errors during NHEJ usually result in small insertions or deletions (indels) to the DNA sequence. These mutations affect the functioning of the targeted sequence, producing the desired trait when the cell is regenerated into a whole organism.

Because they arise through the same biological mechanism, such mutations precisely mimic those that arise in natural processes and traditional techniques, such as those listed in regulation 5(2) of the Genetically Modified Organisms (Deliberate Release) Regulations 2002.

SDN2 and SDN3 are Qualifying higher plants (QHPs)

3.2 SDN2- and SDN3-type changes

Another kind of DNA repair (homologous end joining) is sometimes exploited to create targeted changes to the DNA sequence within a genome. In this case, as with SDN1-type changes, the DNA sequence is broken at a predetermined location, but in addition, a DNA template is introduced to the cell, designed to help direct the DNA repair machinery to generate the precise sequence change that is required.

In many cases that sequence change may be a small insertion or deletion. However, it is possible to use this strategy either to replace a whole or partial gene or allele with an alternate version or to insert a cisgene at a predetermined location.

Each of these scenarios mimics genetic changes that are possible to achieve naturally, and via traditional breeding techniques, when the resulting genetic composition remains within that which is accessible through crossing sexually compatible species.

Prime or base editing are Qualifying higher plants (QHPs)

3.3 Prime or base editing

Using an adaptation of the approach described above, it is possible to precisely direct which specific nucleotide or nucleotides are changed within a genome, without generating a double strand DNA break. To achieve this, a SDN such as CrisprCas9 is modified so that it 'nicks' one of the DNA strands at a predetermined location, and through the presence of a linked enzyme, replaces the incumbent nucleotide with an alternate one. As with SDN1 type alterations, these changes mimic what occurs naturally and is exploited by breeders.

Epigenetic changes are Qualifying higher plants (QHPs)

3.4 Epigenetic changes

Some research, still in its early stages, has demonstrated that SDNs can be engineered to carry out targeted epigenetic changes to genetic material such as (de)methylation. These alterations do not result in a change in DNA sequence but affect gene expression and give rise to phenotypic changes which have been observed to be inherited up to three generations.

In traditional plant breeding, pure epigenetic changes are rare and often unstable. Epialleles are thought more commonly to result from the indirect effects of nucleotide sequence changes either in an 'obligate' or 'facilitate' fashion. Pure epialleles have therefore played a relatively small role in crop improvement.

Nevertheless, for the purposes of guidance to developers, it is appropriate to note that SDN-mediated epigenetic changes rely on the same biochemical mechanisms for altering DNA and chromatin (for example, (de)methylation and (de)acetylation) as those that occur naturally or as a result of chemical induction. Consequently, plants altered in this way are likely to be QHPs.

Cisgenics are also QHPs; but not transgenics or intragenics

Transgenesis, cisgenesis and intragenesis describe cases where a DNA fragment is manipulated in vitro before being inserted into the genome using recombinant DNA technology. As outlined in the guidance, cisgenic plants are QHPs because their genetic composition is consistent with the genetic variation that could occur naturally within that species or as a result of traditional techniques and selection.

Transgenic plants, however, contain genetic material from species that are sexually incompatible or non-crossable and are therefore not QHPs. Intragenic plants are also not QHPs because their genetic composition is unlikely to occur naturally or as a result of traditional techniques and selection

Again, to be counted as a QHP, there can be no transgene elements present, including the gene-editing cassettes, selectable markers and vector genes.

March-2023

John Innes Centre
Unlocking Nature's Diversity

Unlocking research in plants

1 week

- Based on new developments gene editing is now widely used.
- Precision Breeding offers large potentials to contribute to sustainable agricultural development and food security.
- Current regulation allows open-field research trials of precision bred organisms (PBO) in UK.
- Current Precision Breeding bill would allow proportionate science-based regulation to enable PBO to enter commercial cultivation.

THANK YOU

DSW
DELIVERING
SUSTAINABLE
WHEAT

@SadiyeHayta

John Innes Centre
Unlocking Nature's Diversity

UKRI
Biotechnology and Biological Sciences Research Council