New GMOs, New Threat
and what you can do

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November 2019

What is a GMO?

- European law defines a GMO (genetically modified organism) as an organism in which "the genetic material has been altered in a way that does not occur naturally by mating and/or recombination"
- It requires the risks of each GMO to be assessed on a case-by-case basis
- GM foods and crops must pass safety checks and carry a GMO label.

New GMOs are being developed

- New types of genetically modified (GM) foods and crops are being developed
- The GMO industry and associated lobbyists are trying to get “new GMOs” exempted from the GMO regulations – meaning:
  - No safety assessment
  - No GM labelling
  - No choice of non-GM seeds and foods

What are the “New GMOs”?

- Gene-edited crops, foods, and livestock animals, mostly generated using CRISPR gene-editing techniques and RNA interference
- The techniques are cheaper, quicker, and easier to use than older-style “transgenic” genetic engineering techniques
- The pro-GMO lobby calls them “New Plant Breeding Techniques” but they have nothing to do with breeding. They are genetic modification techniques and give rise to GMOs.

Court of Justice agrees

- In July 2018 the European Court of Justice ruled that products of certain new GM techniques are GMOs and fall under the GMO regulation
- So they have to go through the same safety checks as older-style GMOs and carry a GM label
- The court recognised that these new GMOs pose similar risks to the older-style GMOs.

GMO lobby furious

- The pro-GMO lobby is infuriated by the court's ruling
- It has strengthened its campaign to get the EU institutions to open up the EU's GMO regulation and change it so that products of new GM techniques are exempt from the regulation (i.e. no or few safety checks, no labelling).

Who is the lobby?

- The US government and President Trump
- In UK – Boris Johnson
- The GMO industry and its lobby groups – e.g. Europabio, animal feed group FEFAC
- Prominent members of the former European Commission (2014–2019)
- The Commission's Scientific Advice Mechanism (SAM)
- Some pro-GMO EU Member States, e.g. UK, Netherlands, Finland
- Various scientists, often presented as independent but reliant on the GMO industry via funding/patent income; and/or ideologically pro-GMO.

Trump

- On June 11 2019, US President Donald Trump issued an executive order to "streamline" GMO regulations in the US.
- The order has a section on what Trump sees as the imperative "to increase international acceptance of products of agricultural biotechnology in order to open and maintain markets for United States agricultural exports abroad”.

Trump and Boris Johnson

- Boris Johnson is dancing to Trump's tune. He hyped GMOs no less than 3 times in 3 speeches in his first 3 days as prime minister.
- If Brexit happens, the UK will lose its major trading partner – the EU – so Johnson's priority is to make a trade deal with the US.
- The US has made clear that GMOs would be a key part of any trade deal, with the US pushing to de-regulate gene-edited crops (and ultimately all GM crops) in the EU/UK.

Who doesn't want new GMOs de-regulated?

- Most Green Party MPs/MEPs. Some S&D and RE Group MEPs are open to concerns.
- NGOs, e.g. Friends of the Earth Europe, Greenpeace Europe, GM Freeze, GMWatch, Eurogroup for Animals (animals only), Transatlantic Consumer Dialogue
- European Network of Scientists for Social and Environmental Responsibility (ENSSER) – see published statements
- Some organic industry groups, e.g. IFOAM.

Reasons given for why we “need” new GM

Myth: We need gene-edited climate ready crops

Truth: We need climate ready food and farming **systems** based on diversified cropping and soil building

Myth: We need gene-edited crops to “feed the world”

Truth:

- No intrinsic yield increase from GM
- We already produce enough food to feed 14 billion people, more than we’ll ever need.

The real reason we are being forced down the “new GM” route

PATENTS:
All GM organisms are patentable. The push for GM is about money, greed, and corporate control of the food supply from seed to fork.

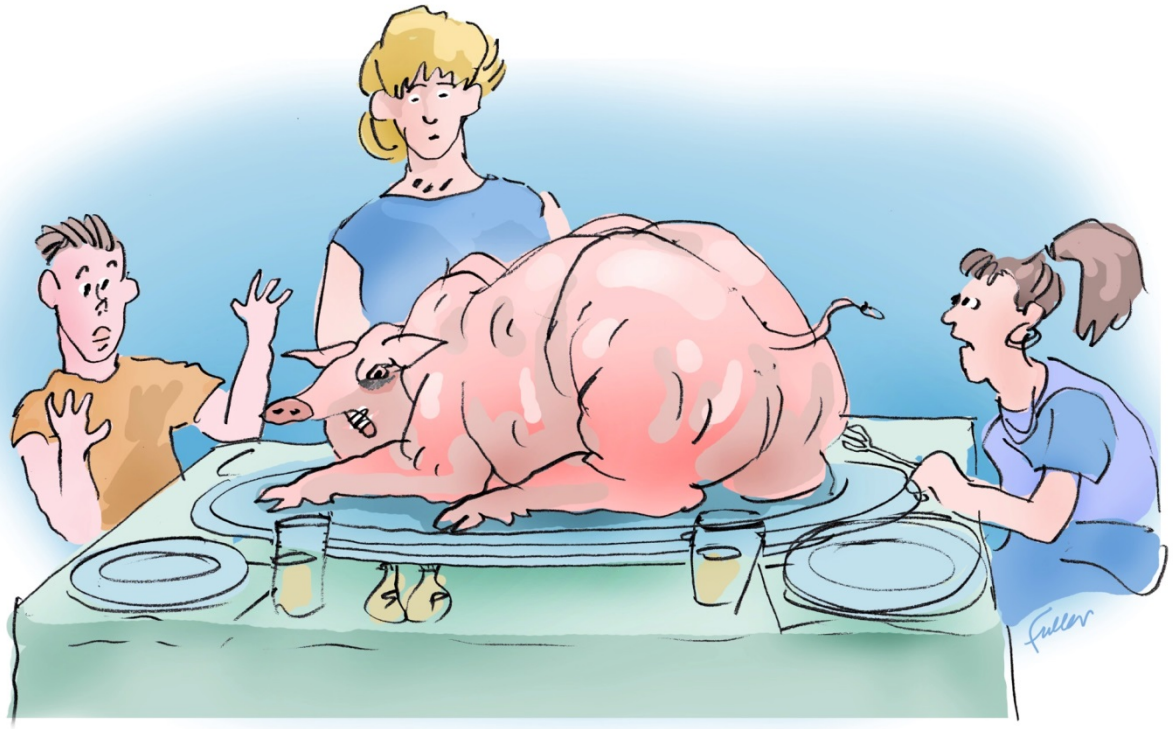
Which "New GM" foods have been de-regulated?

Foods that have been developed using gene-editing or other new GM tools are:

- Soybean engineered to have an altered fat profile (Calyxt/US, commercialised)
- Canola/oilseed rape engineered to survive being sprayed with herbicide (Cibus/US, commercialised)
- Mushroom engineered to be non-browning when cut (Chinese researchers, non-commercialised)

Gene-edited animals

It's not only food crops that are being gene-edited.



Livestock animals are being "gene-edited" to make them super-muscled, to produce more meat

Gene-edited hornless cows

- Cows have been gene edited to make them hornless, a manipulation claimed to help animals and handlers stay safe.
- Developers claimed no unintended effects from the genetic manipulation, but scientists from the US Food & Drug Administration (FDA) found the cows' genomes had unexpectedly incorporated antibiotic resistance genes used in the genetic manipulation process.
- Concern: these genes could transfer to disease-causing bacteria, making them antibiotic-resistant – putting animal/human health at risk.

Gene drive

- Gene editing is also being used to create gene drives, an extreme form of genetic engineering designed to over-ride the usual rules of inheritance and spread the engineered trait through an entire population.
- Gene drive is being proposed to try to wipe out mosquito populations in malaria regions and “invasive mammals” and weeds in areas where they are deemed to be causing problems.
- Major funders: The Gates Foundation and the US military (DARPA).

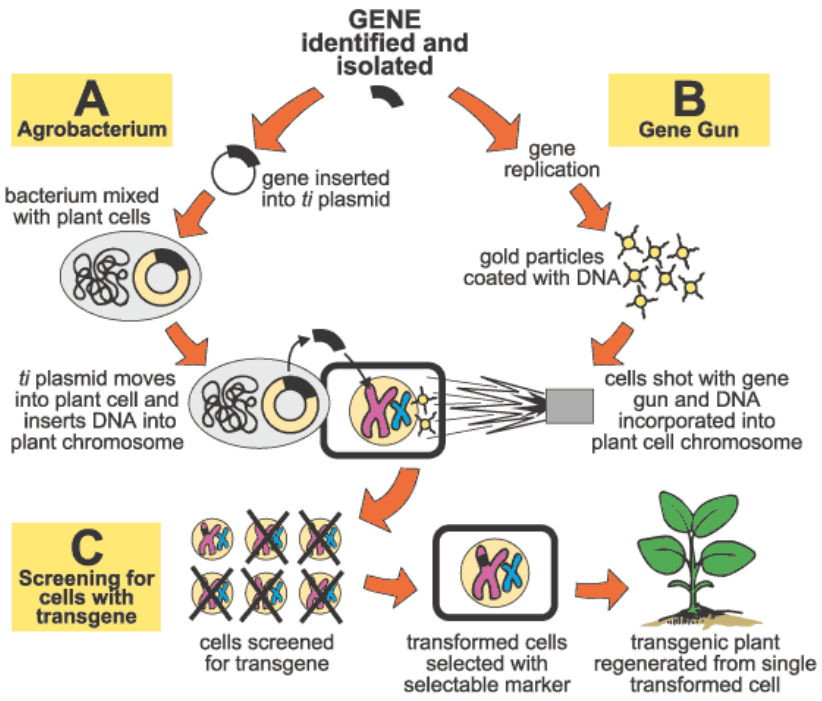
Back to food

- Today we're focusing on food, so Michael will explain what gene editing is and the risks of gene editing our food crops and livestock animals.
- Then I'll conclude by telling you what you can do to ensure your food supply remains safe.

New genetic engineering techniques

Gene editing:
Is it precise?
Is it safe?

Old-style gene-addition transgenic GM



- Old-style GM involves addition of an artificial foreign transgene
- Random insertion of transgene
- Novel gene combinations
- Unwanted and unpredictable mutations
- Result: altered plant biochemistry in undesirable ways

SCIENTIFIC REPORTS

OPEN

Received: 17 August 2016
Accepted: 02 November 2016
Published: 19 December 2016

An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process

Robin Mesnage[1,*], Sarah Z. Agapito-Tenfen[2,*], Vinicius Vilperte[3], George Renney[4], Malcolm Ward[4], Gilles-Eric Séralini[5], Rubens O. Nodari[3] & Michael N. Antoniou[1]

What is genome or gene editing?

Targeted alteration to the DNA of an organism:

- Small base unit changes (deletions/insertions)
- Large deletions
- Small/large insertions

Claim: precise, predictable outcomes, safe

Are plants and animals produced by gene editing for agricultural use genetically modified organisms (GMOs)?

- Proponents claim plants or animals produced by genome editing for agricultural use should not be considered as GMOs (at least in cases of small DNA base unit changes in one or more genes).

- Strong lobby for either deregulated status or light-touch product-based regulated status.

Arguments used for gene editing de-regulation in agriculture

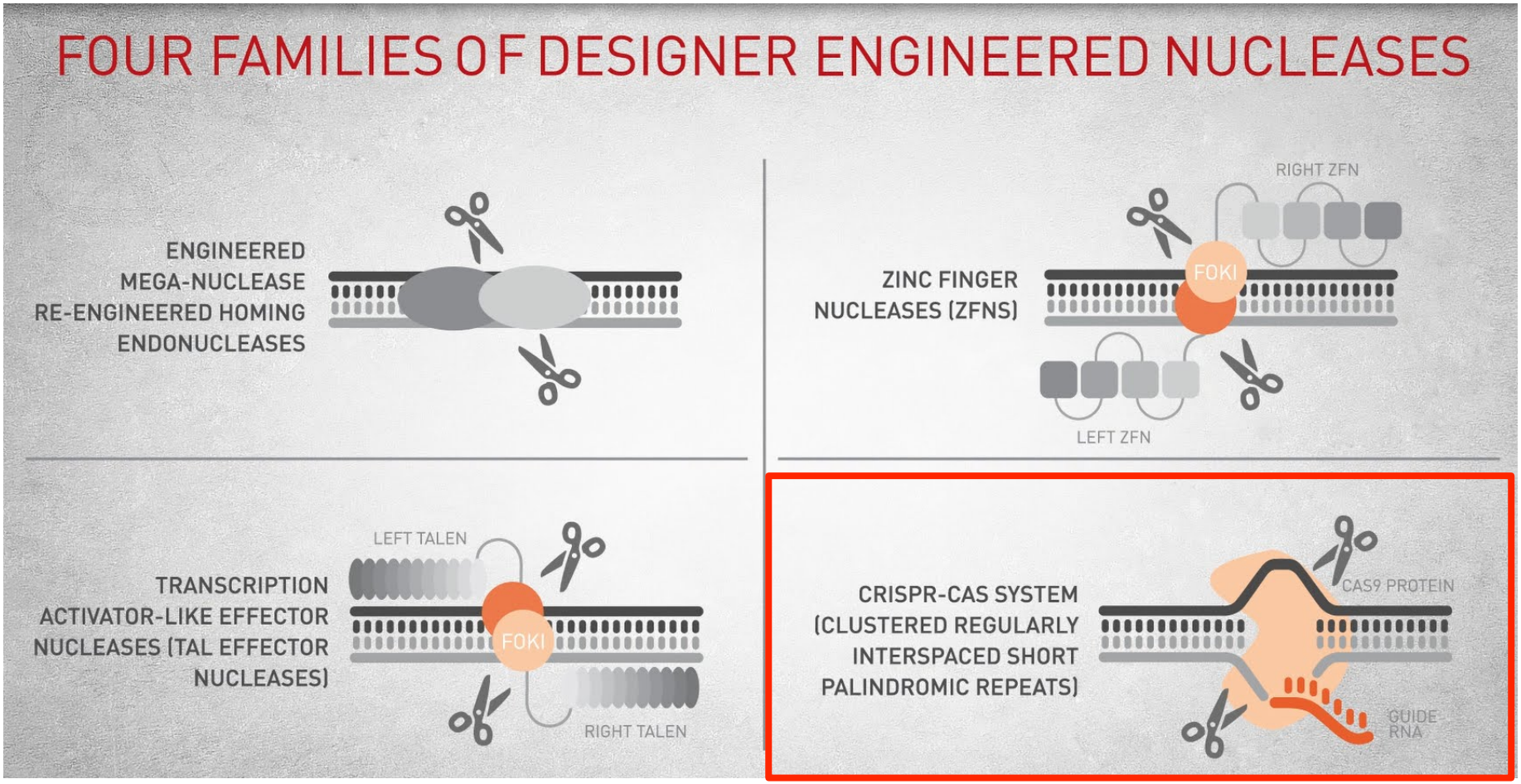
- Only the ***end product*** of the gene editing event(s), whether a microbe, plant or animal, should be considered by regulators, rather than the ***process*** by which the genomic change was obtained.
- The small DNA base unit changes brought about by these methods, which either knock-out (ablate) a gene or modify the function of a gene's protein or RNA product, can ***mimic what may occur naturally through random mutation***.
- The intended changes in a gene(s) are "***precise***" and no other genome alterations occur in the target organism.
- The outcome of the gene editing event(s) is ***totally predictable*** and thus the products derived from this process are ***safe***.

Gene editing: how does it work?

Two approaches:

- Oligonucleotide directed mutagenesis (ODM)
- Site-directed nuclease (SDN)

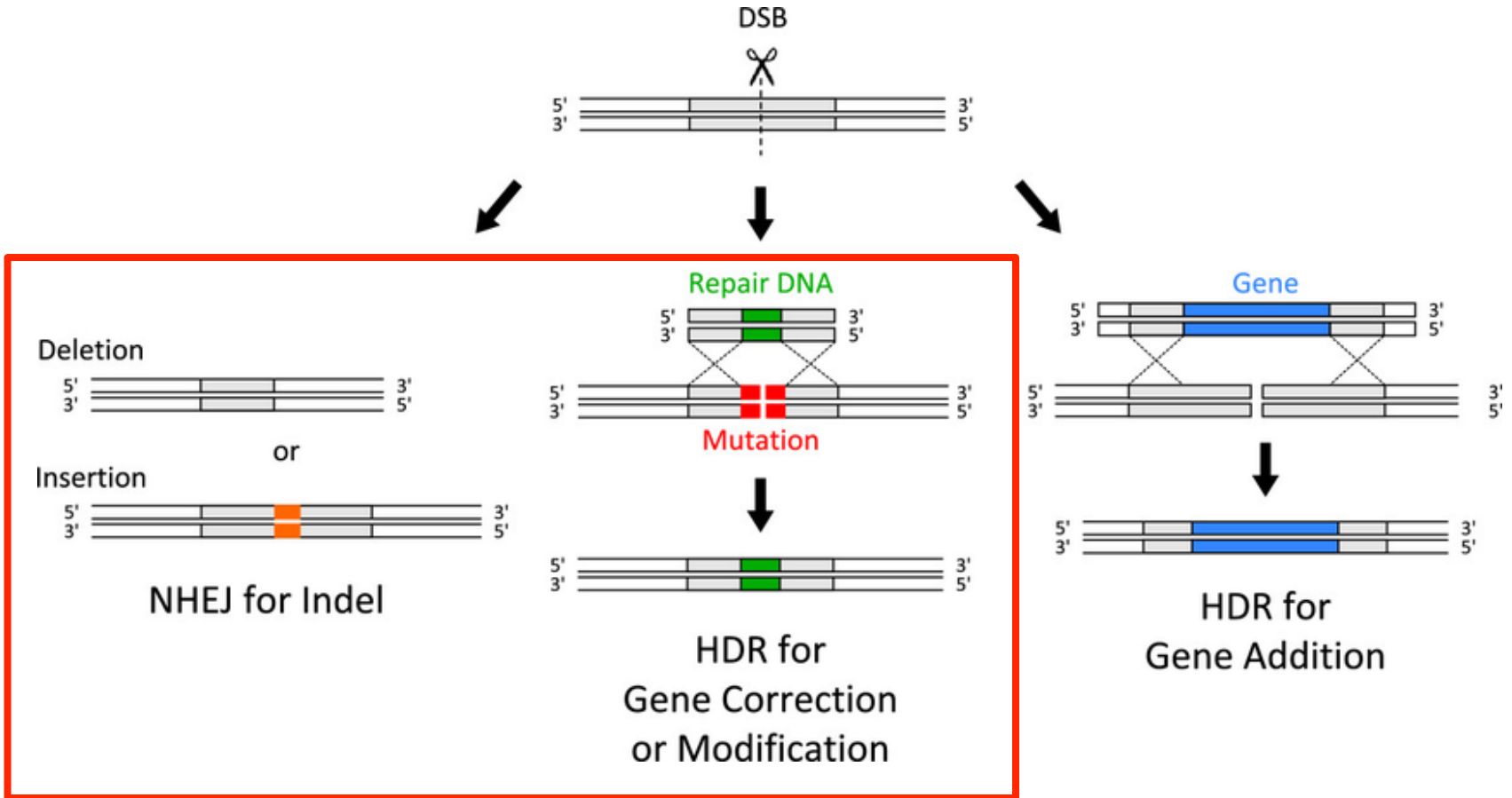
Site-directed nucleases - SDNs



Site-directed nucleases - SDNs

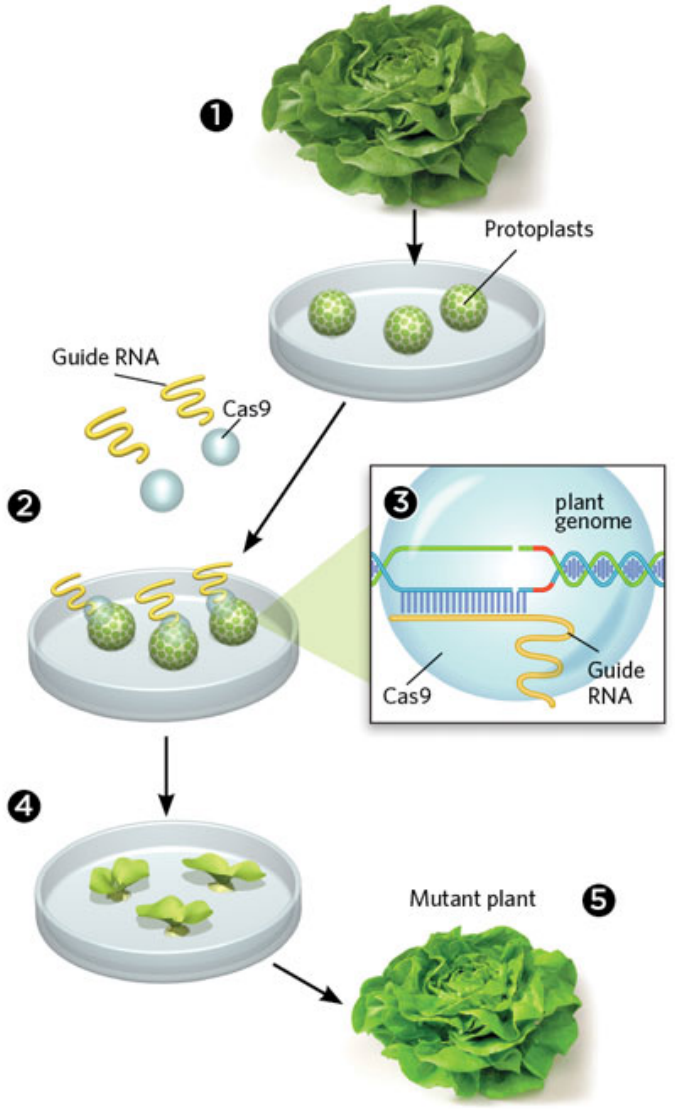
ZFN, TALEN, CRISPR-Cas

Produce double-strand break in DNA at pre-determined site



Procedure of genome editing a plant

Plant tissue culture



Gene-edited CRISPR mushroom escapes US regulation

A fungus engineered with the CRISPR–Cas9 technique can be cultivated and sold without further oversight.

Knock-out of polyphenol oxidase (PPO) gene via NHEJ

The common white button mushroom (*Agaricus bisporus*) has been modified to resist browning

Nature News, 14 April 2016

Huge numbers of gene edited crops and animals await market approval

Calyxt (USA): Edited potato

- TALEN disabled single gene; blocks sucrose conversion to glucose and fructose
- Doesn't accumulate sweet sugars on cold storage; lasts longer
- Won't produce as much acrylamide (suspected carcinogen) when fried

DuPont (USA): low amylose, high amylopectin maize

- CRISPR disabled Waxy gene
- Eliminates amylose
- Kernels with 97% amylopectin

Gene-edited farm animals

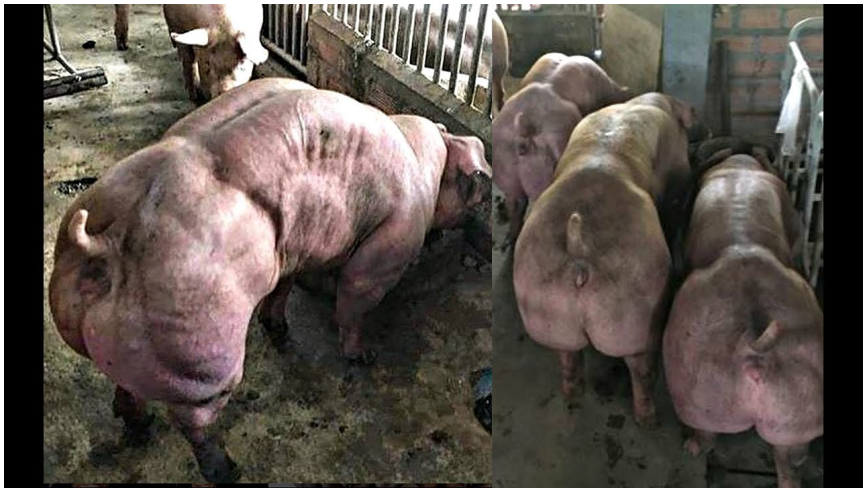
Hornless cattle

TALEN introgression of POLLED gene via cloning
(Carlson DF et al., Nat Biotechnol. 34: 479, 2016)

Super-muscly pigs created by small genetic tweak

Researchers hope the genetically engineered animals will speed past regulators. *NATURE* | NEWS, 30 June 2015

TALEN knock-out of myostatin gene via cloning



Are claims of precision and predictability of gene editing supported by the evidence?

The claim that gene editing-induced gene changes are similar to what may occur naturally is unproven.
Presently this constitutes at best an untested hypothesis.

These techniques are prone to unpredictable "off-target" and "on-target" mutational effects.

Currently recognized gene editing off-target effects

- **Unintended side-effects from the intended alteration.** For example, alteration in enzyme activity can result in chemical reactions other than those that are intended.

- **Unintended alterations or mutations to other genes in addition to the target gene(s).** Includes mutations from plant tissue culture.

Currently recognized gene editing on-target effects

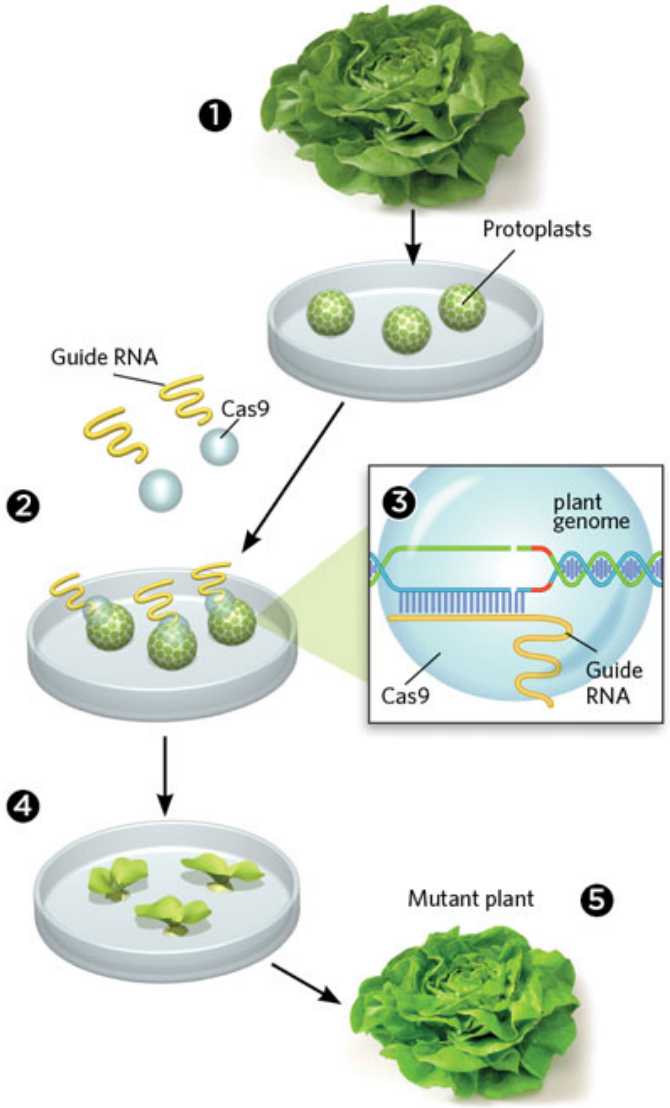
- **Large DNA deletions affecting more than one gene.**
- **Large DNA rearrangements affecting multiple gene functions.**
- **Creation of new gene sequences resulting on new mRNA and proteins.**
- **Insertion of contaminating DNA.**

Consequences of unpredictable off-target and on-target mutations from gene editing

- **Can lead to unintended alterations in the biochemistry of the organism.** In edited plant foods off-target effects could lead to unexpected toxins or allergens, or altered or compromised nutritional value.

- **In order to patent gene-edited organisms, industry and academia must argue for novelty and an inventive step.** Contradicts arguments that edited products are no different from organisms that may occur naturally.

Multiple types and large number of unpredictable mutations from gene editing



Mutations from plant tissue culture and transformation process

Off-target and on-target mutations

Simultaneous and sequential use of gene editing

Gene editing developed to be used simultaneously and/ or sequentially.

- Simultaneous modification of multiple genetic sequences
- Sequential modification of a single or different genetic sequence(s)

Outcome:

- Each change may individually be small, BUT in total will produce an organism radically different from the parent
- May be as different from a parental line (or even more different) as any organism produced with older-style transgenic genetic modification techniques

Products of gene editing must be regulated

- **Gene editing can be used to radically alter an organism, completely changing metabolic pathways**. Such products would require highly stringent regulation.

- **Gene editing outcomes may closely resemble older-style transgenic GM products.** If gene editing-derived organisms were exempted from the regulations applied to transgenic GMOs, then the former would escape regulation, but the latter would be regulated.

Process-based and product-based regulation must be applied

Given that gene editing:

- Uses laboratory-based, artificial DNA modification procedures
- Does not in itself involve natural cross-breeding
- Results in functional alterations of one or more DNA sequences
- Cause unintended and/or unpredictable off-target effects at DNA, RNA and protein levels

Gene editing is a GM procedure and regulations applied to their products should be process-based as well as product-based, as with the current EU GMO regulations.

Advantages of process-based regulation

- Process-based regulation can highlight mechanisms of unintended and off-target gene function disruption effects

- Process-based regulation is true to the state of this science and technology.

- **Attempts to argue that such regulation is superfluous or excessive are disingenuous and place public health and the environment at risk.**

EURACTIV

The EU must not de-regulate gene-edited crops and foods

https://www.euractiv.com/section/agriculture-food/opinion/the-eu-must-not-de-regulate-gene-edited-crops-and-foods/

Scientific and technical facts about genome editing show that organisms produced by these procedures are GMOs and give rise to novel health risks.

This demands that all products of genome editing should be regulated:

- In accord with strictest GMO regulations (e.g. EU regulations)
- As permitted by the Cartagena Protocol on Biosafety and Codex Alimentarius

Evidence of harm from gene editing?

No studies conducted to date

Claims of safety are hypothetical

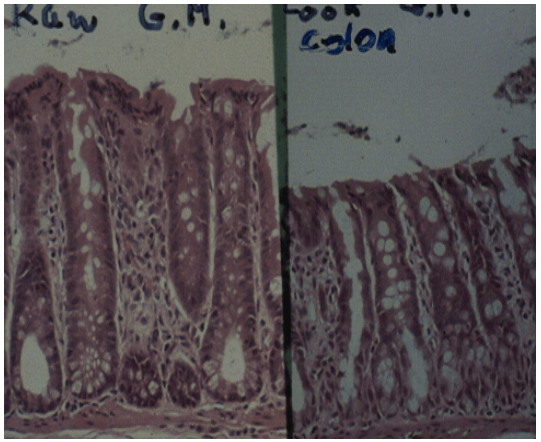
Numerous studies show evidence of harm from consumption of old-style transgenic GM crops

Controlled animal feeding studies show clear signs of toxicity linked with GM crops

Revealed by GM vs isogenic non-GM comparison

Feeding studies conducted by academics: non-commercialised crops

Cell proliferation similar to a pre-cancerous condition in gut of rats fed GM potatoes containing snowdrop GNA insecticide protein (Ewen SWB and Pusztai A, *Lancet*, **354**, 1353-1354, 1999):



GM Non-GM
Rat Colon

Rats fed GM Bt rice: significant differences in gut bacterial populations and organ weights (adrenals, testis, uterus) (Schrøder *et al*., 2007).

GM peas cause surprise allergic reaction: bean a-amylase inhibitor in peas caused marked immune response and allergic type reactions in mice (Prescott VE et al. *J Agri Food Chem.*, **53:** 9023-9030, 2005).

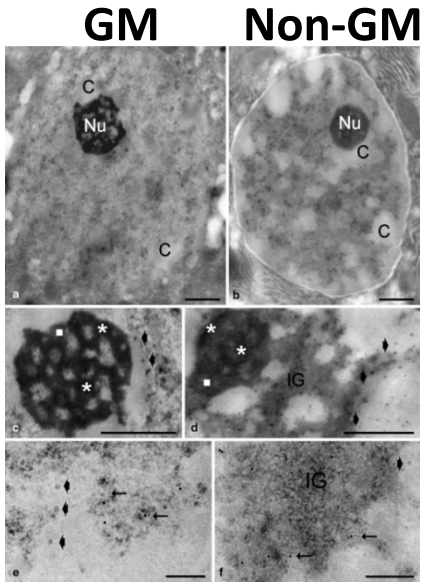
Feeding studies conducted by academics: commercialised crops: Bt maize/corn

- **Rats fed GM Bt corn over three generations:** areas of necrosis to liver and kidneys and alterations in blood biochemistry (Kilic & Akay, 2008).
- **Old and young mice fed GM Bt corn MON810:** marked disturbance in immune system cells and in biochemical (cytokine) activity (Finamore *et al*., 2008).
- **Pigs fed GM Bt corn variety MON810 for 31 days:** differences in immune cell type numbers (e.g. CD4+ T cells, B cells, macrophages) and biochemistry (cytokine levels; e.g. IL-12, IFNg, IL-6, IL-4, IL-8) (Walsh *et al*., 2011).
- **Ewes and their lambs fed GM Bt corn variety Bt176 over three generations:** hyperplasia of ruminal epithelial basal cells in ewes and a disturbed gene functioning of liver and pancreas in lambs (Trabalza-Marinucci *et al*., 2008).
- **Rats fed MON810 GM Bt corn for 91 days:** multiple organ changes in weight, biochemistry; severe damage in structure and function including to *liver, kidney, testes, intestines* (Gab-Alla *et al*., 2012; El-Shamei *et al*., 2012).

Feeding studies conducted by academics: commercialised crops: glyphosate-tolerant soy

- **Mice fed GM soy:** disturbed liver, pancreas and testes function; abnormally formed cell nuclei and nucleoli in liver cells, indicating increased metabolism and potentially altered patterns of gene expression (Malatesta *et al*., 2002; Malatesta *et al*., 2003; Vecchio *et al*., 2004).

- **Mice fed GM soy over their lifetime (24 months):** more acute signs of ageing in the liver; significant changes in the expression of 49 proteins. Significant decrease in senescence markers (e.g. regucalcin, HSPs); lower metabolism. Structure of liver cell nuclei suggest marked lowering of gene function (Malatesta *et al*., 2008):



A long-term toxicity study on pigs fed a combined genetically modified (GM) soy and GM maize diet

Carman JA et al. (2013) *J Organic Systems* **8**: 38-54

Gastric and uterine differences in GM ration fed pigs:

- **Marked increase in severe stomach inflammation (4-fold males; 2.2-fold females)**
- **Uteri 25% heavier**

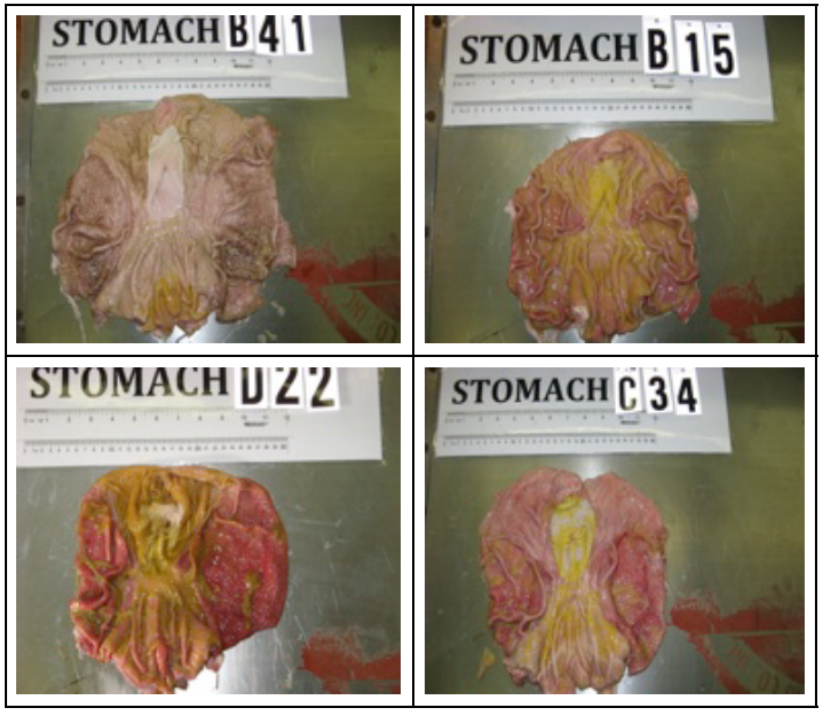
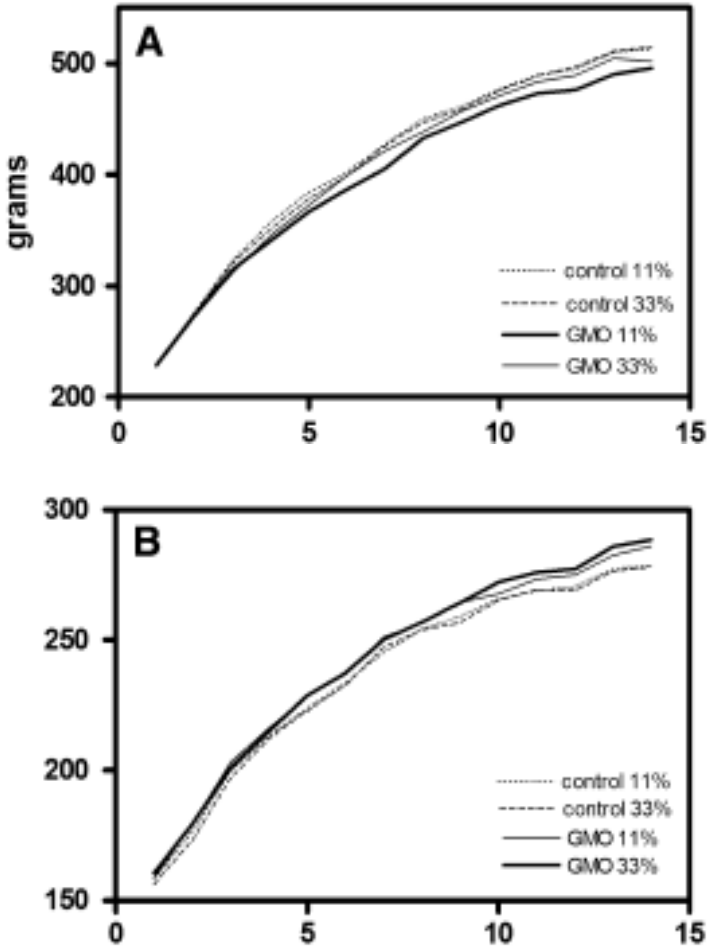


Figure 1. Different levels of stomach inflammation found (clockwise from top left): nil (from a non-GM-fed pig, number B41), mild (from a non-GM-fed pig, number B15), moderate (from a GM-fed pig, number C34) and severe (from a GM-fed pig, number D22).

Feeding studies conducted by industry

Rats fed commercialised insecticide-producing MON863 Bt corn:

- Grew more slowly
- Sex differences
- Showed higher levels of certain fats (triglycerides) in their blood
- Problems with liver and kidney function (Séralini *et al*., 2007).



	Week	m 11%	m 3 %	f 11%	f 33%
Liver parameters					
Albumin/globulin ratio	5	11*	-3	-9	4
Albumin/globulin ratio	14	6	-2	-18**	7
Albumin	5	-3	-2	-2	5*
Albumin	14	-2	3	-6*	5
Globulin	5	-12*	2	9*	1
Globulin	14	-8	7	15*	-2
Alanine aminotransferase	14	-30*	-8	37	4
Total protein	14	-5*	5*	1	3
Triglycerides	5	22	-2	-11	40**
Triglycerides	14	15	-1	24*	6
Liver weight	14	-1	-2	7**	6
Liver/brain ratio	14	-1	-3	6*	4
Kidney parameters					
Creatinin	14	-7	13*	13*	-2
Urine sodium	14	-23	-25*	11	-26
Urine sodium excretion	14	3	-35*	35	-24
Urine chloride excretion	5	35	3	50*	67*
Urine potassium	5	35*	-20	-3	-13
Urine phosphorus	5	3	-35*	24	-15
Urine phosphorus	14	-34	-31*	12	-8
Urea nitrogen	14	-8	4	17*	-1
Kidney weight	14	-3	-7*	3	2
Kidney/brain ratio	14	-3	-7*	1	1
Kidney % body weight	14	-1	-5*	-1	-1
Pancreas					
Glucose	14	-4	9	9*	10**
Bone marrow					
Neutrophils	5	5	22*	-14	3
Eosniophils	14	32	54*	20	0
Reticulocytes	14	15	-17	-35	-52*
Reticulocytes % RBC	14	16	-16	-36	-55*

Note: * & ** indicate statistical significance

Feeding studies conducted by industry

Rats fed commercialised GM Bt corn varieties MON863 and MON810 and Roundup tolerant NK603: signs of toxic effects on liver and kidneys. (de Vendomois *et al*., 2009).

Parameters	Week	Males 11%	Males 33%	Females 11%	Females 33%
BONE MARROW					
Absolute Lymphocytes	14	-12	29	-1	-23 *
Neutrophils	14	13	-34 **	4	16
Lymphocytes	14	-3	8 **	0	-2
Eosinophils (p)	5	38 *	-19	43	-13
Lar Uni Cell	5	4	-6	33 **	6
HEART					
Heart Wt	14	6	11 **	0	4
Heart % Body Wt	14	5	9 **	2	1
Heart % Brain Wt	14	6	9 *	-2	4
KIDNEY					
Urine Phosphorus	5	-15	67 **	-1	40 *
Urine Phosphorus	14	-10	97 **	12	28
Urine Sodium (p)	14	23	44 *	-7	37
Urine Potassium	14	-6	34 *	4	-13
Urine Creatinine Clearance	5	20	42 **	0	29
Blood Urea Nitrogen	5	-14 *	-13 *	13	-14
Creatinine	5	-25 *	-23 **	-6	-17
Phosphorus	5	2	-7 *	2	-8
Potassium	14	4	-2	5	13 **
LIVER					
Liver Wt	14	2	10 *	-4	1
Liver % Body Wt	14	1	5 *	-2	-2
Alkaline Phosphatase	14	2	3	29 *	16

Differences in NK603 fed rats and control animals fed isogenic non-GM maize.

Note: * & ** indicate statistical significance

Séralini et al. Environmental Sciences Europe 2014, 26:14
http://www.enveurope.com/content/26/1/14

Environmental Sciences Europe
a SpringerOpen Journal

RESEARCH Open Access

Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize

Gilles-Eric Séralini[1*], Emilie Clair[1], Robin Mesnage[1], Steeve Gress[1], Nicolas Defarge[1], Manuela Malatesta[2], Didier Hennequin[3] and Joël Spiroux de Vendômois[1]

Not all feeding studies show problems with GM crops/foods

Some studies don't report adverse effects from the GM diet, but:

- Some studies are too short to find long-term ill effects
- For many studies, in-depth scrutiny of the results does reveal signs of toxicity and adverse effects – but statistically significant signs of toxicity are denied or explained away as not biologically relevant without any scientific validity.

Gene editing:
Agricultural vs clinical uses

Gene editing in medical sphere:

- **Unquestionably considered as genetic modification**
- **Strictly regulated**

Regulation of gene editing in agriculture would align these methods with how they are scientifically observed, used, and regulated within the medical sphere.

European Network of Scientists for Social and Environmental Responsibility (ENSSER)

Statement on new GM techniques

[https://ensser.org/publications/ngmt-statement/]

ENSSER Statement
27 September 2017

Products of new genetic modification techniques should be strictly regulated as GMOs

We encourage all scientists to sign on to this statement

Conceptual flaws of agricultural genetic engineering

Bound to fail: The flawed scientific foundations of agricultural genetic engineering (part 2)

Published: 21 November 2018

Share 999 Like 999 Tweet Share

The new understanding of "omnigenics" tells us GM food and crop technology is conceptually flawed - and genome editing won't change that, writes Dr Michael Antoniou

https://www.gmwatch.org/en/news/latest-news/18593

No gene works in isolation

Function of ALL genes required to impart complex traits: "OMNIGENICS"

Genes work as a highly co-ordinated NETWORK

Adding a new gene of altering the function of just one gene will have far reaching consequences in the network

The whole is greater than the sum of its parts; study of parts cannot predict the function of the whole

What you can do

- When the UK is politically stable, write to your MPs (and MEPs if Brexit doesn't happen), asking them to ensure that all GMOs remain strictly regulated and labelled: https://gmwatch.org/en/news/latest-news/18984. Access same page by going to gmwatch.org; in right-hand menu, click "GENE-EDITED CROPS AND FOODS: Help stop the new threat".
- Subscribe to GMWatch's free newsletters to stay up to date at gmwatch.org: click "Subscribe to news".
- Buy our book, **GMO Myths & Truths: A Citizen's Guide to the Evidence on the Safety and Efficacy of Genetically Modified Crops and Foods, 4th Edition,** from Amazon or Chelsea Green Publishing.

Write to retailers

- Write to retailers thanking them for maintaining their GM-free policy for own-brand food products since the 1990s.
- Tell them that just as you didn't want to eat the first generation GMOs, so you don't want to eat second generation gene-edited foods and crops.
- Ask them to tell the EU institutions to uphold and respect the 2018 ruling of the European Court of Justice that gene-edited foods and crops are GMOs, pose the same safety risks as older-style GMOs, and should be regulated as GMOs.
- Ask them to support consumer choice by demanding that gene-edited foods and crops continue to be labelled as GMOs.
- Find a list of retailers here: https://www.gmfreeze.org/retailers/