
New Genetic Technologies

TJ Higgins AO

What is genetics?

Genetics is the study of heredity

- The passing on of characters from one generation to the next
 - ❖ Haemophilia
 - ❖ Eye color

Plant improvement using selection and breeding

- HISTORICAL PERSPECTIVE

8000 BC (5 million people)

2000 BC (50 million people)

1583 (500 million people)

1742

1799

1927

1983 (5 billion people)

2018 (Over 7.7 billion people)



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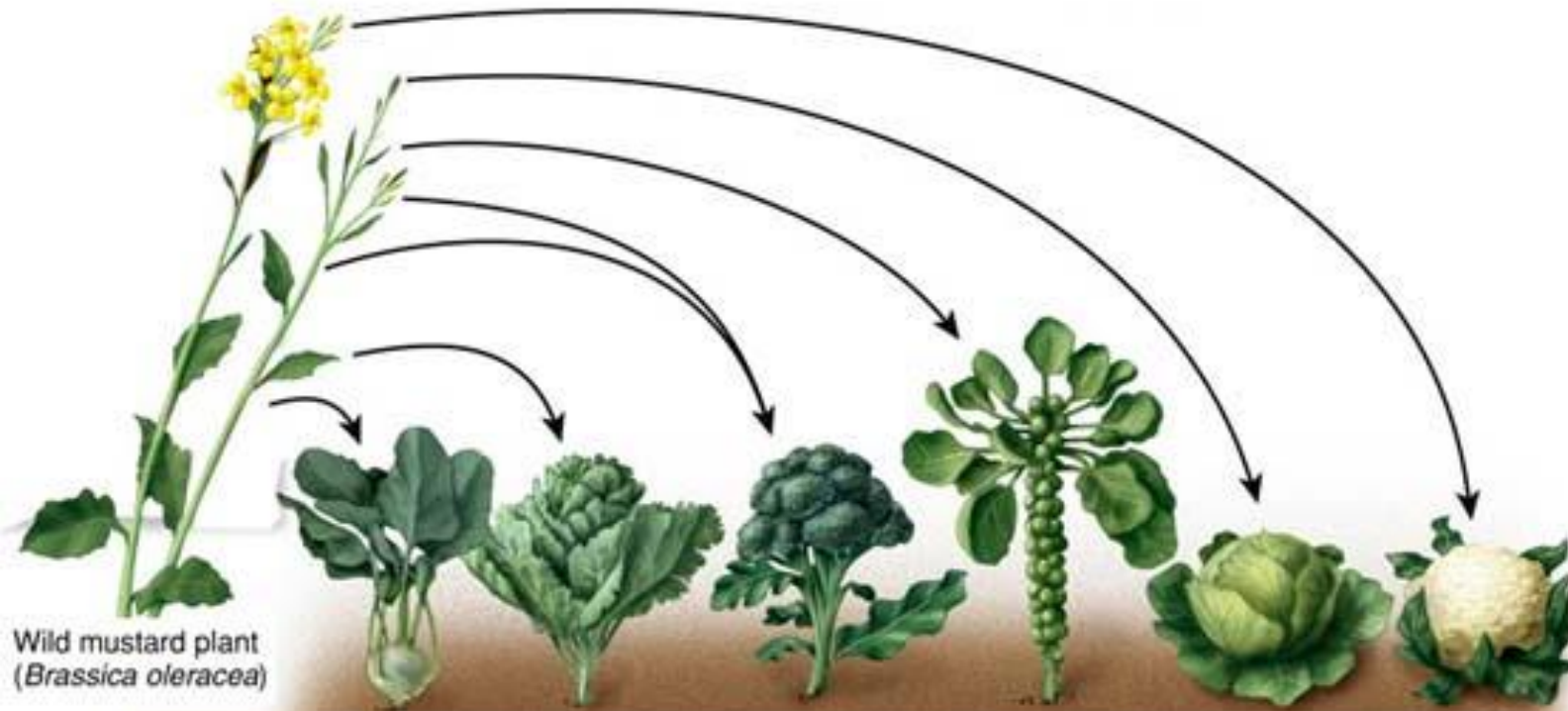
Genetic editing, “broad sense”

**All our food crops are highly “genetically edited”
from their wild ancestors**



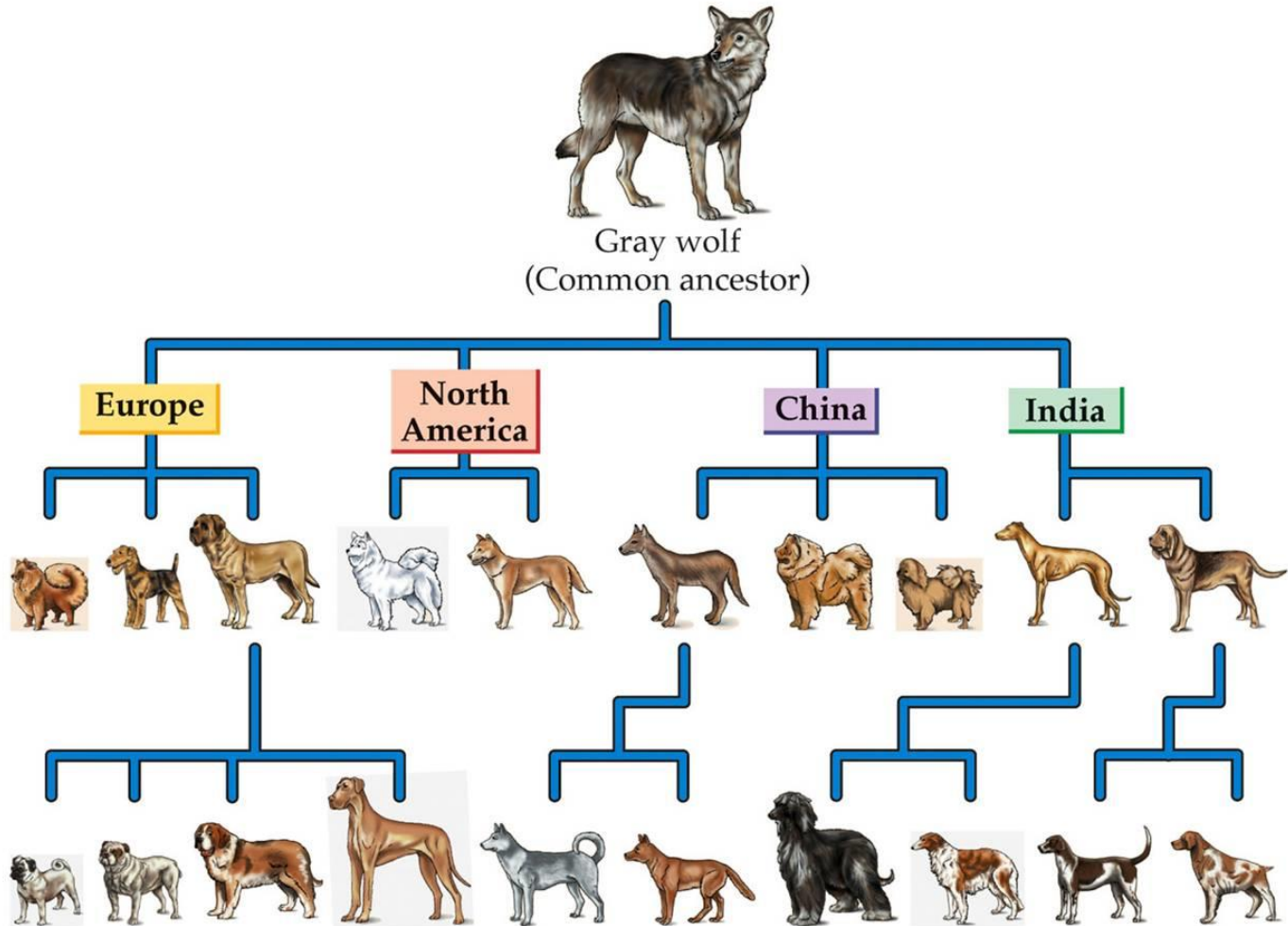
Teosinte Primitive Maize Modern Maize

Plant breeding



Strain	Kohlrabi	Kale	Broccoli	Brussels sprouts	Cabbage	Cauliflower
Modified trait	Stem	Leaves	Flower buds and stem	Lateral leaf buds	Terminal leaf bud	Flower buds

Animal breeding 1



Animal breeding 2



FRIESIAN CHICKEN



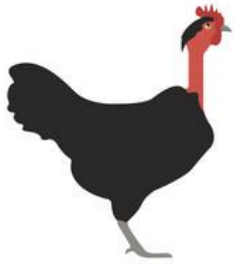
DUTCH BANTAM



GERMAN LANGSHAN



KULANG CHICKEN



TRANSYLVANIAN NAKED NECK



LEGHORN



MINORCA



SERAMA



NEW HAMPSHIRE RED



SUMATRA CHICKEN



POLAND CHICKEN



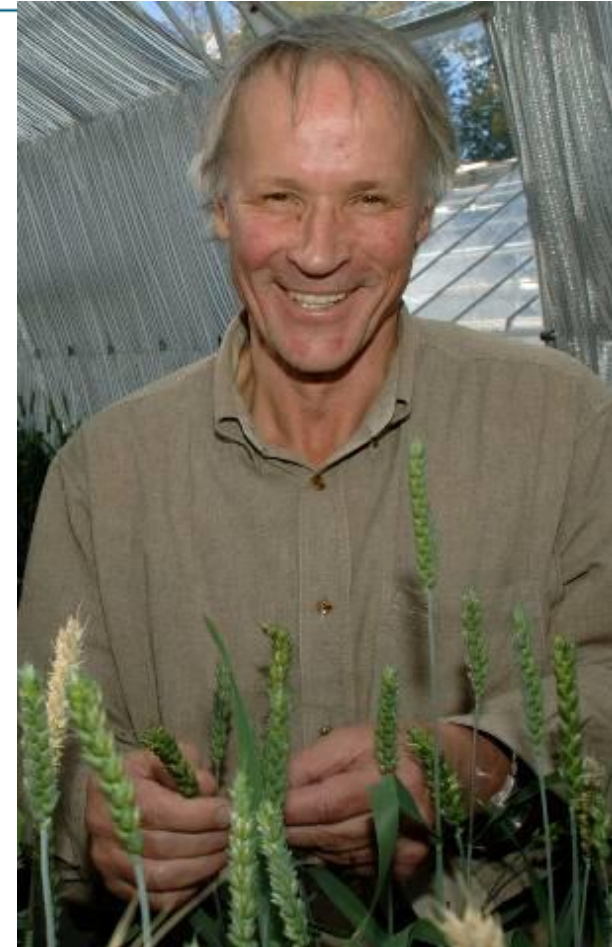
JERSEY GIANT



Australian Academy of Science

Modern genetics in plant improvement

- Modern “conventional” breeding is anything but conventional
 - Employs one or more of :
 - Mutagenesis
 - Interspecific Hybrids
 - Intergeneric Hybrids
 - Molecular Markers
 - Male Sterility for Hybrids
 - Digital Image Phenotyping
 - New Analytical Statistics
 - Genomics and Bioinformatics
 - But not GM for most crops
- Maybe
- Gene Editing



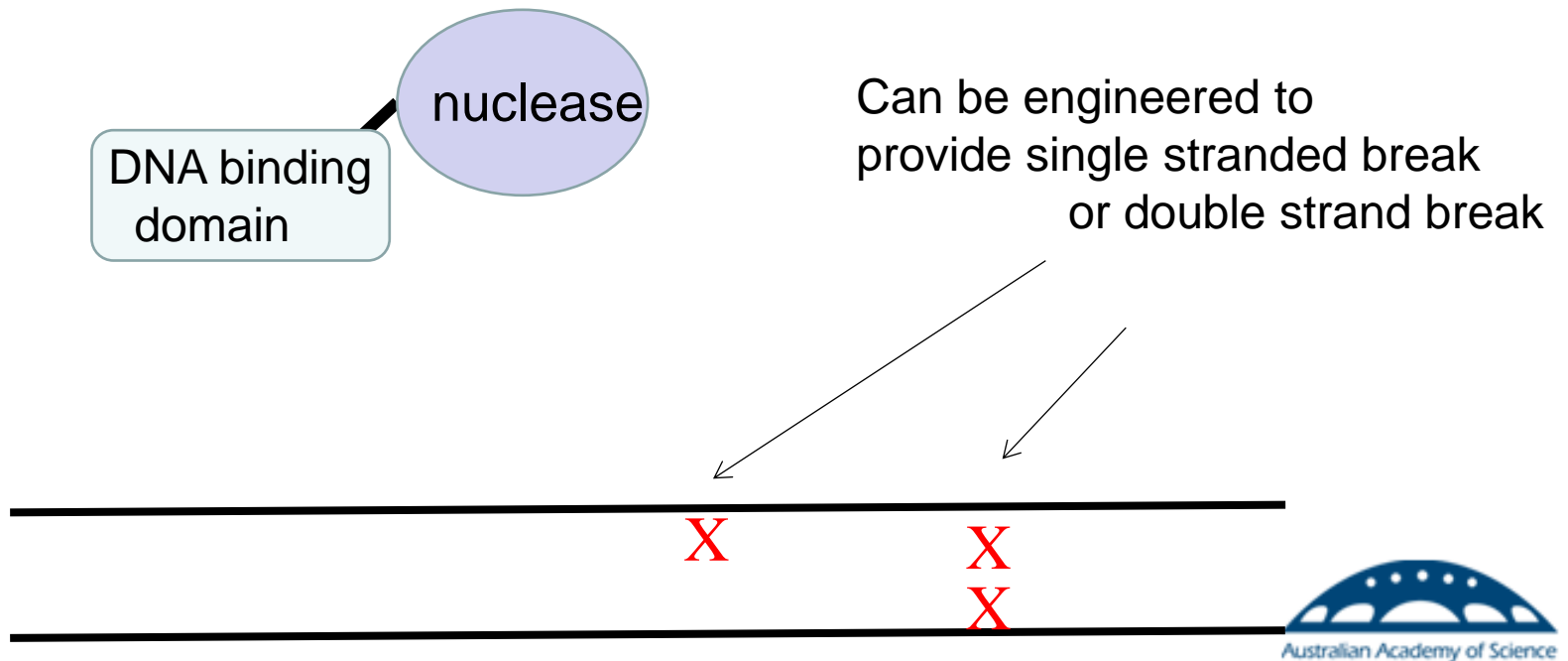
Breeding advances



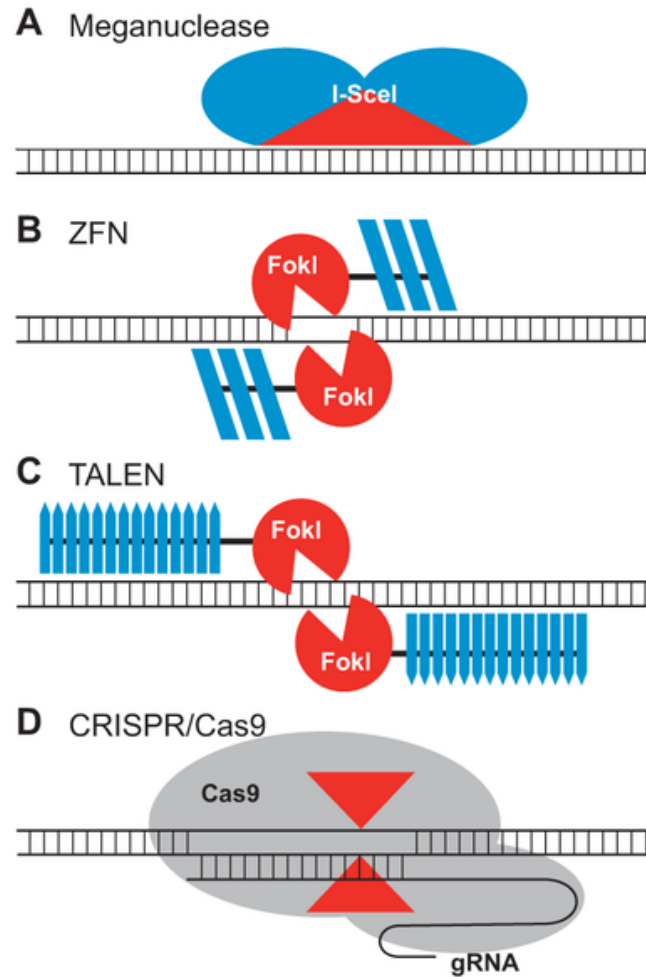
Editing of genes

How does it work?

In ALL cases a specific DNA sequence is first cleaved by a nuclease



Four gene editing techniques



What does CRISPR mean?

It stands for :

Clustered Regularly Interspaced Short Palindromic Repeats

But is really an abbreviation for the CRISPR-Cas9 system that bacteria use to protect themselves from infection by viruses

The system has two components :

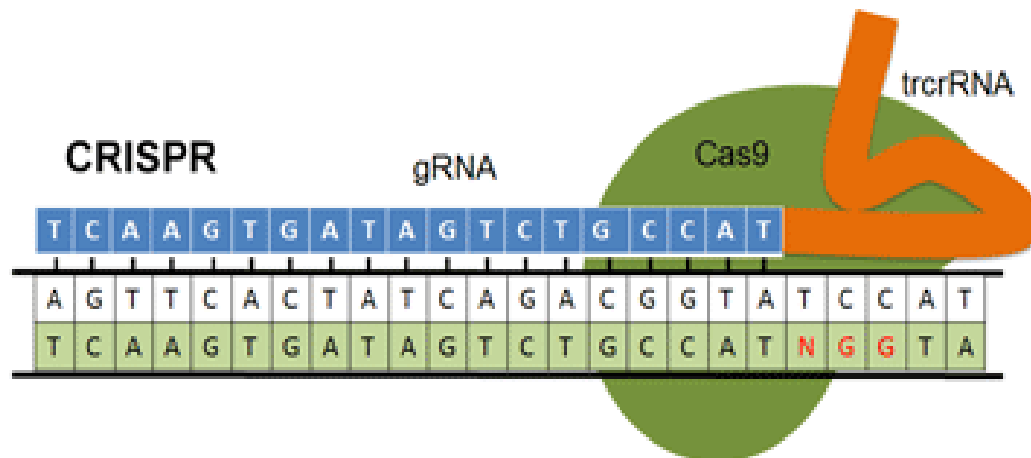
CRISPR which acts like a GPS in finding a target DNA sequence and -

Cas9 which is a protein that snips the DNA at the site identified by the CRISPR

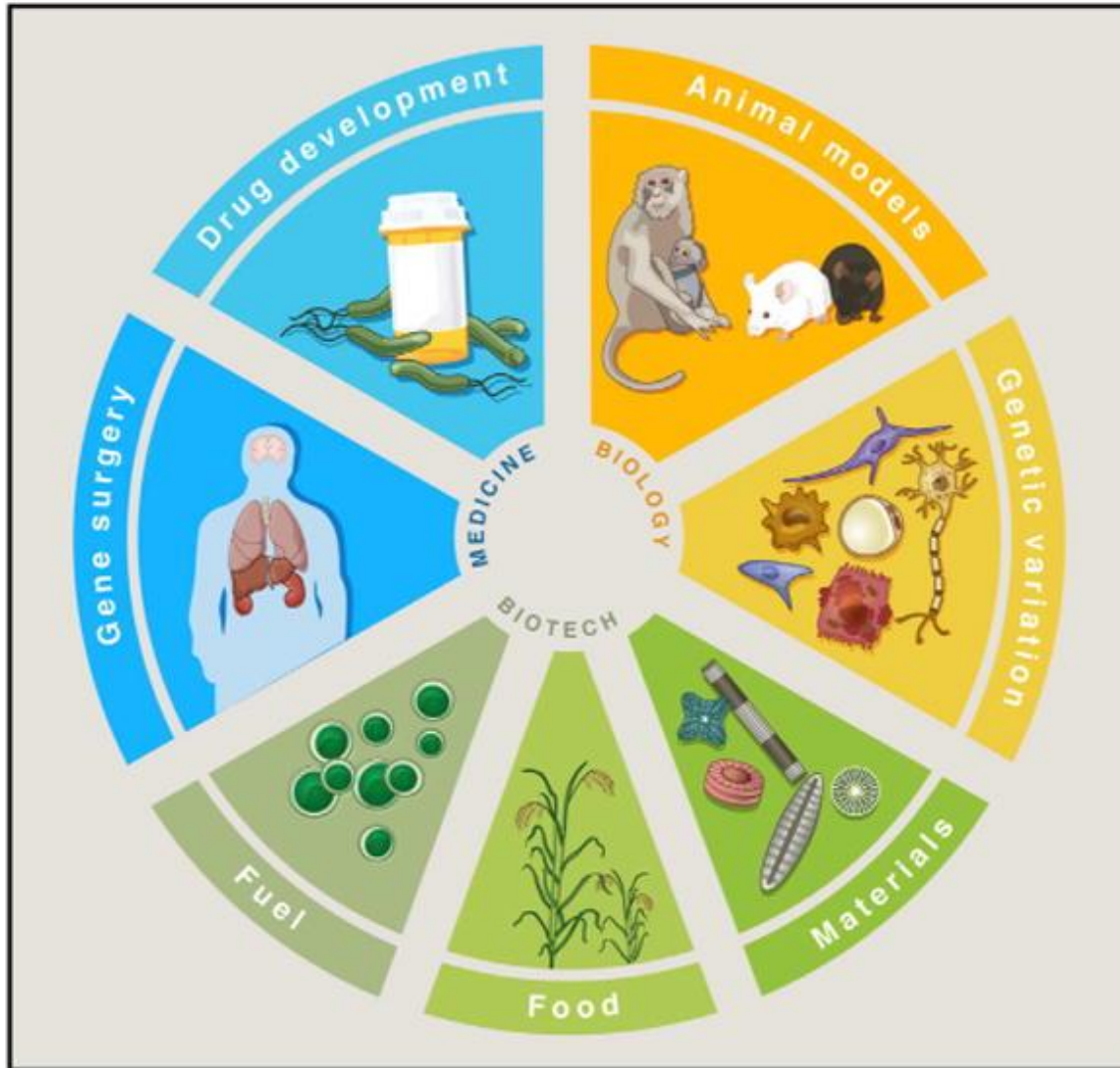
CRISPR-based gene editing

CRISPR – Clustered Regular Interspaced Short Palindromic Repeats

- Bacterial defense system against invading nucleic acids
- An RNA molecule guides the Cas9 nuclease to the target site by complementary base pairing between guide and target



Gene editing applications



*Application of genome editing.
(Modified from Hsu et al. 2014)*

Some uses of gene editing aimed at animal improvement

Cattle

- Hornless
- Reducing milk allergens

Goats

- Long hair(Angora)
- Better muscling

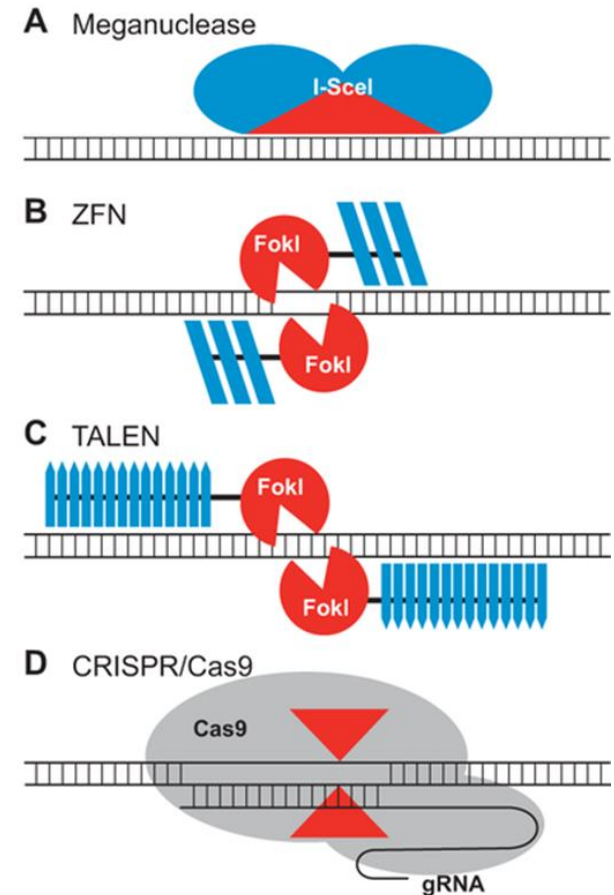
Pigs

- African Swine Fever
- PRRS Virus

Poultry

- Bird Flu
- Reduced allergens in eggs

Silkworms

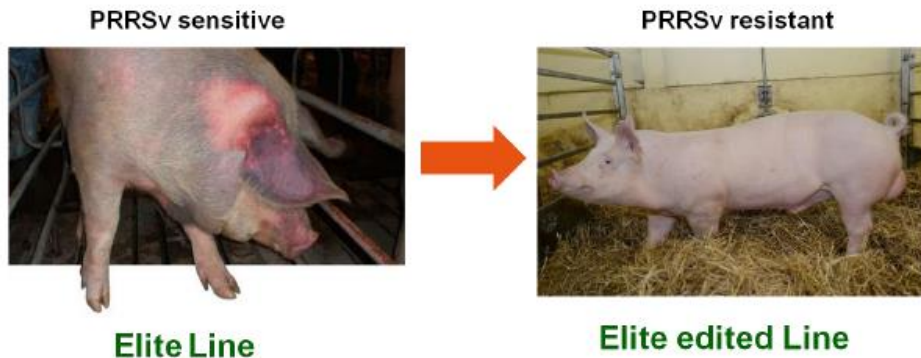


Pig disease

Technology choices



PRRS viral disease in pigs – “Blue Ear”



- Porcine Reproductive Respiratory Syndrome
- Devastating disease; leads to reproductive failure, reduced growth, suffering and premature death
- Causes large economic losses worldwide
- No cure and vaccine is not effective.

Some current uses of gene editing in plants

Non browning mushrooms

Waxy maize

High Oleic Soybean

Rice

- Bacterial Blight

Wheat

- Rusts

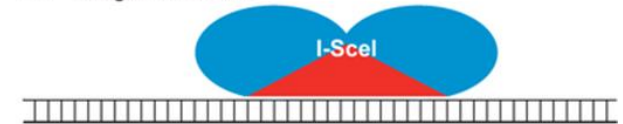
- Powdery Mildew

Tomato

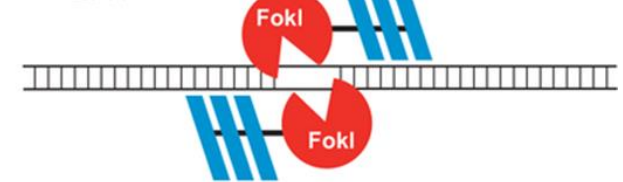
- High anti-oxidants

Understanding gene function

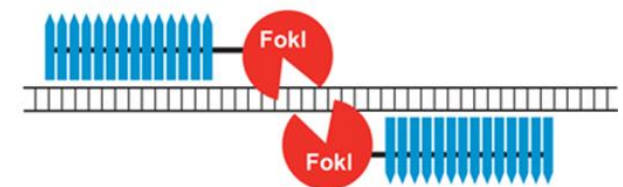
A Meganuclease



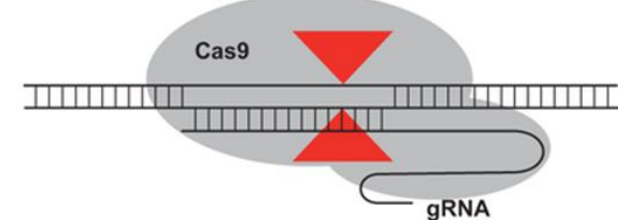
B ZFN



C TALEN



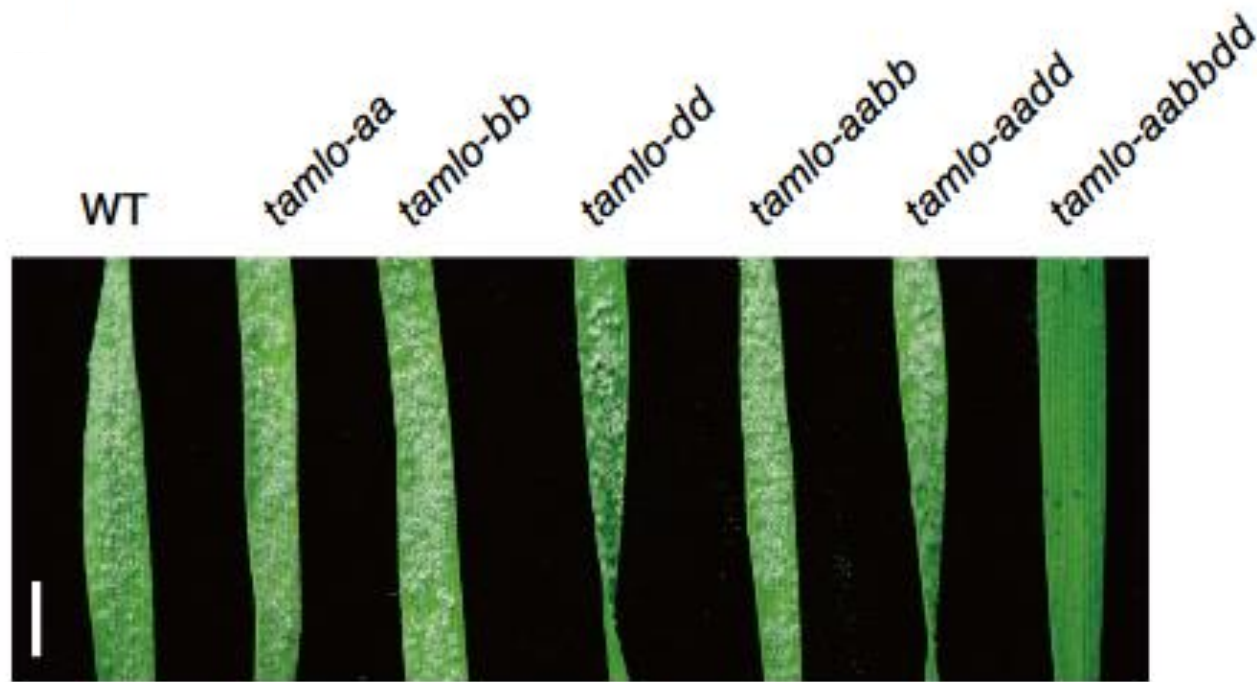
D CRISPR/Cas9



Powdery Mildew Resistance in Wheat

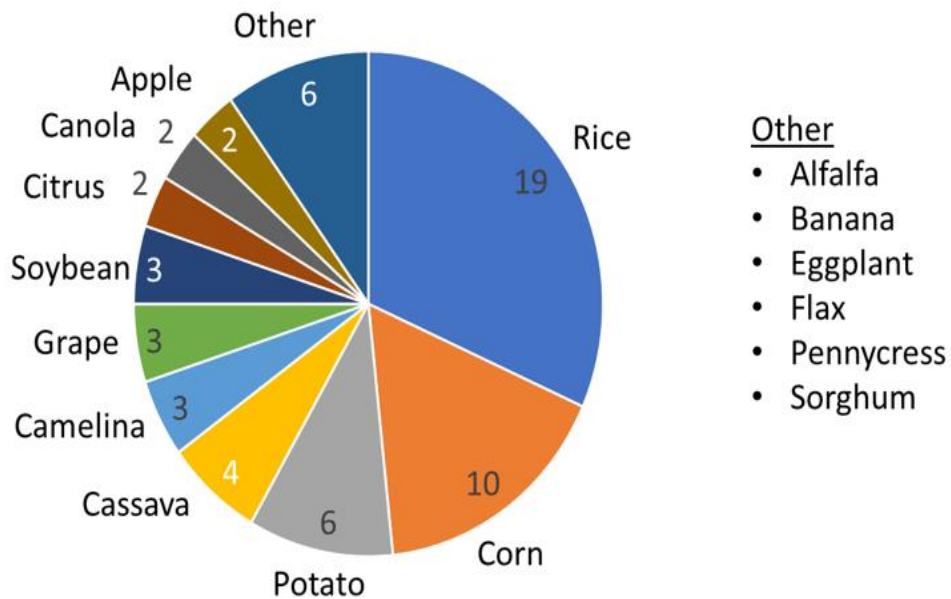
High efficiencies means polyploids can be edited

Knock out of MLO gene in all 3 genomes in wheat gives mildew resistance



In the pipeline

Announced edited crops



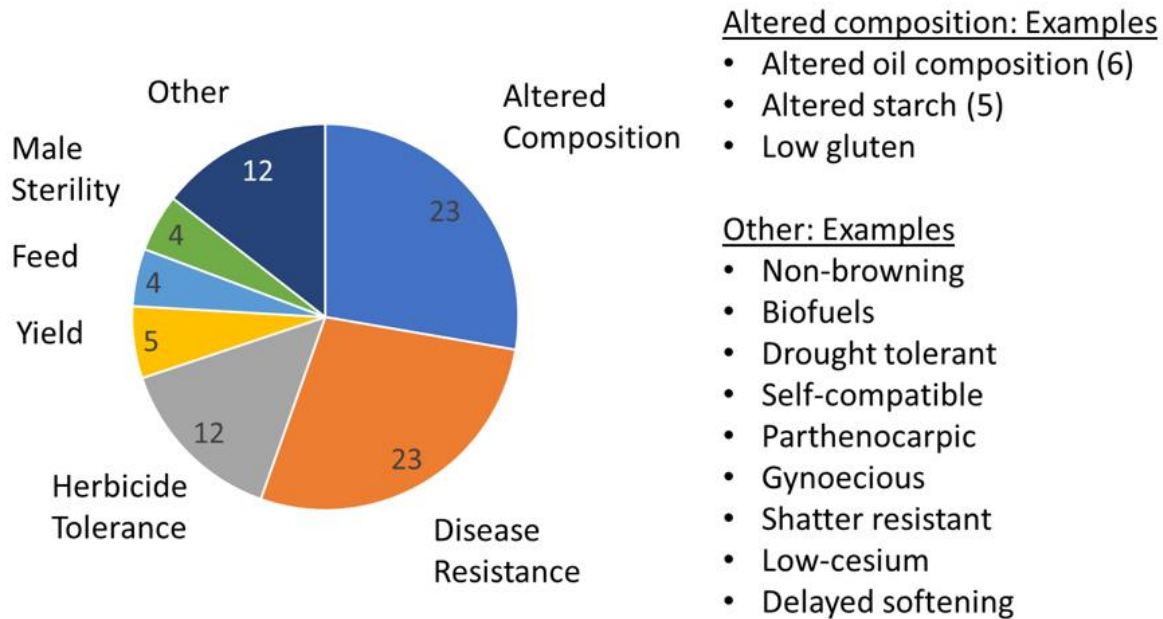
Sources: Scientific literature, scientific conferences, company websites, media reports, USDA "Am I regulated?" Letters/ provided by FDA

EMAC



In the pipeline 2

Announced traits through gene editing

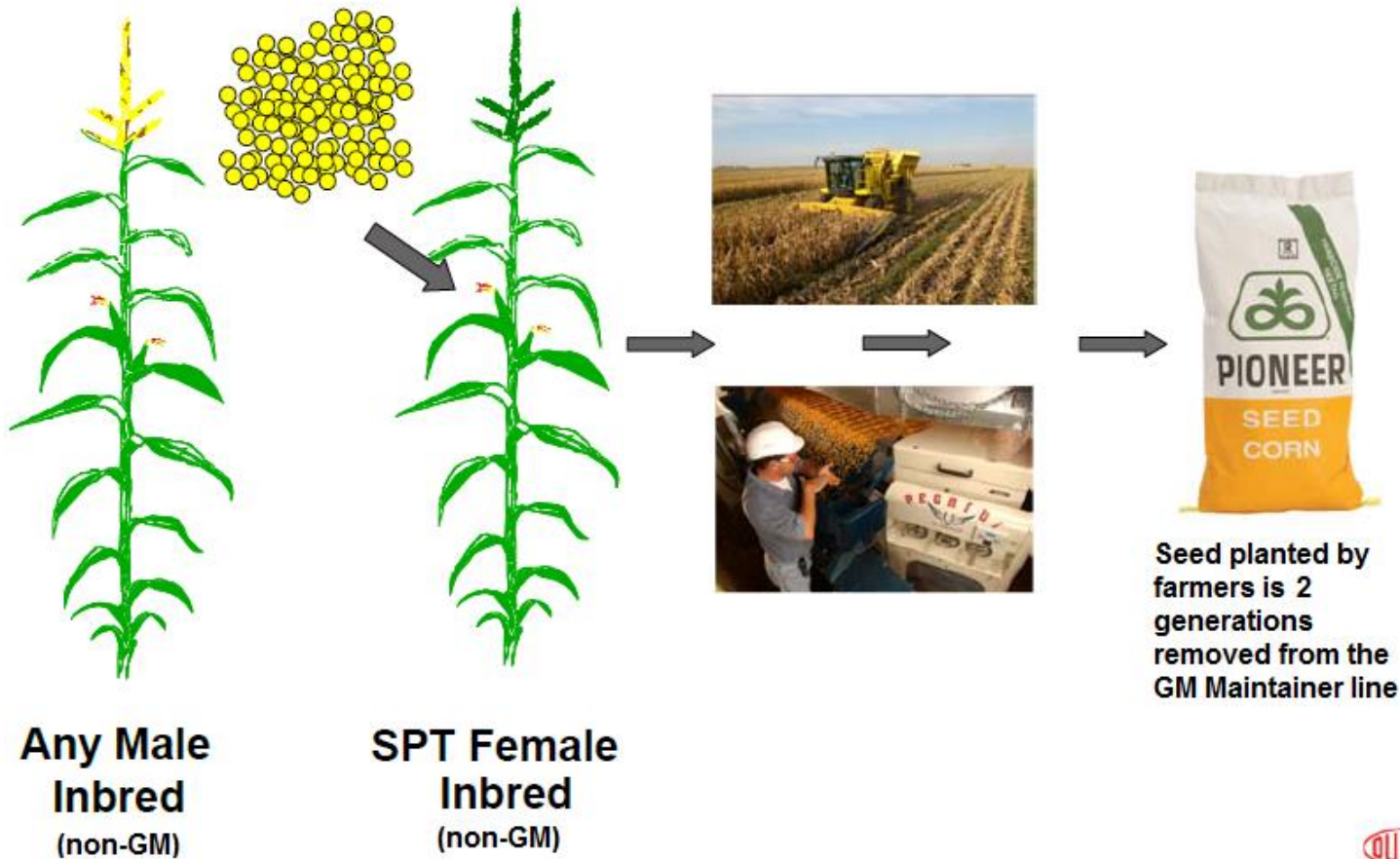


Sources: Scientific literature, scientific conferences, company websites, media reports, USDA "Am I regulated?" Letters/ provided by FDA

EMAC



Pioneer SPT corn is already being grown in the USA



Gene edited canola approved in Canada

Cibus™



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SU CANOLA

The Crop that is changing the Agriculture Industry



Some uses of gene editing aimed at human health

Immune system cell lines for:

HIV

Cancers

Animal models of human diseases:

Hepatitis B

Haemophilia

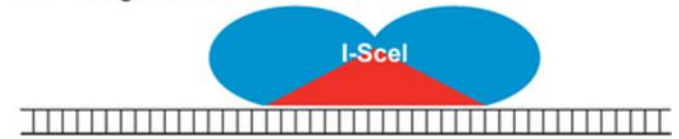
Cystic Fibrosis

Cataracts

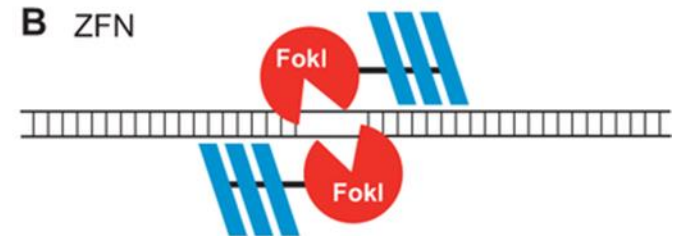
Muscular Dystrophy

Understanding Gene Function

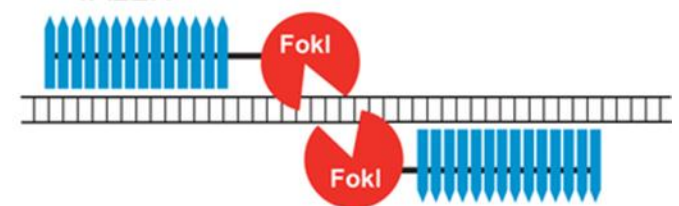
A Meganuclease



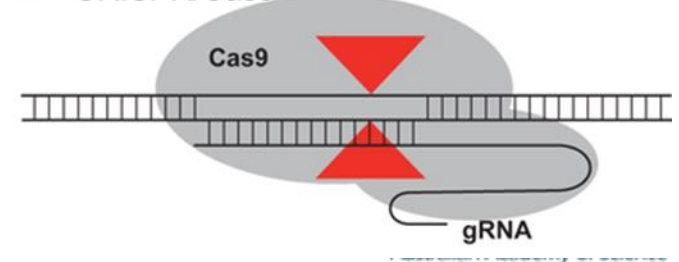
B ZFN



C TALEN



D CRISPR/Cas9



Health Improvement via Gene Editing

Genome surgery for eye disease moves closer to reality

Study shows that a CRISPR-based treatment can restore retinal function in mice

Health Improvement via Gene Editing

Functional Repair of CFTR by CRISPR/Cas9 in Intestinal Stem Cell Organoids of Cystic Fibrosis Patients

Gerald Schwank¹²⁷Bon-Kyoung Koo¹²⁷⁸Valentina Sasselli¹²Johanna F. Dekkers³⁴Inha Heo¹²Turan Demircan¹Nobuo Sasaki¹²Sander Boymans¹Edwin Cuppen¹⁶Cornelis K. van der Ent³Edward E.S. Nieuwenhuis⁵Jeffrey M. Beekman⁵⁶Hans Clevers¹²

Ethics of gene editing

What are the ethical concerns about genome editing?

Bioethicists and researchers believe that human genome editing for reproductive purposes should not be attempted at this time, but that studies that would make [gene therapy](#) safe and effective should continue.

Safety

Informed Consent

Justice and Equity

Genome-Editing Research Involving Embryos

USA policy on gene edited products



Policy considerations in the U.S. pertaining to genome-edited products

High Level Policy Dialogue on Agricultural Biotechnology
Workshop Part Two

Fan-Li Chou
Biotechnology Coordinator
United States Department of Agriculture



Policies on regulation

Organisms with the following alterations are **not** considered regulated under the USDA *current* approach:

- Deletions
- Single base-pair substitution
- Introduction of sequences from sexually compatible plant relatives
- Complete null segregants

USDA plans to maintain this policy as we are updating our regulation.

- June 2018, USDA published a Notice of Intent

Australian Government currently considering what regulations will apply

European Court of Justice ruled all gene editing to be regulated as GM



New knowledge in CRISPR use-

	CRISPER Publications	--%--
Biochemistry, Genetics and Molecular Biology	7172	66%
Medicine	2861	26%
Immunology and Microbiology	1861	17%
Agricultural and Biological Sciences	1510	14%
Multidisciplinary	1072	10%
Chemical Engineering	578	5%
Pharmacology, Toxicology and Pharmaceuticals	530	5%
Neuroscience	501	5%

Mostly to enhance our knowledge of how genes work

