

Can new biotech tools provide genetic solutions-will they be allowed in the EU?

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07 December 2017

ITLUS conference

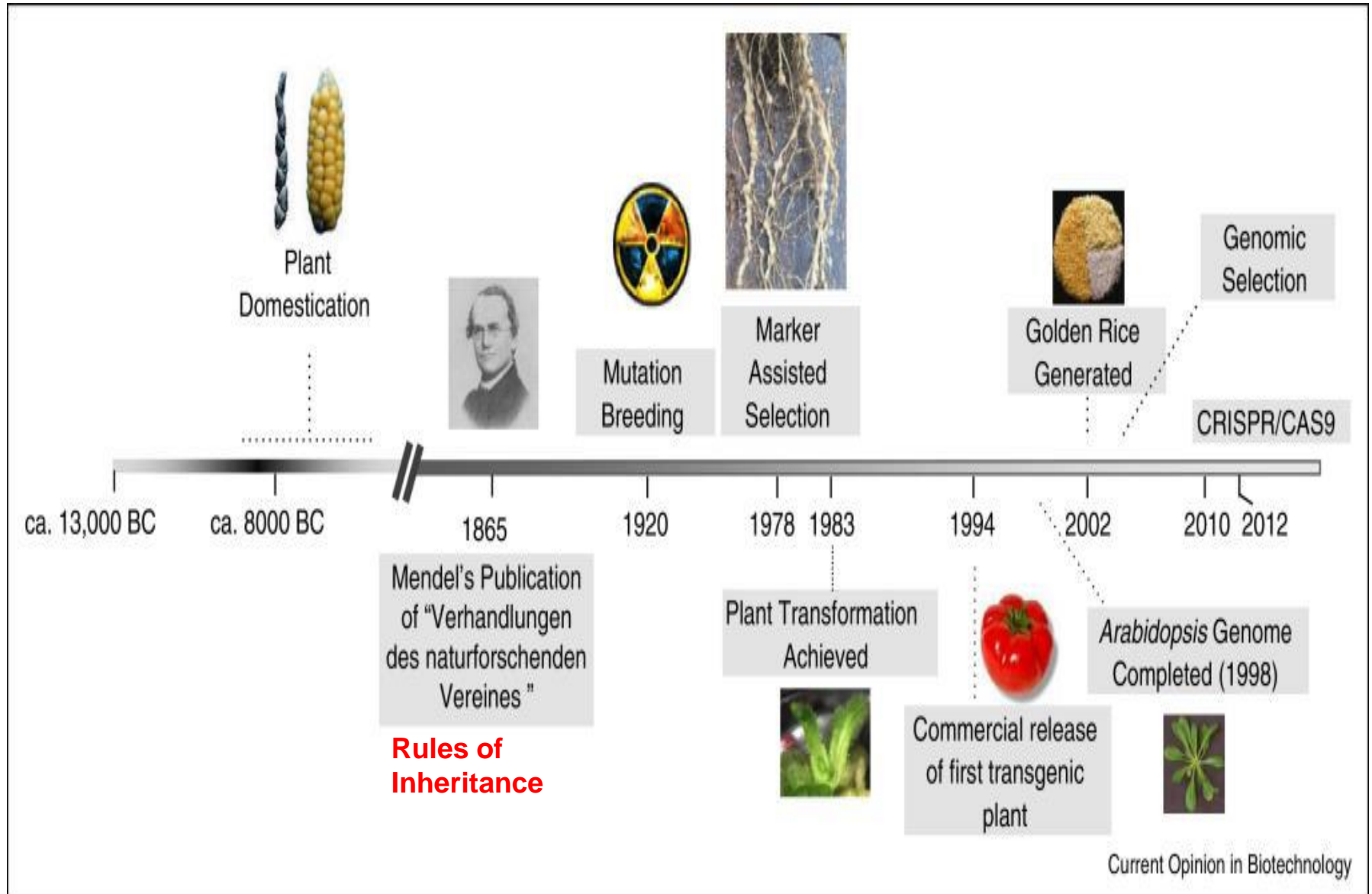
What is Biotechnology?

Biotechnology-Involves harnessing the natural biological processes of microbes, plant & animal cells for the benefit of mankind. It has been practised in agriculture 1000's years, examples include:

- **Farmers select seed-best plants-next year's planting**
- **Plants-cross bred-to produce hybrids**

Timeline of key events in plant breeding

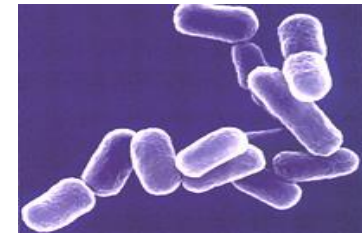
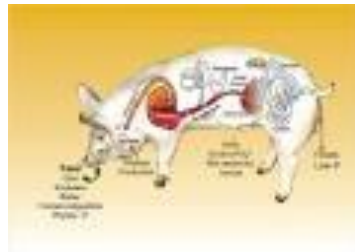
Source: (Francis et al., 2017)



Definitions - Genetically Modified Organism (GMO-DR/GMM-CU)

GMO/GMM:

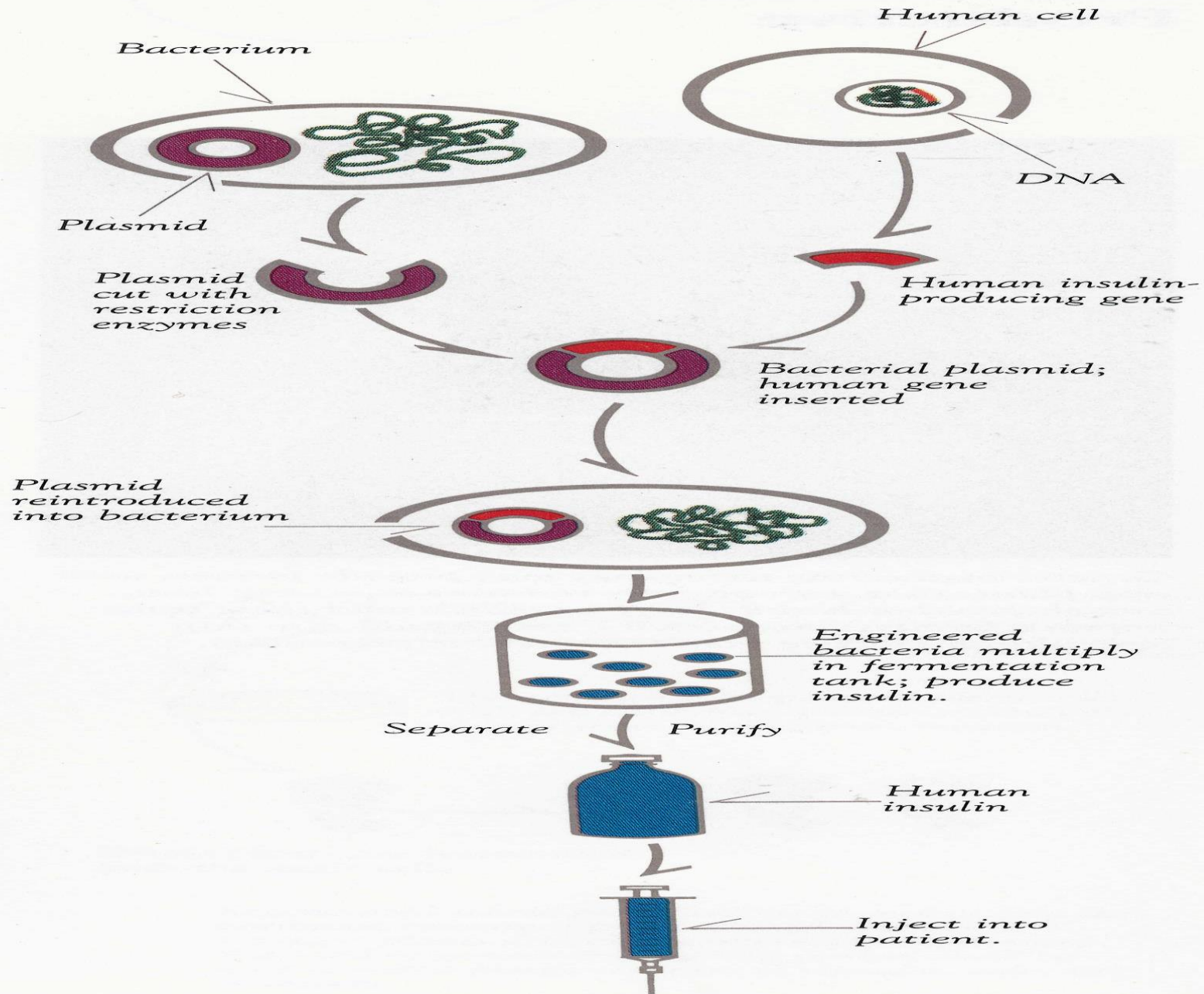
- An organism/micro-organism in which the genetic material has been altered in a way that does not occur naturally by mating or natural recombination



List techniques (under Annexes) that:

- Give rise to genetic modification - 'altering' the genetic material....
- Are **not** considered to result in genetic modification - **conjugation** etc.
- Yield organisms – **are** excluded from the Directive – **mutagenesis, self-cloning-only for CU** etc.

HUMAN INSULIN PRODUCTION



Pharmaceuticals produced with genetic engineering technology are administered to patients by traditional methods.

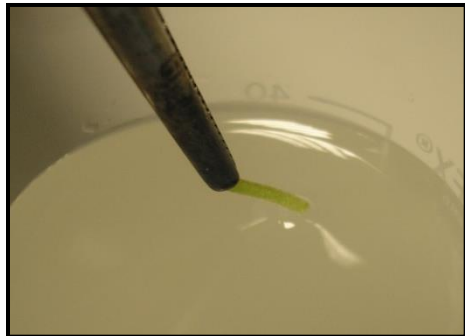
1: Sterile potato culture



2: Excise internodal explant



3: Explant dip in *Agrobacterium* equipped with *RB* gene to confer blight resistance

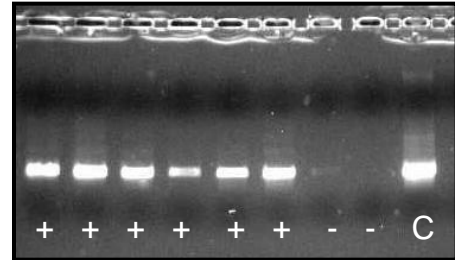


4: Regeneration of GM line from treated explant tissue



5: Growth of GM line in high nutrient media

6: Molecular verification of modification



7: Disease assessment



Conv. potato GM potato

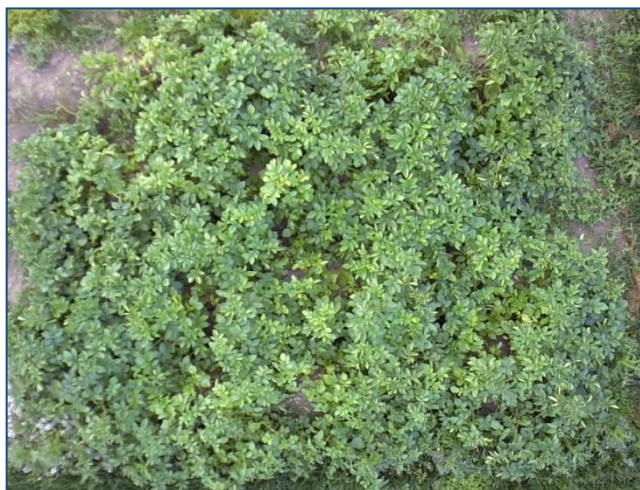
Generation of GM blight resistant potato
(~16 week from phase 1-7)

Source: Dr E. Mullins, Teagasc

2013

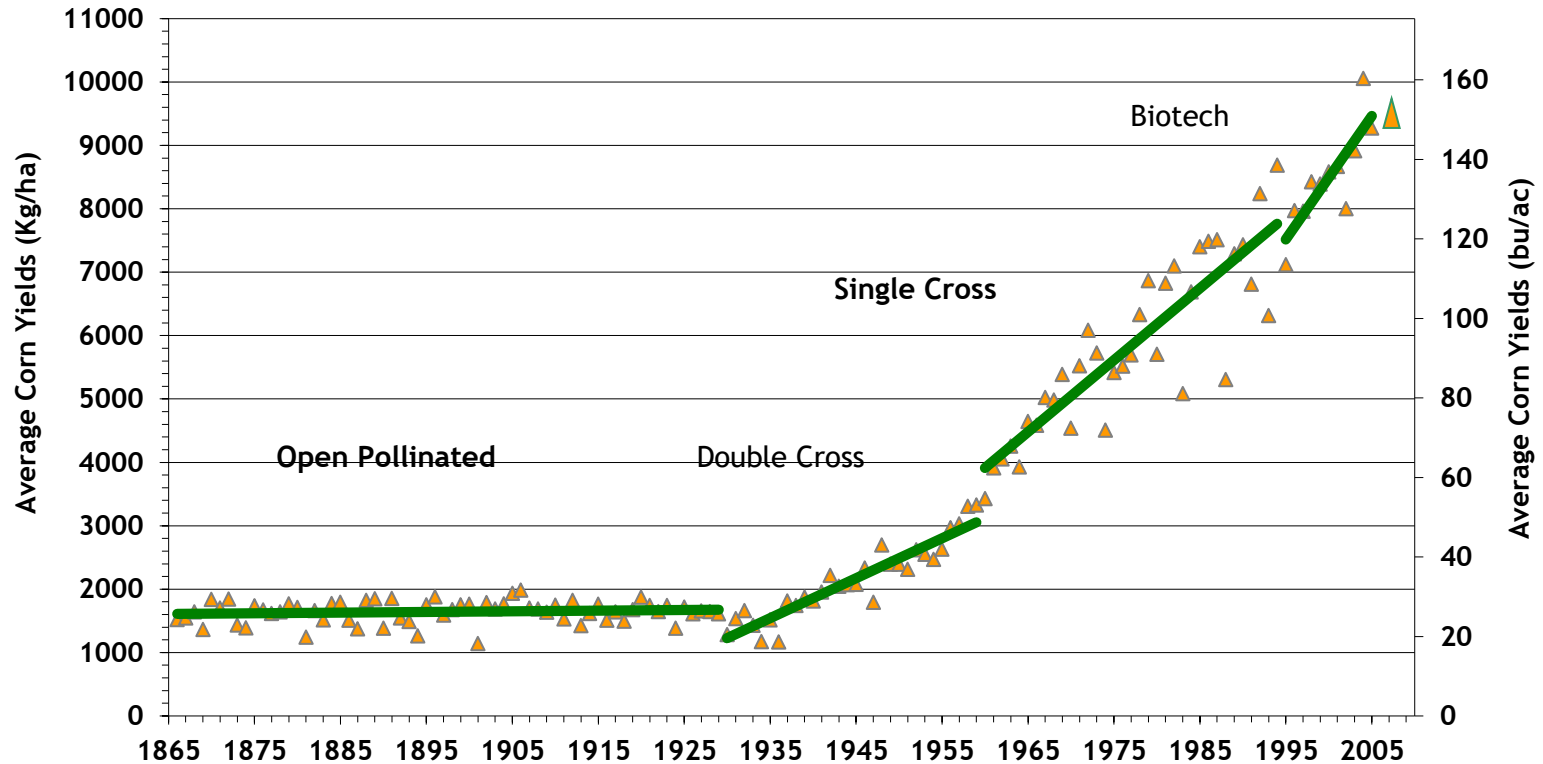


2014



Pictures taken from Irish field study as part of the EU funded AMIGA project. Cisgenic potato line was developed at the University of Wageningen, The Netherlands –source: Dr Ewen Mullins

Technology's Impact On US corn Crop Yields



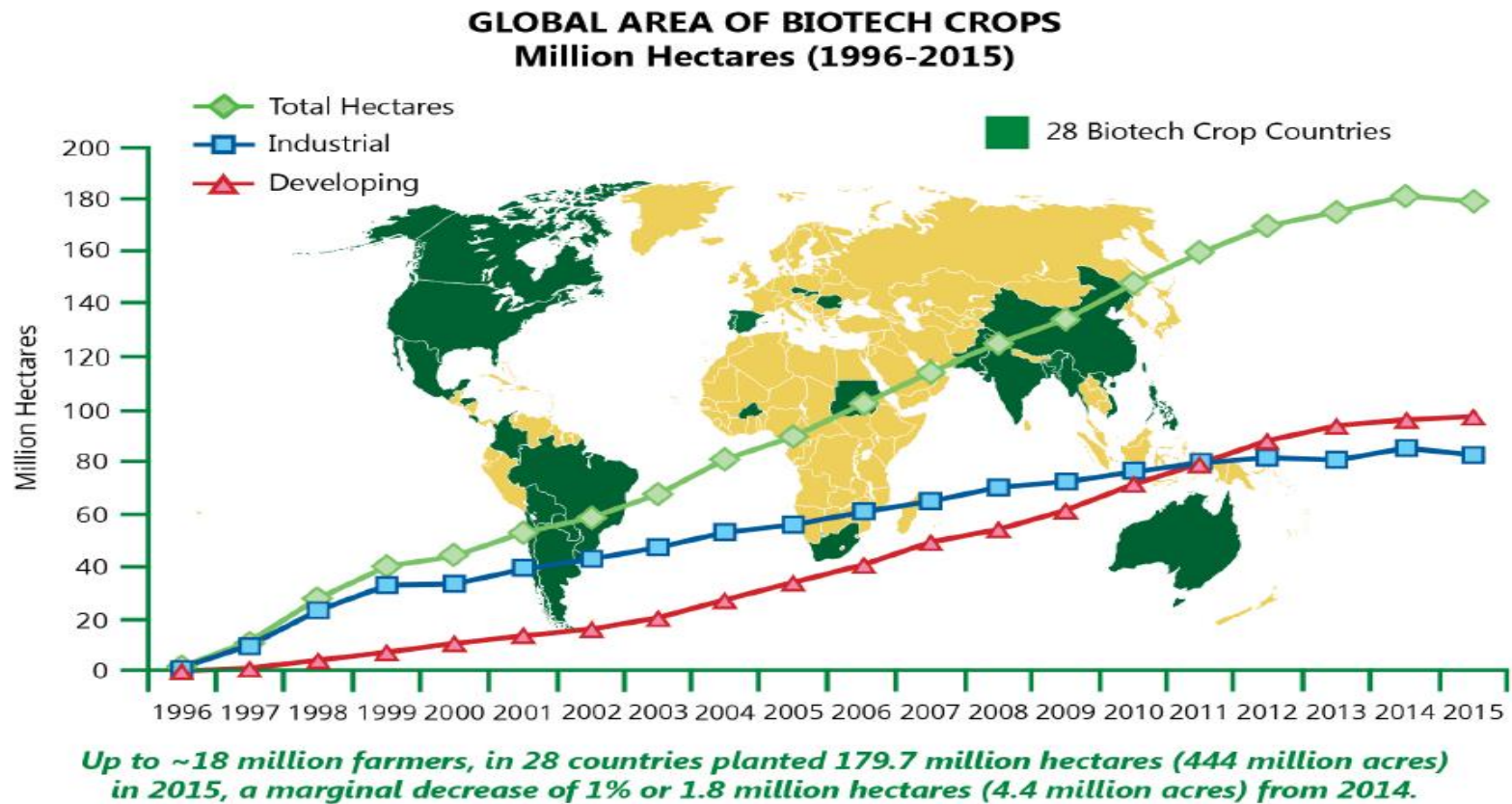
Prof Jimmy
Burke



GMO 2013 EPA Conference-Conclusions

- GMO technology-history of safe use for 40 years-enormous benefits for science & society.
- Huge impact on human medicine, treatment of AIDS, rheumatoid arthritis, vaccines etc.
- GMO technology big impact on Irish pharma industry-50%-exports.
- GMO is not per se riskier than conventional plant breeding –€300m EU funded GMO biosafety research
- EU imports 65% of protein-rich feedstuffs, >50% animal feed Ireland-derived from GMO.

Biotech crops



Source: Clive James, 2015.

Opportunities for NBTs

- **All major crops receptive to NBTs (gene editing)**
- **NBTs are methods that allow the plant breeding industry to develop new plant varieties in a similar-but faster and more precise-manner compared to conventional breeding techniques**

New Breeding Techniques (NBTs)

TARGETED MUTAGENESIS TECHNIQUES

OLIGONUCLEOTIDE DIRECTED MUTAGENESIS



ZINC FINGER NUCLEASE TECHNIQUE



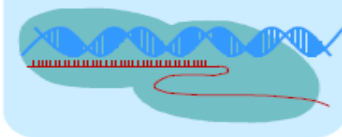
MEGANUCLEASE TECHNIQUE



TALEN TECHNIQUE



CRISPR-Cas SYSTEM



TECHNIQUES RESULTING IN "NEGATIVE SEGREGANTS"

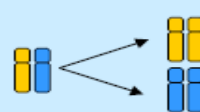
EARLY FLOWERING-accelerated breeding



RNA DIRECTED DNA METHYLATION

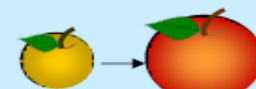


REVERSE BREEDING



VARIANTS OF PLANT TRANSFORMATION TECHNIQUES

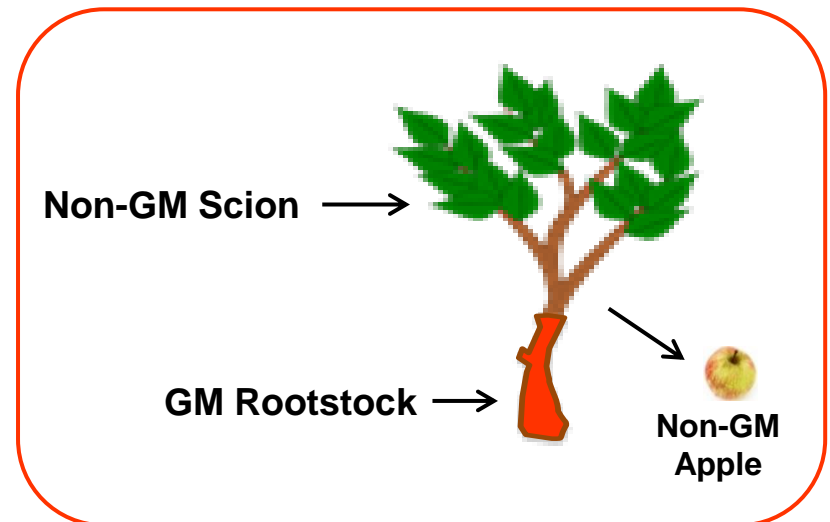
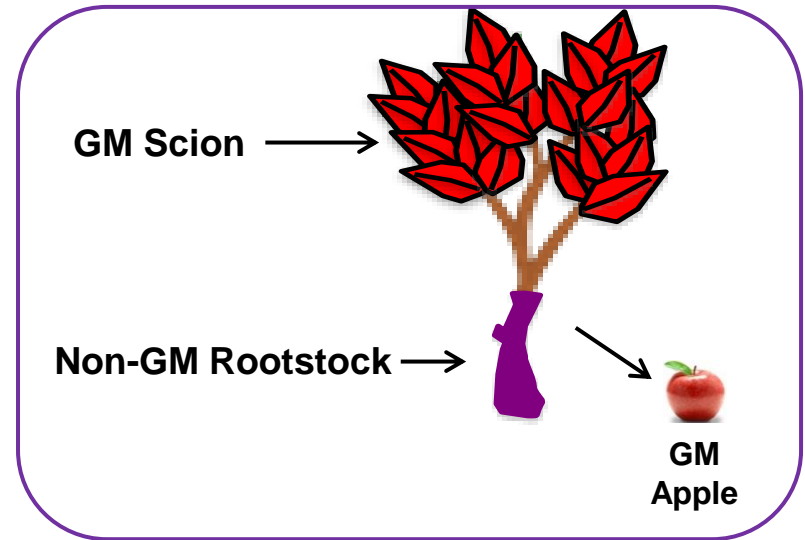
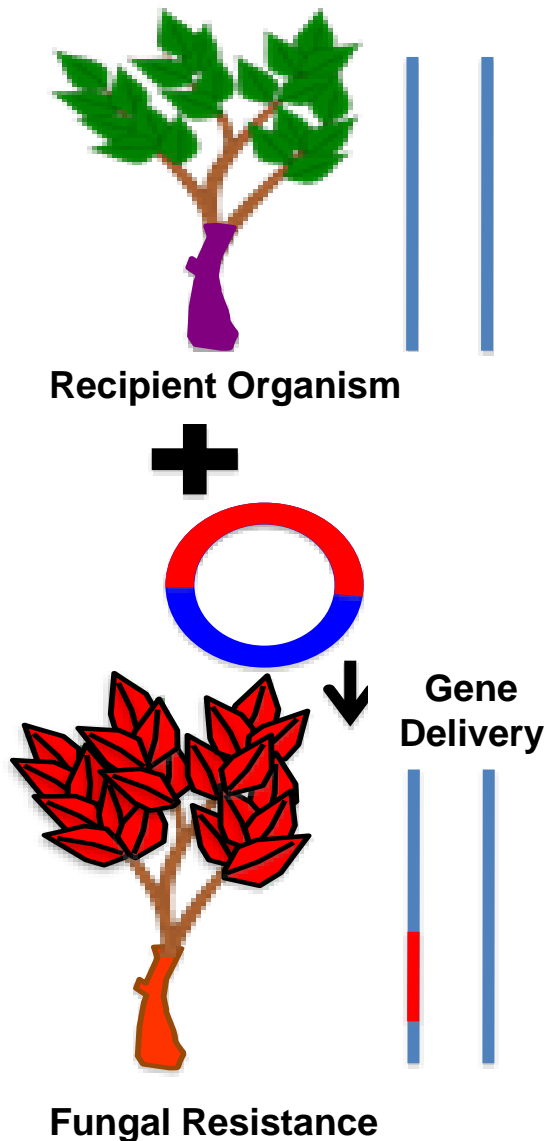
CISGENESIS AND INTRAGENESIS



GRAFTING ON GM ROOTSTOCK



Example of Grafting



Establishment EU working group on NBTs

- **Questions from companies on the regulatory status of NBTs**
- **EU working group was established in 2007 at the request of EU Member States**
- **Objective: examine new techniques in the context of the GMO legislation**
- **Report was finalised in 2012 but never published by the COM!**

What is happening at EU level-NBTs

- **Scientific Advise Mechanism (SAM)-established in 2015-Advise EU Commissioners**
- **High Level Group (SAM) published Explanatory note on NBTs-April 2017**
- **Modern Biotechnologies in Agriculture-Paving the way for responsible innovation Sept 2017-DG Health & Food Safety-webpage**
- **NL proposal 2017-If NBT are as safe as plants obtained by traditional breeding-exempt them!**
- **SW, FI & DE have made decisions on **CRISPR-Cas9**-non-GM**
- ****ODM**-Herbicide tolerant oilseed rape (UK, IE, DE, SW, FI)-non-GM.**
- **EFSA opinions (2012-2015)-ODM, ZFN-1 and ZFN-2 can be considered a form of mutagenesis. Cisgenesis is similar to conventionally bred plants!**

Main observations by SAM

- NBT differ significantly from each other
- NBT are used in combination with conventional breeding/GMO.
- NBT are very versatile and can make a number of types of changes to plants include the insertion of genes from the same or other species in a precise and targeted way, without the addition of DNA to the genome of end-products.
- Some new techniques do not make changes to genetic sequences at all.
- This precision and control over changes made is greater than with the use of conventional breeding or GMO. As a consequence, these new techniques result in **fewer unintended effects**.
- Assessments of the safety of the organisms produced by NBT can be made on a case-by-case basis.

Commercial development of crops via NBTs

Drivers

- Technical potential of NBTs

Economic :

- Faster breeding process than conventional plant breeding

Constraints

- Uncertainty of regulatory status at EU level?
- High costs if regulated as GMO-ramifications for SMEs
- Economic development-keep Biotech jobs in the EU!
- Food Security in the EU
- Brain drain-EU level!
- Labelling-Freedom of choice for consumers?
- Trade implications?
- Plant disease/Climate change/ fewer Plant Protection Products-need NBTs!

France (Council of State) refers questions on NBTs to ECJ-October 2016

Citing a serious difficulty in interpreting European Union law

- **Whether NBTs fall under EU GMO law?**
- **Whether EU countries could ban NBTs?**
- **Exempt-NBTs-EU GMO rules endanger the precautionary principle.**

Considerations

- **How does a point mutation produced by NBT differ from mutagenesis (chemical/radiation)–does it produce a lower higher or the same risk?**
- **Need to apply the Innovation/Better Regulation principles and not just the Precautionary Principle to decide the legal question?**
- **Can a mutation be traced by analytical means? No authorization in the EU without traceability-Cibus oilseed rape?**
- **Proportionate to the risks**
- **Risk vs. benefits**
- **ECJ decision how to interpret EU law-wait and see!**

EU Industry Calls for Innovation-Agriculture

Smart Regulation & Innovation for EU Agriculture

- **Workable regulatory systems & science-based policy-growth for EU productive & sustainable agri sector**
- **Innovation to provide food security, feed a growing population & transition towards a bio-based economy.**
- **Policy shift to prevent EU falling behind- overly cautious approach-uptake of new innovative technologies!**

New agricultural breeding techniques: EU must take off its ideological blinkers-**September 2017**



Norbert Lins (DE) MEP-shadow rapporteur on technological solutions for sustainable agriculture in the EU

*Go raibh maith
agaibh.*

New Plant Breeding Methods

- <http://www.kws.com/aw/Research-and-Breeding/Methods/New-Plant-Breeding-Methods/~hjmg/>