



Inspired by Nature™

**Cibus' Trait Machine is Accelerating Plant Breeding
Using the Rapid Trait Development System (RTDS™)
to Benefit Consumers, Farmers and Processors.**

6th Plant Genomics and Gene Editing Congress: Europe
Greg Gocal, Ph.D.
EVP and CSO

Rotterdam, The Netherlands
May 15, 2018

Cibus™

Cibus – “Food For Man” – Innovation in Breeding



- Cibus is a privately owned biotechnology company with ~120 employees located in San Diego and Minneapolis (US), Kapelle (The Netherlands) and most recently Winnipeg (Canada)
- Cibus is focused on the development of improved characteristics for all crops through the application of precision gene editing technologies
- Nucelis, an independent operating unit of Cibus, applies the same technologies to develop improved fermentation and bio-based products.



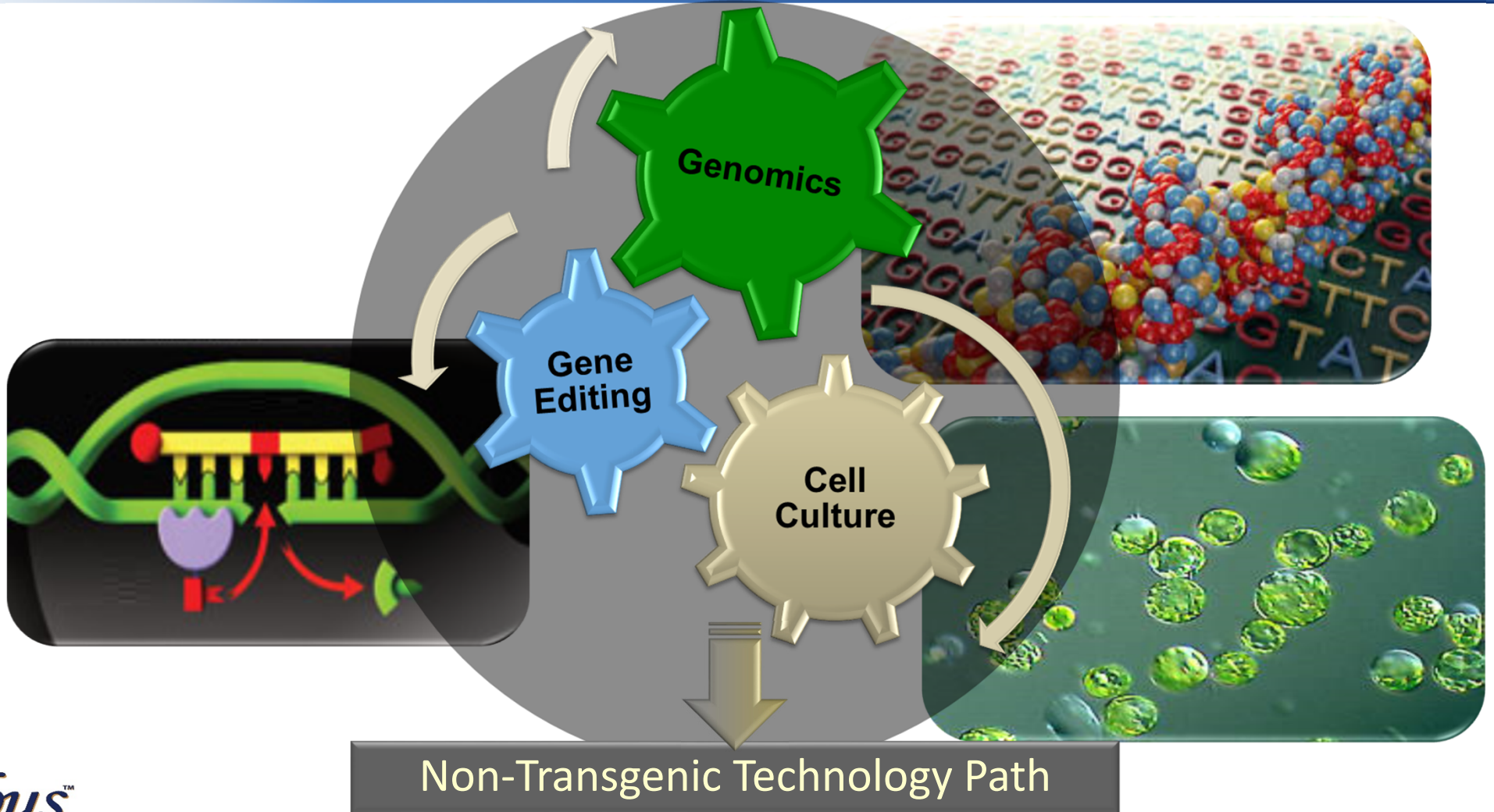
Our Mission

To be leaders in the development of a sustainable global non-transgenic food supply

Inspired by Nature™

Cibus is changing the face of agriculture by innovating plant breeding

Converging Technologies Have Enabled a New Non-Transgenic Approach



Genetic Diversity

*Phenotypic diversity is driven
by genetic diversity*



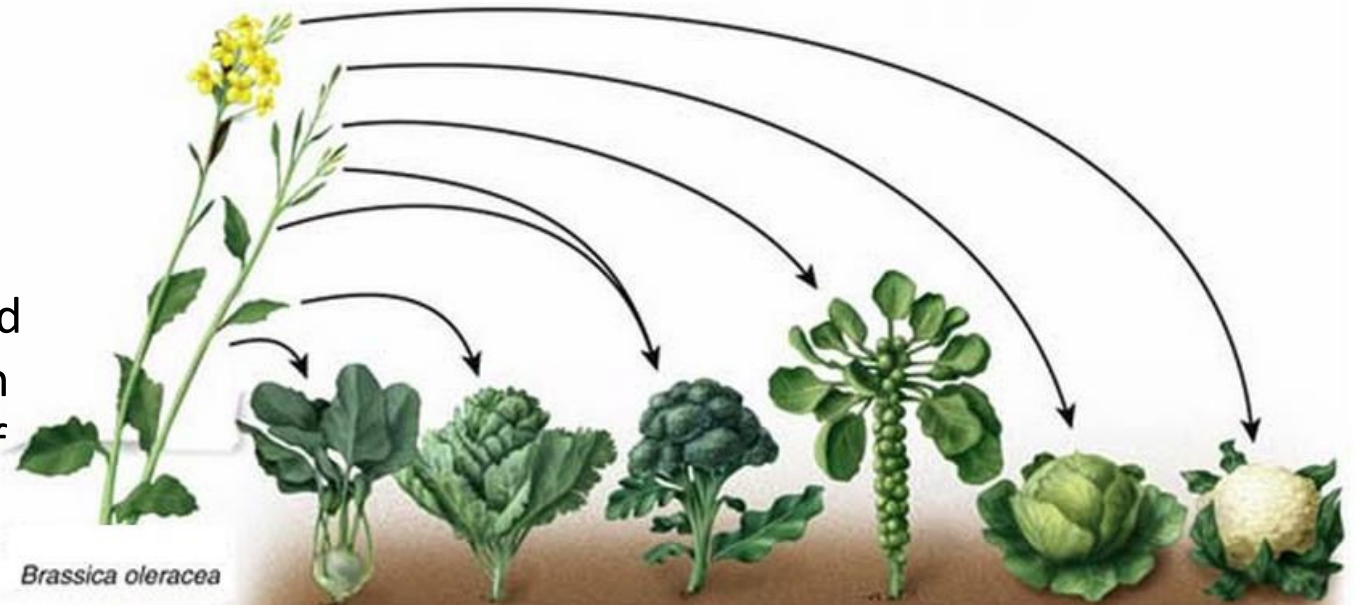
Genetic Diversity and Plant Breeding

2,500 Years of Domestication

Mutations only happen infrequently
 $\sim 1 \times 10^{-9}$ / generation

Plant breeders have harnessed spontaneous genetic variation through thousands of years of crop domestication

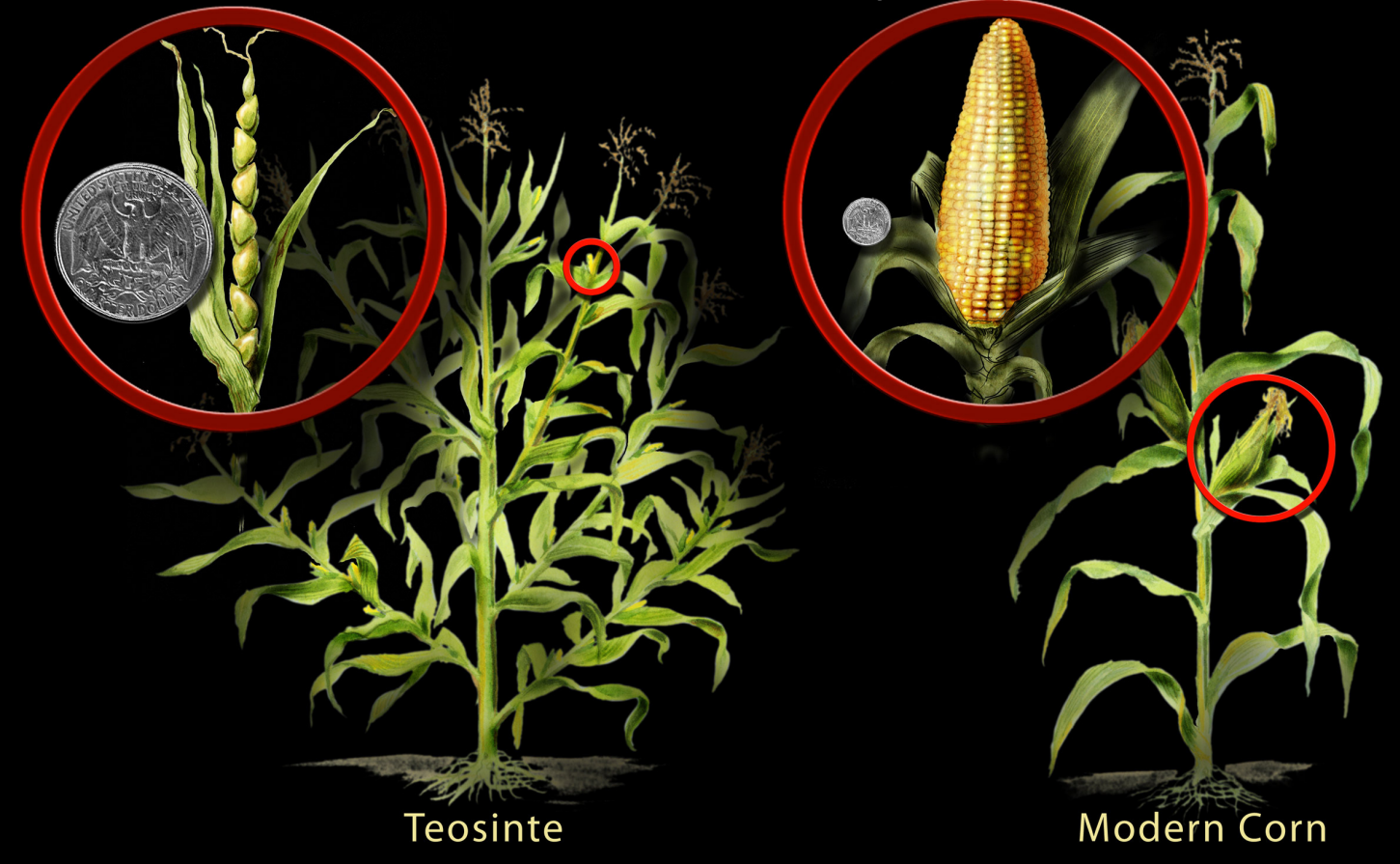
People have eaten much of the diversity that has occurred



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

Traditional Plant Breeding is Slow and Inefficient

Corn domesticated over 9000 years ago



- Cibus' Rapid Trait Development System (**RTDS™**) accelerates plant breeding
- Since the onset of agriculture 10-12 thousand years ago, plant breeders have been searching for useful variation
- Variation occurs when a typographical error is made each time DNA is copied
- New characteristics (traits) such as yield, taste, color, etc. often only occur infrequently

Many Crop Plants Show Hybrid Vigor

Chinese Cabbage

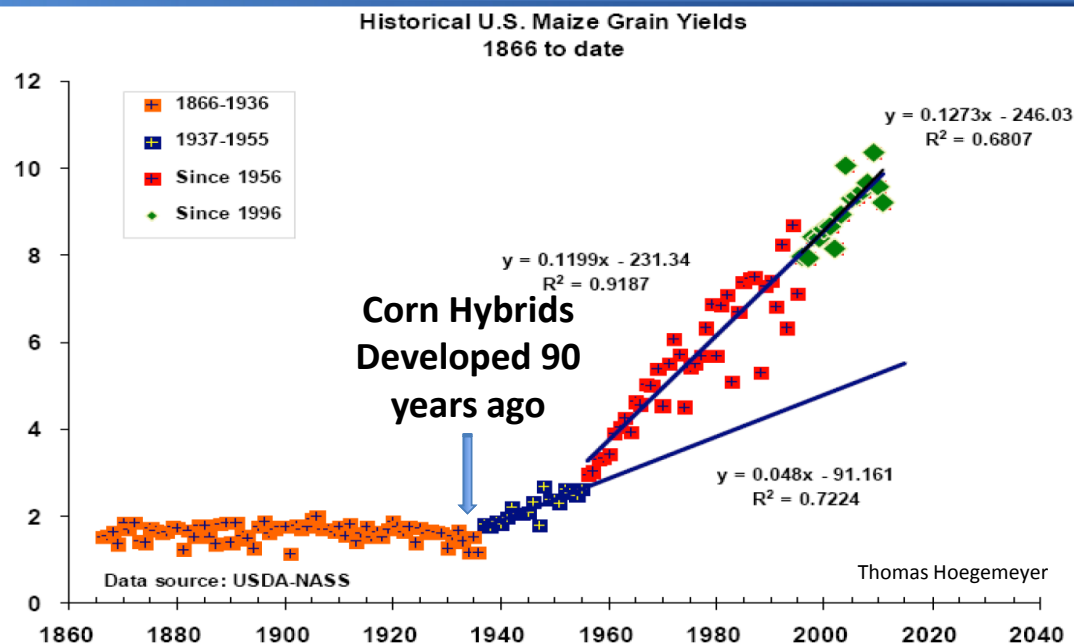


Female F₁ Male

Tomato



Normal parent Hybrid offspring Mutant parent
Krieger et al (2010)



Corn (1973)



Mo17 F₁ B73



Rice



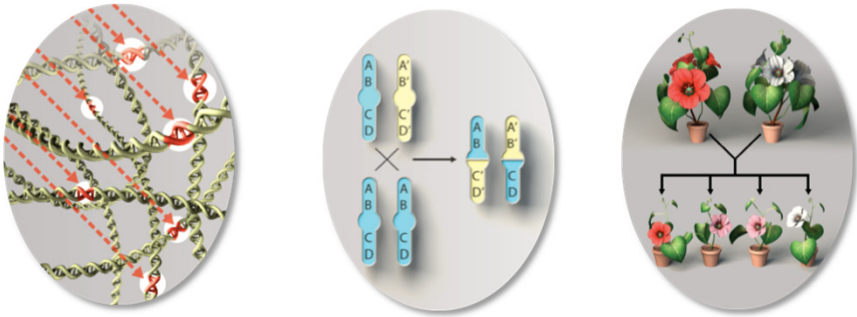
Qifa Zhang

- Crossbreeding two inbred parents to produce hybrid crops such as rapeseed (Canola), rice, corn, sugarbeet, sunflower and others improves performance, size, growth rate, fertility, and yield
- Canola hybrids were first commercialized in 2002
- By developing new characteristics in elite commercial lines or each parent for elite hybrids, Cibus' Rapid Trait Development System (**RTDS™**) accelerates plant breeding

Evolution of Trait Development Technologies

Plant Breeding (traditional)

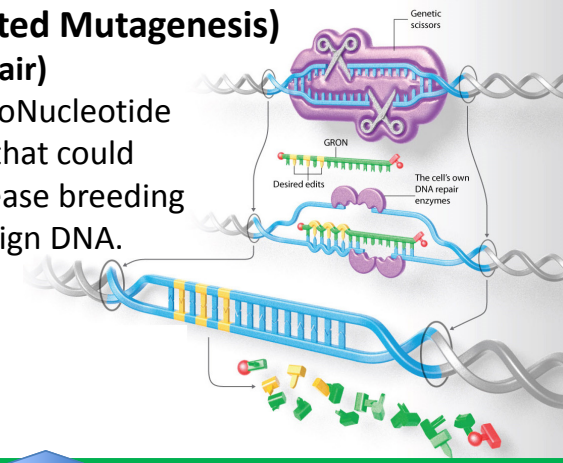
Characteristics derived from natural or induced spelling changes have enabled crops to be developed and improved.



ODM (Oligonucleotide-Directed Mutagenesis) (Homology Directed Repair)

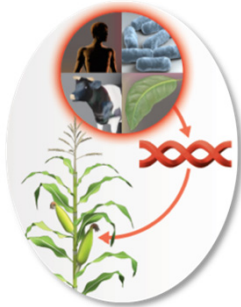
Mediated by the Gene Repair OligoNucleotide (GRON), precise spelling changes that could occur in nature expedite and increase breeding efficiency **WITHOUT** inserting foreign DNA.

RTDS has >400 patents and pending applications.



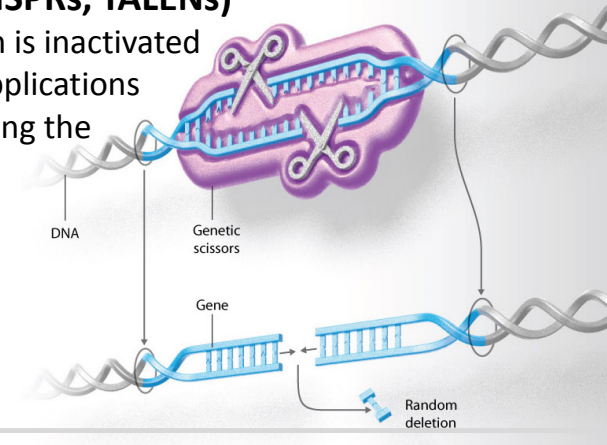
Transgenic (GMO) Plants (old technology)

Foreign DNA is added to develop characteristics that could not occur without adding these sequences.



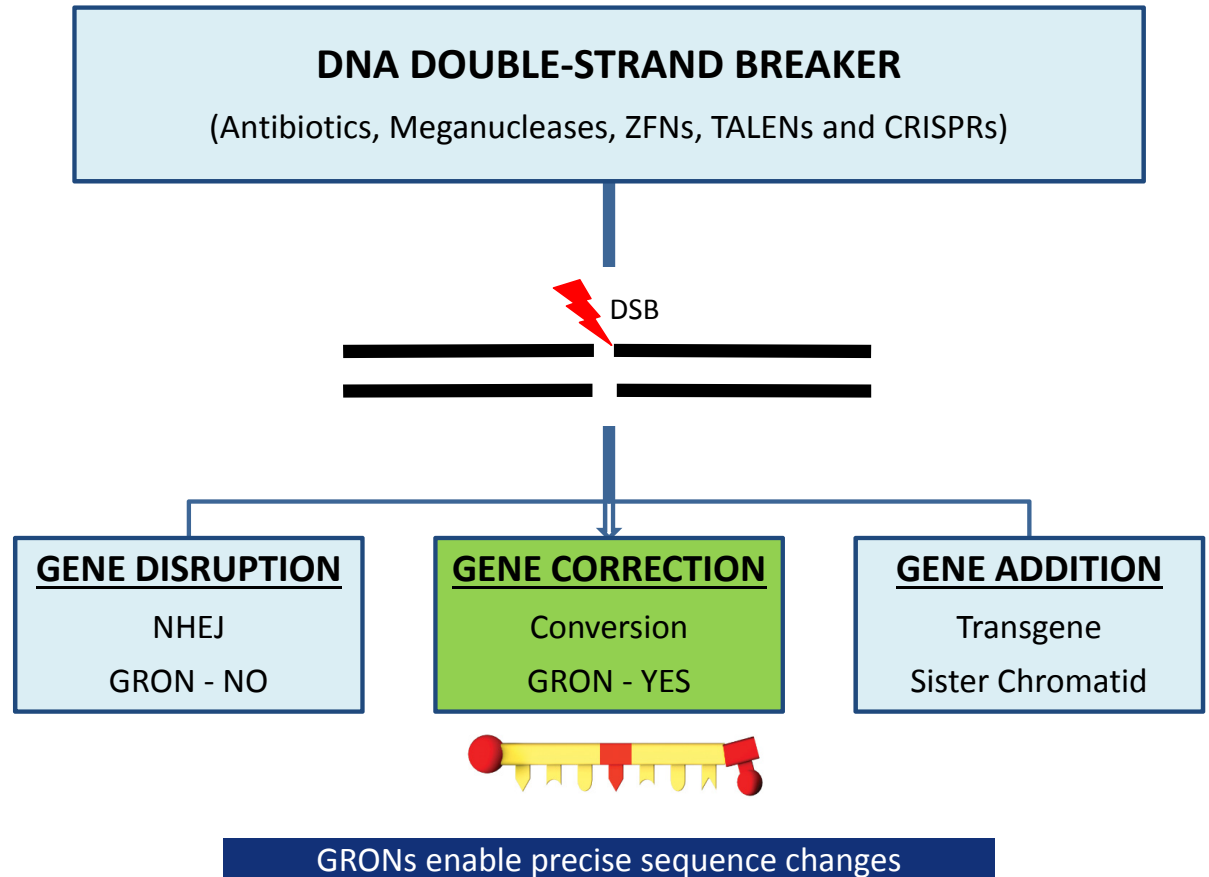
Directed Nucleases (CRISPRs, TALENs)

Without a GRON, gene function is inactivated (knocked out). To date, most applications in plants Insert reagents encoding the directed nuclease.



Cibus Differentiation

- **Focus on Targeted Changes**
 - GRON mediates one or a few nucleotide changes
 - At a specific location
 - Within a specific gene
- **Non-transgenic**
 - No selectable marker
 - Reagents not inserted
- **Without Selection**
 - Conversion frequency sufficient to identify winners by molecular screening alone
- **Efficient Single Cell Culture**
 - Converted single cells regenerated back into entire plants



Mutations Found in Nature Compared to Cibus *RTDS*



Nature induces the changes to make new characteristics

Uses natural DNA repair process

Find the trait: in trillions of plants or millions of acres

Takes a long time for plant breeders to find and use the new trait



Cibus induces the change to make new characteristics

Uses natural DNA repair process

Find the trait: in the Petri dish or in the greenhouse

Fast to find and use new trait. Very precise as no other changes will be made

Identical traits verified through molecular testing

Cassava Twitter Feed – ECJ AG Opinion

[Weigel Lab @PlantEvolution](#)

More Breaking news: **EU Advocate General opinion** -- genome edited organisms exempt from **#GMO** regulations (like X-ray or chemical mutants), as long as no intermediate transgenic step **#CRISPR #GenomeEditing** <https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-01/cp180004en.pdf> ...

[Devang Mehta @ devangm](#) 8:24 AM - 18 Jan 2018

This is still **bad news for crops that need intermediate transgenesis (like cassava** for instance) before crossing out the CRISPR gene.

[Philip A Wigge @PhilWigge](#) Jan 18

Replying to [@ devangm @PlantEvolution](#)

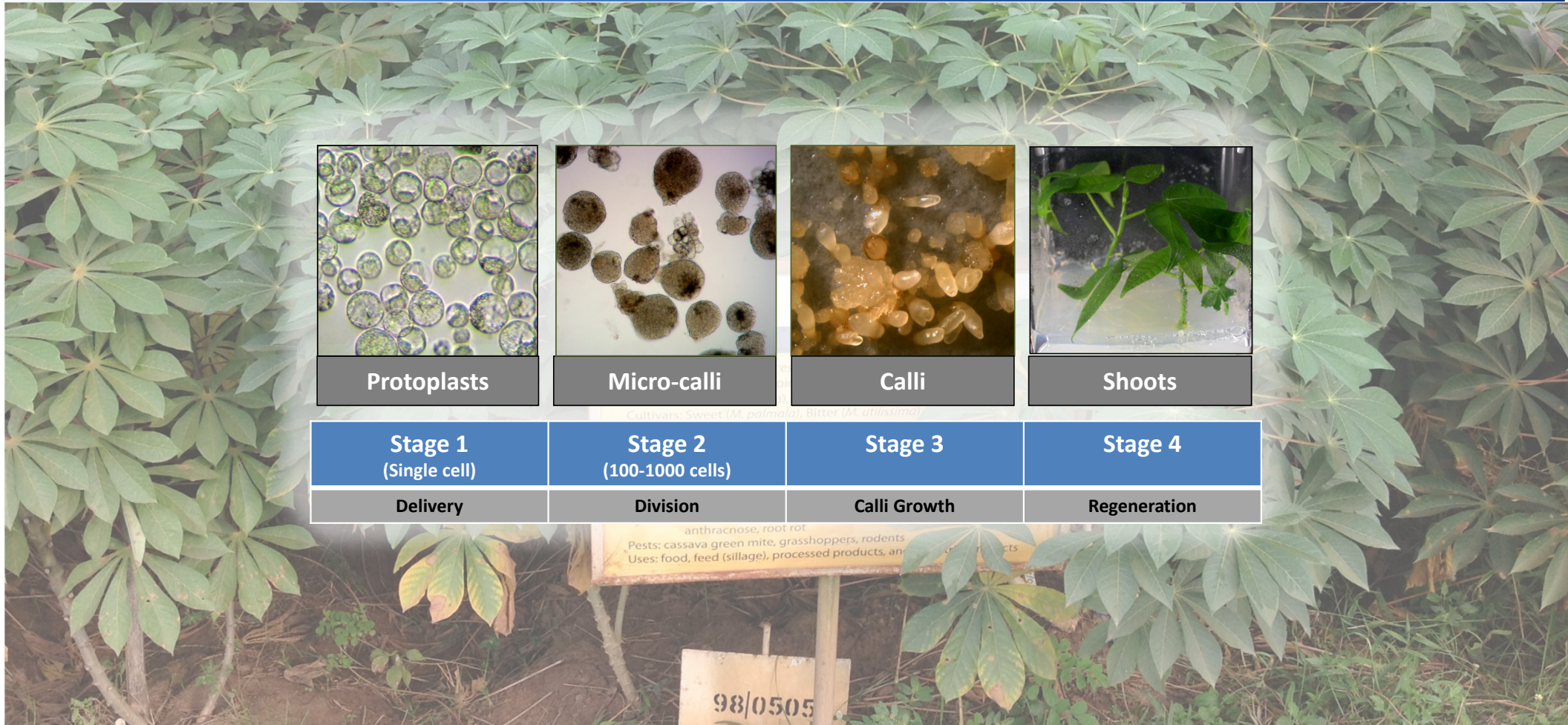
Presumably microinjection/bombardment of pre-assembled Cas9-guide RNA complexes will become routine in all plant systems?

[Devang Mehta @ devangm](#) Jan 18

Unfortunately standardising tissue culture in most crops (and crop varieties) is a bottleneck that **no one is brave/crazy enough** to tackle... For eg we can introduce the complex into cassava protoplasts but it's **impossible to generate plants from protoplasts right now.**



Cassava Platform

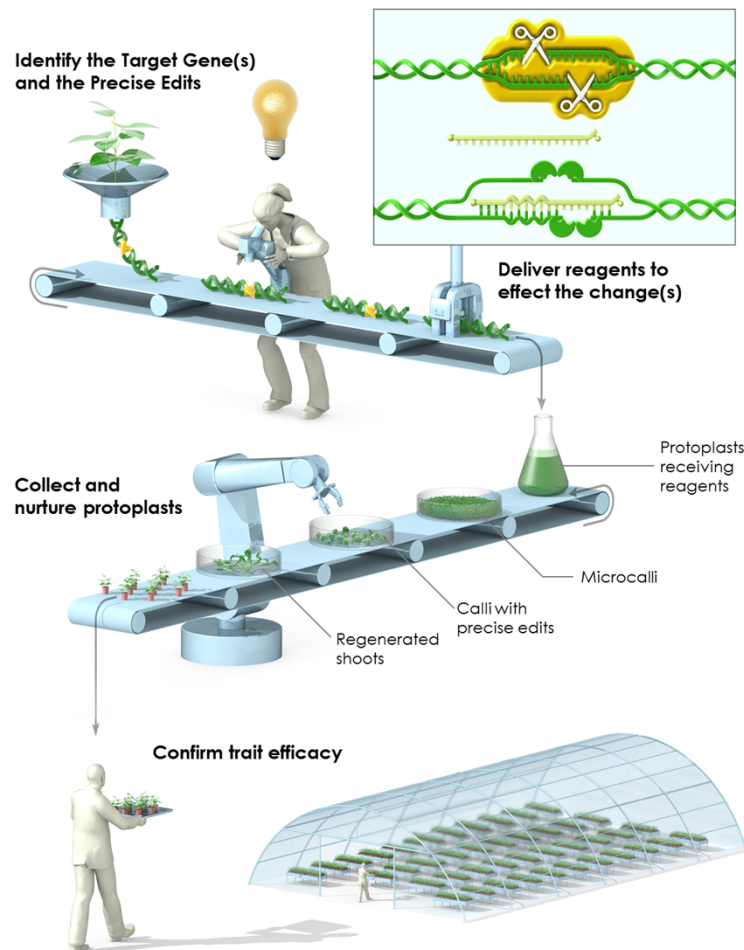


Cibus Trait Machine™



- The trait machine has been enabled in various crops including canola, rice, flax and potato.
- The principles apply to all plants.
- Accessible traits include:
 - Tolerance to environmental stress factors, including heat and drought
 - Crop yield improvement
 - Quality characteristics including oils and starch
 - Herbicide tolerance – multiple modes of action
 - Enhancing the durable natural defense systems of plants to fungal and bacterial diseases

Inside the Cibus Trait Machine

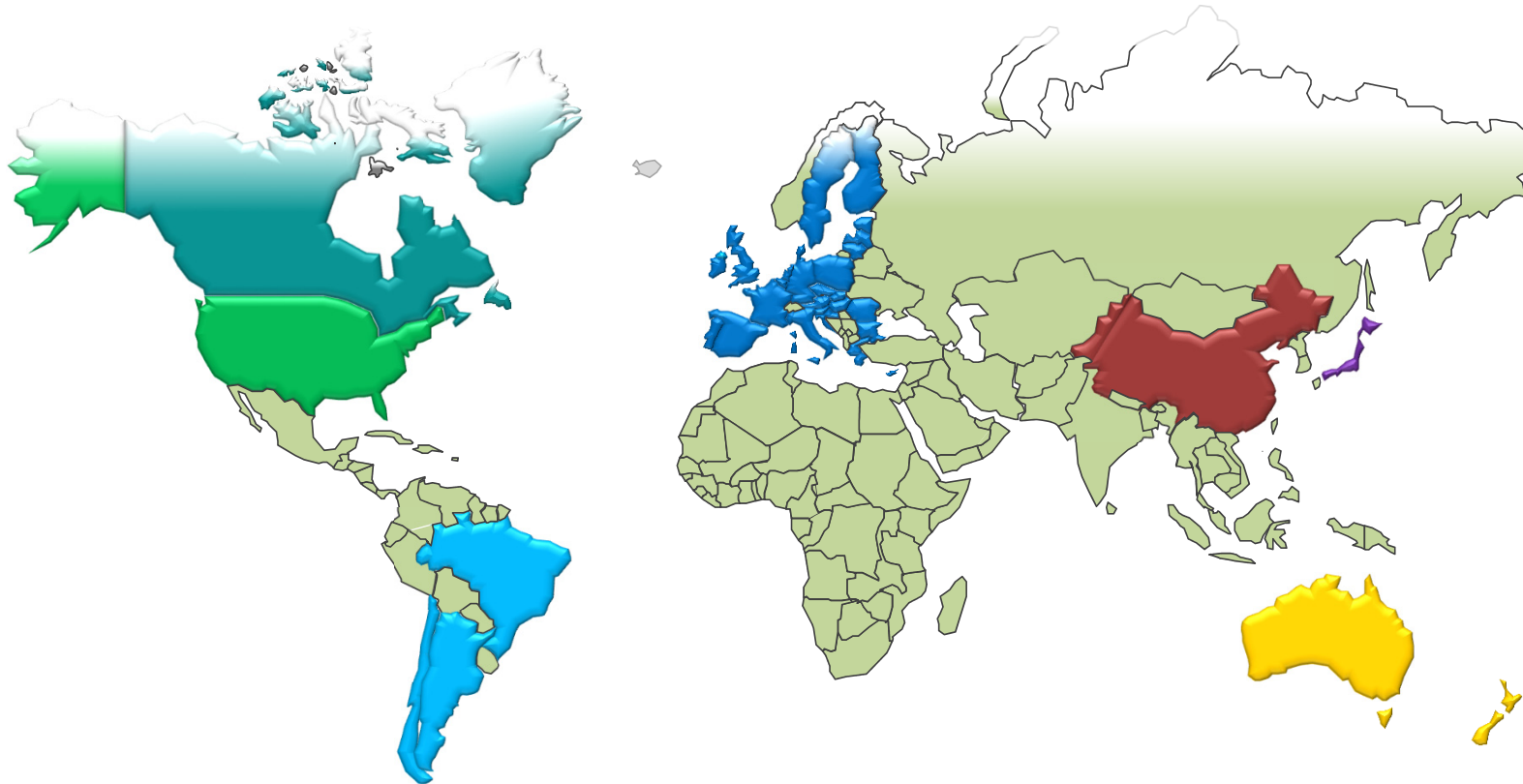


- To accelerate breeding using Cibus' *RTDS*, requires expertise in:
 - What to edit?
 - How to edit?
 - Plant cell culture
- This process can leverage diversity that has only occurred infrequently in nature or perhaps has not been recognized or selected by breeders.
- This diversity to be made in the best genetic package for a particular geography.

Regulatory Overview

Global Regulatory Approach

- Regulatory authorities around the world are adapting their regulations for Plant Breeding Innovation including *RTDS*[™]
- With products available, Cibus is often among the first to meet with authorities to describe the technologies and products





Thank you!

More information about *RTDS* and
the Cibus Team are presented at www.cibus.com

*Cibus*TM

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