Current and future market applications of new genomic techniques (NGTs)

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Joint Research Centre (JRC)

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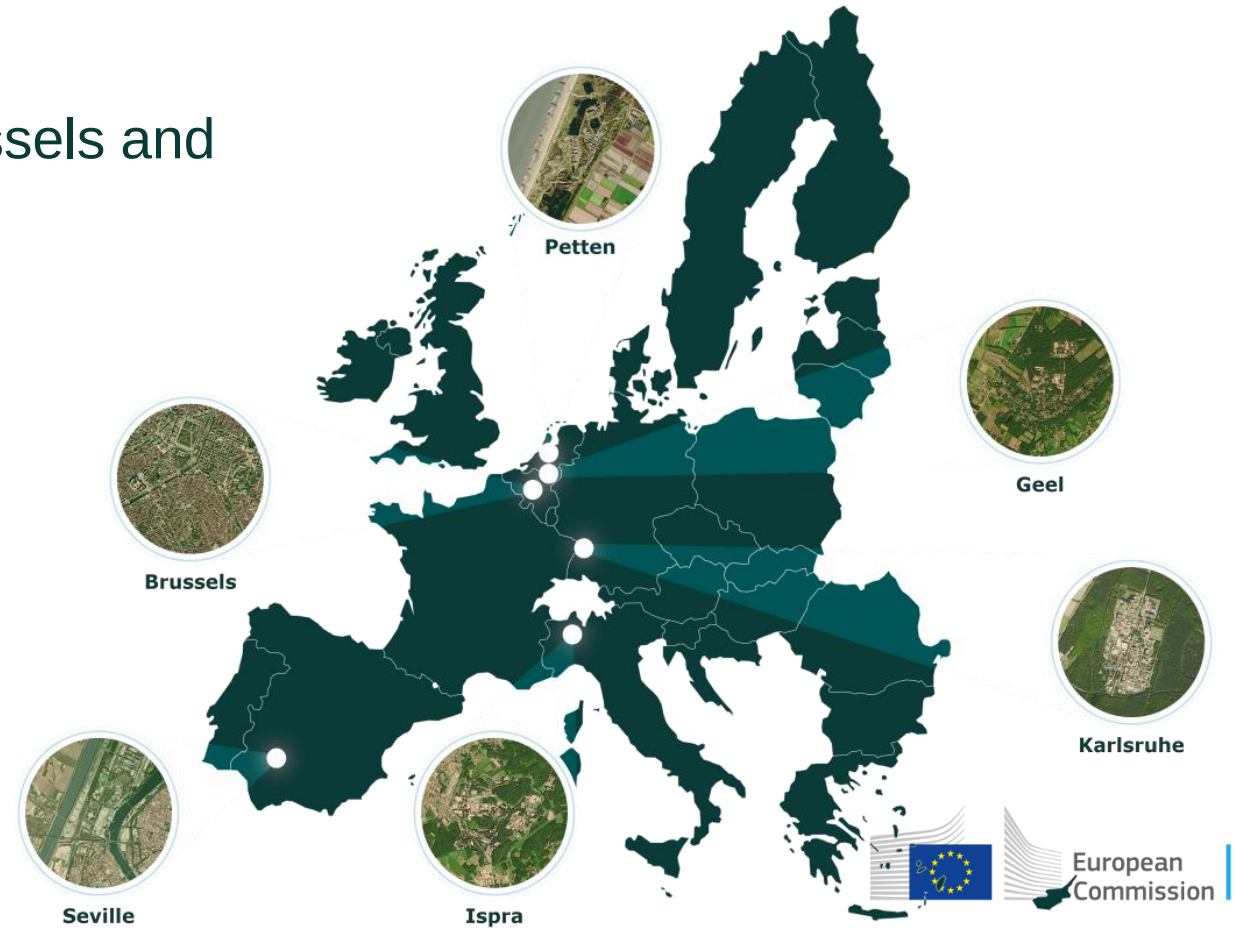
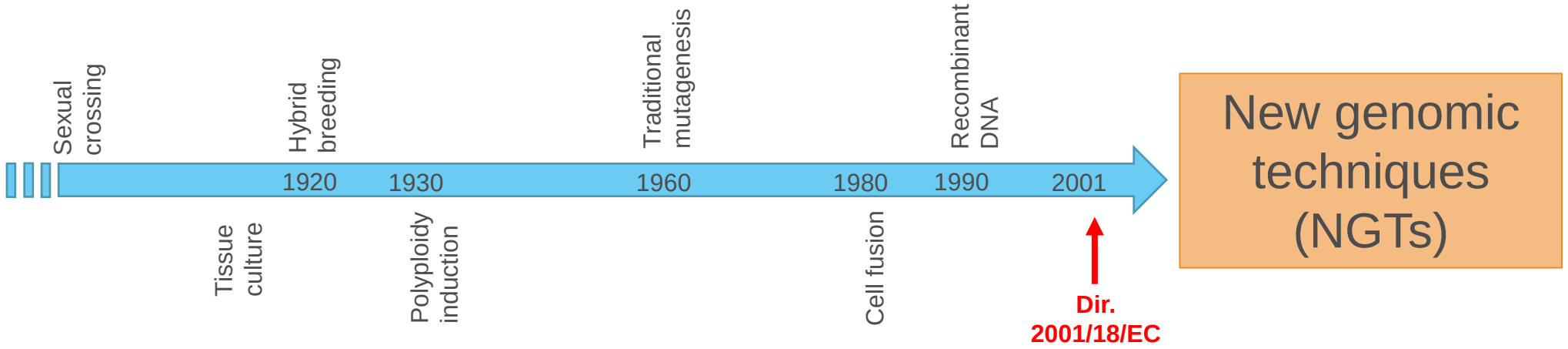


New Genomic Techniques

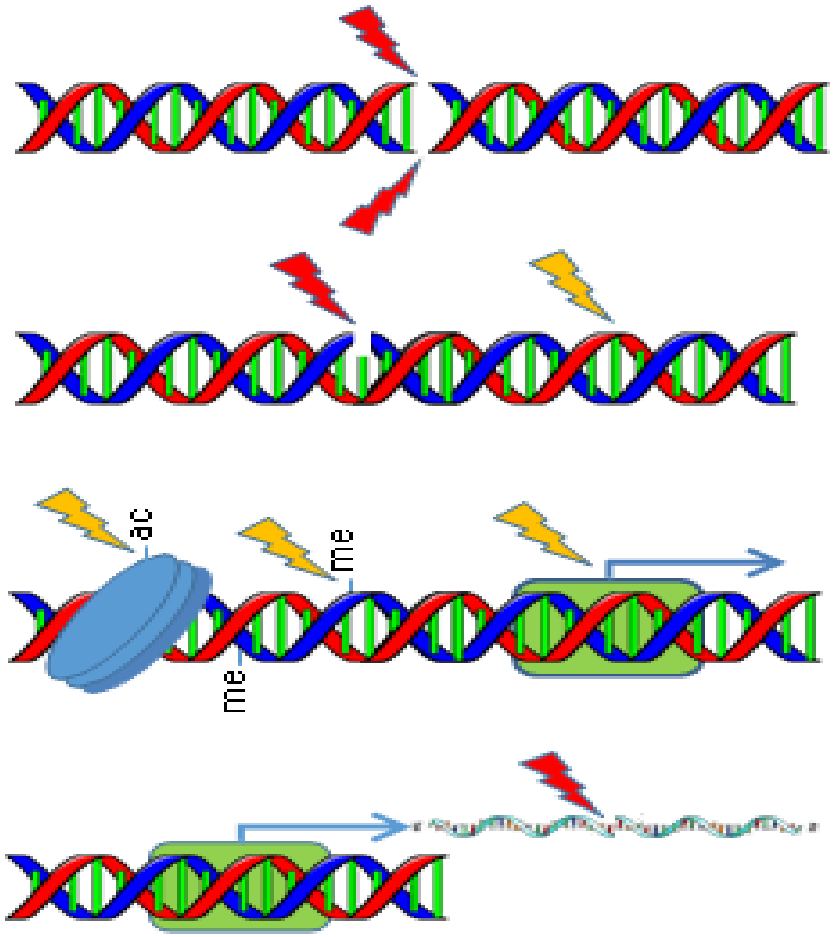


- NGTs = techniques which are capable to alter the genetic material of an organism, developed after the publication of Directive 2001/18/EC

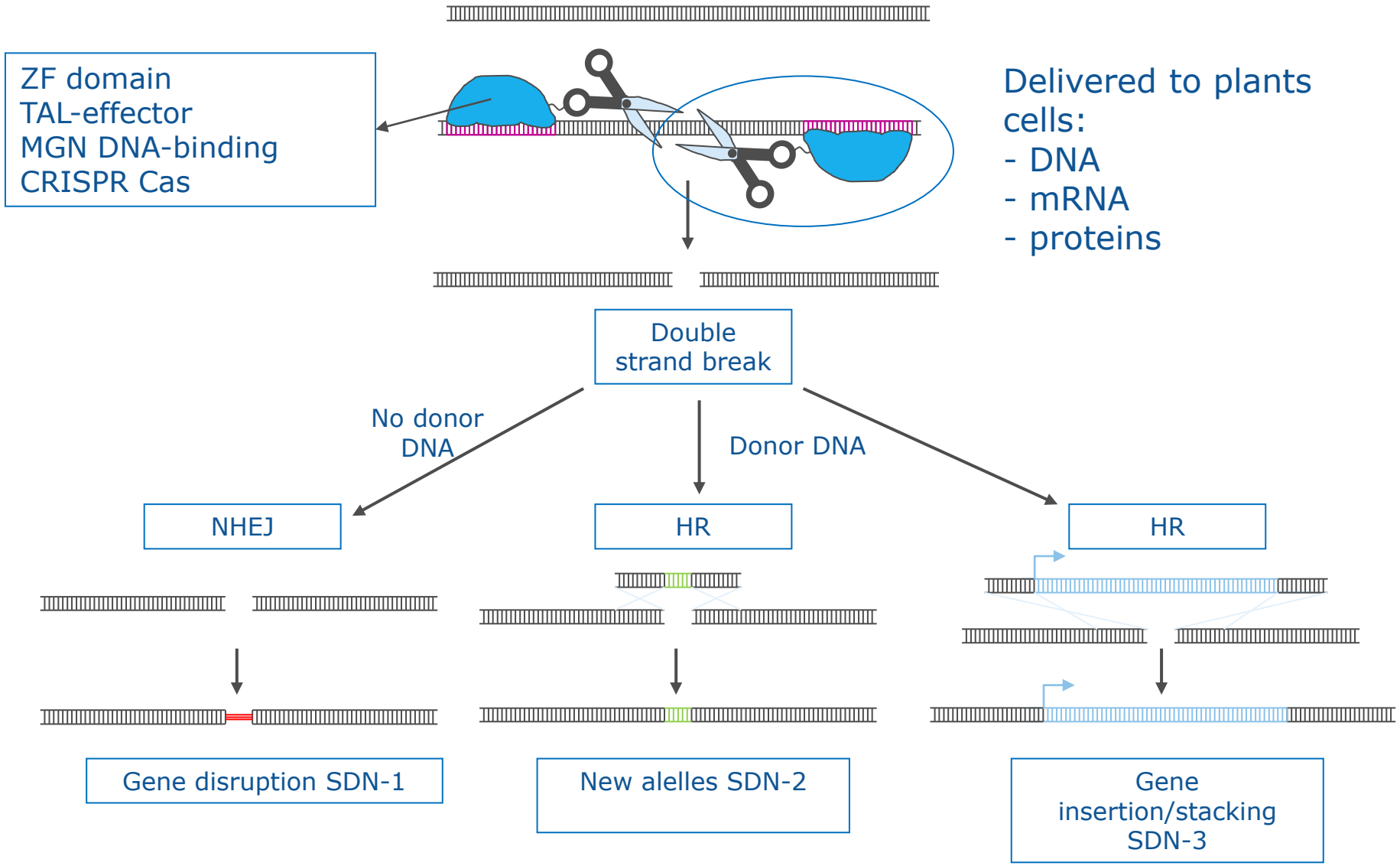
Background

- **July 2018**, the Court of Justice of the European Union (CJEU) clarified that organisms from new mutagenesis techniques fall within the scope of the EU GMO legislation.
- **November 2019**, The EU Council requested the Commission to submit, by 30 April 2021, a study on the status of NGTs.
- The **JRC** was requested to provide, as part of the study, “An overview of current and future scientific and technological developments in New Genomic Techniques as well as of new products that are, or are expected to be marketed”.
- **April 2021** European Commission study published including JRC Reports
- **September 2021** launching of EC initiative that will propose a legal framework for plants obtained by targeted mutagenesis and cisgenesis

Classification of NGTs (Broothaerts el al. 2021, JRC121847)



- **Group 1: Genome editing involving a DNA double-strand break**
- **Group 2: Genome editing without DNA double-strand break**
- Group 3: Editing of the epigenome
- Group 4: Site-directed RNA editing



European Commission

JRC SCIENCE FOR POLICY REPORT

Current and future market applications of new genomic techniques

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2021

European Commission

Scope

Sectors:

- Agriculture
- Bio-based industry
- Medical

Organisms:

- Plants (& mushrooms)
- Animals
- Microorganisms
- Human cells

Uses of NGTs:

Within the scope:

- Product/variety development (traits)
- Use as breeding tool (e.g. reproductive characteristics)

Outside the scope:

- Technology development (e.g. new/improved genome editing tools)
- Gene discovery research

Market applications review - Methodology

NGT APPLICATIONS DATABASE

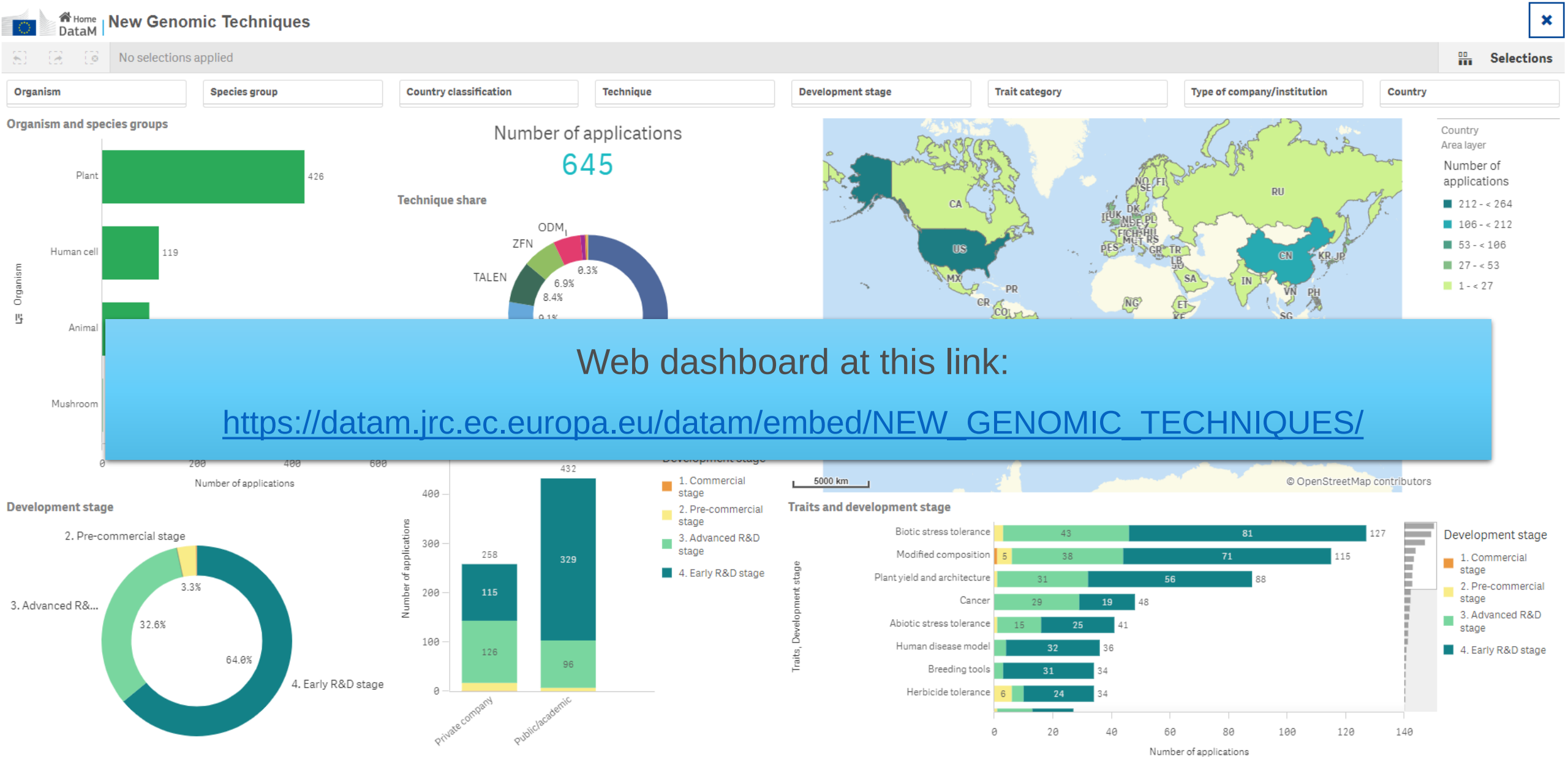
- Screening of public authorities' databases of different countries
- Search in scientific literature and datasets, including clinical trials databases worldwide
- Identification of companies/institutions developing NGT products and screening of their websites and press releases
- Expert consultation: More than 20 videoconferences with regulators and public/private technology providers from several countries worldwide
- Survey of public and private technology developers: 47 organisations participated (37 private companies and 10 public/academic organisations)
- Integration and cleaning of the data from different sources in the database

Market applications review - Methodology

The NGT applications identified were classified, using the information available, as being at the following development stages:

1. Commercial stage	NGT applications currently marketed in at least one country worldwide
2. Pre-commercial stage	NGT applications ready to be commercialised in at least one country worldwide but not yet on the market
3. Advanced R&D stage	NGT applications at a late stage of development and likely to reach the market in the medium term
4. Early R&D stage	NGT applications at proof of concept stage (i.e., testing gene targets for trait enhancement of commercial interest).

Results : web dashboard



Web dashboard at this link:

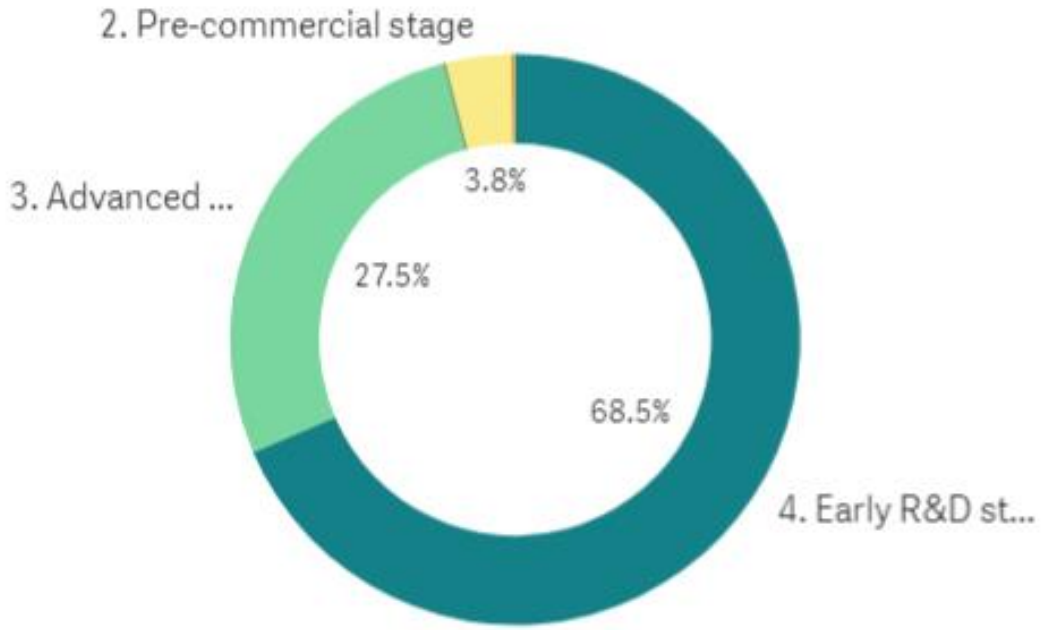
https://datam.jrc.ec.europa.eu/datam/embed/NEW_GENOMIC_TECHNIQUES/

Plants in the NGT database

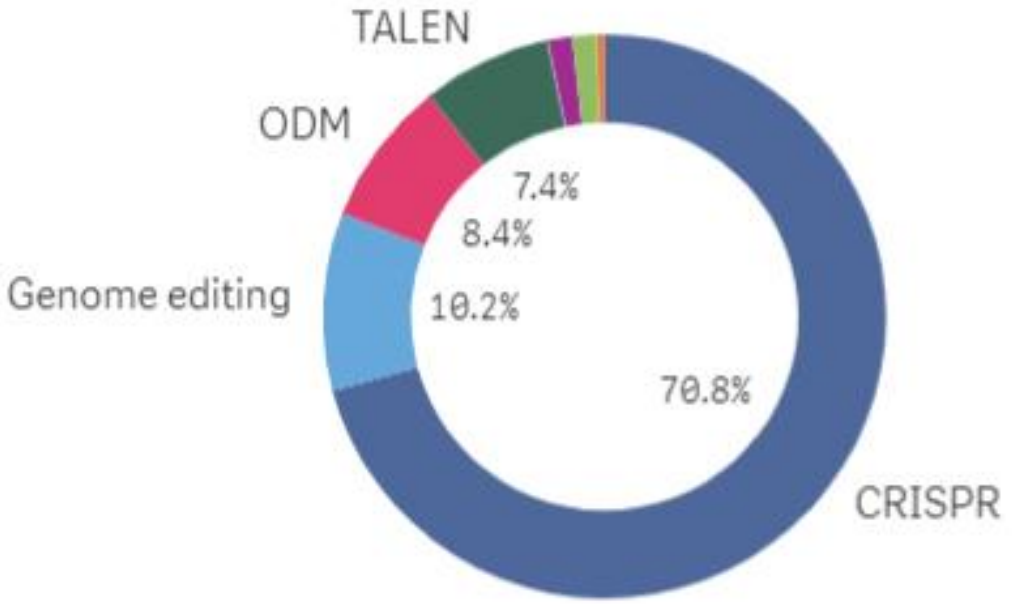
Number of applications

426

Development stage



Technique share



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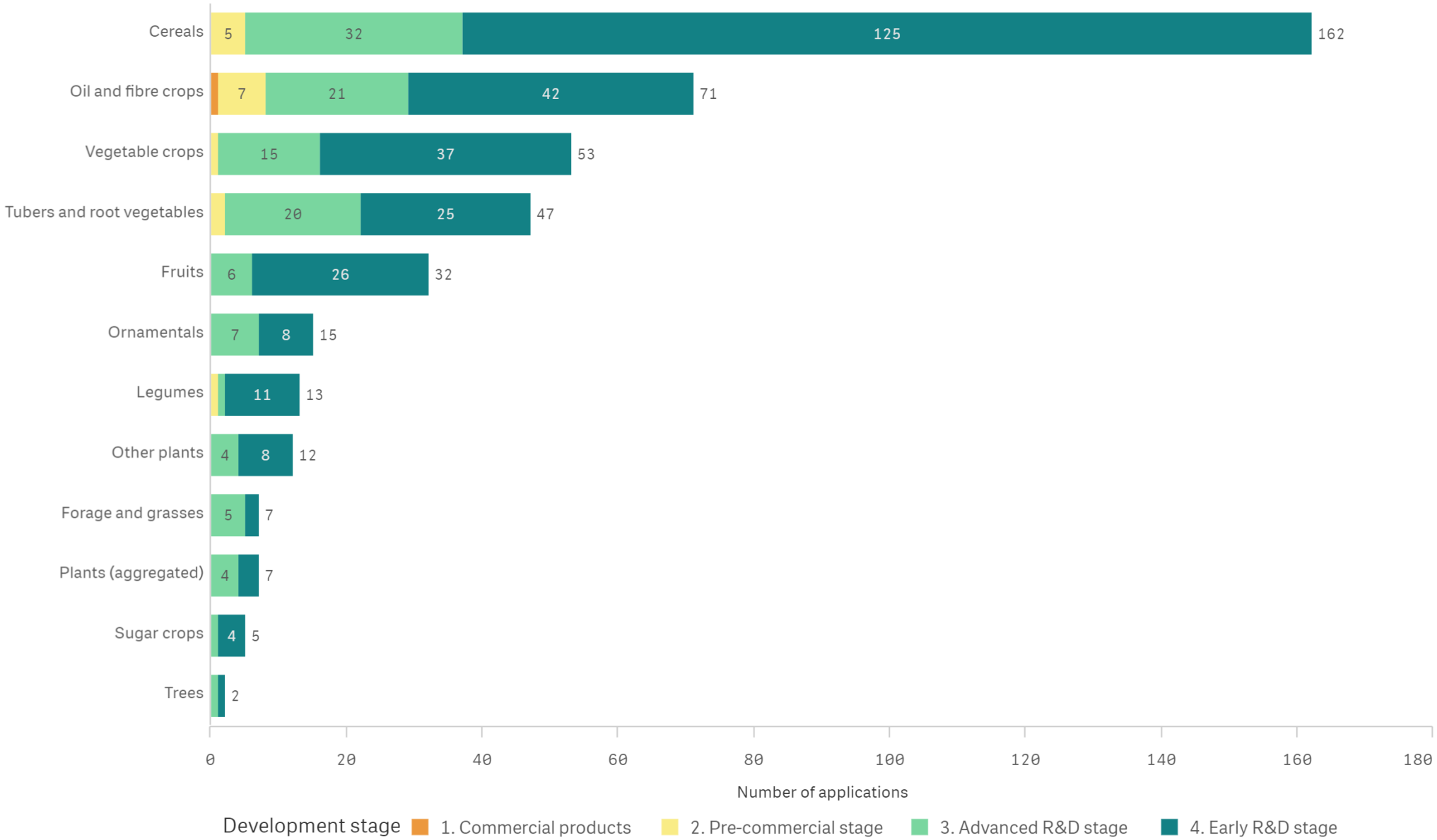
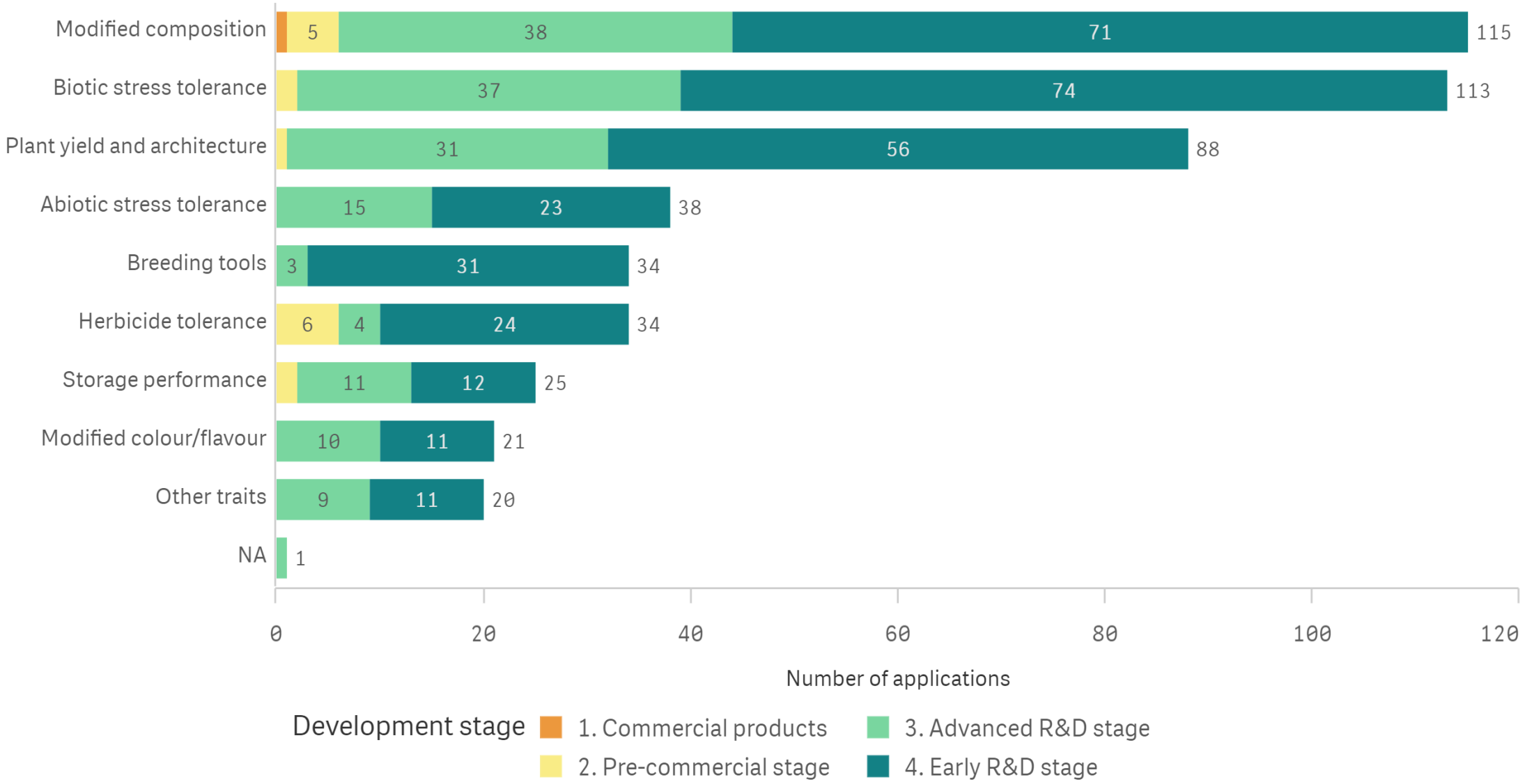
NGTs -Plants –breakdown by crop groups



NGT -plants – breakdown by traits



Modified composition

- Consumers health & consumers convenience

SOYBEAN- High Oleic Calyno

Stage: COMMERCIAL

Technique: TALEN

Trait: High Oleic (Calyno oil)

Developer: Calyxt (US)

TOMATO- Enhanced GABA (“Sicilian rouge”)

Stage: COMMERCIAL

Technique: CRISPR

Trait: high GABA content (low blood pressure association)

Developer: Sanatech (Japan)

B. Juncea greens- low pungency/low bitterness

Stage: field trials

Technique: CRISPR-SDN1

Trait: eliminate bitterness from nutrient rich species in "orphan crop"(new salads)

Developer: Pairwise (USA)

WHEAT- safe gluten for coeliacs

Stage: greenhouse trials

Technique: CRISPR-SDN1

Trait: alfa-gliadin family, reduced alfa-gliadin production

Developer: CSIC (Spain), WUR (NL)

	Celiac Disease (CD)	Wheat allergies (WA)	NCWS
Prevalence	0.2 – 2.4%	0.2 – 2.1%	0.6 – 13%

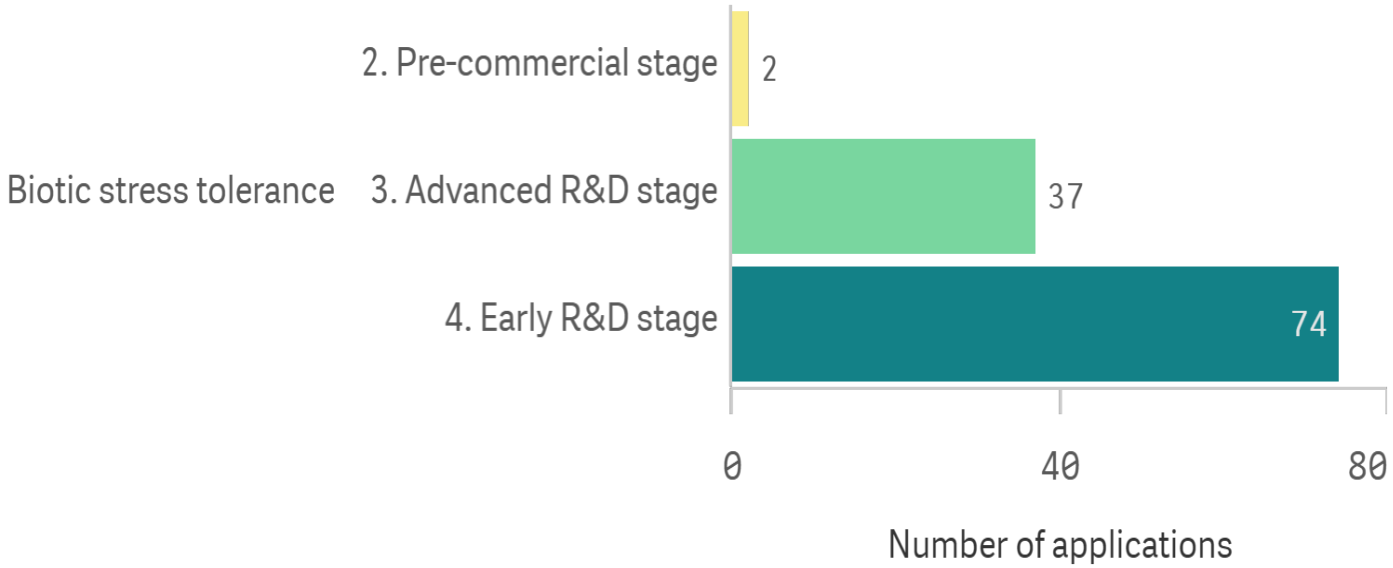
Pest and disease resistance

Resistance to pests and diseases

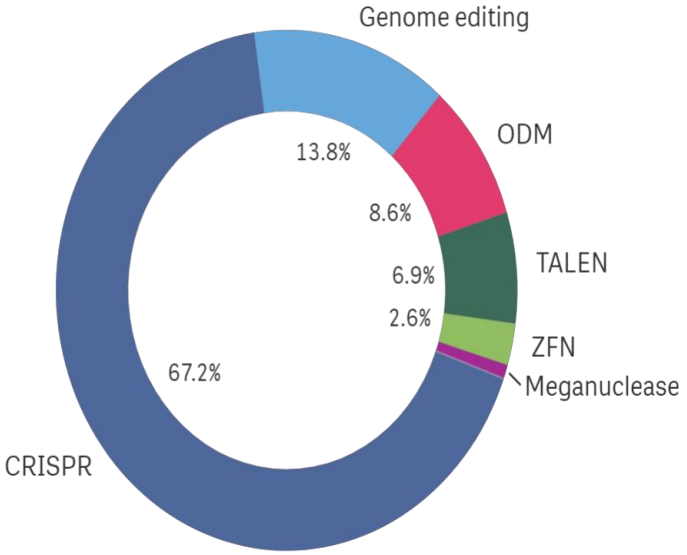
Number of applications

113

Traits and development stage



Technique share



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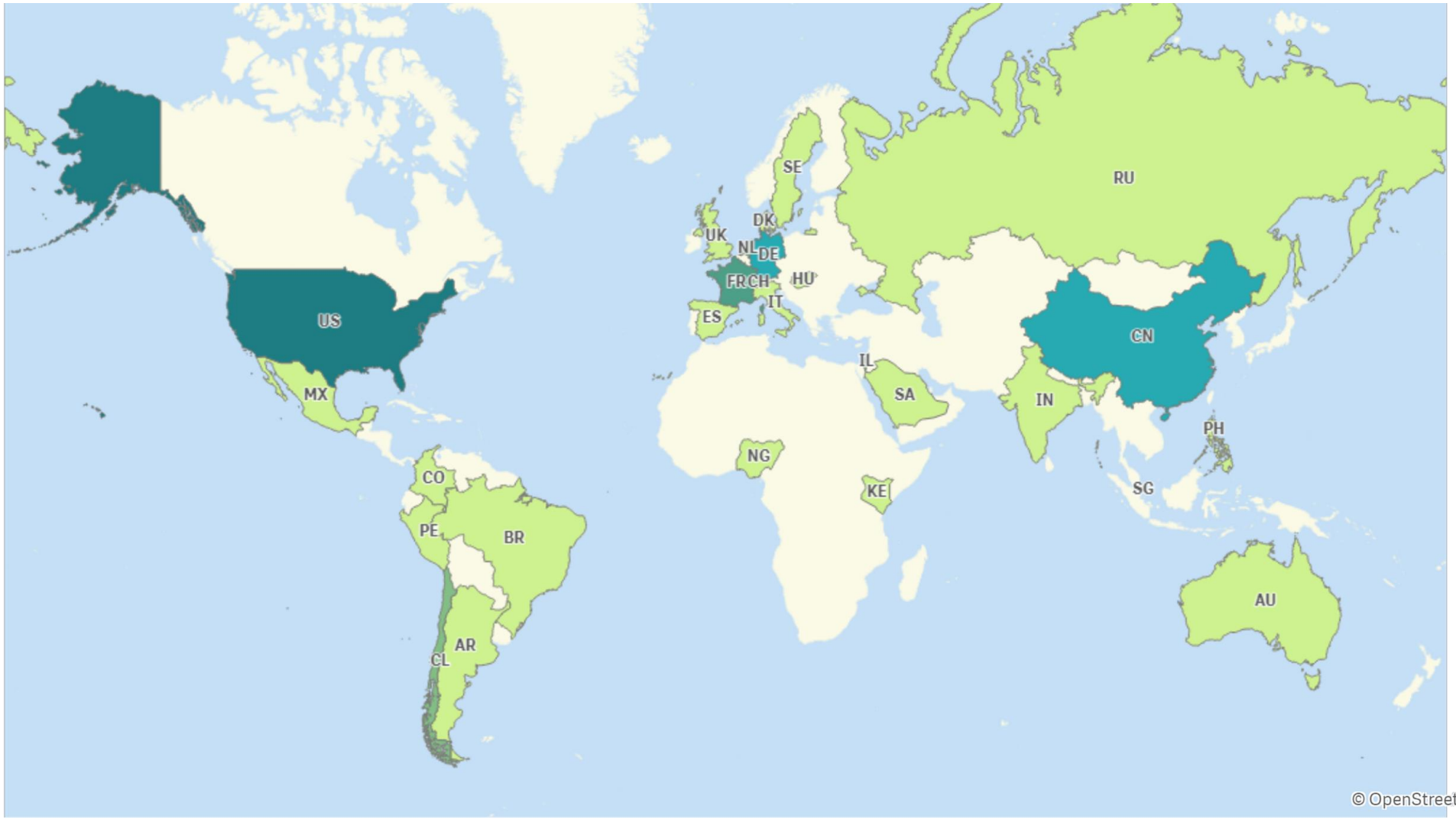

Country
Area layer

Number of applications

- 26 - < 32
- 13 - < 26
- 7 - < 13
- 4 - < 7
- 1 - < 4

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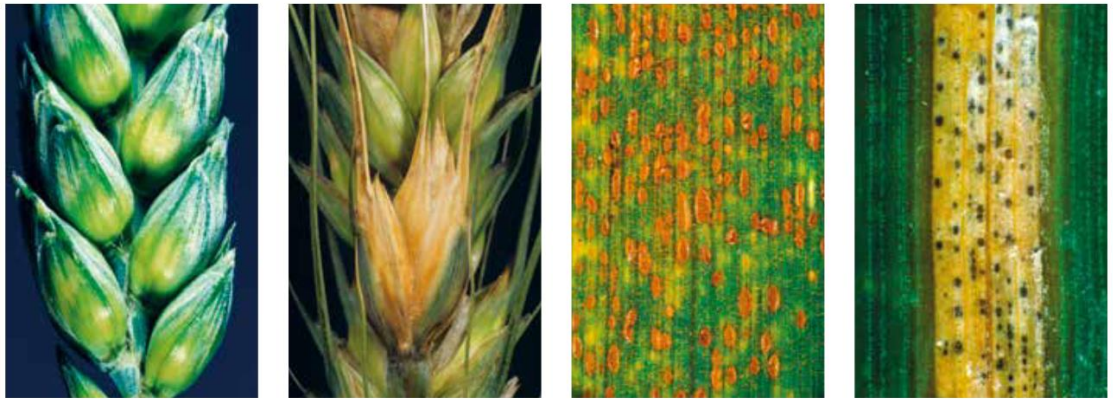
WHEAT- broad and wide fungal R (PILTON)

Establishing multiple and durable fungal disease tolerance in wheat through the latest breeding methods



Stage: close to field trials

Technique: CRISPR SDN1

Traits: KO repressors of natural defense reaction in wheat (rust, Septoria, Fusarium)

Developer: BDP Consortium of DE breeding companies

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WHEAT – powdery mildew-China

Article

Genome-edited powdery mildew resistance in wheat without growth penalties

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Check for updates

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Disruption of susceptibility (*S*) genes in crops is an attractive breeding strategy for conferring disease resistance[1,2]. However, *S* genes are implicated in many essential biological functions and deletion of these genes typically results in undesired pleiotropic effects[1]. Loss-of-function mutations in one such *S* gene, *Mildew resistance locus O* (*MLO*), confers durable and broad-spectrum resistance to powdery mildew in various plant species[2,3]. However, *mlo*-associated resistance is also accompanied by growth penalties and yield losses[3,4], thereby limiting its widespread use in agriculture

CGIAR gene editing plants/animals – developing countries

Research centre	Species	Trait category	SDN type (1, 2, 3)	Development stage
IITA	Banana	Biotic stress tolerance	SDN1	4. Early R & D stage
IITA	Banana	Biotic stress tolerance	SDN1	4. Early R & D stage
IITA	Banana	Biotic stress tolerance	SDN1	4. Early R & D stage
CIAT	Beans	Modified composition	SDN1, SDN2	4. Early R & D stage
CIAT	Cacao	Modified composition	SDN1, SDN2	4. Early R & D stage
CIAT	Cassava	Haploid techniques	SDN1, SDN2	4. Early R & D stage
ICARDA	Chickpea	Abiotic stress tolerance	SDN1	4. Early R & D stage
ICRISAT	Chickpea	Modified composition; plant yield and architecture	SDN1, SDN2	4. Early R & D stage
CIMMYT	Maize	Biotic stress tolerance	SDN1, SDN2	3. Advanced R & D stage
CIMMYT	Maize	Biotic stress tolerance	SDN1	3. Advanced R & D stage
ICRISAT	Millet	Storage performance	SDN1, SDN2	4. Early R & D stage
ICRISAT	Pigeon pea	Reproductive/flowering characteristics	SDN1, SDN2	4. Early R & D stage
CIP	Potato	Biotic stress tolerance	SDN1, SDN2	4. Early R & D stage
CIAT	Rice	Biotic stress tolerance	SDN1, SDN2	3. Advanced R & D stage
CIAT	Rice	Plant yield and architecture	SDN1, SDN2	4. Early R & D stage
IRRI	Rice	Plant yield and architecture	SDN1	4. Early R & D stage
IRRI	Rice	Modified composition	SDN1, SDN2, SDN3	4. Early R & D stage
IRRI	Rice	Reproductive/flowering characteristics	SDN2	4. Early R & D stage
IRRI	Rice	Biotic stress tolerance	SDN1	4. Early R & D stage
ICRISAT	Sorghum	Biotic stress tolerance	SDN1, SDN2	4. Early R & D stage
CIMMYT	Wheat	Biotic stress tolerance	SDN1	4. Early R & D stage
CIMMYT	Wheat	Biotic stress tolerance	SDN1	4. Early R & D stage
ILRI	Cattle	Biotic stress tolerance	SDN3	4. Early R & D stage

MAIZE – Lethal Necrosis viruses- Africa

- Photo Green Venus
- Photo Green Venus

Stage: field trials

Technique: SDN1

Traits: editing African-adapted parental lines to mimic R genes identified in tolerant germplasm

Developer: CYMMIT

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Plant yield

SUGARCANE – Flex I Flex II

- Photo Hugo Molinari (EMBRAPA)

Stage: field trials

Technique: CRISPR

Traits easier digestibility of cell walls (ethanol) and higher yield in sugars

Developer: EMBRAPA Brazil

Improved storage

LETTUCE- non-browning

- Photo Green Venus

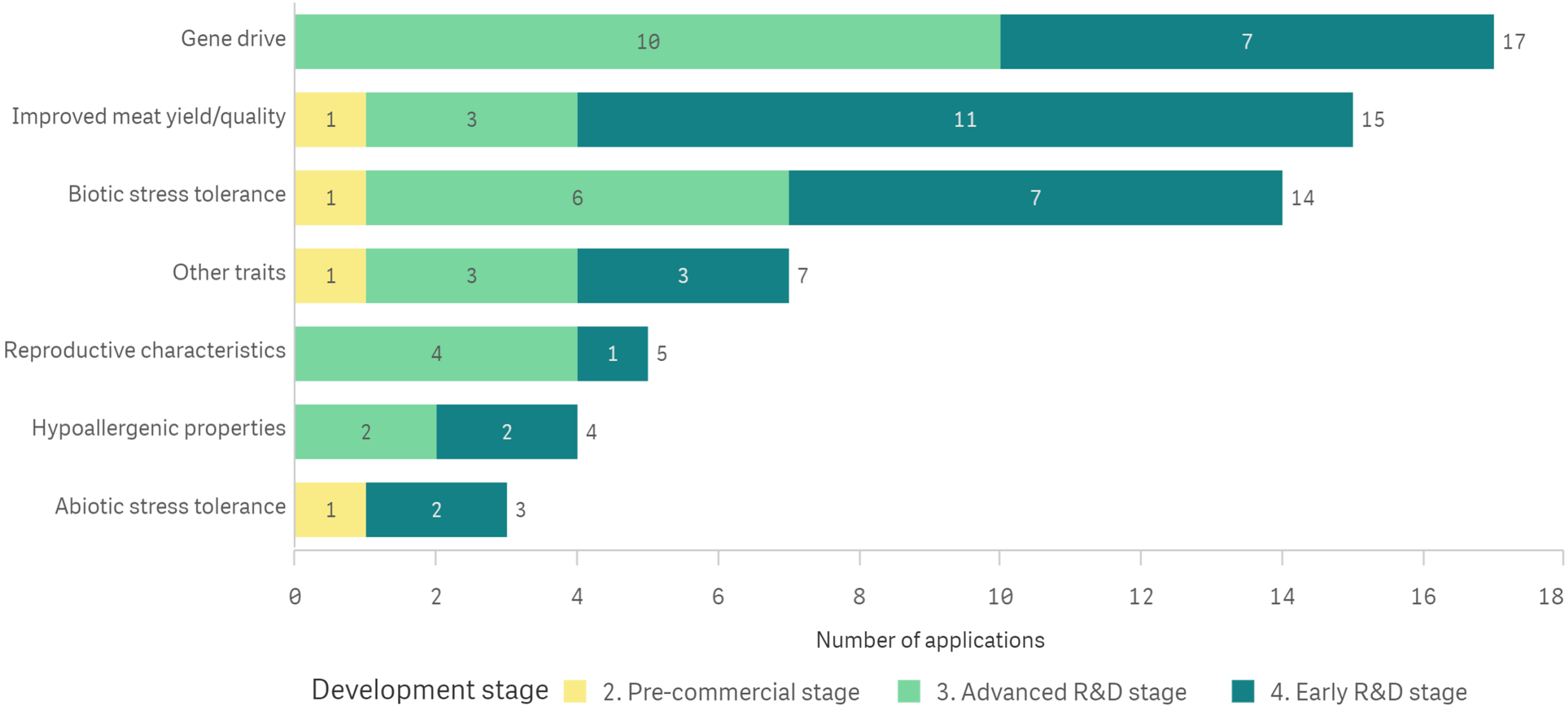
Stage: field trials

Technique: SDN1

Traits: longer storage

Developer: GREEN VENUS (USA)

NGT- Animals- Traits under development



Red Sea Bream (Madai)

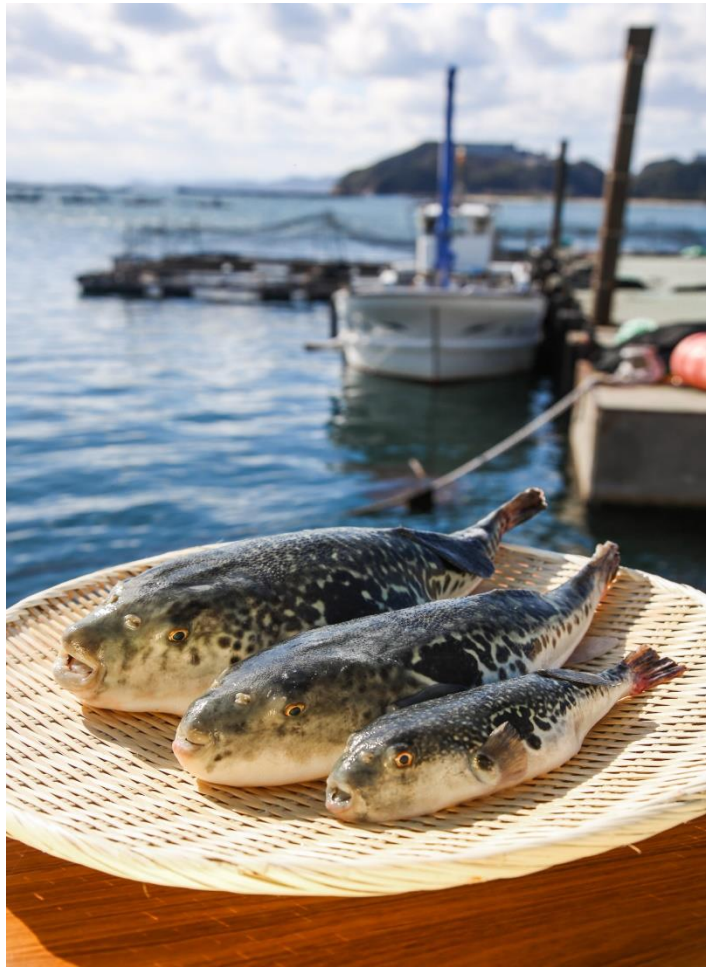
Stage: COMMERCIAL

Technique: CRISPR

Trait: higher flesh/muscle (up to 20%), more feed efficiency (up 14%)

Developer: Regional Fish Institute (start-up) (Kyoto) + Univ. of Kyoto + Kindai University

Tiger pufferfish (Torafugu)



Stage: COMMERCIAL

Technique: CRISPR K.O leptin receptors

Trait: higher flesh/muscle (up to 1.9 times)

Developer: Regional Fish (Kyoto) + Univ. of Kyoto + Kindai University

NGT- microorganisms for contained use

- NGTs are already applied commercially in microorganisms for the bio-production of industrial molecules and the R&D pipeline is active
- Technology developers continuously use genetic techniques (including both established and new) to improve microbial strains
- NGTs (CRISPR) are becoming standard tools in some cases
- NGTs are mainly used to knock out unfavourable genes (e.g. toxins, intrinsic antibiotic resistance or by-products)
- It is difficult to estimate the current share of microorganism strains used by bio-industry worldwide that have been improved with NGTs.
- Sectors: biofuels, bio-based enzyme production…

NGT microorganisms for deliberate release Klebsiella-N fixing-corn specific

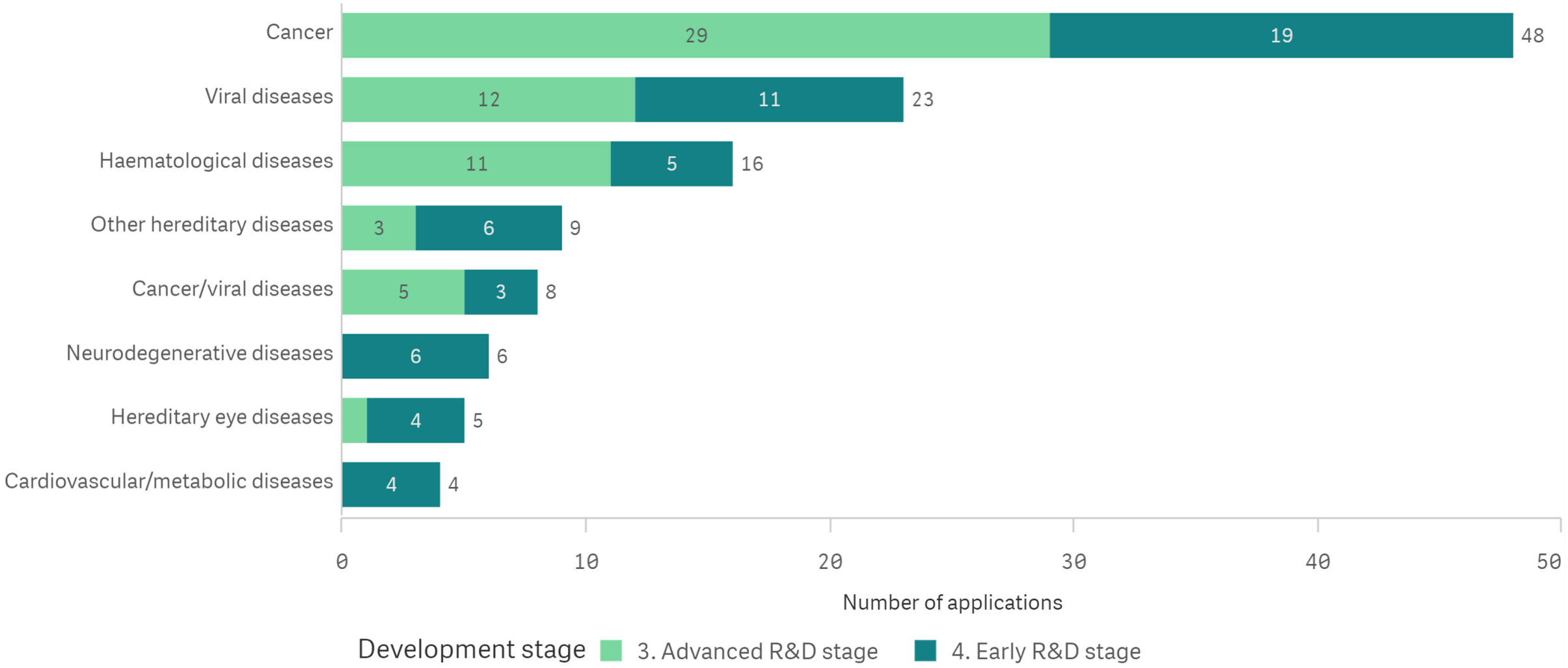
Stage: COMMERCIAL

Technique: Gene editing, synthetic biology

Trait: sup: Nitrogen-fixing-bacteria associated to maize/sorghum seeds

Developer: Pivot Bio (US)

Results in human health applications - conditions



Conclusions I

- NGTs Group I (mainly CRISPR) are actively and increasingly used in agri-food, industrial and medicinal applications (over 600 items identified)
- NGTs Group I used in >90% of cases
- Few applications are marketed worldwide (two crop plants, two fish, one microorganism for release and microorganisms for contained production of industrial molecules)
- Plants the largest pipeline (>400), composition and resistance to pests and diseases the largest pipelines

Conclusions II

- NGT now incorporated in toolkit for improving strains of microorganisms for contained use commercial (biofuels/enzymes).
- NGT microorganisms for release on agricultural soil commercial (N fixation) Pipeline active
- NGTs actively used to tackle several human diseases, and many applications have already reached patients (phase I and phase I/II clinical trials).
- United States and China are the most frequent countries of origin, particularly in the stages closest to market. The EU, particularly Germany and France, is also active in the use of NGTs. Several developing countries very active, mostly in the agricultural sector.
- Private and public sector both source of applications

Thank you

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