EuropaBio
The European Association for Bioindustries

Genome-Edited Products and Projects: Resources and Examples

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This is a non-exhaustive list of over 200 genome-editing or viral vector related products and research projects, drawn from various resources and covering healthcare, industrial and agricultural biotech. Some of the sources include products from techniques other than genome editing. It is noteworthy that viral vectors modified through new genomic techniques for pharmaceutical applications are usually incapable of replicating in the environment, and therefore do not pose any environmental risks.

Contents

1. Sources with examples of various applications

1.1 US regulator's database 'Am I regulated'? 43 "NGT" applications, mostly plants, some micro-organisms

https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated/Regulated_Article_Letters_of_Inquiry

As of 6 May 2020, a total of 93 Letters of Inquiry have been published by USDA replying to product developers inquiring whether their biotech applications are regulated as "GMOs" under USDA's current regulations. In the vast majority of cases, the reply by APHIS was 'No'. Please note: the majority of these letters (50 of 93) **do not involve** organisms developed using New Genomic techniques (e.g., genome editing, cisgenesis, intragenesis). Those products not developed using NGTs are excluded from analysis here. Some of these letters date back to 2011. It is not clear how many of these **43 NGT-derived organisms** that USDA has provided an opinion on are close to commercialisation. Some of them are likely not intended for commercialisation.

- **Many species**: All are plants and one mushroom. Just 34% concern one four large area crops (maize, soya, wheat, rice). The biggest group are cresses, fruit & vegetables.

- **Mainly medium companies & public research**: Only 12% of the developers are multinationals.
- **Many and varied traits:** including product quality, stress or disease tolerance. Herbicide tolerance is the rarest.

(See annex for more detailed breakdown)

1.2 EuropaBio's What if examples

https://www.europabio.org/cross-sector/publications/genome-editing-%E2%80%94-what-if-we-embraced-its-potential

11 applications: 4 healthcare, 3 plant, 3 industrial biotech & 1 animal factsheet (listed individually under the relevant sections below)

1.3 Innovature Website

https://innovature.com/

BIO and ASTA website, organised into 3 sections exploring the potential of gene-editing for our planet, our health, and our food, with about 15 concrete examples and many more conceptual examples (e.g. many examples of organisms, both plants and animals, whose genomes have been sequenced paving the way for identification of interesting genes. This could one day lead to interesting projects in these organisms.)

1.4 **Gene editing regulation tracker** hosted by Genetic Literacy Project

https://crispr-gene-editing-regs-tracker.geneticliteracyproject.org/

This tracker informs and compares regulatory approaches in different countries/regions for human health (distinguishing between therapeutic/stem cell and germline/embryonic), gene drives, and agriculture (distinguishing between crops/food and animals).

2. Industrial Biotech

- 3 EuropaBio industrial biotech factsheets (algae to make biofuel, enzymes to produce hydrogen peroxide without petroleum, wood into food preservatives)
- Shaping CRISPR scissors for gene editing in yeast. Research Project Wageningen
- 2 examples from Innovature (jet fuel from gene-edited pennycress, soil fertilizing microbes)
- Olefine, EU-funded research project to develop safely produced and affordable insect pheromones as an alternative to conventional insecticides
- iFermenter, EU-funded research project aiming to use biotechnology to convert forestry residual sugar streams to antimicrobial proteins by intelligent fermentation
- Genome editing for microbial protein : Microbial protein has the potential to become a sustainable, healthy, and nutritious alternative to meat and plant proteins. Genetic modification can be used to tailor the amino acid and taste profiles to serve the demands of different food applications or to eliminate potential antibiotic resistance genes.

3. Healthcare biotech

- 4 EuropaBio healthcare factsheets (targeted cancer treatments, Childhood blindness, sick blood cells, AIDS)
- Characterization of virulence genes in Streptococcus, Research Project Wageningen
- Adaptive Immunity in Prokaryotes, Research Project Wageningen

3.1 14 examples in the Gene editing regulation tracker hosted by Genetic Literacy Project:

- Liver disease - a stem cell treatment for severe liver disease was introduced in 2019 with a clinical trial to be conducted across eight European countries.
- Cancer vaccine - in 2019, researchers in Germany tested an RNA-based vaccine for patients with melanoma.
- Wiskott-Aldrich syndrome - in 2019, researchers from France and England successfully treated a rare genetic disease that causes bleeding, severe and recurrent infections, severe eczema and in some patients autoimmune reactions and the development of cancer.
- Blood disorder - gene therapy to treat beta thalassemia that reduces a patient's ability to produce hemoglobin, the protein in red blood cells that contains iron, leading to life-threatening anemia. Approved in 2019.
- Fatal muscle disease - clinical trials ongoing for gene therapy for a muscle disease in which patients typically survive only into early childhood.
- Rare form of blindness - congenital (present at birth) blindness usually caused by inherited eye diseases,
- Lymphoma - gene therapy to treat large B cell lymphoma, approved in 2018.
- Crohn's disease symptoms - A cell therapy used to treat specific severe symptoms of Crohn's disease, approved in 2018.
- Leukemia - gene therapy for patients with B cell lymphoblastic leukemia, approved in 2018.
- Vein disease - gene therapy to treat a disorder in which the small veins of the liver become obstructed, in patients who have received a bone marrow transplant, Approved in 2017.
- "Bubble boy" disease – treatment for ADA Severe Combined Immune Deficiency, a disease in children that causes them to be extremely susceptible to infections, approved in 2016.
- Eye damage – the first stem cell therapy was approved in Europe in 2015 to treat physical or chemical burns to the eye.
- Melanoma - a genetically engineered virus used to treat inoperable melanoma, conditionally approved in Europe in 2015.
- Inability to digest fats - approved in Europe in 2012 to treat lipoprotein lipase deficiency, a rare disease that leaves individuals unable to digest fats and can cause life-threatening pancreatitis.

- EU funded research: DG RTD regularly publishes success stories from EU-funded projects in biotech, specifically in health.

3.2 Other examples:

Research is currently underway on clinical applications of genome editing technologies to treat the following genetic disorders:

- Amyloidosis (abnormal proteins build up in organs, such as the heart, kidneys, liver, and can lead to their failure). and
- Clinical trials for sickle cell disease (red blood cells taking a crescent shape causing anaemia and jaundice) are ongoing.
- Haemophilia (inherited bleeding disorder where the blood does not clot properly) treatments are currently under development.
- Lysosomal storage disorders (abnormal build-up of toxic materials in cells as a result of enzyme deficiencies affecting e.g. the skeleton, brain, skin, heart, and central nervous system).
- Progress is being made on gene therapies for cystic fibrosis (the production of thick and sticky mucus, sweat or digestive juices which damages the lungs, digestive system and other organs).
- In addition, significant progress in therapeutic genome editing has been demonstrated in cancer and infectious diseases, such as HIV and Hepatitis.

3.3 EU-funded projects on CRISPR applications in healthcare, retrieved in mid-2019
The EU appears to have invested close to 200 million EUR in these projects as of mid-2019 in the 148 projects below.

Nr.	EU-funded project name	EU investment (€)	Nr.	EU-funded project name	EU investment (€)
1	Uncovering viral sabotage of host CRISPR-Cas immune systems	177.598	**75**	TRACT	2.877.077
2	Identification and Characterization of Host and Phage Proteins Interacting with the CRISPR System	100.000	**76**	CleverGenes	2.437.500
3	Prokaryotic Evolution of CRISPR Targeting	221.606	**77**	INTEGHER	1.810.747
4	PHAGECOM	183.454	**78**	ENHANCEME	161.969
5	Prokaryotic Evolution of CRISPR Targeting	221.606	**79**	OPTOLOCO	183.470
6	CRISPR-EVOL	2.495.625	**80**	LincRNA	183.470
7	CRISPAIR	1.499.763	**81**	NACHO	185.857
8	EcCRISPR	1.499.000	**82**	ACMO	2.439.996
9	REMEMBER	1.499.184	**83**	relieve-IMDs	1.500.000
10	THALAMOSS	5.020.000	**84**	editCRC	2.499.405
11	CRISPR-GQ	88.799	**85**	DUNHARROW	375.806
12	EARN	100.000	**86**	TransposonsReprogram	1.499.055
13	COHESIN CONTROL	2.421.212	**87**	FIGHT-CANCER	1.998.000
14	DIAMONDCOR	1.490.529	**88**	METLINK	173.857
15	MASTFAST	148.914	**89**	VIAR	171.461
16	IMGENE	2.068.409	**90**	Sialoglycan Array	200.195
17	SUPERSIST	5.999.997	**91**	UB-RASDisease	1.999.796
18	SYSNORM	354.112	**92**	MemCHAPS	177.599
19	EURATRANS	10.500.000	**93**	DNAProteinCrossRep	212.195
20	CVGENES-AT-TARGET	5.995.449	**94**	PathAutoBIO	200.195
21	PhageResist	2.000.000	**95**	NEMoCuRe	195.455
22	CRISS	1.372.839	**96**	UNNAMEd-2	200.195
23	PromoTeRapy	195.455	**97**	EScORIAL	1.980.434
24	ANTIVIRNA	1.467.180	**98**	INTERGLU	212.195
25	QuantFung	3.859.190	**99**	ImmunoFit	1.999.721
26	KILLINGTYPHI	183.455	**100**	iPS-ChOp-AF	1.988.750
27	eCHO Systems	4.044.794	**101**	NonChroRep	2.000.000
28	INsPiRE	2.495.050	**102**	Alpha-Synuclein	200.195
29	mTORmorS	187.420	**103**	ORGANOMICS	1.500.000
30	PlasmaCellControl	2.500.000	**104**	ANTIViR	1.499.794
31	DMD2CURE	185.076	**105**	deFIBER	1.498.544
32	UNEXPECTED	2.000.000	**106**	MALEPREG	1.499.989
33	transLEISHion	195.455	**107**	SC-EpiCode	1.500.000
34	Xchromosome	1.912.369	**108**	ELONGAN	1.480.880
35	CRISTONE	265.840	**109**	CELLNAIVETY	2.000.000
36	REACT	185.076	**110**	PD UpReg	1.999.987
37	BCSC-ST	195.455	**111**	TelMetab	2.118.431

38	PRION2020	2.500.000	**112**	MechAGE	2.500.000
39	LincRNA	183.470	**113**	Secret Surface	2.000.000
40	PLASMOESCAPE	1.815.480	**114**	SystGeneEdit	2.499.995
41	REGAIN	1.471.840	**115**	ContraNPM1AML	1.883.750
42	CHROMATINPRINCIPLES	2.495.080	**116**	GenEdiDS	2.000.000
43	EvISC	200.195	**117**	IAV-m6A	264.668
44	Cytokineproteomics	159.461	**118**	INTUMORX	1.972.905
45	HOST-SELECT	159.461	**119**	CORFEDITING	149.995
46	HemTree2.0	2.000.000	**120**	CHI-ZEF	158.122
47	3D_Tryps	1.498.175	**121**	EXO-EYE	269.858
48	HepatoRiSK	212.195	**122**	LIGER	154.721
49	MiniBRAIN	166.157	**123**	GSTHgNDD	183.455
50	SmallDrugRheuma	170.122	**124**	COLGENES	1.498.618
51	CANCER-DC	1.500.000	**125**	RetroNets	1.993.858
52	CARiPSCTcells	165.599	**126**	SPACEVAR	1.499.883
53	HD-DittoGraph	2.040.943	**127**	3D-REPAIR	1.999.750
54	DROSADAPTATION	2.392.521	**128**	reLIVE	2.571.694
55	EDPAS	158.122	**129**	MacAGE	2.499.994
56	MELANOPARK	183.455	**130**	CAVEHEART	1.499.429
57	DecipherBILU	183.455	**131**	circRTrain	3.870.807
58	MIMIC	1.057.324	**132**	HOXA9 degradome	239.861
59	Mosimann Zebrafish	100.000	**133**	CHROMTOPOLOGY	1.500.000
60	ThDEFINE	1.980.685	**134**	EpiTarget	200.195
61	HGSOC	177.599	**135**	UNICODE	1.971.846
62	NeuroRhomboid	183.455	**136**	SYNVIA	1.999.438
63	Syncrip_2014	183.455	**137**	HairGen	195.455
64	HOPE	2.484.325	**138**	EpigenomeProgramming	1.281.205
65	BRCANCER	207.584	**139**	EpiMIRgen	187.866
66	EPICut	2.196.414	**140**	INFANTLEUKEMIA	2.000.000
67	TRANSREG	1.977.148	**141**	CFS modelling	1.499.711
68	GrowCELL	2.500.000	**142**	ReachingCompleteness	1.500.000
69	ZNEOPSIN_II	183.455	**143**	SPICE	1.996.428
70	DNAmethAML	200.195	**144**	IntestineUb	195.455
71	MiRCHOL	200.195	**145**	CureCKDHeart	1.497.888
72	MeGa	195.455	**146**	IMSTREV	171.461
73	DREMATURE	187.420	**147**	LYSOSOMICS	2.362.563
74	Repro_organoid	171.461	**148**	HRMECH	1.999.014
Total Crispr-related EU investments: **196.603.910 EUR in 148 projects**					

4. Agricultural biotech, including plants and mushrooms

4.1 Products on the market

Innovator	Product	Status	Technology	Info resources
Calyxt	Soybean Calyno™ High Oleic Soybean Oil	Closed loop cultivation USA	TALEN	Calyxt PR, AgProfessional, The Scientist

4.2 US regulator's database 'Am I regulated?

93 plant applications, of which 43 developed using NGTs – see section 1.1 and annex

4.3 National Geographic: Why gene editing is the next food revolution

https://www.nationalgeographic.com/environment/future-of-food/food-technology-gene-editing/

9 plant applications

Virus resistant cocoa, fungus-resistant banana (virus / fungus threatens a large part of the world's cocoa - banana plantations), grapevines protected against mildew (mold), coffee beans without caffeine, higher yielding rice, enhanced flavor tomatoes, drought-tolerant maize, non-browning mushroom, gluten-free wheat.

Biotech Now expands more on these same examples.

(See annex for an overview graphic)

4.4 EuropaBio 'What If' plant factsheets

https://www.europabio.org/cross-sector/publications/genome-editing-%E2%80%94-what-if-we-embraced-its-potential

Plant applications : gluten free wheat, low acrylamide potatoes, healthier oil soya.

4.5 Julius-Kühn Institut list of plants

https://www.bmel.de/SharedDocs/Downloads/DE/_Landwirtschaft/Gruene-Gentechnik/NMT_Uebersicht-Zier-Nutzpflanzen.pdf?__blob=publicationFile&v=3

This list, which is probably the biggest list of plants made with 'new molecular biological techniques', is compiled by the Julius Kühn Institut (German federal research centre for cultivated plants). The JKI list is based on the 'Am I regulated' database (see 1,1), as well as on many scientific publications and lists 140 plants. The list is structured by group of traits:

- Food and Feed quality: 35, including alfalfa, cassava, peanut, potato, penny cress, camelina, maize, mushroom, millet, rapeseed, rice, sage, soy, lettuce, tomato, poppy, wheat and durum wheat. 9 market ready ('Marktreife').
- Tolerance to abiotic stress: 5, including potato, maize, rice, soy, wheat. 1 market ready.
- Tolerance/resistance to biotic stress: 23, including grapefruit, cucumber, cacao, maize, orange, rice, tomato, wine grapes, wheat, rapeseed, cassava, potato, barley, cotton, banana. 3 market ready.
- Agronomically relevant traits: 43, including cotton, cucumber, maize, rapeseed, rice, switchgrass, kiwi, lettuce, potato, soy, tomato, wild strawberry, wheat. 2 market ready.
- Plants for industrial use: 5, including pennycress, potato, dandelion, switchgrass, tobacco, sugarcane. 2 market ready.
- Ornamental plants: 6, including morning glory, orchid, petunia, flowering tobacco, torenia. 0 market ready.

- Genome editing to improve plant breeding: 6, including potato, maize, rice, wheat.
- Herbicide tolerant plants: 11, including cotton, flax, potato, maize, cassava, rapeseed, rice, soy, tomato, watermelon, wheat. 1 market ready.
- Miscellaneous: 6, including cabbage, maize, physalis, rice, and wild tomato.

Of these 140 applications, only 11 are being developed by the Big 4, with the vast majority developed by universities, research institutes, or smaller enterprises.
Of these 140 applications, 26 are carried out within the EU ((6x food / feed quality, 5x biotic stress, 7x agronomic, 3xindustrial use, 3x herbicide tolerance, 1x abiotic stress and 1x multiple categories).
The majority of these applications focus on economically important crops like rice (81 applications), tomato (26), maize (25), wheat (14), potato (14) and soy (12). However, the list also highlights the diversity of crops currently being genome edited (peanut, kiwi, lettuce, banana, cocoa, cassava, to name a few).

4.6 Wageningen brochure examples

The brochure 'opportunities of new plant breeding techniques' by Wageningen University and Research lists 6 examples (p. 19 ff) : late blight (phytophthora) -resistant potato using cisgenesis, blight resistant rice, powdery mildew resistant wheat, improved oil quality in soybean, resistance to AHAS (ALS)- targeting herbicides in various crops, early flowering in trees.

4.7 Plant Genome Editing Database

http://plantcrispr.org/cgi-bin/crispr/index.cgi
8 plant species
Hosted by Boyce Thompson Institute (Ithaca, NY). As of 6 March 2020, it features various entries on the following species: *Brachypodium distachyon* (grass), cassava, groundcherry, *Medicago truncatula* (barrel clover, a small legume), *Nicotiana benthamiana* (a relative of tobacco), rice, strawberry, tomato.

4.8 CropLife International

https://croplife.org/resources/
CropLife has a **case study series on Innovations in Plant Breeding** exploring the gene editing work being done to improve cassava (eliminating toxins), oranges (disease resistance), wheat (low gluten), lettuce (heat resistance), rice (rice blast resistance), and beans (drought tolerance, nutrition, storage).

4.9 CRISPR Advent Calendar from Progressive Agrarwende

https://progressive-agrarwende.org/crispr-adventskalender-blog/
In December 2019 Progressive Agrarwende released a CRISPR advent calendar with 24 case studies covering a variety of traits:

- Disease resistance (7 case studies: barley, cassava, potato, rapeseed, banana, orange, wine)
- Agronomic traits e.g. drought tolerance, seed dormancy, growth characteristics (10 case studies: Wheat, Watermelon*, Cucumber, Cotton, Maize, Rapeseed, Kiwifruit, Wild tomato, and 2 traits in rice (salt tolerance and reduced arsenic content)) *herbicide resistance
- Consumer benefits e.g. increased vitamins, improved oil quality or benefits to a processor e.g. starch composition, increased biomass (5 case studies: Dandelion, Lettuce, Tomato, Potato, Soybean)
- Ornamentals e.g. enhanced flower longevity or modified colours (2 case studies: petunia, wishbone flower)

4.10 Innovature

Innovature cites examples like compactly-growing cherry tomatoes, acceleration of domestication of the wild tomato, disease resistant apple, banana, cacao, pumpkin, sweet potato, reduced-browning potatoes.

4.11 Genetic Literacy Project Gene editing regulation tracker

https://crispr-gene-editing-regs-tracker.geneticliteracyproject.org/

The Gene editing regulation tracker hosted by Genetic Literacy Project cites 87 products and research projects, only 4 of which are linked to herbicide resistance (canola, soybean, maize). These are broadly distributed worldwide:

- North America (USA, Canada): 25 projects, including apple, canola, potato, alfalfa, soybean, tomato, wine grapes, rice, wheat, camelina, mushroom. These examples cover disease/pest resistance (tomato, wine grapes, wheat, rice), abiotic stress tolerance (rice, soybean, maize), agronomic benefits (cereal crops, alfalfa), consumer benefits (soybean, tomato, apple, wheat, camelina, potato, mushroom)
- Central and South America (Brazil, Colombia, Chile, Uruguay, Argentina): 17 projects, including rice, cassava, cacao, soybean, mandarin, tomato, potato, alfalfa, camelina, maize, yeast. These examples cover disease/pest resistance (soybean, rice, cassava), abiotic stress tolerance (maize, rice, alfalfa), consumer benefits (tomato, maize, mandarin, soybean, camelina, cacao, potato, cassava), biofuel production (yeast).
- Africa: 10 projects, including cassava, bananas, yam, maize, sorghum, cacao. These projects focus on disease or pest resistance (cassava, bananas, yam, maize, sorghum, cacao), abiotic stress tolerance (banana) or on nutritional qualities (cassava, sorghum).
- Europe, Russia, Israel: 16 projects, including tomato, petunias, jasmine tobacco, cucumber, maize, banana, canola, wheat, potato, camelina, barley, beetroot, sugar beet. These mainly cover disease resistance (banana, cucumber, tomato, potato, sugar beet), abiotic stress tolerance (maize, barley) or consumer benefits (wheat, potato, camelina, beetroot, petunia, jasmine tobacco).
- Asia (concentrated in China, India and Japan): 21 projects, including rice, banana, maize, wheat, grape, kiwifruit, poplar, soybean, morning glory, apple, tomato, potato, canola. The examples cover disease/pest resistance (wheat), consumer benefits (rice, morning glory, tomato, potato, banana), agronomic benefits (rice, wheat, soybean), research (grape, kiwi, poplar, apple, tomato).
- Australia and NZ: 10 projects, including sorghum, wheat, barley, cottonseed, canola, potato, rice, grass. These examples cover disease/pest resistance (barley, wheat), agronomic traits (wheat, canola, grass), consumer benefits (cottonseed, potato, rice, sorghum).

4.12 Resources about specific plant applications

- ALFALFA: improved digestibility (2021): Calyxt pipeline website
- BANANA: fungus resistance (against the devastating Panama disease): Wageningen & Queensland.
- BERRIES: including raspberries and blackberries, to extend growing season, improve nutrition – Pairwise in partnership with Plant Sciences Inc
- CABBAGE: earlier flowering (Chungnam and Seoul National Universities), male sterility (Southwest University, China)
- CASSAVA: resistance to cassava brown streak disease (Donald Danforth Plant Science Center) and lower toxin production (by Innovative Genomics Institute – collaboration between UC Davis and UC Berkeley)
- CITRUS fruits, incl. ORANGE: resistance to citrus greening Innovature, CLI & ASTA video

- COCOA: fungus resistance – Pennsylvania State
- COFFEE: disease & pest resistance. Research project UC Davis (via Innovature)
- DANDELION: enhanced agronomic performance (easier to cultivate & harvest taproot phenotype, higher root biomass, increased natural rubber biosynthesis) – University of Münster, Ohio State University
- GRAPE mildew resistance, saving fungicides: Articles in GLP, Innovature
- GROUNDCHERRY research project Cornell University (also here and here)
- LETTUCE Video : Climate vs. Lettuce. CLI & ASTA Video
- MAIZE: Thermosensitive male-sterile maize (Chinese Academy of Agricultural Sciences)
- MAIZE: haploid breeding lines (Chinese Academy of Agricultural Sciences)
- MAIZE: reduced epicuticular wax (Iowa State University, China Agricultural University)
- MUSHROOM non-browning (non-regulated in USA): articles in Nature, Washington Post
- OILSEED RAPE research project University of Kiel
- OILSEED RAPE resistance against sclerotinia stem rot Yangzhou University
- PLANTAIN with inactivated endogenous Banana streak virus (International Institute of Tropical Agriculture & UC Davis)
- POPLAR TREE – Thuenen Institute
- POTATO *Phytophthora* resistance and starch: Swedish University of Ag Sciences.
- POTATO: cold storable (post 2024): Calyxt pipeline website
- POTATO: Resistance to potato virus Y which also confers salt and osmotic stress tolerance (Moscow State University)
- RICE : more robust rice (attacking TAL effectors) : Research project Cornell Univ.
- RICE: haploid breeding lines (Chinese Academy of Sciences)
- SUGARCANE: improved saccharification efficiency (University of Florida and Korea Institute of Science and Technology)
- TOMATO : disease resistance. Research project Boyce Thompson Institute
- WHEAT : reducing acrylamide in processed wheat. Project Rothamsted.
- WHEAT : high fiber (2022): Calyxt pipeline website
- WHEAT : mildew resistance: Chinese Academy
- WHEAT : longer seed dormancy period (Japanese National Agriculture and Food Research Organization)
- WINE GRAPES : fungal resistance: University of Udine

4.13 23 EU-funded projects on CRISPR applications in agriculture (retrieved in mid-2019)

The EU appears to have invested close to 27 million EUR in these projects as of mid-2019.

Nr.	EU-funded project name	EU investment (€)
1	PlantMYCcellWall	265.263
2	CRISPR/Cas9 technology implementation for improved resistance to Abiotic Stress in cereals:	72.500
3	Next generation disease resistance breeding in plants	2.496.835
4	Multidimensional CRISPR/Cas mediated engineering of plant breeding	2.499.981
5	Mechanisms of natural auto immunity triggered by plant NLR immune receptors	159.460
6	Tracking and Targeting a T-DNA Vector for Precise Engineering of Plant Genomes	1.958.408
7	Implementation of CRISPR/Cas9 technology in melon to edit fruit ripening and CMV resistant genes	170.121
8	New insights into wheat meiosis: Crossover resolution in the absence of the Ph1 locus	183.454
9	Control of meiotic recombination: from Arabidopsis to crops	3.645.642

10	BIO: Banana IN and OUT - engineering resistance against Panama disease in banana	183.454
11	DISCO	6.485.847
12	BREED4FUTURE	265.263
13	Increasing reproductive success in crops under high ambient temperature	158.121
14	GENETICS OF TEMPERATURE MODULATION OF PLANT IMMUNITY	100.000
15	Molecular inventions underlying the evolution of the nitrogen-fixing root nodule symbiosis	2.494.114
16	GREEN-SPECIALISTS	200 194
17	Max-imising the potential of CROP researchers	1.467.957
18	SiPoMorph	183.454
19	SynthHotSpot	1.999.953
20	CVI_ADAPT	1.609.375
21	MEPOL	165.598
22	MetKnock	150.000
23	CHIC project (see below)	7.300.000
Total Crispr-related EU investments		**34.214.994**

4.14 Other EU projects

- Moritz Nowack - ERC consolidator grant 1/06/20-31/05/2025
  EXECUT.ER exploits CRISPR-based mutant screens and multiplex genome editing to dissect the molecular mechanisms that execute developmental programmed cell death in plants. (EXECUT.ER)
- Dirk Inzé - ERC Advanced grant 1/09/2019-31/08/2024
  A novel breeding strategy using multiplex genome editing in Maize (BREEDIT)
  BREEDIT combines multiplex genome editing with classical breeding to select for maize plants with superior growth characteristics.
- Wout Boerjan - ERC Advanced grant 1/07/2019-30/06/2024
  Large-scale identification of secondary metabolites, metabolic pathways and their genes in the tree model poplar (POPMET)
  POPMET will use gene editing as a reverse genetics tool in the discovery of metabolic pathways in poplar.
- CHIC: The CHIC project aims to develop chicory varieties that can be used to produce dietary fibre with enhanced prebiotic effects to promote gut health. At the same time, given its biosynthetic capacity, high yields and low agronomic requirements, chicory has significant potential as a versatile production host in molecular farming for the production of many additional health-related products with benefits for consumers. CHIC also aims to harness this potential for the extraction of other types of health-related compounds (terpenes) as potential lead molecules for drug development.

4.15 Other relevant plant focused resources

- Plant Ed (EU funded COST action project): https://plantgenomeediting.eu/about-planted/objectives/ (no product examples)
- Video (ASTA): Plant Breeding Innovation: https://www.youtube.com/watch?v=nYMoWtTXkwI
- TED talk from Jennifer Doudna: How CRISPR lets us edit our DNA
- KWS video: usefulness of genome editing in crops explained generally: yield, climate, disease; good legislation important; also transparency and discussion important (pictures of some crops, e.g. potatoes, maize, etc.). Also, lots of good general GE explanation (e.g. glossary on KWS website).
- Pioneer video on CRISPR-Cas

- ASTA-CLI: PBI video and CLI infographic with general benefits explained
- Good pictures links for before and after domestication (e.g. teosinte versus modern maize) here and here.
- PRRI resources; ISAAA website

5. Animals

- The FLI report (Friedrich-Loeffler-Institut : Institute reporting to the German Ministry of Agriculture) lists ca. 100 animals, mostly transgenic, both green and red (animals to produce medicines).
- EuropaBio animal factsheet (hornless cows, sterile pigs to avoid manual dehorning and pig castration)
- Pigs disease resistance. Research project Roslin Institute (Edinburgh)
- Tilapia, which allows for a 70% yield increase, Intrexon press release
- Innovature cites the following examples: Lyme-disease resistant mice, malaria-resistant or sterile mosquitoes, flu-resistant chickens
- Gene editing regulation tracker hosted by Genetic Literacy Project cites 78 products and research projects. These are broadly distributed worldwide:
  - North America (USA, Canada): 12, including Aquadvantage salmon, cows, pigs, catfish, lizards, coral
  - Central and South America (Brazil, Chile, Uruguay, Argentina): 9, including fruit flies, cows, tilapia, horses, salmon
  - Africa: 7, chicken, rhino, mostly cows
  - Europe and Israel: 12, including pigs, sheep and chickens, mice, flies
  - Asia (concentrated in China, India and Japan): 29, including pigs, monkeys, dogs, cows/heifers, goats, mosquitoes, mice, rats, coral, and fish (tuna, anchovy, red sea bream)
  - Australia and NZ: 9, including toad, carp, cattle, chickens, mice, coral

Annex 1: US regulator's database 'Am I regulated?'

https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated/Regulated_Article_Letters_of_Inquiry

Status 6 May 2020

As of 6 May 2020, a total of 93 Letters of Inquiry have been published by USDA replying to product developers inquiring whether their biotech applications are regulated as "GMOs" under USDA's current regulations. In the vast majority of cases, the reply by APHIS was 'No'. The majority of these letters (50 of 93) **do not involve** organisms developed using New Genomic techniques (e.g., genome editing, cisgenesis, intragenesis). Those products not developed using NGTs are excluded from analysis here.

MAINLY MEDIUM COMPANIES AND PUBLIC RESEARCH

The signatory organisations (mostly developers) of the 43 requesting letters were:

1. 46% medium sized and smaller companies : 20 letters;
2. 42% public institutions : 18 letters ; mainly universities;
3. 12% multinational companies which also market transgenic GMO plants (BASF, Bayer, Corteva (DupontPioneer and Dow), Syngenta, Simplot) : 5 letters

Only 12 % of the developers are multinational companies

MANY DIFFERENT ORGANISMS, MOSTLY PLANTS, BUT MANY SPECIES

The letters with relevance to plants covered a very wide variety of species:

1. 16% Fruit & vegetables : 7 (tomato, grapevine, apple, citrus, lettuce)
2. 14% Maize : 6
3. 12% Forages & Cresses : 5
4. 12% Soy : 5
5. 7% Potato: 3
6. 5% Wheat : 2
7. 5% Rice : 2
8. 23% Other: 10 (flowers, Camelina, Setaria, tobacco, sorghum)
9. 5% no crop specified: 2
10. 2% Mushroom : 1

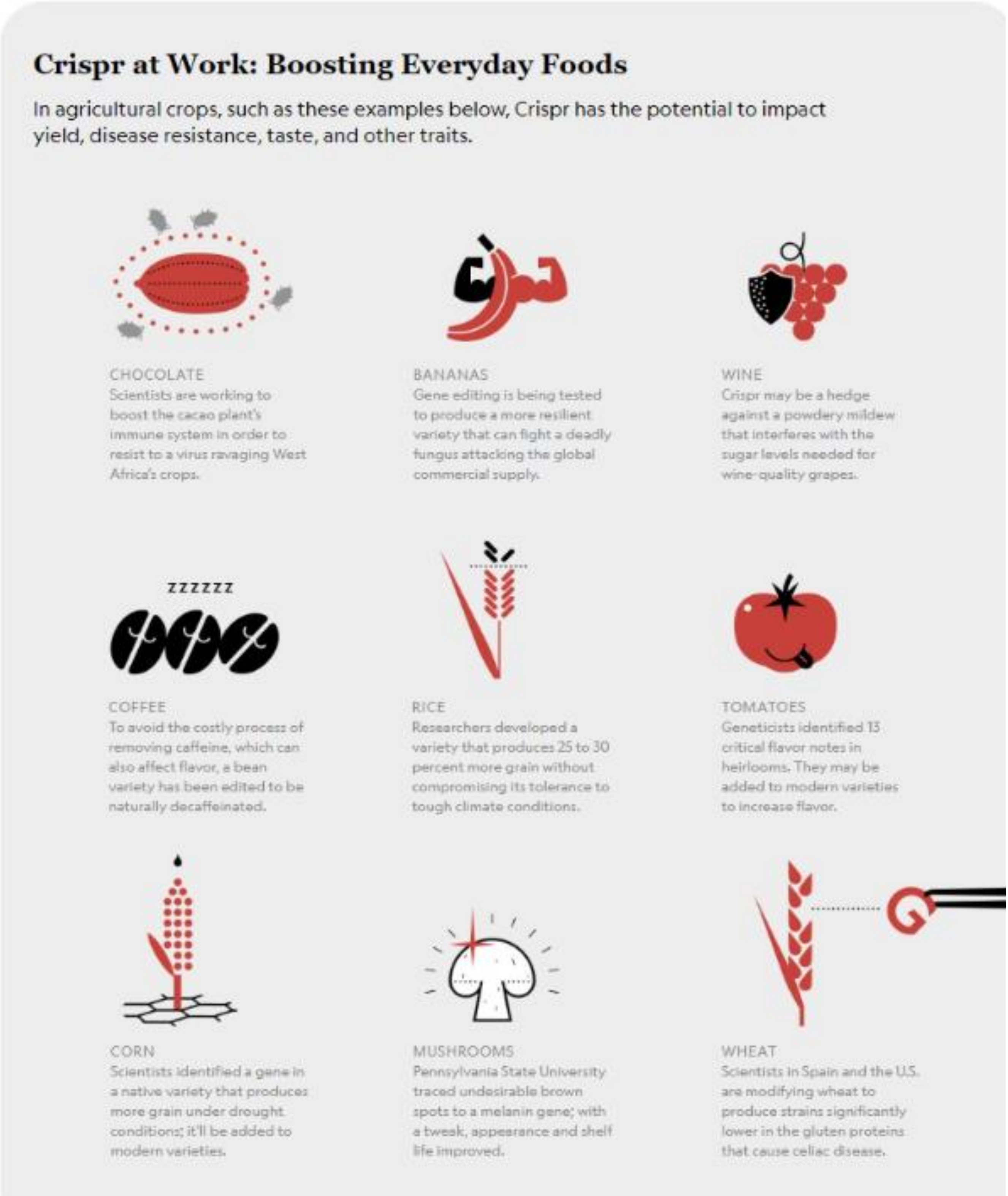
Only 26% concern the big four crops (soy, maize, oilseed rape and cotton), namely 6 maize and 5 soy

MANY DIFFERENT TRAITS

1. Product Quality: 18
2. Pest Resistance: 6
3. Agronomic Phenotype: 5
4. Stress Tolerance: 3
5. Other traits: 7
6. CBI: 3

The biggest group of traits concern product quality, disease resistance and stress tolerance, and agronomic phenotype. Herbicide resistance seems to be the rarest trait.

Annex 2: Screenshot of National Geographic reporting on 9 plant applications



Why gene editing is the next food revolution
https://www.nationalgeographic.com/environment/future-of-food/food-technology-gene-editing/
9 Plant Applications (National Geographic)

Annex 3: Screenshot of DG Research Success Stories Health & Life Sciences: Biotechnology

☐ **Advanced molecular technique boosts cancer research**

After cardiovascular diseases, cancer is the second leading cause of death and morbidity in European countries and is one of the most significant health challenges worldwide. An EU-funded project is developing new tools for diagnosing cancer and for understanding the role of proteins in this and other major diseases.

Published: 14 March 2019

☐ **Light-sensitive molecules for new disease therapies**

Peptidomimetics are small molecules that mimic short natural proteins - peptides - and produce the same effects as their natural counterparts. An EU-funded project is developing peptidomimetics that can alternate between biologically active and inactive forms when exposed to light. The technique could lead to new light-controlled drugs which can be turned off and on when needed to treat cancers and other diseases.

Published: 4 March 2019

☐ **Personalised brain cancer treatment shows potential**

EU-funded researchers have demonstrated huge potential for treating aggressive brain cancer using actively personalised immunotherapy in a first first-stage clinical trial to test the vaccine's safety.

Published: 27 February 2019

DG RTD project website: "Success Stories Health & Life Sciences: Biotechnology"
https://ec.europa.eu/research/infocentre/theme_en.cfm?item=Health%20%26%20life%20sciences&subitem=Biotechnology