LGN0232 - Genética Molecular

Introdução a Genética Molecular

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LGN0232 - Genética Molecular

Método de avaliação

- 1ª Prova Teórica: **26 de setembro**
- 2ª Prova Teórica: **12 de dezembro**
- Apresentação do trabalho : **5 de dezembro**

A média final = (Prova I x 0,35) + (Prova II x 0,35)
+ (Trabalho x 0,2) + (+ (Testes x 0,1);

Não haverá prova substitutiva ou repositiva

Aprovado => 5,0 e frequência => 70%

Questões semanais melhoram a média final!

As normas para a nota do trabalho estarão em breve no *site*!

O que é Genética Molecular?

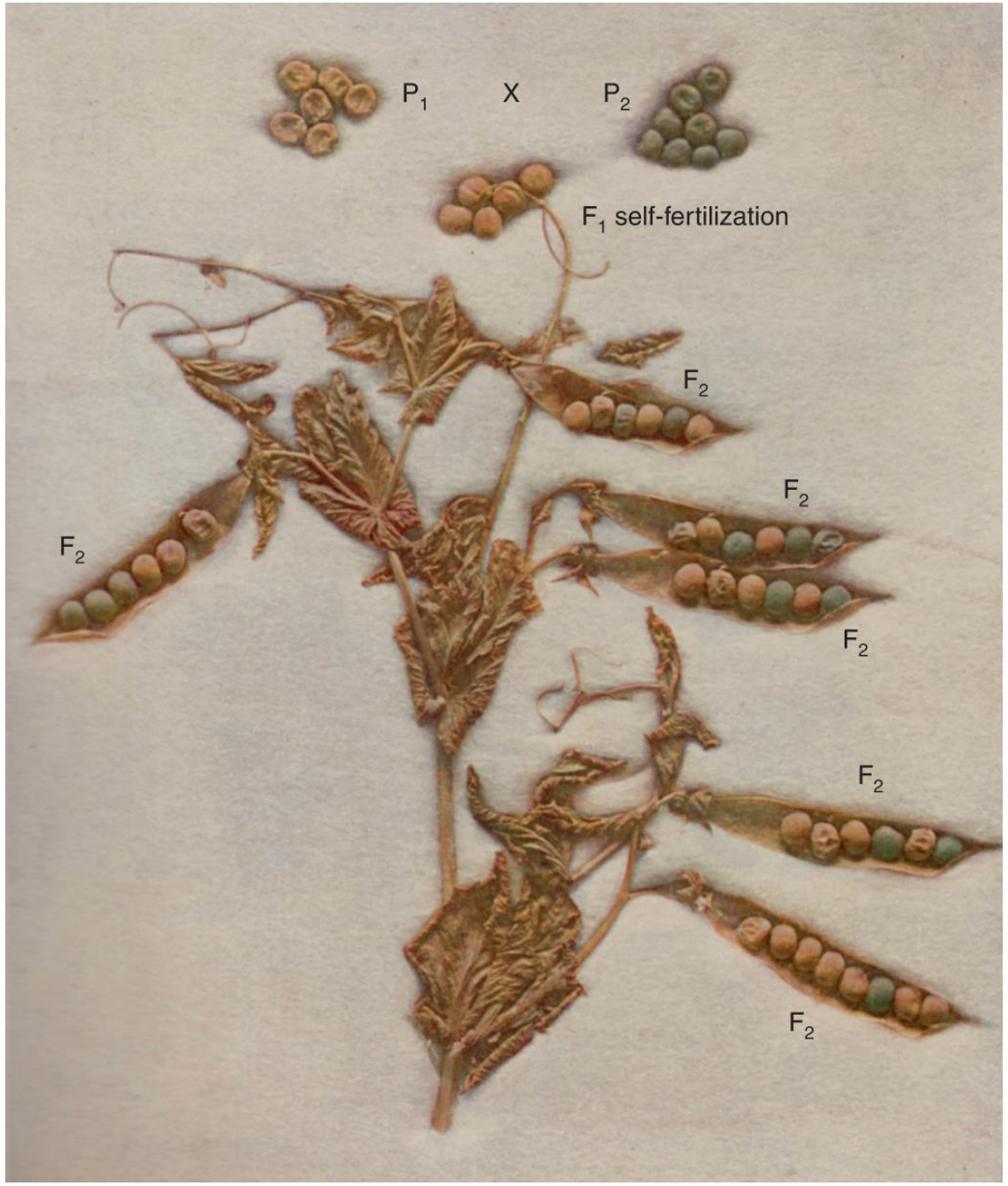
- O que é **Genética**?
- O que é **Gene**?
- O que é **Genética Molecular**?
- O que é **Biotecnologia**?

O que é Genética Molecular?

- O que é **Genética**?
  - **ciência voltada para o estudo da hereditariedade e da estrutura e funções dos genes**
- O que é **Gene**?

- O que é **Genética Molecular**?

- O que é **Biotecnologia**?



Fundador da Genética

Gregor Mendel – 200 anos de nascimento!

How did Mendel arrive at his discoveries? | Nature Genetics

O que é Genética Molecular?

- O que é **Genética**?
  - **ciência voltada para o estudo da hereditariedade e da estrutura e funções dos genes**
- O que é **Gene**?

- O que é **Genética Molecular**?

- O que é **Biotecnologia**?

O que é Genética Molecular?

- O que é **Genética**?
  - Ciência voltada para o estudo da hereditariedade e da estrutura e funções dos **genes**
- O que é **Gene**?
  - **Unidade fundamental, física e funcional da hereditariedade, constituída pelo segmento de uma cadeia de DNA,** responsável por determinar a síntese de uma proteína
- O que é **Genética Molecular**?

- O que é **Biotecnologia**?

O que é Genética Molecular?

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  - Ciência voltada para o estudo da hereditariedade e da estrutura e funções dos genes
- O que é **Gene**?
  - Unidade fundamental, física e funcional da hereditariedade, constituída pelo segmento de uma cadeia de DNA responsável por determinar a síntese de uma proteína
- O que é **Genética Molecular**?
  - **A área da biologia que estuda a função dos genes em nível molecular. A genética molecular usa métodos de genética e biologia molecular, dentre essas a tecnologia do DNA recombinante**
- O que é **Biotecnologia**?

Biotecnologia – histórico do termo

- 1917 - Termo criado por Karl Ereky
  - para descrever processo de produção de porcos em larga escala usando beterraba açucareira
  - Definiu como "*all lines of work by which products are produced from raw materials with the aid of living things*"
- 1961 – microbiologista Carl Gören Hedén recomendou troca de nome de periódico:

  Journal of Microbiological and Biochemical Engineering and Technology
  para -> *Biotechnology and Bioengineering*
- 1970s – microbiologia em engenharia química
  - *The application of scientific and engineering principles to the processing of material by biological agents to provide goods and services*

Biotecnologia

- Associado a fermentações
  - Panificação, álcool, iogurte, penicilina, ...
- Biotecnologia industrial usa microrganismos para produção comercial
  - Enzimas, antibióticos, inoculantes,..
- Fermentação/Biotransformação/Bioprocessos
- Biorreatores – otimizações
- Técnicas no processo –> seleção, mutação
- **Técnicas de DNA recombinante - revolução**

Biotecnologia

- Definição do *U.S. Office of Technology Assessment (1995)*:

  - *Any technique that uses living organisms to make or modify products, to improve plants or animals, or to develop microorganisms for specific purposes.*

  - Qualquer técnica que use organismos vivos para produzir ou modificar produtos, para melhorar plantas ou animais, ou para desenvolver microrganismos com propósito específico

There is a wide array of "biotechnologies" with different techniques and applications. The Convention on Biological Diversity (CBD) defines biotechnology as:

"any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use".

http://www.fao.org/biotech/fao-statement-on-biotechnology/en/

There is a wide array of "biotechnologies" with different techniques and applications. The Convention on Biological Diversity (CBD) defines biotechnology as:

"qualquer aplicação tecnológica que usa sistemas biológicos, organismos vivos, ou seus derivados, para ***fazer ou modificar produtos ou processos para uso específico****".*

Definição muito abrangente!

http://www.fao.org/biotech/fao-statement-on-biotechnology/en/

Interpreted in a narrow sense, which considers ***only the new DNA techniques, molecular biology*** *and reproductive technological applications, the definition covers a range of different technologies such as gene manipulation and gene transfer, DNA typing and cloning of plants and animals.*

http://www.fao.org/biotech/fao-statement-on-biotechnology/en/

Interpreted in a narrow sense, which considers ***only the new DNA techniques, molecular biology*** *and reproductive technological applications, the definition covers*

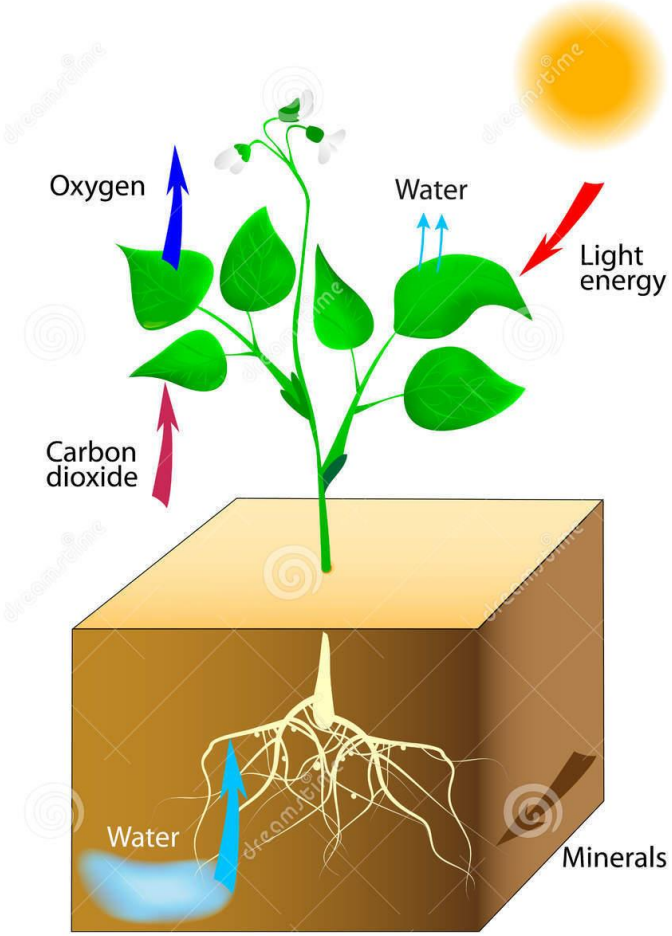
"uma gama de tecnologias diferentes tais como manipulação gênica e transferência de genes, tipificação de DNA e clonagem de plantas e animais."

Inclui apenas técnicas de DNA recombinante, biologia molecular e aplicações reprodutivas tecnológicas

http://www.fao.org/biotech/fao-statement-on-biotechnology/en/

Mas, porque eu preciso saber de Genética Molecular?

Porque aprender Genética Molecular?



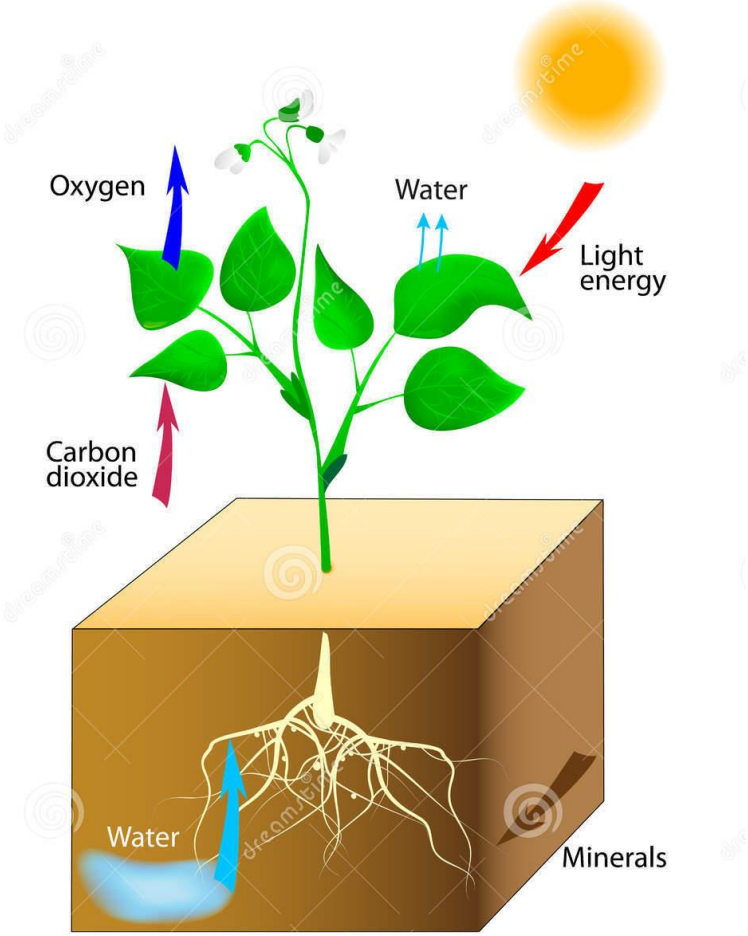
APLICAÇÕES

Planta

Microrganismos e Solos

Pragas, Doenças, Daninhas

Porque aprender Genética Molecular?



APLICAÇÕES

Planta

- Cultivar – OGM, genotipagem, melhoramento por seleção genômica, CRISPR,..

Microrganismos e Solos

- Endofíticos: inoculação com organismos melhorados, GM, microbioma...
- Rizosfera – Fixadores de N, estimuladores de crescimento, solubilizadores de fosfato,...

Pragas, Doenças, Daninhas

- RNAi, controle biológico,..

Ferramentas da Genética Molecular

- Técnicas de DNA recombinante – clonagem moelcular
- PCR
- Genotipagem e marcadores moleculares
- Sequenciamento de genoma, genes, transcritos, proteínas, metabolitos,..
- Organismos Geneticamente Modificados, Plantas Transgênicas
- Expressão Heteróloga
- Edição Genômica (CRISPR/Cas9)
- Interferência por RNA (RNAi)
- *To be continued*.....

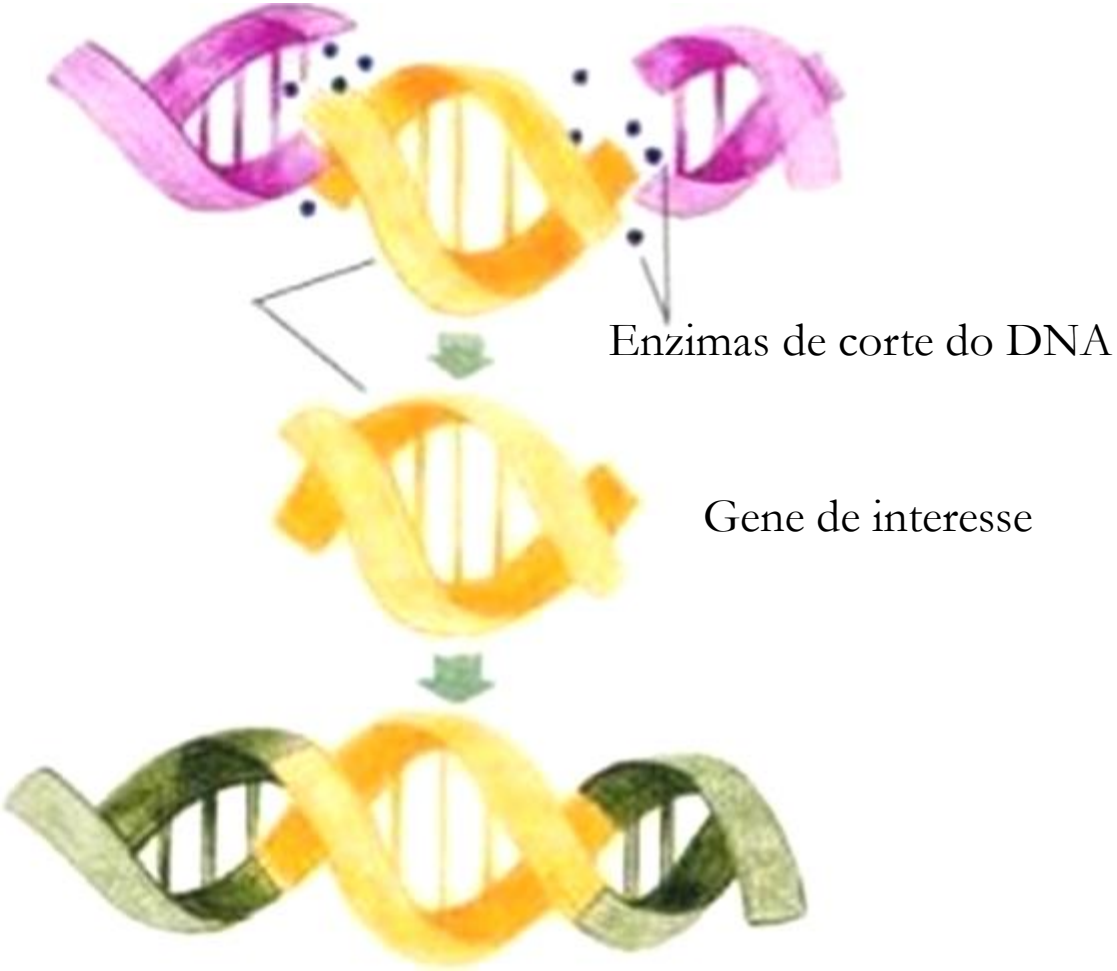
DNA Recombinante: quebra de barreiras entre espécies!

Ex. Gene Bt promove resistência a insetos

DNA de bacteria

Enzimas são usadas para isolar o gene de interesse

DNA de milho



Organismos Geneticamente Modificados (OGM)

X

Transgênicos

Lei de Biossegurança - definições

- Liberação Planejada
- Liberação Comercial
- Processo Importação
- Publicações no Diário Oficial da União

NORMAS E LEIS

- Constituição Federal
- Tratados Internacionais
- **Leis**
- Medidas Provisórias
- Decretos Legislativos
- Portarias
- Decretos
- Instruções Normativas
- Notas Técnicas
- Resoluções Normativas
- Comunicados
- Orientações
- Regimento Interno da CTNBio

Art. 3o Para os efeitos desta Lei, considera-se:

I – organismo: toda entidade biológica capaz de reproduzir ou transferir material genético, inclusive vírus e outras classes que venham a ser conhecidas;

II – ácido desoxirribonucléico - ADN, ácido ribonucléico - ARN: material genético que contém informações determinantes dos caracteres hereditários transmissíveis à descendência;

III – moléculas de ADN/ARN recombinante: as moléculas manipuladas fora das células vivas mediante a modificação de segmentos de ADN/ARN natural ou sintético e que possam multiplicar-se em uma célula viva, ou ainda as moléculas de ADN/ARN resultantes dessa multiplicação; consideram-se também os segmentos de ADN/ARN sintéticos equivalentes aos de ADN/ARN natural;

IV – engenharia genética: atividade de produção e manipulação de moléculas de ADN/ARN recombinante;

V – organismo geneticamente modificado - OGM: organismo cujo material genético – ADN/ARN tenha sido modificado por qualquer técnica de engenharia genética;

VI – derivado de OGM: produto obtido de OGM e que não possua capacidade autônoma de replicação ou que não contenha forma viável de OGM;

VII – célula germinal humana: célula-mãe responsável pela formação de gametas presentes nas glândulas sexuais femininas e masculinas e suas descendentes diretas em qualquer grau de ploidia;

VIII – clonagem: processo de reprodução assexuada, produzida artificialmente, baseada em um único patrimônio genético, com ou sem utilização de técnicas de engenharia genética;

IX – clonagem para fins reprodutivos: clonagem com a finalidade de obtenção de um indivíduo;

X – clonagem terapêutica: clonagem com a finalidade de produção de células-tronco embrionárias para utilização terapêutica;

XI – células-tronco embrionárias: células de embrião que apresentam a capacidade de se transformar em células de qualquer tecido de um organismo.

§ 1o Não se inclui na categoria de OGM o resultante de técnicas que impliquem a introdução direta, num organismo, de material hereditário, desde que não envolvam a utilização de moléculas de ADN/ARN recombinante ou OGM, inclusive fecundação in vitro, conjugação, transdução, transformação, indução poliplóide e qualquer outro processo natural.

§ 2o Não se inclui na categoria de derivado de OGM a substância pura, quimicamente definida, obtida por meio de processos biológicos e que não contenha OGM, proteína heteróloga ou ADN recombinante.

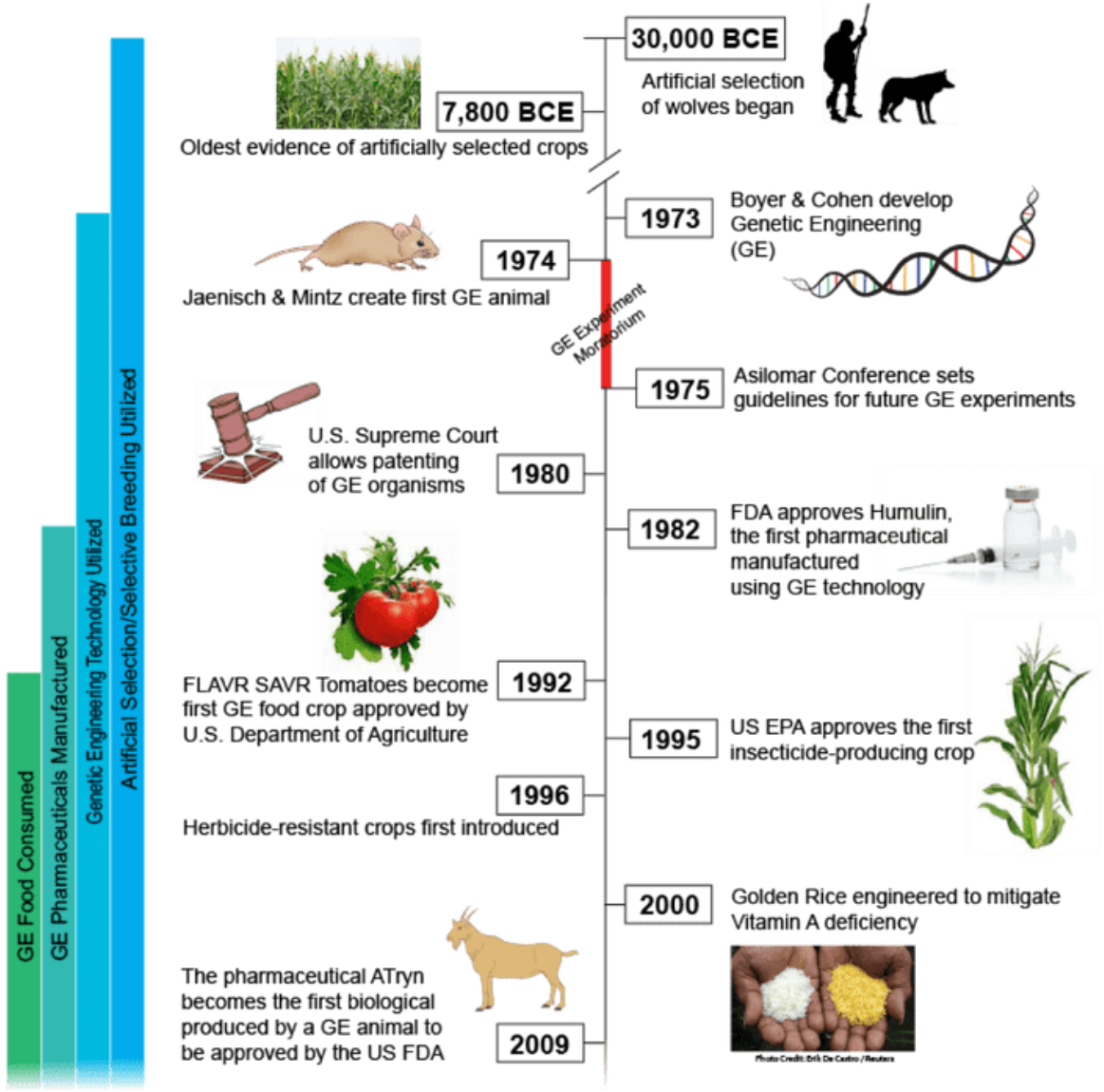
Art. 4o Esta Lei não se aplica quando a modificação genética for obtida por meio das seguintes técnicas, desde que não impliquem a utilização de OGM como receptor ou doador:

I – mutagênese;

II – formação e utilização de células somáticas de hibridoma animal;

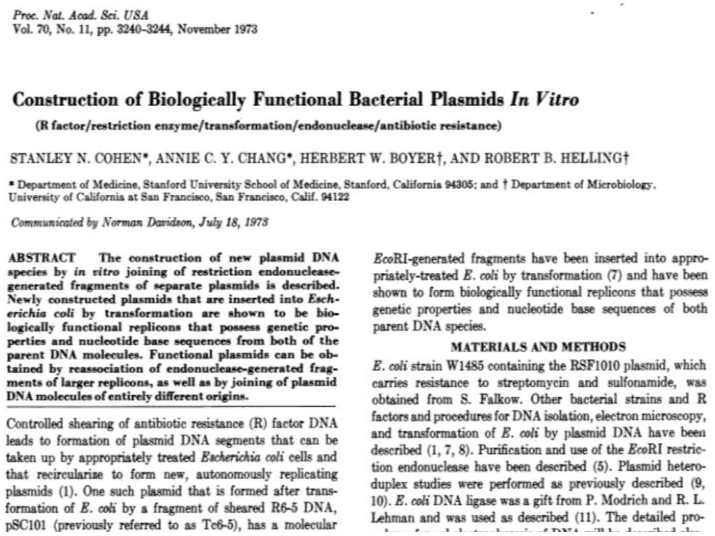
Linha Cronológica OGM

A longa cronologia de OGMs



http://sitn.hms.harvard.edu/flash/2015/from-corgis-to-corn-a-brief-look-at-the-long-history-of-gmo-technology/

O Primeiro Transgênico!!!



Proc. Nat. Acad. Sci. USA
Vol. 70, No. 11, pp. 3240–3244, November 1973

Construction of Biologically Functional Bacterial Plasmids *In Vitro*

(R factor/restriction enzyme/transformation/endonuclease/antibiotic resistance)

STANLEY N. COHEN*, ANNIE C. Y. CHANG*, HERBERT W. BOYER†, AND ROBERT B. HELLING†

* Department of Medicine, Stanford University School of Medicine, Stanford, California 94305; and † Department of Microbiology, University of California at San Francisco, San Francisco, Calif. 94122

Communicated by Norman Davidson, July 18, 1973

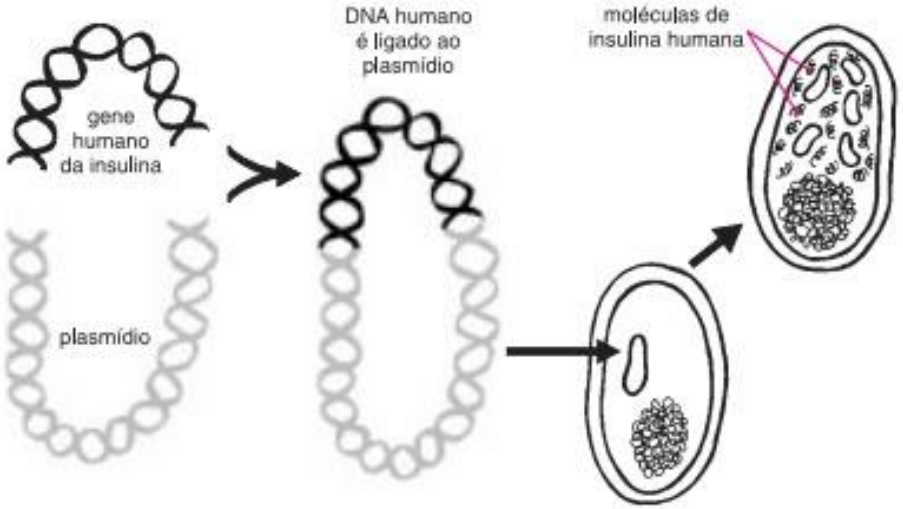
ABSTRACT **The construction of new plasmid DNA species by *in vitro* joining of restriction endonuclease-generated fragments of separate plasmids is described. Newly constructed plasmids that are inserted into *Escherichia coli* by transformation are shown to be biologically functional replicons that possess genetic properties and nucleotide base sequences from both of the parent DNA molecules. Functional plasmids can be obtained by reassociation of endonuclease-generated fragments of larger replicons, as well as by joining of plasmid DNA molecules of entirely different origins.**

Controlled shearing of antibiotic resistance (R) factor DNA leads to formation of plasmid DNA segments that can be taken up by appropriately treated *Escherichia coli* cells and that recircularize to form new, autonomously replicating plasmids (1). One such plasmid that is formed after transformation of *E. coli* by a fragment of sheared R6-5 DNA, pSC101 (previously referred to as Tc6-5), has a molecular

*Eco*RI-generated fragments have been inserted into appropriately-treated *E. coli* by transformation (7) and have been shown to form biologically functional replicons that possess genetic properties and nucleotide base sequences of both parent DNA species.

MATERIALS AND METHODS

E. coli strain W1485 containing the RSF1010 plasmid, which carries resistance to streptomycin and sulfonamide, was obtained from S. Falkow. Other bacterial strains and R factors and procedures for DNA isolation, electron microscopy, and transformation of *E. coli* by plasmid DNA have been described (1, 7, 8). Purification and use of the *Eco*RI restriction endonuclease have been described (5). Plasmid heteroduplex studies were performed as previously described (9, 10). *E. coli* DNA ligase was a gift from P. Modrich and R. L. Lehman and was used as described (11). The detailed pro-



Herbert Boyer

Stanley Norman Cohen

Um dos primeiros produto derivado de um organismo transgênico chegou ao mercado em 1982. Era **insulina**, produzida por uma bactéria geneticamente modificada com um gene humano. Até então, a insulina injetada por diabéticos tinha de ser **extraída de bois e porcos**, por ser parecida com a humana, mas não idêntica, o que causava reações alérgicas. A insulina recombinante acabou com o problema, pois é exatamente igual à humana.

Genentech

1976, 13.539 empregados

Flavr Savr (Calgene)

O tomate **Flavr Savr**, foi desenvolvido pela **Calgene**, uma companhia de biotecnologia com base em Davis, na Califórnia. Vários anos se passaram até que o FDA aprovasse o transgênico. O FDA não exige aprovação, no entanto a Calgene submeteu voluntariamente o Flavr Savr para aprovação em 1989. Em 1994, o Departamento de Agricultura dos Estados Unidos aprovou que este não apresentava risco ao ambiente.

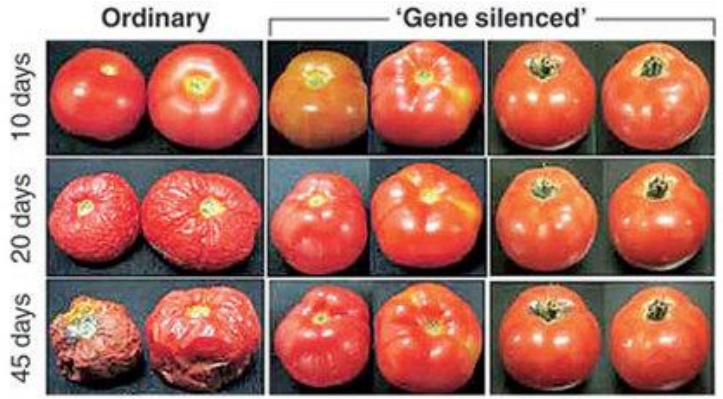


Image shows three sets of tomatoes. The ordinary control tomatoes (extreme left) soften and shrivel up, while texture of gene-silenced tomatoes remains intact for up to 45 days.

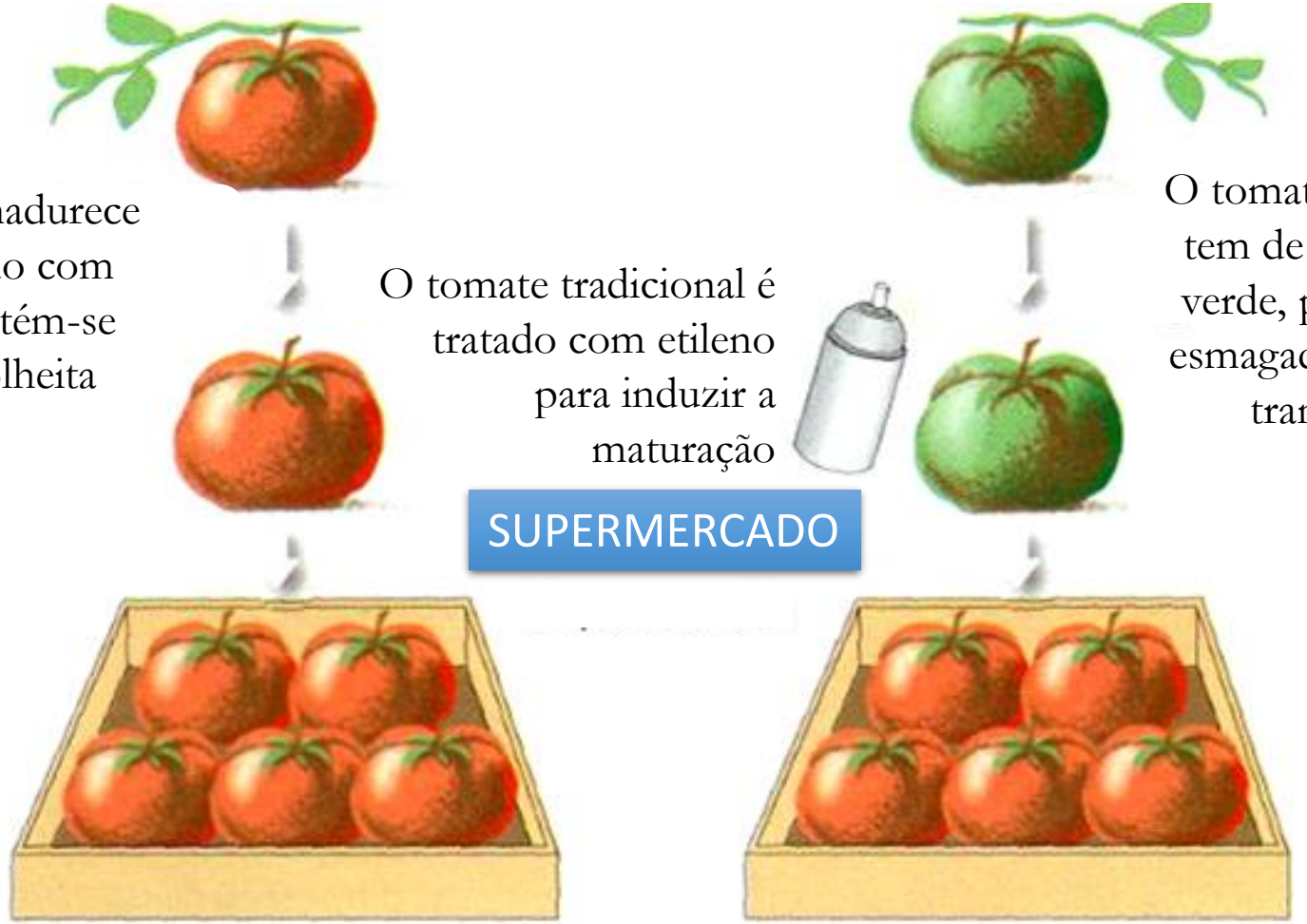
Photo credit: Asis Datta, Subhra Chakraborty, National Institute of Plant Genome Research, New Delhi

FlavrSavr

Flavr Savr (Calgene)

Tomate geneticamente modificado

Tomate tradicional



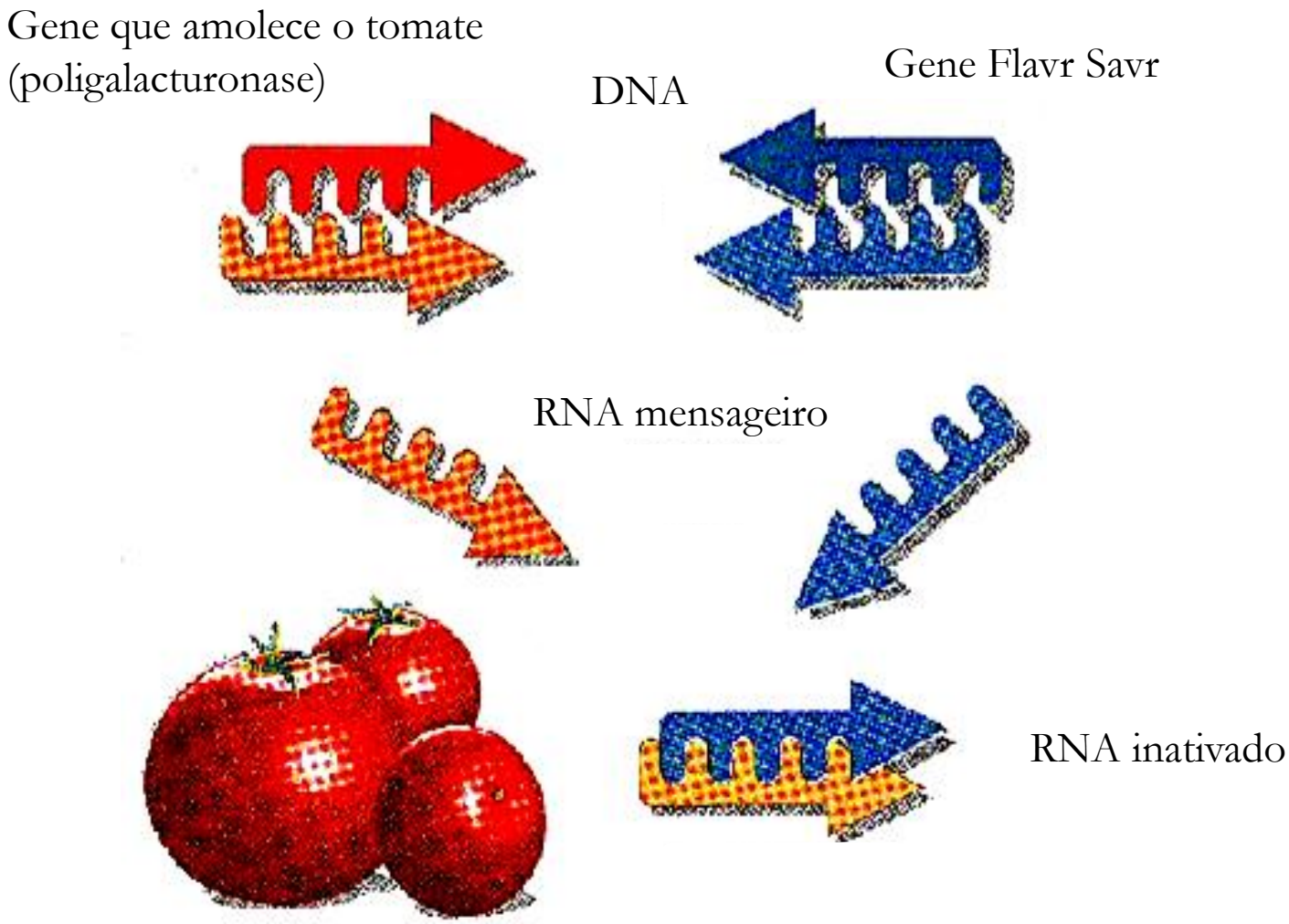
O tomate GM amadurece na planta, ficando com mais sabor. Mantém-se firme após a colheita

O tomate tradicional é tratado com etileno para induzir a maturação

O tomate tradicional tem de ser colhido verde, para não ser esmagado durante o transporte.

SUPERMERCADO

Flavr Savr (Calgene)



A história do *ROUNDUP READY*

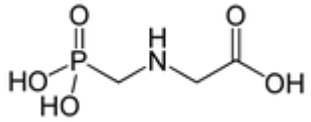
Glifosato (*Glyphosate*) é um herbicida de amplo espectro

• Ingrediente ativo do herbicida *Roundup;*
• Mata todas as plantas com que entra em contato;
• Inibe uma enzima chave (**EPSP synthase**) no metabolismo de aminoácidos aromáticos (fenilalanina, tirosina, triptofano)
•Rota do ácido chiquímico

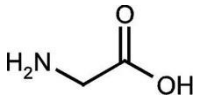
• Planta morre porque faltam aminoácidos

• Um gene que codifica uma enzima resistente (EPSP synthase) ao glifosato isolado de uma bactéria (*Agrobacterium* CP4) permite que as culturas sobrevivam mesmo quando pulverizadas

Plantas sensíveis ao Roundup



glifosato



glicina (amino ácido)

Ácido chiquimico + fosfoenolpiruvato

+ glifosato

Planta EPSP synthase

Ácido 3-Enolpiruvil chiquímico -5-fosfato (EPSP)

Aminoácidos aromáticos

Sem aminoácidos, planta morre

Plantas resistentes ao Roundup

Ácido chiquimico + fosfoenolpiruvato

+ Glifosato

Bacteria
EPSP synthase

RoundUp não tem efeito;
Enzima é resistente ao herbicida

Ácido 3-Enolpiruvil chiquímico -5-fosfato
(EPSP)

Com amino ácidos, planta sobrevive

Aminácidos
aromáticos

Transgênico Natural!!

Batata doce!

Qual foi o 1º transgênico mesmo?

PNAS

The genome of cultivated sweet potato contains *Agrobacterium* T-DNAs with expressed genes: An example of a naturally transgenic food crop

Tina Kyndt[a,1], Dora Quispe[a,b,1], Hong Zhai[c], Robert Jarret[d], Marc Ghislain[b], Qingchang Liu[c], Godelieve Gheysen[a], and Jan F. Kreuze[b,2]

[a]Department of Molecular Biotechnology, Ghent University, 9000 Ghent, Belgium; [b]International Potato Center, Lima 12, Peru; [c]Beijing Key Laboratory of Crop Genetic Improvement/Laboratory of Crop Heterosis and Utilization, Ministry of Education, China Agricultural University, Beijing, China, 100193; and [d]Plant Genetic Resources Unit, US Department of Agriculture, Agricultural Research Service, Griffin, GA 30223

Edited by Eugene W. Nester, University of Washington, Seattle, WA, and approved March 16, 2015 (received for review October 13, 2014)

Agrobacterium rhizogenes **and** ***Agrobacterium tumefaciens*** **are plant pathogenic bacteria capable of transferring DNA fragments [transfer DNA (T-DNA)] bearing functional genes into the host plant genome. This naturally occurring mechanism has been adapted by plant biotechnologists to develop genetically modified crops that today are grown on more than 10% of the world's arable land, although their use can result in considerable controversy. While assembling small interfering RNAs, or siRNAs, of sweet potato plants for metagenomic analysis, sequences homologous to T-DNA sequences from** ***Agrobacterium*** **spp. were discovered. Simple and quantitative PCR, Southern blotting, genome walking, and bacterial artificial chromosome library screening and sequencing unambiguously demonstrated that two different T-DNA regions (*Ib*T-DNA1 and *Ib*T-DNA2) are present in the cultivated sweet potato (*Ipomoea batatas* [L.] Lam.) genome and that these foreign genes are expressed at detectable levels in different tissues of the sweet potato plant. *Ib*T-DNA1 was found to contain four open reading frames (ORFs) homologous to the tryptophan-2-monooxygenase (*iaaM*), indole-3-acetamide hydrolase (*iaaH*), C-protein (*C-prot*), and agrocinopine synthase (*Acs*) genes of *Agrobacterium* spp. *Ib*T-DNA1 was detected in all 291 cultigens examined, but not in close wild relatives. *Ib*T-DNA2 contained at least five ORFs with significant homology to the *ORF14*, *ORF17n*, rooting locus (*Rol*)*B/RolC*, *ORF13*, and *ORF18/ORF17n* genes of *A. rhizogenes*. *Ib*T-DNA2 was detected in 45 of 217 genotypes that included both cultivated and wild species. Our finding, that sweet potato is naturally transgenic while being a widely and traditionally consumed food crop, could affect the current consumer distrust of the safety of transgenic food crops.**

horizontal gene transfer | *Agrobacterium* spp. | food safety | sweet potato | transgenic crops

Horizontal gene transfer (HGT) has long been recognized as a natural phenomenon, especially between bacteria, but it is

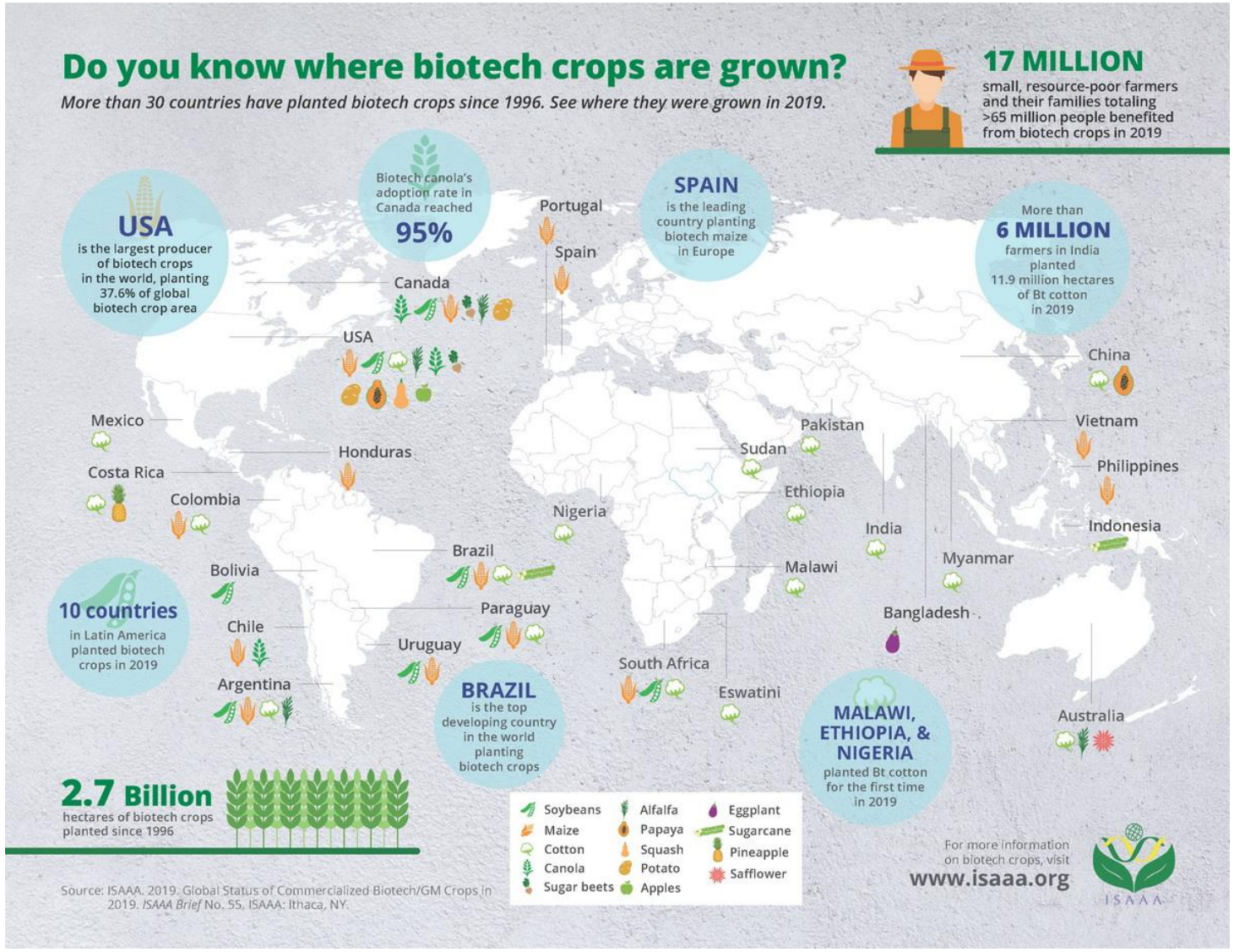
Crown gall is a disease that afflicts orchards and vineyards in particular. It has long been known to be caused by a bacterial agent (9). In the late 1970s, it was shown that the disease resulted from the transfer of a part of the tumor-inducing (Ti) plasmid, the T-DNA, from *Agrobacterium tumefaciens* into the host plant genome (10). The transfer of the T-DNA from the root-inducing (Ri) plasmid in a related bacterium, *Agrobacterium rhizogenes*, induces abundant root proliferation (hairy roots) at the infection site (11). Once integrated, the genes of the T-DNA are expressed and are responsible for tumor (crown gall) or hairy root formation, as well as the production of opines, in the infected plant tissue. The types of opines synthesized have been used to classify Ti and Ri plasmids into octopine, nopaline, and agropine-type plasmids (12–14).

Agrobacterium rhizogenes agropine strains contain two physically separated T-DNA regions (the TR-DNA and the TL-DNA)

Significance

We communicate the rather remarkable observation that among 291 tested accessions of cultivated sweet potato, all contain one or more transfer DNA (T-DNA) sequences. These sequences, which are shown to be expressed in a cultivated sweet potato clone ("Huachano") that was analyzed in detail, suggest that an *Agrobacterium* infection occurred in evolutionary times. One of the T-DNAs is apparently present in all cultivated sweet potato clones, but not in the crop's closely related wild relatives, suggesting the T-DNA provided a trait or traits that were selected for during domestication. This finding draws attention to the importance of plant–microbe interactions, and given that this crop has been eaten for millennia, it may change the paradigm governing the "unnatural" status of transgenic crops.

Culturas GM no mundo



Culturas GM no mundo

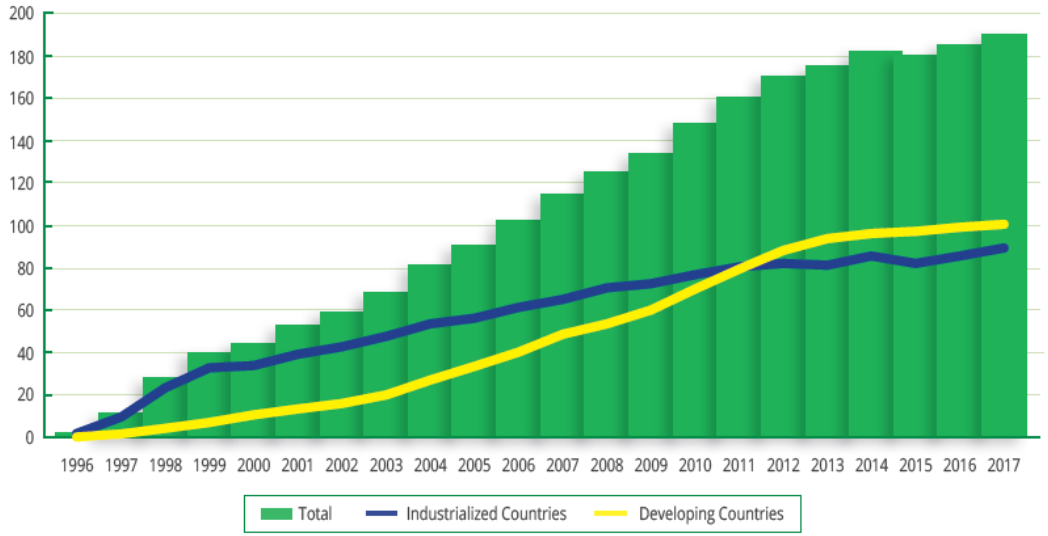


Figure 1. Global Area of Biotech Crops, 1996 to 2017: Industrialized and Developing Countries (Million Hectares)

Source: ISAAA, 2017

Table 1. Global Area of Biotech Crops in 2019: by Country (Million Hectares)**

Rank	Country	Area (Million Hectares)	Biotech Crops
1	USA*	71.5	Maize, soybeans, cotton, alfalfa, canola, sugar beets, potatoes, papaya, squash, apples
2	Brazil*	52.8	Soybeans, maize, cotton, sugarcane
3	Argentina*	24.0	Soybeans, maize, cotton, alfalfa
4	Canada*	12.5	Canola, soybeans, maize, sugar beets, alfalfa, potatoes
5	India*	11.9	Cotton
6	Paraguay*	4.1	Soybeans, maize, cotton
7	China*	3.2	Cotton, papaya
8	South Africa*	2.7	Maize, soybeans, cotton
9	Pakistan*	2.5	Cotton
10	Bolivia*	1.4	Soybeans
11	Uruguay*	1.2	Soybeans, maize
12	Philippines*	0.9	Maize
13	Australia*	0.6	Coton, canola, safflower
14	Myanmar*	0.3	Cotton
15	Sudan*	0.2	Cotton
16	Mexico*	0.2	Cotton
17	Spain*	0.1	Maize
18	Colombia*	0.1	Maize, cotton
19	Vietnam*	0.1	Maize
20	Honduras*	<0.1	Maize
21	Chile	<0.1	Maize, canola
22	Malawi	<0.1	Cotton
23	Portugal	<0.1	Maize
24	Indonesia	<0.1	Sugarcane
25	Bangladesh	<0.1	Brinjal/Eggplant
26	Nigeria	<0.1	Cotton
27	Eswatini	<0.1	Cotton
28	Ethiopia	<0.1	Cotton
29	Costa Rica	<0.1	Cotton, pineapple
	Total	**190.4**	

*19 biotech mega-countries growing 50,000 hectares, or more, of biotech crops
**Rounded-off to the nearest hundred thousand.

Source: ISAAA, 2019

http://www.isaaa.org/resources/publications/briefs/53/default.asp

Culturas GM no mundo

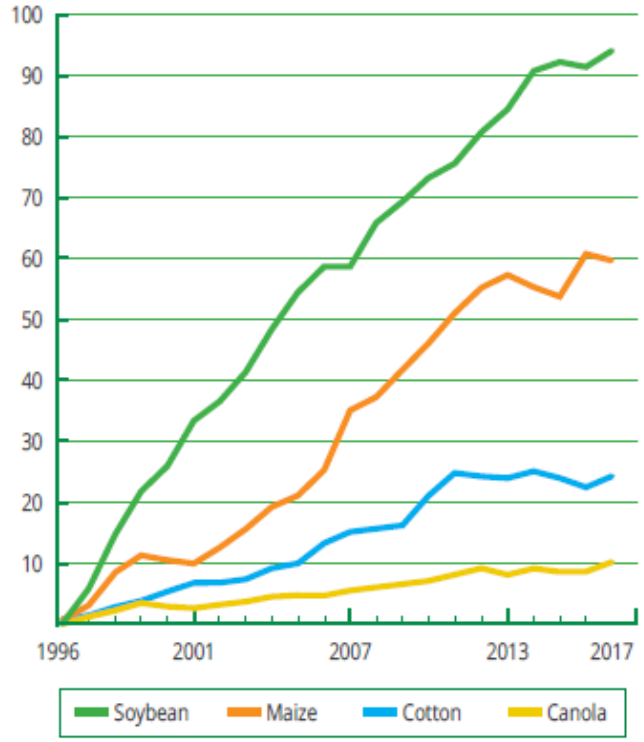


Figure 16. Global Area of Biotech Crops, 1996 to 2017: by Crop (Million Hectares)

Source: ISAAA, 2017

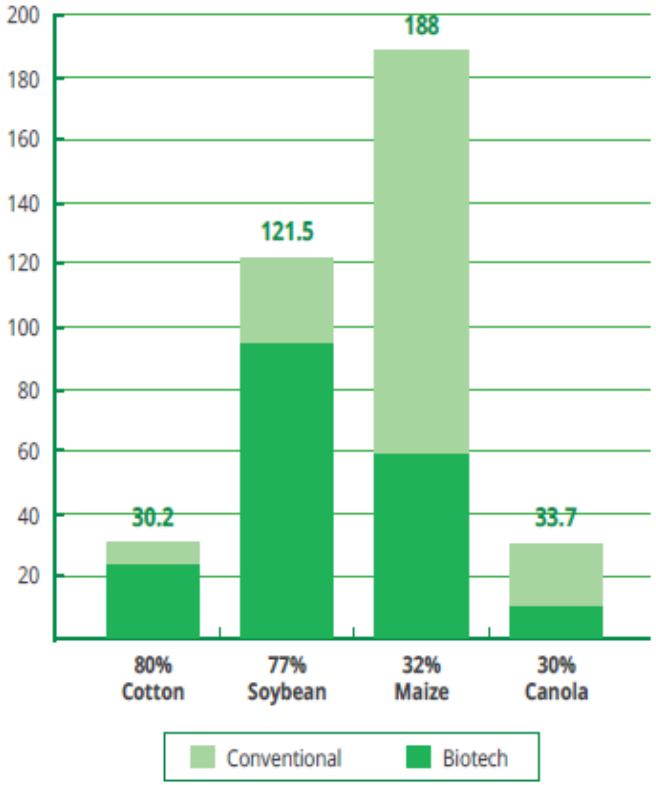


Figure 17. Global Adoption Rates (%) for Principal Biotech Crops, 2017 (Million Hectares)

Source: ISAAA, 2017

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Algodão GM na Índia

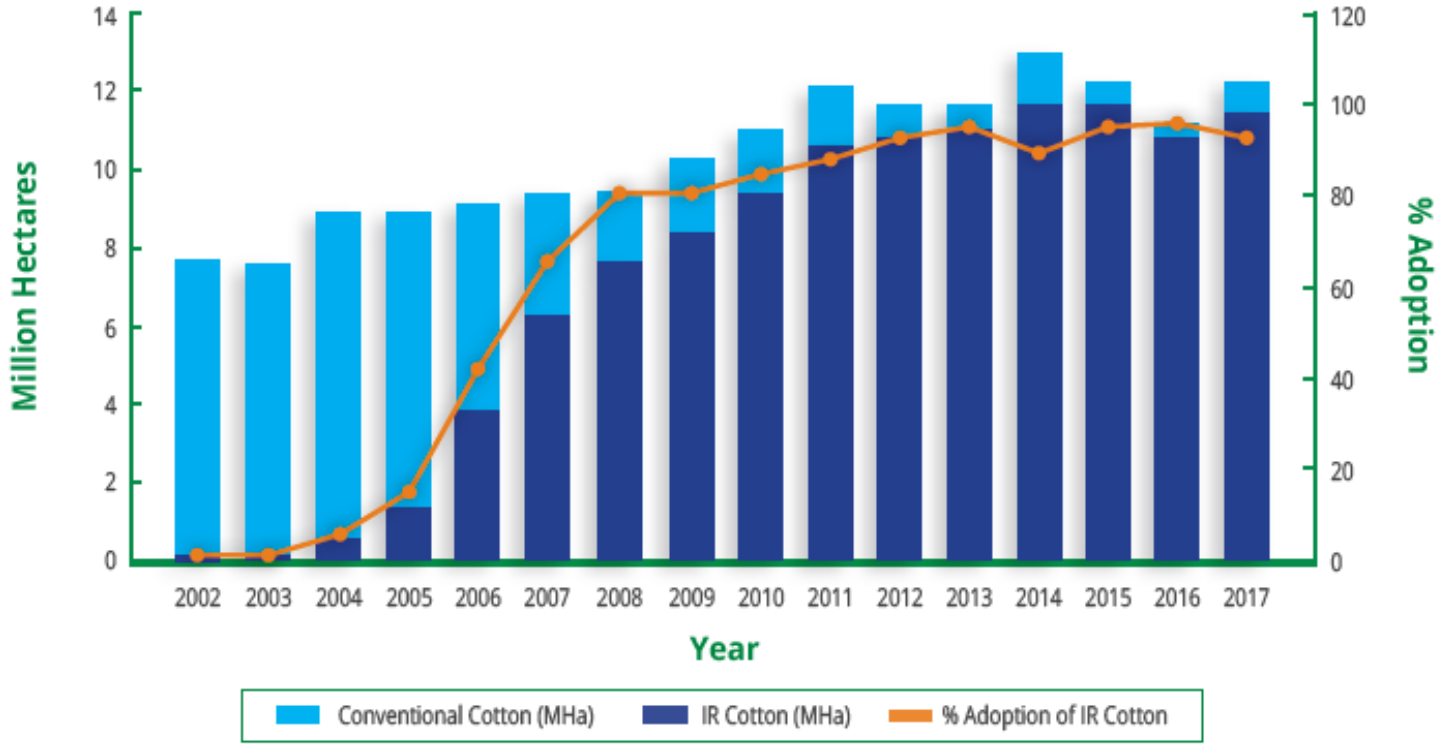


Figure 7. Sixteen Years of Adoption of IR (Bt) Cotton in India, 2002 to 2017

Source: ISAAA, 2017

http://www.isaaa.org/resources/publications/briefs/53/default.asp

Culturas GM no mundo

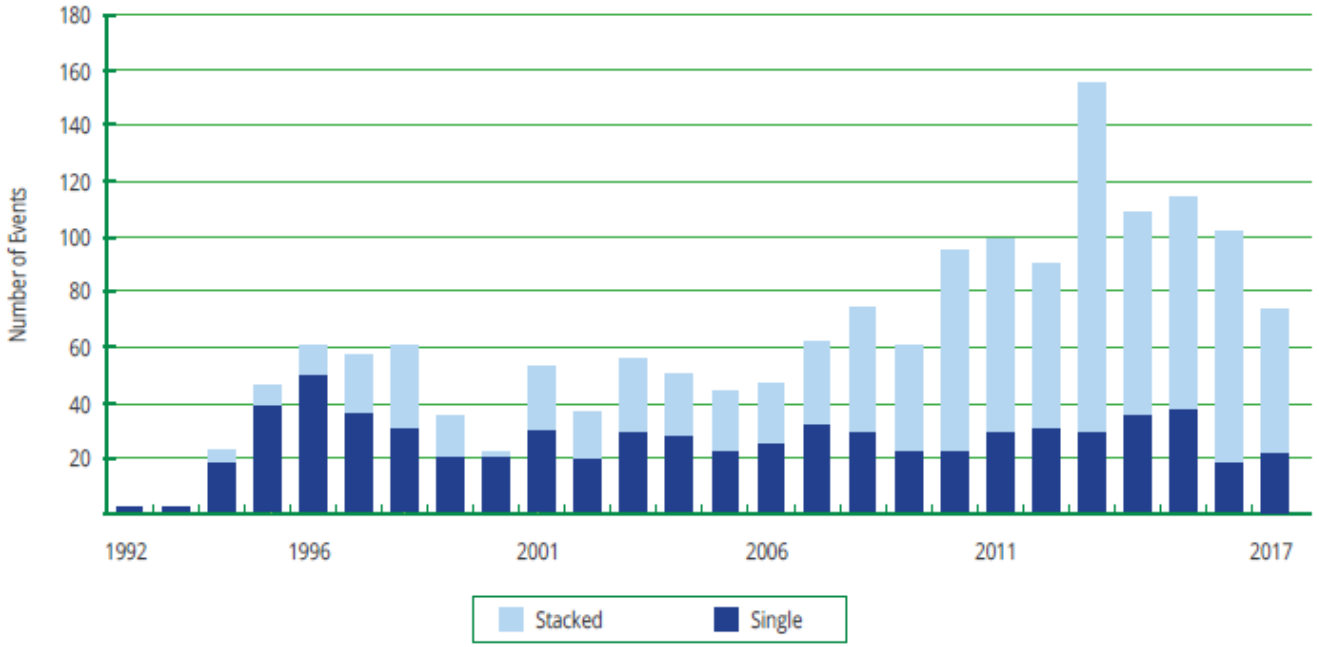


Figure 20. Number of GM Events Approved per Year

Source: ISAAA, 2017

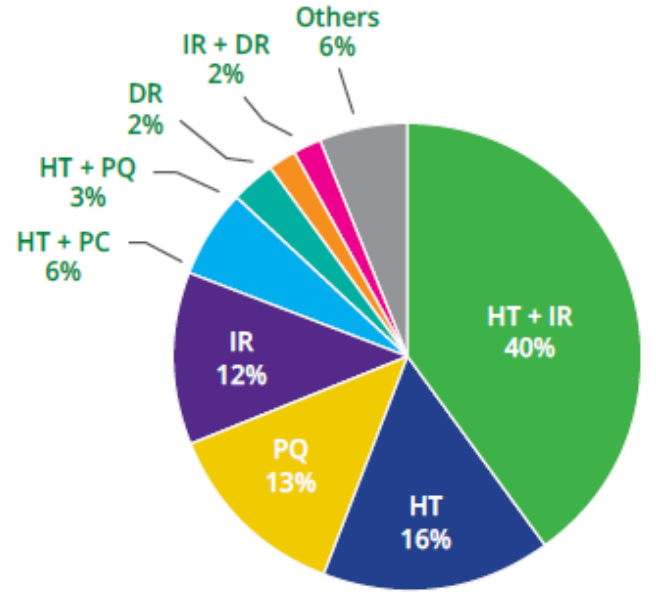


Figure 21. Distribution of Traits of Approved GM Events

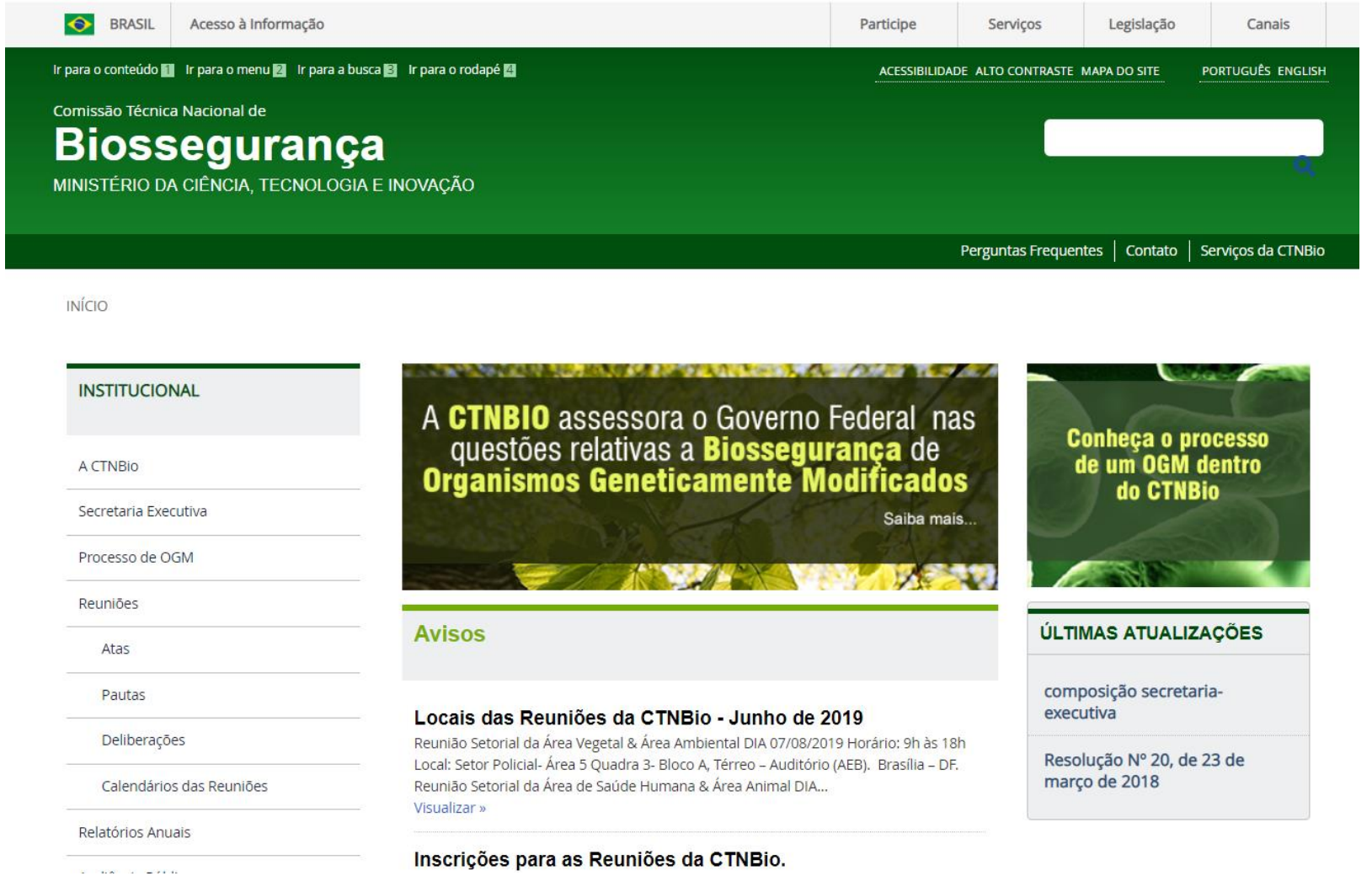
Source: ISAAA, 2017

OGM, transgênicos,..

- Qual é a opinião de vocês?

- Quais são os riscos?
  - Ambiental?
  - Saúde humana?
  - Agrícola?
  - Social?
  - Cultural?

Comissão Técnica Nacional de Biossegurança



http://ctnbio.mctic.gov.br/inicio

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Liberações Comerciais

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Plantas Plantas Subpastas: Algodão, Eucalipto, Feijão, Milho, Soja, Mais »
Outros Subpastas: Parecer Técnico nº 261-470_2004 - Importação e Liberação Comercial de Enzimas - Processo 01200.00374, Parecer Técnico nº 3964 - 2014 - OX513A de Aedes aegypti
Microorganismos Subpastas: Parecer Técnico nº 2281 - 2010, Parecer Técnico nº 3287 - 2012, Parecer Técnico nº 3775 - 2013, Parecer Técnico nº 3877 - 2013, Parecer Técnico nº 4203 - 2014, Mais »
English Version Subpastas: Crops, Microorganisms, Others, Vacccines

Mostrando 5 resultados.

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Nova geração de GM - RNAi

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/ ISAAA / GM Approval Database / GM Crop Events List / MON87411

See all events of crop:

Maize (*Zea mays L.*)

See all events developed by:

Monsanto Company (including fully and partly owned companies)

See all events with trait introduction method:

Agrobacterium tumefaciens-mediated plant transformation

See all events with commercial trait:

Herbicide Tolerance

Insect Resistance

See all events with GM trait:

Glyphosate herbicide tolerance

Coleopteran insect resistance

See all events with gene:

cry3Bb1

cp4 epsps (aroA:CP4)

dvsnf7

Lists

Crops List

Events List

Genes List

Event Name: MON87411

Event Code : MON-87411-9
Trade Name: not available

Crop: *Zea mays L.* - Maize, Corn

Basic Information | Authorizations | Documents and Links

Developer:
Monsanto Company (including fully and partly owned companies)

Method of Trait Introduction:
Agrobacterium tumefaciens-mediated plant transformation

GM Trait s :
Glyphosate herbicide tolerance , Coleopteran insect resistance

Commercial Trait:
(Stacked) Herbicide Tolerance + Insect Resistance

Summary of Basic Genetic Modification

Gene Introduced	Gene Source	Product	Function
cry3Bb1	*Bacillus thuringiensis* subsp. kumamotoensis	Cry3Bb1 delta endotoxin	confers resistance to coleopteran insects particularly corn rootworm by selectively damaging their midgut lining
cp4 epsps (aroA:CP4)	*Agrobacterium tumefaciens* strain CP4	herbicide tolerant form of 5-enolpyruvulshikimate-3-phosphate synthase (EPSPS) enzyme	decreases binding affinity for glyphosate, thereby conferring increased tolerance to glyphosate herbicide
dvsnf7	Western Corn Rootworm (Diabrotica virgifera virgifera)	double-stranded RNA transcript containing a 240 bp fragment of the WCR Snf7 gene	RNAi interference resulting to down-regulation of the function of the targeted Snf7 gene leading to Western Corn Rootworm mortality.

OPEN ACCESS Freely available online

PLOS ONE

Ultrastructural Changes Caused by Snf7 RNAi in Larval Enterocytes of Western Corn Rootworm (*Diabrotica virgifera virgifera* Le Conte)

Juraj Kočí[1], Parthasarathy Ramaseshadri[2], Renata Bolognesi[2], Gerrit Segers[2], Ronald Flannagan[2], Yoonseong Park[1]*

1 Department of Entomology, Kansas State University, Manhattan, Kansas, United States of America, 2 Department of Biotechnology, Monsanto Company, Chesterfield, Missouri, United States of America

SCIENTIFIC REPORTS

OPEN

Control of Western Corn Rootworm (*Diabrotica virgifera virgifera*) Reproduction through Plant-Mediated RNA Interference

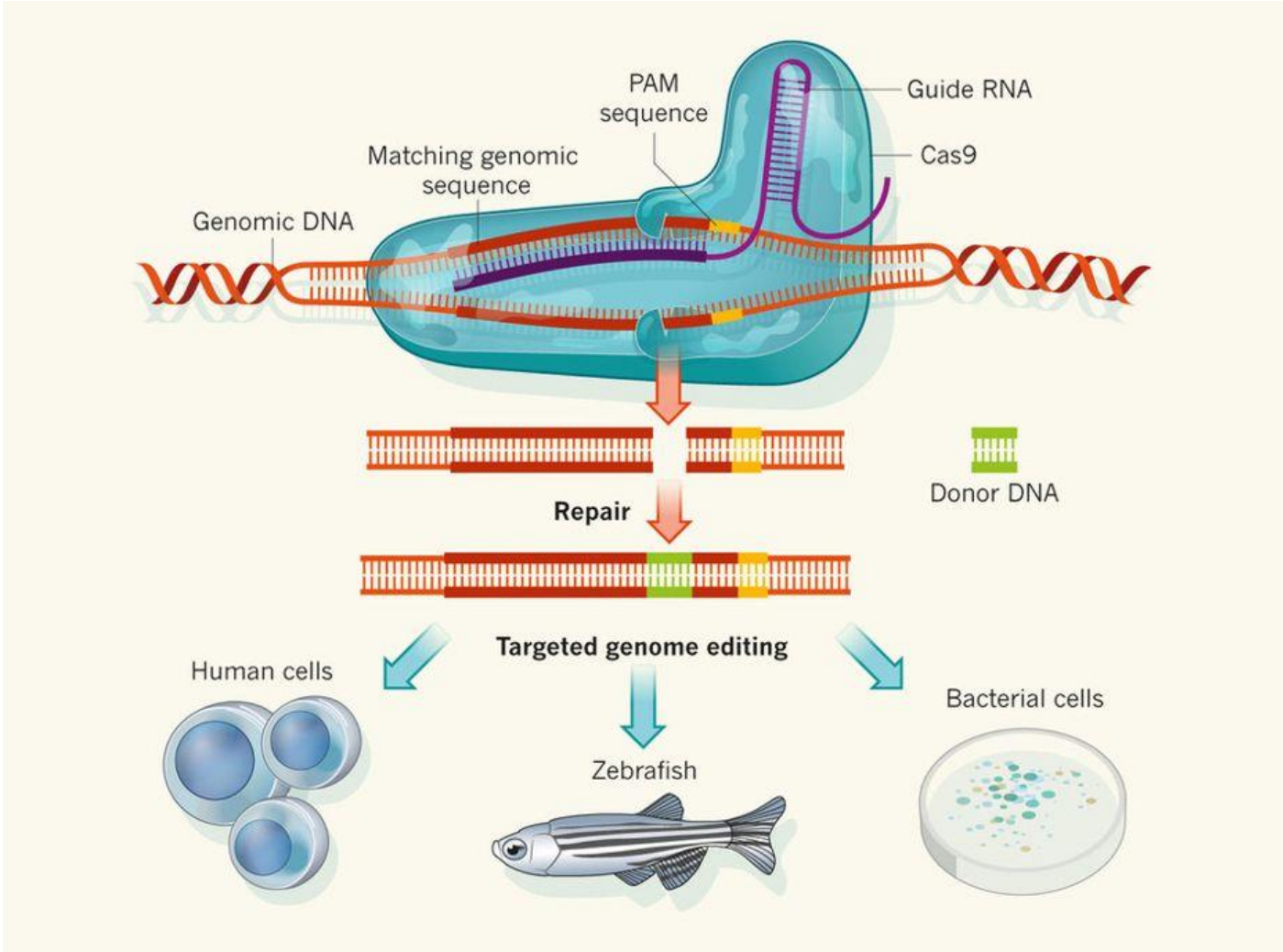
Received: 30 May 2017
Accepted: 13 September 2017
Published online: 03 October 2017

Xiping Niu[1], Adane Kassa[1], Xu Hu[1], Jonathan Robeson[1], Mollie McMahon[1], Nina M. Richtman[1], Joseph P. Steimel[1], Bliss M. Kernodle[1], Virginia C. Crane[1], Gary Sandahl[1], Julie L. Ritland[1], James K. Presnail[1,2], Albert L. Lu[1] & Gusui Wu[1]

RNA interference (RNAi) in transgenic maize has recently emerged as an alternative mode of action for western corn rootworm (*Diabrotica virgifera virgifera*) control which can be combined with protein-based rootworm control options for improved root protection and resistance management. Currently, transgenic RNAi-based control has focused on suppression of genes that when silenced lead to larval mortality. We investigated control of western corn rootworm reproduction through RNAi by targeting two reproductive genes, *dvvgr* and *dvbol*, with the goal of reducing insect fecundity as a new tool for pest management. The results demonstrated that exposure of adult beetles, as well as larvae to *dvvgr* or *dvbol* dsRNA in artificial diet, caused reduction of fecundity. Furthermore, western corn rootworm beetles that emerged from larval feeding on transgenic maize roots expressing *dvbol* dsRNA also showed significant fecundity reduction. This is the first report of reduction of insect reproductive fitness through plant-mediated RNAi, demonstrating the feasibility of reproductive RNAi as a management tool for western corn rootworm.

Edição Genômica – CRISPR/Cas9

Clustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeat = **CRISPR**
CRISPR- **as**sociated = **Cas**



https://www.nature.com/articles/495050a

CRISPR – liberação Europa

nature International weekly journal of science 22/02/17

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Archive > Volume 542 > Issue 7642 > Editorial > Article

NATURE | EDITORIAL

Gene editing in legal limbo in Europe

The European Union is dragging its feet on gene-editing rules and scientists should push the issue.

22 February 2017

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NEWS · 19 JANUARY 2018

European court suggests relaxed gene-editing rules

Judicial opinion says restrictive regulations may not apply to plants and animals bred using CRISPR technique.

THIS WEEK EDITORIALS

Legal limbo

Europe is dragging its feet on gene-editing rules and scientists should push the issue.

Germany is having trouble deciding whether plants that are gene-edited should be regulated as if they were genetically modified (GM). Confused? You're not alone: the issue has split the German government and has left scientists across Europe in limbo.

Plant scientists say that new editing tools, including CRISPR–Cas9, involve no more than making tiny, precisely targeted changes to a gene that are indistinguishable from natural mutations. But opponents say that any form of meddling with genes is potentially perilous.

Germans attach great value to public dialogue. So on 14 February, the Leopoldina, Germany's national science academy, hosted a debate on the issue. Officials from the federal environment ministry and its office for nature protection spoke passionately in favour of ever-greater regulation, whereas the agriculture ministry and the office for consumer protection and food safety disagreed.

The debate might never have taken place if the European Union itself had been able to decide on the issue. But it is habitually paralysed whenever genetic modification is discussed. Two years ago the European Commission requested all member states to hold back on giving the all-clear on gene editing while it considered its options. Now its hand is being forced, ever so slowly, by the referral of the issue by France to the European Court of Justice (ECJ) last October. French non-governmental organizations and trade unions had called on the French state to regulate organisms created through all methods of mutagenesis, including classical methods. They argued that easy-to-use, modern gene-editing tools will encourage large numbers of new plants to be created whose environmental impacts are uncertain. At the Leopoldina meeting, the German office for nature protection aligned itself with this argument.

The ECJ told *Nature* that a decision is not expected before 2018 because the case is so politically sensitive. That's a long time to wait, given that so much is at stake. GM-style regulation is complex and exorbitantly costly. CRISPR technology, although very new, has already led to many gene-edited plants that are ready for outdoor field trials. Such studies should not be held up. Some are intended to shed light on basic plant biology, such as how plants adapt themselves so readily to their environments. Others will determine whether the gene-edited plants have new traits that make them better crops. European scientists are competing with countries such as the United States, where gene-edited products are not considered equivalent to GM products, at least for now. And earlier this month the European Ombudsman stated that the legal limbo does not mean that gene editing should be put on freeze.

Some EU member states are forging their own way through the muddle. In 2015, Sweden decided that the technical and legal issues in favour of non-regulation were crystal clear and told its plant scientists that they could go ahead. It has promised to reverse its position should the EU decide on regulation. Stefan Jansson at Umeå University made such swift progress that he hosted a press lunch last summer where he served up 'tagliatelle with CRISPRy fried vegetables' using ingredients from his garden, including a gene-edited cabbage. According to those present, it was delicious. Last year, Finland chose a similar path, although no field trials have begun.

"CRISPR technology has already led to many gene-edited plants that are ready for outdoor field trials."

Sabres are rattling in the Netherlands, where the parliament's lower house called on the government last week to consider the exclusion of most forms of gene editing from GM regulation. The United Kingdom has maintained silence, and will in any case be under no obligation to follow EU rules once Brexit is complete.

Germany, meanwhile, is being forced to wait for the ECJ decision. In 2015, the consumer protection office told the San Diego-based biotechnology company Cibus that its herbicide-resistant oilseed rape, created using one of the earlier gene-editing technologies, would not need to be regulated in the country. Opponents immediately brought a court case — but that local court is now awaiting ECJ guidance. And during this election year, the German government is highly unlikely to risk making sensitive decisions.

The ECJ has an unfortunate history of delivering highly conservative or scientifically confused verdicts on complex biological issues. In 2011, it outlawed patents that depended even indirectly on human embryonic stem-cell lines, adding that similar basic research was immoral. And in the same year it nearly upended the European honey market with a muddled decision about alleged traces of pollen from GM maize.

Plant scientists should spend the waiting time engaging in public dialogue like the one Germany is leading about the safety and value of gene editing. Reason and science need to prevail this time. ■

CRISPR – liberação Europa

IN FOCUS NEWS

BIOTECHNOLOGY

Gene-edited CRISPR mushroom escapes US regulation

A fungus engineered using CRISPR–Cas9 can be cultivated and sold without oversight.

BY EMILY WALTZ

The US Department of Agriculture (USDA) will not regulate a mushroom that has been genetically modified with the gene-editing tool CRISPR–Cas9, the agency has confirmed. The long-awaited decision means that the mushroom can be cultivated and sold without passing through the agency's regulatory process — making it the first CRISPR-edited organism to receive a green light from the US government.

"The research community will be very happy with the news," says Caixia Gao, a plant biologist at the Chinese Academy of Sciences Institute of Genetics and Developmental Biology in Beijing, who was not involved in developing the mushroom. "I am confident we'll see more gene-edited crops falling outside of regulatory authority."

Yinong Yang, a plant pathologist at Pennsylvania State University (Penn State) in University Park, engineered the fungus — the common white button mushroom (*Agaricus bisporus*) — to resist browning. The effect is achieved by targeting the family of genes that encodes polyphenol oxidase (PPO), an enzyme that causes browning. By deleting just a handful of base pairs in the mushroom's genome, Yang knocked out one of six PPO genes — reducing the enzyme's activity by 30%.

STUART MCCALL/GETTY

The common white button mushroom (*Agaricus bisporus*) has been modified to resist browning.

AGENCY RULES

The mushroom is one of about 30 genetically modified organisms (GMOs) to sidestep the USDA's regulatory system in the past 5 years. In each case, the agency's Animal and Plant Health Inspection Service (APHIS) has said that the organisms — mostly plants — do not qualify as something that the agency must regulate. (Once a crop passes the USDA reviews, it may still undergo a voluntary review by the US Food and Drug Administration.)

Several of the plants that bypassed the USDA were made using gene-editing techniques such as the zinc-finger nuclease (ZFN) and transcription activator-like effector nuclease (TALEN) systems. But until now, it was not clear whether the USDA would give the same pass to organisms engineered with science's hottest tool, CRISPR–Cas9.

Yang first presented the crop to a small group of USDA regulators in October 2015, after being encouraged to do so by an APHIS official. "They were very excited," Yang says: "There was certainly interest and a positive feeling" at the meetings. He followed up with an official letter of enquiry to the agency later that month.

The USDA's answer came this week. "APHIS does not consider CRISPR/Cas9-edited white button mushrooms as described in your October 30, 2015 letter to be regulated," the agency wrote to Yang on 13 April.

> ***"I am confident we'll see more gene-edited crops falling outside of regulatory authority."***

Yang's mushroom did not trigger USDA oversight because it does not contain foreign DNA from 'plant pests' such as viruses or bacteria. Such organisms were necessary for genetically modifying plants and fungi in the 1980s and 1990s, when the US government developed its framework for regulating GMOs. But newer gene-editing techniques that do not involve plant pests are quickly supplanting the old tools.

The United States is revamping its rules for regulating GMOs, which collectively are known as the Coordinated Framework for Regulation of Biotechnology. To that end, the US National Academies of Sciences, Engineering and Medicine have convened a committee that is charged with predicting what advances will be made in biotechnology products over the next five to ten years. It will hold its first meeting on 18 April.

In the meantime, Yang is mulling over whether to start a company to commercialize his modified mushroom. Fruits and vegetables that resist browning are valuable because they keep their colour longer when sliced, which lengthens their shelf life. In the past 18 months, biotech companies have commercialized genetically engineered non-browning apples and potatoes.

"I need to talk to my dean about that. We'll have to see what the university wants to do next," says Yang about the prospect of bringing his mushroom to market. But he notes that in September 2015, Penn State filed a provisional patent application on the technology. ■

21/04/2016

NEWS IN FOCUS

CHRIS RATCLIFFE/BLOOMBERG/GETTY

In the EU, gene-edited crops and food will be treated in the same way as genetically modified organisms.

GENE EDITING

EU law deals blow to CRISPR crops

Top court's ruling threatens research on gene-edited plants.

BY EWEN CALLAWAY

Gene-edited crops should be subject to the same stringent regulations that govern conventional genetically modified (GM) organisms, Europe's highest court ruled on 25 July.

The decision, handed down by the Court of Justice of the European Union (ECJ) in Luxembourg, is a major setback for proponents of gene-edited crops, including many scientists. They had hoped that organisms created using relatively new, precise gene-editing technologies such as CRISPR–Cas9 would be exempted from existing European law, which has limited the planting and sale of GM crops.

Instead, the ECJ ruled that crops created using these technologies are subject to a 2001 directive. That law was developed for older breeding techniques, and it puts high hurdles in the way of developing GM crops for food.

"It is an important judgment, and it's a very rigid judgment," says Kai Purnhagen, a legal scholar at Wageningen University and Research in the Netherlands who specializes in European and international law. "It means for all the new inventions, such as CRISPR-Cas9 food, you would need to go through the lengthy approval process of the European Union."

That is likely to hinder investment in crop research using these tools in the EU, says Purnhagen. "From a practical perspective, I don't think this will be at all of interest for business. So they will move somewhere else," he says.

The ruling is "tremendously disappointing", says Nigel Halford, a crop geneticist at Rothamsted Research in Harpenden, UK. "It's a real hit to the head," he says. Gene-editing techniques will still be used as a research tool for developing crops, he adds, but he doubts that companies in Europe will have much appetite to develop them. "They are not going to invest in a technology they see not having any commercial application," Halford says.

Environmental organization Friends of the Earth in Amsterdam, meanwhile, applauded the court's decision in a statement. It also called for all products made through gene editing to be regulated, assessed for their health and environmental impacts, and labelled.

DNA CHANGES

The 2001 EU directive behind the ECJ's decision concerns the intentional release of GM organisms into the environment — and was aimed at species into which entire genes, or long stretches of DNA, had been inserted. The law exempts organisms whose genomes were modified using 'mutagenesis' techniques, such as irradiation, which introduce changes to an organism's DNA but don't add foreign genetic material.

In 2016, the French government asked the ECJ to interpret the directive in light of plant-breeding techniques that have since emerged.

Many plant breeders and scientists contend that gene-editing techniques such as CRISPR–Cas9 should be considered mutagenesis, just like irradiation, and thus be exempt from the directive, because they can involve changes to DNA and not the insertion of foreign genes. But people opposed to GM organisms contend that the deliberate nature of alterations made through gene editing means that they should fall under the directive.

In January, an advocate-general with the court, Michal Bobek, issued a 15,000-word opinion that both sides claimed was partly in their favour. He said that gene-edited crops do constitute GM organisms under the original directive, but also that species modified using technologies discovered since 2001 — such as those used for gene editing — could be exempted, as long as they don't contain DNA from other species, or artificial DNA.

But in its ruling, the ECJ determined that only mutagenesis techniques that have "conventionally been used in a number of applications and have a long safety record are exempt from those obligations". Organisms made using mutagenesis techniques developed after 2001 — including gene editing — are not exempt from the directive.

NO INCENTIVE

"This will have a chilling effect on research, in the same way that GMO legislation has had a chilling effect for 15 years now," says Stefan Jansson, a plant physiologist at Umeå University in Sweden. Gene-edited crops will not vanish from European research labs, but he worries that the funding to develop them could dry up. "If we cannot produce things that society finds helpful, then they will be less likely to fund us."

Jansson also has practical concerns about the ruling. He developed a 'CRISPR cabbage' that he has consumed, and which was growing in his home garden as he spoke to *Nature*. "I took a photo yesterday, and I took another after the ruling. It's still the same plant. Yesterday it wasn't a GMO, and now it's a GMO. I'm a bit curious what I have to do. Do I have to remove it?"

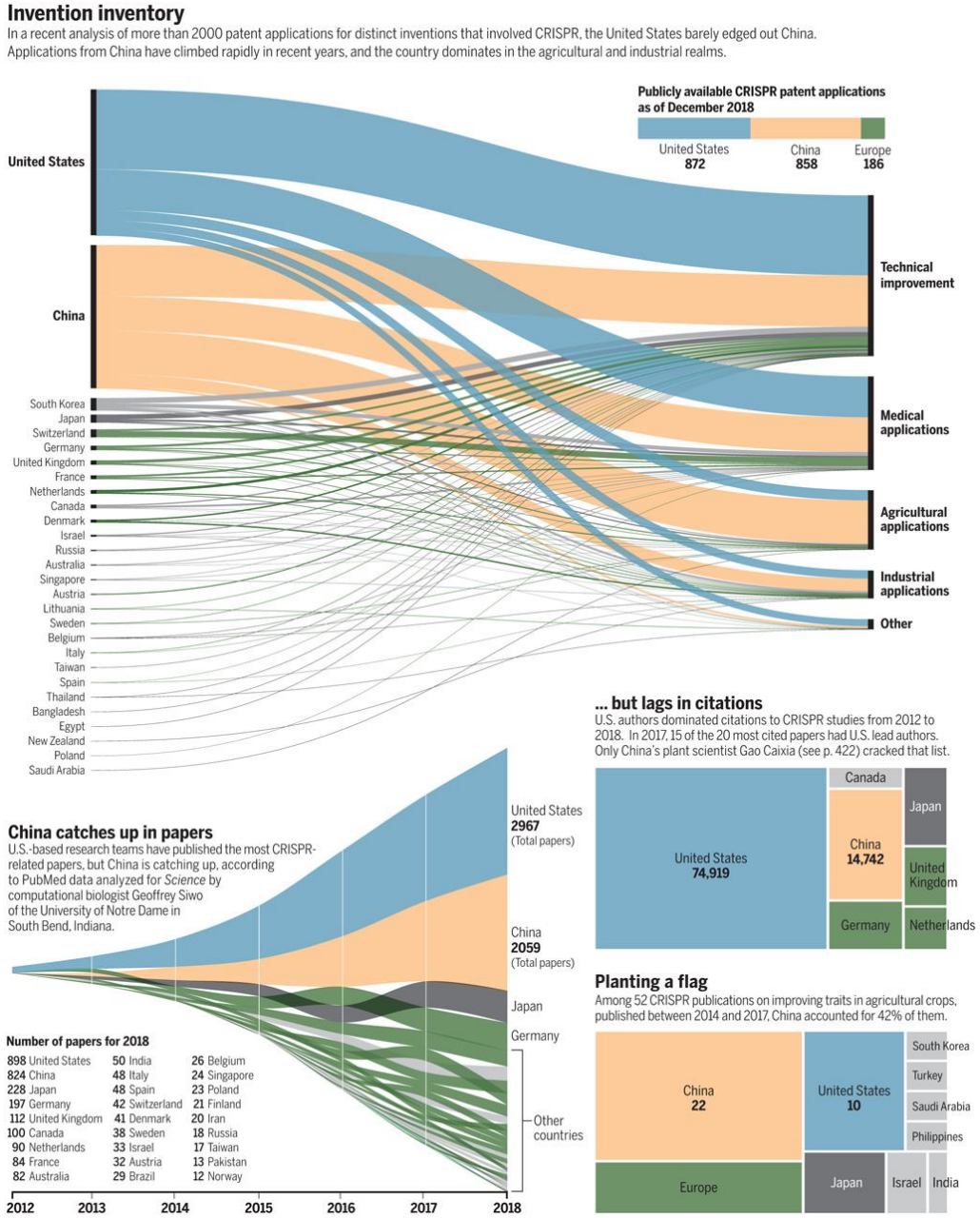
Purnhagen says that the ruling leaves open a possible loophole, whereby if scientists can prove that gene-editing techniques are as safe as mutagenesis methods already exempt from the law, such as irradiation, the new techniques, too, could earn an exemption.

But he doubts that researchers and businesses developing gene-edited crops will hold out hope. "I can't see CRISPR–Cas9 and all these new technologies will be profitable in the European Union. I can't see this happening. I think this research will move somewhere else." ■

02/08/2018

CRISPR na China

02/08/2019



CRISPR

MENU

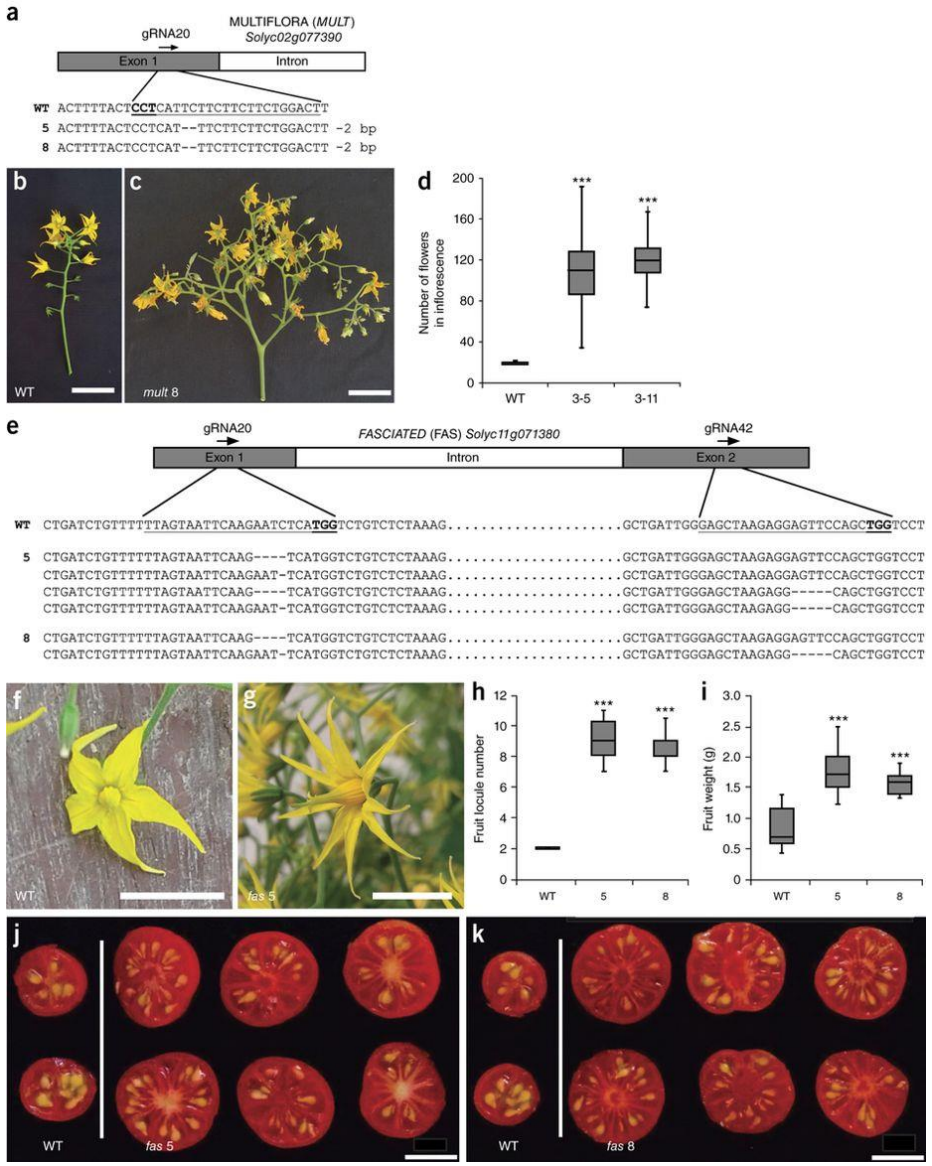
nature biotechnology

Article | Published: 01 October 2018

De novo domestication of wild tomato using genome editing

Agustin Zsögön, Tomáš Čermák, Emmanuel Rezende Naves, Marcela Morato Notini, Kai H Edel, Stefan Weinl, Luciano Freschi, Daniel F Voytas, Jörg Kudla ✉ & Lázaro Eustáquio Pereira Peres ✉

Nature Biotechnology **36**, 1211–1216 (2018) | Download Citation ⬇



Salmão Atlântico Transgênico

SCIENTIFIC AMERICAN

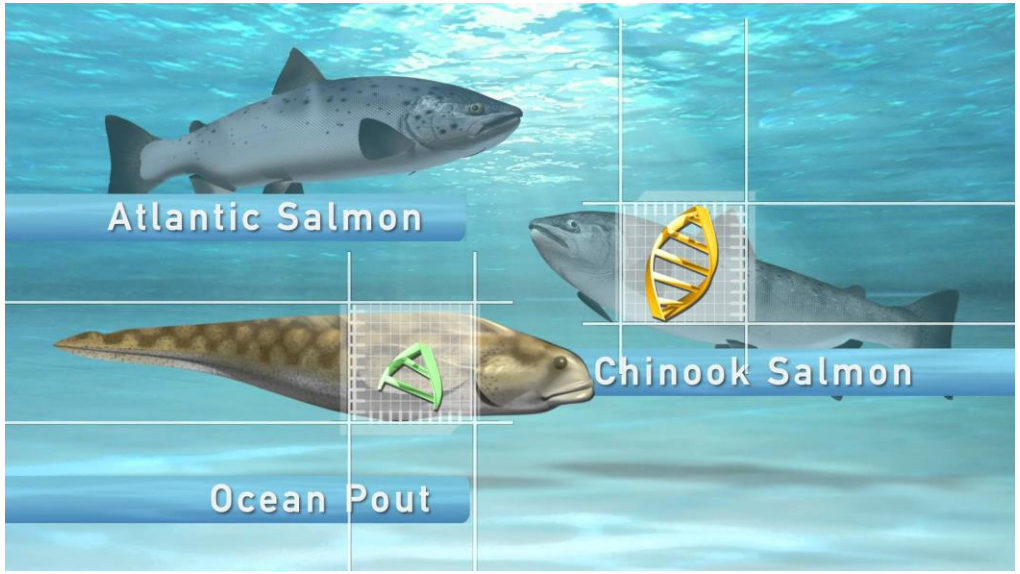
nature

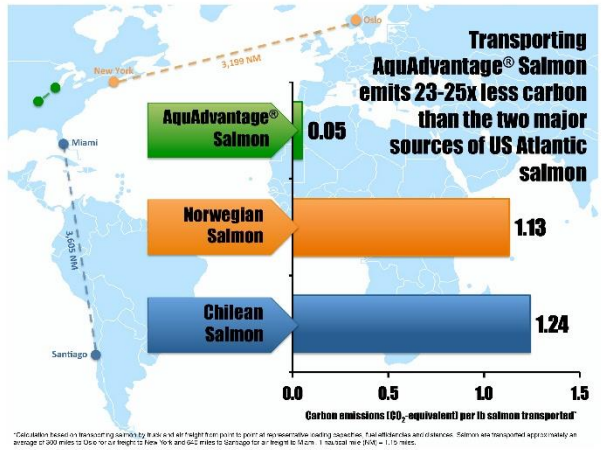
MEDICAL & BIOTECH

First Genetically Engineered Salmon Sold in Canada

US firm AquaBounty Technologies says that its transgenic fish has hit the market after a 25-year wait

By Emily Waltz, Nature on August 7, 2017





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Estudo Dirigido

1. O que é genética molecular e biotecnologia?
2. Importância e aplicação da genética molecular na agricultura
3. Diferença entre organismo geneticamente modificado (OGM) e transgênico
4. Papel da CTNBio na legislação de OGMs

Leitura recomendada (*site* stoa)

ISAA – 2017
OGM – Floresta
OGM - Agronomia