“Bio-Medical Technology Foresights”

Spring 2010

Special Lectures on Agricultural Biotechnology

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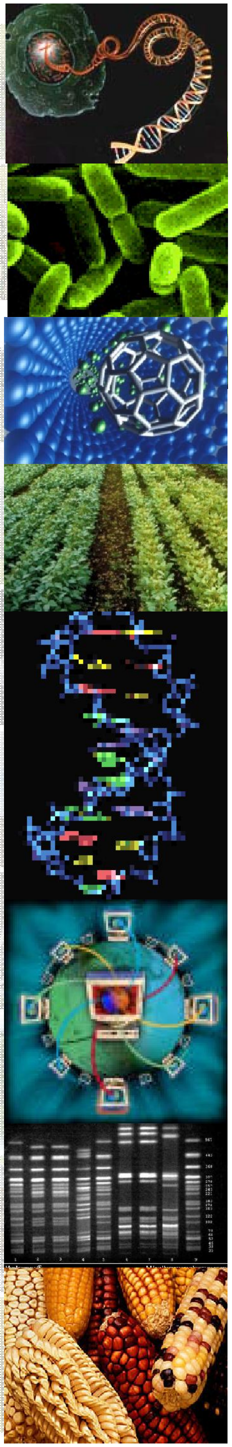
Embrapa Labex Korea
Suwon - Republic of Korea



Bottom line…

No single technology will do the trick…

Mix of Technologies and Strategies…

Technology

Consolidated Institutions

Policies

Capacity Building

Convergent Agendas

Foresight and Vision

Bottom line…

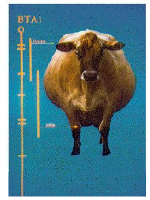
Modern Biotechnology is an important alternative…

Agricultural Biotechnology

GENETIC ENGINEERING

TRANSGENIC TECHNOLOGY

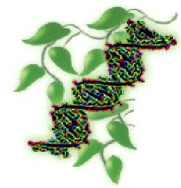
Biotic Stress Tolerance
Abiotic Stress Tolerance
Quality/Functionality
New Bioproducts



MOLECULAR MARKERS

MOLECULAR MAPS

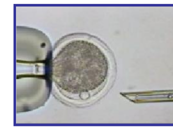
Gene/Trait Mapping
Genetic Resources Charc.
Function Characterization
Molecular Breeding



GENOMIC SCIENCES

GENOMICS
PROTEOMICS

Coffee
Eucalyptus
Banana/Rice
Bovine & Others



ADV. ANIMAL PRODUCTION

CLONING
IN-VITRO FERTILIZATION

Animal Breeding
GR Conservation
Germplasm Enhancement
Biofactories

GENETICS, PHYSIOLOGY, TISSUE CULTURE, BIOINFORMATICS, BIOSAFETY, ETC...

Agricultural Biotechnology

GENETIC ENGINEERING

TRANSGENIC TECHNOLOGY

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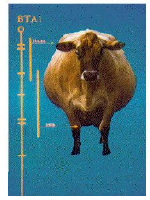
Abiotic Stress Tolerance
Quality/Functionality
New Bioproducts

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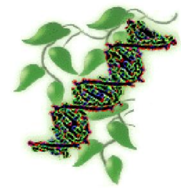

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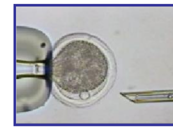


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GENETICS, PHYSIOLOGY, TISSUE CULTURE, BIOINFORMATICS, BIOSAFETY, ETC...

The Timeline of Biotechnology

1859 - Charles Darwin publishes “The Origin of Species”, establishing the Theory of Evolution and its mechanism, natural selection...

1865 - The age of genetics begins when Gregor Mendel, studying inherited traits of pea plants. Outlines the basic laws of heredity that still hold true today for all organisms...

1910 - Thomas Hunt Morgan proposes the chromosomal theory of inheritance. Establishes that genes are located on chromosomes…

1941 - One gene, one enzyme: George Beadle and Edward Tatum establish that one gene makes one enzyme or protein...

1952 - Martha Chase and Alfred Hershey demonstrate that DNA is the substance that transmits inherited characteristics from one generation to the next...

The Timeline of Biotechnology

1953 - James Watson and Francis Crick deduce the structure of the DNA molecule - a double helix...

1967 – Genetic code cracked. Har Khorana, Robert Holley and Marshall Nirenberg decipher the mechanism that enables DNA to be translated into proteins...

1968 - Stanley Cohen determines that bacteria carry genes for antibiotic resistance on plasmids, extrachromosomal circles of DNA...

1970 - Restriction enzymes discovered. In the ensuing years, hundreds of different restriction endonucleases are found that cleave DNA at specific sites...

1972 - Recombinant DNA technology begins. Stanford biochemist Paul Berg splices together two blunt-ended fragments of DNA from the SV40 virus and E. coli, creating recombinant DNA...

The Timeline of Biotechnology

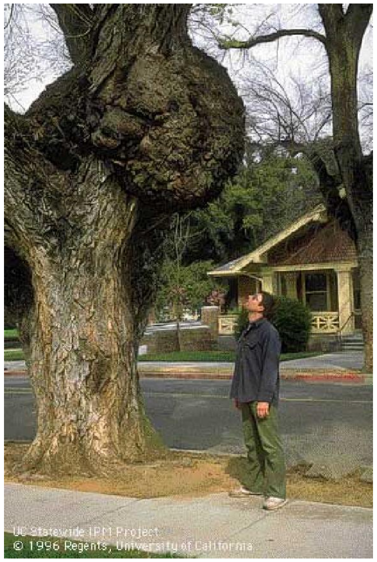
1972 - Sticky ends of "restricted" DNA can be linked together or "spliced" with DNA ligases. Insertion of desired DNA into bacterial plasmids - the basis of the biotechnology industry...

1975 - Asilomar Conference held in Pacific Grove CA. A conference on recombinant DNA technology with over 100 other scientists to discuss what they knew (and didn't know) about recombinant DNA and to draw up guidelines that would let the science proceed without undue risk. The scientists agree to suspend research involving recombinant DNA technology research until potential risks could be evaluated.

1975 - DNA sequencing developed. Walter Gilbert and Allan Maxam of Harvard University and Fred Sanger of Cambridge University simultaneously come up with two techniques for determining the exact sequence of bases that make up a gene.

1980 - The Birth of Plant Biotech…

Genetic Engineering
Learning with nature….

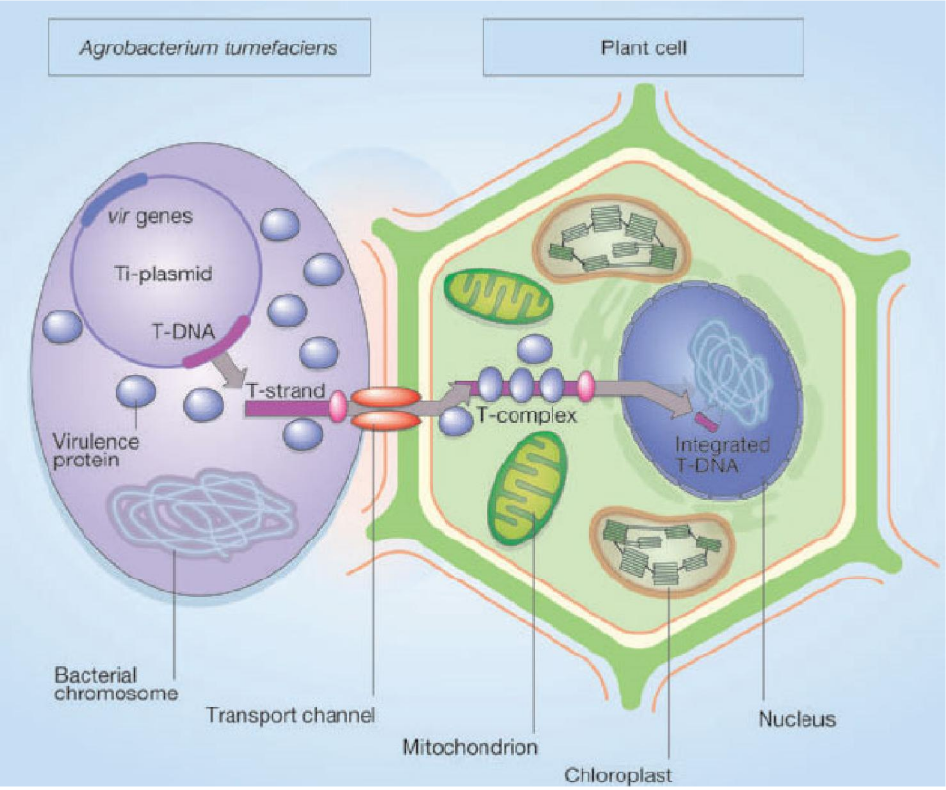


http://www.ag.ndsu.edu/pubs/plantsci/crops/a1219-3.jpg

http://www.bio.uio.no/plfys/haa/gen/gmo.htm

Agrobacterium tumefaciens is the causal agent of crown gall disease (that lead to formation of tumors) in plants.

Symptoms are caused by the insertion of a small segment of DNA (known as the T-DNA, for 'transfer DNA') into the plant cell, which is incorporated at a semi-random location into the plant genome.



Source: http://www.biotecheambiente.com/

Genetic Engineering

1980: First transgenic plants.

Several research groups used *Agrobacterium tumefaciens* to insert a Ti plasmid DNA into tobacco. Showed that the bacterium could be used as a gene vector, creating tobacco plants that were kanamycin resistant.

Doors opened for plant genetic engineering

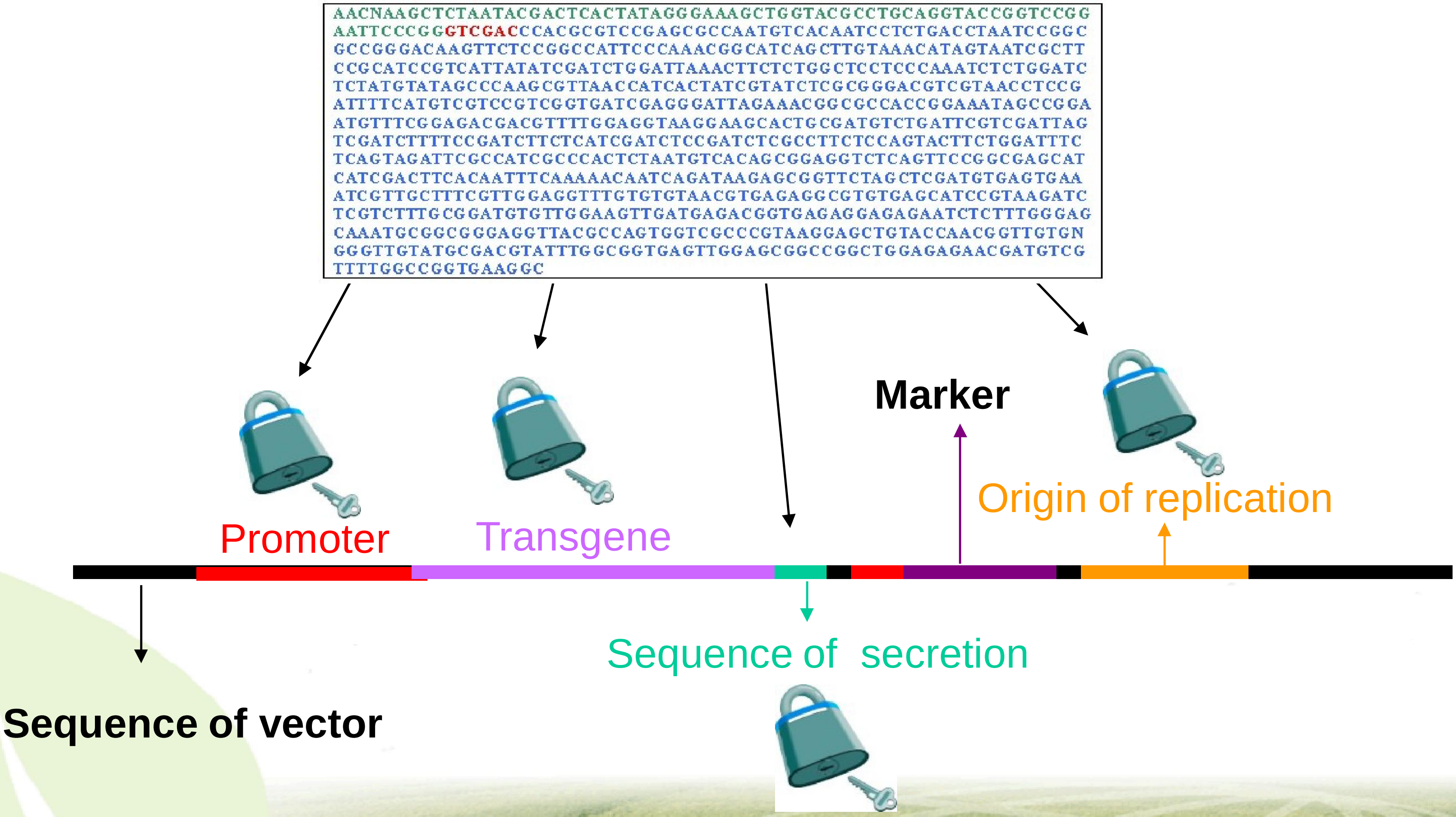
Find the genes for some specific traits

Place genes in organisms where they did not originate

Get those genes to work in their new location

Genetic Engineering

“Building” and transferring genes between organisms



Genetic Engineering

Advances in processes and sophistication of tools

Genetic Engineering

Basic Principles

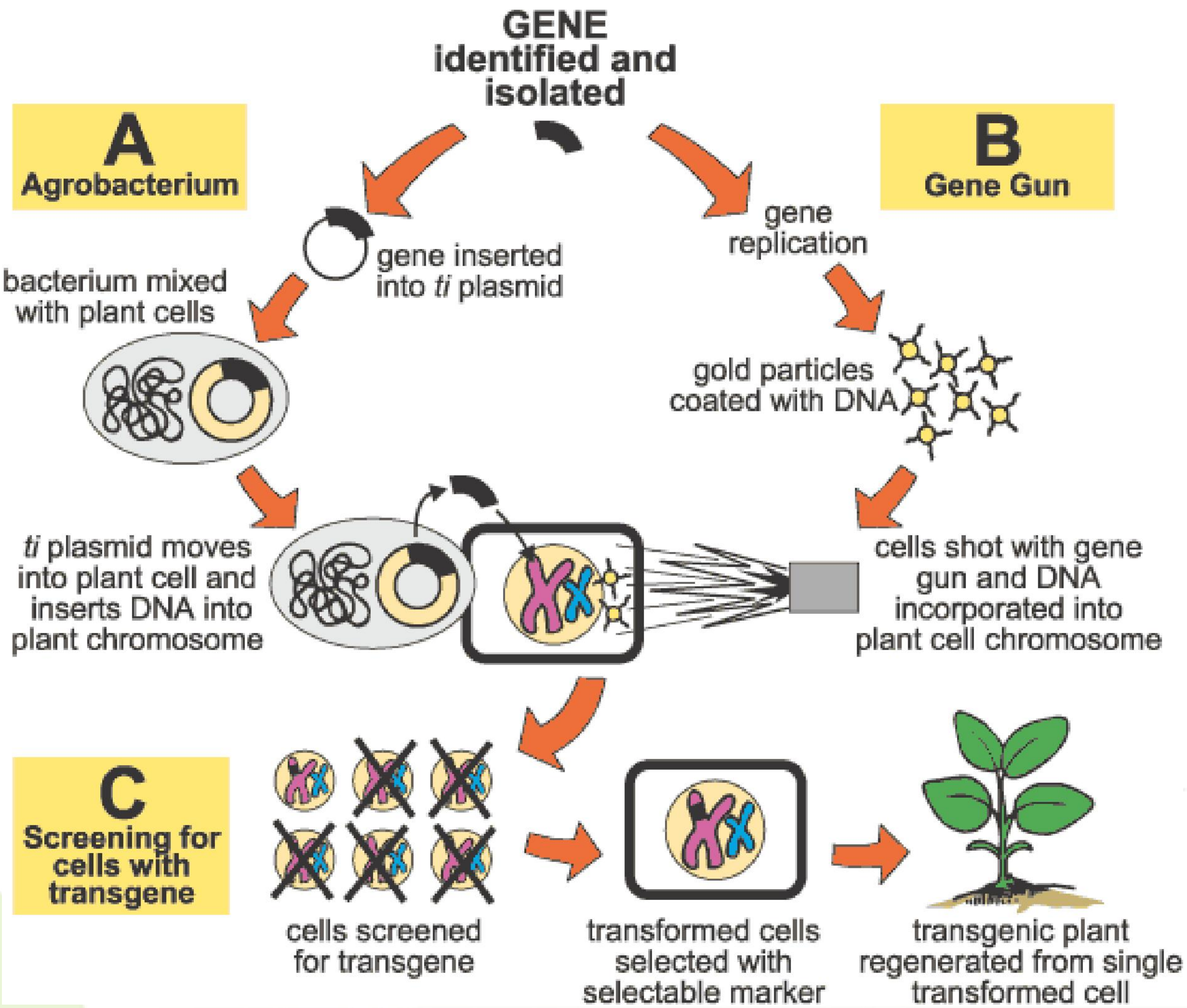
Genetic transformation requires a:

1) Vector or way to transfer the genetic material into the cell;

2) Means of screening for transformed cells;

3) Means of regenerating the organism from the individual cell that is transformed.

Genetic Engineering



Source: A Basic Primer on Biotechnology , http://www.ag.ndsu.edu

Genetic Engineering – Traits Targeted

<u>Agronomic Traits</u> – (*input traits*)

- **Biotic Stress**
  - Insect Resistance
  - Disease Resistance - Viral, Bacterial, Fungal, Nematode
  - Weed- herbicide tolerance
- **Abiotic Stress**
  - Drought, Cold, Heat, Poor soils
- **Yield**
  - Nitrogen Assimilation, Starch Biosynthesis, O2 Assimilation

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Quality Traits (*output traits*)

- Processing
- Shelf-life
- Reproduction: sex barriers, male sterility, seedlessness
- Nutrients (Nutraceuticals)
  - Macro: Protein, Carbohydrates, Fats
  - Micro: vitamins, antioxidants, minerals, isoflavonoids, glucosinolates, phytoestrogens, lignins, condensed tannins
  - Anti-nutritionals: Phytase, Toxin removal
- Taste
- Architecture
- Fiber
- Ornamentals: color, shelf-life, morphology, fragrance

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Novel Crop Products

- Oils
- Proteins: nutraceuticals, therapeutics, vaccines
- Polymers

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Novel Crop Products

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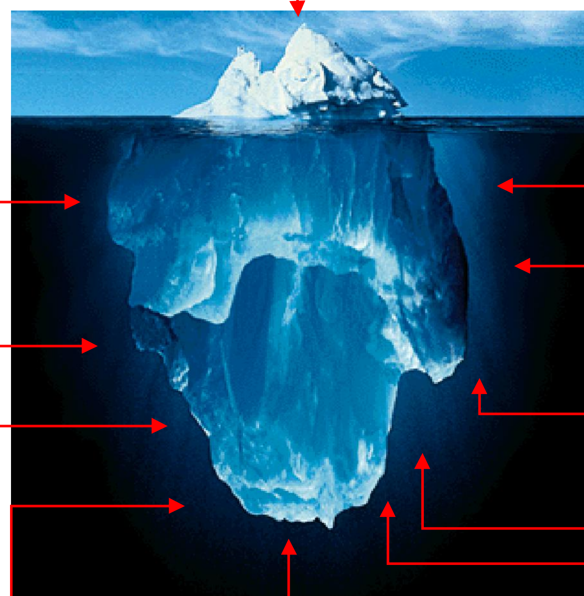
Renewable resources

- Biomass conversion, feedstocks, biofuels

Genetic Engineering – Traits Targeted

Very few products available commercially

Herbicide tolerance and insect resistance



drought

Soil acidity

Nutritional Quality

Nutrient use efficiency

Biofactories

New functionalities

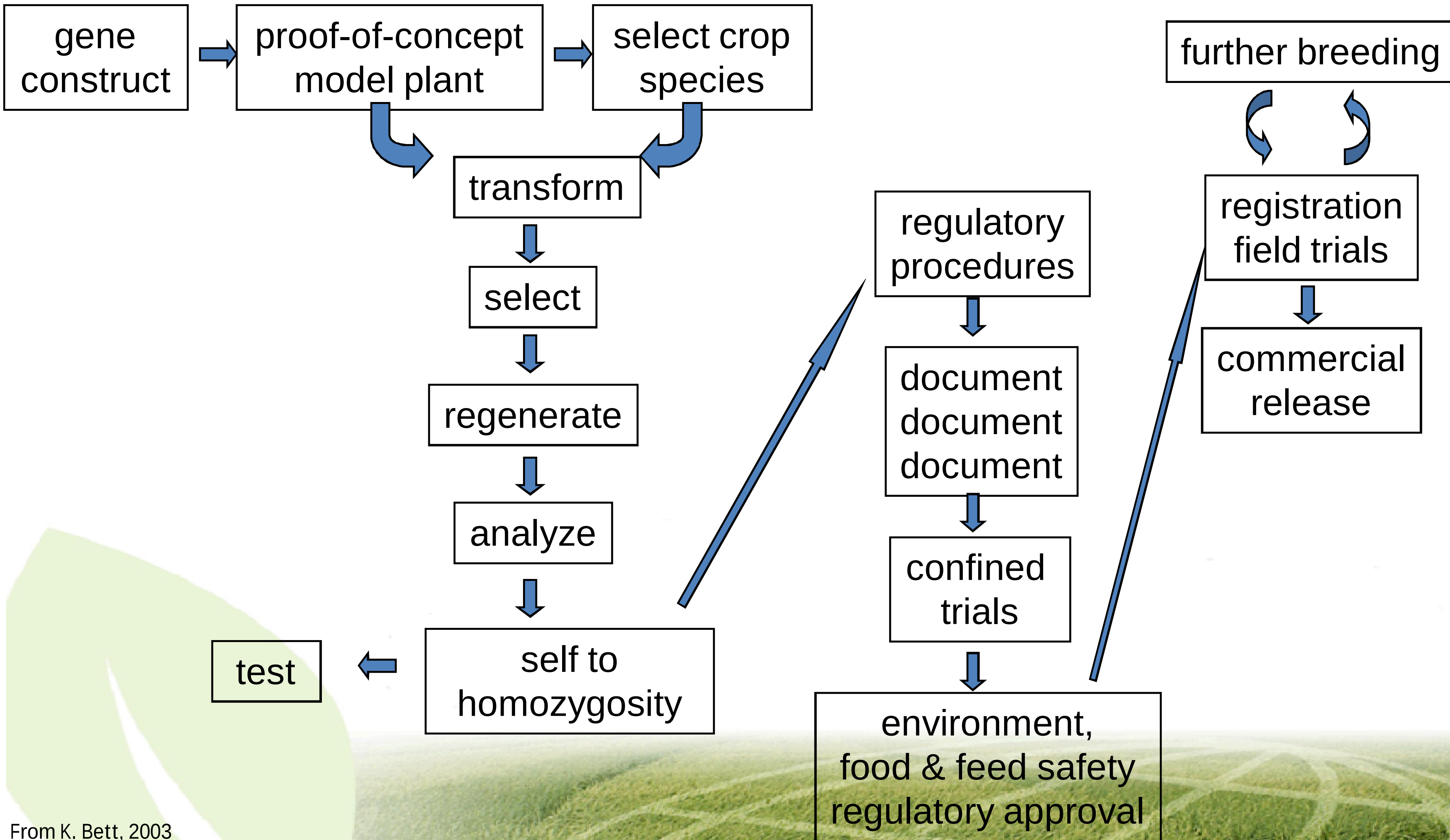
Changed morphology

New compounds

Biosensors

Possibilities not yet anticipated

Genetic Engineering
From Concept to Products



From K. Bett, 2003

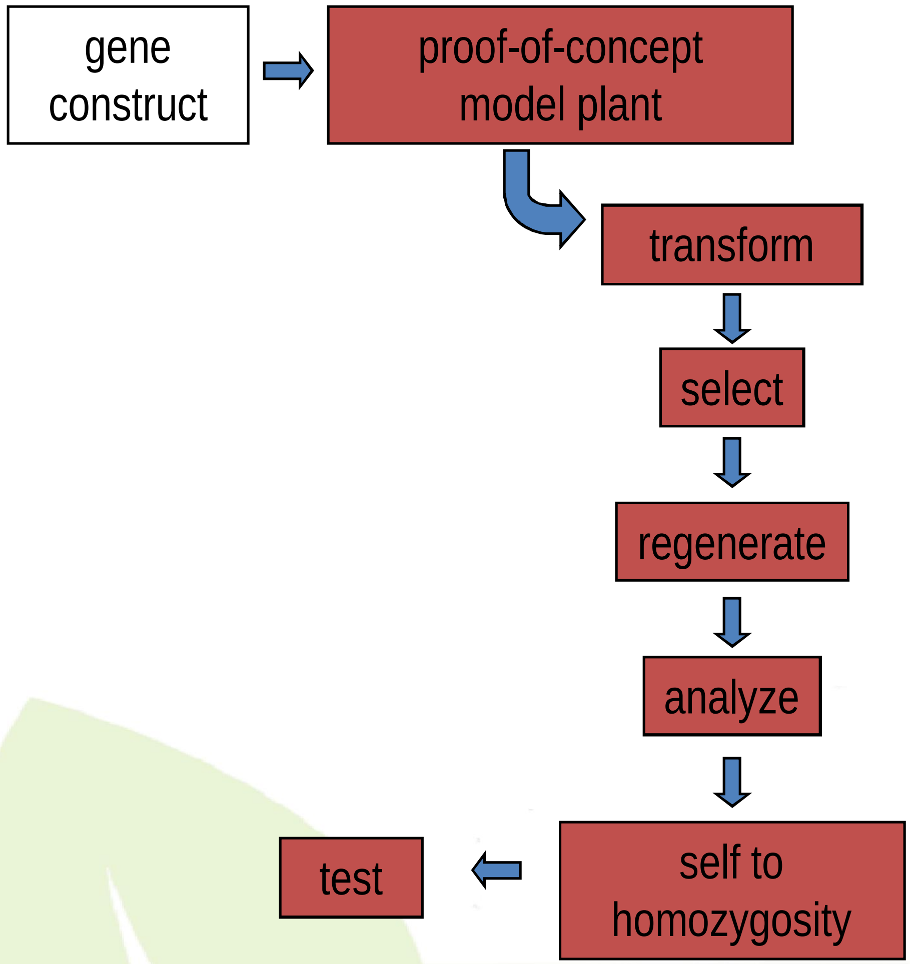
Genetic Engineering
From Concept to Products

gene construct

- gene of interest
- promoter
  - constitutive
  - tissue-specific
  - temporal
- selectable marker
- enhancer elements

From K. Bett, 2003

Genetic Engineering
From Concept to Products



- Agrobacterium
- biolistics

- using selectable markers
  - antibiotic resistance
  - herbicide resistance

- copy number
- presence of gene activity
- phenotype

From K. Bett, 2003

Genetic Engineering

From Concept to Products

Regulatory Procedures

↓

document
document
document

↓

confined trials

↓

environment, food & feed safety regulatory approval

- scientific and common names
- description of life cycle and habitats
- where is it a known pest?
- tendency towards weediness & dormancy
- mechanism of pollen, seed and vegetative dispersal
- mechanism of out-crossing
- information of known toxins

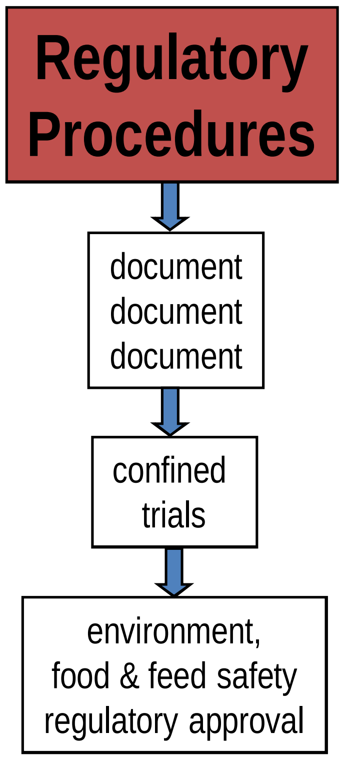
- map + description of biodiversity at site
- isolation distances; border/guard rows
- prevention of pollen movement
- info on pesticide use, harvest methodology, post-harvest use of land
- contingency plan in case of accidental release
- monitoring during and post trial

- description of trait and method of modification
- description of expression
  - tissue specificity
  - developmental stage
  - stability
- confirm no change to dormancy or weediness
- toxicity, allergenicity, nutritional studies
- fate of gene product when ingested

From K. Bett, 2003

Genetic Engineering
From Concept to Products

up to 90% of the cost of getting the product to market can occur at these regulatory steps



From K. Bett, 2003

Genetic Engineering
Herbicide Tolerant Crops

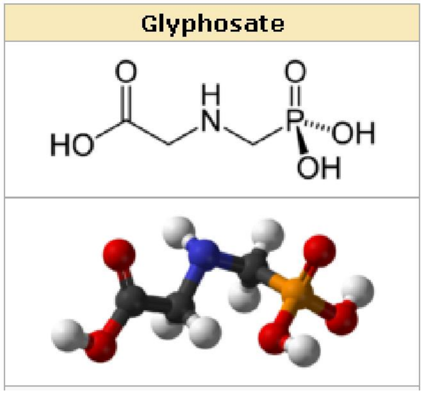
Herbicides target specific enzymes or processes

- Target is usually specific and key to plant metabolism.
- Engineering resistance involves modification of the target enzyme or introduction of an enzyme that detoxifies the herbicide.
- The modified or introduced enzyme can usually be obtained from bacteria, fungi, or other plants.

Genetic Engineering
Herbicide Tolerant Crops

The Case of Roundup Ready™

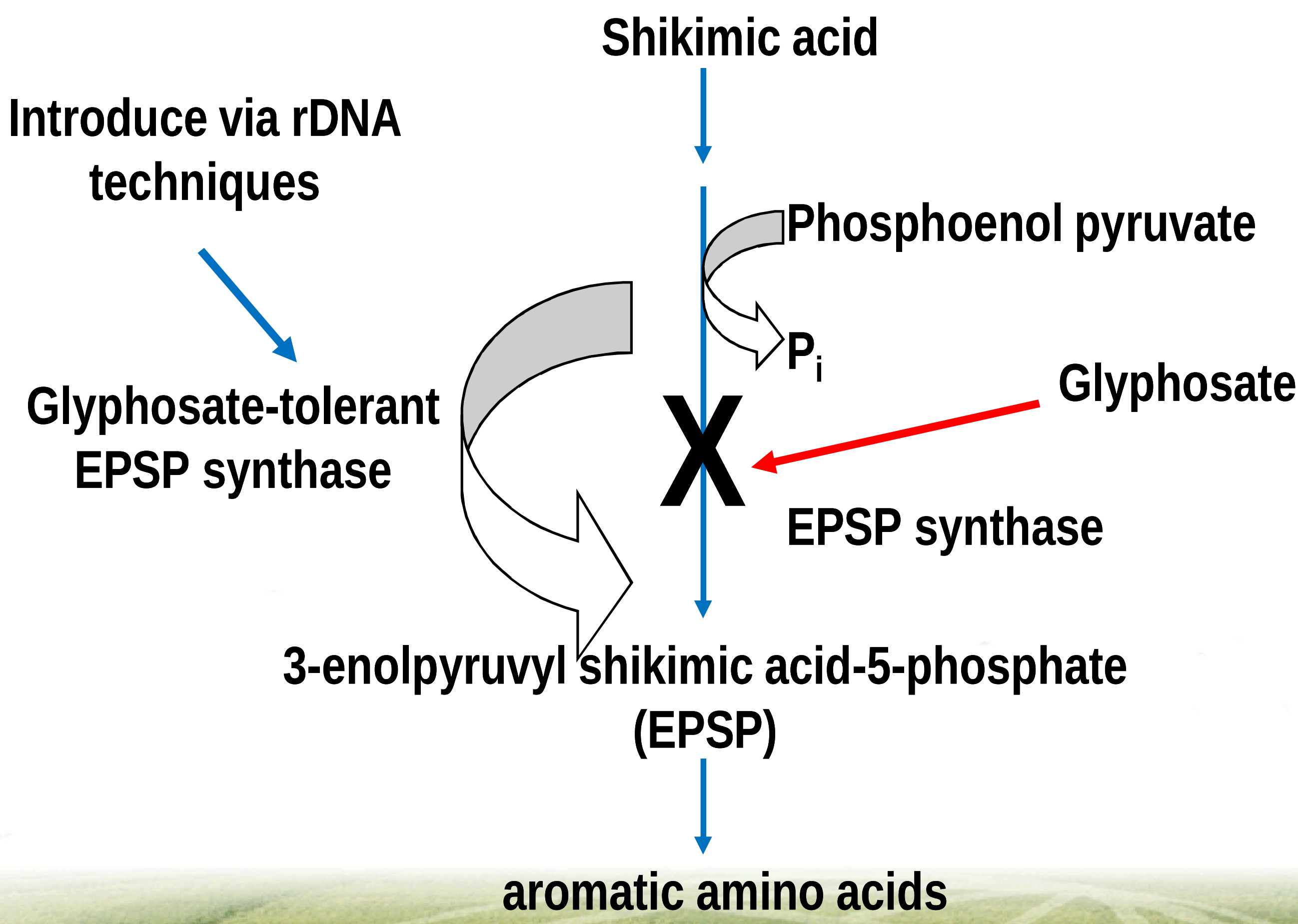
Genetic engineered crops resistant to the molecule Glyphosate (N-(phosphonomethyl) glycine), that is a broad-spectrum systemic herbicide used to kill weeds. It is typically sprayed and absorbed through the leaves. Initially patented by Monsanto Company in the 1970s under the tradename Roundup, its U.S. patent expired in 2000.



http://www.answers.com/topic/glyphosate

Genetic Engineering
Herbicide Tolerant Crops

The Case of Roundup Ready™



Genetic Engineering
Herbicide Tolerant Crops

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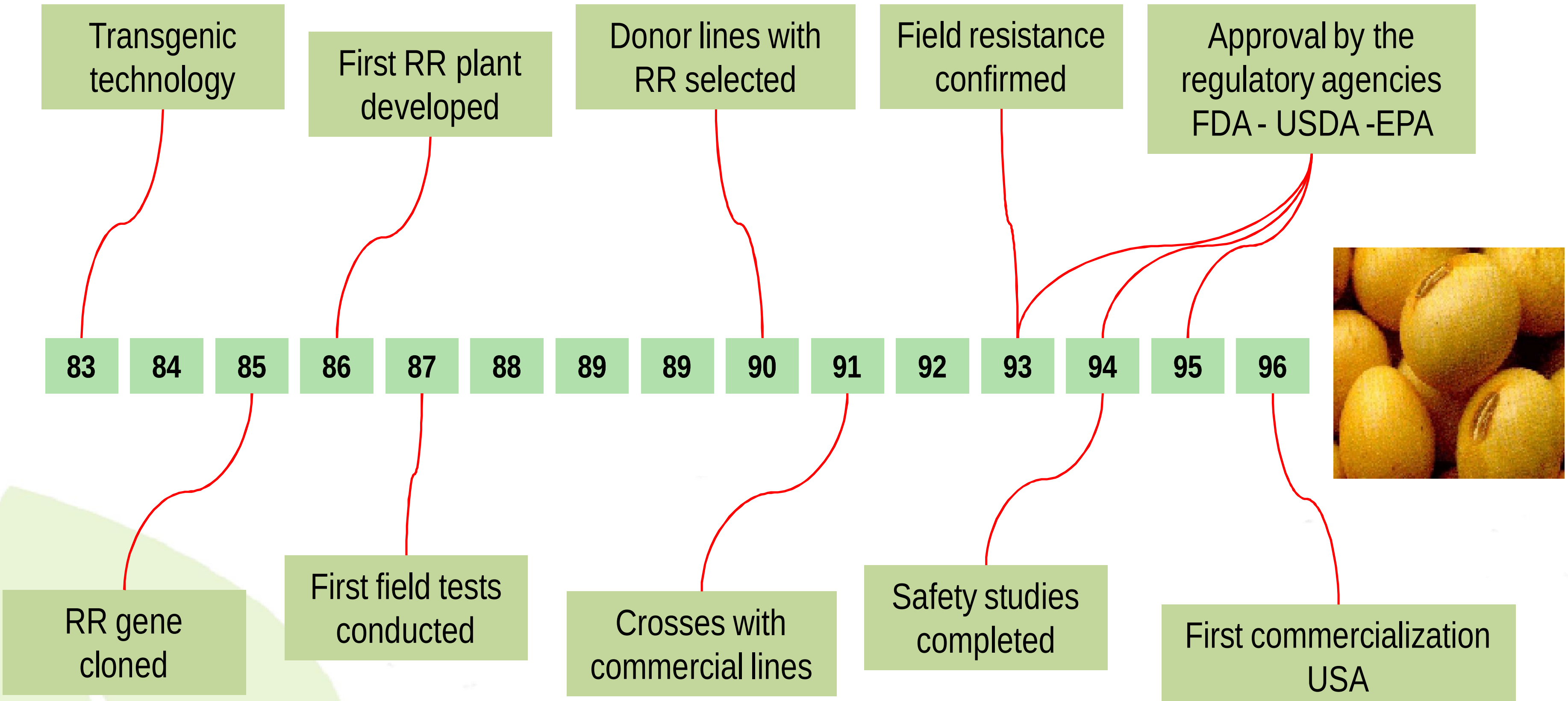
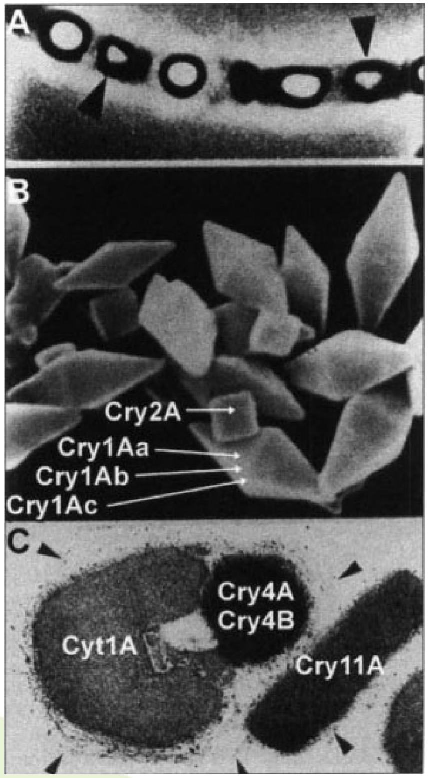


Genetic Engineering

Insect-Resistant Crops – Bt Technology



Sporulated culture and parasporal bodies of *Bacillus thuringiensis (Bt)*.

Identify specific Bt strain active on target pest.

↓

Isolate DNA coding for *cry* protein from bacteria.

↓

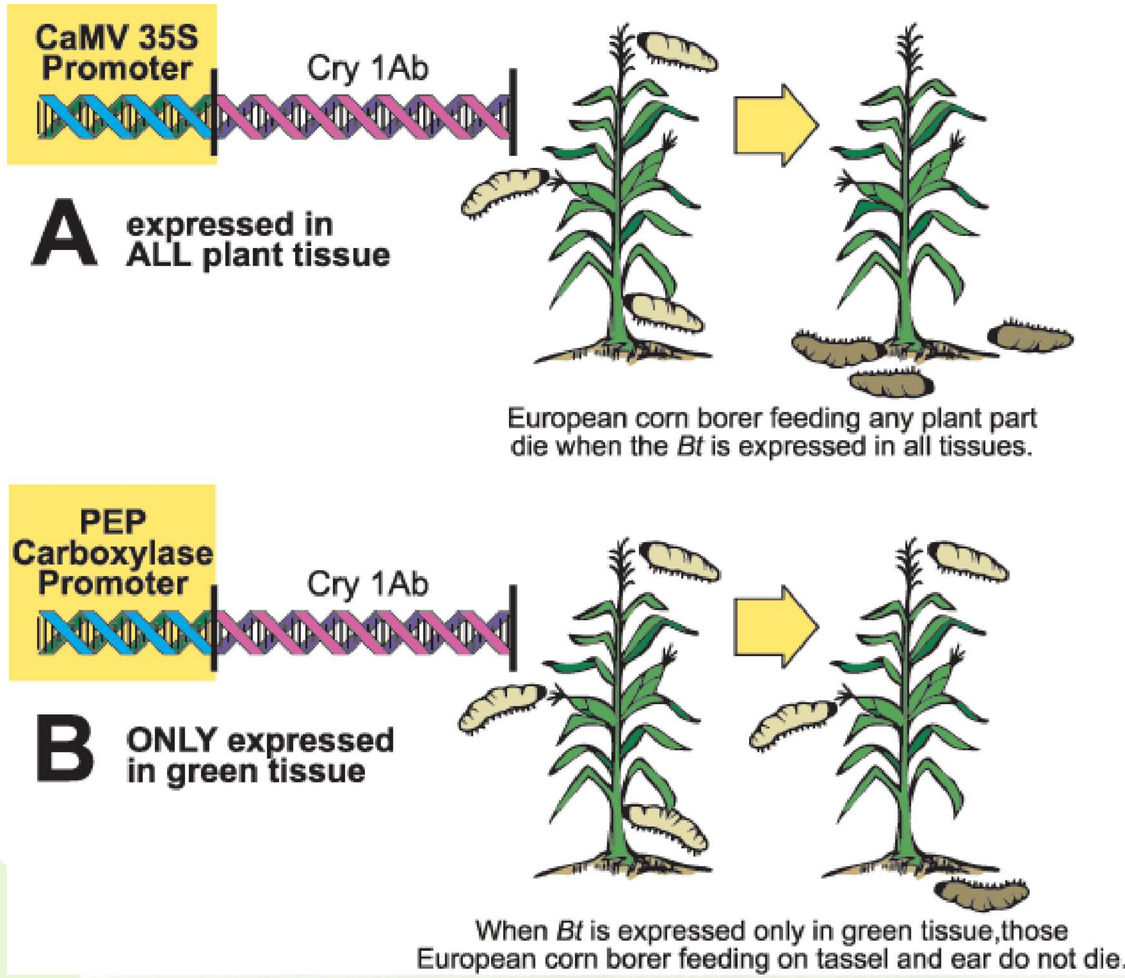
Introduce DNA coding for *cry* protein into crop plant.

↓

Test for expression, stability, effectiveness and safety.

Source: B.A. Federici, UC Riverside, USA. http://tinyurl.com/25uj2qc

Genetic Engineering
Insect-Resistant Crops



Source: A Basic Primer on Biotechnology , http://www.ag.ndsu.edu

Genetic Engineering
Insect-Resistant Crops

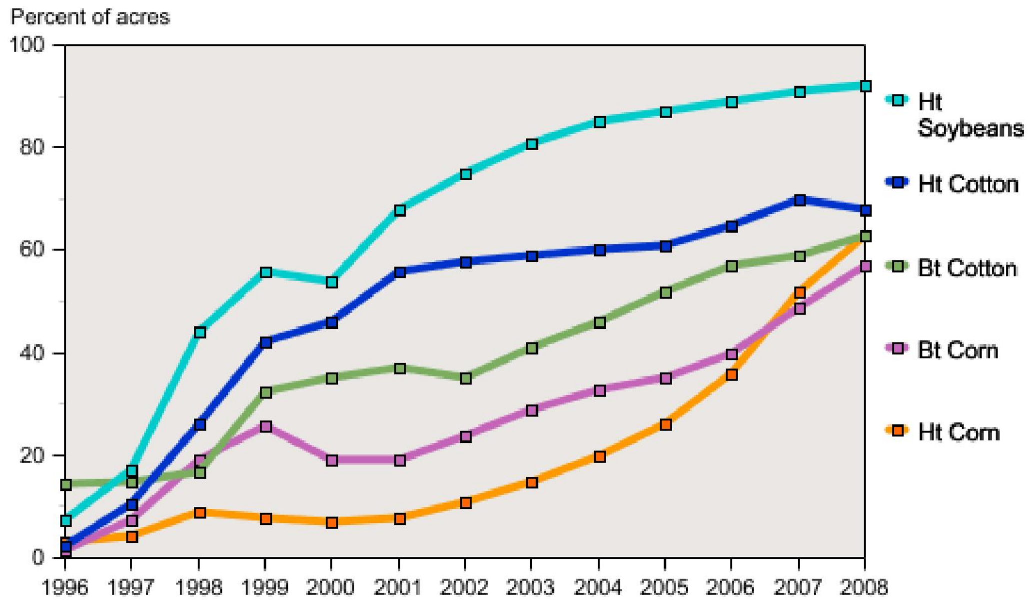
Reduce applications of insecticides to control pests.

Reduce occurrence of secondary toxins (e.g., reduced fumonisin in Bt corn).

Preserve beneficial insects.

Adoption of GM Technology

Adoption of Genetically Modified Crops in the U.S.



Source: Adoption of Genetically Engineered Crops in the U.S., data obtained by USDA's National Agricultural Statistics Service (NASS) in the June Agricultural Survey for 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, and 2008.

Adoption of GM Technology

Country Areas Cultivated with GM Crops in 2008

Rank	Country	Area (million hectares)	Biotech Crops
1*	USA*	62.5	Soybean, maize, cotton, canola, squash, papaya, alfalfa, sugarbeet
2*	Argentina*	21.0	Soybean, maize, cotton
3*	Brazil*	15.8	Soybean, maize, cotton
4*	India*	7.6	Cotton
5*	Canada*	7.6	Canola, maize, soybean, sugarbeet
6*	China*	3.8	Cotton, tomato, poplar, petunia, papaya, sweet pepper
7*	Paraguay*	2.7	Soybean
8*	South Africa*	1.8	Maize, soybean, cotton
9*	Uruguay*	0.7	Soybean, maize
10*	Bolivia*	0.6	Soybean
11*	Philippines*	0.4	Maize
12*	Australia*	0.2	Cotton, canola, carnation
13*	Mexico *	0.1	Cotton, soybean
14*	Spain *	0.1	Maize
15	Chile	<0.1	Maize, soybean, canola
16	Colombia	<0.1	Cotton, carnation
17	Honduras	<0.1	Maize
18	Burkina Faso	<0.1	Cotton
19	Czech Republic	<0.1	Maize
20	Romania	<0.1	Maize
21	Portugal	<0.1	Maize
22	Germany	<0.1	Maize
23	Poland	<0.1	Maize
24	Slovakia	<0.1	Maize
25	Egypt	<0.1	Maize

* 14 biotech mega-countries growing 50,000 hectares, or more, of biotech crops
Source: Clive James, 2008.

Adoption of GM Technology

Major Biotech Crops

Soybean

- 70% (65.8 million has.) of total global soybean planted is biotech
- US$4B increase in farmer income in 2007
- Countries growing biotech soybean: *Argentina, Bolivia, Brazil, Canada, Chile, Mexico, Paraguay, Uruguay, South Africa, and the USA.*

Cotton

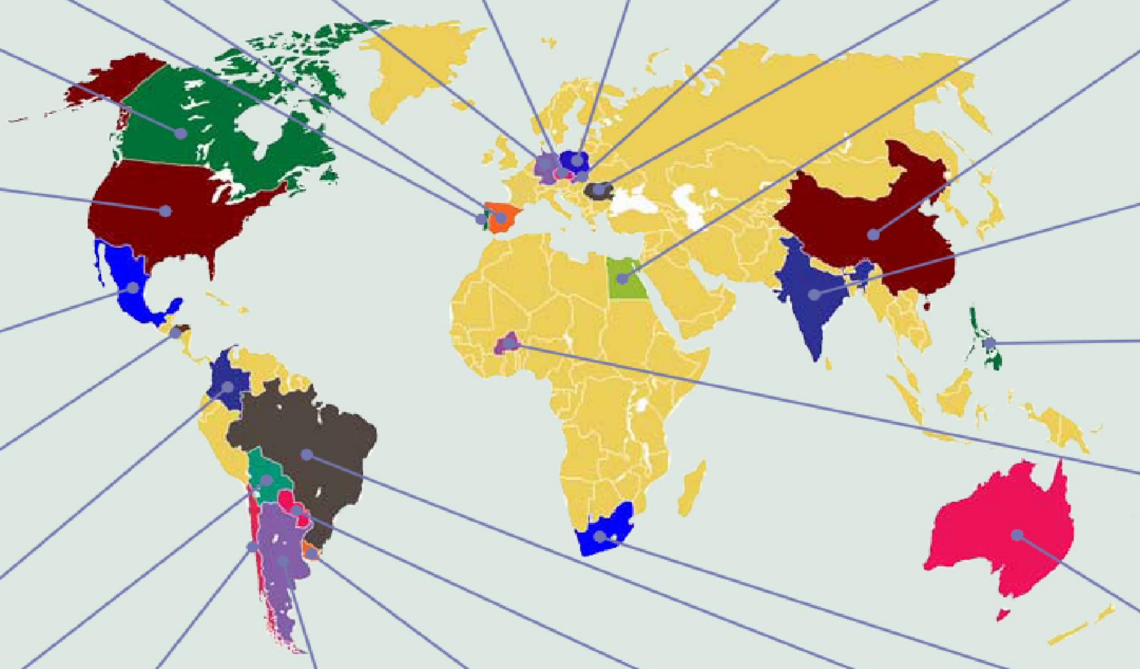
- 46% (15.5 million has.) of total global cotton planted is biotech
- US$3.3B increase in farmer income in 2007
- Countries growing biotech cotton: *Argentina, Australia, Brazil, Burkina Faso, China, Colombia, India, Mexico, South Africa, and the USA.*

Maize

- 24% (37.3 million has.) of total global maize planted is biotech
- US$2.4B increase in farmer income in 2007
- Countries growing biotech maize: *Argentina, Brazil, Canada, Chile, Czech Republic, Egypt, Germany, Honduras, Philippines, Poland, Portugal, Romania, Slovakia, South Africa, Spain, Uruguay, and the USA.*

Canola

- 20% (5.9 million has.) of total global canola planted is biotech
- US$0.4B increase in farmer income in 2007
- Countries growing biotech canola: *Canada, Chile, and the USA.*



#21 *Portugal*
<0.05 Million Has.
Maize

#14 *Spain**
0.1 Million Has.
Maize

#22 *Germany*
<0.05 Million Has.
Maize

#19 *Czech Republic*
<0.05 Million Has.
Maize

#23 *Poland*
<0.05 Million Has.
Maize

#24 *Slovakia*
<0.05 Million Has.
Maize

#20 *Romania*
<0.05 Million Has.
Maize

#25 *Egypt*
<0.05 Million Has.
Maize

#5 *Canada**
7.6 Million Has.
Canola, Maize, Soybean, Sugar beet

#1 *USA**
62.5 Million Hectares
Soybean, Maize, Cotton, Canola, Squash, Papaya, Alfalfa, Sugar beet

#13 *Mexico**
0.1 Million Hectares
Cotton, Soybean

#17 *Honduras*
<0.05 Million Hectares
Maize

#16 *Colombia*
<0.05 Million Hectares
Cotton, Carnation

#6 *China**
3.8 Million Has.
Cotton, Tomato, Poplar, Petunia, Papaya, Sweet Pepper

#4 *India**
7.6 Million Has.
Cotton

#10 *Philippines**
0.4 Million Has.
Maize

#18 *Burkina Faso*
<0.05 Million Has.
Cotton

#11 *Australia**
0.2 Million Has.
Cotton, Canola, Carnation

#10 *Bolivia**
0.6 Million Hectares
Soybean

#15 *Chile*
<0.05 Million Hectares
Maize, Soybean, Canola

#2 *Argentina**
21.0 Million Hectares
Soybean, Maize, Cotton

#9 *Uruguay**
0.7 Million Hectares
Soybean, Maize

#7 *Paraguay**
2.7 Million Hectares
Soybean

#3 *Brazil**
15.8 Million Has.
Soybean, Maize, Cotton

#8 *South Africa**
1.8 Million Has.
Maize, Soybean, Cotton

* 14 biotech mega-countries growing 50,000 hectares, or more, of biotech crops.

For more information about ISAAA, contact the Center nearest you:

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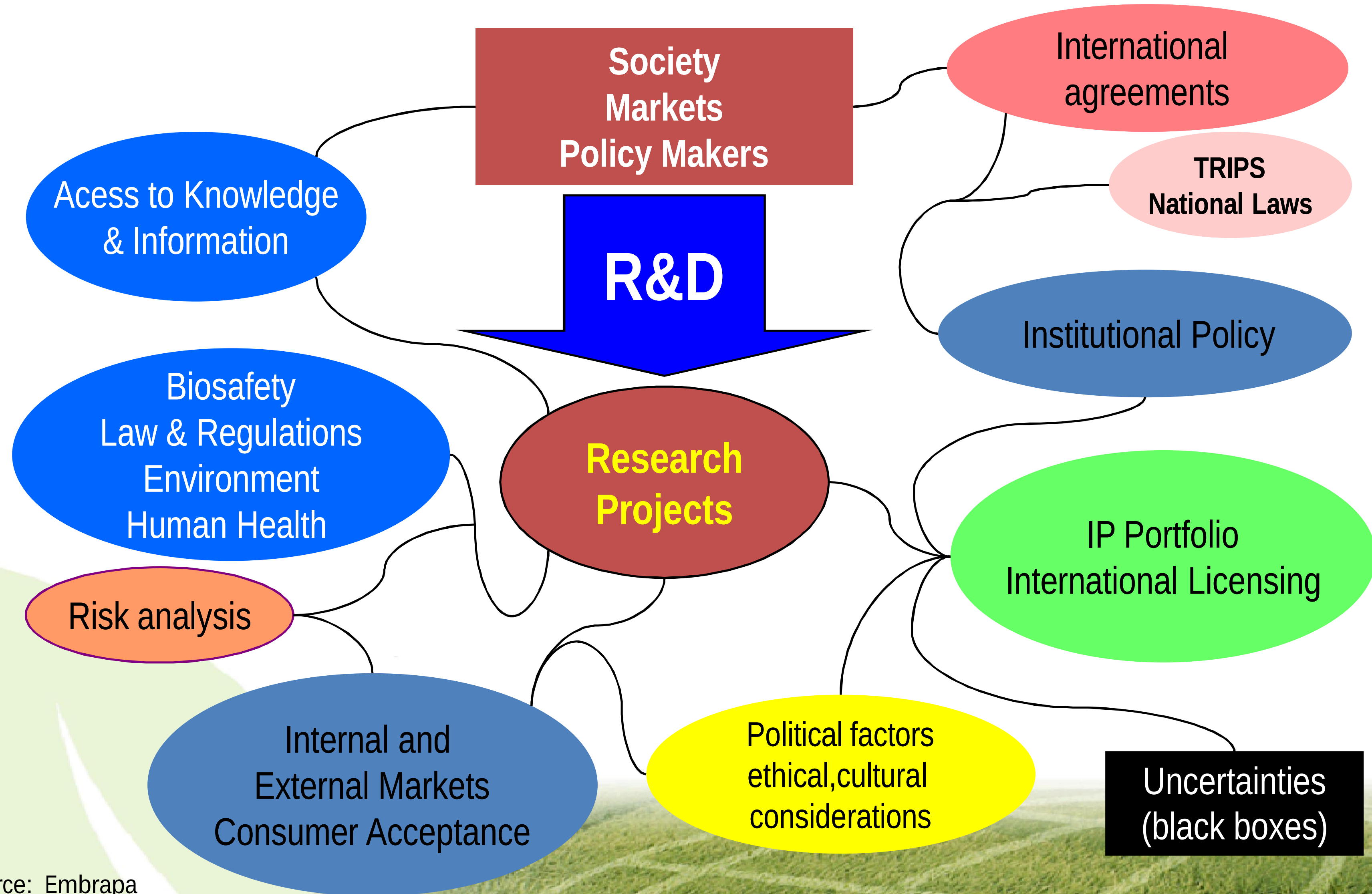
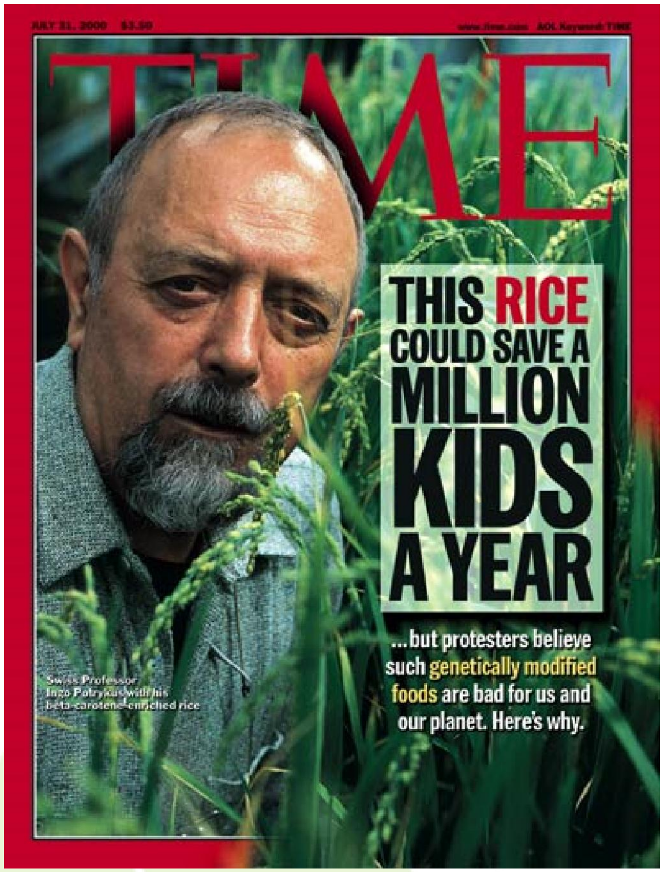
Complexities of GM Technology Development & Application
Society – Policy - Markets

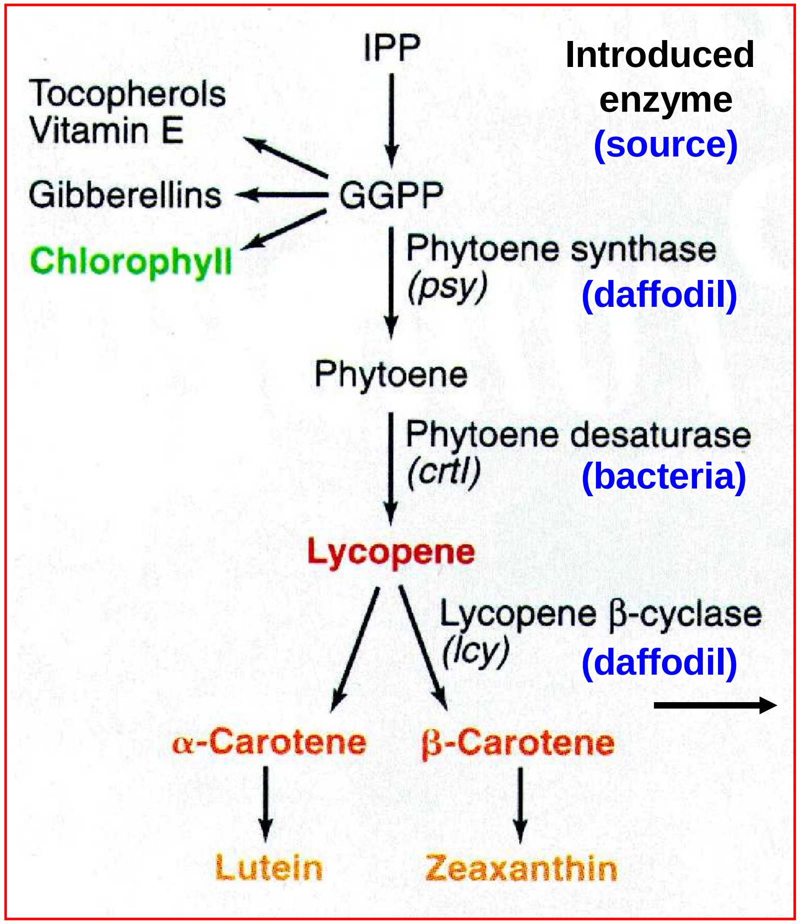


Source: Embrapa

Genetic Engineering
Output traits



http://www.time.com/time/

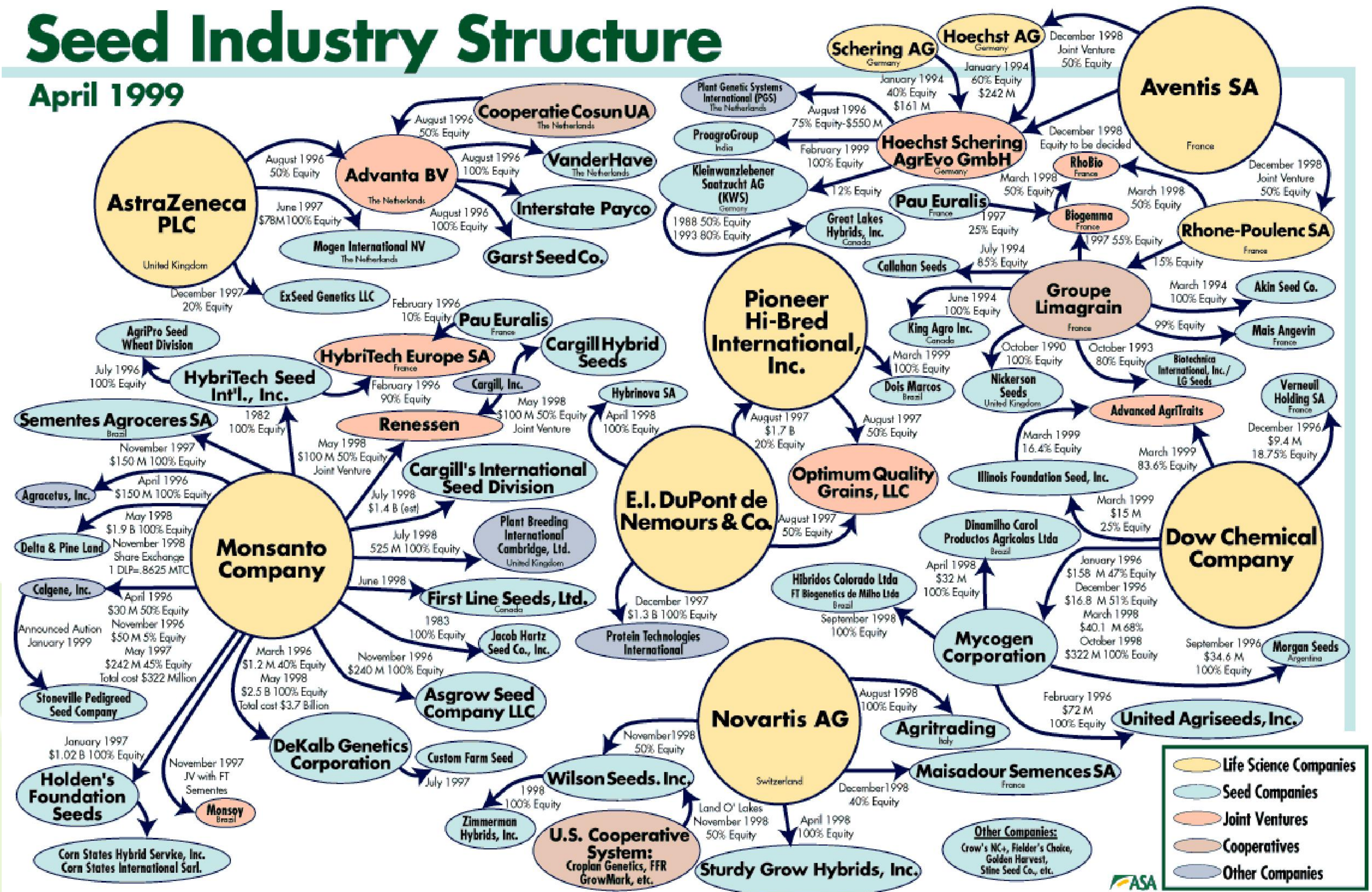


Ye et al. (2000) Science 287: 303-305.

"*Golden*Rice™"

Adoption of GM Technology

Market Impacts



Adoption of GM Technology
Market Impacts

Vertical Integration

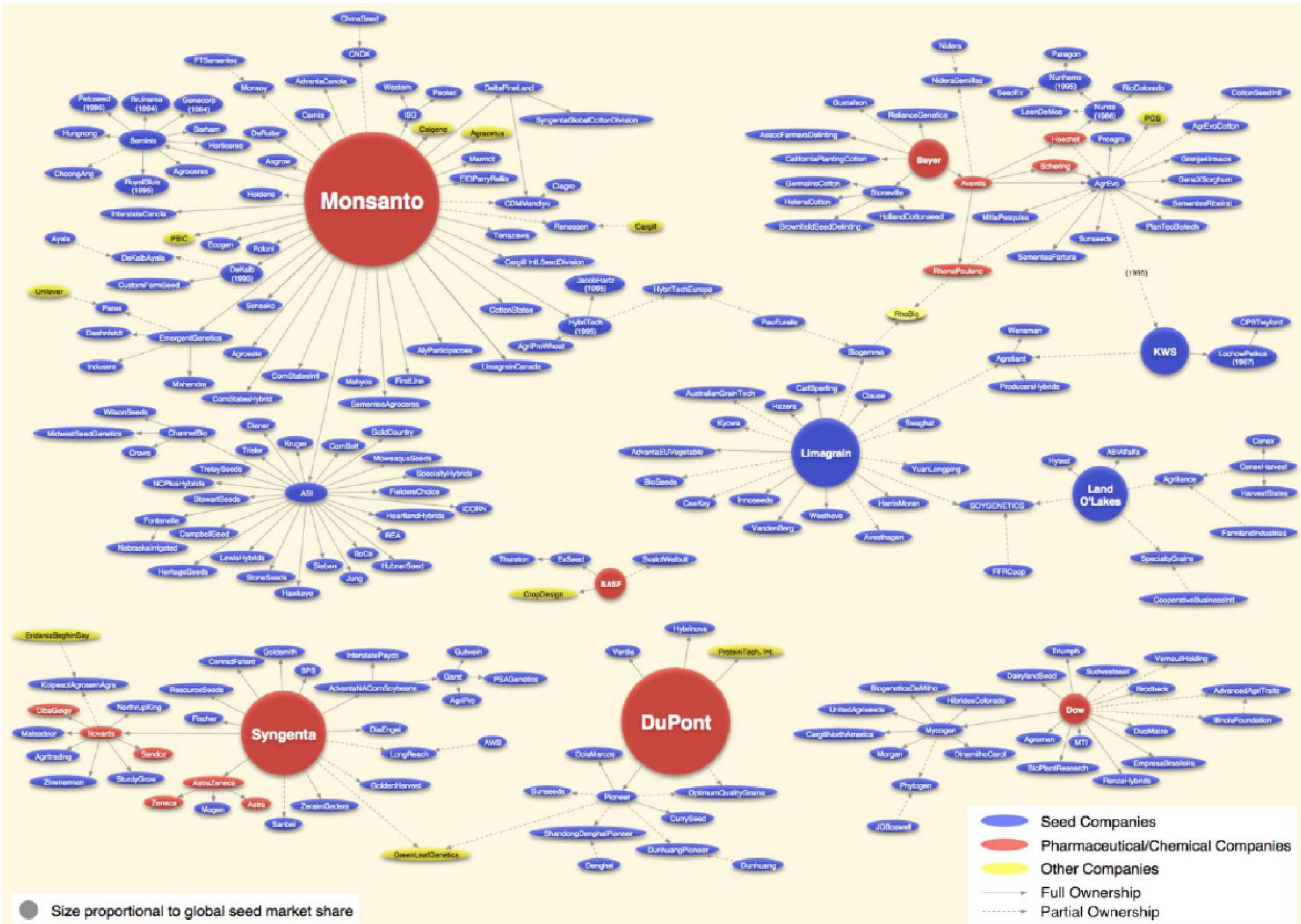
SEEDS – A GOOD PACKAGE FOR TECHNOLOGY
INPUTS - HERBICIDES
PROCESSING
DISTRIBUTION

MICROSOFT – MS Office Package

“EVERYTHING IN A BOX”

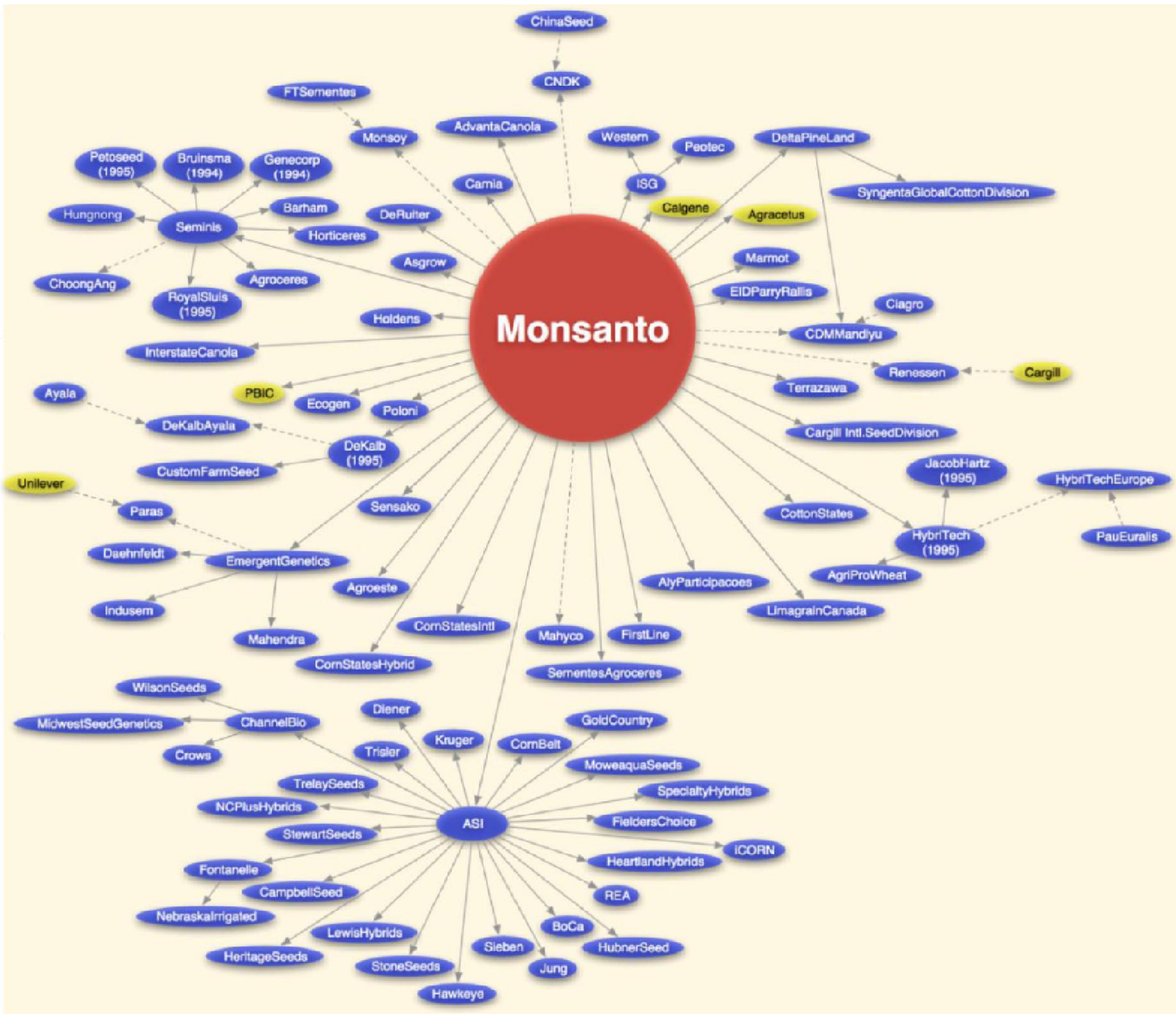
Adoption of GM Technology

Market Impacts – Seed Industry Structure – 1996-2008



Available at: http://www.mdpi.com/2071-1050/1/4/1266/pdf

Adoption of GM Technology
Market Impacts

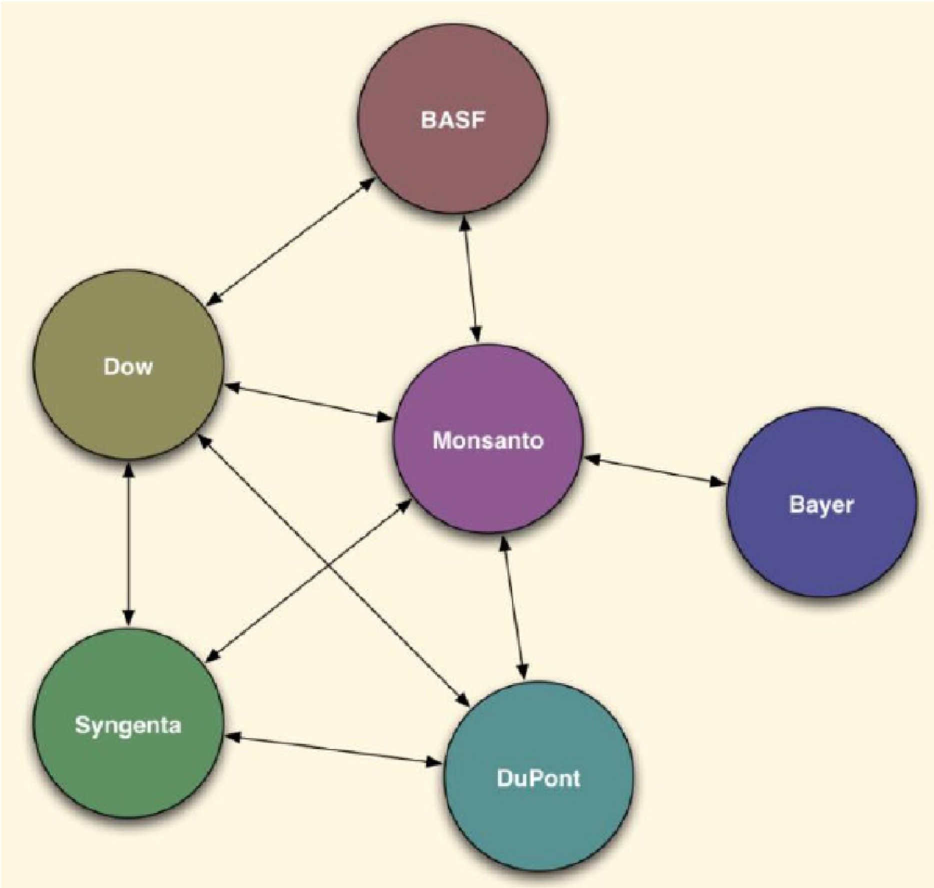


Available at: http://www.mdpi.com/2071-1050/1/4/1266/pdf

Adoption of GM Technology
Market Impacts

Cross-licensing

Cross-licensing agreements involving pharmaceutical/chemical companies for transgenic seed traits.
Monsanto has a central position in this network, as it is the only firm to have agreements with each of the other 5 firms.



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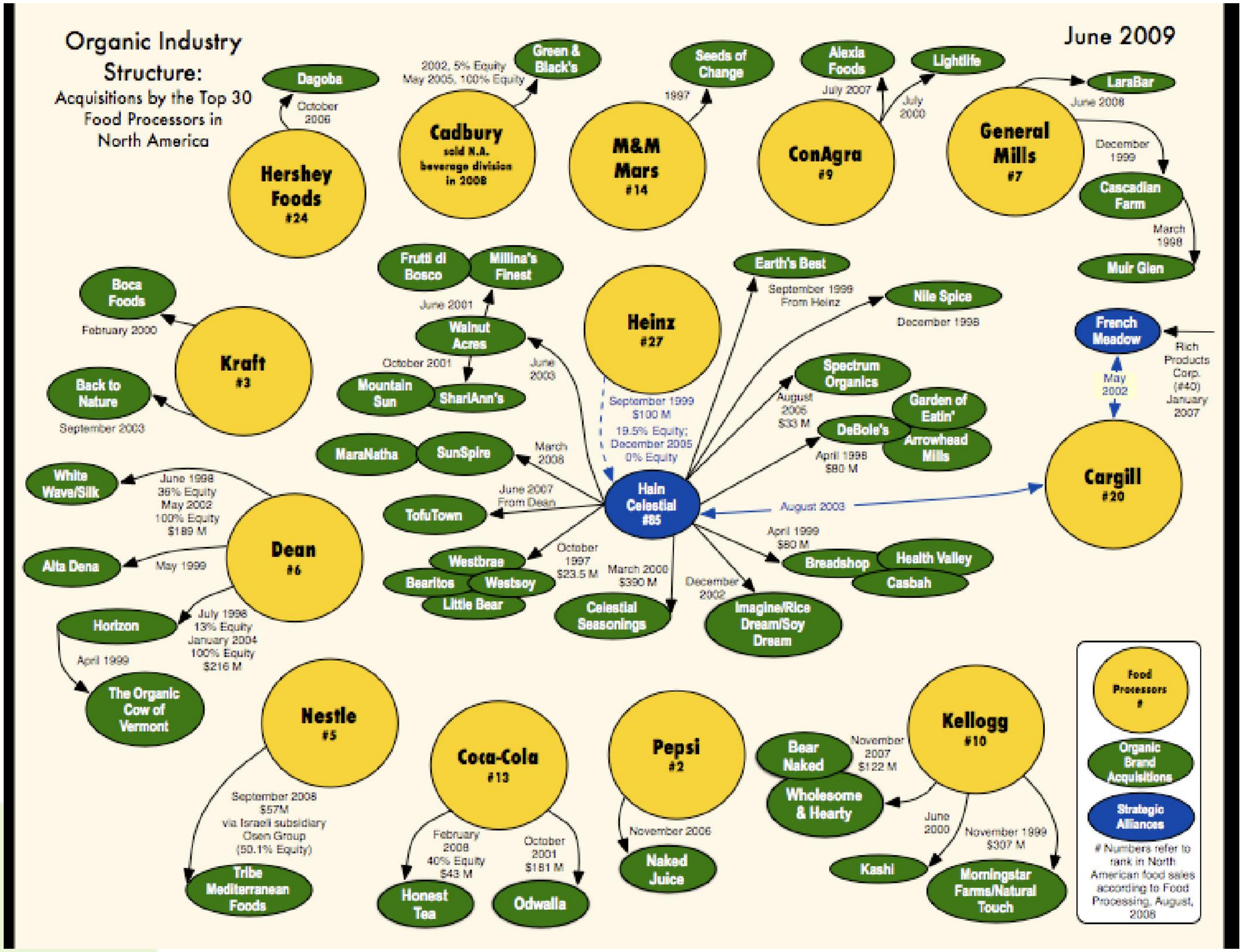
Organic Industry Structure



Howard, Philip H. 2009. *International Journal of Sociology of Agriculture and Food* 16(1), 13-30
Available at http://www.ijsaf.org/archive/16/1/howard.pdf

Foresight – Future Applications of GM Technology

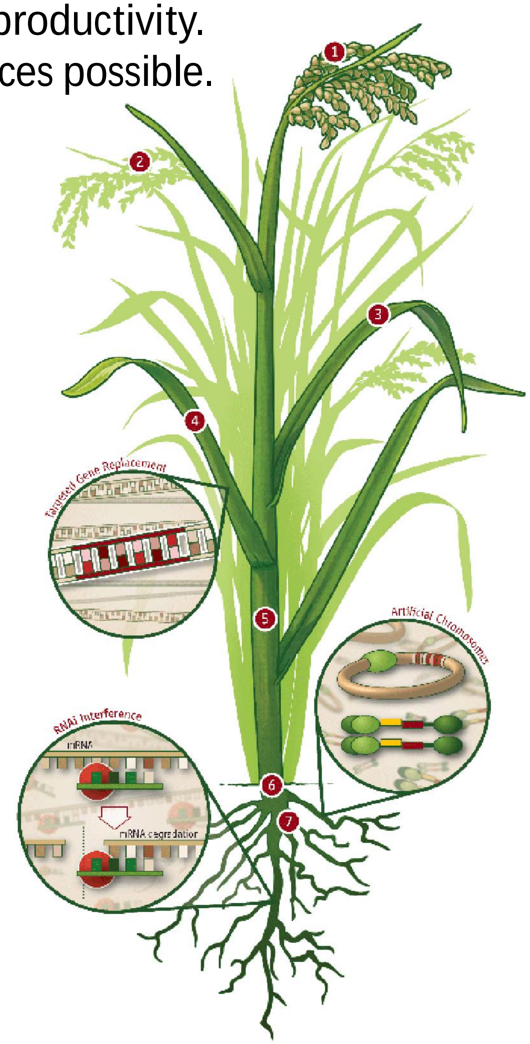
Examples of current and potential future applications of GM technology for crop genetic improvement.

Time scale	Target crop trait	Target crops
Current	Tolerance to broad-spectrum herbicide	Maize, soybean, oilseed brassica
	Resistance to chewing insect pests	Maize, cotton, oilseed brassica
Short-term (5–10 years)	Nutritional bio-fortification	Staple cereal crops, sweet potato
	Resistance to fungus and virus pathogens	Potato, wheat, rice, banana, fruits, vegetables
	Resistance to sucking insect pests	Rice, fruits, vegetables
	improved processing and storage	Wheat, potato, fruits, vegetables
	Drought tolerance	Staple cereal and tuber crops
Medium-term (10–20 years)	Salinity tolerance	Staple cereal and tuber crops
	Increased nitrogen-use efficiency	
	High-temperature tolerance	
Long-term (>20 years)	apomixis	Staple cereal and tuber crops
	Nitrogen fixation	
	Denitrification inhibitor production	
	Conversion to perennial habit	
	Increased photosynthetic efficiency	

Sources: Royal Society of London, *Reaping the Benefits: Science and the Sustainable Intensification of Global Agriculture* (Royal Society, London, 2009).
J. Gressel, Genetic Glass Ceilings (Johns Hopkins Univ. Press, Baltimore, 2008).

Foresight – Future Contributions of Modern Biotechnology

Researchers' wish list includes traits that could boost plant productivity.
New technologies are needed to make some of these advances possible.



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1.

Improve the nutrient content of seeds and edible plant parts.

For biofuels, the right mix of plant cell-wall components is needed to ease processing.

Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

Foresight – Future Contributions of Modern Biotechnology

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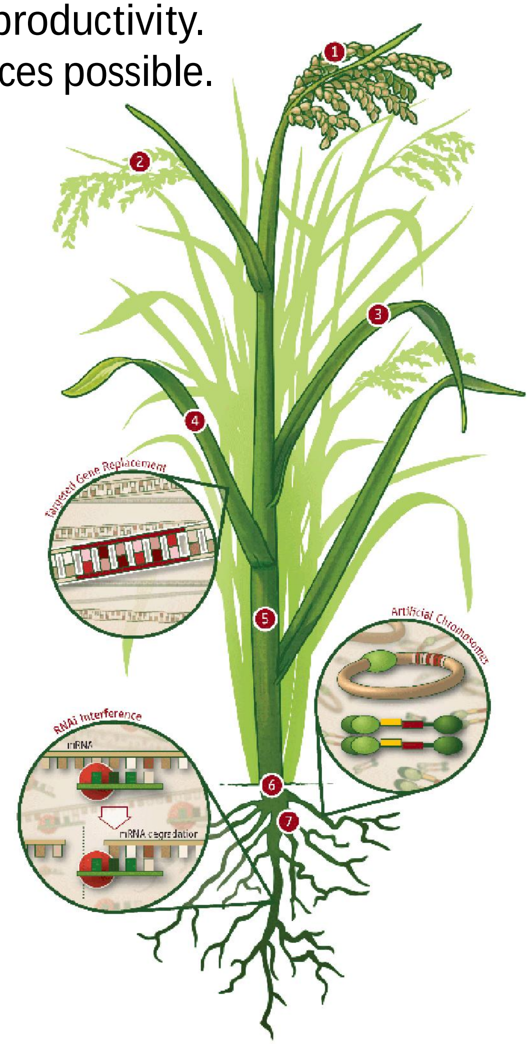
2.

No more sex. Hybrid seeds often produce more vigorous plants, but farmers can't always afford to buy new hybrid seeds.

Get hybrids to reproduce asexually through a process called apomixis.

Having apomixis in rice, for example, could save small farmers $4 billion a year. (An alternative to apomixis is to tweak the genetics of annual crop plants—which die each year—so that they become perennials.)



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Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

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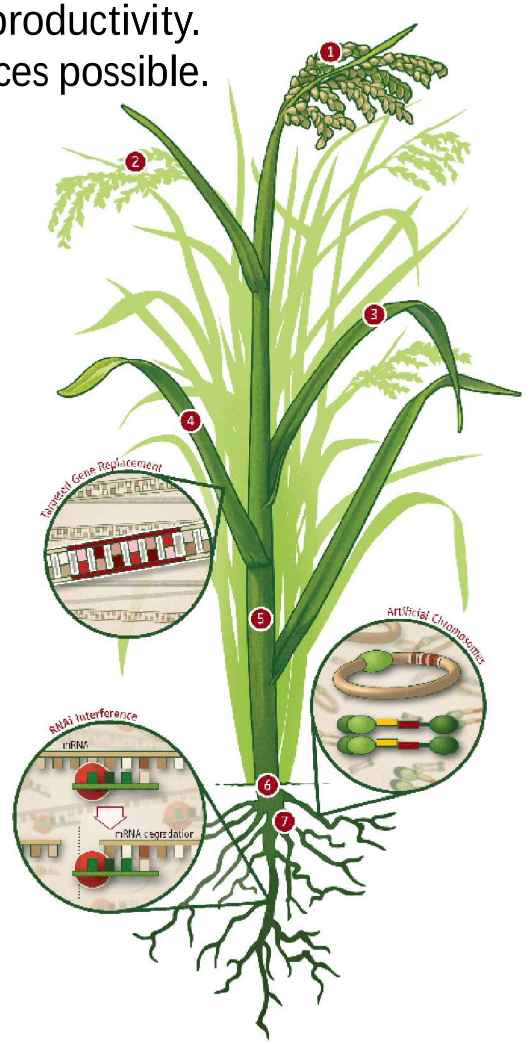
3.
Install warning lights.

A pigment gene that turns on in times of stress could cause a crop's leaves or stems to change color—and alert farmers to take remedial action.



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Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

Foresight – Future Contributions of Modern Biotechnology

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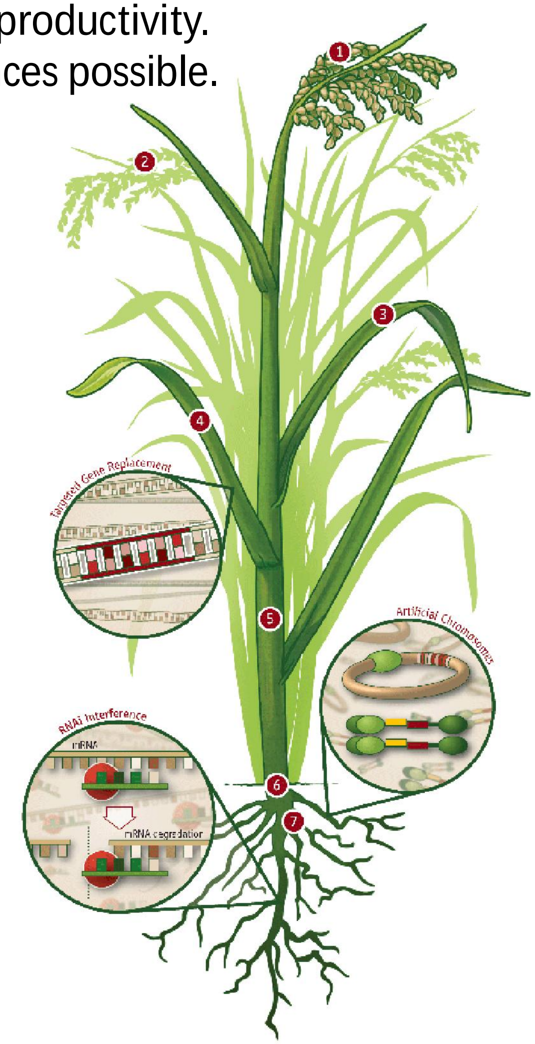
4.

More crop per drop.

Restructuring root and leaf architecture—and upgrading drought-response biochemical pathways—could increase water-use efficiency.

Shallower roots can better tap soil-surface moisture.



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Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

Foresight – Future Contributions of Modern Biotechnology

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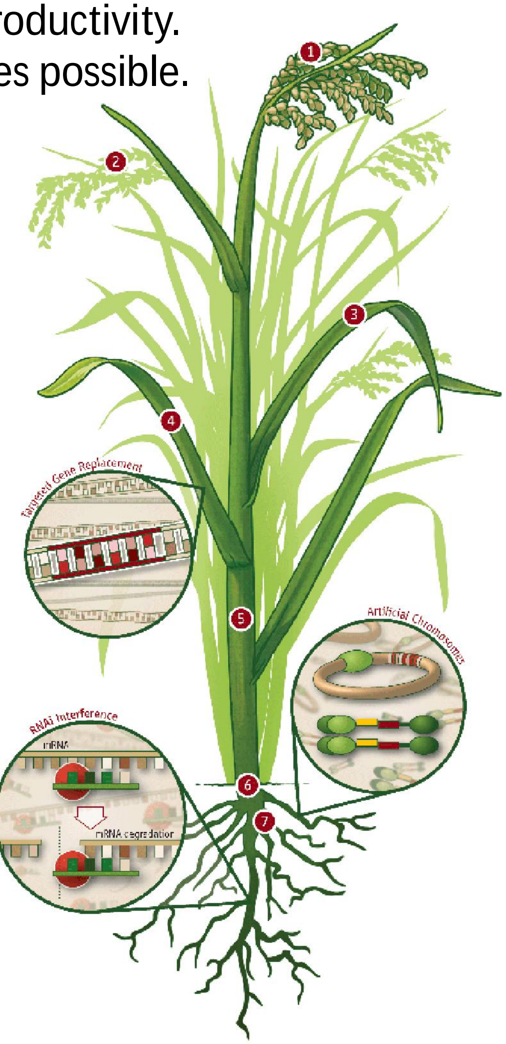
5.
Longer shelf life.

Enhanced control of ripening and senescence could reduce the amount of spoiled harvest.



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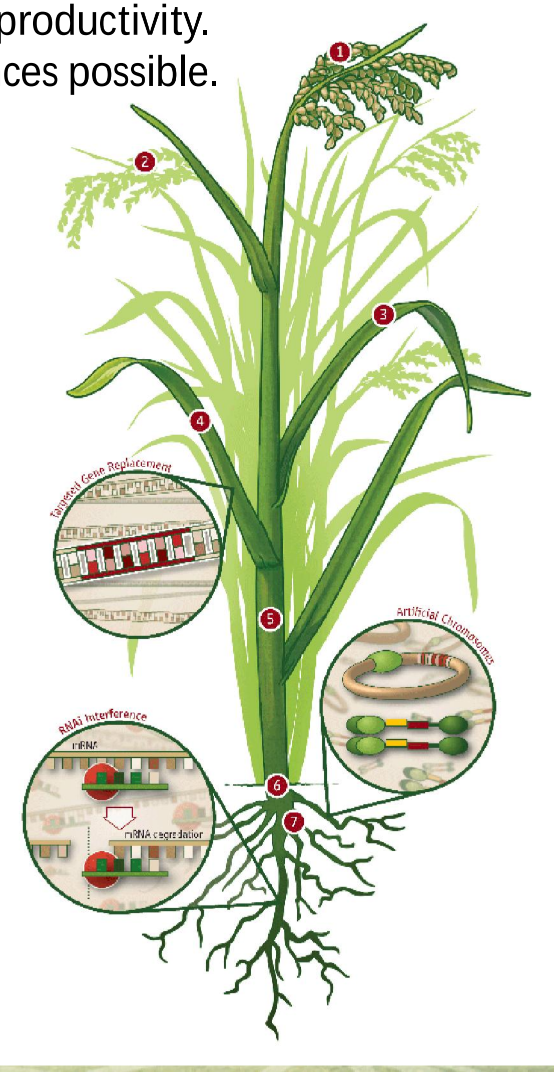

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6.

Improve nitrogen efficiency.

Fertilizers are costly to farmers and the environment.

Improving a plant's uptake and use would be a big help.

Better yet, build into the plant the genes necessary to carry out nitrogen fixation.

Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

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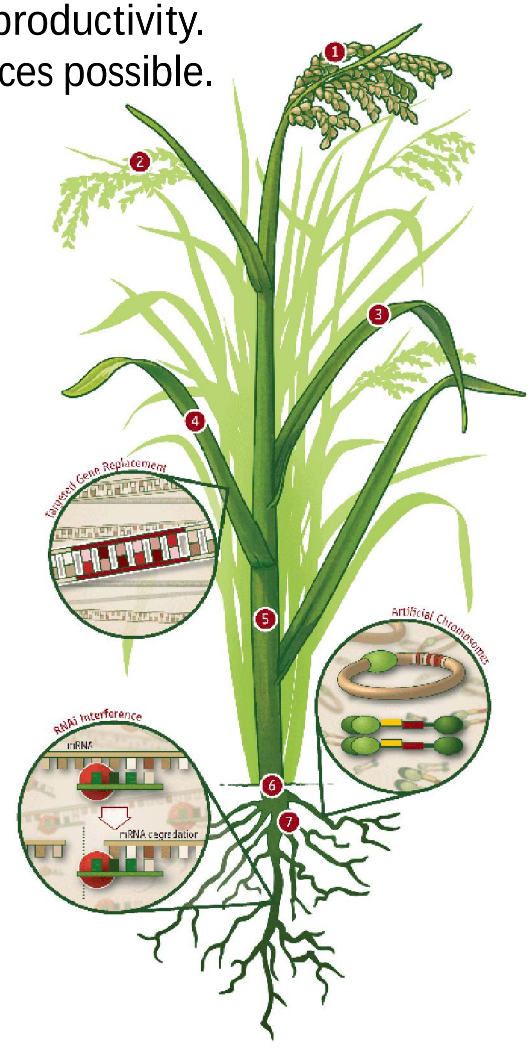

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7.

Tougher pest defenses.

Adding genes for toxins that kill only pest insects or nematodes

Addition of genes that attract the enemies of pests.

Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

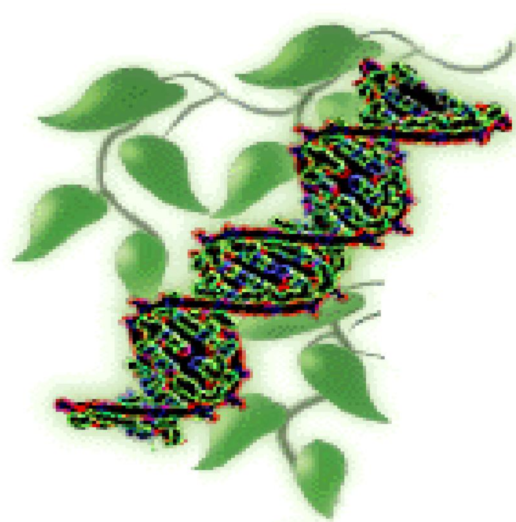
Agriculture – the industry of the future?

Agriculture and the Emerging Bioeconomy (“Global Green Growth”)

Food

Chemical

Fiber



Pharma

Energy

Biomaterials

Foresight – Synthetic Biology

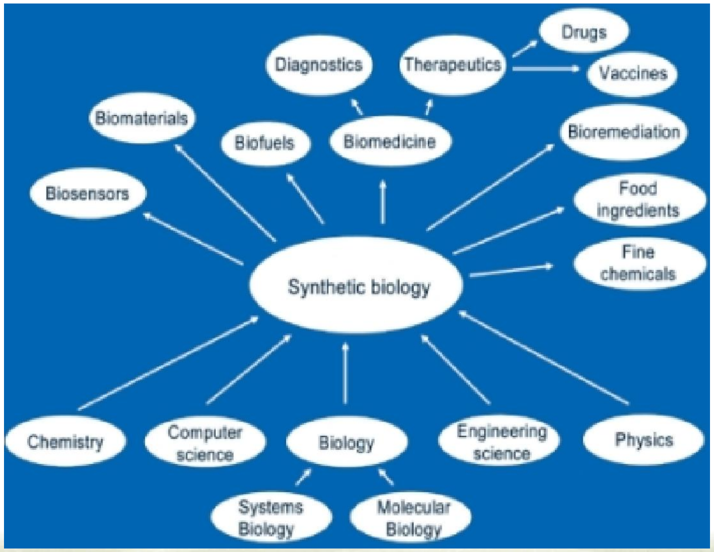
Synthetic biology is a new area of biological research that combines science and engineering.

Synthetic biology encompasses a variety of different approaches, methodologies and disciplines… convergence…

What they all have in common, however, is that they see synthetic biology as the design and construction of new biological functions and systems not found in nature.

A) the design and construction of new biological parts, devices, and systems, and

B) the re-design of existing, natural biological systems for useful purposes.



http://syntheticbiology.org/

Foresight – Synthetic Biology

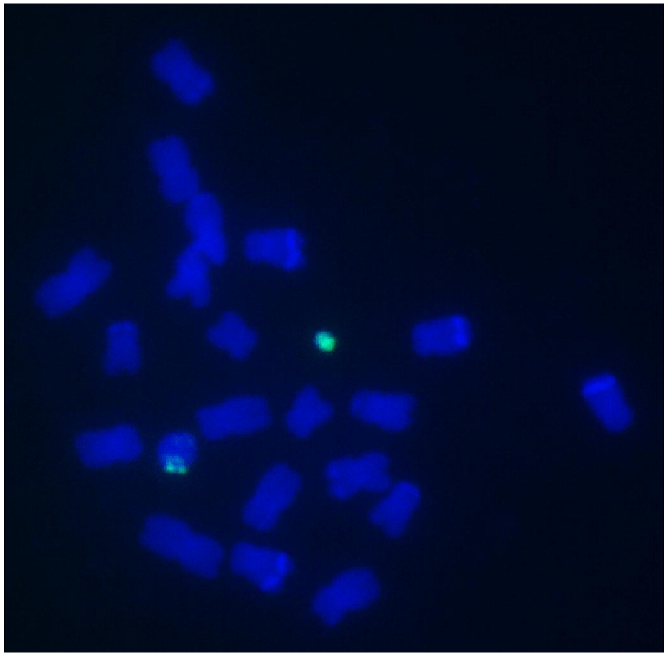
Artificial Chromosomes

If one gene is good, more genes are better. That's the mantra of plant biologists working to improve crops. Already, companies have engineered varieties that carry both herbicide and insect-resistance genes. Ultimately, researchers have set their sights on tweaking complex multigene processes, such as nitrogen fixation, which might involve 20 genes, or a special type of photosynthesis called C4 that works particularly well in tough conditions. Coordinating the expression of whole suites of genes, however, is an easier feat if the genes are grouped together. Here's where artificial chromosomes come into play.

Such "minichromosomes" come in several flavors. A company called Chromatin, for instance, has developed a way to attach useful suites of genes to a "platform" made from a ring of maize DNA. It encodes the repetitive regions of the centromere, the region near the middle of chromosomes that is important during DNA replication. Once loaded with the desired genes, the ring is put into the target plant.

Several teams are also making use of a plant's own "extra" DNA—such as the B chromosome in maize, or extra chromosomes in tetraploid versions of barley, rice, or Arabidopsis. They insert DNA containing the desired genes and the repetitive sequence of a telomere, which caps off chromosomes. That DNA inserts into the plant's chromosome and truncates it, creating a new minichromosome.

These techniques are promising, but it's not clear how stable the minichromosomes will be over multiple generations—or if the right amount of gene expression will be maintained over time.



The isolated green dot marks the centromere of a minichromosome.

CREDIT: RICK E. MASONBRINK AND JAMES BIRCHLER

Source: Pennisi, 2010. Science Vol. 327. no. 5967, pp. 802 - 803

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Brazilian Presence in the Korean Science and Technology Scene
http://is.gd/bJyUC

Building a Green Economy http://is.gd/bJyzQ

EMBRAPA LABEX

The concept of Virtual Laboratory – or Labex, was created by the Brazilian Agricultural Research Organization, Embrapa, as means of increasing its scientific and technological ties with advanced research organizations around the world. Instead of building its own platform abroad, Embrapa uses the concept of virtual lab, or lab without walls, to negotiate access to its partner organizations' existing facilities. The concept, which has been tested and validated in the United States and in Europe, is now being extended to Asia, in partnership with the Rural Development Administration – RDA, of South Korea. More here.

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Labex Korea is hosted by Rural Development Administration

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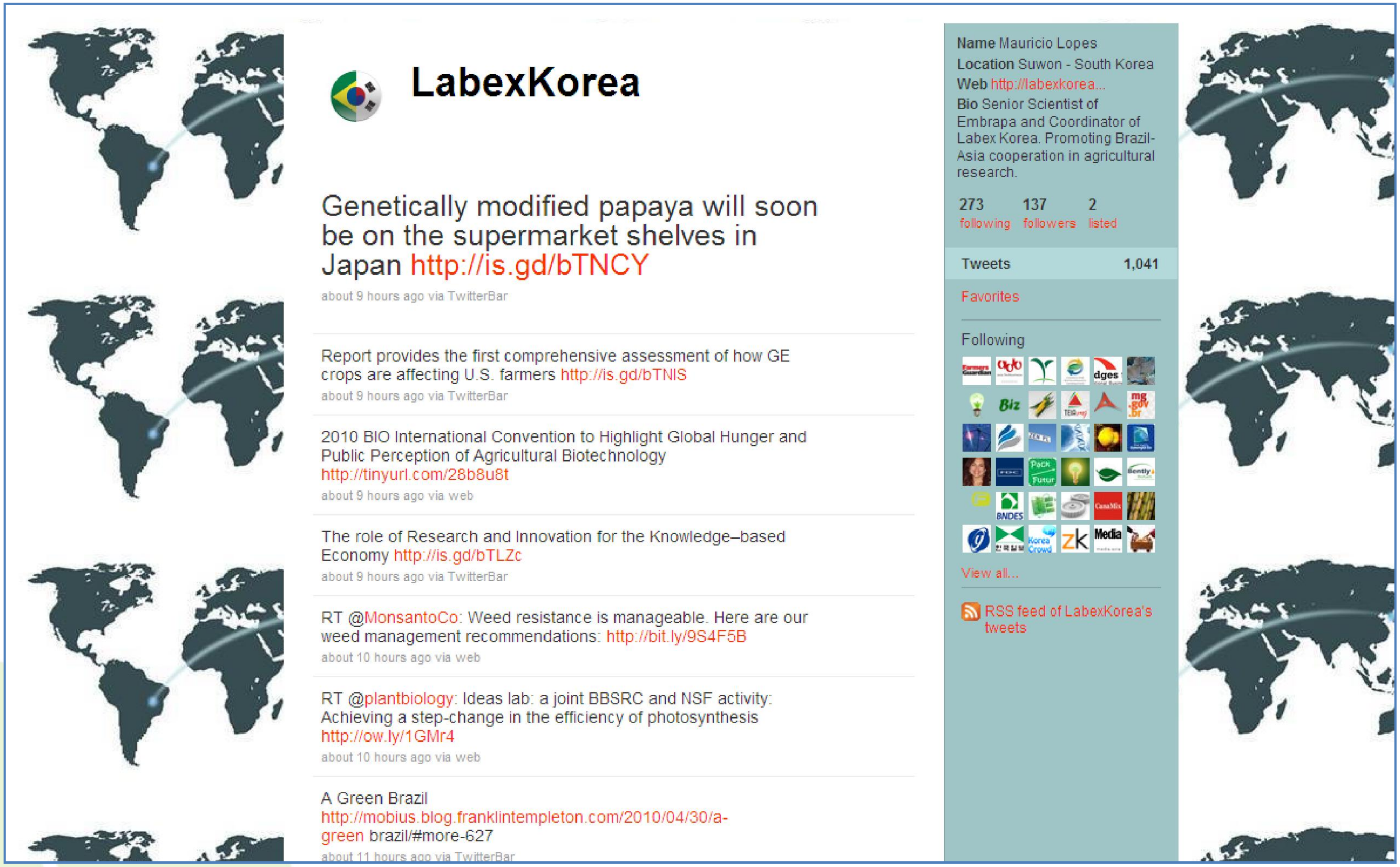

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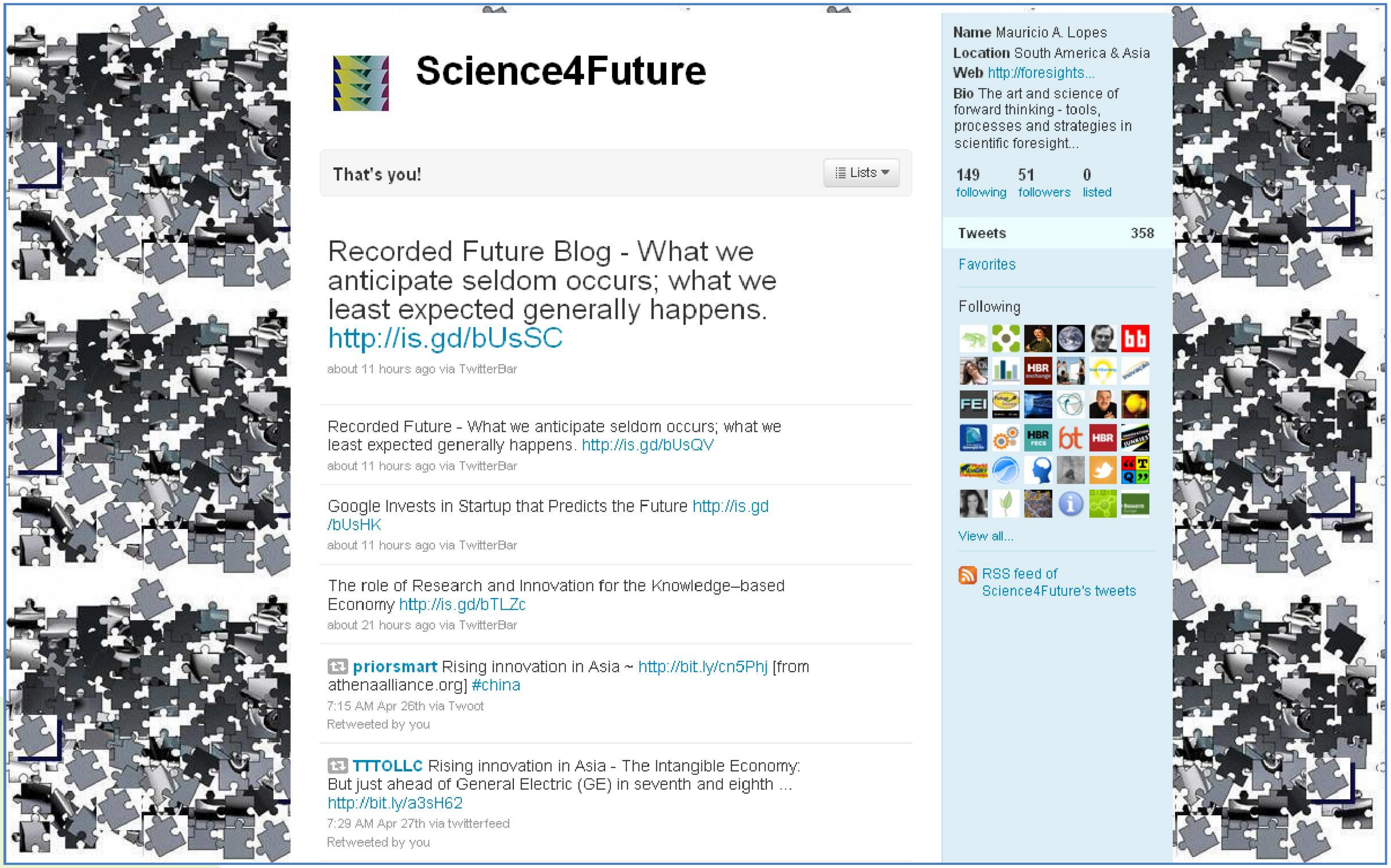

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