GENETICALLY-ENGINEERED VIRUS RESISTANCE IN PLANTS

"I never eat anything with DNA in it"

"You don't know, my dear boy, with what little reason the world is governed."
[Letter to his son, 1648] - *Axel Gustafsson, Count Oxenstierna, 1583-1654*

Mechanisms of Resistance

1. Immunity
2. Genetic Host Resistance
3. Systemic Acquired Resistance
4. Post-transcriptional Gene Silencing
5. Engineered (Transgenic and edited) Resistance

Two broad means of engineering plants for resistance to viruses:

A. Genome engineering based on “pathogen-derived resistance”

B. Genome engineering based on CRISPR/Cas9 directed changes to the host or viral genome

A. Genome engineering based on “pathogen-derived resistance”

Opportunities for engineering resistance to pathogens:

- We have the ability to identify, isolate, and introduce a virus specific resistance into unlimited varieties of crops

  - irrespective of their sexual compatibility
  - without compromising desirable agronomic traits
  - and avoiding the need for extensive back-crossing

- This is a viable alternative to traditional plant breeding for virus and pathogen resistance.

A. Engineering based on “pathogen-derived resistance”

1. **Transformation of Plants**

2. **Strategies for Engineering Virus Resistance**

3. **The Politics of Engineered Resistance**

A. Engineering based on “pathogen-derived resistance”

1. Transformation of Plants

Biotechnology is a powerful set of tools used by scientists to alter the genetic makeup of plants and animals

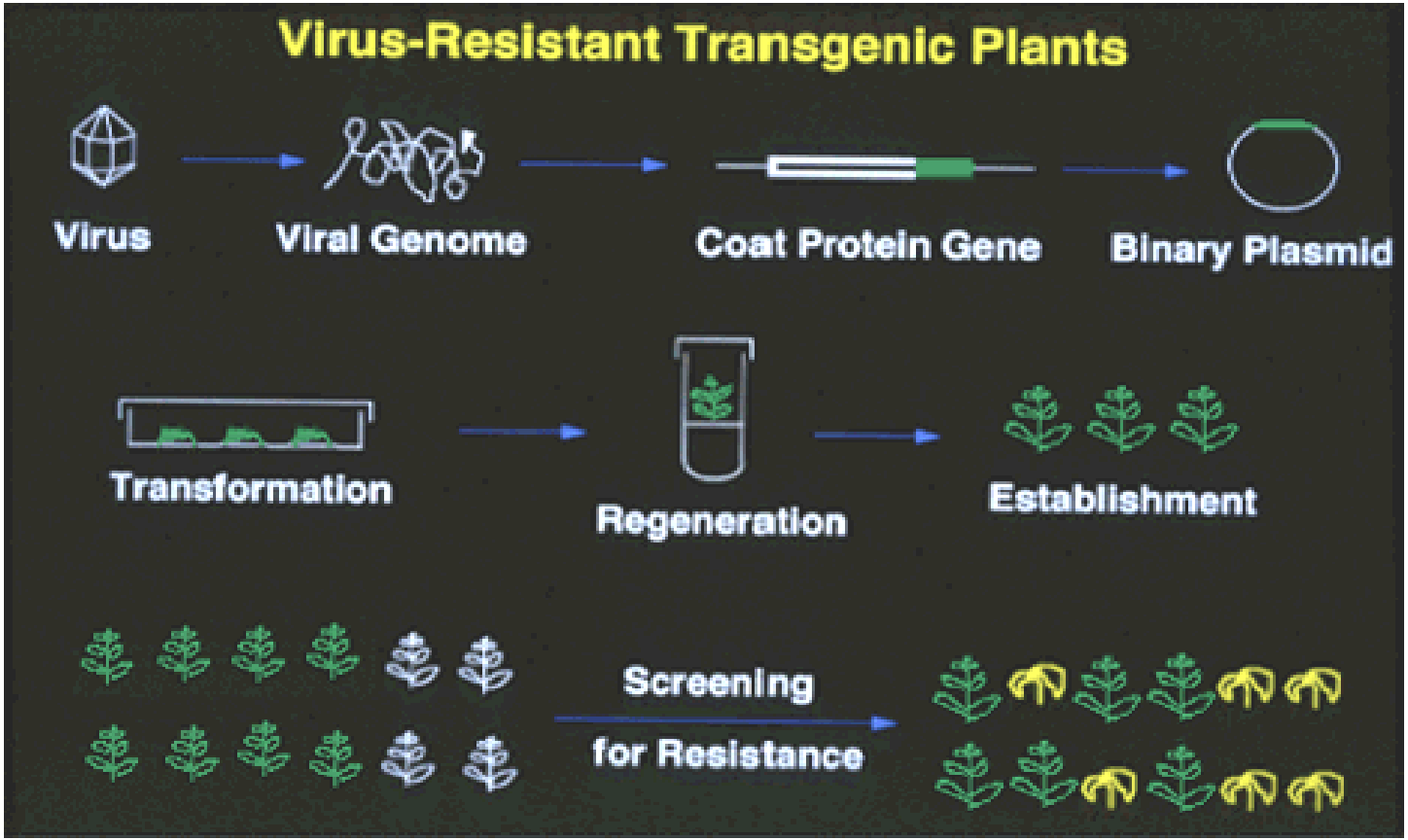
Genetic engineering enables the genetic modification of a plant by adding new traits through recombinant DNA technology.

Two important developments in the 1980’s make it possible to improve crop plants by incorporating pathogen-derived genes.

1. Cloning and sequencing of viral genes

2. Transformation techniques

A. Engineering based on “pathogen-derived resistance”



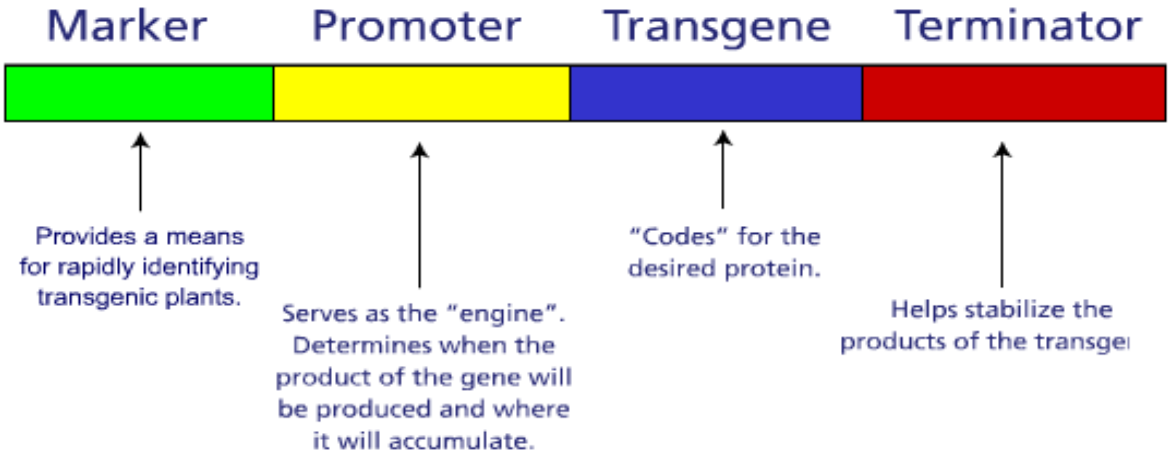
Steps in the research process.

A. Engineering based on “pathogen-derived resistance”

1. Transformation = DNA transfer

Requires transformation vectors:

Plant promoter (35S) from *Cauliflower mosaic virus* which can drive levels of expression of foreign genes in plants in various plant tissues, leader sequence, gene of interest, sequences which provide for transcription termination and polyadenylation signals, and a selectable marker gene.



A. Engineering based on “pathogen-derived resistance”

1. Transformation

2 methods used to transform plants:

a. **Agrobacterium-mediated transformation**.

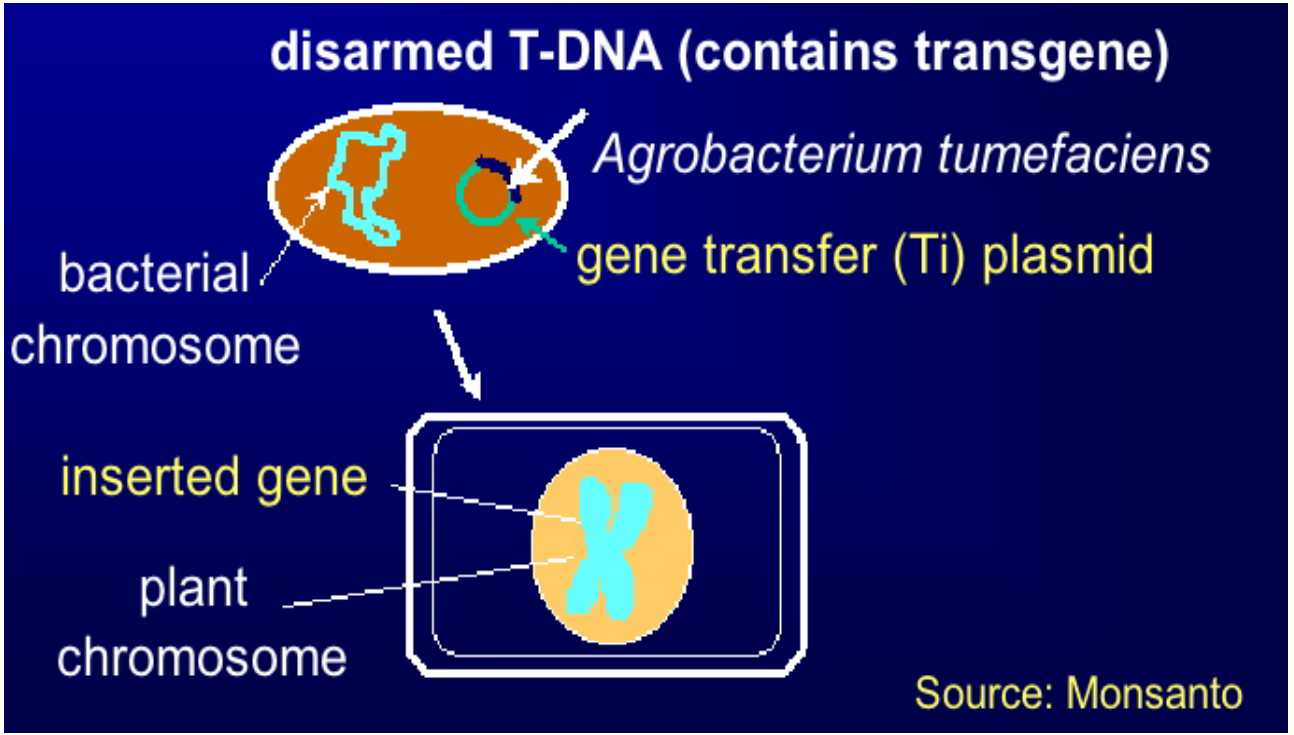
b. **Microprojectile bombardment**.

A. Engineering based on “pathogen-derived resistance”

1. Transformation of Plants

a) Agrobacterium-mediated transformation

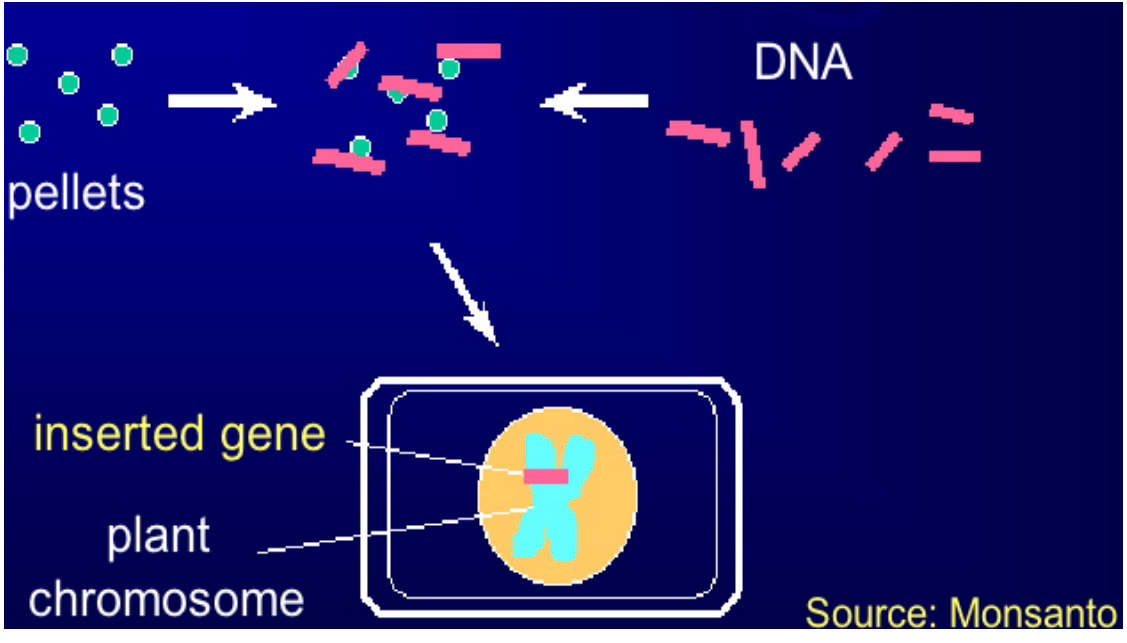
Limited to plants that can be infected with Agrobacterium (genotype dependent)



A. Engineering based on “pathogen-derived resistance”

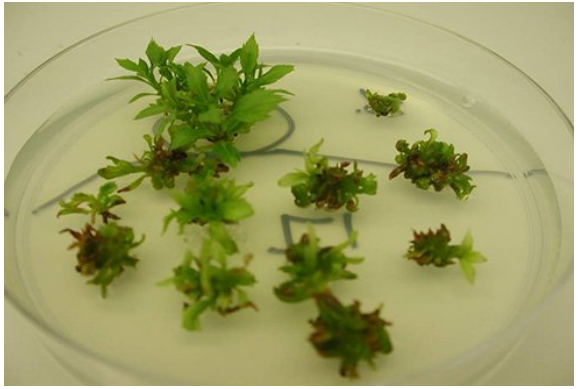
1. Transformation of Plants

b) Microprojectile bombardment. Particle bombardment wherein microscopic metal particles coated with genetically engineered DNA are explosively accelerated into plant cells. This is genotype-independent transformation.

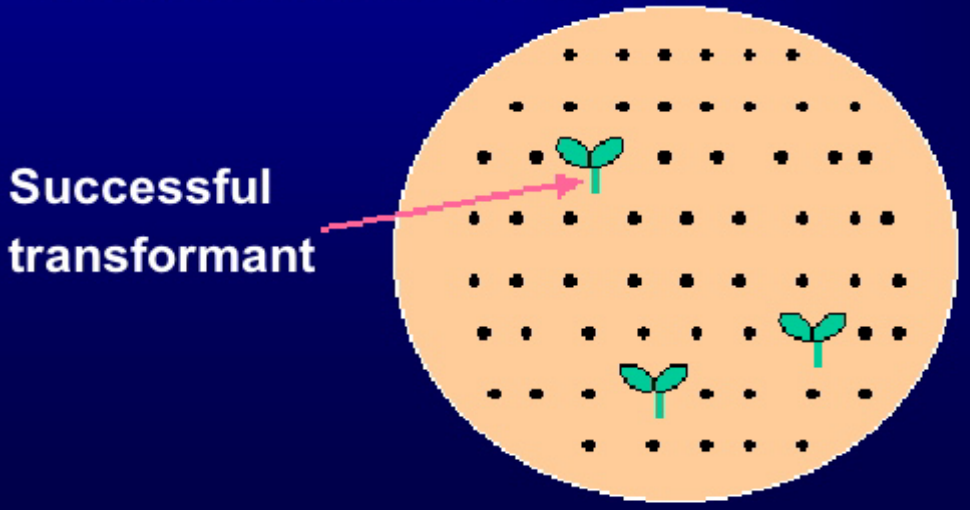


A. Engineering based on “pathogen-derived resistance”

1. Transformation of Plants



To identify cells/tissues in which new genes are incorporated into plant’s DNA, grow in media containing antibiotics or herbicides.



A. Engineering based on “pathogen-derived resistance”

1. Transformation of Plants

For both transformation methods:

- Whole plants with inserted genes are regenerated from single transformed cells through tissue culture
- Resulting plants are screened for desired characteristics

A. Engineering based on “pathogen-derived resistance”

2. Strategies for Engineering Resistance to Viruses:

a. Virus Resistance through use of non-viral genes

- Transferring genes for virus resistance from one host to another
- Least common approach

b. Virus Resistance through Pathogen-mediated Resistance (PDR)

A. Engineering based on “pathogen-derived resistance”

- Can transfer plant virus resistance genes to hosts where there are none, where they can confer resistance

Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 8776–8781, August 1996
Plant Biology

The *N* gene of tobacco confers resistance to tobacco mosaic virus in transgenic tomato

(hypersensitive response/plant disease resistance)

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Communicated by Frederick M. Ausubel, Massachusetts General Hospital, Boston, MA, April 24, 1996 (received for review December 25, 1995)

A. Engineering based on “pathogen-derived resistance”

2. Strategies for Engineering Resistance to Viruses:

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b. Pathogen-derived Resistance (PDR) 1985

- Initial basis of genetic engineered virus resistance (starting in the 1990's):

- Sanford and Johnson proposed and developed the concept of pathogen-derived resistance:

  Natural host-pathogen relationships could be disrupted if the host organism expresses a pathogen gene product:

  - in excess amounts,
  - at the inappropriate developmental stage,
  - or in a defective form

- They proposed that a disruption of the normal replicative cycle of the pathogen could result in an attenuated or aborted infection of the host.

Sanford and Johnston (1985; J. Theor. Biol. 113, 395-405)

A. Engineering based on “pathogen-derived resistance”

First recognition of the association of what was later recognized as “PTGS” with virus resistance in plants was the mid 1980’s

Whole or partial sequences of viral genes were used to engineer PTGS-meditated resistance to viruses in plants from the early 1990’s to the present.

Mechanism of PDR:

RNA-Mediated Resistance (Gene Silencing)

This approach to creating resistance has been shown to be due to cytoplasmic activity that inactivates and eliminates specific RNA sequences from a cell (PTGS).

Two types of resistance responses to inoculation are commonly observed:

1. Plants are highly resistant with no virus replication
2. Plants are susceptible but recover from systemic infection

Researchers select for the type of resistance they want in early generations (soon after transformation) – usually its high levels of resistance rather than recovery

Strategies for Engineering Resistance to Viruses

a. Virus Resistance through use of non-viral genes

- Transfering genes for virus resistance from one host to another
- Least common approach

b. Virus Resistance through Pathogen-mediated Resistance (PDR)

Strategies can be:

- **RNA-mediated: due to mechanism of gene silencing)**
  most examples of engineered virus resistance are this type
- **Protein-mediated resistance:** (resistance conferred due to expression of a protein.
- **RNA- and protein-mediated**

A. Engineering based on “pathogen-derived resistance”

b. Virus Resistance through Pathogen-mediated Resistance (PDR), RNA-mediated resistance

1. Using sequences of structural protein genes (coat proteins)
2. Using sequences of non-structural protein genes
3. Using antisense sequences of genes
4. Use of hairpin sequences

- **Viral sequence must be at least 100 nucleotides to be effective**
- **Coat protein gene most commonly used viral gene**

A. Engineering based on “pathogen-derived resistance”

b. Virus Resistance through Pathogen-mediated Resistance (PDR), RNA-mediated resistance

Coat Protein-mediated Resistance

1. The resistant phenotype can be expressed as:
    a. temporary delay in symptom development
    b. an attenuation of normal virus-induced symptoms
    c. lower virus titer in infected tissue
    d. the ability of infected plants to recover from infection

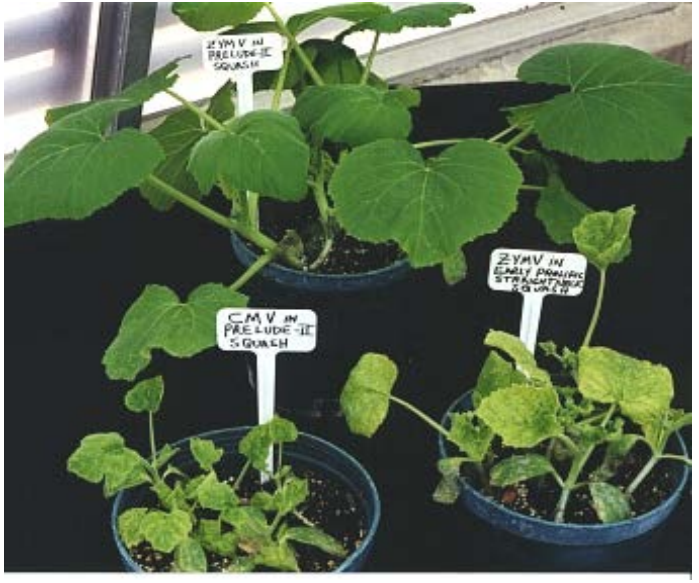
2. Induced resistance tends to be virus-specific

3. No good correlation between coat protein accumulation and resistance.

4. This resistance has been shown to be durable

Multiple Virus Resistant Yellow Crookneck Squash

- ZW-20 squash resists infection by *Zucchini yellow mosaic* and *Watermelon mosaic viruses* because the coat proteins of those viruses were inserted into the line. It was field tested under 14 APHIS permits at 46 sites in 10 states.
- Released as 'Freedom II'. Deregulated - December 13, 1994, began selling Feb 1995 with field resistance to ZYMV and WMV



- Later came 'Prelude II' with resistance to WMV and improved horticultural traits

- This resistance bypasses the need for aphid control and significantly increased yields.

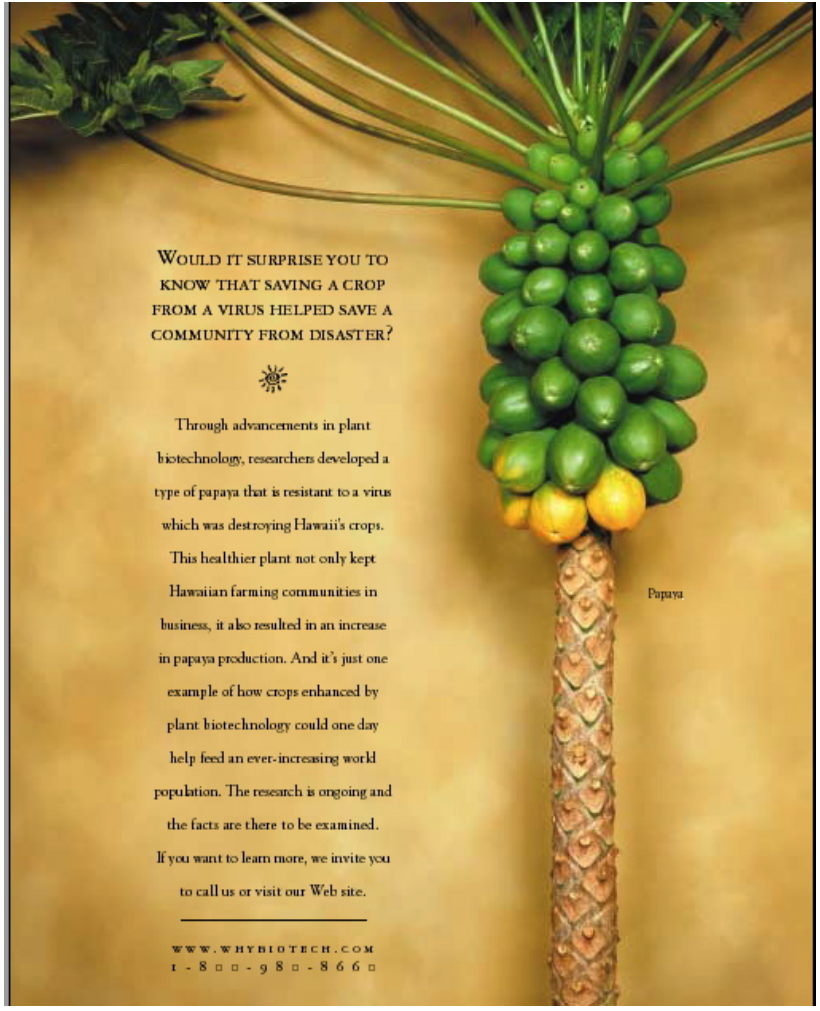
A. Engineering based on “pathogen-derived resistance”

The story of Papaya ringspot virus (PRSV) resistant papaya

After inoculation with PRSV:

Transformed

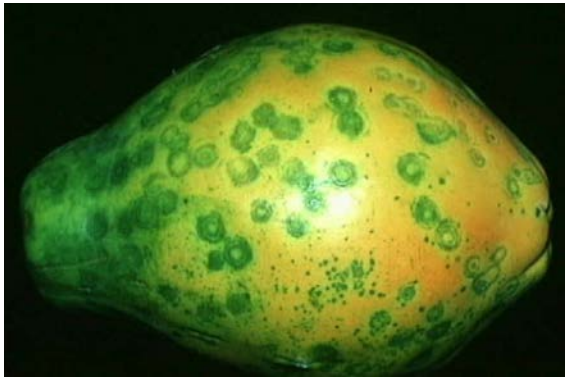
Non-transformed



Papaya ringspot virus (PRSV) had been present in the Hawaiian Islands for nearly 100 years, and farmers managed it by escape (moving their farms) and by roguing until about the 1980's. By then, despite many attempts to move farms to other areas, the virus made its way across the state, and devastated the industry. PRSV decreases yields, and what fruit is produced is inedible.

Hawaii papaya farm

picture taken between 1992 - 1997



Cornell Univ.

Dennis Gonsalves

https://medium.com/@gmoanswers/gm-papaya-story-c9a666c4bd5b

A. Engineering based on “pathogen-derived resistance”

June 1996

Gonsalves began the research in 1985

Oct. 1995: First field trial of transgenic 'UH Rainbow' and 'UH SunUp’ in Puna

Non-transgenic papaya (left) 'UH Rainbow' (right) in all images.

Nov. 1996

March 1997

A. Engineering based on “pathogen-derived resistance”

Gonsalves, D., Gonsalves, C., Ferreira, S., Pitz, K., Fitch, M, Manshardt, R. and Slightom, J. 2004.

Transgenic Virus-Resistant Papaya: From Hope to Reality in Controlling Papaya Ringspot Virus in Hawaii.

APS*net* Features.
Online. doi:10.1094/APSnetFeature-2004-0704

Fig. 2. Kapoho field trial started in 1995, showing a solid block of PRSV-resistant Rainbow growing well while the surrounding susceptible non-transgenic Sunrise is severely infected with PRSV. Picture taken 19 months after start of the field trial.

A. Engineering based on “pathogen-derived resistance”

b. Virus Resistance through Pathogen-mediated Resistance (PDR),

1. Using sequences of structural protein genes (coat proteins)
2. **Using sequences of non-structural protein genes (entire genes, truncations, mutations)**
3. Using antisense sequences of genes
4. Use hairpin sequences

Non-structural Protein-mediated Resistance

Replicase/Rep genes.

Works well in antisense or sense orientation.

Proteases

Transgenic tobacco expressing *Potato virus Y* truncated N terminus NIa (protease) was found to be highly resistant to PVY (Vardi et al., 1993, Proc. Natl. Acad. Sci. USA 7513-7517).

Movement proteins

Interference with virus movement from the infection initiation site theoretically could be a very effective control strategy but so far results have not been promising.

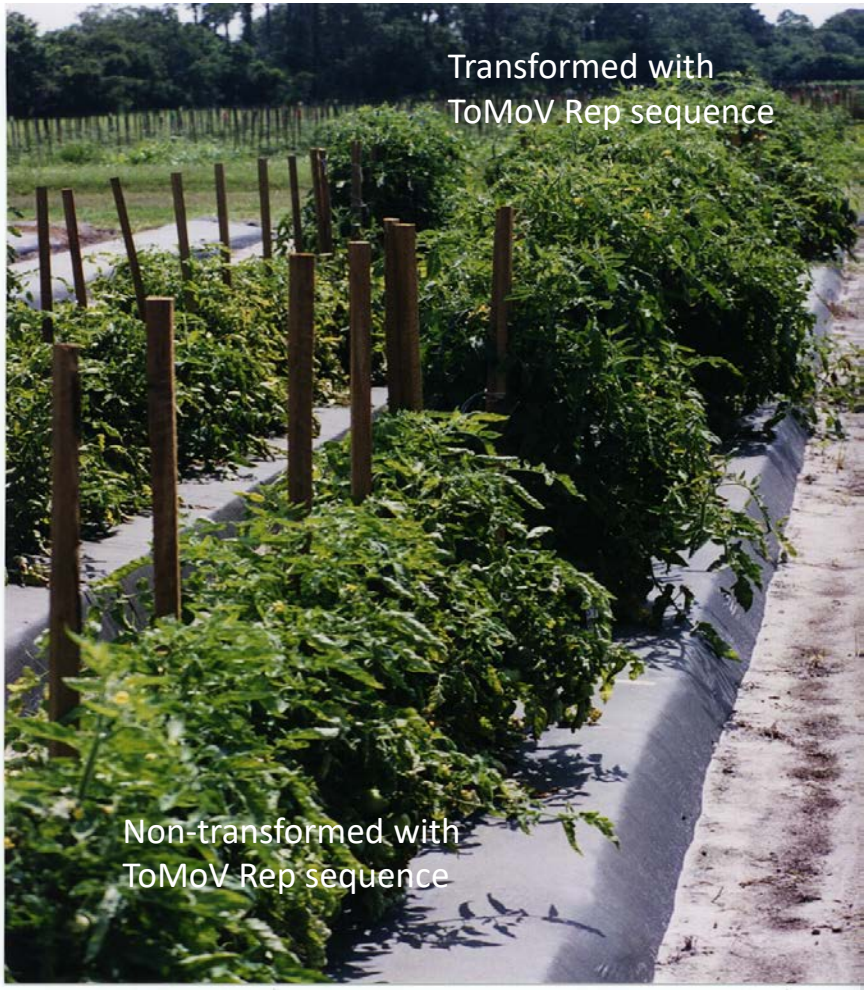
In general:
blocking of earlier steps in replication is more effective than blocking later steps

A. Engineering based on “pathogen-derived resistance”

b. Virus Resistance through Pathogen-mediated Resistance (PDR)

2. Using sequences of non-structural protein genes

- Mutated viral genes which interfere with the function of a wild-type gene can be used as transgenes.
- A strategy involving a mutation (defective) in one motif of a multi-motif protein is a useful strategy for interfering with viral replication.
- This interference with the function of the wild-type gene has been coined as a **dominant negative mutant**.



All plants inoculated with ToMoV

Tomato transformed with the partial *Tomato mottle begomovirus* (ToMoV) *Rep* gene showing resistance to ToMoV

Non-transformed tomato

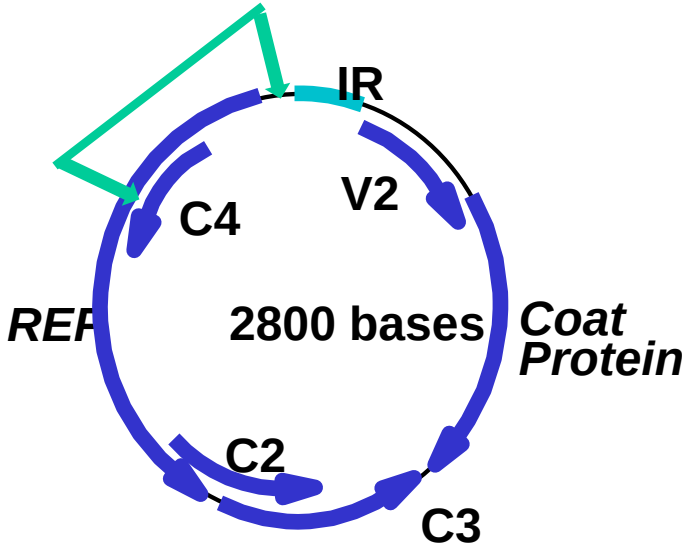
Yield Trials of Tomatoes Genetically Engineered for Resistance to *Tomato mottle virus*

Tomato Line	Total Marketable Yield (ca/A)	
	Inoc. With ToMoV	Non-Inoc. With ToMoV
4	1702.9 a	1503.7 ab
11	1689.0 a	1747.6 ab
12	1905.0 a	1742.4 ab
FL 7324	325.2 b	1184.8 bc
Agriset	580.8 b	1381.4 abc

- Yields of inoc. transgenic plants were 3-5 times greater than inoc. non-transgenic plants.
- Yields of inoc. transgenic plants were equal to non-inoc. plants

Fall 1998

Equivalent results obtained with 2/5 TYLCV *Rep*



Transformed tomatoes show "non-host resistance" to TYLCV

Transgenic virus resistance using Rep sequences

- Resistant plant appears to be immune.
- No symptoms are ever produced.
- Virus never detected in non-inoculated leaves of inoculated plants.
- Plants are not considered immune because the virus is presumed to have limited replication in order to turn on the resistance. Some non-hosts are thought to have the same kind of resistance.

Inoc. and transformed

Inoc. and non-transformed

b. Virus Resistance through Pathogen-mediated Resistance (PDR),

Types of viral genes used tested or used successfully

1. Using sequences of structural protein genes (coat proteins)

2. Using sequences of Non-structural protein genes

3. **Using antisense sequences of genes**

   Design a DNA sequence that when transcribed results in a single-stranded RNA that is complementary to the messenger RNA (mRNA) sequence of a viral gene. This won't result in a gene product and it still turns on PTGS.

4. **Use hairpin sequences**

   This turns on PTGS.

A. Engineering based on “pathogen-derived resistance”

In Development or Waiting Registration:

- Fruit trees with resistance to *Plum pox virus* (an exotic virus) whose presence would severely limit exports (now in process of being released)
- Turfgrass that only needs to be mowed once/month
- Plants that express human proteins that are currently obtained through the slaughter of animals
- Plants that lack common allergens (ie peanuts)
- Ornamentals with increased fragrances
- Improved flavor of tomatoes
- Many more….

Two broad means of engineering plants for resistance to viruses:

A. Genome engineering based on “pathogen-derived resistance”

B. Genome engineering based on CRISPR/Cas9 directed changes to the host genome

Systems that improve crop plant resistance to viruses by:

1) directly targeting viral genomes OR
2) targeting host factors

Most successful system: CRISPR/Cas9

B. Genome engineering based on CRISPR/Cas9 directed changes to the host genome

CRISPR/Cas9) System: CRISPR: Clustered regularly interspaced short palindromic repeat.

- Some bacteria have a similar, built-in, gene editing system to the CRISPR-Cas9 system that is used to respond to invading pathogens like viruses.
- The bacterial system was used to create the gene editing tool, known as CRISPR/Cas9

CRISPR/Cas9:

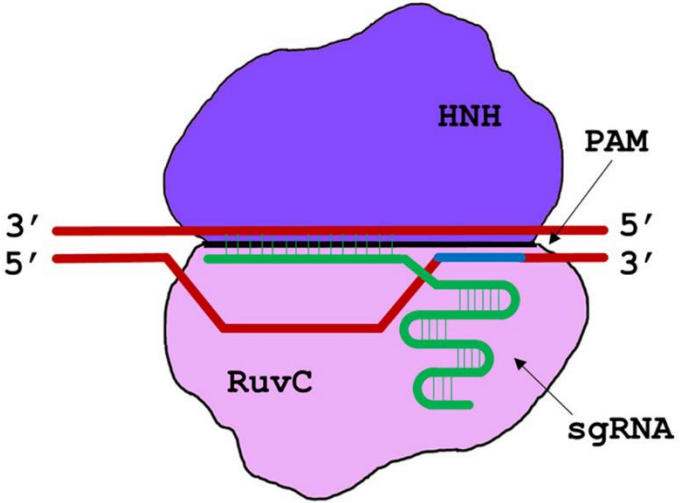
- It is faster, cheaper and more accurate than previous techniques for editing DNA
- CRISPR-Cas9 is a unique technology that enables geneticists to edit parts of the genome by removing, adding or altering sections of the DNA sequence.
- Has a wide range of potential applications

B. Genome engineering based on CRISPR/Cas9 directed changes to the host genome

Cas9: endonuclease from *Streptococcus pyogenes*, with two domains, RuvC and HNH. These act as scissors to cut DNA.

This system consists of a single guide RNA (sgRNA) and Cas9. The sgRNA defines the specific site to be targeted where Cas9 nuclease produces double stranded breaks (DSBs) 3 base pairs upstream of protospacer adjacent motif (PAM in the case of *S. pyogenes*).

The repair of these DSBs by endogenous systems results in targeted genome modifications.

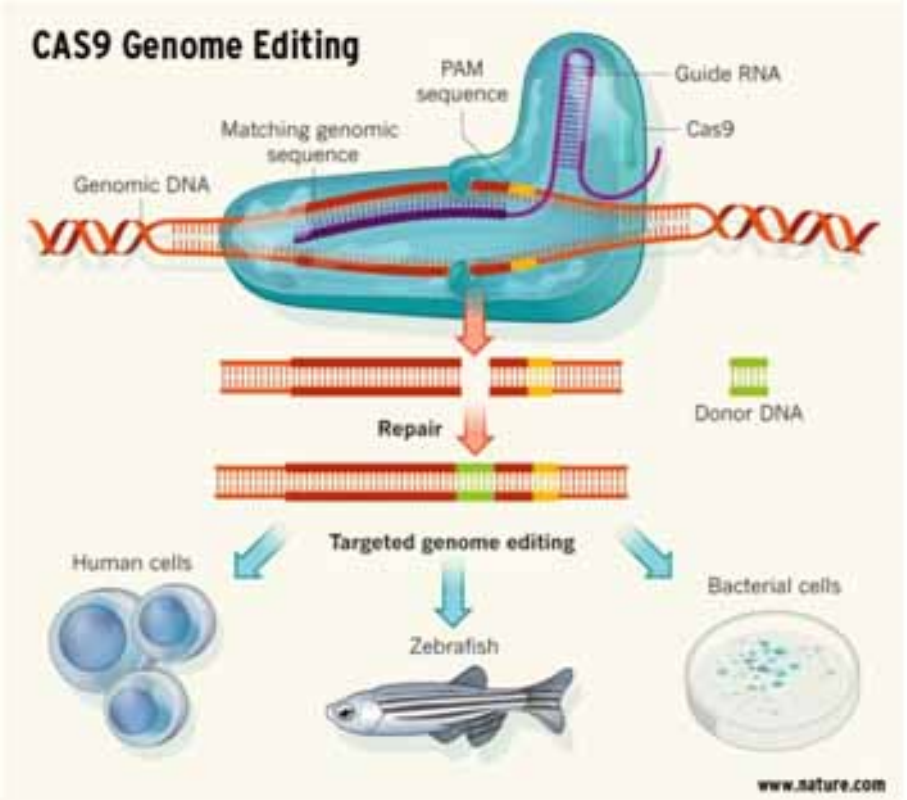


B. Genome engineering based on CRISPR/Cas9 directed changes to the host genome

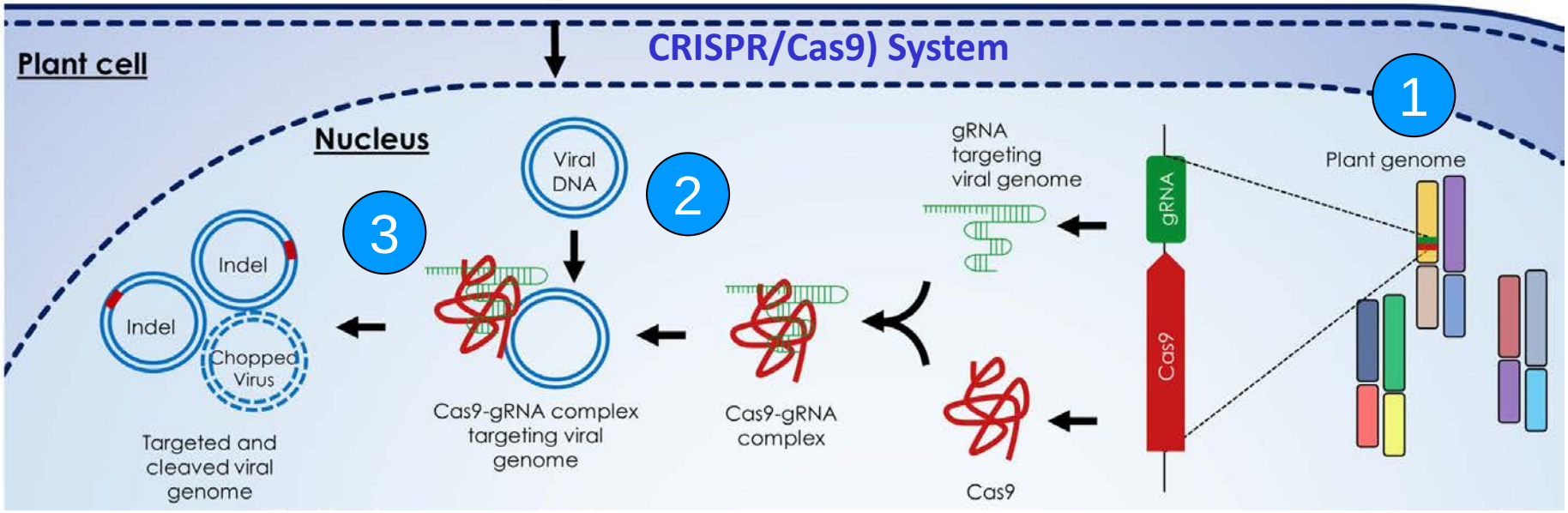
Used to successfully edit genes in plants, animals, bacteria, fungi…

System is commercially available from many sources

Editing services using CRISPR/Cas9 are commercially available



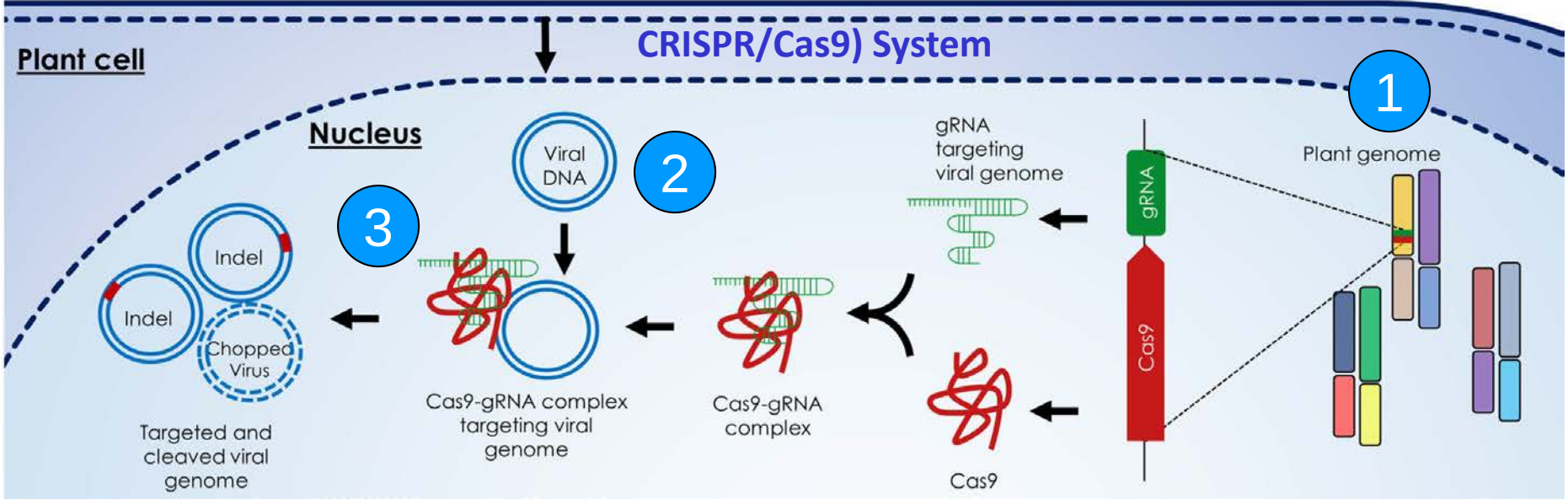
Youtube video (4:12 min) :
https://www.youtube.com/watch?v=2pp17E4E-O8



Proposed use to develop resistance to a DNA plant virus:

1. Components of the CRISPR/Cas9 machinery, gRNA, and Cas9, are expressed from the plant genome (transgenic or otherwise) and once produced form the gRNA-Cas9 complex.

2. Upon viral infection, the viral DNA replicates through the dsDNA replicative forms inside the nucleus of host cell.



3 The gRNA-Cas9 complex targets the viral dsDNA at target sites complementary to the gRNA sequence and cleaves the viral genome via double strand breaks (ds breaks). The breaks have 2 outcomes:

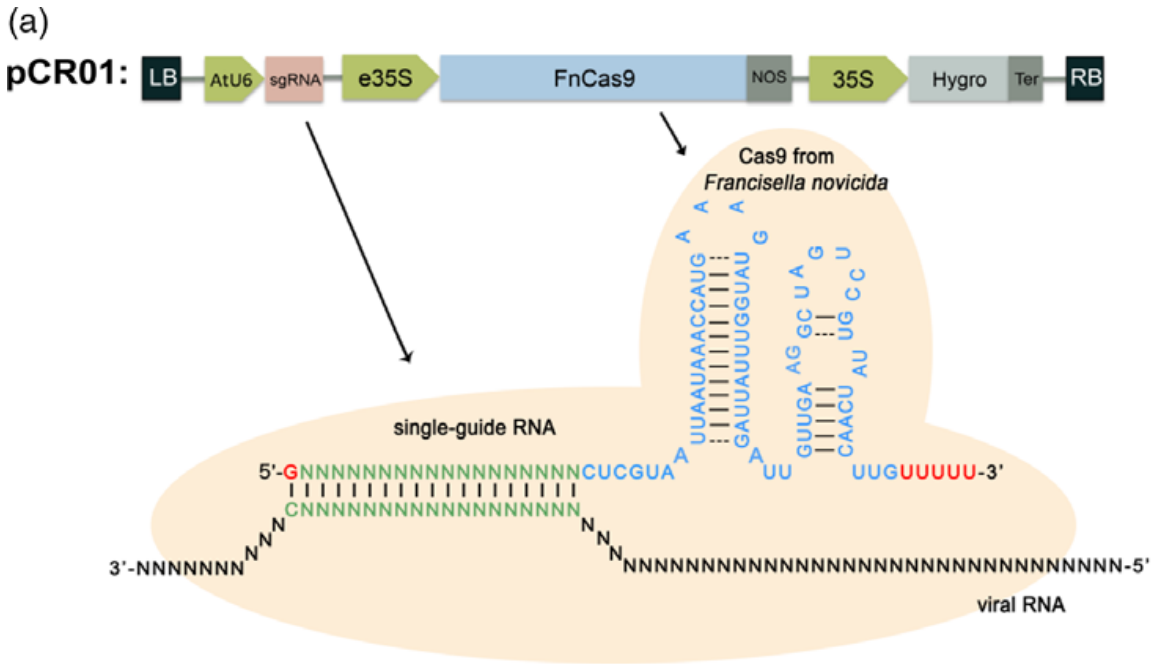
- can be repaired by non-homologous end joining (NHEJ) repair which can result in mutations and loss of function in the gene.
- ds breaks are susceptible to enzymatic degradation which results in the degradation of the virus genome.

For RNA viruses:

First example of RNA virus resistance using gene editing:

Researchers selected a modification of the CRISPR/Cas9 system (which targets DNA):

Used Cas9 from *Francisella novicida* (FnCas9) and the type VI-A CRISPR/Cas effector from *Leptotrichia shahii* (LshCas13a) or *L. wadei* (Lwa-Cas13a), which were reported to target RNA *in vivo*.

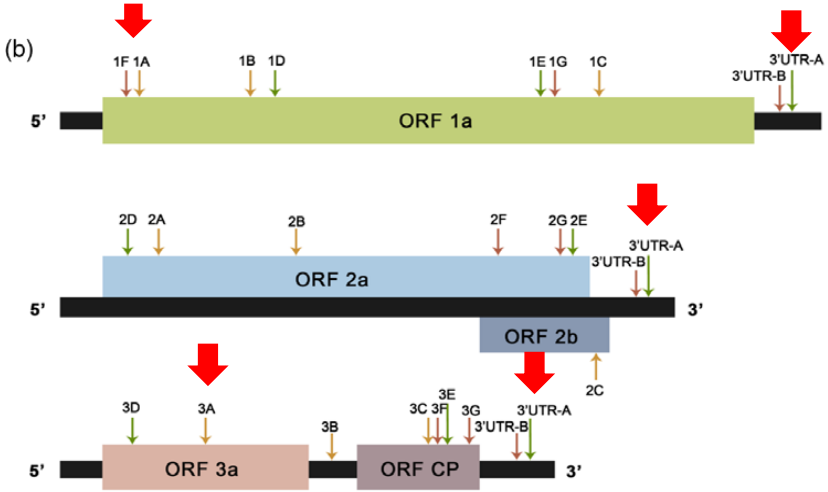


Zhang T, et al. Plant Biotechnology Journal (2018) 16, pp. 1415–1423

For RNA viruses:

First example of RNA virus resistance using gene editing:

- They selected 30 sites in the genome and evaluated various sequences to use as sgRNAs (using a detached leaf assay)
- Selected 3 sites for further evaluation:
  pCR01-**1A**, pCR01-**3C**, pCR01-**30UTR-A**, with the pCR01 (control).
- Plants were inoculated with CMV and results were evaluated 2 weeks later



Zhang T, et al. Plant Biotechnology Journal (2018) 16, pp. 1415–1423

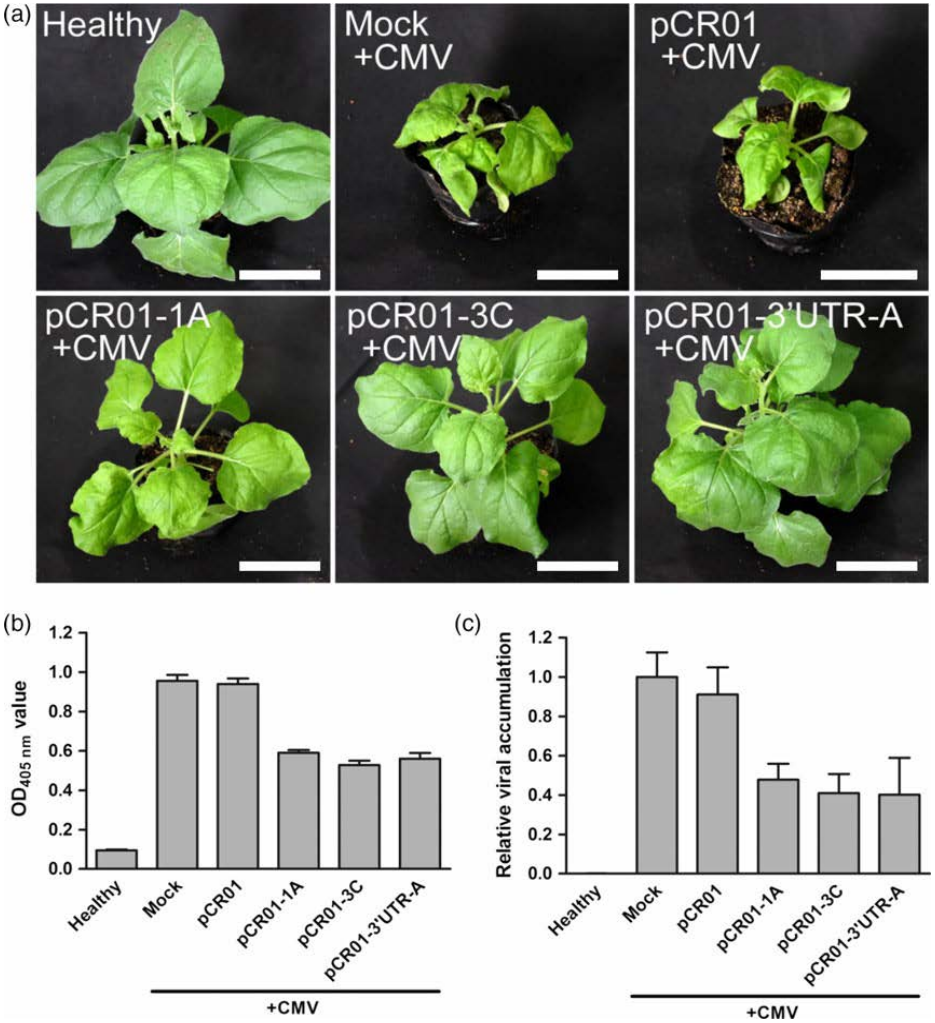
For RNA viruses:

First example of RNA virus resistance

Results:

- Symptoms (above) were reduced in plants treated with either of the sgRNAs.

- Abs values using ELISA (below) showed that virus coat protein accumulation in plants inoculated with the three pCR01-sgRNAs were reduced by 40–50%, compared with mock inoculated.



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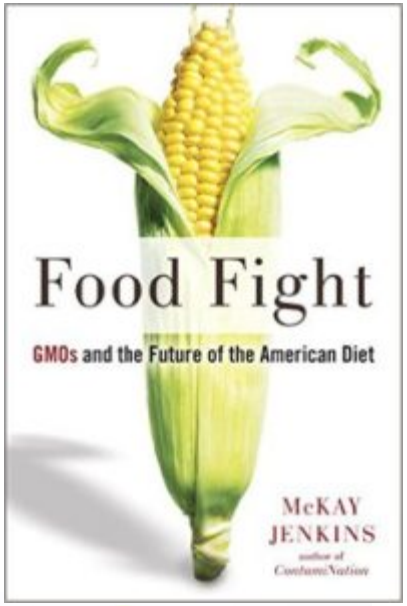
Genetically engineered/Genome edited Virus Resistance:

- Many crops that have resistance to viruses for which no other sources of resistance have been found.
- With traditional breeding methods, the available gene pool is restricted by sexual incompatibility of many interspecific and intergeneric crosses.
- Genetic engineering and gene editing provide a means of for broadening the pool of resistance

You did WHAT to my plants?

Oh noes…. My plants aren’t natural!

The Politics of Genetically Modified Plants



Gonsalves, D., Gonsalves, C., Ferreira, S., Pitz, K., Fitch, M, Manshardt, R. and Slightom, J. 2004. Transgenic Virus-Resistant Papaya: From Hope to Reality in Controlling Papaya Ringspot Virus in Hawaii. APS*net* Features. Online. doi:10.1094/APSnetFeature-2004-0704

PRSV Resistant Papaya in Thailand

Forbidden Fruit: Transgenic Papaya in Thailand
S. N. Davidson, Plant Physiol. 2008 June; 147(2): 487–493.
doi: PMCID: PMC2409016

Fig. 2. Kapoho field trial started in 1995, showing a solid block of PRSV-resistant Rainbow growing well while the surrounding susceptible non-transgenic Sunrise is severely infected with PRSV. Picture taken 19 months after start of the field trial.

Dec 5th 2013
Ban on all GMO crops approved by Kona Hawaii County Council (6-3 vote)
[A Lonely Quest for Facts on Genetically Modified Crops]

February 6 2014

Right-to-farm legislation wilts in state Legislature

By TOM CALLIS
Stephens Media Hawaii

Right-to-farm legislation that could have threatened Hawaii County's law restricting the use of transgenic crops appears to have been defeated in the state Legislature.
- See more at: http://westhawaiitoday.com/news/local-news/right-farm-legislation-wilts-state-legislature#sthash.70mpui1v.dpuf

Maui's GMO Ban Blocked By Federal Judge

AP | AUDREY McAVOY | Posted 11.14.2014 | **Green**

HONOLULU (AP) — A federal judge says Maui County may not implement a new law banning the cultivation of genetically modified organisms until he can consider arguments in a lawsuit against the measure.

Judge Barry Kurren said Friday that both sides have agreed to delay the date the law goes into effect.

Monsanto Co. and a unit of Dow Chemical Co. sued the county earlier this week to stop the law. Local businesses joined the lawsuit.

Maui voters passed a ballot initiative last week creating the law. The measure was to take effect after officials certified the election results. That was expected late this month.

Kenneth Robbins, an attorney for the plaintiffs, says Kurren is saying the plaintiffs have shown they could potentially suffer irreparable harm if the law goes into effect.

Judge: Maui ban on GMO crops is invalid

A federal judge has ruled that federal and state law pre-empts Maui County GMO-crop ban

June 30, 2015 10:55PM ET Updated July 1, 2015 2:34AM ET

Big concerns about use of pesticides in Hawaiian paradise

Residents say they're being poisoned by chemicals used on seeds on farms. Jacob Ward goes to Kauai to investigate (Part 1)

Hawaii Counties Can't Regulate GMOs and Pesticides According to New Ruling

The Associated Press

Nov 19, 2016

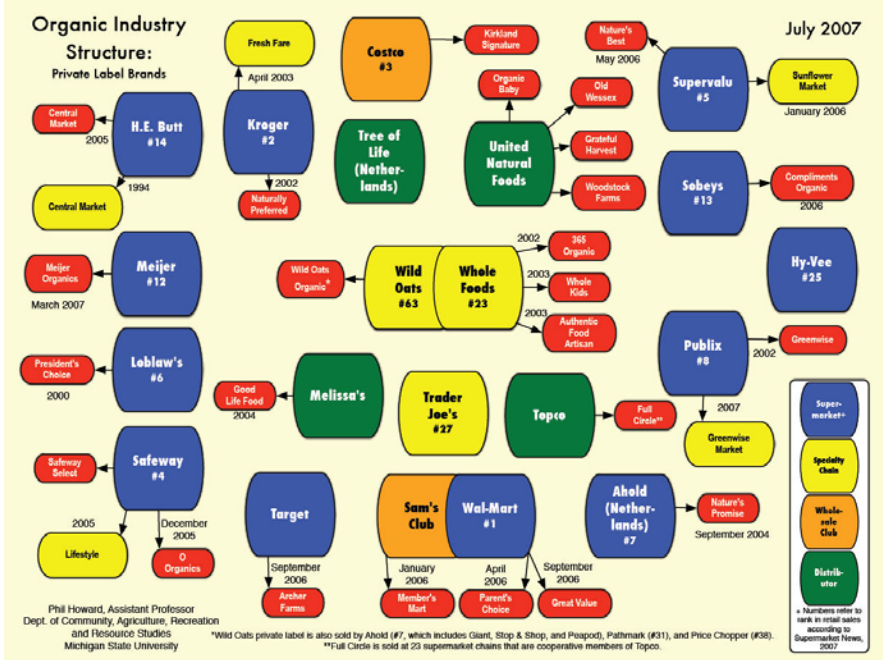
A federal judge has ruled that three Hawaii counties can't enact their own bans or regulations on genetically modified crops and pesticides, handing a victory to the major agriculture companies that fought the regulations.

$$$$


GMO
Organic

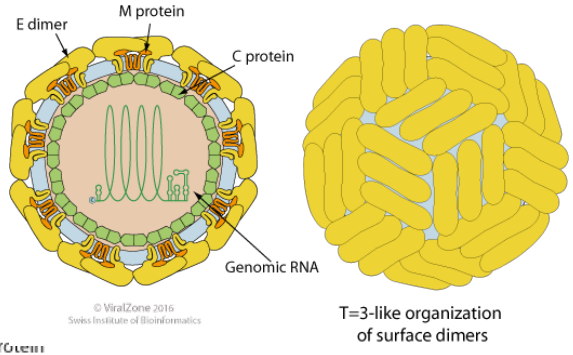
$$$$

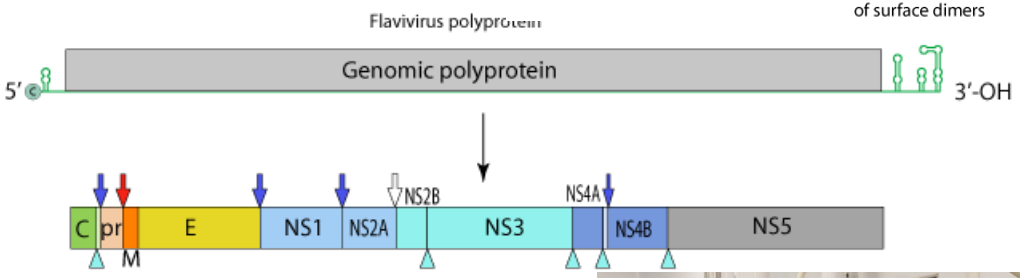

THESE COMPANIES
$$ OPPOSE $$
GMO LABELING
Source: http://cal-access.sos.ca.gov/Campaign/Committees/Detail.aspx?id=1344135&session=2011&view=late1


Organic Industry Structure:
Private Label Brands
July 2007
Phil Howard, Assistant Professor
Dept. of Community, Agriculture, Recreation and Resource Studies
Michigan State University
*Wild Oats private label is also sold by Ahold (#7, which includes Giant, Stop & Shop, and Peapod), Pathmark (#31), and Price Chopper (#38).
**Full Circle is sold at 23 supermarket chains that are cooperative members of Topco.

Many medicines are vaccines are genetically engineered:

Zika virus
Flaviviridae
(+) ssRNA genome





Ex.: insulin, human growth hormones, follistim (for treating infertility), human albumin, monoclonal antibodies, blood clotting factors, many vaccines, and many more.

Frederick plant manufacturing Zika vaccine.
Sep 15, 2016

At a specially designed manufacturing plant in Frederick, workers and machines have been filling hundreds of tiny vials with a vaccine that could prevent more Zika virus infections.

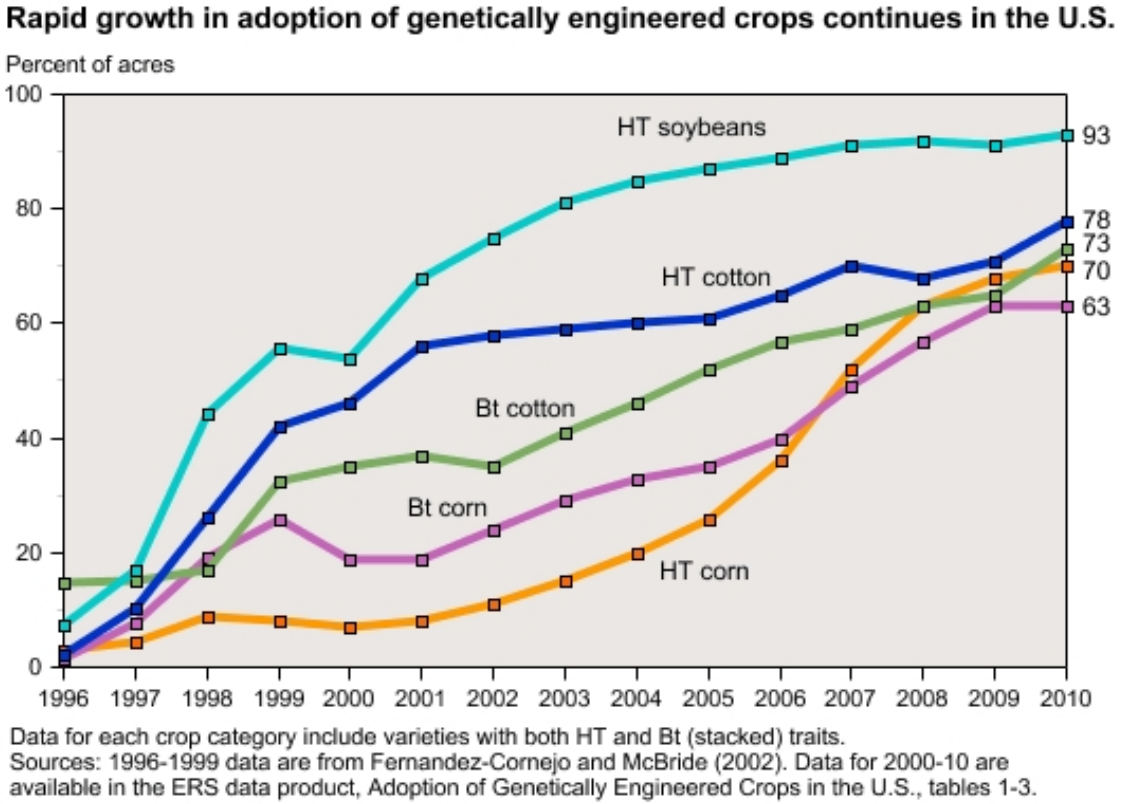
When the vaccine is injected into the body, genetically engineered DNA assembles into a non-replicating form of the Zika virus that provokes the immune system to respond.

DNA vaccines do not contain infectious material, so this Zika vaccine cannot infect a patient with the Zika virus.

Cultivation areas with genetically modified plants

Big value crops: Soybean, Corn, Cotton, ….

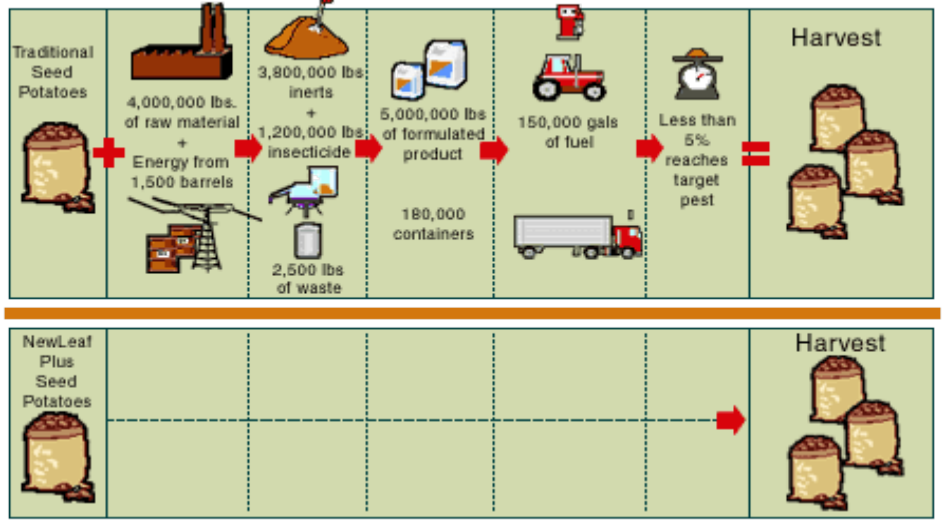
Primarily transformed for insect resistance, herbicide resistance

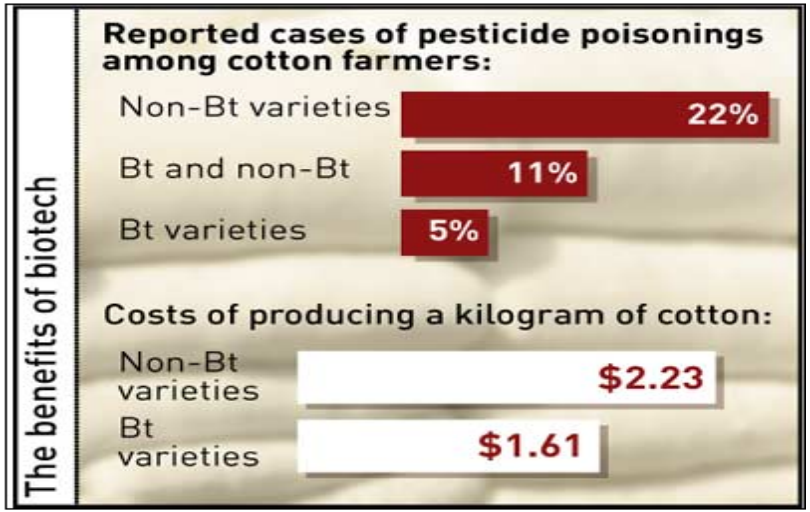


Benefits to genetic engineering of crops for growers:

Reduction in Inputs and Wastes

Fewer pesticide applications increases safety for growers





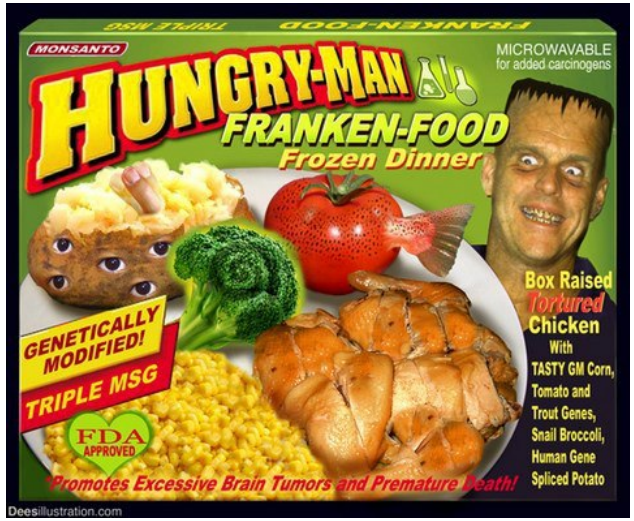
Pesticide poisoning among cotton farmers

Environmental Risks Proposed by GMO opponents:

- Creating new or more vigorous pests and pathogens
- Harm to "non target" beneficial species — soil organisms, helpful insects, birds, or other animals
- Decreased nutritional value
- Unwanted gene flow to non-target plants (wild, weed, etc..)
- Evolution of super-resistant weeds
- Irreparable changes in species diversity and genetic diversity within a species.


"IF IT CAME FROM A PLANT, EAT IT; IF IT WAS MADE IN A PLANT, DON'T."
-MICHAEL POLLAN
GMOINSIDE.org
Coalition Powered by Green America


Frankenfood
Bite some before it bites you!


MONSANTO
MICROWAVABLE
for added carcinogens
HUNGRY-MAN
FRANKEN-FOOD
Frozen Dinner
GENETICALLY MODIFIED!
TRIPLE MSG
FDA APPROVED
*Promotes Excessive Brain Tumors and Premature Death!
Box Raised Tortured Chicken With TASTY GM Corn, Tomato and Trout Genes, Snail Broccoli, Human Gene Spliced Potato
Deesillustration.com

Public Perception of GMO Risks

Famed horticulturist Luther Burbank produced a book in1893 entitled ***New Creations In Fruits And Flowers*** that described hundreds of new hybrid plant species.

Burbank was immediately denounced by groups who claimed that **only God could "create" a new plant**.

Once the controversy subsided, ***New Creations…*** made Burbank internationally famous and by 1901 Burbank plums and Burbank potatoes were introduced coast-to-coast to the delight of consumers.

Proposed:

Genetic Engineering/Editing at the beginning of the 21st century is the equivalent of Electricity at the beginning of the 20th century

ELECTRIFIED PORTSMOUTH, NH BRIGHT IDEA IN 1900?

JANUARY 1900

A Reporter's Notebook

Electric, electric, electric! The way people bandy that word about nowadays, you'd think electricity is the new salvation of mankind. That attitude is particularly "on the wire" this week as the Old Town by the Sea hurtles relentlessly from the comfortably familiar 19th century into the unknown landscape of the 20th.

This writer, however, urges caution as we contemplate the coming Electric Age, admonishing readers not to entertain Utopian flights of fancy. Certainly this modern miracle has its usefulness, but **for every labor-saving benefit, electricity brings us -- something, we fear, is lost in the trade**. We have long acknowledged the value of the telegraph, bringing us speedy long distance communication, but bringing with it, an unsightly army of poles and wires that pollute the view of our historic city. Now comes the electric telephone, which offers promise. It promises, detractors fear, to strike at the very sociability of our community. People who would normally seek out each other's company, may now speak over a wire, and so far, with minimal fidelity. Still, the prophets (or should we say "profits") tell us that some two million telephone receivers may be in use by this time next year in 1901.

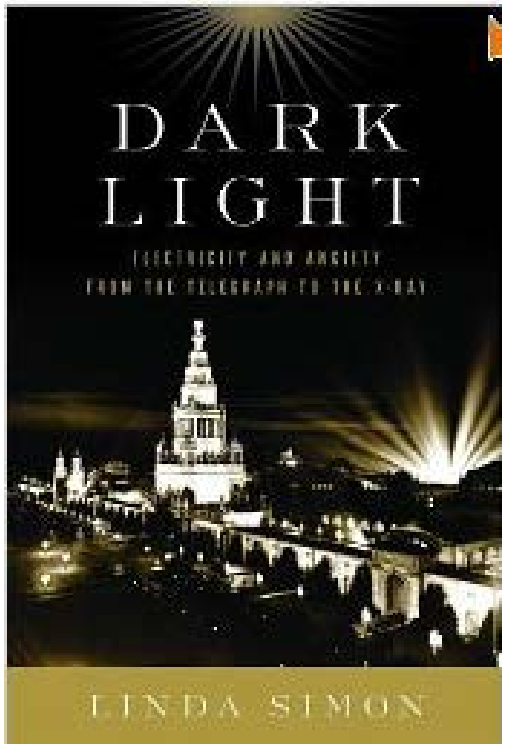
Whether all these gentle people truly have something worthy to say, remains a mystery.

We were pleased, years back, to see electric bells made available to area businesses in need of alarms to protect goods from theft and fire. Here, at last, was a use above reproach, but progress waits for no man. Today we see that Trafton & Sons of 36 Congress Street are advertising electric light wiring for business and for homes. **Electrified stores and electrified street lamps we can applaud -- but electrified homes?** To date, thanks to the "shocking" cost of power from the Rockingham Electric Light and Power Company on Daniel Street near the ferry to Kittery, few residents can afford the conversion from the dependability of gas.

But to see the future, a local pundit informs me, one need only walk down Water Street at night where the incandescent glow of electrical lights beckon hapless sailors from across the Piscataqua to visit houses of adult entertainment. Vice and corruption, it seems, have deep pockets. **Electricity is the new Jezebel**, seducing our young men into the arms of immorality……

http://www.seacoastnh.com/Places_%26_Events/NH_History/Electricity_Sparks_Fears__in_1900?/

“Thirty years after Edison invented a successful light bulb, only ten percent of American homes were wired. Edison could not conquer the public fear that "nature would extract retribution for harnessing its power."



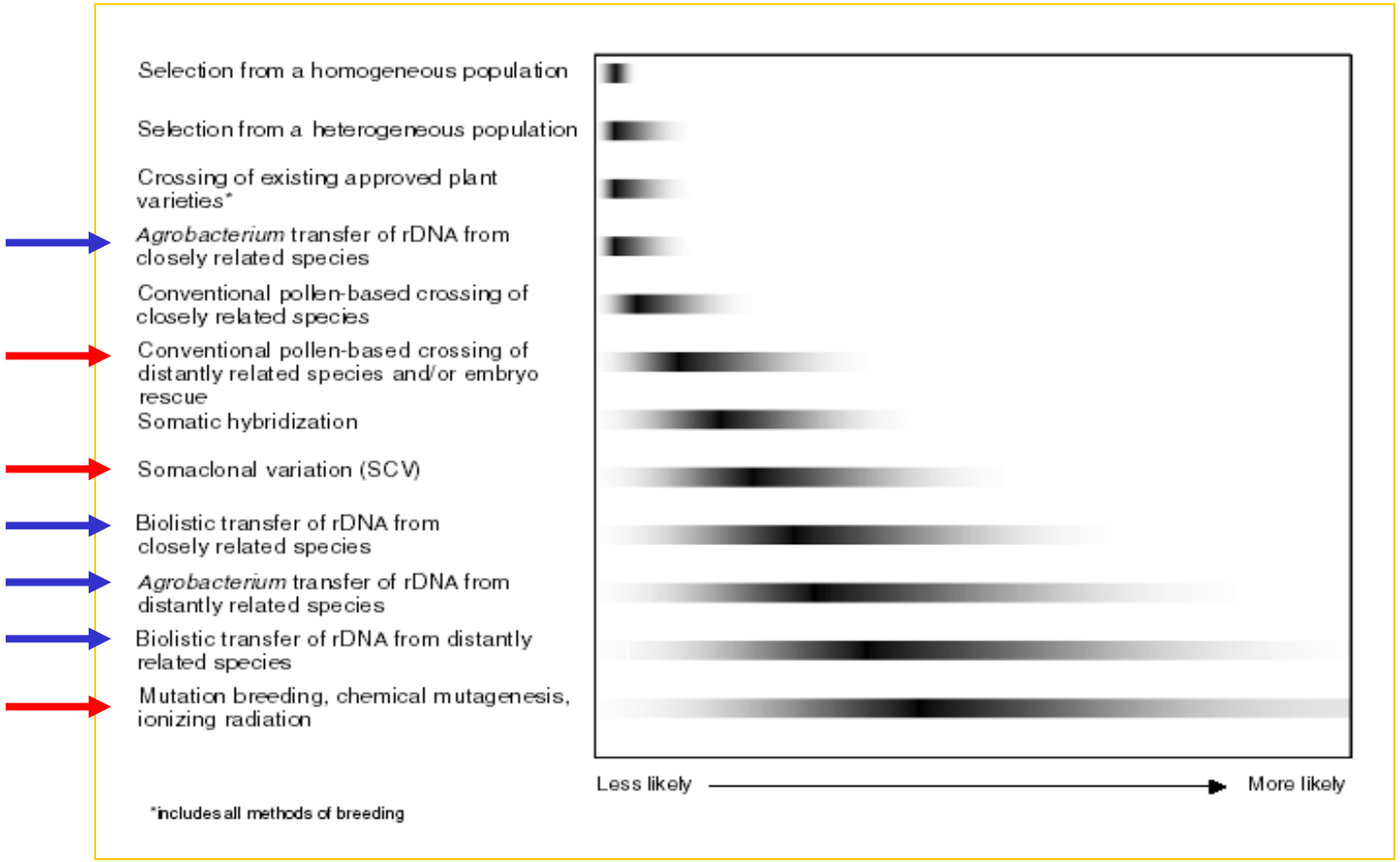
Registration of GMO's

Registration not required for conventionally-derived resistance
Registration Process takes 3-5 years
Involves USDA-APHIS, EPA, FDA
Approx. $5 million per event
Event = one gene in one background (cultivar)
Each GMO cultivar costs approx. $5 million to register – NOT ECONOMICALLY FEASIBLE FOR MOST CROPS

"The screening of transgenic crops is far more intense than that of the products of traditional breeding. Transgenic plants have to go through more hoops before they are even considered for field release. "

Roger Hull, PhD
John Innes Centre
Initiator of CaMV research at JIC

Potential for "Unintended Consequences"

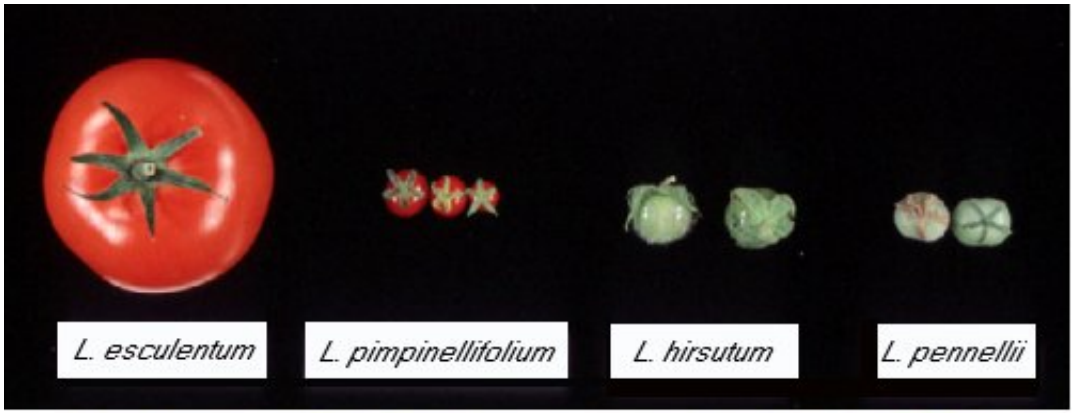


Genetic engineering

Conventional Breeding

National Research Council (2004) http://books.nap.edu/execsumm_pdf/10977.pdf

Fruits of wild tomato species



Fruits of resistant breeding line containing TYLCV-resistance derived from *L. hirsutum.*

https://theaggie.org/2019/05/01/you-hate-gmos-and-youre-so-hip-and-broke/