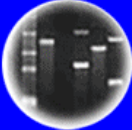


DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

HC70A, PLSS530, & SAS70A Spring 2015

Genetic Engineering in Medicine, Agriculture, and Law

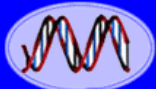
**Professors Bob Goldberg,
Channapatna Prakash, & John Harada**

Lecture 2 The Age of DNA: What Is Genetic Engineering-Part Two

UCLA



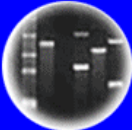
UC DAVIS
UNIVERSITY OF CALIFORNIA



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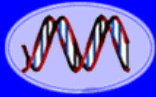
Cloning: Ethical Issues
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Plants of Tomorrow

THEMES

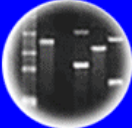
1. Spectacular Examples of Genetic Engineering 1.0 - What Can Be Done?
2. What Does Genetic Engineering Tell Us About Basic Genetic Processes in All Organisms?
3. The Future is Here - Genetic Engineering 2.0!
4. Genetic Engineering - Anything New?
5. Are Vegetables Engineered - Demonstration
6. Classical vs. 21st Century Genetic Engineering -
7. Is Science Hocus Pocus or a Precise Process?
8. Understanding Basic Genetic Processes → Understanding How Genetic Engineering Uses Natural Rules of the Cell (i.e., it isn't magic)!



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Plants of Tomorrow

Last Lecture - Age of DNA & Genetic Engineering: Part One

Today's Class - Age of DNA & Genetic Engineering: Part Two

Genetic Engineering - Spectacular Examples

Genetic Engineering - Anything New?

Recall: The Era Of DNA Manipulation Means.....

1. Specific DNA Sequence and/or Gene Can Be Isolated From Any Organism
2. DNA Segments of Any Kind From Any Organism Can Be Combined
3. Isolated Genes Can Be Re-Inserted Into the Chromosomes of Any Organism and Made to Work

The Critical Point - There Are No Genetic Limits. All Biological Organisms Use the Same Genetic Rules. The Implications Are Enormous!!



What Can Be Done With Genetic Engineering?

A Few Examples of Genetic Engineering 1.0

Using a Jellyfish Gene to Make Bacteria, Animals, and Plants Glow!!!!

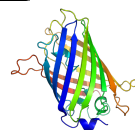


Aequoria victoria

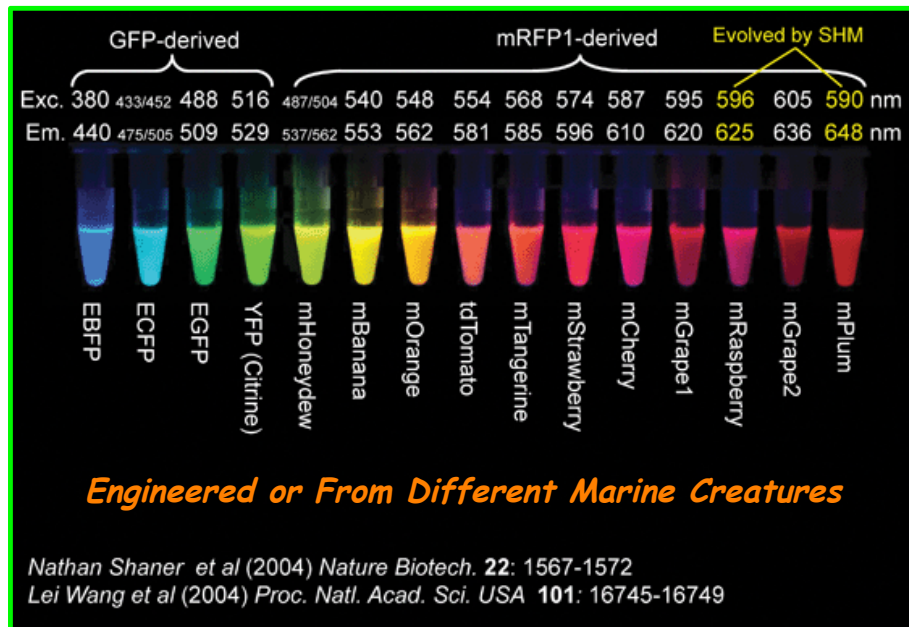
Green Fluorescence Protein (GFP)

(238 amino acids)

Nobel Prize in Chemistry - 2008 - Shimomura, Chalfie, & Tsien



There Are Many Different Kinds of Fluorescing Proteins!



Nobel Prize in Chemistry – 2008 – Shimomura, Chalfie, & Tsien

DNA
Genetic Code of Life

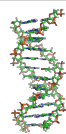
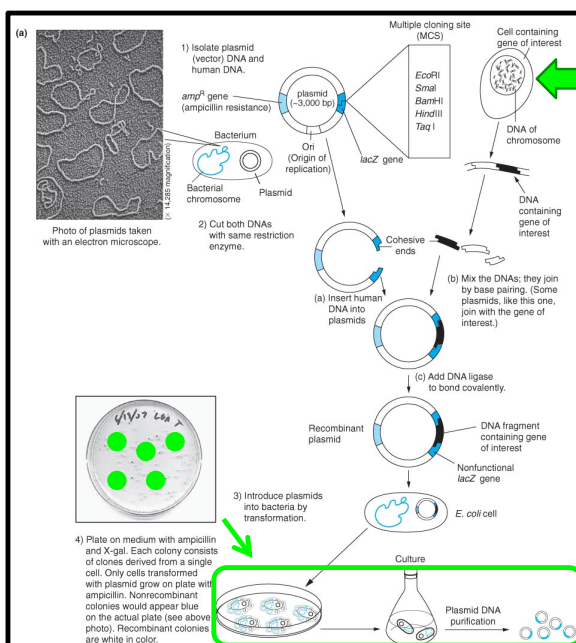
Entire Genetic Code of a Bacteria

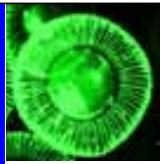
DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

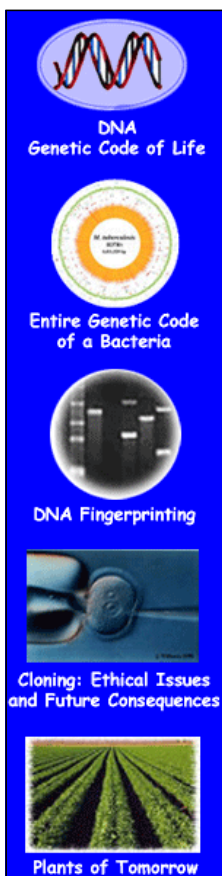
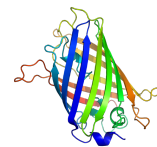
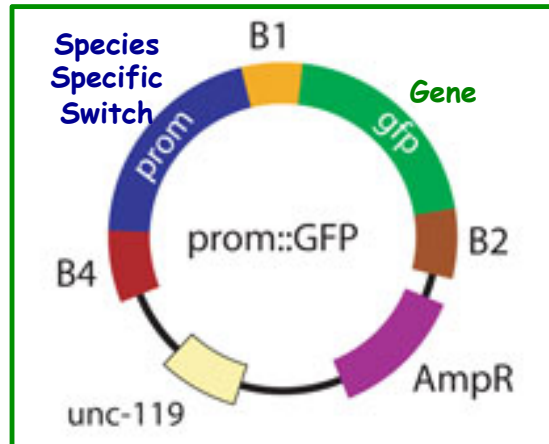
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Using Recombinant DNA to Clone the Jellyfish GFP Gene

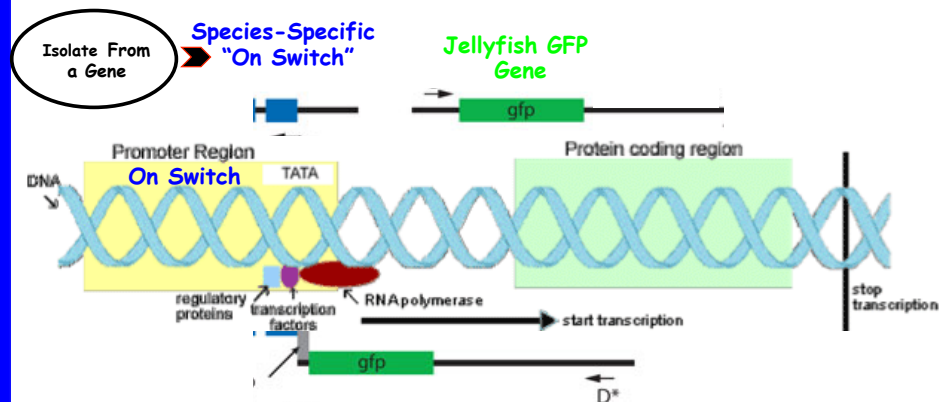




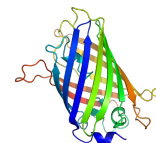
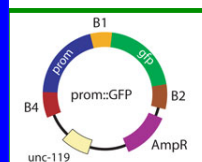
A Recombinant Plasmid Containing the GFP Gene



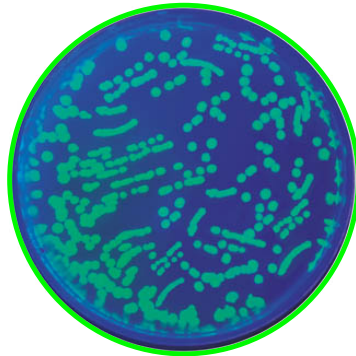
Engineering the Jellyfish GFP Gene to Be Active in Different Organisms



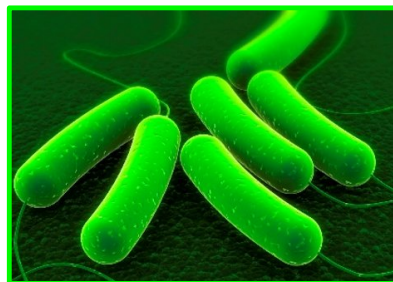
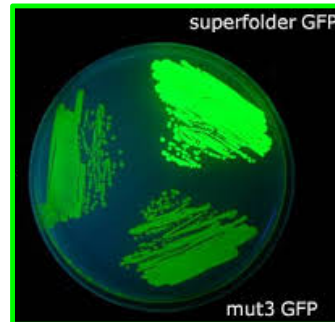
Engineered Chimeric GFP Gene



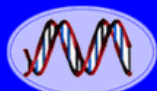
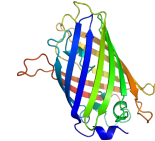
GloColi - *E. coli* Engineered With the Jellyfish GFP Gene!



E. coli Switch +
Jellyfish GFP Gene



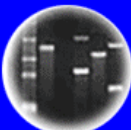
E. coli Synthesizes
GFP Protein!



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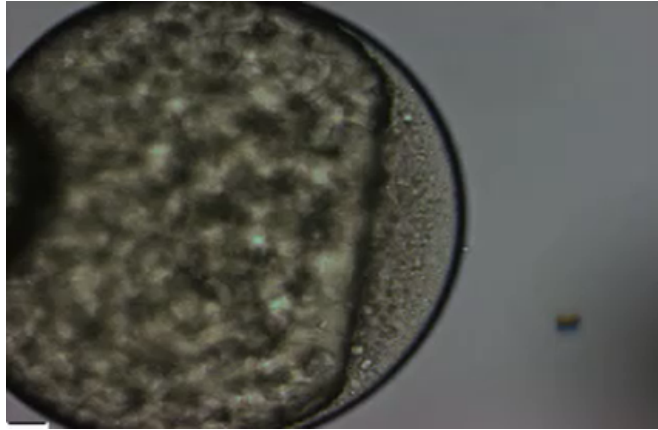
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Question One

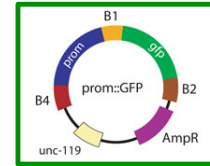
Engineering *E. coli* to Express a Jellyfish *GFP Gene* Implies That Genetic Processes in Bacteria and Jellyfish Are Similar Even Though They Are Separated By One Billion Years of Evolution!

- a. Yes
- b. No

Engineering a “GloFish”

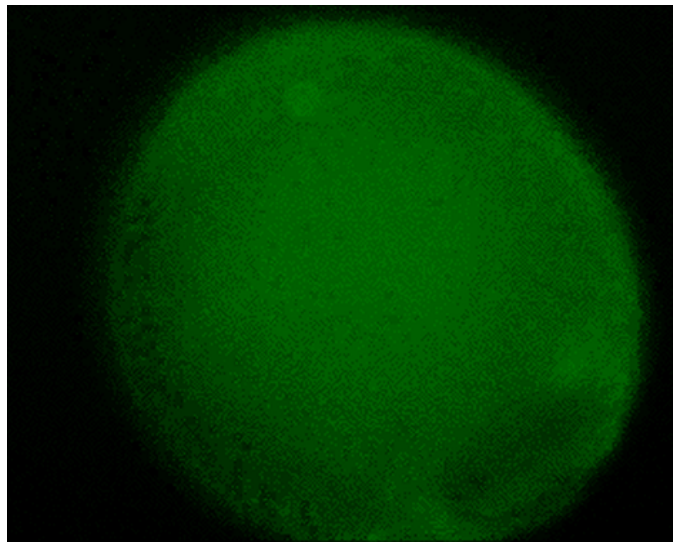


Zebrafish
Danio rerio



.....Using Genetic Engineering To Insert
A Jellyfish Gene into a Zebrafish Egg!

A “GloFish” Embryo!!

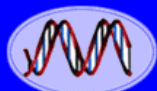


Zebrafish - Danio rerio

Genetically Engineered "GloFish!!"



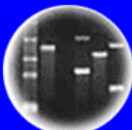
Note Different Fluorescing Colors - Due to Different Jellyfish Genes



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GloFish Are Not Sold In California (& Canada, or Europe)

- **Cal. Fish and Game Code § 15007 (2007)**

Regulation Makes it illegal to spawn, cultivate, or incubate any transgenic fish in the state controlled waters of the Pacific Ocean.

- **Title 14, Section 671.1 CA Code of Regulations (2003)**

Regulation. Movement of live transgenic aquatic animals from facilities is prohibited unless specifically permitted by the Department. **Release of transgenic aquatic animals or their progeny into waters of the state is prohibited.**

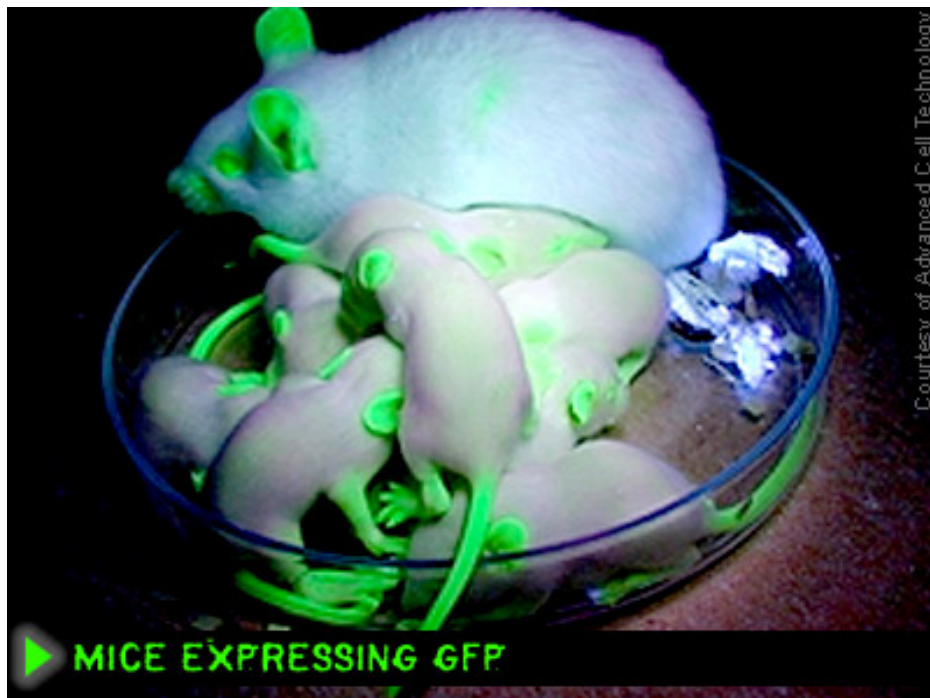
Genetic Engineering & the Law!!



How About a GloFly!



What About “GloMice!!!”



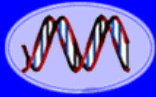
And Glo Monkeys, Cats and Pigs as Well!!!



***Engineering a GloPlant With the
Same Jellyfish Gene!!!***



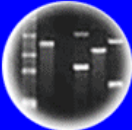
***What are the Philosophical and Biological
Implications of These Experiments?***



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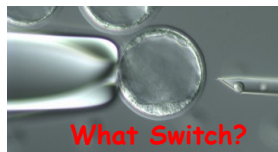
Question Two

Does Engineering Different Organisms With a Chimeric GloFish Gene Indicate that Genes Work Independently of Other Genes?

- a. Yes
- b. No

Dramatic growth of mice that develop from eggs microinjected with metallothionein–growth hormone fusion genes

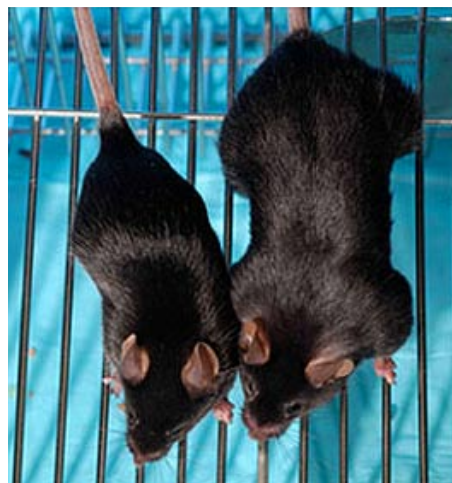
Richard D. Palmiter[†], Ralph L. Brinster[†], Robert E. Hammer[†],
Myrna E. Trumbauer[†], Michael G. Rosenfeld[‡], Neal C. Birnberg[§]
& Ronald M. Evans[§]



What Switch?

Nature,
December, 1982
~33 Years Ago!

Engineering "Mighty Mouse" With a Rat Growth Hormone Gene



How About a Salmon That Grows Faster Using a Fish Growth Hormone Gene?



GENETIC ENGINEERING

Genetically-modified salmon are closer than ever to a dinner plate near you

The super salmon are (almost) here. The Food and Drug Administration has reportedly finished its evaluation of the environmental impacts of the first fish genetically engineered (GE) for human consumption.

FDA expected to approve Genetically Modified Salmon

AQUAADVANTAGE SALMON | JANUARY 3, 2013 | BY: MARK WACHTLER | [Subscribe](#)

FDA faces opposition over genetically engineered salmon

A group of eight senators is asking the FDA to cease consideration of the fish as food, and is threatening to pull funding for the study if the agency does not comply.

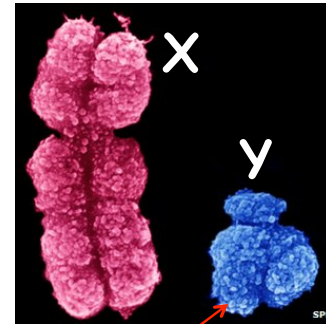
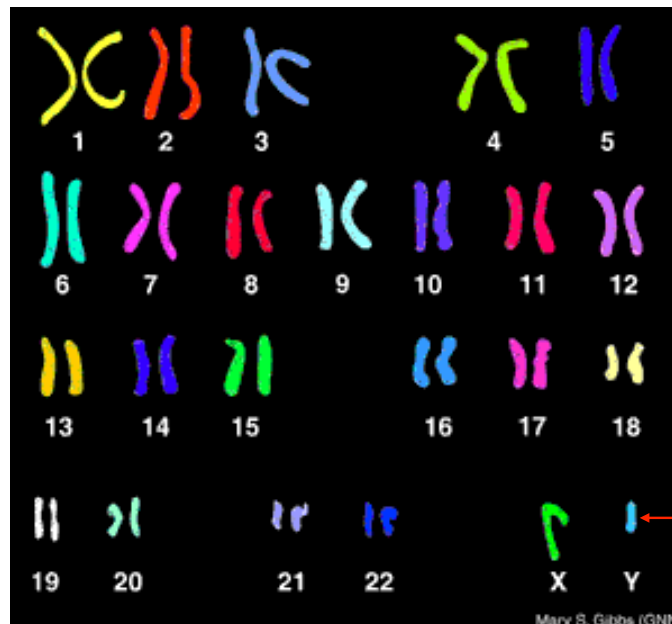
What's a GMO?



How About Changing The Sex Of An Organism?



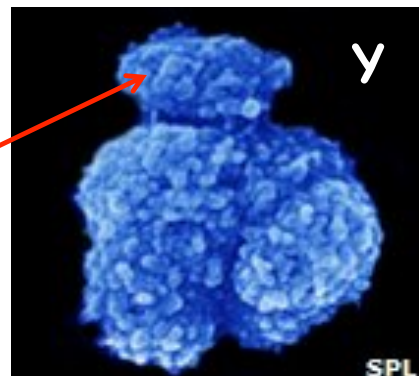
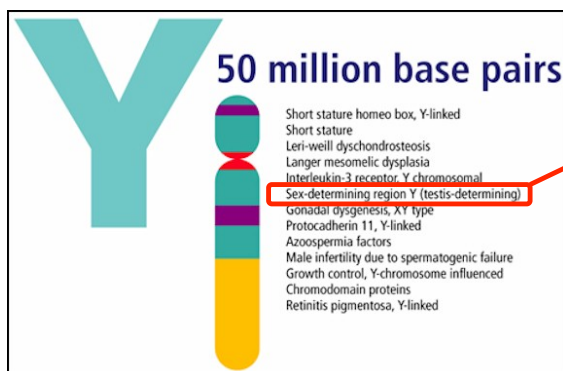
Males and Females Differ By the Presence or Absence Of the Y Chromosome (simplistically!!)



*Male SRY Gene
(Sex Determining
Region Y)*

The Human SRY Gene For Maleness Controls Gender

Y chromosome: Why men contribute so little

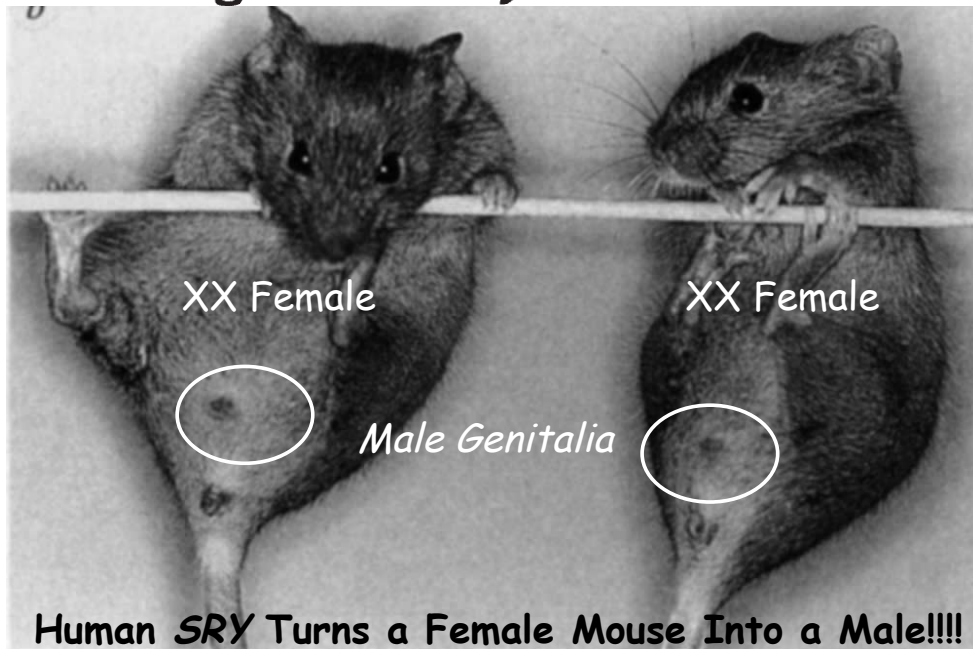


Two Y Genes Can Replace the Entire Y Chromosome for Assisted Reproduction in the Mouse

Science. November 25, 2013

Male development of chromosomally female mice transgenic for *Sry*

Nature, May 9, 1991



Human *SRY* Turns a Female Mouse Into a Male!!!!

Functional Proof That SRY Controls Male Development


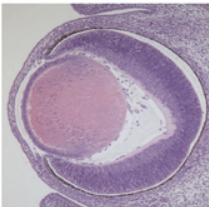
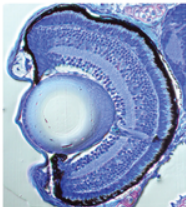

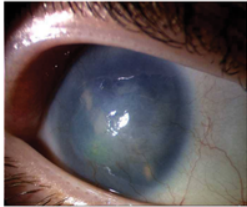
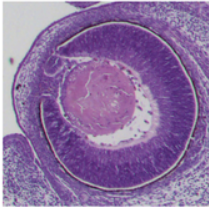
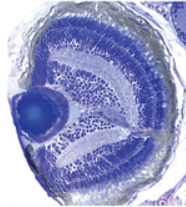
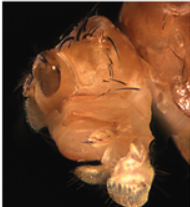
What Does This Experiment "Say" About Human & Mice Genes?

What Are the Conclusions of This Experiment?

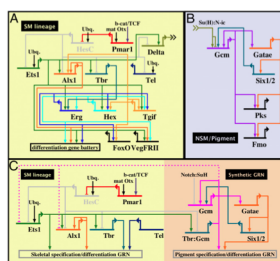
- *Ground State of Mammalian Development is FEMALE!*
- *ONE Gene Switches Development From Male to Female!*
- *Eve Had a Y Chromosome and LOST the SRY Gene!!*

"So the LORD God caused a deep sleep to fall upon the man, and while he slept took one of his ribs and closed up its place with flesh; and the rib which the LORD God had taken from the man he made into a woman and brought her to the man. Then the man said, "This at last is bone of my bones and flesh of my flesh; she shall be called Woman, because she was taken out of Man." Genesis, Chapter 2

Using Genetic Engineering to Change Body Architecture-Engineering Eyes on a Fly's Leg With a Single Gene!

	Human	Mouse	Zebrafish	Drosophila
WT				
mut				
	PAX6^{-/-}	Pax6^{-/-}	pax6b^{-/-}	ey^{-/-}
EQs	cornea opaque <u>iris absent</u> retina degenerate lens opaque aqueous humor of eyeball increased pressure	eye decreased size lens fused_to cornea iris morphology absent anterior chamber absent	eye decreased size lens decreased size retina malformed	eye absent

Induction of Ectopic Eyes by Targeted Expression of the *eyeless* Gene in *Drosophila* *Science* 267, 1788, 1995



Mouse PAX-6 Gene (*eyeless* in flies)
Engineered To Work

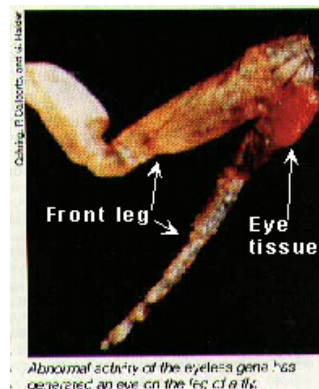


Different Fly Regions

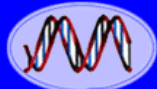
Fly Leg Switch + Mouse Eye Gene



What Does This Experiment Tell Us About Mouse & Fly Eye Genes?



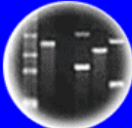
Abnormal activity of the *eyeless* gene has generated an eye on the leg of a fly.



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Plants of Tomorrow

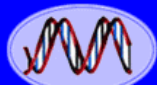
What About Inserting **Bacterial** **Genes** Into **Plants** To Produce a Result With Significant Agricultural Application?

GARDEN GUIDE **SUNSET**

WHAT TO DO IN YOUR GARDEN IN SEPTEMBER

Southern California Checklist

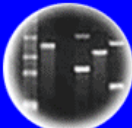
☒ **PROTECT CABBAGE CROPS.** The minute you plant a brassica, squadrons of cabbage white butterflies seem to descend on it to lay their eggs. The easiest way to thwart them is to cover your cabbage crops with row covers right from the start. The next best option is spraying with *Bacillus thuringiensis* to kill the young caterpillar larvae. ♦



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Plants of Tomorrow

How to Use Bt Pesticide as an Organic Pest Control

Learn how to use Bt pesticide to kill cabbage worms, tomato hornworms and other pests in your organic vegetable garden.

By Barbara Pleasant
April 24, 2013



Bt is one of the safest natural pesticides you can use to control caterpillar pests without harming beneficial insects.

Photo Courtesy Safe Brand

FOR ORGANIC GARDENING **OMRI**

Monterey

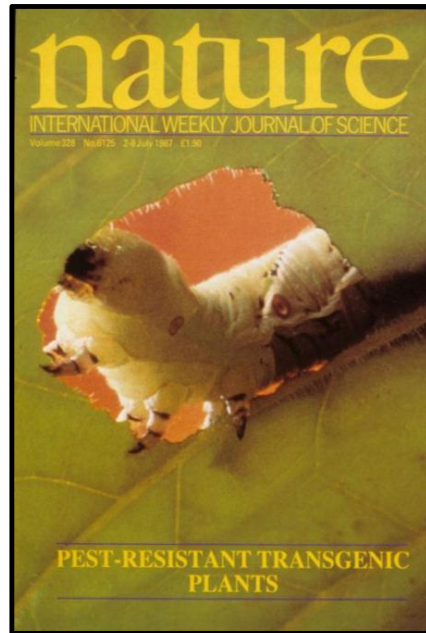
Active Ingredient:
Bacillus thuringiensis subspecies *kurstaki* strain SA-12 solids,
spores and Lepidopteran active toxins (At least 6 million
viable spores per mg)* 98.35%
Other Ingredients: 1.65%
Total: 100.00%

*The percent active ingredient does not indicate product performance and potency measurements are not federally standardized.

Transgenic plants protected from insect attack

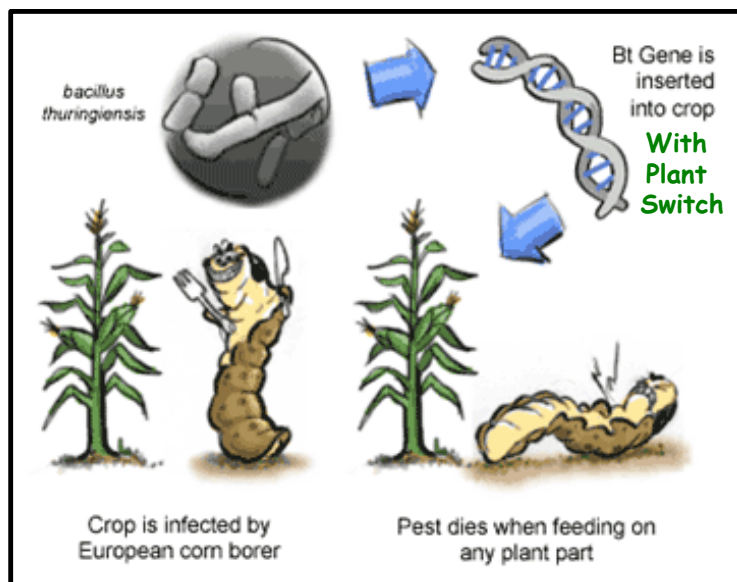
Mark Vaeck, Arlette Reynaerts, Herman Höfte, Stefan Jansens, Marc De Beuckeleer, Caroline Dean*, Marc Zabeau, Marc Van Montagu & Jan Leemans

Plant Genetic Systems NV, Jozef Plateaustaat 22, B-9000 Gent, Belgium

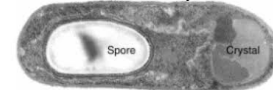


July, 1987
28 Years Ago
Old Technology!

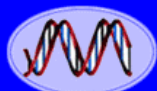
Crops Can Be Engineered With Bt For Insect Resistance



Bt Toxin in Spores



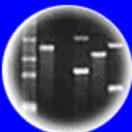
Genetic Engineering a Plant to Resist Worms! Implications For Agriculture



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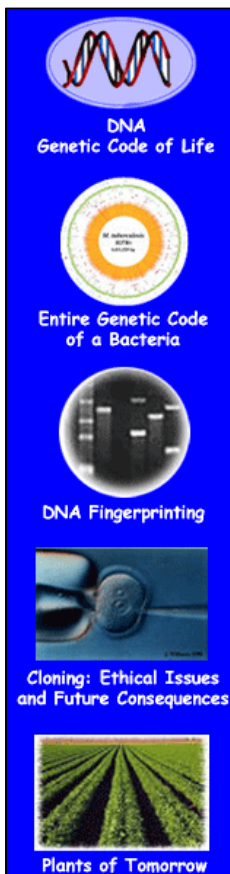
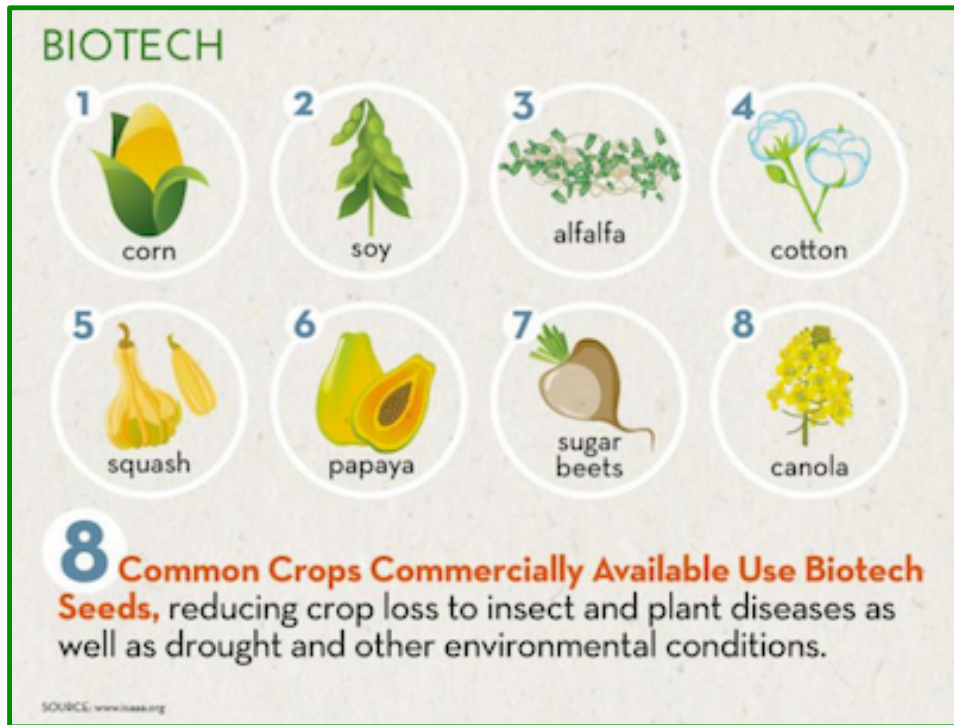
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Question Three

Does the Same Bt Protein in Engineered Crops
& Organic Sprays Protect Plants From Insect
Damage?

- a. Yes
- b. No

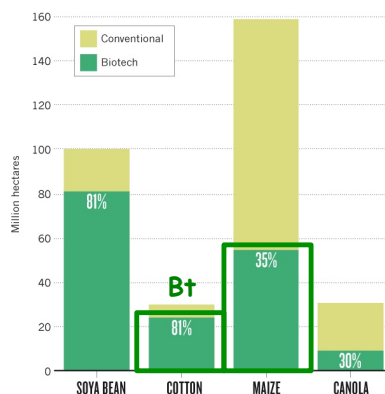
Genetically Engineered Crops in Cultivation Today



The 2013 GMO Landscape

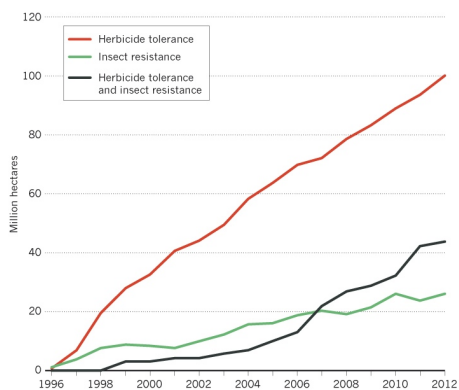
Popular crops

GM soya bean, maize (corn), cotton and canola crops accounted for nearly all GM crops grown in 2012.



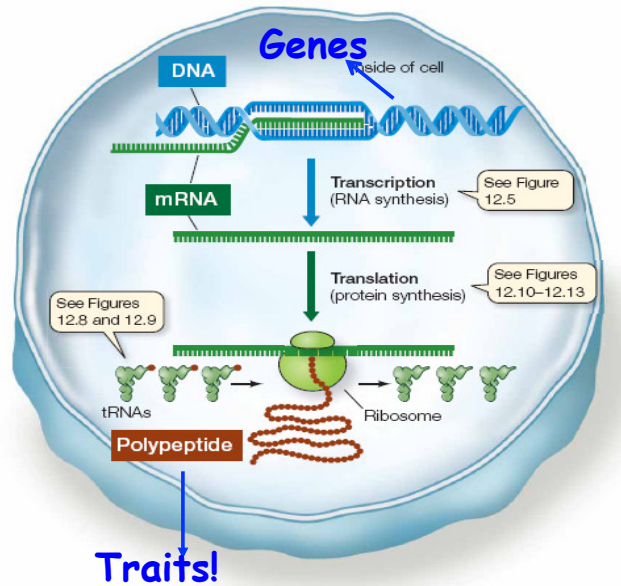
Popular traits

Of some 30 traits that are currently engineered into plants for commercial use, the most popular are those that confer herbicide tolerance, insect resistance or both 'stacked' traits.





What Can We Infer FROM These Genetic Engineering Experiments About How Genes “Work” and Genetic Processes in All Living Organisms?

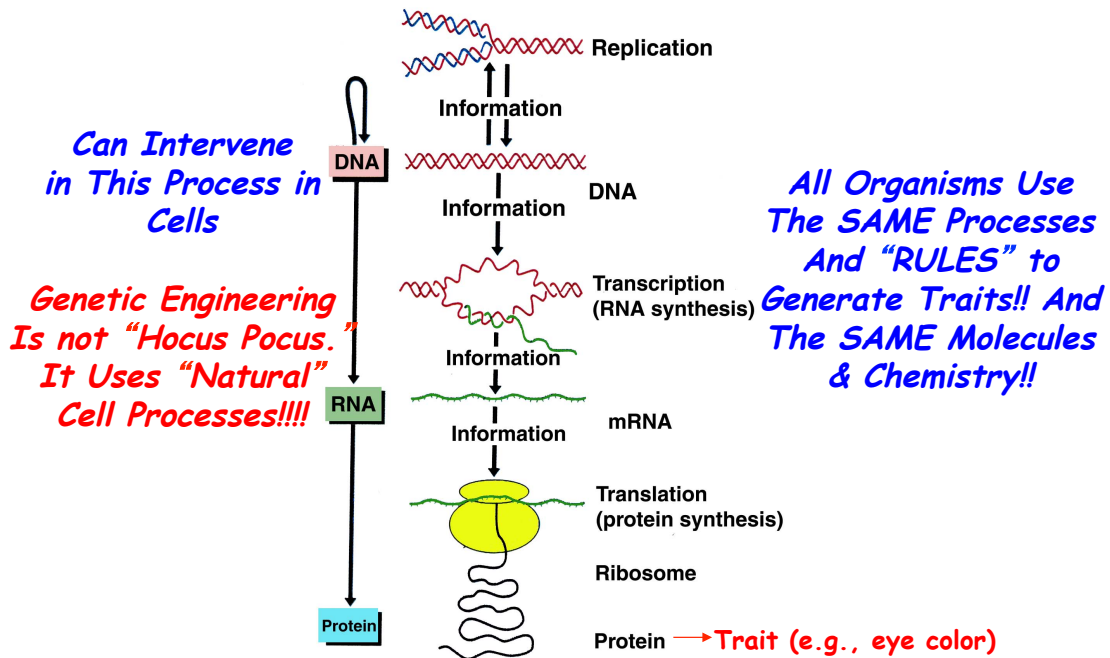


Observations and Inferences From Genetic Engineering Experiments

1. Genes Can Work Independently of Each Other -
E.G. - *The Jellyfish Fluorescence Gene Works Perfectly in a Variety of Organisms*
2. Basic Genetic Processes Are Universal (Replication & DNA to RNA to Protein) -
E. G. - *The Bt Gene Directs the Production of BT Protein in Crops.*
3. Basic Genetic Processes Can Be Used to Engineer or Transfer Genes From One Organism to Another and Transfer Them Stably Generation After Generation -
E.G. - *The Chimeric GloFish & Bt Genes Are Inherited Generation After Generation.*



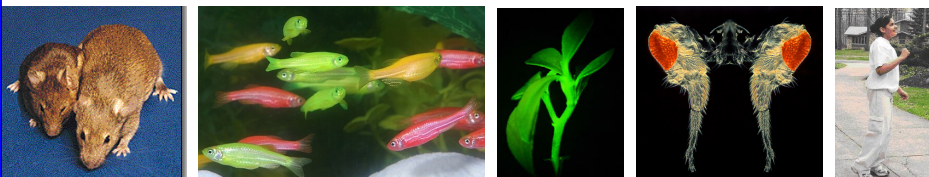
Translating The Genetic Code Into Proteins is a Conserved Process



- DNA Genetic Code of Life** (Icon: DNA double helix)
- Entire Genetic Code of a Bacteria** (Icon: Circular plasmid map)
- DNA Fingerprinting** (Icon: Gel electrophoresis image)
- Cloning: Ethical Issues and Future Consequences** (Icon: Cloning flask)
- Plants of Tomorrow** (Icon: Green field of crops)

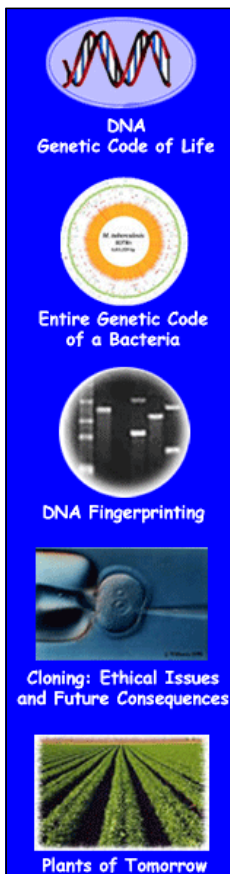
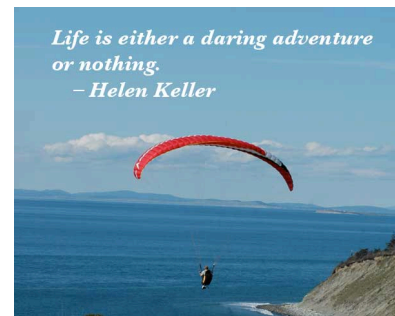
Summary - Age of DNA - There Are NO Genetic Limitations to What Can Be Done Using Genetic Engineering

- Synthetic Chromosomes & Microbes (GE 2.0)
 - Recombinant Plasmids & Bacteria
 - GlowFish, GloMice, GloMonkey, GloPlant
 - Mighty Mice and Giant Fish
 - Insect Resistant Crops
 - Novel Fly Body Plans (e.g., eye on leg)
 - Engineered Humans
- GE 1.0** (Red text annotation pointing to the list)





**We Are Only Limited By Our
Ingenuity and Our “Fear”
of the Unknown**

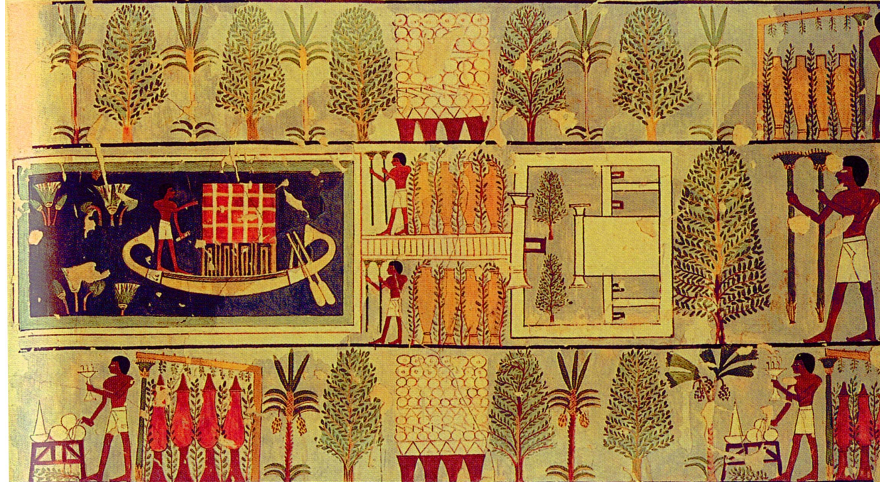


**There is Nothing New About
Genetic Engineering!**

**Manipulating Genes IS
Manipulating Genes No Matter
What Technology or Processes
Are Used!!**

This is Genetic Engineering 0.0!!

**Breeding And Cultivation Of Plants
Have Taken Place Over Thousand Of Years**

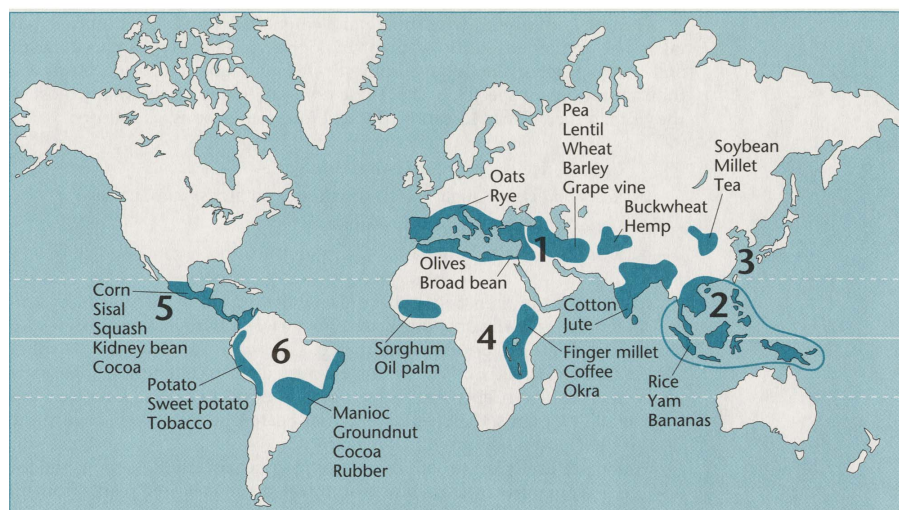


Genetic Engineering is Not New

Crops of Egypt 400 B.C.

*Most Major Crops Were Engineered From Wild Relatives
by Early "Bioengineers" Over 10,000 Years Ago!!*

Regions Where Major Crops Were Established



Breeding Involves Gene Manipulation Using EXISTING Genetic Variability!

**Breeding Uses Natural Genetic Variability of Genes
As Raw Material - *Variability Generated by Mutations***



*Mutations in a Gene That Change Its Chemical Sequence
& Slightly Alters Its Function (e.g., fruit size, color)*

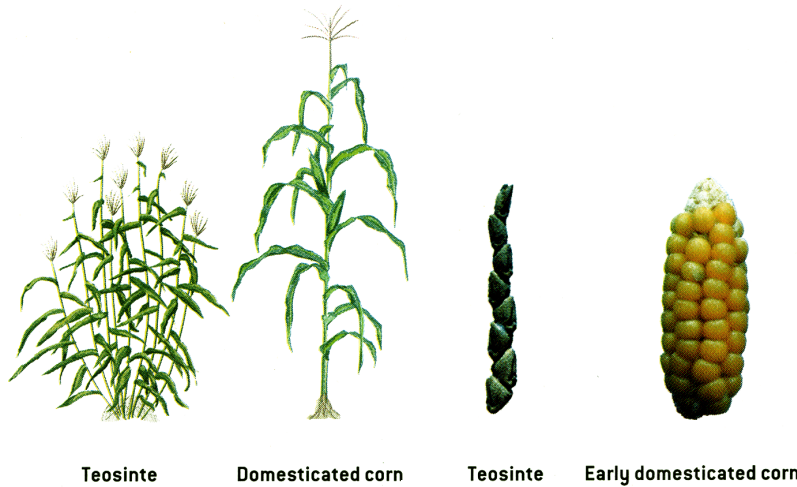
***Tomatoes Were Engineered From Small Wild Relatives
Because of Mutations in Fruit Size Genes!***



*The Early Tomato “Bioengineers” Selected For Large
Fruit Size Because it Provided More Food!*

What They Were Selecting Was a Different Form (Allele) of a Fruit Size Gene!

Engineering Teosinte Into Domesticated Corn

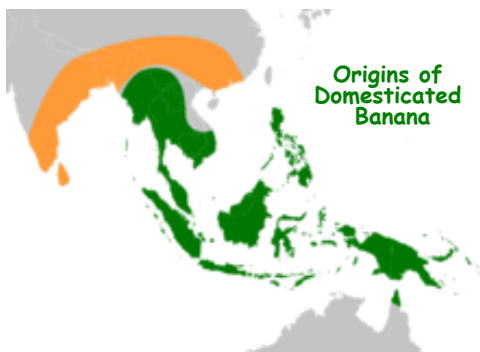


Note: Architecture and Fruit (cob) Size

*Only Five Genes Cause These Plants to Differ
& We Now Know What They Are*

How Does This Differ From Putting an Eye on a Fly's Leg?

Engineering the Modern Banana

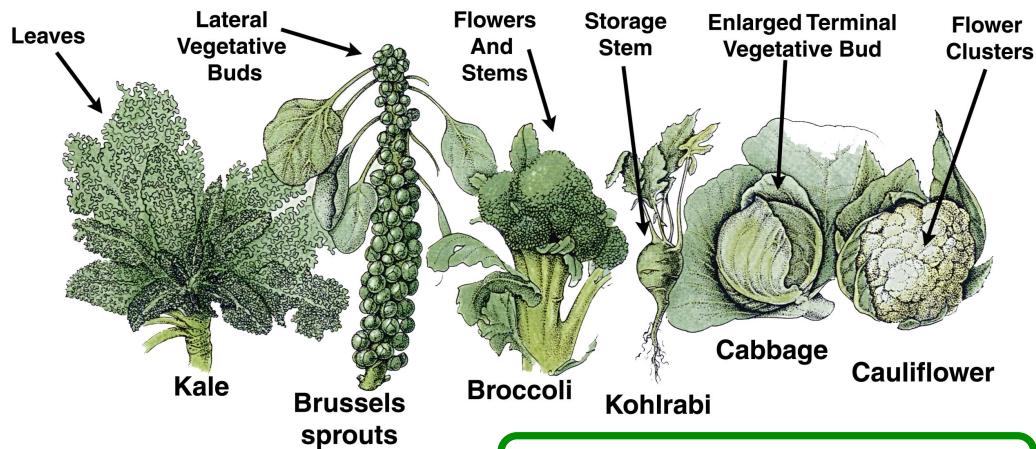


Modern Banana



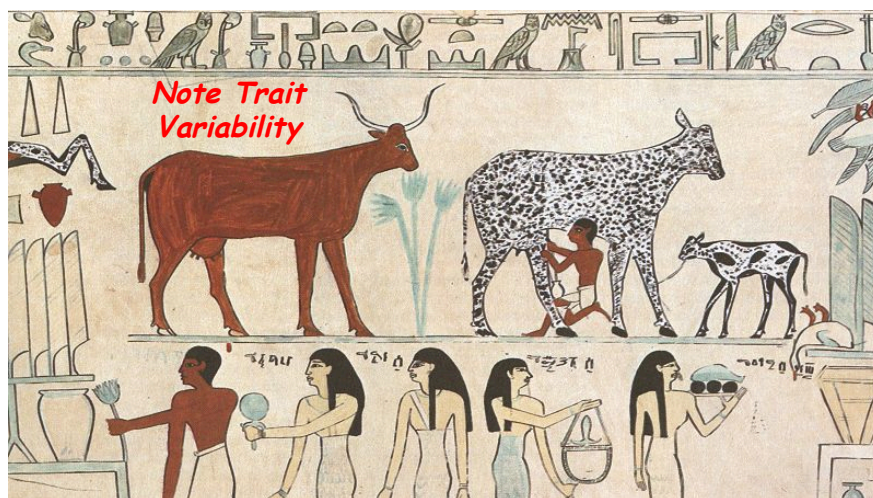
**Note: Fruit Architecture
and Presence of Seeds**

**Breeders Have Selected For
Variability In Plant Control Genes To
Generate Novel Crops**



How Are These Plants Related?

**Farm Animals Were Also “Engineered” By
Breeding Wild Relatives
Cattle Breeding in Egypt 4,000 Years Ago!**



**Manipulating Existing Genetic Variability
Brought About By Chance Mutations!**

Even Domesticated Pets Were “Engineered” By Breeding Wild Relatives

Vol 438 | 8 December 2005

nature

Nature, December 2005

NEWS & VIEWS



GENOMICS

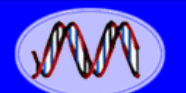
The dog has its day

Hans Ellegren

Domestication and selective breeding have transformed wolves into the diversity of dogs we see today. The sequence of the genome of one breed adds to our understanding of mammalian biology and genome evolution.

The Dog Genome Has Been Sequenced!

Canine DNA
Forensic Testing



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

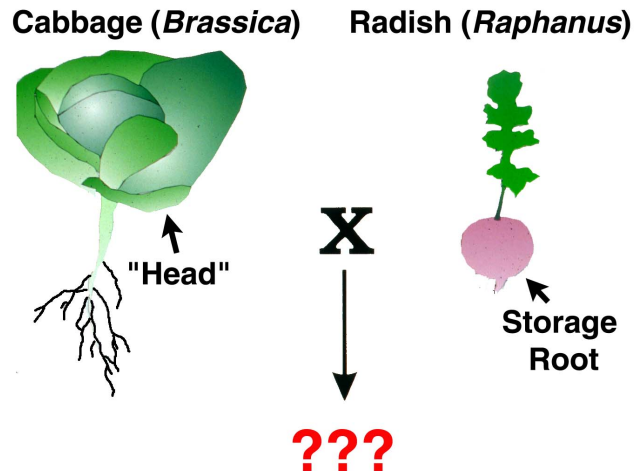
The Problem With Breeding the “Old Fashioned Way”

Cannot Predict Results!



The Problem With Breeding the "Old Fashioned Way"

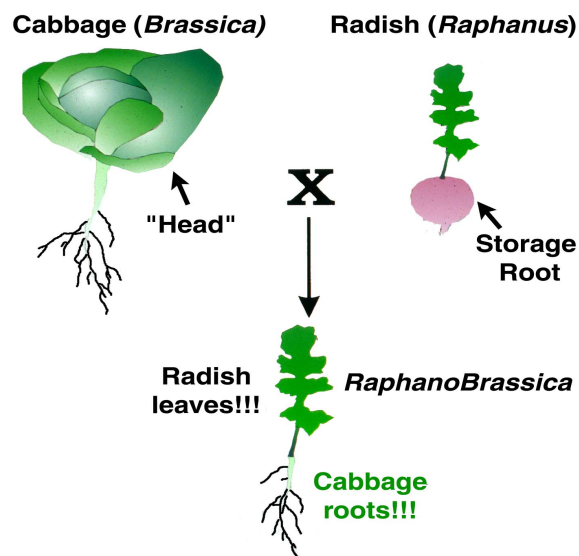
Engineering A Novel Crop By "Wide" Breeding



Karpechenko, G.D., 1928. *Polyloid hybrids of Raphanus sativus L. X Brassica oleracea L.* Zeitschrift für induktive Abstammungs- und Vererbungslehre 48, 1-85.



Engineering A Novel Crop By "Wide" Breeding



*Results Show the Unpredictability of Classical Breeding Approaches!!
Compare With the Modern Genetic Engineering Examples Shown Previously*

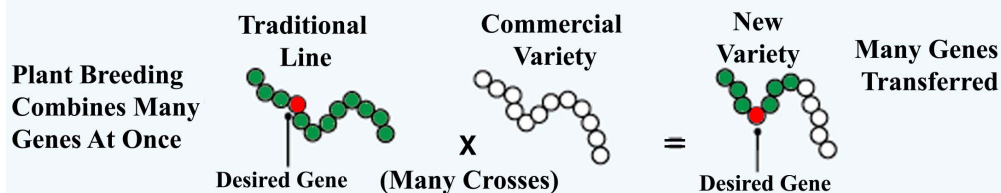


Genetic Engineering is a TECHNIQUE!

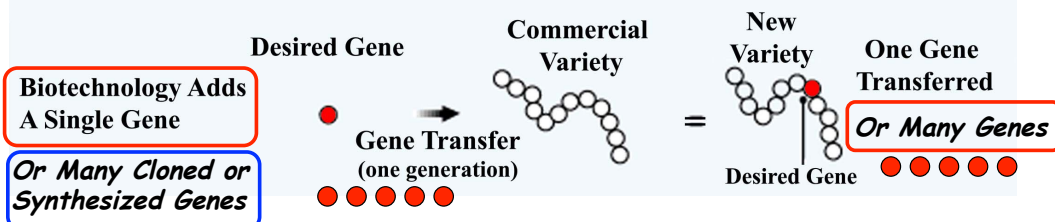
How Do Classical Genetic Engineering Methods Differ From Those Using DNA and 21st Century Technologies?

Classical vs. Molecular Genetic Engineering Techniques

TRADITIONAL PLANT BREEDING

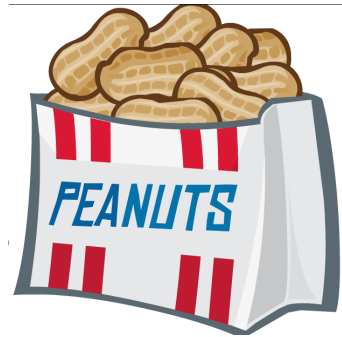


PLANT BIOTECHNOLOGY



Both Manipulate Genes - But in Different Ways!!

Classical vs. Molecular Genetic Engineering



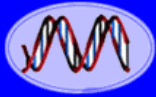
What Are The Limitations of Classical Breeding/Genetic Engineering?

1. Limited To Genes of Interbreeding Organisms and, Clearly, Severe Ethical Issues With Humans (Eugenics)
2. Only Can Make New Combinations of EXISTING Genes - Genes Created By "Natural" Mutations
3. Can't Make Existing Genes "Better" - Just Better or More Useful Combinations of Existing Genes and/or Alleles
4. Takes Time - Limited To Generation Time of Organism - Decades For Some Crop Plants
5. Only Useful For "Obvious" Traits - One's That Can Be Observed or Followed
6. Unpredictable Outcomes (Bringing in Thousands of Genes at Once - Some With Deleterious Consequences)

What Are The Advantages of Using 21st Century Genetic Engineering Methods?

1. Any Gene From Any Organism Can Be Used In Any Organism - There Are No Breeding Barriers (e.g., genes of all sequenced genomes)
2. New Genes Can Be Engineered - Genes That Work Better and/or Produce New Proteins (i.e., create new genetic variability and/or alleles)
3. Existing Genes Can Be Engineered to be Switched On in "Places" That They Are Normally Off - Gene Control or Regulation Altered (e.g., fly eye on leg)
4. Speed - Can Engineer a New Organism in a Generation
5. Can Change, Alter, Manipulate, Synthesize and/or Control the Genetic Blueprint of Any Organism
6. Very Precise (Working With Known Genes & Proteins)

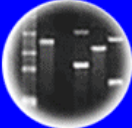




DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



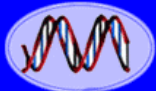
Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

HOW IS SCIENCE CARRIED OUT?

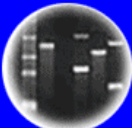
**SCIENTIFIC
KNOWLEDGE IS
OBTAINED BY A
PRECISE & SPECIFIC
PROCESS**



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

Science is **NOT** "Hocus Pocus" or
Based on Opinions and Beliefs



**• Science is Based on
Observation, Hypothesis Testing,
Rigorous Experimentation, and
Verification**

**• Technology, or the Application
of Scientific Knowledge, Has
Transformed Dramatically Our
Lives and How We Live**

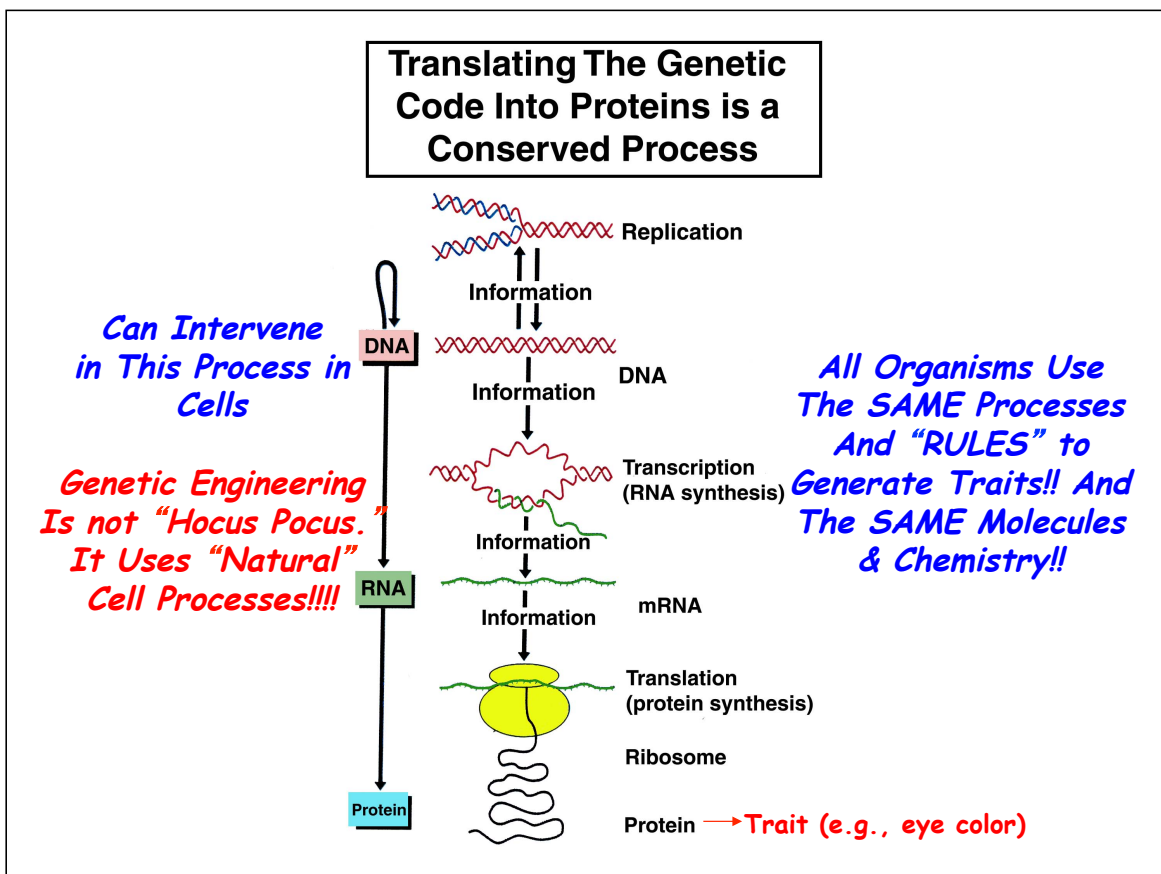
What Are the Data!!!!



It Has Lead to Civilization and Culture as We Know It!

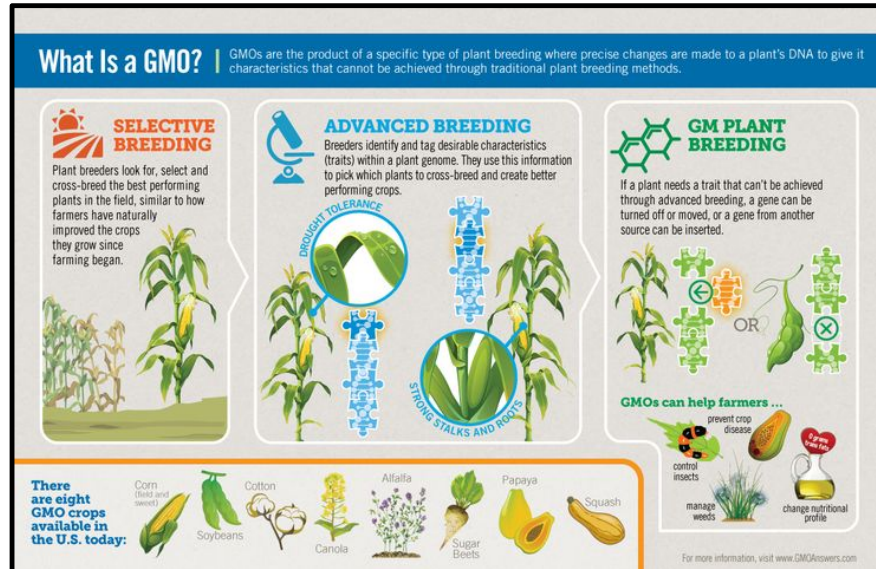
- Agriculture
- Medicine
- Computers and Automation
- Airplanes, Cars, and Satellites
- Countries and Cities
- Political Systems
- Art and Literature
- Etc., Etc., Etc.

Simply Put:Our Way of Life!

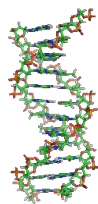




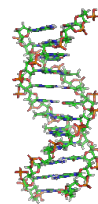
Genetic Engineering is a TECHNIQUE!



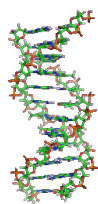
**Breeding or DNA - It's the Same
& Called *Gene Manipulation***



**We Live in the
The Age of DNA!**



**Genetic Engineering Is
Manipulating DNA Either Classically or By
Exciting Modern Approaches (GE 1.0 and 2.0)!
It's a Scientific Process
Not Hocus Pocus**



**Understanding Genetic Engineering
Requires a Basic Understanding of Genes
And How They Work**

