

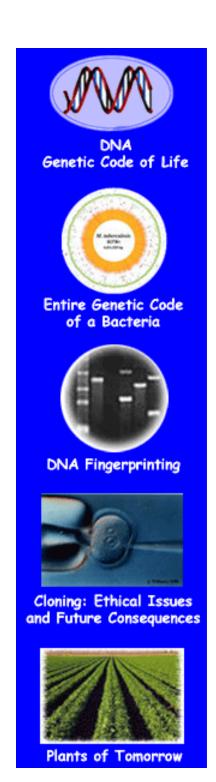
HC70A & SA570A Winter 2016 Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg & John Harada

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







THEMES

- 1. What is Genetic Engineering A Review.
- 2. What Are the Ethical and Legal Issues That Arise Because of Recombinant DNA?
- 3. The Future is Here Synthetic Genomes Work of Craig Venter.
- 4. What Has and Can Be Done With Genetic Engineering Spectacular Examples.
- 5. What Does Genetic Engineering Tell Us About Basic Genetic Processes in All Organisms?
- 6. Genetic Engineering Anything New?
- 7. Are Vegetables Engineered Demonstration.
- 8. Classical vs. 21st Century Genetic Engineering.
- 9. Is Science Hocus Pocus or a Precise Process?
- 10. Understanding How Genetic Engineering Uses Natural Rules of the Cell (i.e., It Isn't Magic)!

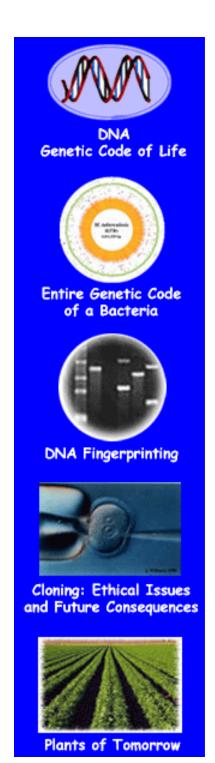


Last Lecture - Age of DNA & Genetic Engineering: Part One

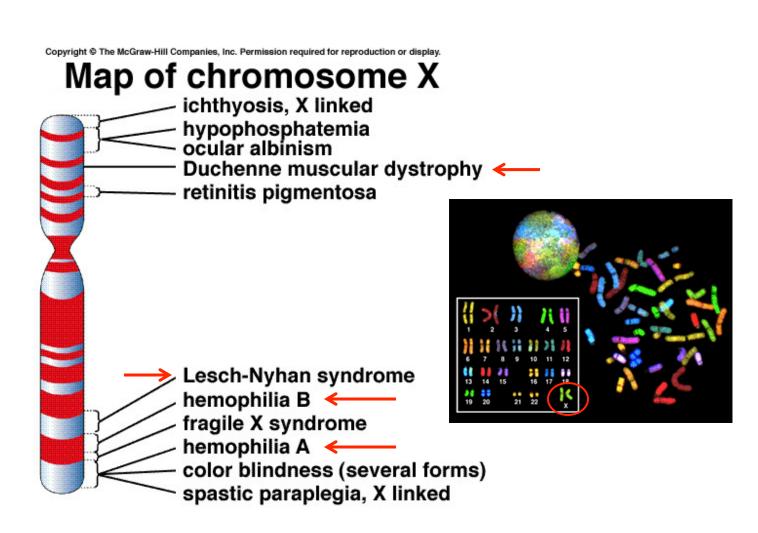
Today's Class - Age of DNA & Genetic Engineering: Part Two

Genetic Engineering - Spectacular Examples

Genetic Engineering - Anything New?



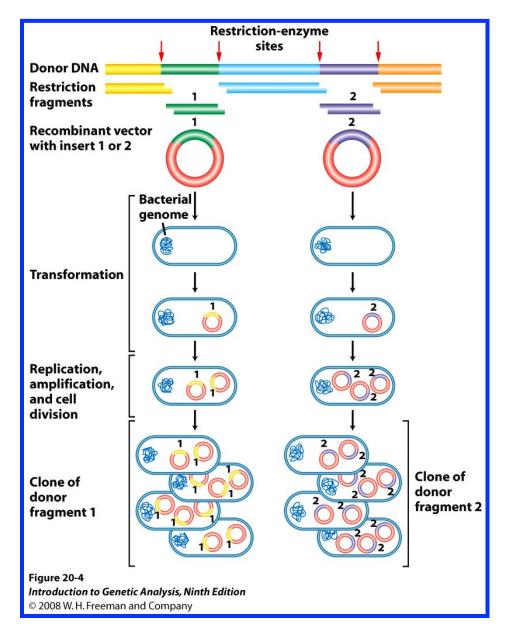
"Why" Clone Genes - Simply Put....Genomes & Chromosomes Contain Thousands of Genes



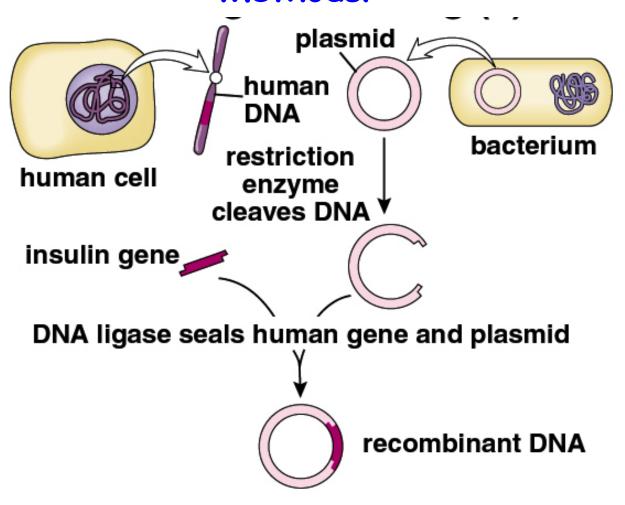
How Can a Single Gene Be Studied?

Genetic Code of Life Entire Genetic Code of a Bacteria DNA Fingerprinting Cloning: Ethical Issues and Future Consequences Plants of Tomorrow

Any Gene Can Be Isolated Using Genetic Engineering



For Example.....The Human Insulin Gene Can Be Separated From Other Human Genes and Cloned in Bacteria Using Recombinant DNA Methods!





And Used to Treat Diabetes!



Recombinant DNA Manipulation Means.....

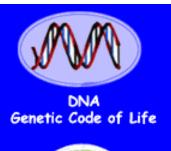
- 1. Specific DNA/Genes Can Be <u>Isolated</u> From Any Organism
- 2. DNA Segments of Any Kind From Any Organism Can Be Combined (Genetic Engineering!!!!!!)
- 3. Isolated Genes Can Be Re-Inserted Into the Chromosomes of Any Organism and Made to Work
- 4. Genes and Genomes Can Be <u>Synthesized and</u> <u>Made To Work</u> in Any Organism

There Are No Genetic Limits. <u>All Biological</u> <u>Organisms Use the Same Genetic Rules.</u> The <u>Implications Are Enormous!!</u>















Cloning: Ethical Issues and Future Consequences



Plants of Tomorrow

Genetic Engineering......

Is the Most Revolutionary Technology in Biology to Have Been Invented in Human History!

Has Generated the Vast Majority of New Biological Knowledge Over the Past 40 Years From Experiments in Biology Laboratories Around the Globe

Has Changed Our Lives Dramatically!

And Has Led to Many New Legal and Ethical Issues

- 1. Patenting Genes, Cells, & Living Organisms?
- 2. Regulating Experimentation on DNA, Cells, Transgenic Organisms ("GMOs")?
- 3. Regulating the Release of Genetically Modified Organisms into the Environment?
- 4. Labeling of Genetically Modified Foods?
- 5. Genetic Testing: DNA Databases, Newborn Genetic Screening, Genetic Privacy, Involuntary or Voluntary Testing?
- 6. Genetic Discrimination?
- 7. Genetic Enhancement and Eugenics: Right to Enhance Your Child? Editing the Human Germline!
- 8. Gender Selection and Prenatal Diagnosis of Genetic Diseases?
- 9. Gene Therapy: Correcting Human Genetic Diseases?
- 10. Human Cloning and Genetic Improvement?
- 11. Gene Testing Companies (e.g., 23andMe): Liability?
- 12. Synthetic Genomes: Constructing New Organisms (Genetic Engineering 2.0)?
- 13. Gene Drive Systems That Permanently Change Genes in a Population

Creating Life: Synthetic Microbes J. Craig Venter

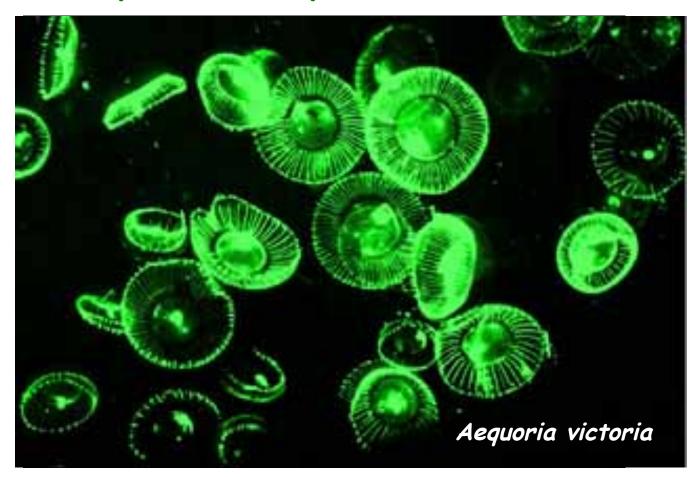
60 Minutes-December 2010



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!!!!

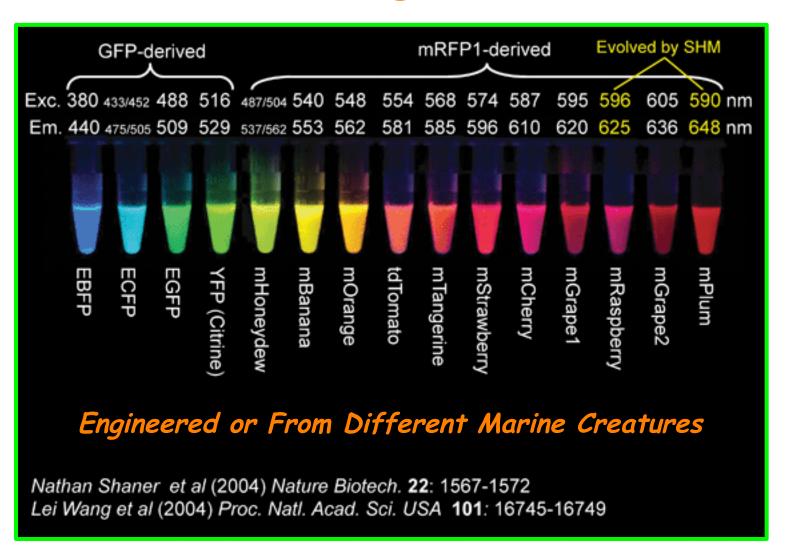


Green Fluorescence Protein (GFP) 🖾

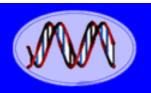
(238 amino acids)

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

There Are Many Different Kinds of Fluorescing Proteins!



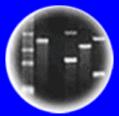
Nobel Prize in Chemistry - 2008 - Shimomura, Chalfie, & Tsien



DNA Genetic Code of Life



Entire Genetic Code of a Bacteria



DNA Fingerprinting



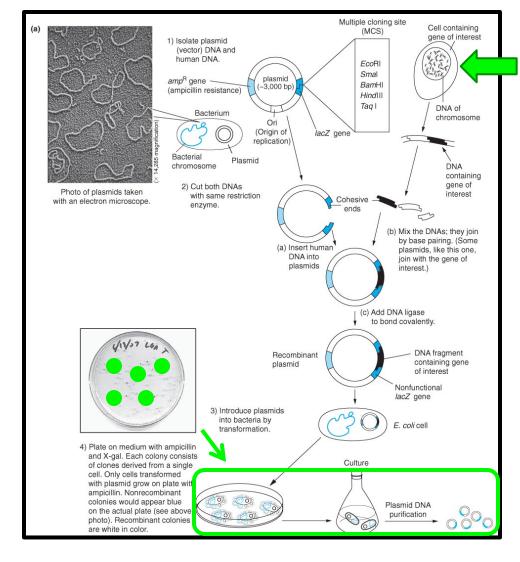
Cloning: Ethical Issues and Future Consequences



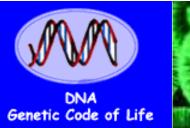
Plants of Tomorrow

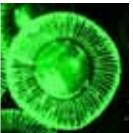
Using Recombinant DNA to Clone the Jellyfish GFP Gene







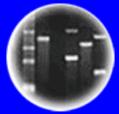




A Recombinant Plasmid Containing the GFP Gene







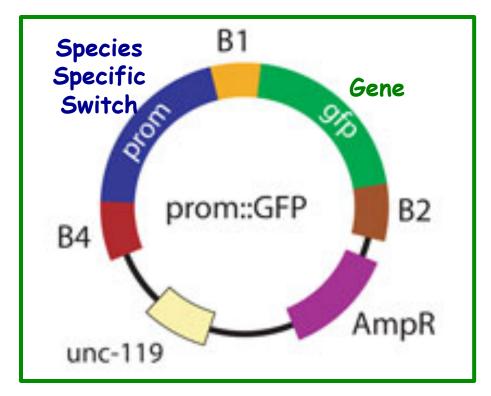
DNA Fingerprinting



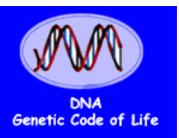
Cloning: Ethical Issues and Future Consequences



Plants of Tomorrow



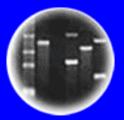




Engineering the Jellyfish GFP Gene to Be Active in Different Organisms



Entire Genetic Code of a Bacteria

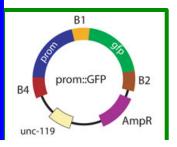


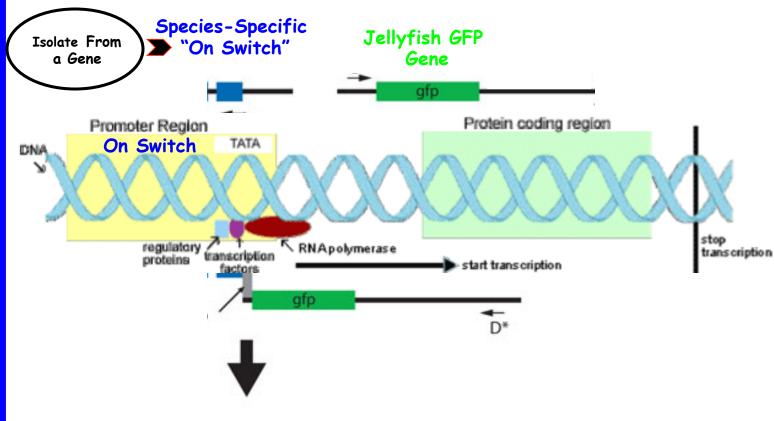
DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences

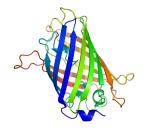






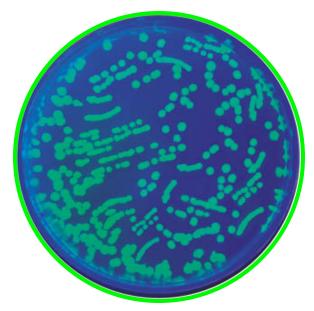


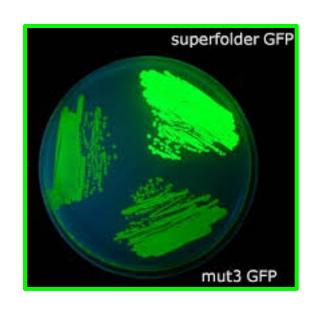




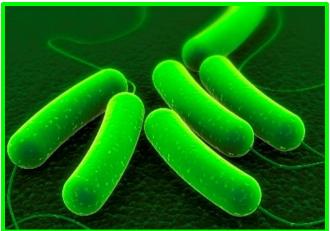
GloColi - *E. coli* Engineered With the Jellyfish GFP Gene!

What Are the Conceptual Implications of This Experiment?





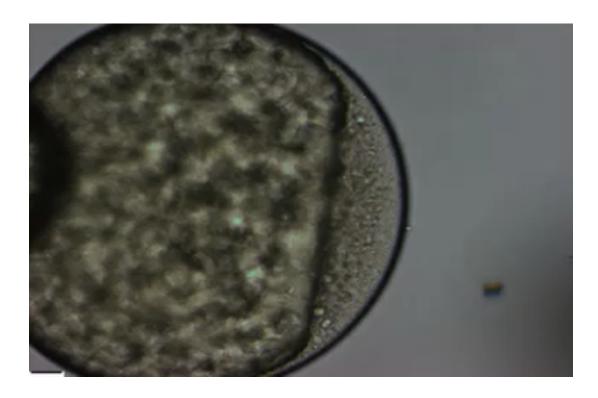
E. Coli Switch + Jellyfish GFP Gene



E. Coli Synthesizes GFP Protein!

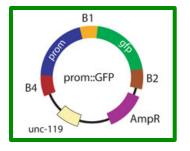


Engineering a "GloFish"......



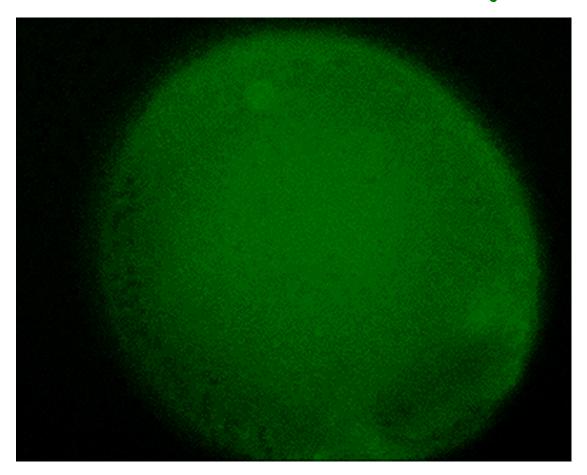
ZebrafishDanio rerio





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

A "GloFish" Embryo!!



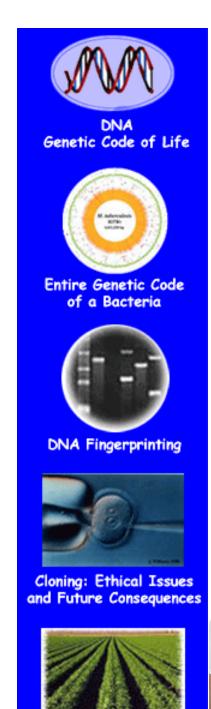


Zebrafish - Danio rerio

Genetically Engineered "GloFish!!"



Note Different Fluorescing Colors - Due to Different Jellyfish Genes



Plants of Tomorrow

GloFish Can Be Sold In California

(But Not in Canada, or Europe)

- Cal. Depart. of 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.
- Cal. Depart. of Fish and Game Code Ruling (2015)
 The Dept. of Fish and Game will propose the addition of an exception to Section 1.92 that would allow the sale of transgenic tropical aquarium fish that the Dept. has determined pose no foreseeable risk or harm to native fish or wildlife.

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?



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

a. Yes

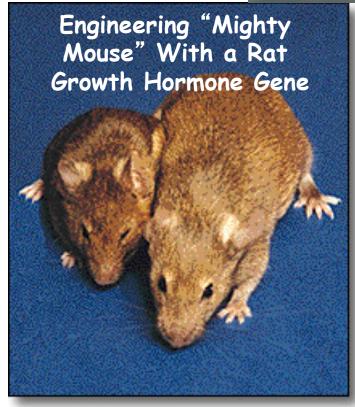
b. No

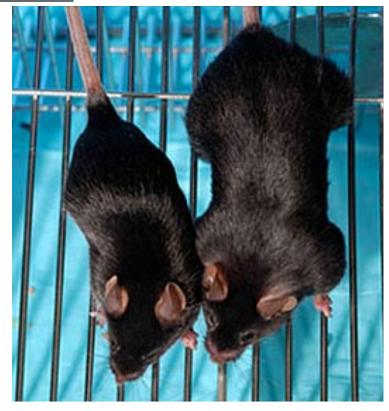
Dramatic growth of mice that develop from eggs microinjected with metallothionein-growth hormone fusion genes

Richard D. Palmiter*, Ralph L. Brinster*, Robert E. Hammer*, Myrna E. Trumbauer*, Michael G. Rosenfeld*, Neal C. Birnberg* & Ronald M. Evans*



Nature, December, 1982 ~33 Years Ago!

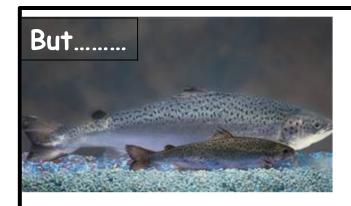




How About a Salmon That <u>Grows Faster</u> (Not Bigger) Using a Fish Growth Hormone Gene?

Genetically Engineered Salmon Approved for Consumption

By ANDREW POLLACK NOV. 19, 2015



GMO Salmon

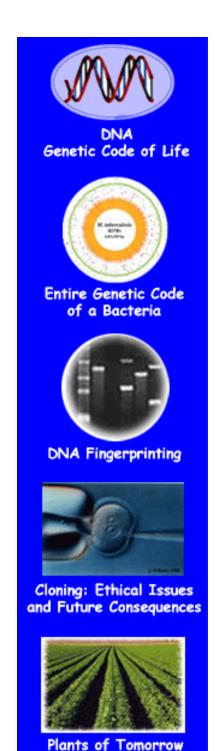
FDA won't be able to allow the sale of genetically modified salmon until it has a plan for labeling the fish. And out of FDA's budget "not less than \$150,000 shall be used to develop labeling guidelines and implement a program to disclose to

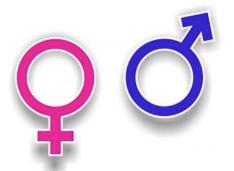
consumers whether salmon offered for sale to consumers is a genetically engineered variety." When FDA approved GM salmon last month it said companies didn't have to label it, provoking the fury of anti-GMO groups.

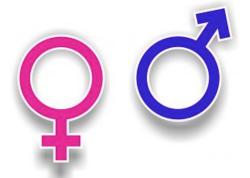
What Are The Issues?

a. Regulation?
b. Environment?
c. Same as "Natural"
Salmon for Food?
d. Consumer Acceptance
of GMOs?
e. All of the Above?

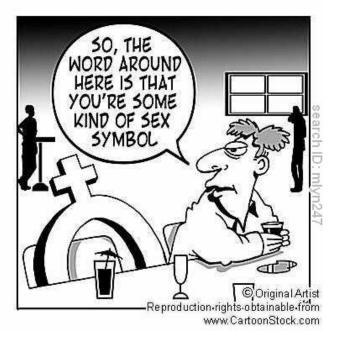
Genetically Modified Salmon Is Safe To Eat, FDA Says



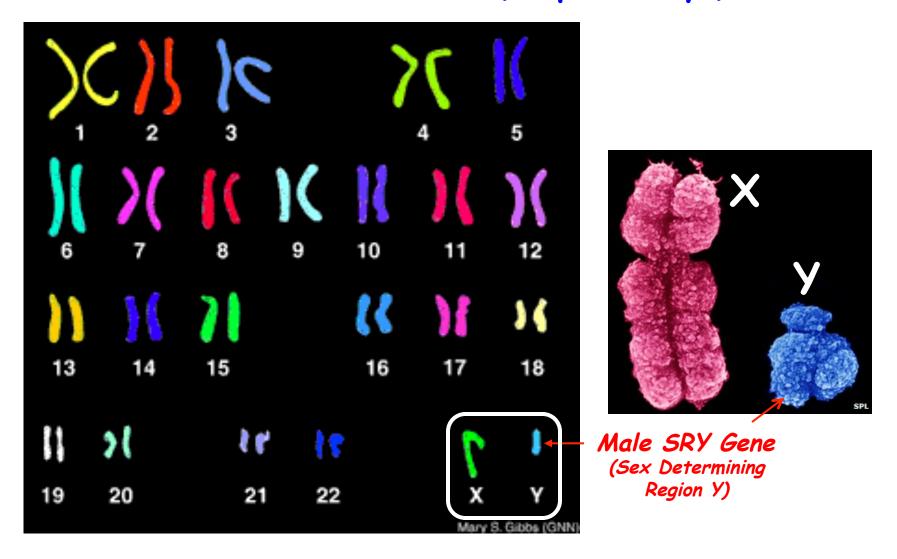




How About Changing The Sex Of An Organism?

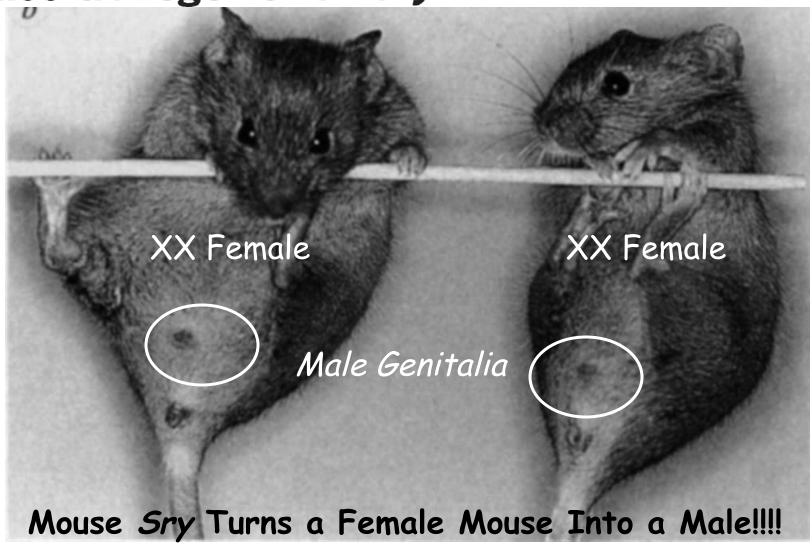


Males and Females Differ By the Presence or Absence Of the Y Chromosome (simplistically!!)



The Human SRY Gene For Maleness Controls Gender

Male development of chromosomally female mice transgenic for *Sry* Nature, May 9, 1991



Functional Proof That Sry Controls Male Development

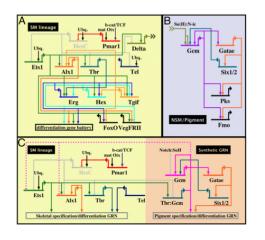
Using Genetic Engineering to Change Body Architecture-Engineering Eyes on a Fly's Leg With a Single Gene!

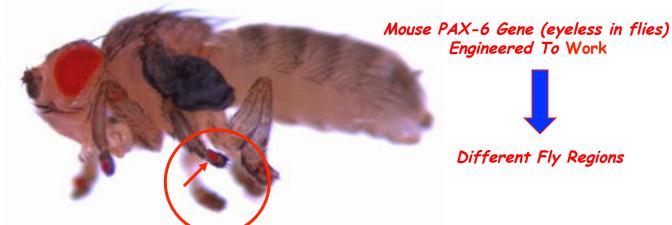
Mouse Zebrafish Drosophila Human WT mut ey⁄-PAX6+/-Pax6-/pax6b-/eye decreased size eye decreased size cornea opaque eve absent **EQs** iris absent lens decreased size lens fused to cornea retina malformed

retina degenerate lens opaque aqueous humor of eveball increased pressure

iris morphology anterior chamber absent

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





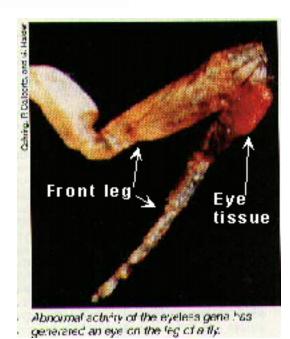
Engineered To Work

Different Fly Regions



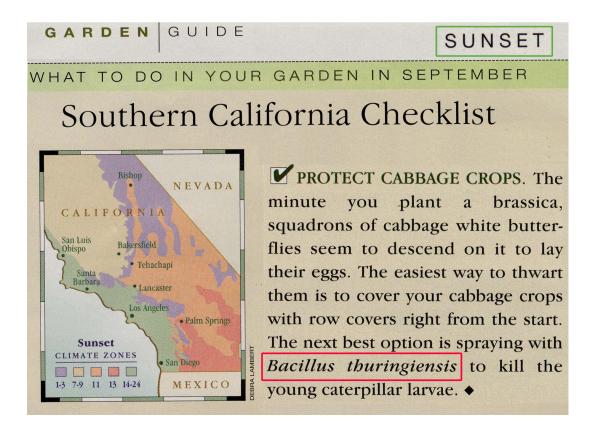


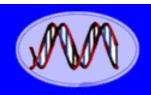
What Does This Experiment Tell Us About Mouse & Fly Eye Genes?





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

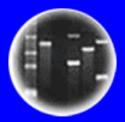




DNA Genetic Code of Life



Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences



Plants of Tomorrow

How to Use Bt Pesticide as an Organic Pest Control

Learn how to use Bt pesticide to kill cabbage worms, tomato homworms 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





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%

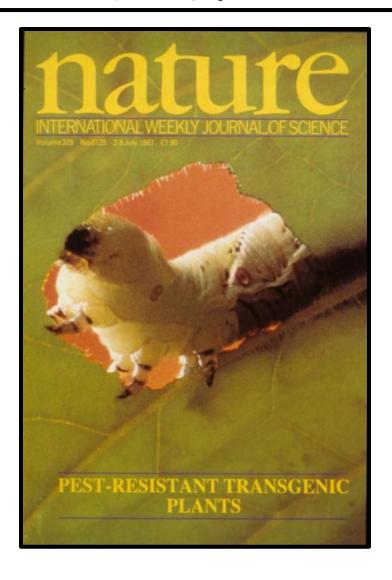
 Total:
 .100.00%

*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

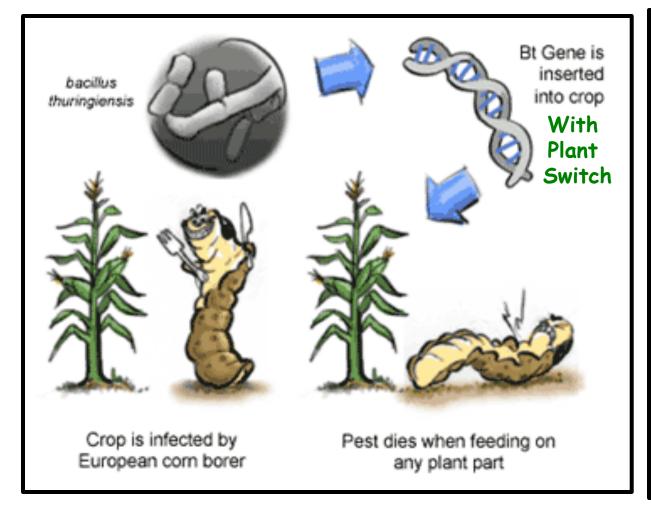
Plant Genetic Systems NV, Jozef Plateaustraat 22, B-9000 Gent, Belgium



July, 1987 28 Years Ago Old Technology!

Crops Can Be Engineered With Bt For Insect Resistance







Genetic Engineering a Plant to Resist Worms! Implications For Agriculture





Question

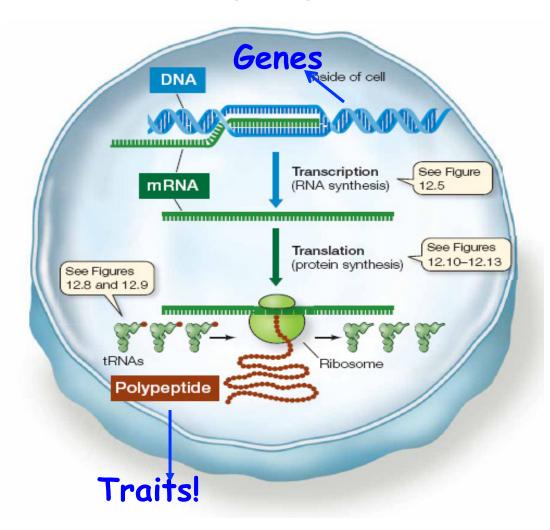
Does the Same Bt Protein in Engineered Crops & Organic Sprays Protect Plants From Insect Damage?

a. Yes

b. No



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



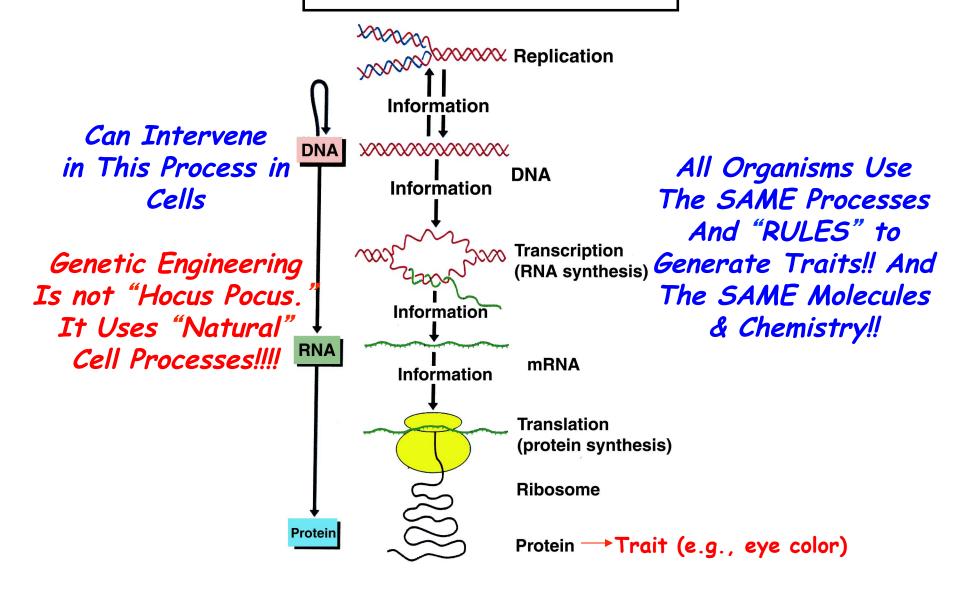
Observations and Inferences From Genetic Engineering Experiments

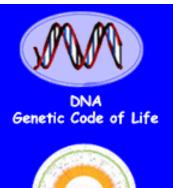
- 1. Genes Can Work Independently of Each Other E.G. The Jellyfish Fluorescence Gene Works Perfectly in a Variety of Organisms
- 2. Basic Genetic Processes Are Universal (Replication & DNA to RNA to Protein)
 E. G. The Bt Gene Directs the Production of BT Protein in Crops.
- 3. Basic Genetic Processes 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









of a Bacteria

DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences



Plants of Tomorrow

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

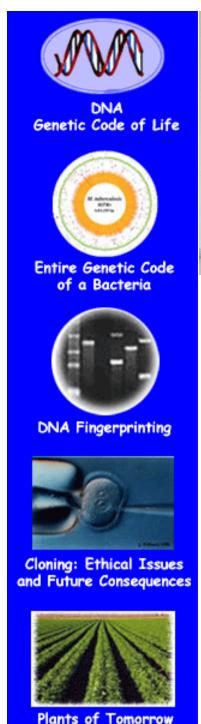






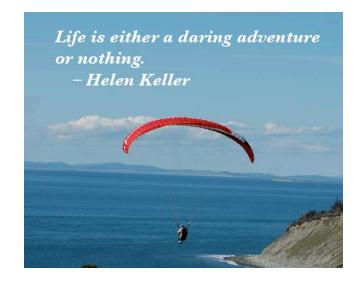


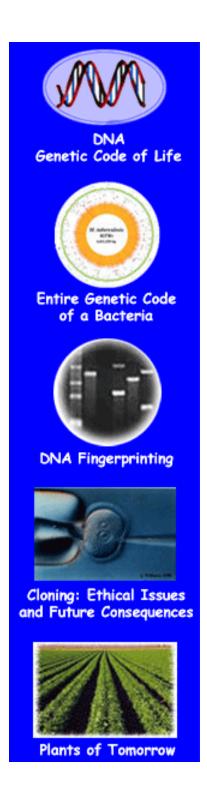
GE 1.0





We Are Only Limited By Our Ingenuity and Our "Fear" of the Unknown



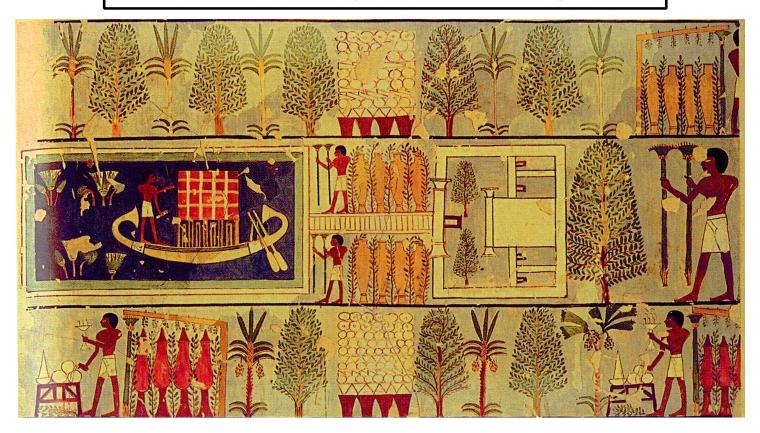


There is Nothing New About Genetic Engineering!

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

This is Genetic Engineeering 0.0!!

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

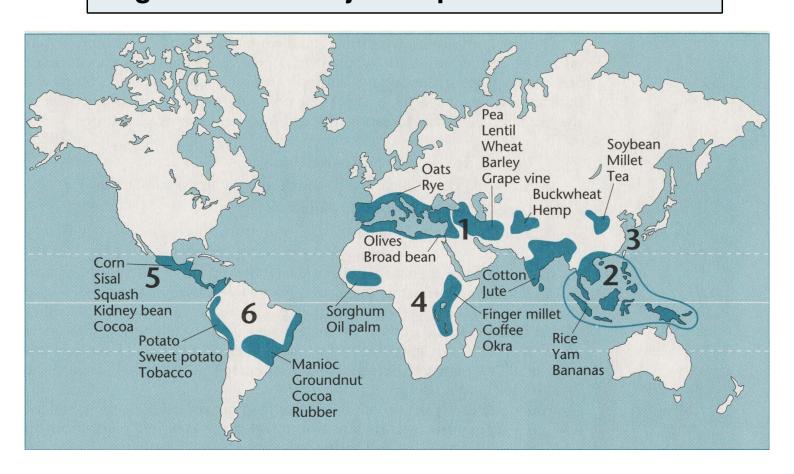


Genetic Engineering is Not New

Crops of Egypt 400 B.C.

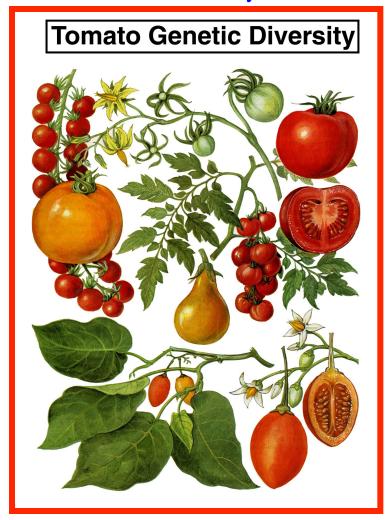
Most Major Crops Were Engineered From Wild Relatives by Early "Bioengineers" Over 10,000 Years Ago!!

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)

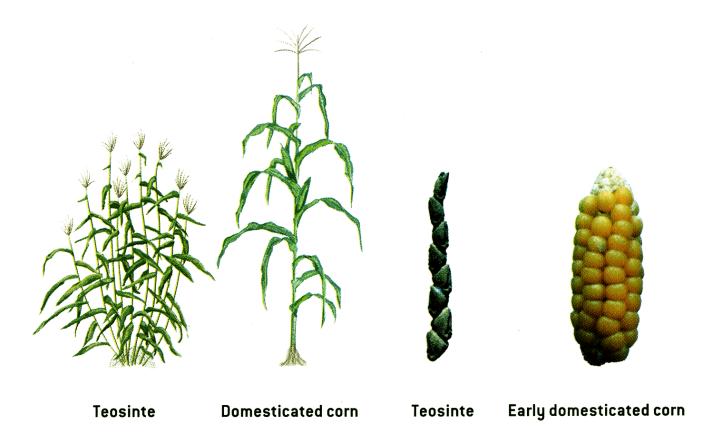
Tomatoes Were Engineered From Small Wild Relatives Because of Mutations in Fruit Size Genes!



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

Engineering the Modern Banana

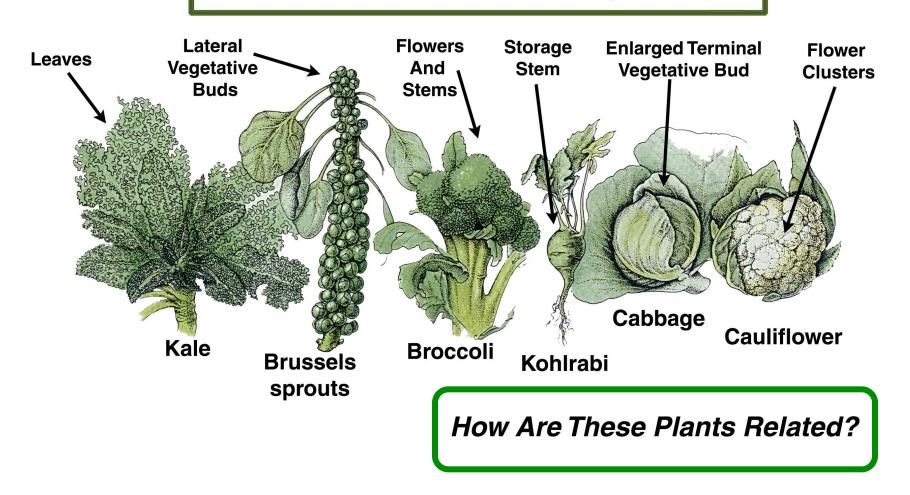




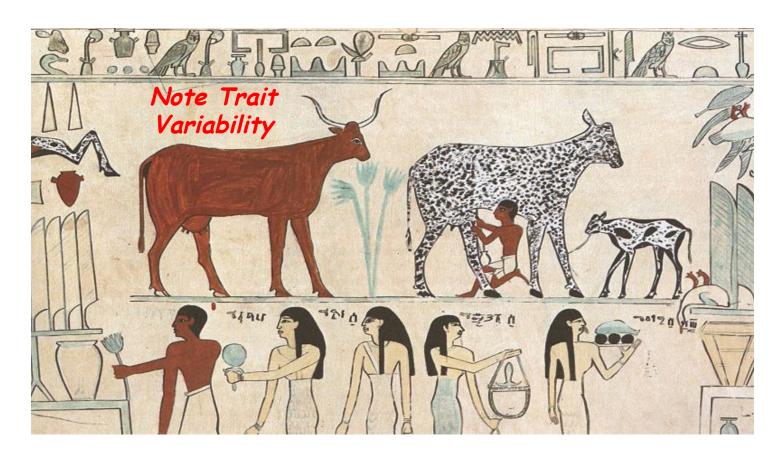


Note: Fruit Architecture and Presence of Seeds

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



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, 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!





Plants of Tomorrow

The Problem With Breeding the "Old Fashioned Way"

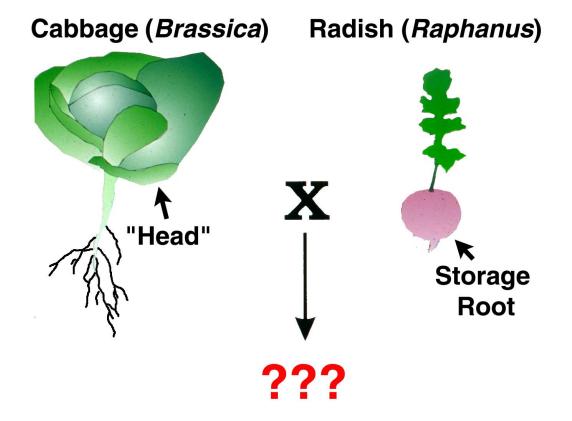
Cannot Predict Results!





The Problem With Breeding the "Old Fashioned Way"

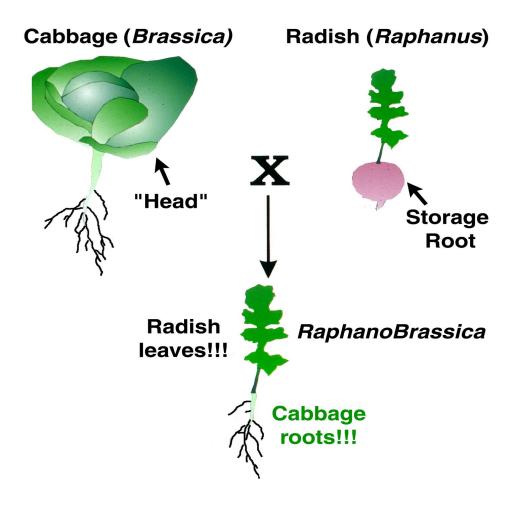
Engineering A Novel Crop By "Wide" Breeding





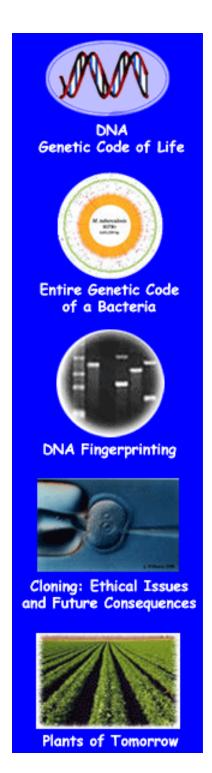
Karpechenko, G.D., 1928. *Polyploid hybrids of Raphanus sativus L. X Brassica oleracea L.* Zeitschrift für induktive Abstammungs- und Vererbungslehre 48, 1-85.

Engineering A Novel Crop By "Wide" Breeding



Results Show the Unpredictability of Classical Breeding Approaches!!

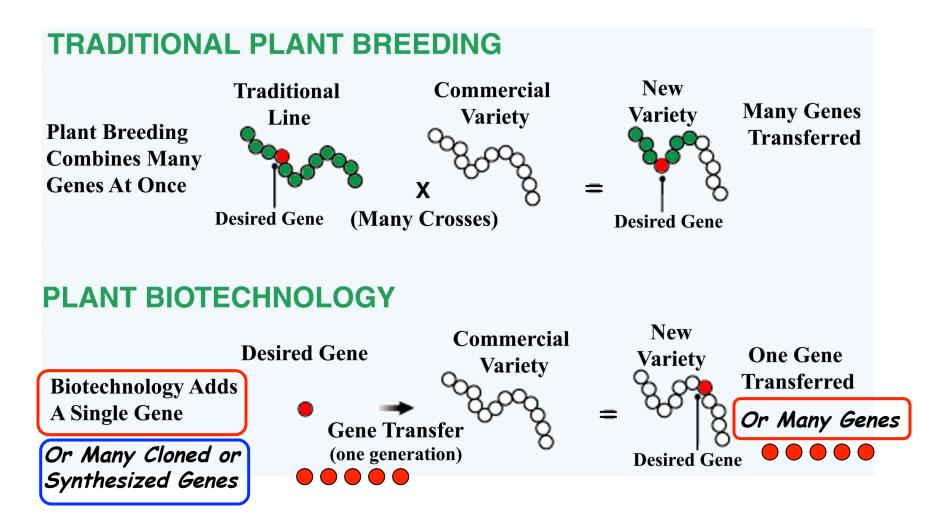
Compare With the Modern Genetic Engineering Examples Shown Previously



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



Both Manipulate Genes - But in Different Ways!!

Focus on the Product NOT the Process!!





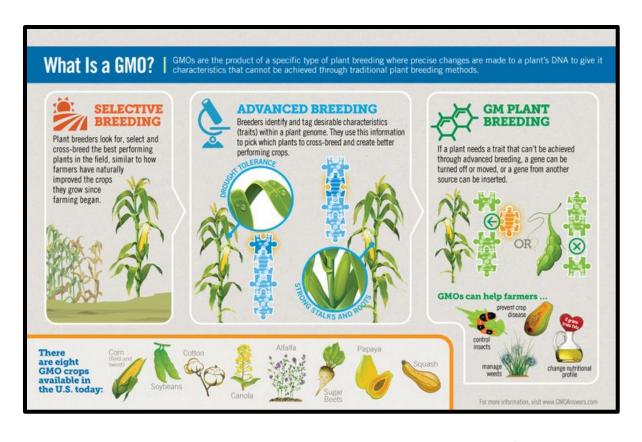




Genetic Code of Life Entire Genetic Code of a Bacteria DNA Fingerprinting Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Genetic Engineering is a **TECHNIQUE!**



Breeding or DNA - It's the Same & Called Gene Manipulation WHAT IS A GMO!!!!!

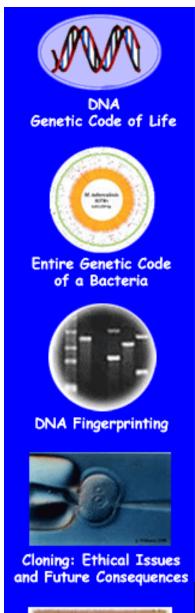
What Are The Limitations of Classical Breeding/Genetic Engineering?

- 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)





Plants of Tomorrow

WHAT IS SCIENCE?

WEBSTER: Knowledge about, or study of, the natural world based on facts learned through experiments and observation.

Technology, like Genetic Engineering, is the <u>application</u> of science <u>knowledge</u>









HOW IS SCIENCE CARRIED OUT?



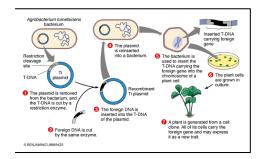




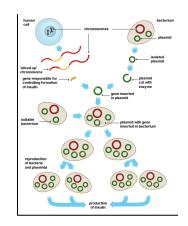
Scientific Knowledge is Based on Observation, Hypothesis Testing, Rigorous Experimentation, Results, Facts, and Verification

What Are the Data!!!!!

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



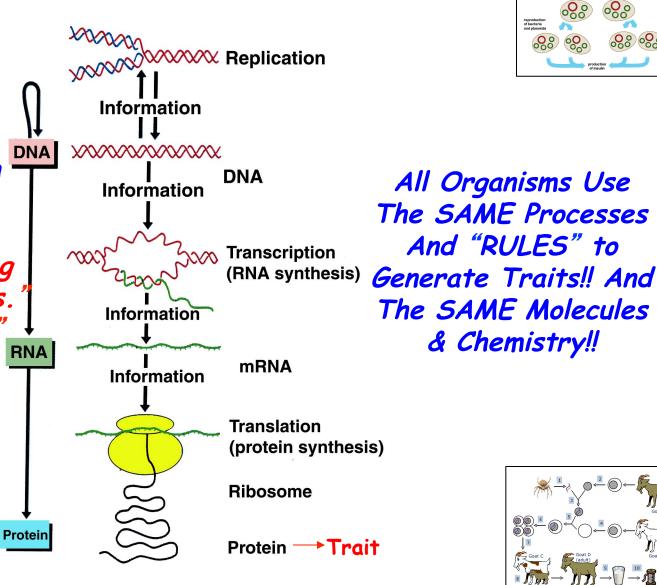
THE FACTS ARE:

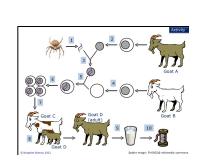


Can Intervene in This Process in Cells

Genetic Engineering Is not "Hocus Pocus." It Uses "Natural" Cell Processes!!!!

Gene Therapy





& Chemistry!!





We Live in The Age of DNA & Genetic Engineering!

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



