

HC70A, PLSS530, & SAS70A
Winter 2013
Genetic Engineering in Medicine,
Agriculture, and Law

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Channapatna Prakash, & John Harada

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

THEMES

1. What is the Significance of Genetic Engineering & What is the Purpose of Cloning Genes??
2. How Has Genetic Engineering Affected Our Lives and Raised New Legal and Ethical Issues??
3. Spectacular Examples of Genetic Engineering 1.0 - What Can Be Done?
4. What Does Genetic Engineering Tell Us About Basic Genetic Processes?
5. Genetic Engineering - Anything New?
6. Classical vs. 21st Century Genetic Engineering - Demonstration
7. Era of Genomics - Impact For Genetic Engineering Future?
8. What Is the Scientific Method & How is Science Carried Out?

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: We Live in the
The Age of DNA!

Genetic Engineering Is
Manipulating DNA!

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

What is Genetic
Engineering?
&
What Does It Do?

Genomes & Chromosomes Contain
Thousands of Genes

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Map of chromosome X

- ichthyosis, X linked
- hypophosphatemia
- ocular albinism
- Duchenne muscular dystrophy
- retinitis pigmentosa

- Lesch-Nyhan syndrome
- hemophilia B
- fragile X syndrome
- hemophilia A
- color blindness (several forms)
- spastic paraplegia, X linked

How Can a Single Gene Be Studied?

The Era Of DNA Manipulation Means.....

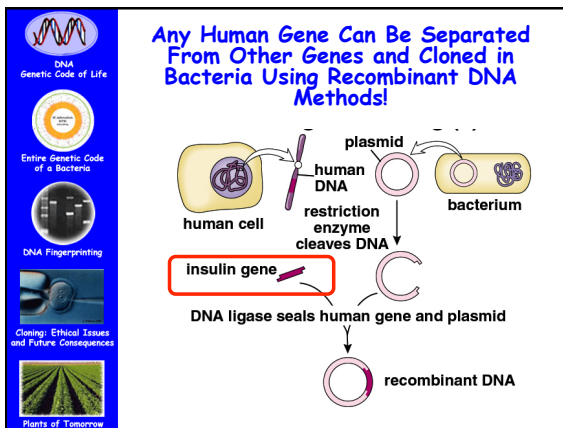
1. **Specific DNA Sequence and/or Gene Can Be Isolated From Any Organism**
2. **DNA Segments of Any Kind From Any Organism Can Be Combined**
3. **Isolated Genes Can Be Re-Inserted Into the Chromosomes of Any Organism and Made to Work**
4. **Genes and Genomes Can Be Synthesized and Made To Work in Any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

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

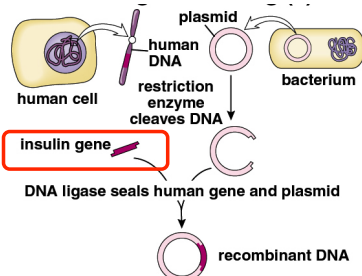
"Why" Clone Genes From An Organism's Genome?

1. **PURIFY** Individual Genes From the Genome (e.g., One of 25,000 Human Genes)
2. **AMPLIFY** The Gene to Obtain Enough DNA For Study
3. **Use the Cloned Gene To:**
 - a) Study Gene Structure & Function (THE Major Use!)
 - b) Use to Convert Cells Into Factories To Make Drugs and Pharmaceuticals
 - c) Use to Diagnose Genetic Diseases
 - d) Use to Identify Individuals (e.g., paternity, forensics)
 - e) Use to Correct Genetic Disease
 - f) Use to Engineer New Crops and Farm Animals
 - g) Synthesize New Genomes and Many Other Uses

Genetic Engineering Has Led to New Knowledge About How Cells and Genes Function and Has Led to Applications That Have Improved Our Lives!!



Any Human Gene Can Be Separated From Other Genes and Cloned in Bacteria Using Recombinant DNA Methods!



The Age of DNA & Genetic Engineering Has Affected Our Lives in Many Ways

1. Basic Understanding of Living Processes and Ourselves
2. Basic Understanding of Genes and Their Functions
3. The Era of Genomics and the Sequence of the Human Genome and Those of Other Organisms
4. Basic Understanding of Human Diseases Such as Cancer and Novel New Treatments
5. A Multibillion Dollar Biotechnology Industry
6. New Legal Fields Such as Genetic Privacy, Forensics, and Patents on Genes and Genetically Engineered Organisms
7. An New Understanding of Human Origins and the Diversity of Human Populations (e.g., where we come from)
8. New Understanding of the Evolutionary Relationships Between Organisms (e.g., sequence of mammalian genomes, including mouse, human, dog, cat, chimpanzee)
9. Ability to Sequence the Genomes of Extinct Organisms
10. New Ethical Issues in "How Far" We Should Go in Using Genetic Engineering Technology


Genetic Engineering Technology 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?** NO. 37
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?
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?


Question One

Would You Use DNA Tests To Select the Gender of In Vitro Fertilized Embryos?


a. Yes
b. No




DNA Genetic Code of Life




Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences




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Question Two

Should Your Insurance Company Be Able to See Your Genetic Profile?


a. Yes
b. No




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Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences




Plants of Tomorrow


Question Three

Should We Be Able To Patent Human Genes?


a. Yes
b. No




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Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences




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Question Four

Should We be Able to Genetically Engineer Our Own Children?


a. Yes
b. No




DNA Genetic Code of Life




Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences




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Question Five

Should Children Born With Incurable Genetic Diseases Be Able to Sue Their Parents in "Wrongful Life" Suits IF The Parents Knew That There Were Genetic Tests Available For Most Inherited Diseases But Decided Not to Be Tested?


a. Yes
b. No




DNA Genetic Code of Life




Entire Genetic Code of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues and Future Consequences




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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!!!!



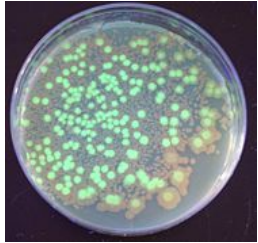
Aequoria victoria


Green Fluorescence Protein (GFP)
(238 amino acids)

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




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







DNA
Genetic Code of Life




Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



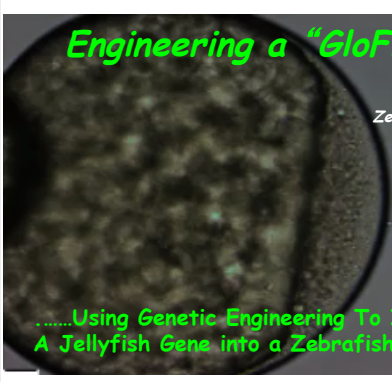
Plants of Tomorrow

Question Six


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



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



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GloFish Are Not Sold In California

- **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!



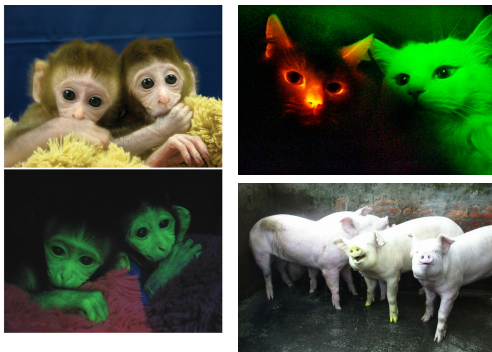
What About "GloMice!!!"



Courtesy of Advanced Cell Technology

MICE EXPRESSING GFP

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



Engineering a GloPlant With the Same Jellyfish Gene!!!



What are the Philosophical and Biological Implications of These Experiments?



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Cloning: Ethical Issues and Future Consequences



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

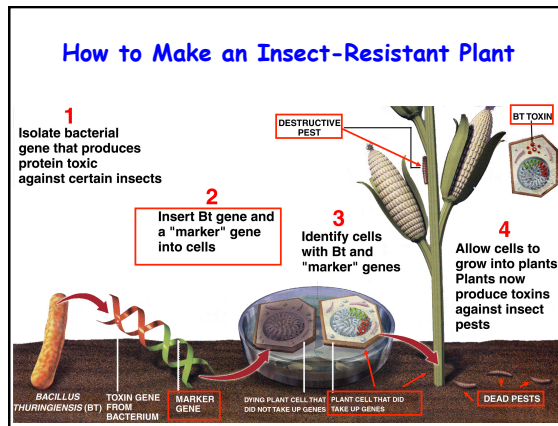
GARDEN GUIDE SUNSET

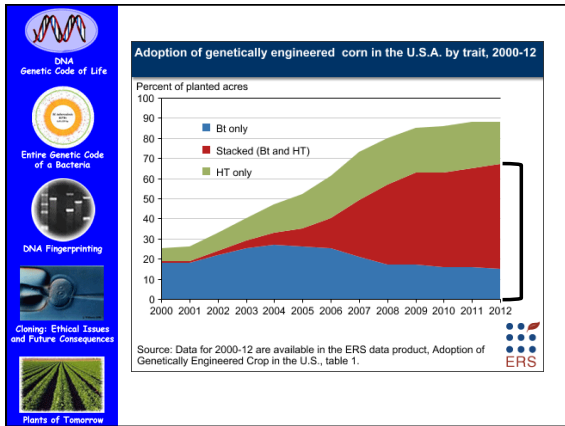
WHAT TO DO IN YOUR GARDEN IN SEPTEMBER

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. ♦







Genetic Engineering a Plant to Resist Worms!

INSECT RESISTANCE with Bt

Implications For Agriculture?

CONTROL Bt

Engineering "Mighty Mouse" With a Rat Growth Hormone Gene

How About a Fish That Grows Faster?

Genetically Engineered Salmon

Wild Salmon

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

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.

Question Seven


Have you ever eaten genetically engineered food?

a. yes
b. no

Question Eight

Would you eat food obtained from genetically modified plants and animals?


a. yes
b. no



Question Nine

Would You Use a Genetically Engineered Drug?



a. yes
b. no




Question Ten

Can the Federal Government Regulate Genetically Engineered Organisms (GMOs) Used For Human Consumption (Food)?

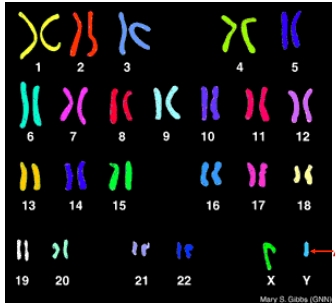
a. yes
b. no

How About Changing The Sex Of An Organism?



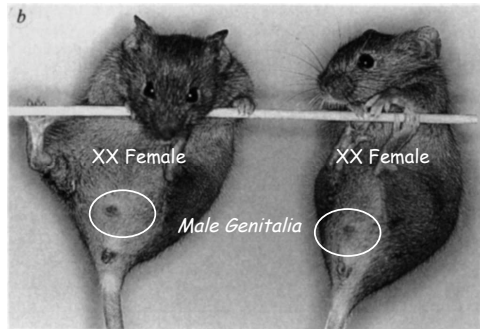
Males and Females Differ By the Presence or Absence Of the Y Chromosome (simplistically!!)



Male SRY Gene (Sex Determining Region Y)

The Human SRY Gene For Maleness Can.....

.....Turn a Female Mouse Into a Male!!!!



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!

Abnormal ectopic expression of the eyeless gene-522 genetically at eye on the leg of a fly.

How About Genetically Engineered Humans?

THE

Treatment for Blood Disease Is Gene Therapy Landmark
By NICHOLAS WADE
Published December 10, 2011

Gene therapy has emerged from exile with breakthrough treatments for blindness, cancer, and the deadly, hereditary disease. By Jill Neimark

In Girl's Last Hope, Altered Immune Cells Beat Leukemia
December 3, 2012

Gene therapy helps blind children see
By Jocelyn Kaiser
ScienceNOW Daily News
24 October 2009

a CURE

Humans Have Been Genetically Engineered To Cure a Lethal Genetic Disease (SCID)

The Age of Human Genetic Engineering Began Almost Twenty Years Ago Treating Severe Combined Immunodeficiency Disease (SCID) With Normal ADA Genes!!!

Several Teenagers Are Alive Because They Have Been Engineered With an ADA Gene That They Were Not Born With!!!

Adenosine Deaminase Gene (ADA)

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

DNA Genetic Code of Life

Entire Genetic Code of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Genes

Transcription (RNA synthesis) See Figures 12.8, 12.9

Translation (protein synthesis) See Figures 12.10-12.13

mRNA

tRNA

Ribosome

Polypeptide

Traits!

Observations and Inferences From the GloGene Experiments

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

Translating The Genetic Code Into Proteins is a Conserved Process

Can Intervene in This Process in Cells

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

All Organisms Use The SAME Processes And "RULES" to Generate Traits!! And The SAME Molecules & Chemistry!!

Replication

Information

DNA

Information

Transcription (RNA synthesis)

Information

mRNA

Information

Translation (protein synthesis)

Ribosome

Protein → Trait (e.g., eye color)

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

REPLACE FEAR OF THE UNKNOWN WITH CURIOSITY

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

Life is either a daring adventure or nothing.
—Helen Keller

Question Eleven

Is Genetic Engineering a New Technology?

a. yes
b. no

There is Nothing New About Genetic Engineering!

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

This is Genetic Engineering 1.0!!

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)

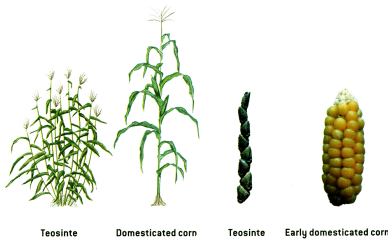
Tomatoes Were Engineered From Small Wild Relatives Because of Mutations in Fruit Size Genes!



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



Wild Banana



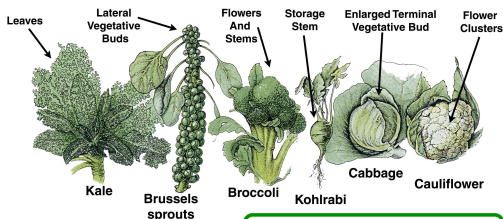
Origins of Domesticated Banana



Modern Banana

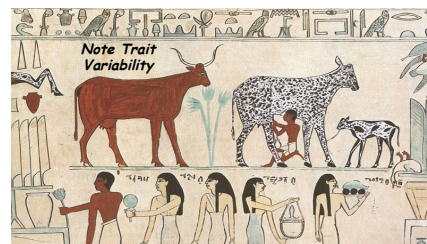
Note: Fruit Architecture and Presence of Seeds

Engineering Vegetables With Different Plant Architectures



How Are These Plants Related?

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



Note Trait Variability

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!

Canine DNA Forensic Testing

The Problem With Breeding the "Old Fashioned Way"

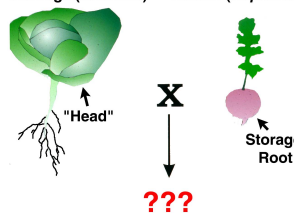
Cannot Predict Results!



The Problem With Breeding the "Old Fashioned Way"


Engineering A Novel Crop By "Wide" Breeding

Cabbage (*Brassica*) Radish (*Raphanus*)



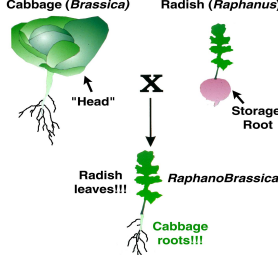
???

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

Cabbage (*Brassica*) Radish (*Raphanus*)



Radish leaves!!! RaphanoBrassica Cabbage roots!!!

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

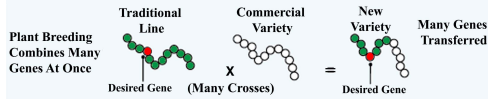


Genetic Engineering is a TECHNIQUE!

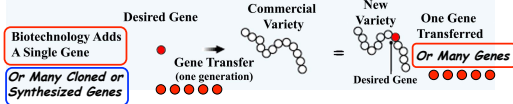
How Do Classical Genetic Engineering Methods Differ From Those Using DNA and 21st Century Technologies?

Classical vs. Molecular Genetic Engineering

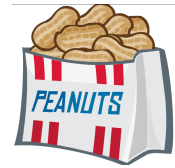
TRADITIONAL PLANT BREEDING



PLANT BIOTECHNOLOGY



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)

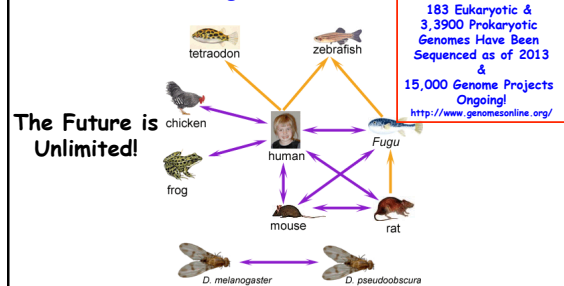
The Era of 21st Century Genomics Will Provide Access to ALL Genes of Every Organism on the Earth




Gene + Chromosome = Genome
(Winkler, 1920)



The Genomes of Many Organisms Have Been Sequenced Providing New Knowledge About Our Origins and Cellular Functions





Providing Thousands of New Genes and Proteins To Be Engineered For Practical Applications (e.g., cellulases in termite gut bacteria for biofuel production)



HOW IS SCIENCE CARRIED OUT?

SCIENTIFIC KNOWLEDGE IS OBTAINED BY A PRECISE & SPECIFIC PROCESS

The Scientific Method

- What are the Observations?
- What is Your Hypothesis to Explain the Observations?
- What are the Predictions?
- How Test Hypothesis?
- What are the Experimental Data?
- Have the Data Been Verified & Peer Reviewed?



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!



- What are the Observations?
- What is Your Hypothesis to Explain the Observations?
- What are the Predictions?
- How Test Hypothesis?
- What are the Experimental Data?
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