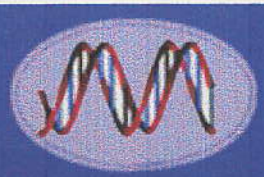
HC 70A Winter 2006
Professor Bob Goldberg

Learning Unit #1
The Age of DNA – What is Genetic Engineering

THEMES

1. Age of DNA, Genes, Genetic Engineering, Genomics, & Mammalian Cloning
2. What do genes look like – DNA demonstration
3. DNA into the Home – DNA Testing – Age of DNA
4. Genetic Engineering into the Home – Glofish – Age of Genetic Engineering
5. Glofish, GloFly, GloMouse – what do these experiments tell us about unity in Gene Processes?
6. How does the Scientific process work – No opinions!
   Stop 1/10/06 talk about HC70A
7. Other Examples of Genetic Engineering – GloPlant, Insect R, GloMonkey, Super Mouse, Obese Mouse, XX♂ Mouse, SCID-Gene Therapy
8. ASILomar Conference – History & Meaning – DVD
9. What is Genetic Engineering & How Affect Society?
10. Genetic Engineering – Anything New?
11. PLANT / crop Engineering / Vegetable demonstration
12. Genetic Variability / Alleles
    Stop 1/24/06
13. Genetics of Mankind / Eugenics
14. ERa of Genomics
15. ERa of Mammalian Cloning / Stem Cells / Reproduction



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

We Live in the Era of....

DNA

Genetic Engineering

Whole Genome Sequencing & Genomics

Mammalian Reproduction & Cloning

And the SYNTHESIS of These Technologies!!!

DNA DEMONSTRATION

1. What Does DNA Look Like?
2. How CARRY out an "Experiment" to "Touch" DNA?
3. Hypothesis Testing - Which Flask has the DNA? How test Prediction?

1. What is a gene?
2. What is a gene made of?
3. How would you study a gene?

4. What's a Hypothesis
5. How test?
   - Predictions?
6. Can prove true - false?

WE LIVE IN THE Age of DNA

The Age of the Gene

DNA Comes Into Your Home!

April 4th...

DNA®

PERFUME

by bijan

DNA...

it's not just
a perfume...
it's gene therapy.

We have begun to Control our Biological Destiny!

WHAT DOES DNA LOOK & FEEL LIKE?

An Age of DNA that comes into the home....

MOLECULAR GENEALOGY RESEARCH PROJECT Uses mouthwash. **FREE.**
molecular-genealogy.byu.edu

FAMILY TREE DNA No blood—just swab your cheek. **$149 AND UP.**
dnafamilytree.com

SCIENCE

DO-IT-YOURSELF DNA

If you've tried and tried but your family tree is still just a seedling, mail-order DNA testing may be for you. Comparing your genetic profile with those of other genealogy buffs—and potential relatives—can provide new leads. For $149 and up, Family Tree DNA will give you a list of 25 markers (or genetic traits) you carry, based on a swab from the inside of your cheek. For a bit more—$220 and up—Oxford Ancestors (**oxfordancestors.com**) will check 10 markers and tell you which "Seven Daughters of Eve" clan you belong to. If that's too steep, the Molecular Genealogy Research Project will test 250 markers for free. Run by Brigham Young University, it hopes to create a worldwide database. The catch: the data must be kept anonymous. In other words, the project will create a map of ancestry lines—not an indvid-ual report for you.

—MATTHEW MACROBERTS

Do it yourself DNA testing to find family history!!
$200

YOU will have a DNA test this Quarter!

VOL. 24, NO. 7

Pheromones: Profoundly Mysterious | Dust Devils

Discover

JULY 2003

SCIENCE, TECHNOLOGY, AND MEDICINE

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It Starts With a Single **Drop of Blood** Taken From Each Newborn

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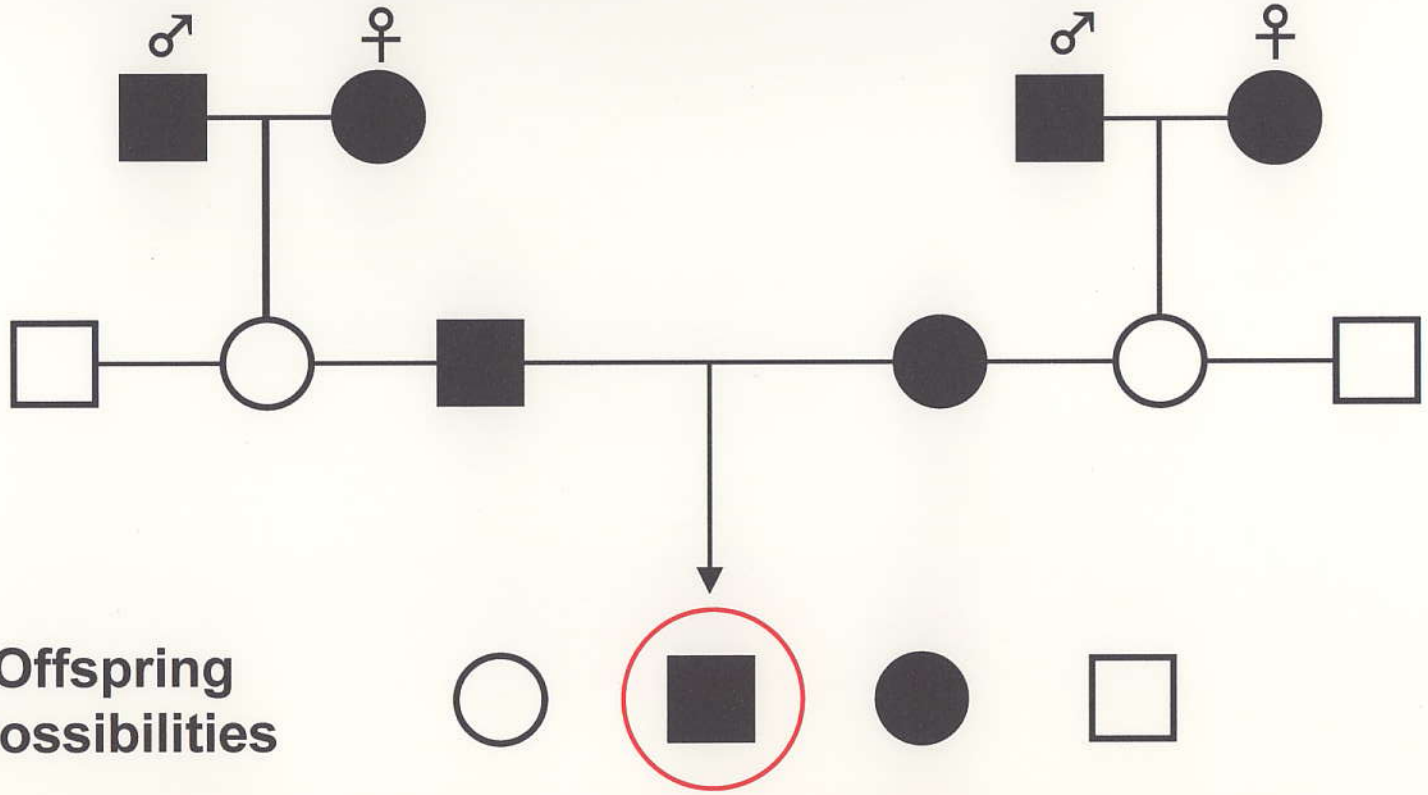
A Hypothetical Genetic Case Study

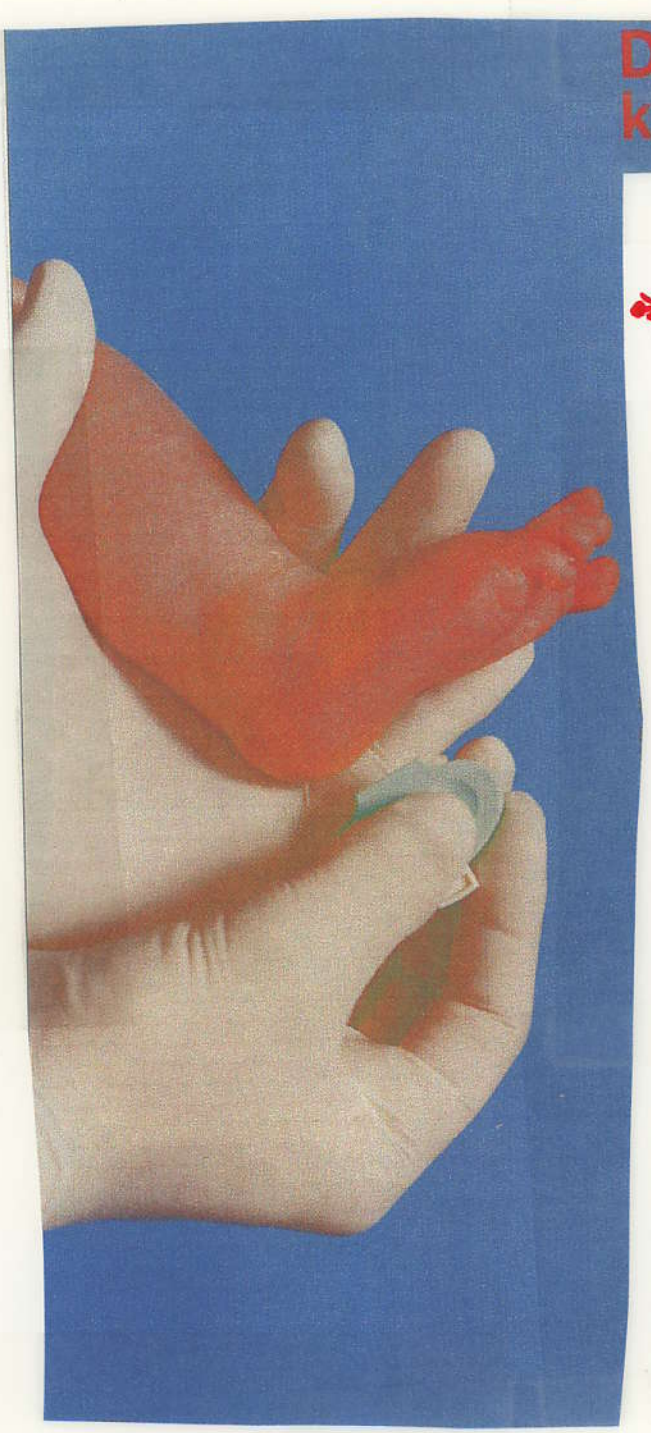
FAMILY ONE
Dominant Genetic Disease X

FAMILY TWO
Dominant Genetic Disease X



How Can DNA Testing be Used to Determine Whether the Parents and Children Carry the "Defective" Gene?

TO TEST OR NOT?



Do you want to know your future?

Every state in the country requires that infants be tested for a list of obscure diseases. Before long, some states could move on to DNA testing of all newborns. Now is the time to decide a critical question: How much do we want to know and when do we want to know it?

By Jeff Wheelwright
Photography by Catherine Ledner

DNA TESTING FAMILIES FOR CARRIERS OF "DEFECTIVE" GENES!

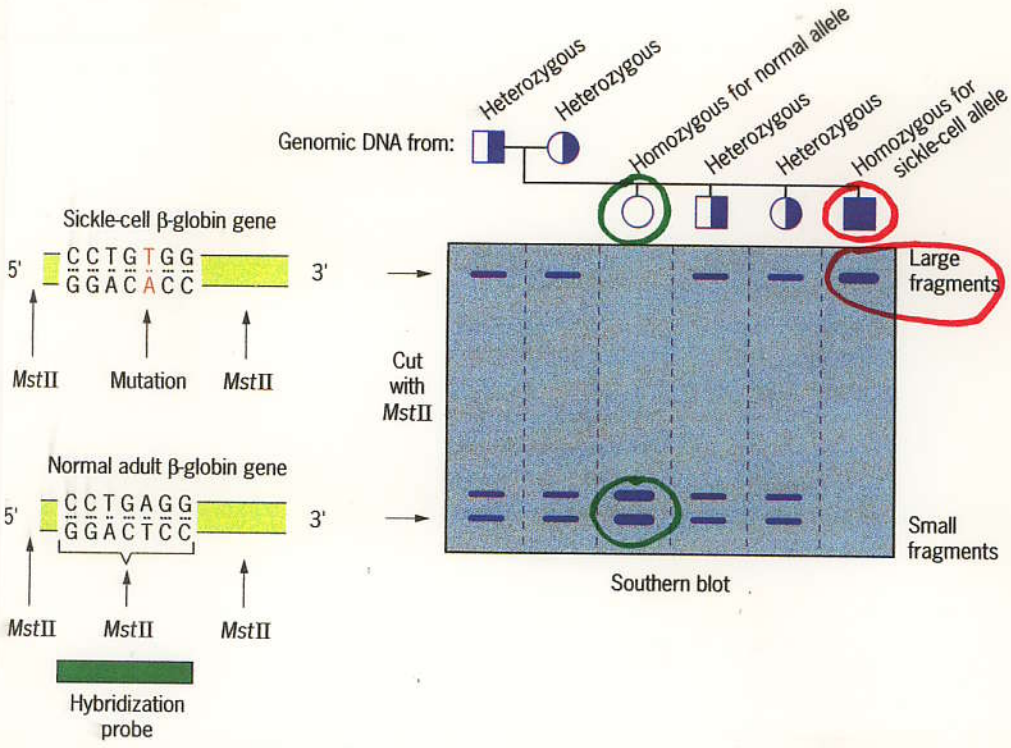


Figure 22.7 Detection of the sickle-cell hemoglobin mutation by Southern blot analysis of genomic DNAs cut with restriction enzyme *Mst*II.

DNA TESTING IS USED IN MANY situations involving Identity — in addition to Humans

DNA Confirms Infected Cow's Origin

Next in the inquiry into a Washington state case of mad cow disease is a focus on feed.

By JOHANNA NEUMAN
Times Staff Writer

WASHINGTON — DNA tests have confirmed that the Holstein found last month to be infected with mad cow disease originated in Alberta, Canada, U.S. Department of Agriculture officials said Tuesday.

The DNA testing on the cow and her offspring, as well as earlier-reported records showing that the cow had been sold by an Alberta farmer disposing of his dairy herd, "makes us confident in the accuracy of this trace-back," said W. Ron DeHaven, the department's chief veterinarian.

The confirmation, based on DNA tests at two laboratories — one in the United States and one in Canada — leaves unanswered the question of how the cow from a farm in Washington state became infected. Officials will now concentrate on the feed used by the cow's original owner in Alberta.

Dr. Brian Evans, chief veterinary officer for the Canadian Food Inspection Agency, said on a USDA conference call Tuesday that investigators would also try to determine whether the feed source for the Holstein was the same as that for an Alberta cow diagnosed with mad cow disease in May.

Scientists believe that bovine spongiform encephalopathy, or BSE, the brain-rotting illness commonly known as mad cow disease, can be transmitted to cattle that eat feed containing the remains of infected cows. In the past, leftover parts of slaughtered animals — including the brain and the spinal cord, which are believed to harbor the source of the infection — were ground up and used in animal feed.

In 1997, the U.S. and Canada banned the use of the remains of ruminants, or cud-chewing animals, in feed used for cattle, but both North American cows diagnosed with BSE — the one discovered in Canada in May and the one found in the United States in December — were born several months before that ban went into effect. The human form of the illness, variant Creutzfeldt-Jakob disease, has been associated with consumption of food made from BSE-infected animals.

Agriculture Secretary Ann M. Veneman announced Dec. 23 that a cow slaughtered Dec. 9 had tested positive for BSE. The cow was tagged for testing because it was a "downer" cow that was unable to walk to slaughter. The cow's meat products had already been distributed before Veneman's announcement, primarily to retail outlets in Washington and Oregon.

While officials recalled the meat, it is not known how much was recovered.

Veneman has since announced a series of reforms to bolster U.S. defenses against BSE, including a ban on accepting downer cows for slaughter and a rule that would hold all meat products from an animal tested for disease until results are completed.

But after Tuesday's announcement of the DNA results confirming the cow's origin, some producers said the Agriculture Department had moved too slowly to determine the source of the infection.

"They knew the leads pointed back to Canada, and if they had made the announcement immediately, it might have mitigated a great deal of our loss," said John Lockie, executive director of R-CALF USA, a national association of cattle producers.

Identifying species / Pathogens (Flu viruses, etc.)
Poaching - Animal Identity
Plant/crop Identity / Forensics
etc.

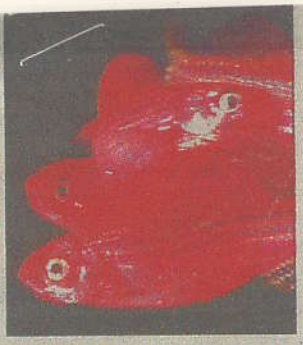
THE AGE OF GENETIC ENGINEERING COMES INTO THE HOME.....

Genetically Engineered Zebra fish

State Takes Dim View of GloFish, Bans Sale

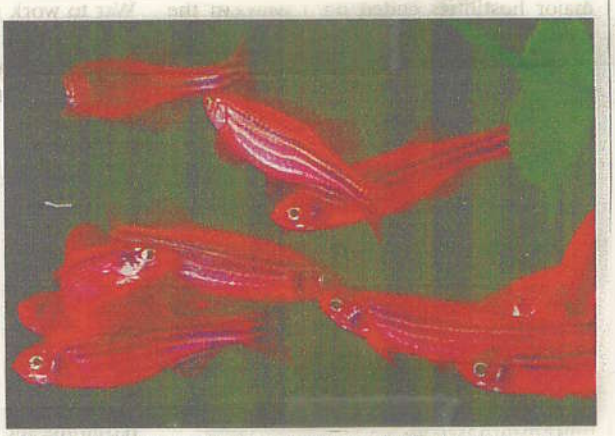
By KENNETH R. WEISS
Times Staff Writer

State Game Panel Bans Sale of GloFish



PR News

RED ZEBRA: *GloFish are implanted with a gene from sea anemones.*

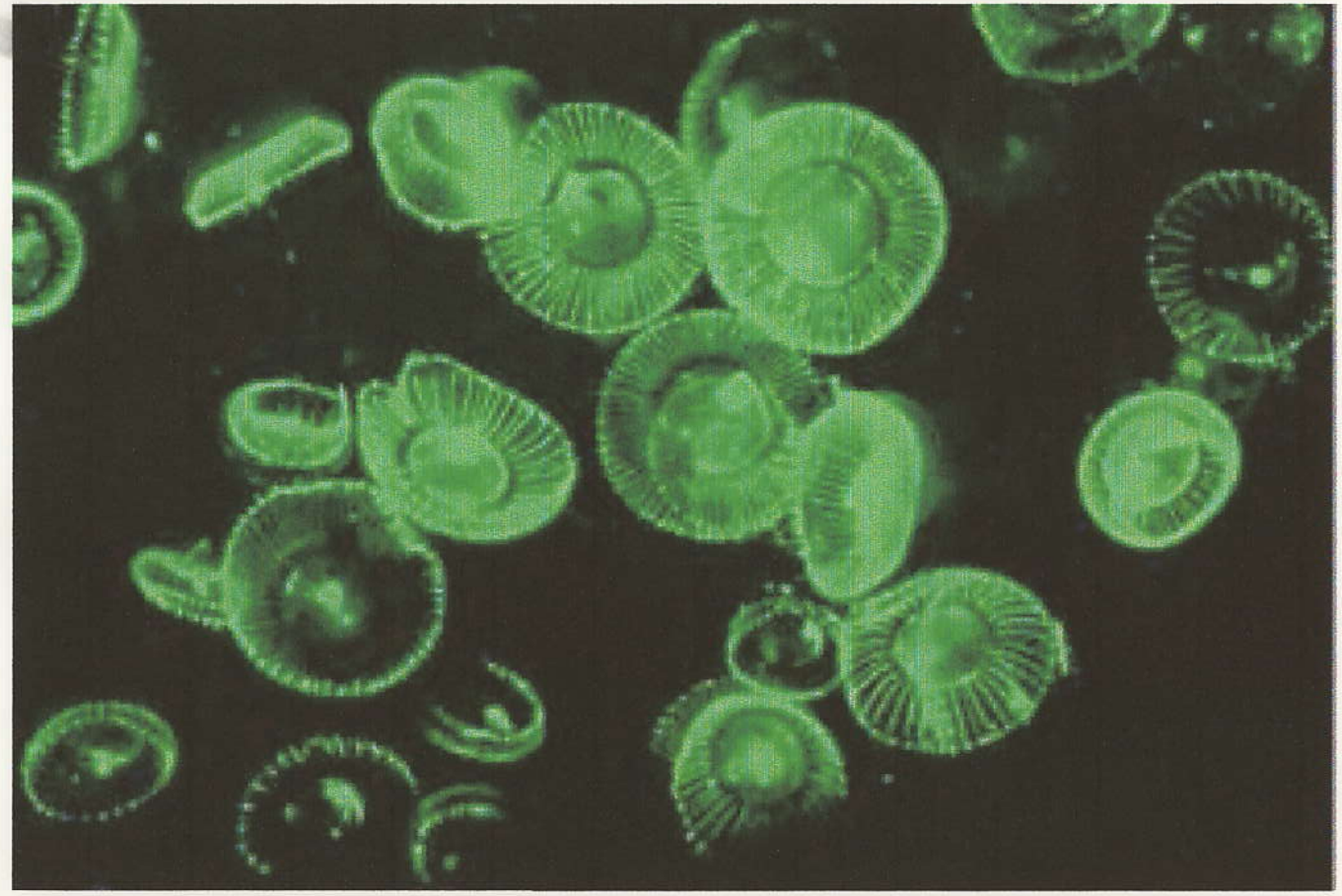


Glowing review: watchdogs want tighter rules for transgenic pets.

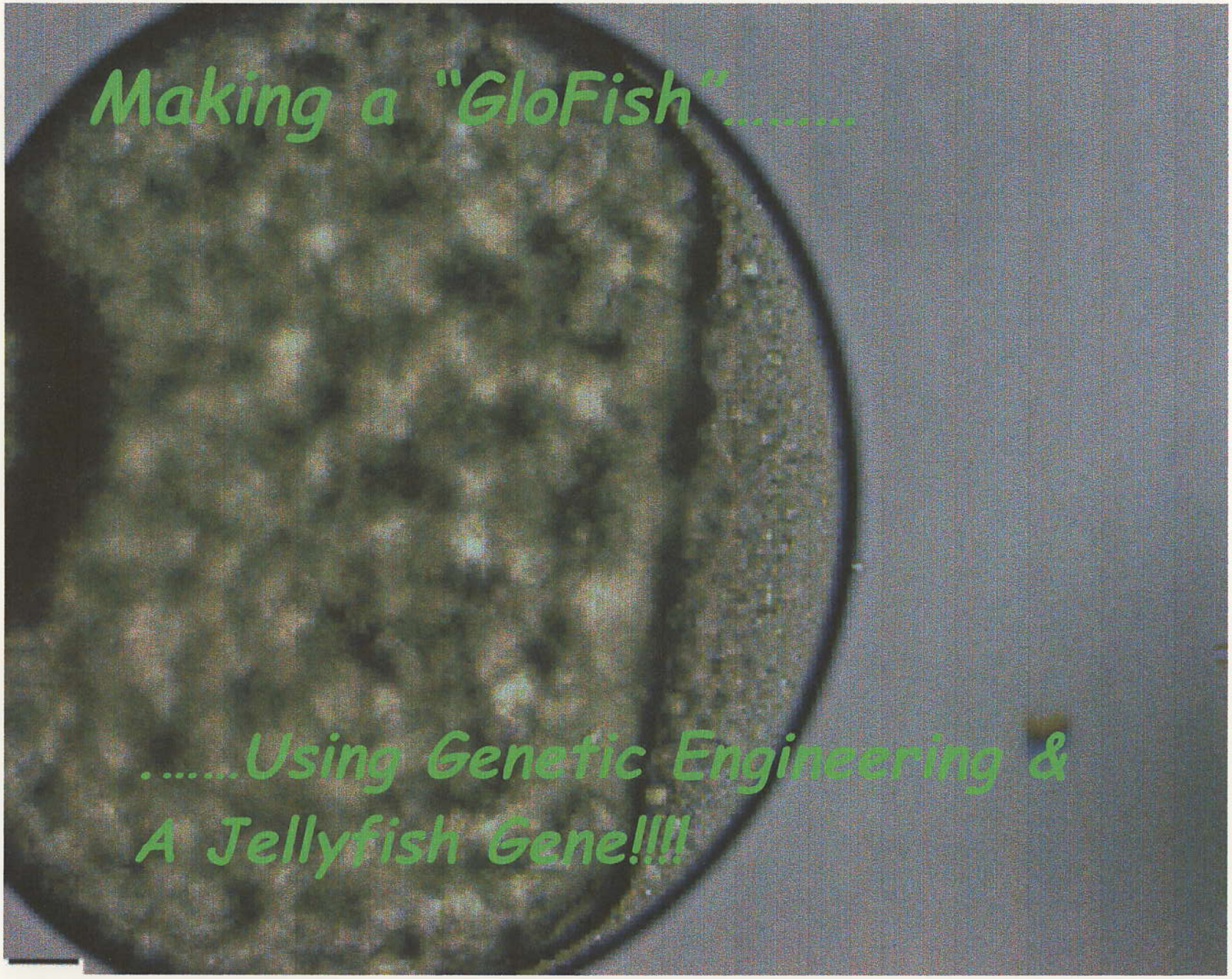
pet GLO fish!!

go to slide

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

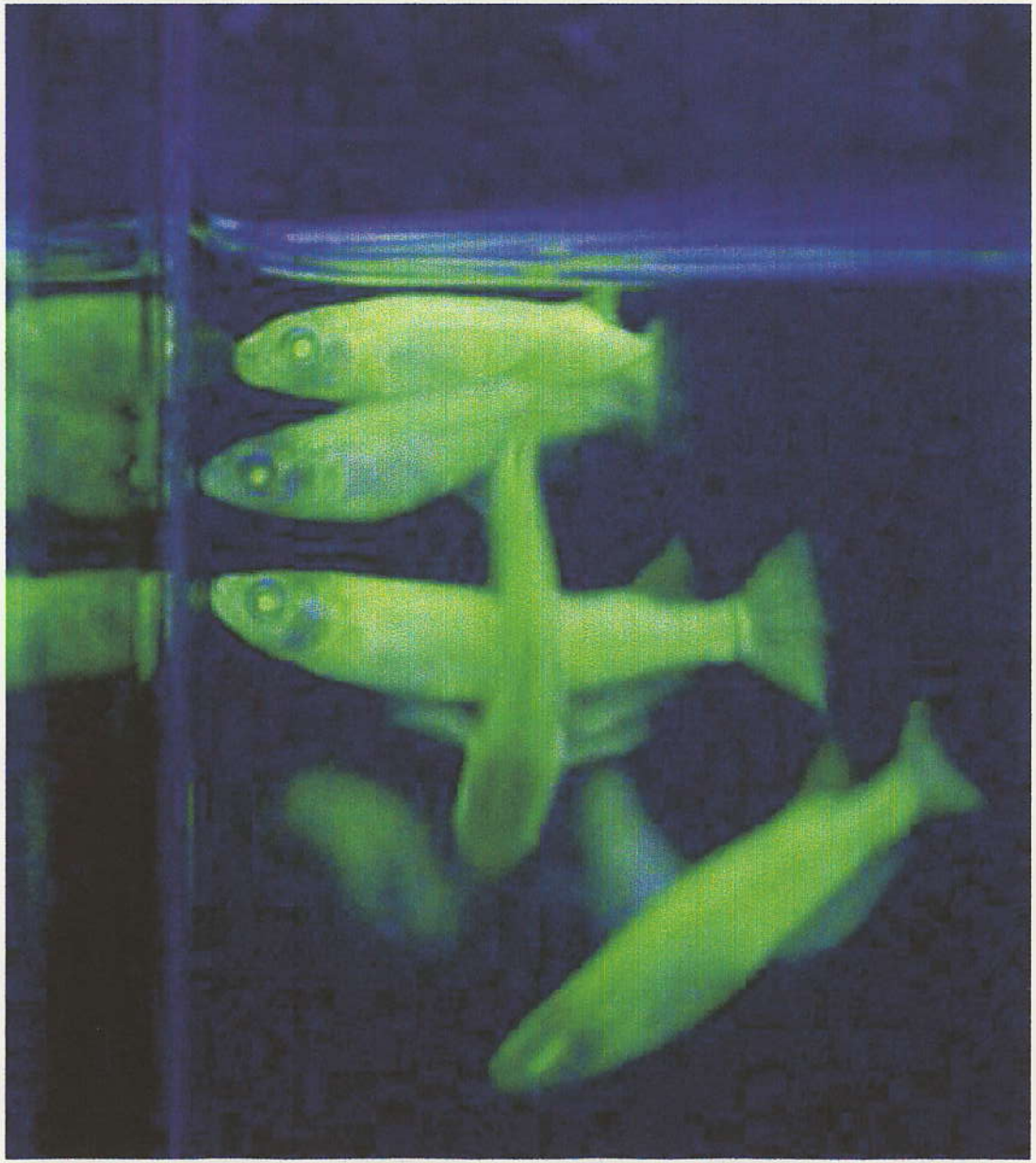


Green Fluorescence Protein


Making a "GloFish".....
.....Using Genetic Engineering &
A Jellyfish Gene!!!!


A "GloFish" Embryo!!!!!

A "GloFish!!!!!"



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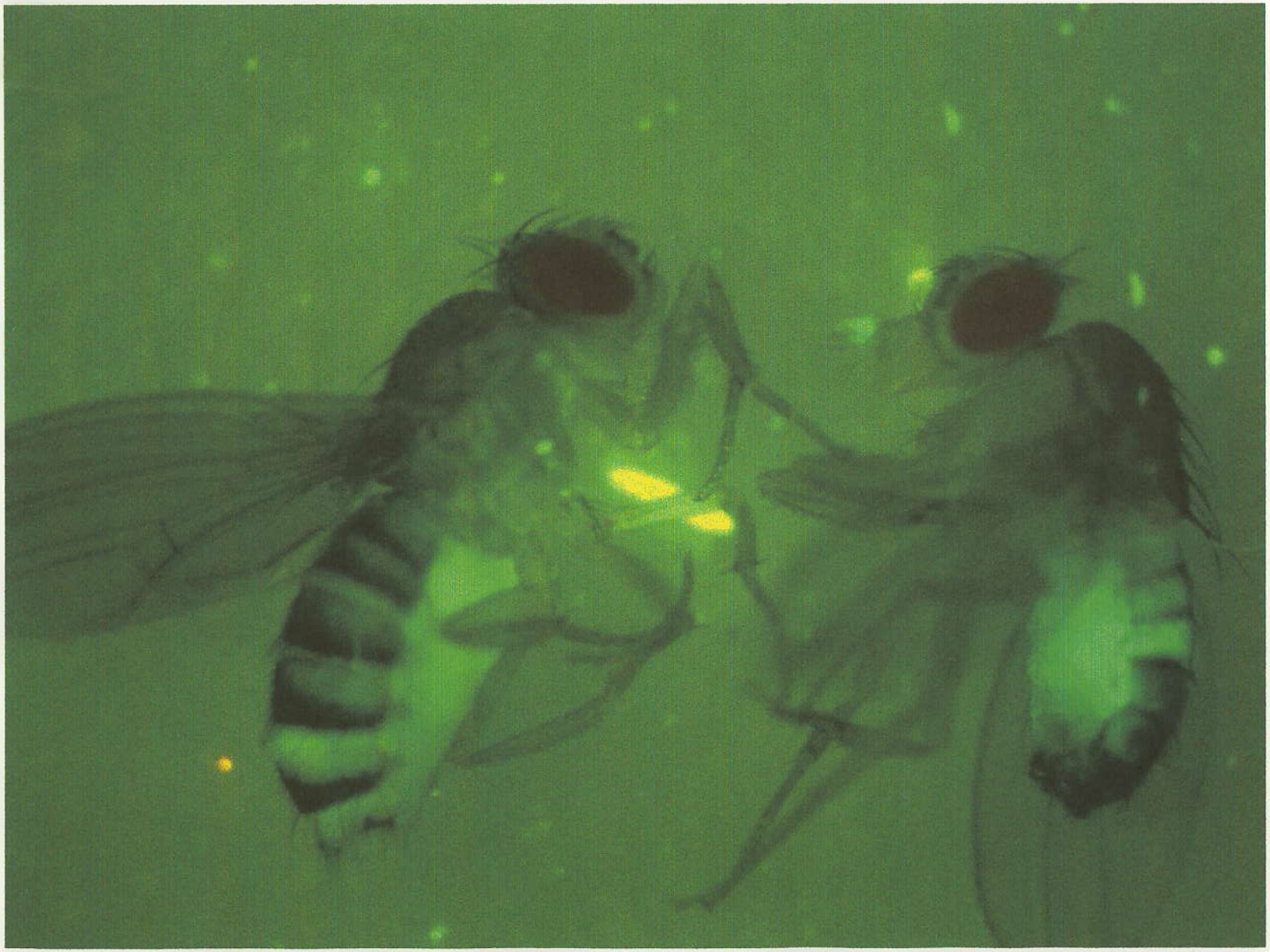
How About a GloFly!!!!!!



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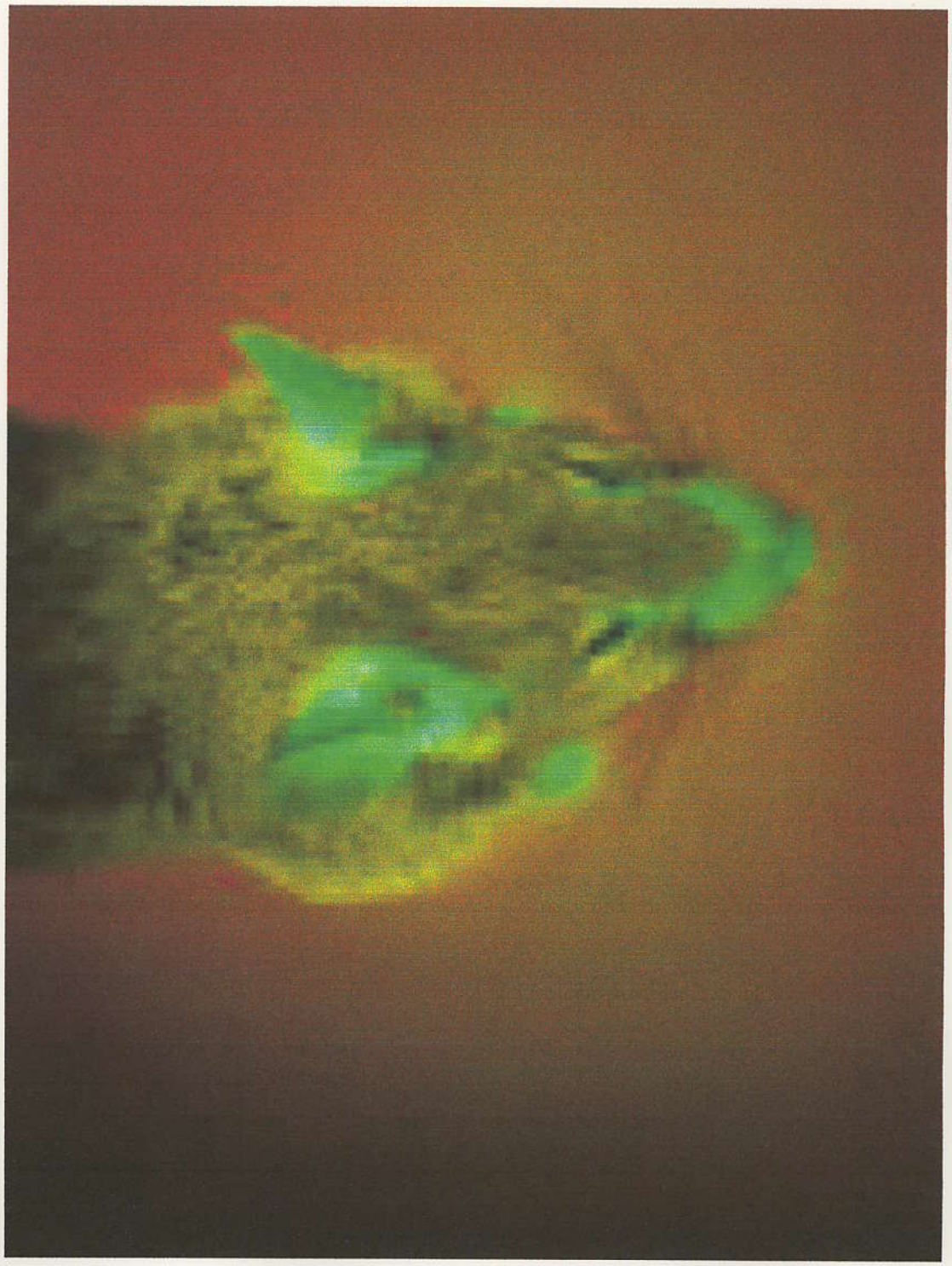
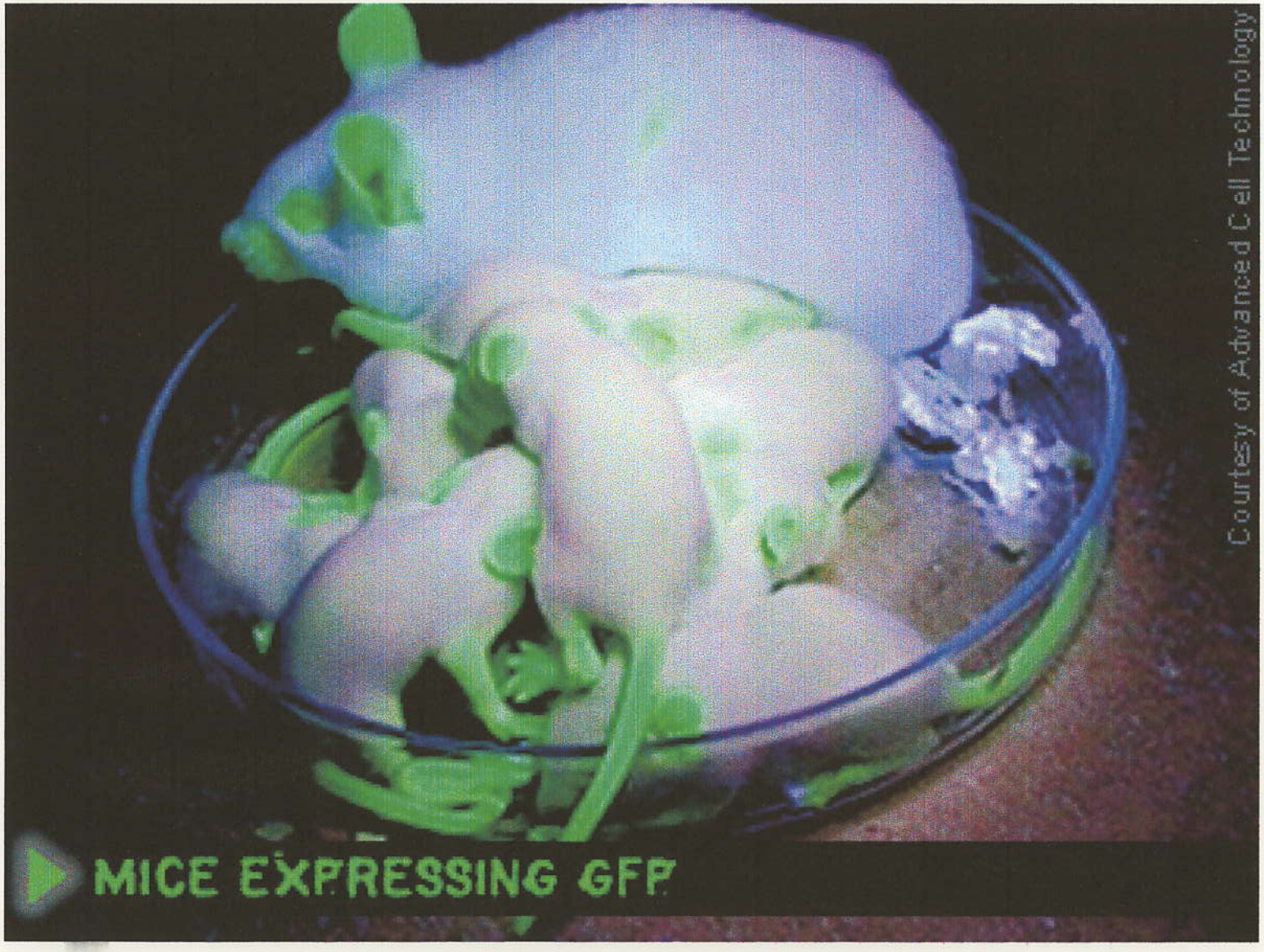
What do these experiments tell us about what DNA/Gene CAN Do? About Unity & Genetic Processes?

How About a "GloMouse!!!"



How About "GloMice!!!"

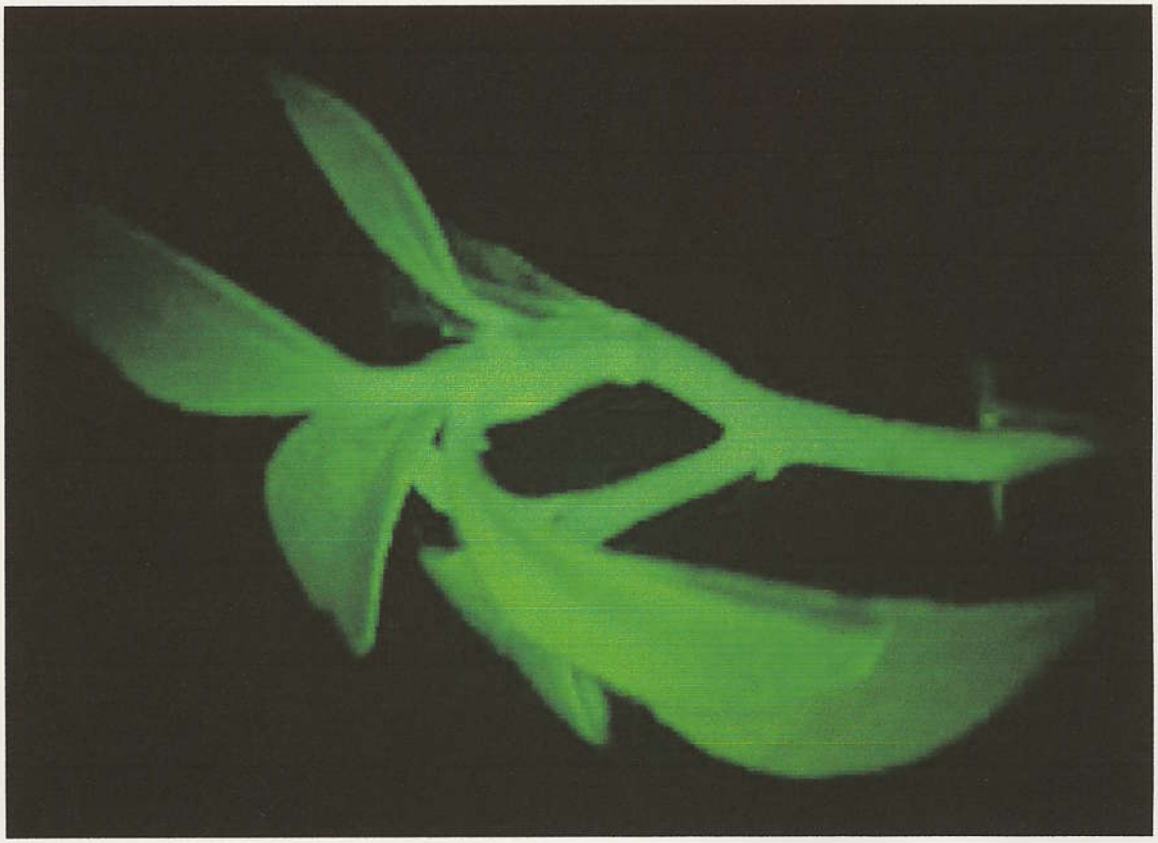


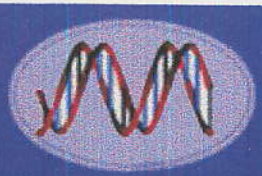
(51)

Note - Glow only in ears, feet + Tail
What's your hypothesis to explain?

Note - The SAME gene is active in a fish, fly, mouse, & plant - what does this imply about DNA, genes, & genetic processes?

A GloPlant With the Same Jellyfish Gene!!!





DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

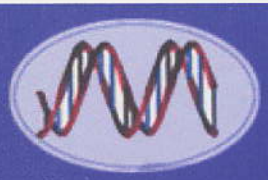
Plants of Tomorrow

What Do These GloGene Experiments "Say" About Unity of Genetic Processes?

What is the Hypothesis?

What are the Predictions?

What Experiment(s) to Test Predictions?



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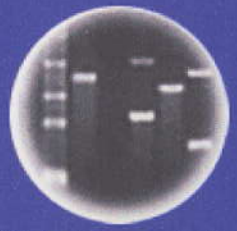

DNA Fingerprinting

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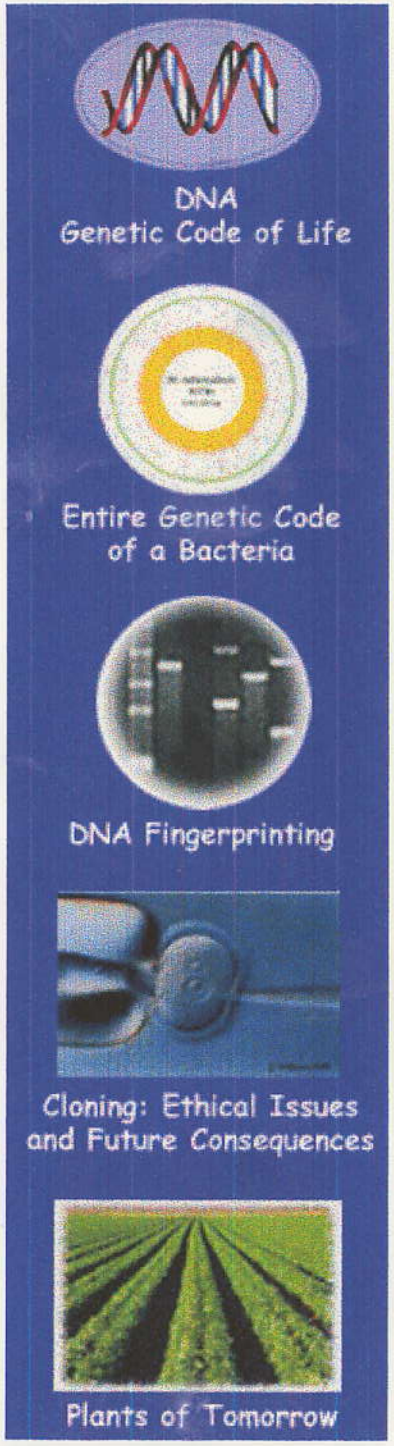
Plants of Tomorrow

Scientific Process

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



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

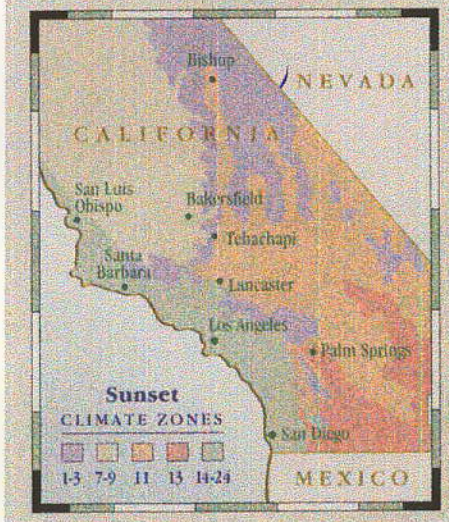
Other Examples of Genetic Engineering - Bacterial Gene into a Plant

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. ◆

How to Make an Insect-Resistant Plant

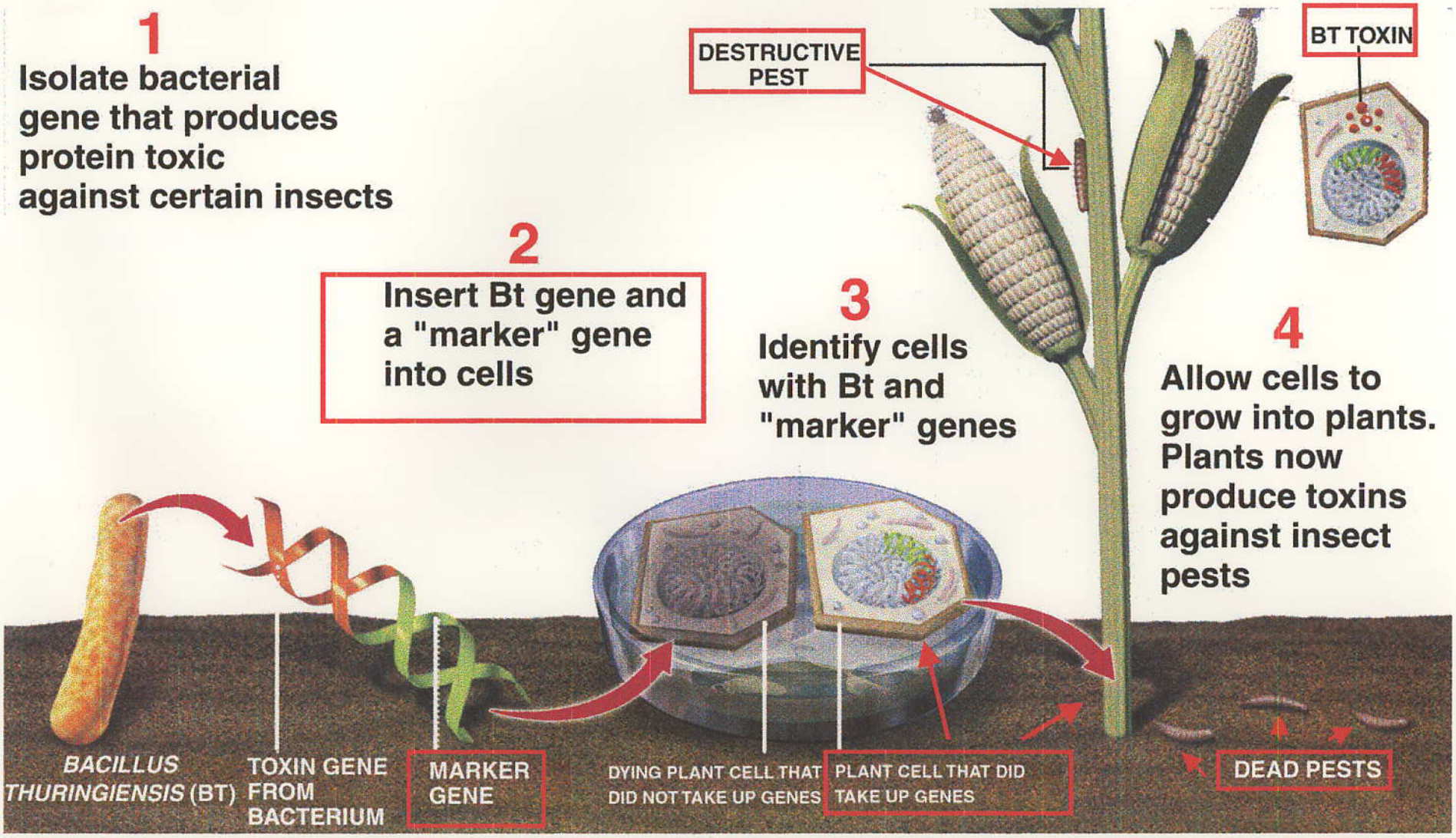
Bacterial Gene → Plant!

1
Isolate bacterial gene that produces protein toxic against certain insects

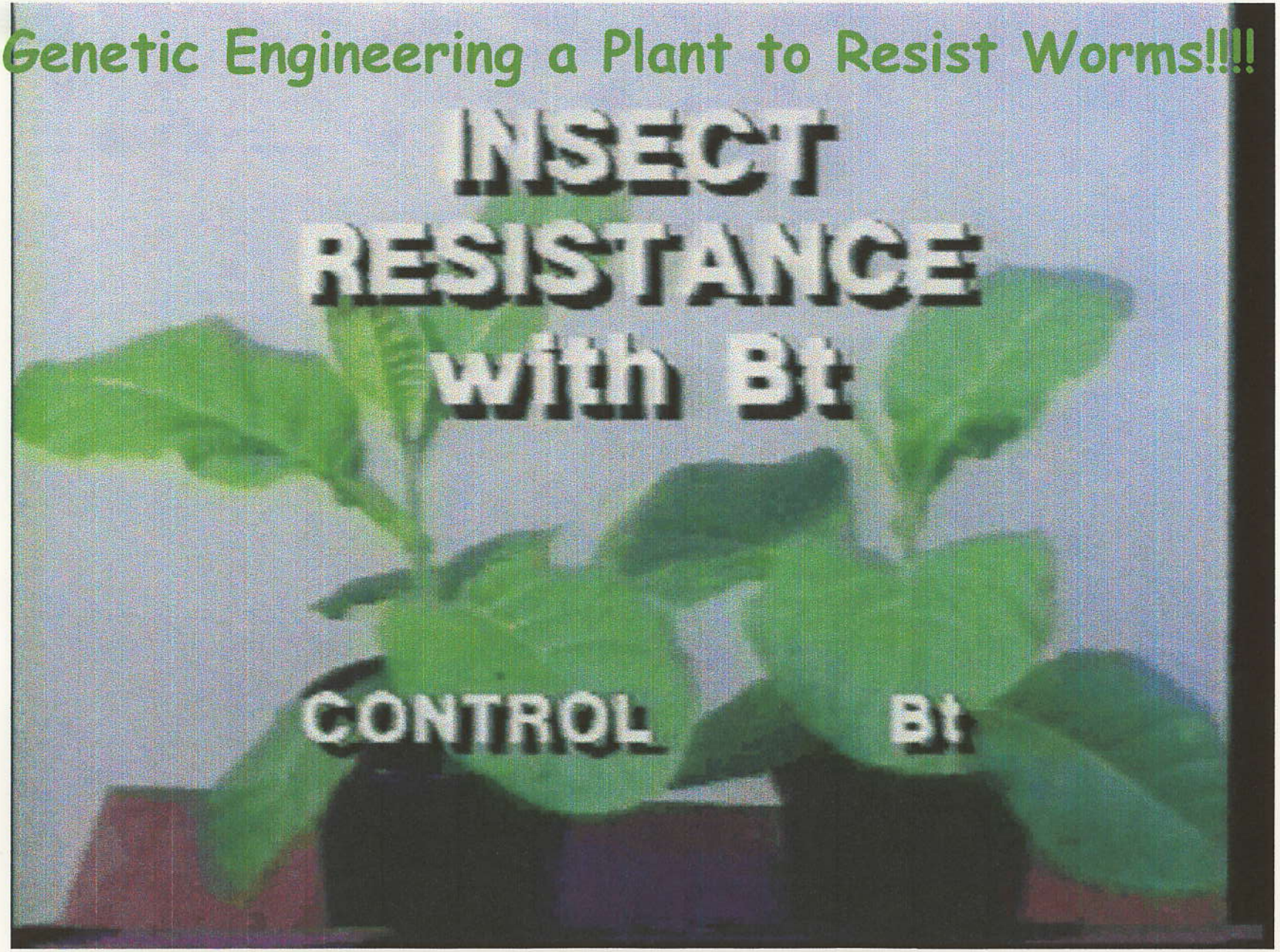
2
Insert Bt gene and a "marker" gene into cells

3
Identify cells with Bt and "marker" genes

4
Allow cells to grow into plants. Plants now produce toxins against insect pests



Genetic Engineering a Plant to Resist Worms!!!!



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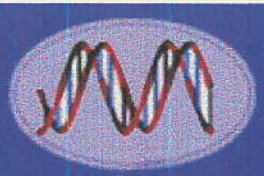
What do Farmers Say About This Technology?



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22

What Else Can Be Done With Genetic Engineering?

How About a "GloMonkey!!!"

(23)

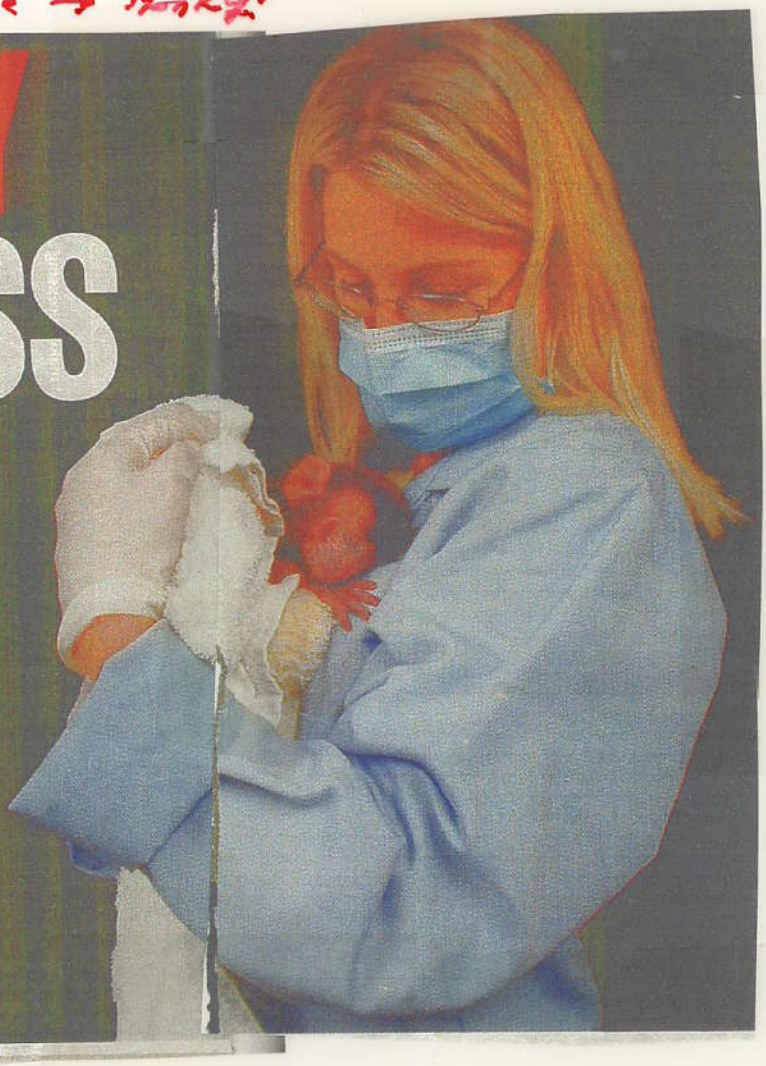
Using red fluorescence protein

WHAT ABOUT A GLO Monky - ANDi?

Jellyfish Gene → Monkey!

MONKEY BUSINESS

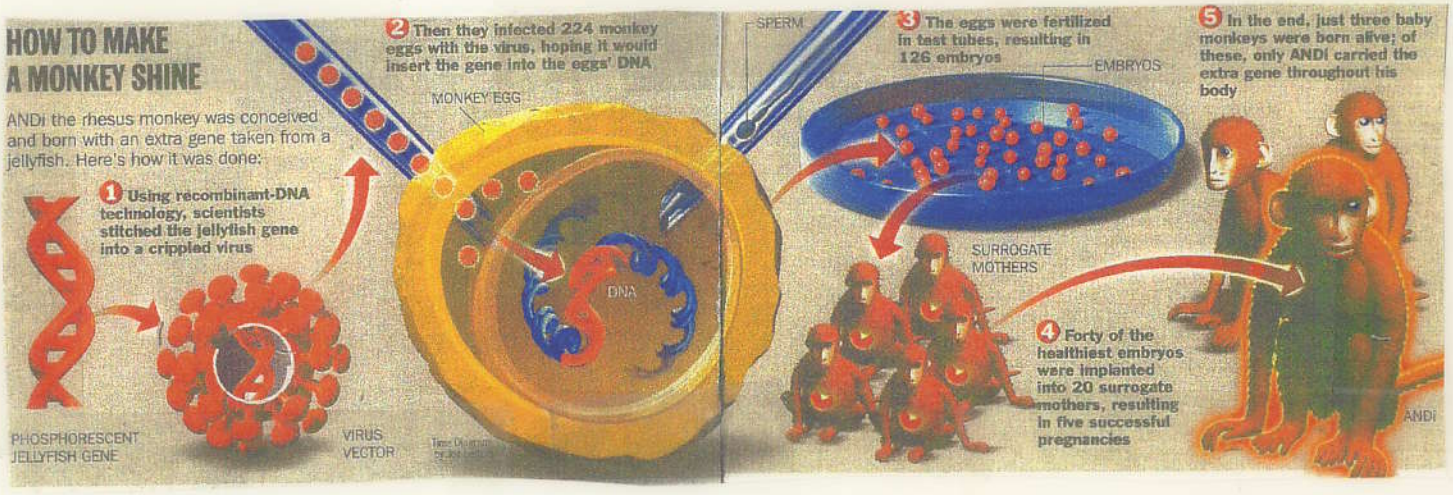
A tiny primate with a gene from a jellyfish raises scientists' hopes—and some serious ethical questions



MADONNA AND MONKEY Researcher Christa Martinovich cradles ANDi soon after birth; his temperament, she says, was "perfect"

HOW TO MAKE A MONKEY SHINE

ANDi the rhesus monkey was conceived and born with an extra gene taken from a jellyfish. Here's how it was done:



How CAN this technology help human beings?

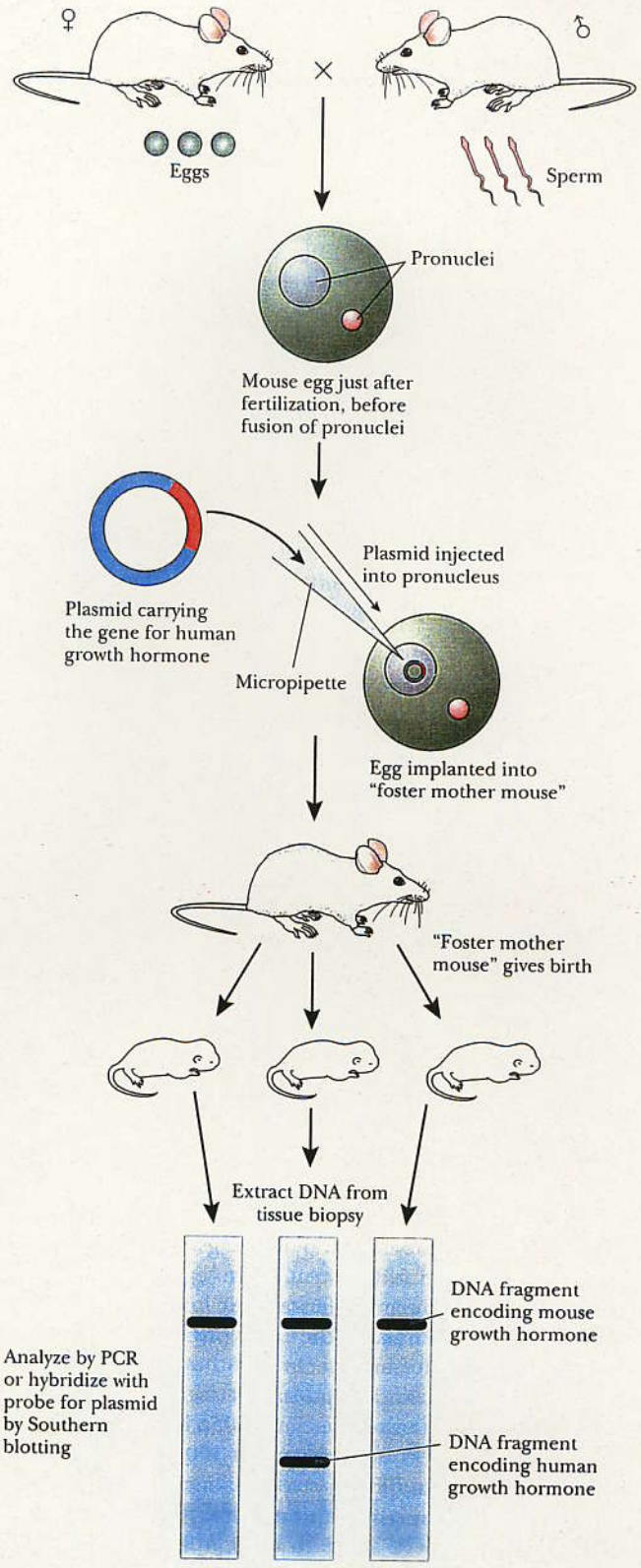
(24) Are there ethical issues in genetically engineering Monkeys? Humans? ← Has it been done?

MORE EXAMPLES OF THE POWER OF GENETIC ENGINEERING

DNA ⇝ SPECIFIC TRAIT

1. Super Mouse
2. XX ♀ → ♂
3. Obese Mouse
4. SCID - Severe Combined Immunodeficiency
   ↳ Human Gene Therapy

Human Growth Hormone Gene CAN BE ENGINEERED into A Mouse



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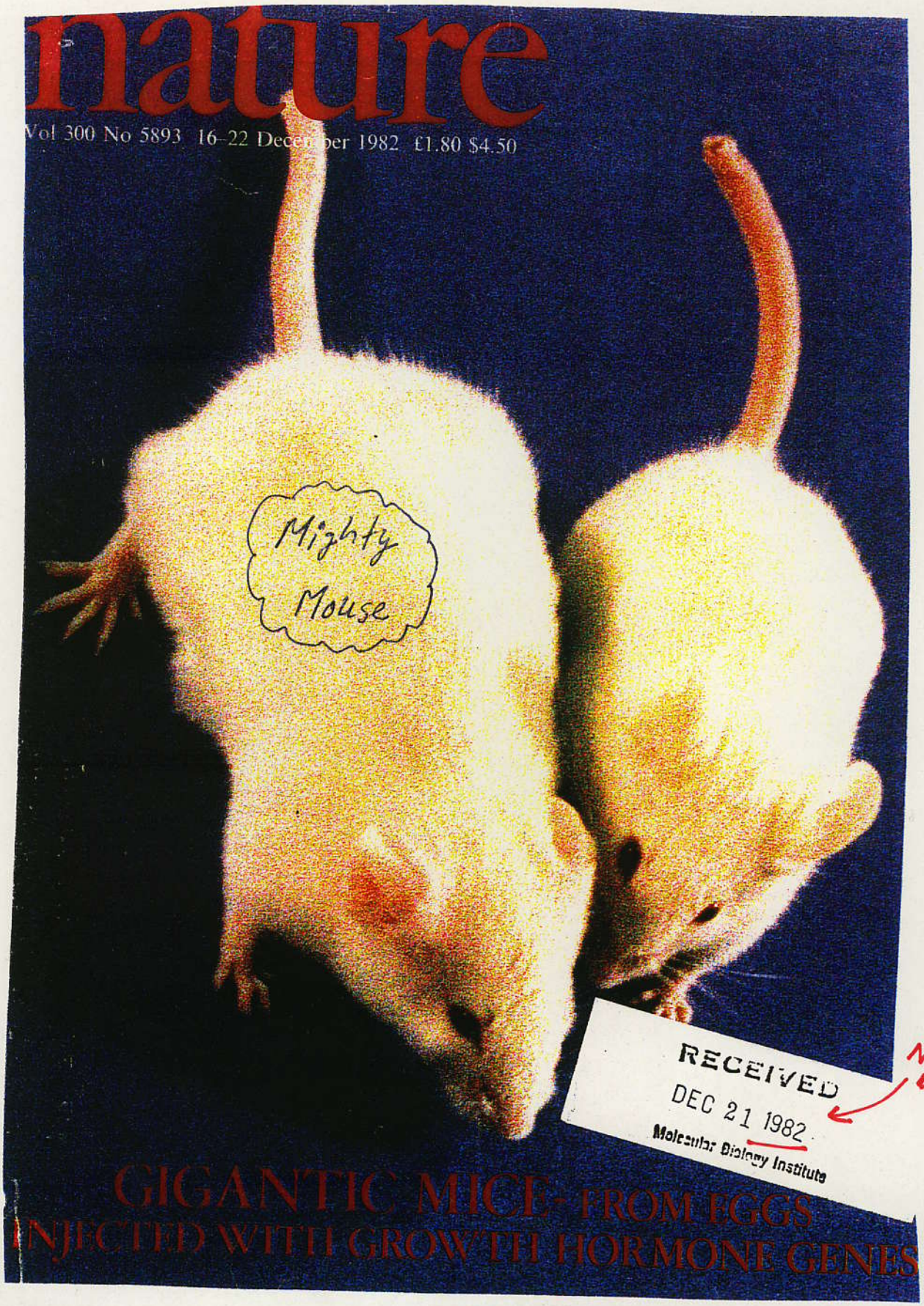
nature
Vol 300 No 5893 16–22 December 1982 £1.80 $4.50



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GIGANTIC MICE - FROM EGGS INJECTED WITH GROWTH HORMONE GENES

Animals can be Genetically Engineered with New Genes that Specify New Traits

Human Gene → Mouse!

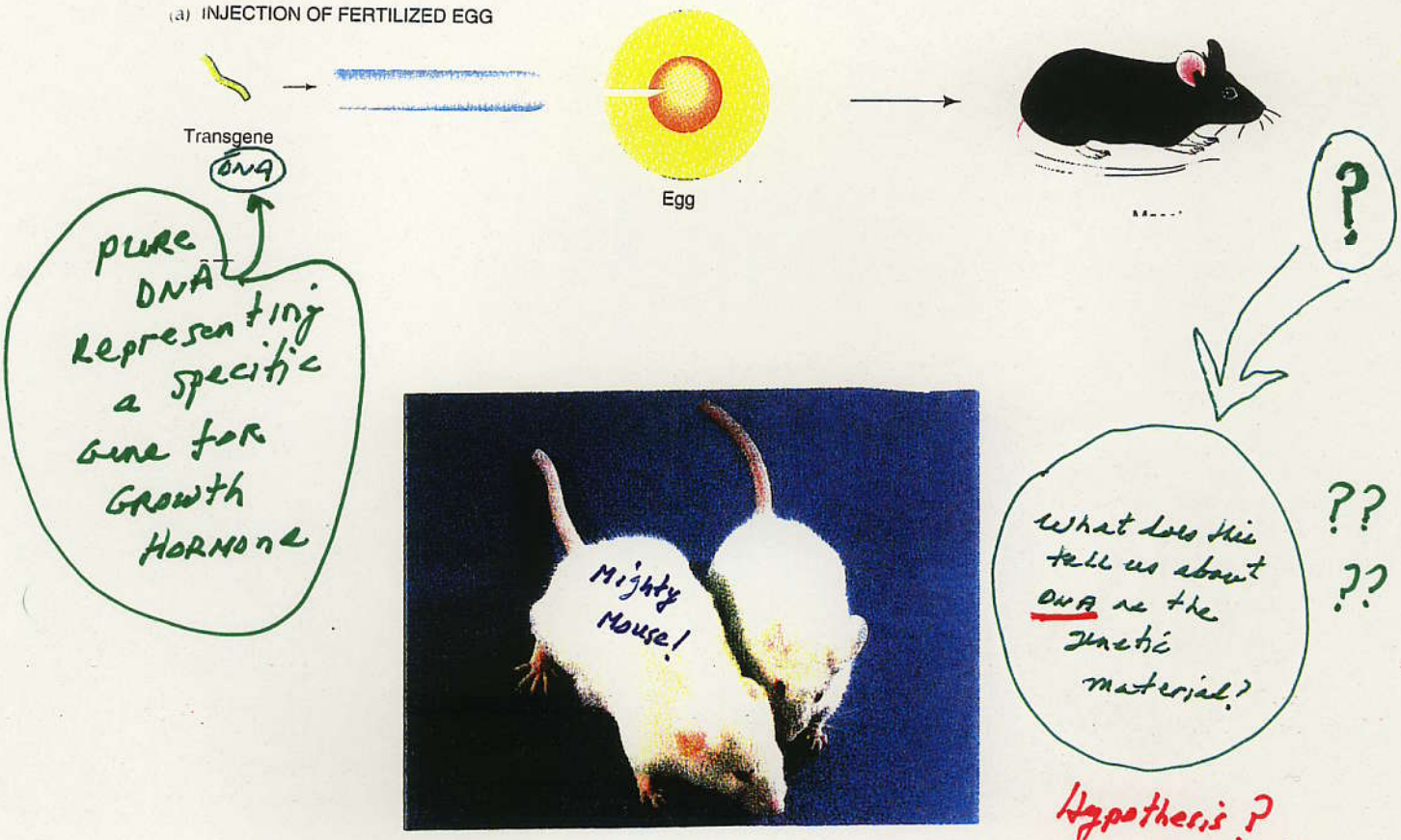


Figure 15-31 Transgenic mouse. The mice are siblings, but the mouse on the left was derived from an egg transformed by injection with a new gene composed of the mouse metallothionein promoter fused to the rat growth hormone structural gene. (This mouse weighs 44 g, and its untreated sibling 29 g.) The new gene is passed on to progeny, in a Mendelian manner, and so is proven to be chromosomally integrated. (R. L. Brinster)

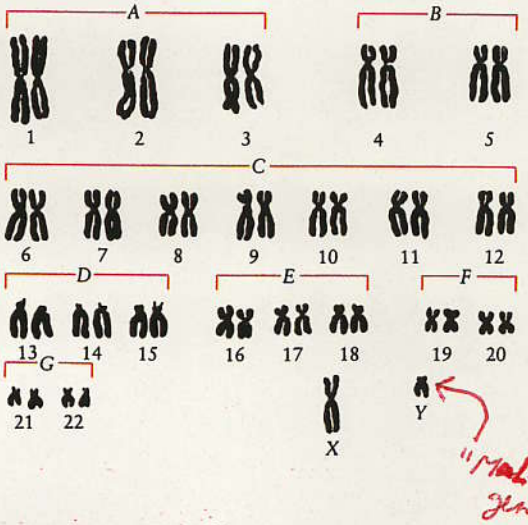
We ARe Entering the ERa of "Designer" ORGANISMS!

ALgo → Glofish, ANDi

SAME TECHNOLOGY!!!

Males & Females differ by only the presence or absence of the Y chromosome (simplistically!)

19–2 *The normal diploid chromosome number of a human being is 46, 22 pairs of autosomes and two sex chromosomes. The autosomes are grouped by size (A, B, C, etc.), and then the probable homologues are paired. A normal woman has two X chromosomes and a normal man, shown here, an X and a Y.*



What Genes are on the Y chromosome?

How do you "naturally" obtain a XY ♂?

XX ♀?

The Human Gene For Maleness

CAN - - - - - - - - →?

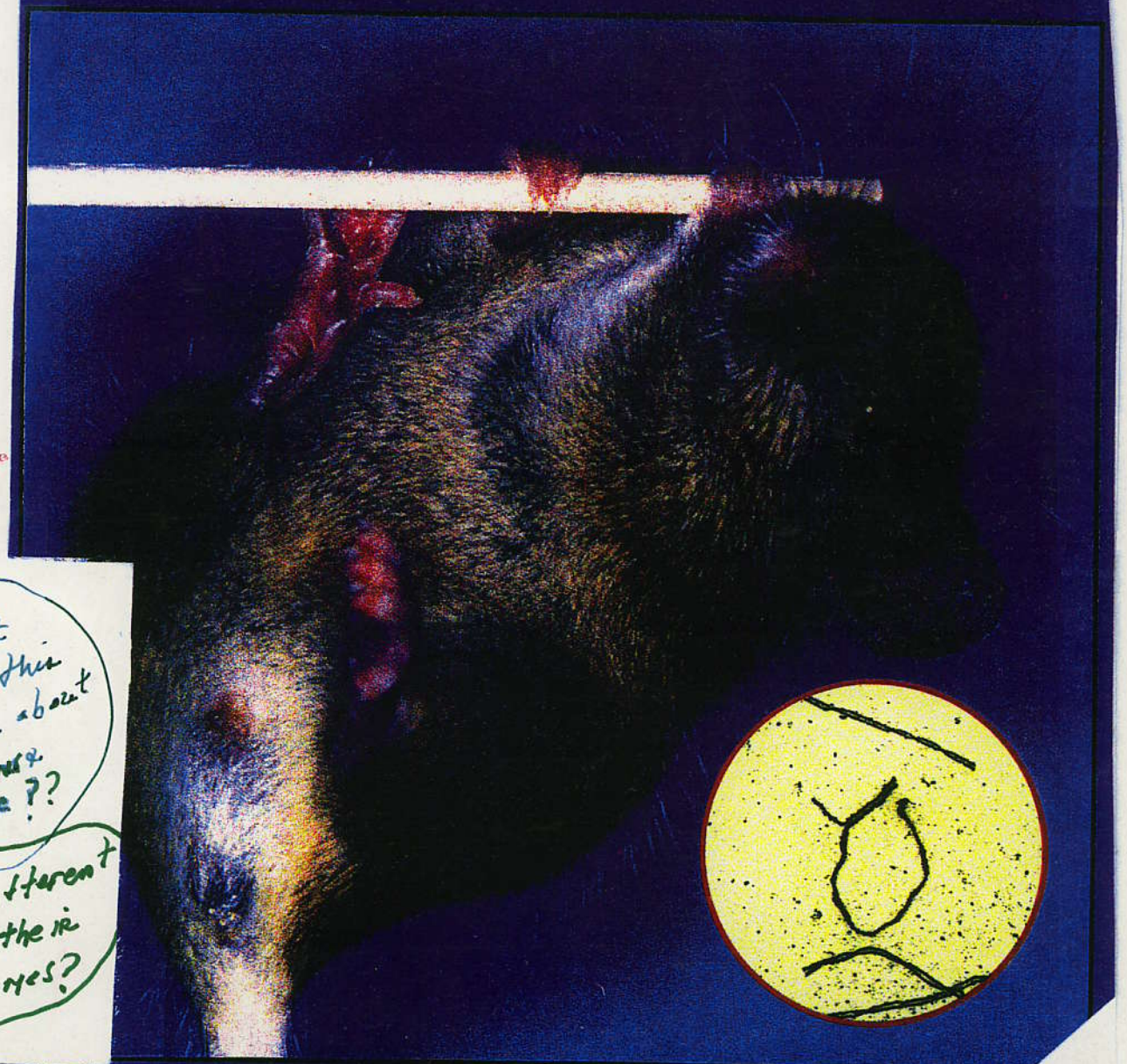
Make A "Female" Mouse Be A Male!

Human Gene → Mouse!

nature

INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Volume 351 No. 6322 9 May 1991 $6.95



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What does this say about Humans & Mice??

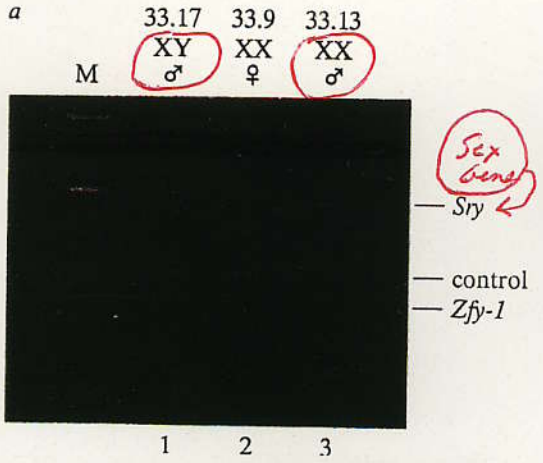
How different ARE their genomes?

MAKING A MALE MOUSE

?? CAN we use the Mouse to Study HUMAN Genes? Disease Models?

30

The Human Sry Gene CAN Make a Female (XX) Mouse into a Male!



Sex Gene

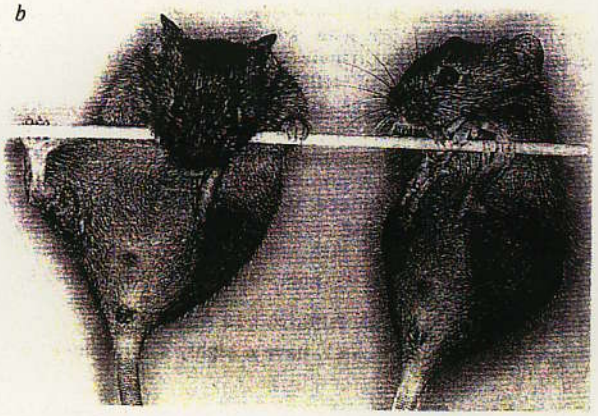


FIG. 3 Analysis of adult sex-reversed transgenic mouse m33.13. *a*, PCR analysis of genomic DNA from m33.13 (lane 3), showing *Sry* and control (myogenin) bands. No band corresponding to *Zfy-1* was seen, demonstrating the lack of a Y chromosome; this result was confirmed by Southern blotting using Y-chromosome probes Y353B (ref. 40) and Sx1 (ref. 41) (not shown). Normal XX female and XY male littermates (33.9, lane 2 and 33.17, lane 1) are shown for comparison. M, marker bands (1,018, 510, 396, 344, 298, 220, 201, 154 and 134 base pairs). *b*, External genitalia of mice 33.17 (left) and 33.13 (right). *c*, Histology of testis sections from mice 33.17 (left) and 33.13 (right). Bar, 90 μm.

METHODS. For PCR analysis, 0.1 μg genomic DNA was added to a 50-μl reaction mixture containing 1.5 mM each dNTP, 50 mM Tris–HCl, pH 9, 15 mM ammonium sulphate, 7 mM $MgCl_2$, 0.05% Nonidet P-40, 0.5 U *Taq* polymerase (Anglian Biotec) and 500 ng each oligonucleotide primer. Amplification consisted of 30 cycles of 94 °C for 5 s, 65 °C for 30 s and 72 °C for 30 s in a Techne PHC-2 thermocycler. An 8-μl aliquot was electrophoresed on a 2% agarose–TBE gel. Primers for *Sry* were (5′–3′) TCATGAGACTGCCAACCACAG and CATGACCACCACCACCACCAA (indicated as triangles in Fig. 1) and for *Zfy-1*, CCTATTGCATGGACTGCAGCTTATG and GACTAGACATGTCTTAACATCTGTCC; myogenin primers corresponded to nucleotides 656–675 and 882–901 of the rat complementary DNA sequence[42]. PCR products were 441, 180 and 245 bp, respectively. Testes were processed for histological examination as described in Fig. 2 legend.

?

How work?

What's your hypothesis?

The "ground state" of human development is a female! Need ONE gene to switch development into a Male

∴ Eve had to have lost a Y chromosome from Adam's Rib! or Eve gave rise to Adam!

31

Mice Can Be Engineered to be Obese!

Mouse Gene → Mouse!

nature

INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Volume 372 No. 6505 1 December 1994 $8.50

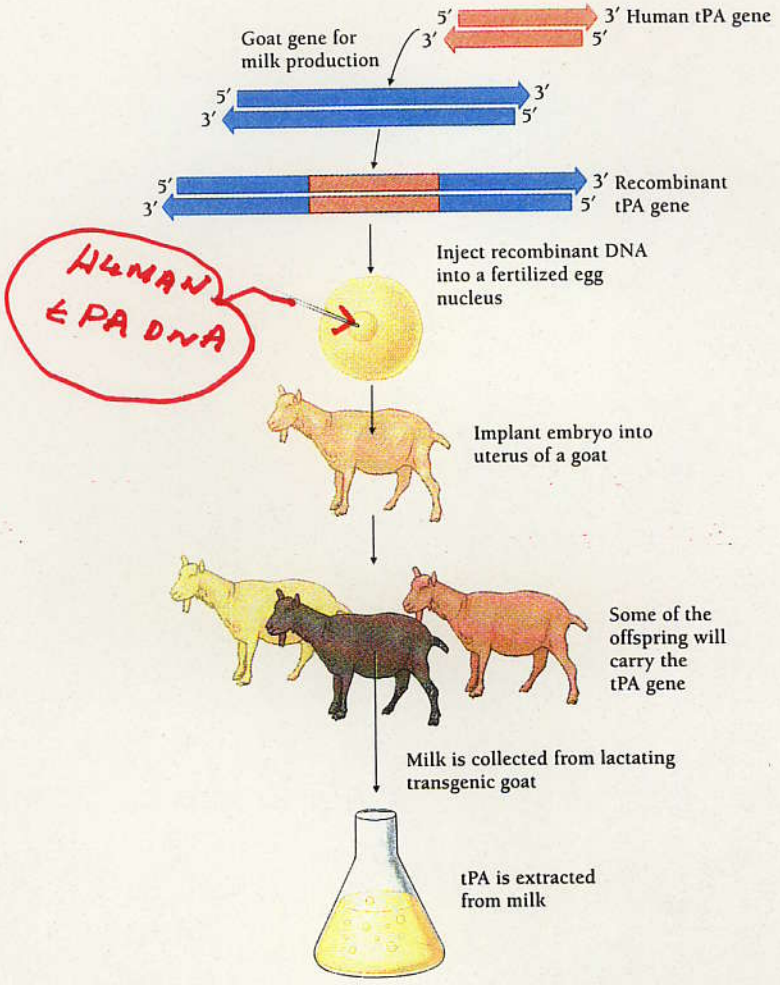
Genetically Engineered Mouse

Mouse weighed down by genetics

Implications?

Goats CAN Be TURNED into "FACTORIES" to Produce Medically-Important Human Proteins

HUMAN Gene → Goats!



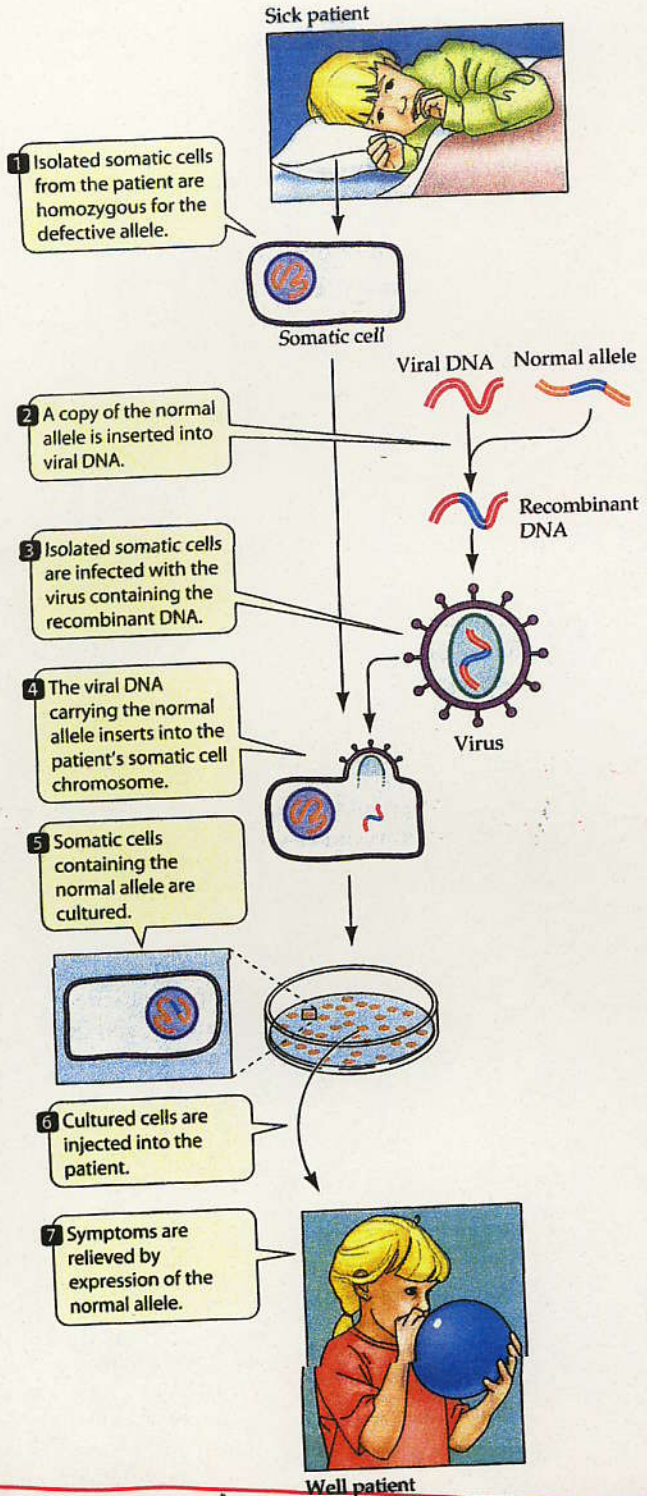
Natural?

Any Different than Breeding Cattle? Cows? For maximum "food" production?

tPA = tissue plasminogen activator
↳ dissolves blood clots & prevents heart attacks!

CORRECTING Genetic Defects in Humans using Genetic ENGineering

HUMAN Gene → HUMANS!



HUMAN Gene Therapy is a ~20-year-old Technology

CORRECTING SCID – Severe Combined IMMUNO Deficiency using the ADA Gene

Adenosine Deaminase Gene → Nucleic Acid Metabolism

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

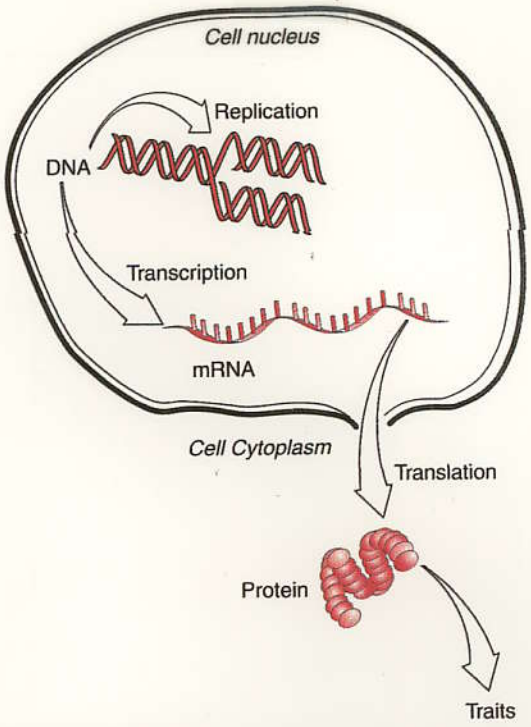


Figure 2.10 The Flow of Genetic Information in Cells DNA is copied into RNA during the process of transcription. RNA directs the synthesis of proteins during translation. Through proteins, genes control the metabolic and physical properties or traits of an organism.

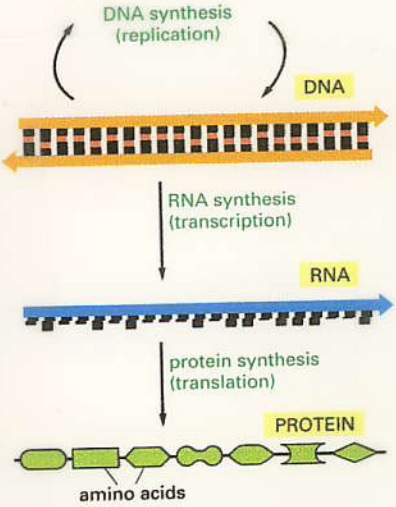


Figure 1–4 From DNA to protein. Genetic information is read out and put to use through a two-step process. First, in *transcription*, segments of the DNA sequence are used to guide the synthesis of molecules of RNA. Then, in *translation*, the RNA molecules are used to guide the synthesis of molecules of protein.

(1) Genes CAN "work" independently of other genes - unique units!

(2) BASIC Genetic PROCESSES Universal
   a. DNA Replication
   b. DNA → RNA → Protein

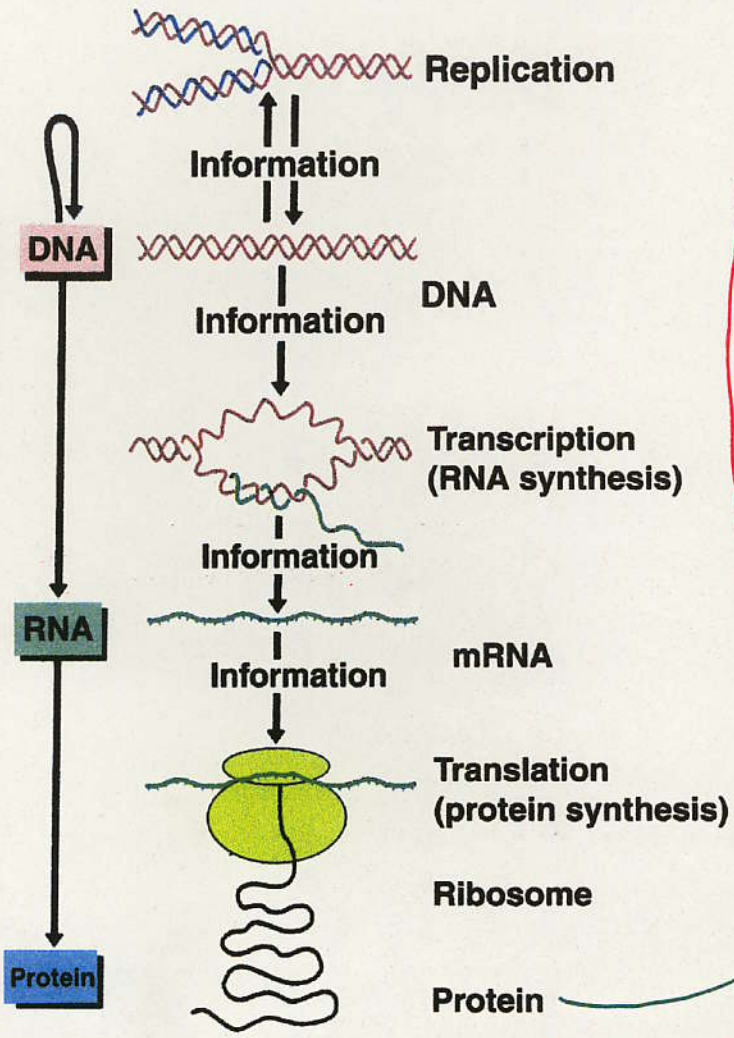
(3) BASIC Genetic PROCESSES CAN Be used to Engineer/TRANSfer Genes FROM one organism to another — stably

The process of Gene to Trait is the "SAME" in all organisms!

UNIVERSAL PROCESS!

Translating The Genetic Code Into Proteins is a Conserved Process

The reason "why" genetic engineering is possible



CAN INTERVENE in this Process in Living Cells

What is the "Big" Implication of "this" for Biology?

TRAIT (e.g. eye color)

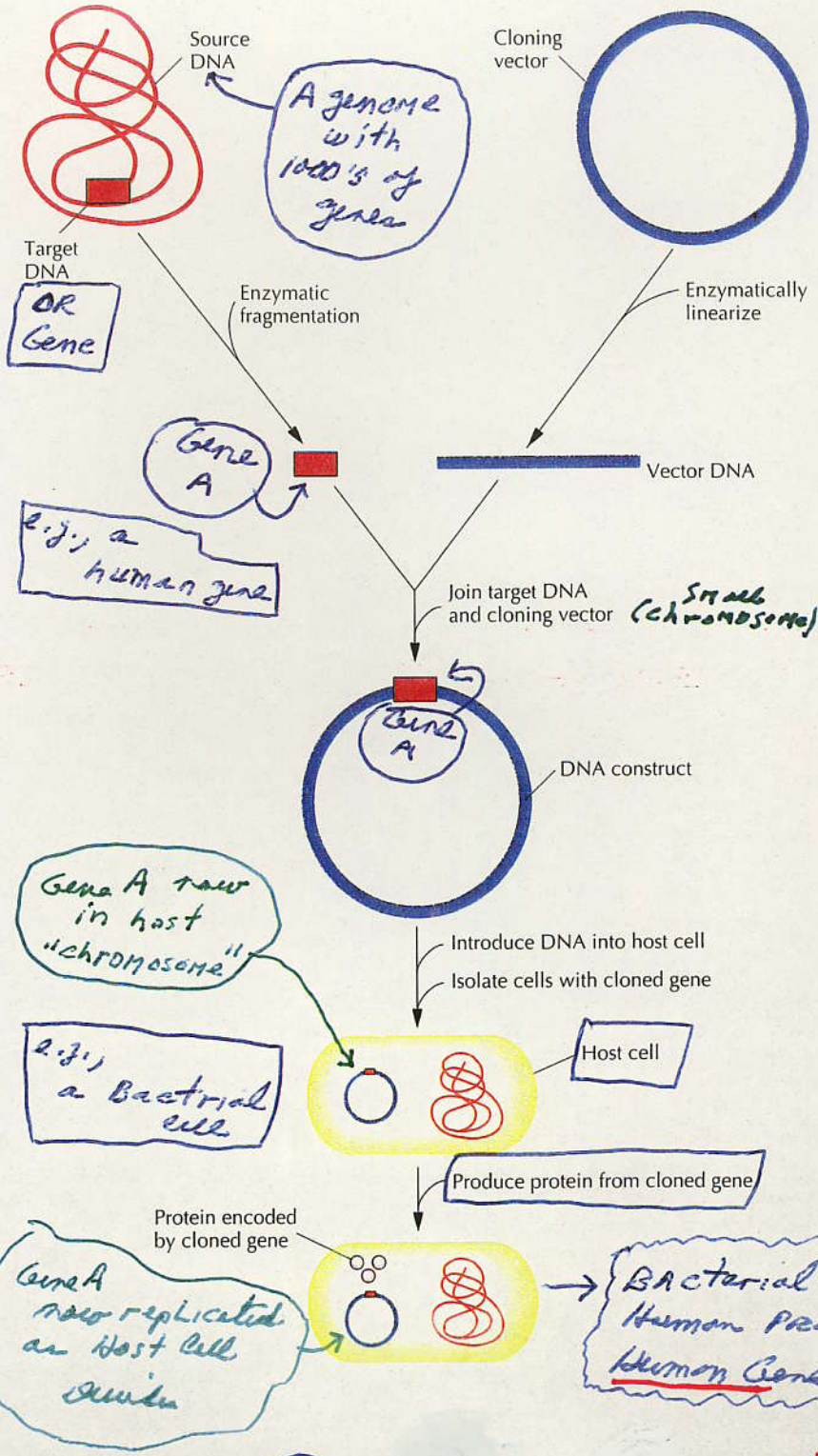
ALL ORGANISMS USE THE SAME PROCESSES and "RULES" to Generate TRAITS!!
And the SAME MOLECULES/CHEMISTRY is involved!

What is Genetic Engineering & What Does it Do?

DNA Cloning OR Genetic Engineering

Uses **Natural PROCESSES** of Living Cells to Isolate Single Genes

NO "HOCUS POCUS"
It's Not Magic!



"Why" Clone Genes from the Genome of an Organism?

Purify Individual Genes from the Genome --- Separate from rest of Genes

Amplify the Gene to obtain enough DNA to Study and/or Engineer

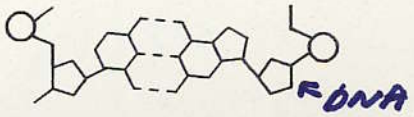
Use the cloned Gene to:

(a) Study Gene Structure & Function !! THE Major use
(b) Use to make pharmaceuticals
(c) Use in animal & plant gene therapy
(d) Use to diagnose diseases
(e) Use to correct diseases
(f) Use to Identify individuals
(g) Use to convert cells into factories

Gene Engineering has lead to new knowledge About how Living Cells function and to Applications that improve all of our Lives!

DNA CLONING ALLOWS "US" TO ISOLATE, MANIPULATE & STUDY INDIVIDUAL GENES

The average atomic mass of one base pair is 635 daltons (a dalton is 1/12 the mass of a carbon atom)



The β globin gene is approximately 2000 bp in length

So, the atomic mass of the β globin gene is:

2000 bp
×
635 daltons/bp
$= 1.27 \times 10^6$ daltons

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635 daltons/bp
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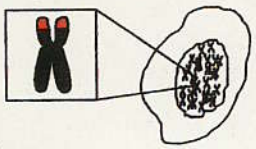
Mass of β globin gene in an adult human

There are two copies of the β globin gene per cell



There are 10^{13} cells per individual

So, the total atomic mass of β globin DNA per individual is:

1.27×10^6 daltons/gene
×
2 genes/cell
×
10^{13} cells/individual
$= 2.54 \times 10^{19}$ daltons

If there are 6.02×10^{23} daltons per gram, then:

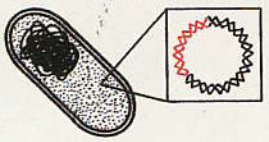
$$\frac{2.54 \times 10^{19} \text{ daltons}}{6.02 \times 10^{23} \text{ daltons/gram}}$$

$= 0.000042$ grams
$= 0.042$ mg

= .042 μg β globin DNA per human

Mass of β globin gene in a liter of *E. coli*

There are 500 copies of the β globin gene per cell



There are 5×10^{11} cells per liter

So, the total atomic mass of β globin DNA per liter is:

1.27×10^6 daltons/gene
×
500 genes/cell
×
5×10^{11} cells/liter
$= 3.175 \times 10^{20}$ daltons

If there are 6.02×10^{23} daltons per gram, then:

$$\frac{3.175 \times 10^{20} \text{ daltons}}{6.02 \times 10^{23} \text{ daltons/gram}}$$

$= 0.000527$ grams
$= 0.527$ mg

= 527 μg β globin DNA per liter!

Mass of β Globin DNA in Adult Human vs. 1-liter Culture of *E. coli* Carrying β Globin Gene on Plasmid

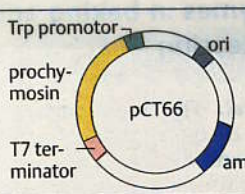
CAN PRODUCE 10X MORE OF A SINGLE HUMAN GENE IN A 1 LITER BACTERIA CULTURE THAN IN THE ENTIRE HUMAN BODY USING GENE ENGINEERING METHODS!

Even Cheesemaking is Helped By DNA Cloning & Genetic Engineering

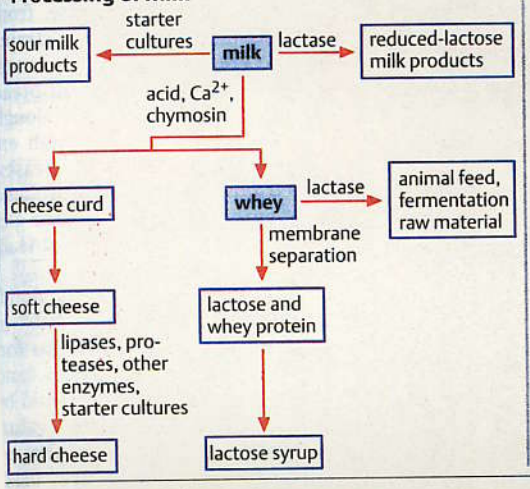
Composition of milk

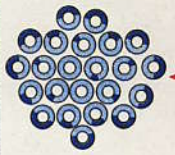
	milk (%)	whey (%)
water	~ 88	~ 94
fat	~ 3–4	~ 0.5
protein	~ 3.3	~ 1
casein	~ 2.6	–
lactose	–	~ 4.8

Plasmid for the expression of chymosin in *E. coli*

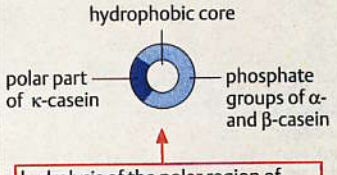


Processing of milk





oil-in-water emulsion with mixed micelles from α-, β- and κ-casein



hydrolysis of the polar region of κ-casein by chymosin (rennin) leads to destruction of micelles, resulting in coagulated milk (salted out by Ca^{2+})

Manufacture of chymosin

native	microbial	recombinant
stomachs of young animals	**preculture**	**recombinant microorganism**
cutting, activation at pH <5	high-yield mutants of *Mucor miehei* or *M. pusillus*	*Escherichia coli*
extraction	**bioreactor**	**bioreactor**
salt water, 14 d	dextrose syrup, soy meal, 30 °C, 72 h	maltodextrins, 37 °C, 36 h
purification	**purification**	**purification**
ultrafiltration standardization	separation of mycelium, re-verse osmosis, precipitation	isolation of inclusion bodies, Tritron-X100/EDTA, urea-/alkali-extract, ion-exchange chromato-graphy, acid treatment
200 U/kg stomach	5000 U/m^3 in 72 h	20000 U/m^3 in 36 h

← 100X more in a bacterial culture!

The cow chymosin gene is cloned & amplified in Bacteria Leading to an infinite amount of Chymosin to Make Cheese!

What about religious issues? Kosher laws?

IN ITS SIMPLEST FORM

GENETIC Engineering

Means.....

(1) ISOLATing A Gene FROM a CHROMOSOME of An Organism AND

(2) CLONING (REPLICATING IDENTICAL COPIES) the Gene in BACterial CELLS

(CLONING DNA/genes in cells - not cell/organism cloning

(3) TO: (1) Study A/that Gene

(2) ultimately Find out what it Does

Using BACteria As FACTORIES to PRODUCE LARGE AMOUNTS of ONE Gene For Study

BUT THE USE, BENEFITS, AND IMPLICATIONS ARE MUCH, MUCH BIGGER!

The ERA of DNA MANIPULATION MEANS.....

(1) DNA/GENES CAN BE CLONED/ISOLATED FROM ANY ORGANISM

(2) DNA Segments of Any Kinds and FROM Any ORGANISMS CAN BE COMBINED

(3) Engineered Gene/DNA Molecules CAN BE Re-Inserted into the CELLS of Any ORGANISM & Made to WORK — Clotish

(4) Whole Genomes & "ORGANISMS" CAN be Synthesized!

There ARE NO Genetic Limits — All of Biology Uses the SAME Rules!

We Have Known How to Manipulate Genes FOR 25 years!

The Implications are ENORMOUS!

THE AGE OF DNA AND GENE CLONING HAS AFFECTED SOCIETY IN MANY WAYS!

AND WE HAVE JUST BEGUN!

1. BASIC Understanding of Living Processes! What is life? What is the BASIS of Biological Diversity?
2. BASIC Understanding of Genes
3. Medicine → Diagnosis & Treatment of Diseases
4. Agriculture → Higher yielding Crops
5. Business / COMMERCE → Biotec Industry
6. The LAW / FORENSICS
   - → Patents
   - → Identification
   - → Privacy Issues
7. Anthropology → Human origins / diversity & unity of Humans
8. Evolution → Where did we come from?
9. Philosophy / Religion → How we view ourselves in relation to God & nature (e.g., synthetic genomes)

Novel Applications of Genetic Engineering / Recombinant DNA Technology

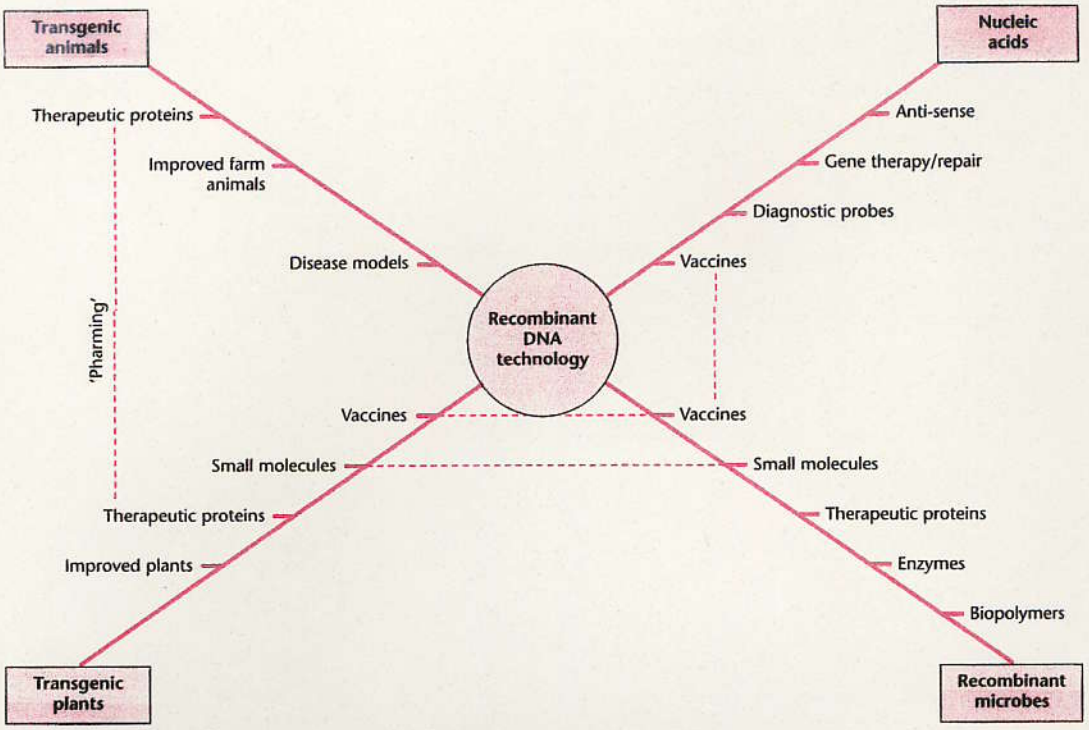


Fig. 14.1 The different ways that recombinant DNA technology has been exploited.

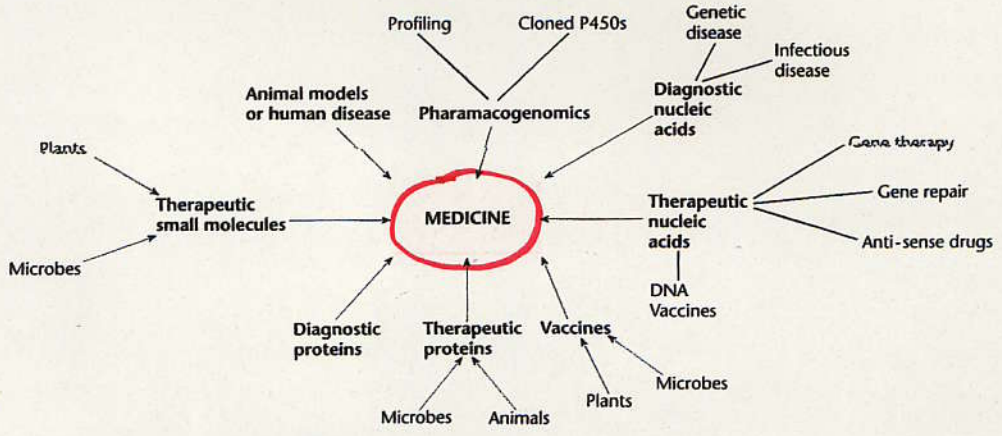


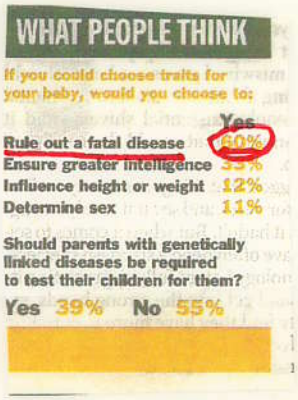
Fig. 1.1 The impact of gene manipulation on the practice of medicine.

Genetic Engineering Technology
Has Led to Many Legal + Ethical
issues

1. Patenting Living organisms, Cells, & Genes ?
2. Regulating "Experimentation" — recombinant ? DNA, stem cells, transgenic plants and animals
3. Regulating Release of genetically modified ? organisms into environment — crops, farm animals, mosquitos
4. Genetic Testing — genetic data bases, voluntary, involuntary, newborn screening, criminals, suspects
5. Genetic Discrimination — insurance, workplace, society
6. Eugenics — Genetic Enhancement —
7. Reproductive Rights — genetic enhance child, wrongful birth suits
8. Gene therapy — correcting genetic disorders
9. Gene Testing Companies — Liabilities
10. Human Cloning — Reproductive Rights — Regulate ?
11. Synthetic Genomes — What is life ?

Issues that need to be Resolved By Informed Public Choices

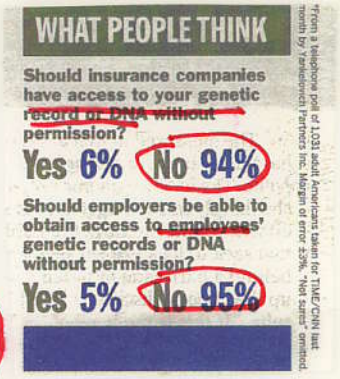
Genetic Testing



Gene Therapy

Genetic Privacy

Genetic Discrimination



Genetic Databases

Genetically Engineered Food

and need to be guided by sound science!!

HC70A Winter 2006
Opinion Survey
Professor Bob Goldberg

---

1. If you could choose traits for your baby, would you choose to.
   a. Rule out a genetic disease 74%
   b. Ensure greater intelligence 8% Choose All:10%
   b. Influence height or weight or hair/eye color 2%
   c. Select gender (male or female) 5%
2. Should parents with a genetic disease be required to test their children to determine whether they are carriers or have the disease?
   a. Yes 50%
   b. No 50%
3. If you carried a gene for an incurable fatal disease, would you have your unborn child tested for the disease?
   a. Yes 90%
   b. No 10%
4. If the test showed that the baby would have the fatal disease, would you consider ending the pregnancy through abortion?
   a. Yes 69%
   b. No 31%
5. Should a child that is born with a genetic disease be allowed to sue their parents for failing to test for the disease that is causing them so much "misery;" i.e., sue for wrongful life liability?
   a. Yes 15%
   b. No 85%
6. Should the government regulate gene therapy – that is, altering genes to cure or prevent diseases – by passing specific legislation at the state and/or federal levels?
   a. Yes 70%
   b. No 30%
7. Should the state and/or federal government regulate funding for stem cell research?
   a. Yes 59%
   b. No 41%
8. Should the state and/or federal government ban the cloning of human beings?
   a. Yes 50%
   b. No 50%
9. Should cloning of human embryos be permitted to obtain patient-specific stem cells to cure diseases such as diabetes, Parkinson's, and muscular dystrophy?
   a. Yes 82%
   b. No 18%

10. Should insurance companies have access to your genetic records or DNA fingerprints without your permission?
    a. Yes 5%
    b. No 95%
11. Should every individual who is arrested for a crime be required to have their DNA fingerprinted and deposited in a National Criminal DNA database?
    a. Yes 64%
    b. No 36%
12. Should the government regulate the engineering of animals and plants for use in agriculture and/or medicine?
    a. Yes 78%
    b. No 22%
13. Should employers be able to obtain access to employees' genetic records and/or DNA without permission?
    a. Yes 2%
    b. No 98%
14. Should employers be allowed to require their employees to undergo DNA testing?
    a. Yes 30%
    b. No 70%
15. Should the police be allowed to collect DNA information gathered from suspected criminals as they currently do with fingerprints?
    a. Yes 66%
    b. No 35%
16. Is it a good or bad idea for the FBI to create a DNA database with information gathered from suspected criminals and crime scenes throughout the country?
    a. Good Idea 78%
    b. Bad Idea 22%
17. If parents choose to give birth to a child with a genetic disease, should the parents or society pay for the health care for their child?
    a. Parents 73%
    b. Society 27%
18. Over the past 30 years how many genetic engineering "disasters" have occurred?
    a. 100 24%
    b. 0 41%
    c. 10 34%
19. If you could undergo gene therapy and change any of your genetic traits (e.g., eye color, hair color, skin color, presence/absence of body hair, etc.) without any adverse affects, would you do it?
    a. Yes 46%
    b. No 54%
20. If food were labeled as genetically engineered, would you buy it for yourself or your family?
    a. Yes 75%
    b. No 25%

21. Are the building blocks of genes made of DNA, RNA, or proteins?
    a. DNA 55%
    b. RNA 0%
    c. Proteins 45%
22. How many years ago was DNA discovered?
    a. 50 68%
    b. 100 28%
    c. 10 4%
23. Should genetically enhanced food be labeled?
    a. Yes 90%
    b. No 10%
24. Is organically grown food more nutritious than food grown using conventional agriculture?
    a. Yes 31%
    b. No 69%
25. How many genes have you eaten within the last 24 hours?
    a. 0 8%
    b. 1,000 8%
    c. 10,000,000 or more 84%
26. Have you tasted any foods that were produced by genetic engineering within the last week?
    a. Yes 84%
    b. No 16%
27. What year are you in school?
    a. First 34%
    b. Second 24%
    c. Third 27%
    d. Fourth 15%
    e. Fifth 0%
28. Are you a science or a non-science major?
    a. Science 34%
    b. Non-Science 66%
29. Have you ever had an exciting, dynamic science class that made you think that "science is neat, fascinating, and important for society?"
    a. Yes 79%
    b. No 21%
30. How many hours do you watch of television a week?
    a. 0 hrs. 17%
    b. 1-3 hrs. 58%
    c. 4-7 hrs. 23%
    d. 7-10 hrs. 2%
    e. 10+ hrs.
31. How many hours to you spend listening to, watching, or reading the news a week?
    a. 0 hrs. 10%
    b. 1-5 hrs. 70%
    c. 5-15 hrs. 20%

Issues Raised By Genetic Engineering Technology - Like all new technologies society & people are affected

Science-philosophy arguments concerning genetic engineering

categorical argument

Some human activities such as genetic engineering are fundamentally reprehensible. Developing this technology, "man plays God" and claims competencies beyond his capacities, degrading nature to the course of his technical manipulations.

pragmatic argument

The key objective of genetic engineering is to reduce the suffering of diseased individuals. The procedures which are applied must, however, be safe, and the patient must be able to decide if he or she wishes to apply genetic diagnosis or therapy.

social policy argument

The social effects of genetic engineering cannot be estimated. In genetic therapy, wrong priorities are chosen, better prophylaxis would be more desirable. We start down a slippery slope that will lead us involuntarily to inhumane practices towards the next generations ("eugenics bottom up")

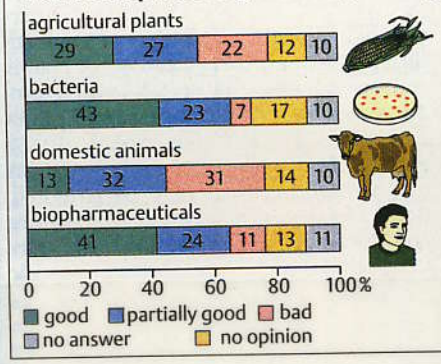
Problematic areas of genetic research

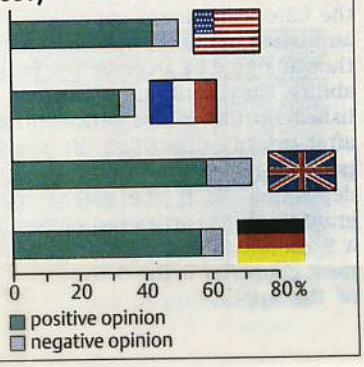
	topic	state of the art	regulation or trend
(1)	cloning of humans	cloning of animals possible	not permitted
(2)	use of embryonic stem cells	growing expertise	permitted, but regulated
(3)	artificial insemination, sexing, surrogate mothers	state of the art in animals	artificial insemination permitted, sexing and surrogate mothers forbidden
	prenatal diagnosis	cytological methods established, DNA-based diagnosis partially established	permitted, abortion permitted after medical indication
(4)	identifying genetic risks by genetic screening	possible for some monogenic diseases	under debate if one gene defect is predictive and if diagnosis is acceptable for incurable diseases; strict data protection required towards employers, insurance companies
(5)	knockout animals for drug research	widely established	generally accepted, but hotly debated by animal protection groups
(6)	food and biopharmaceutical production using transgenic animals or plants	many techniques established	debated in view of consumer protection, animal protection, ecological consequences
(7)	transgenic microorganisms or cell lines for production of biopharmaceuticals	established	widely accepted

VARIES

VARIES

Public acceptance of genetic engineering (survey 2001)





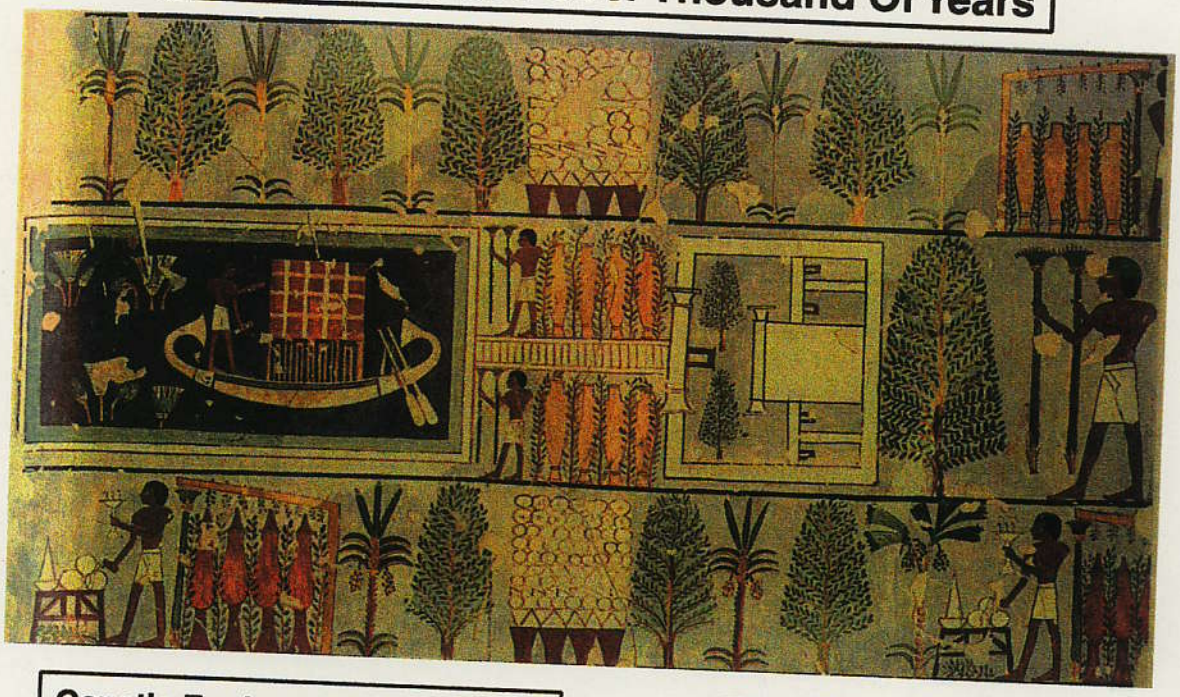
Why it is IMPORTANT TO UNDERSTAND the SCIENCE BEHIND Genetic Engineering!!!!!

That's what this CLASS is About!

GENETIC MANIPULATION / ENGINEERING

ANYTHING NEW?

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



Genetic Engineering is Not New

Crops of Egypt 400 B.C.

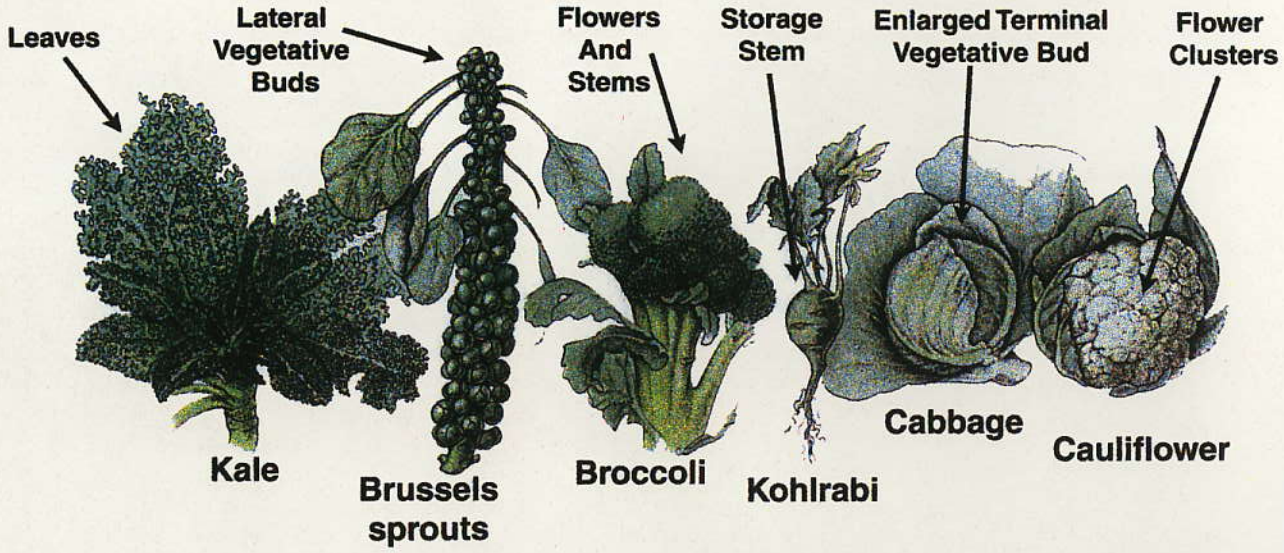
PLANT Breeding / Classical Genetic Engineering demonstration

(1) What is the origin of Genetic Engineering?

(2) Who were the first individuals to Manipulate Genes & organisms?

(3) What plants & Animals were Engineered & How?

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



How Are These Plants Related?

Breeding For Parts of Plants!
What is Being Manipulated?

PLANTS

What did the EARLY "Genetic Engineers" select FOR to generate these Vegetables?

Genes? How do we know Genes Exist?

Gene VARIANTS? Mutations?

ARE Genes Controlling these TRAITS?

Do we <u>NOW</u> know what they are?

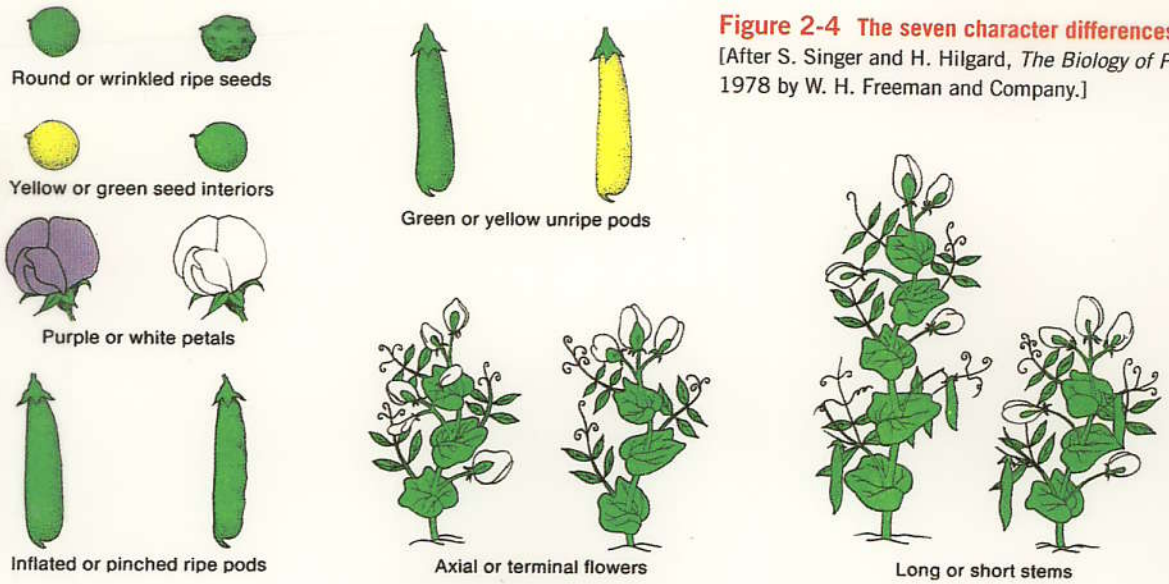


Figure 2-4 The seven character differences studied by Mendel. [After S. Singer and H. Hilgard, *The Biology of People*. Copyright 1978 by W. H. Freeman and Company.]

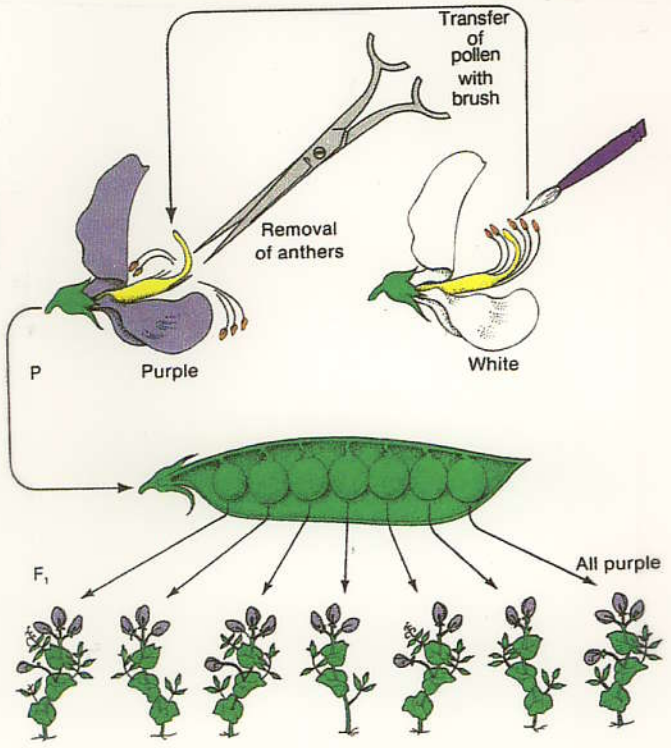
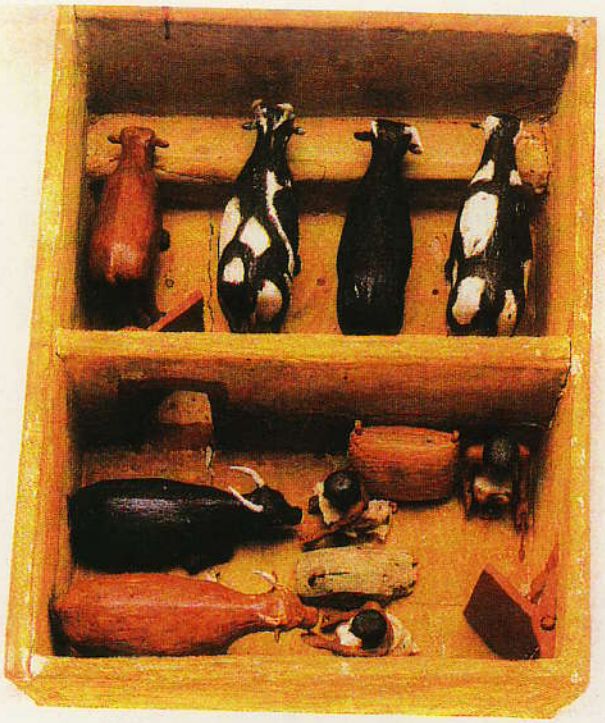


Figure 2-5 Mendel's cross of purple-flowered ♀ × white-flowered ♂ yielded all purple-flowered progeny.

FARM ANIMALS WERE ALSO "ENGINEERED" BY BREEDING WILD RELATIVES



Notice Variability in traits –

Figure 11-2 The ancient Egyptians were successful cattle breeders. This miniature stable, which dates from about 2000 BC, shows longhorn cattle. Other cattle breeds had short horns or no horns. *(Metropolitan Museum of Art, Rogers Fund and Edward S. Harkness Gift, 1920)*

CATTLE BREEDING in Egypt 4000 years Ago!

Manipulating Existing Genetic Variability

Variability Brought About By Chance Mutations!

Biologists chase down pooches' genetic and social past

A Shaggy Dog History

Dog father. Dogs might have evolved from an ancestor of this Chinese wolf.

Genetic variability

Traced using DNA testing!

CAN only arise by selecting for existing variability

15,000 years ago in Europe Asia

Genetic VARIABILITY

Common pedigree. From Chihuahuas (*left*) to Great Danes, dogs of all shapes and sizes share common ancestors.

What are the genetic differences & how did they arise?

Science V. 298 (2002)

Vol 438|8 December 2005 nature

NEWS & VIEWS

C. COLLINS/CORBIS

GENOMICS

The dog has its day

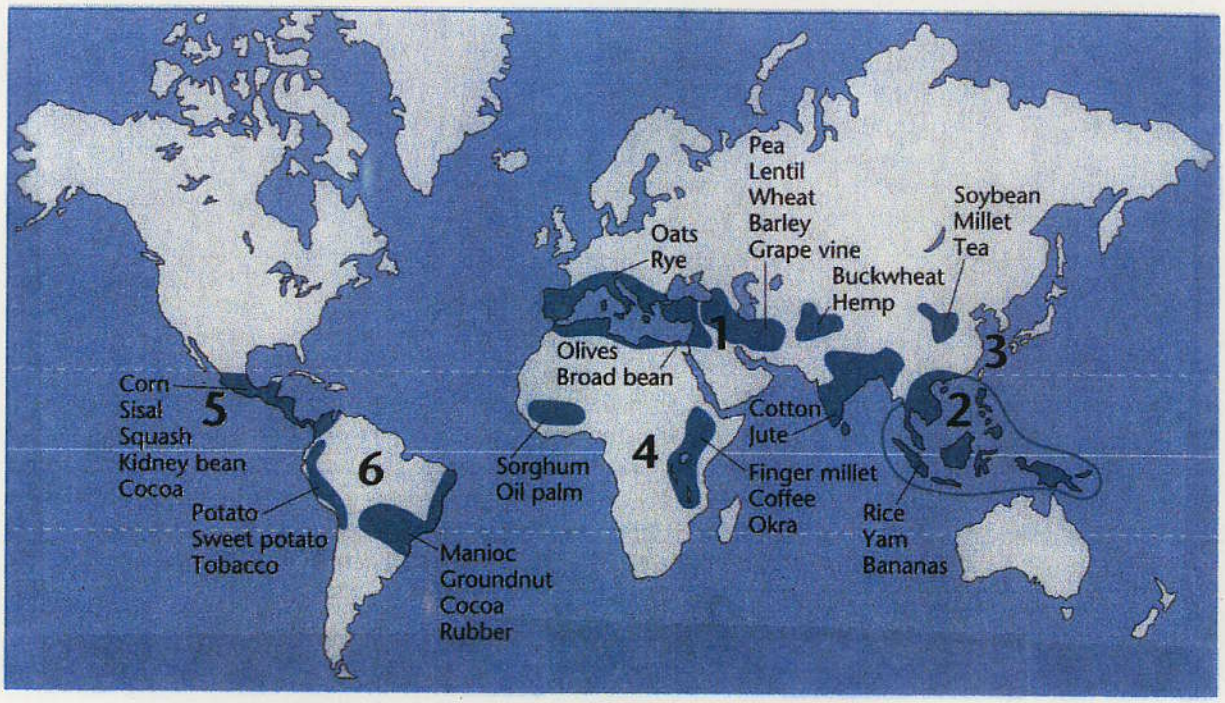
Hans Ellegren

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.

56a

MAJOR CROPS WERE "ENGINEERED" FROM NON-PRODUCTIVE WILD RELATIVES 10,000 years Ago!

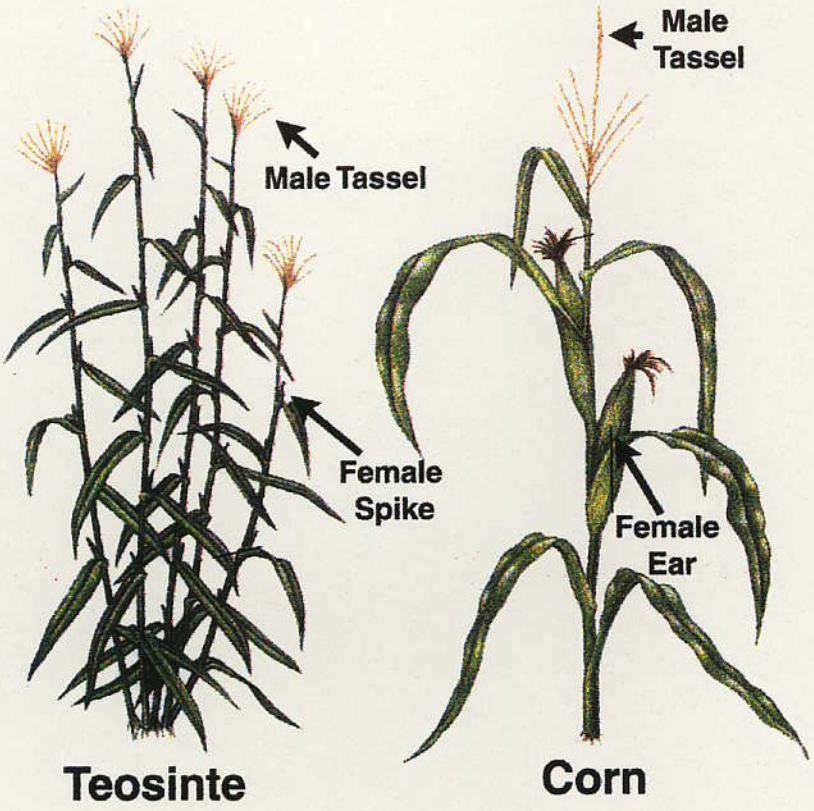
Regions Where Major Crops Were Established



Breeding involves gene Manipulation!

using Existing Gene Variability!

Corn And Its Ancestor Teosinte

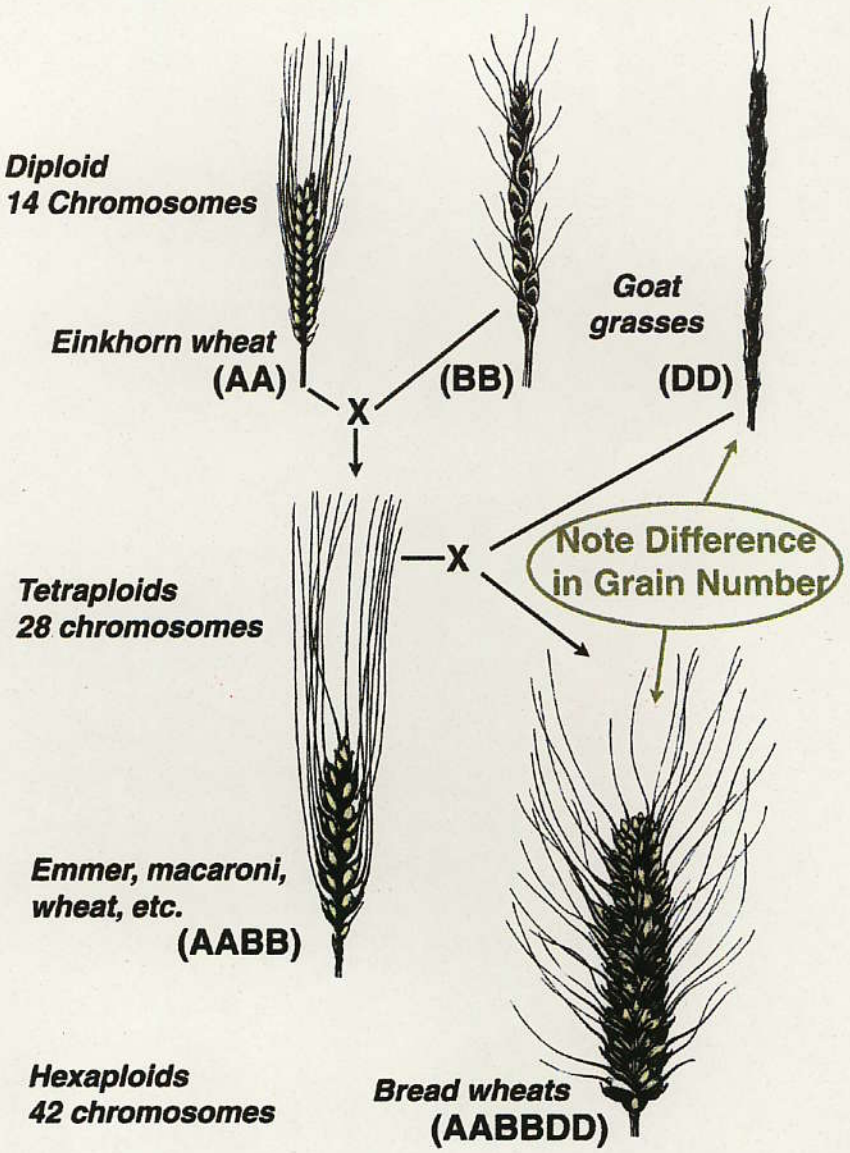


Note Differences in Plant Architecture Yet They Are The Same Species

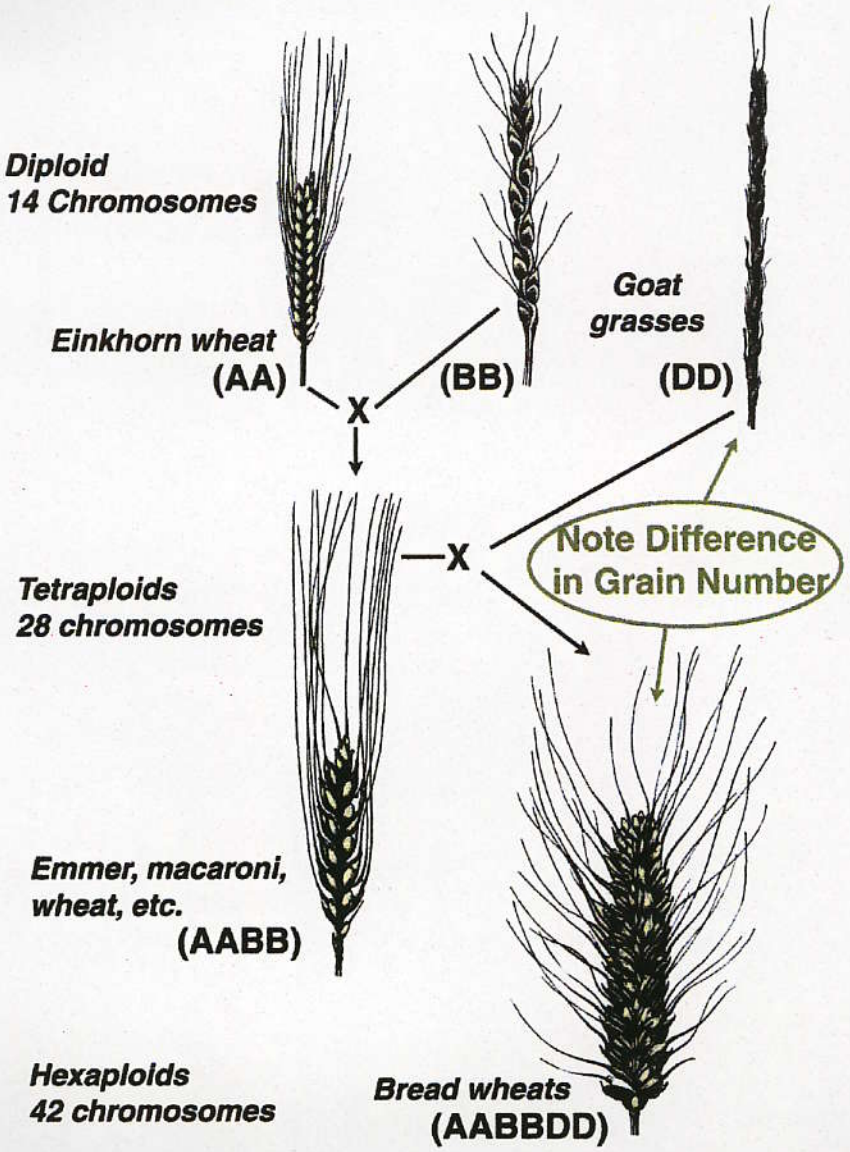
ONLY 5 genes cause these PLANTS to be different!

NOW KNOW what they are!

Domestication of Wheat



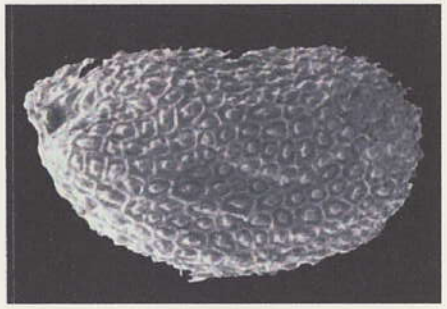
Domestication of Wheat



Domesticating Crops Caused Increased Seed Size

10,000 Years Ago….

Genetic Engineering for Big Seeds



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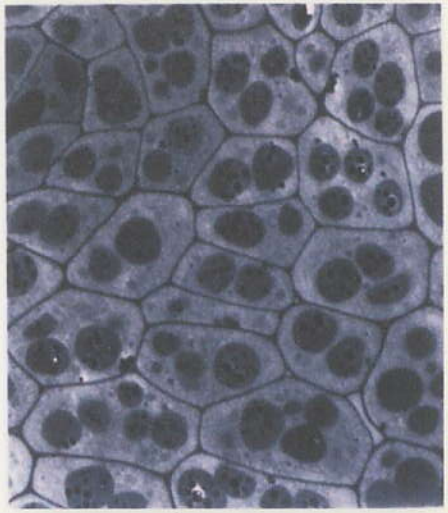
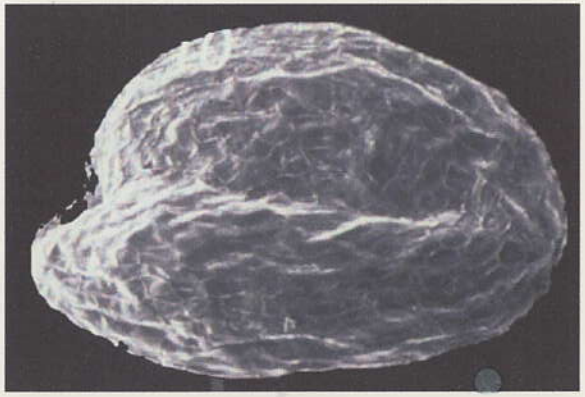
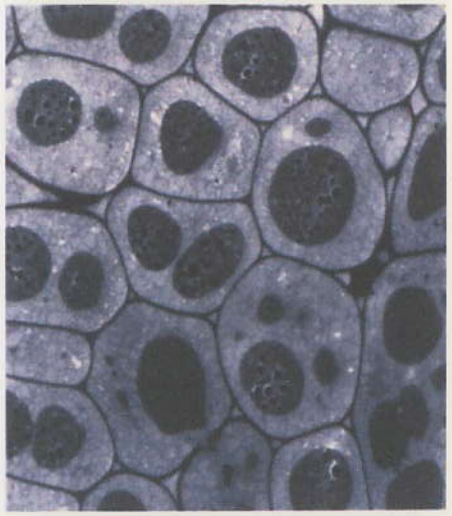


....2006



ap2-10



J. Okamuro
D. Jofuku
UC Santa Cruz

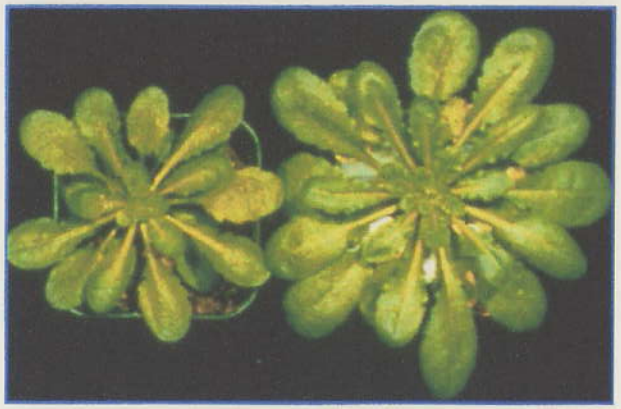
Domesticating Crops Caused Increase Seed Head Size

Foxtail Millet

Wild **Domesticated**

10,000 Years Ago….

Genetic Engineering for Organ Size



35S:ANT

....2006!!

Bob Fischer
UC Berkeley

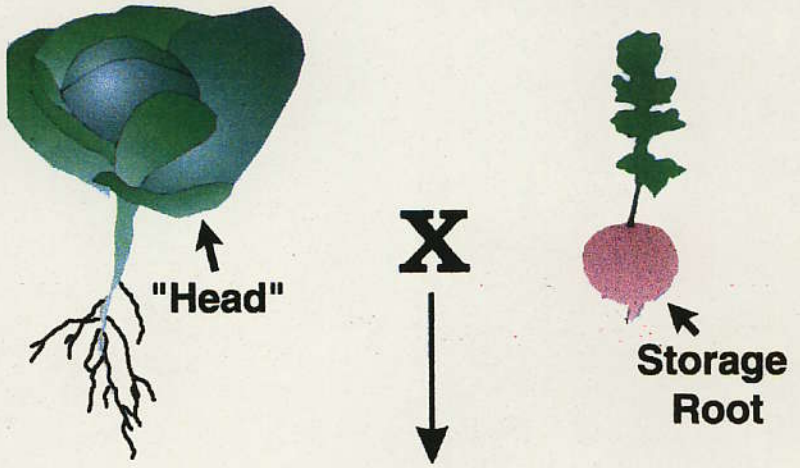
Berkeley

Breeding A "New organism"

The problems with doing it the "Old Fashioned" way

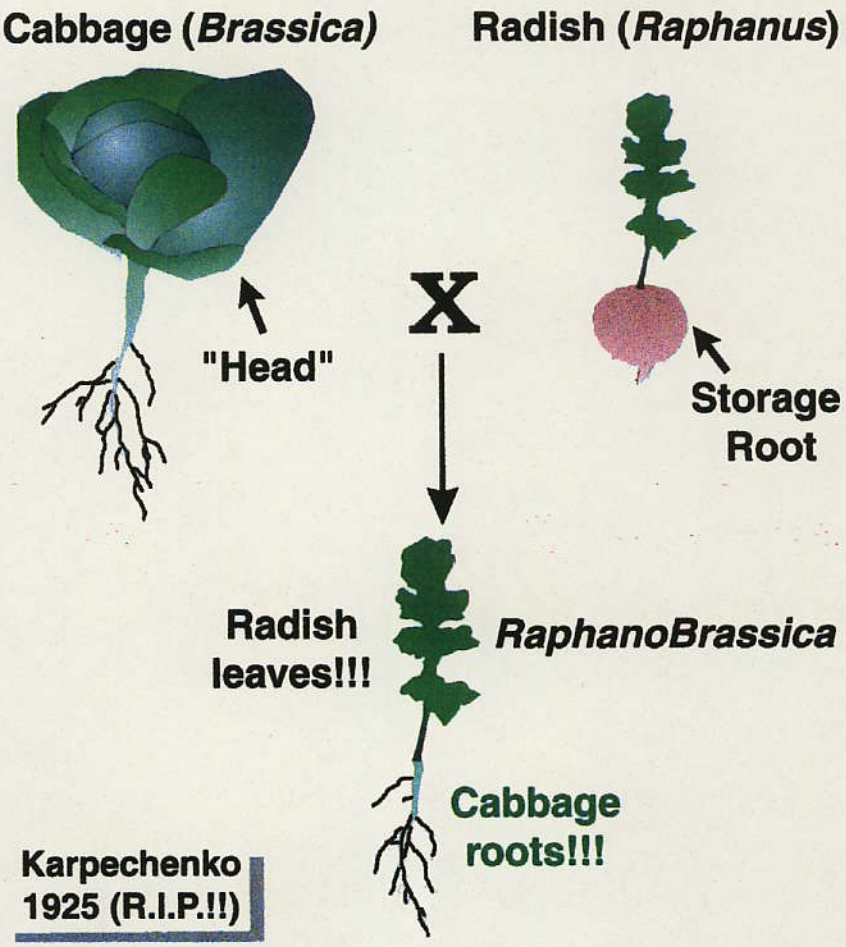
Engineering A Novel Crop By "Wide" Breeding

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



Karpechenko 1925

Engineering A Novel Crop By "Wide" Breeding



Result shows the unpredictability of classical Breeding Approaches

Breeding Uses Natural Variability of Genes As Raw Material

Tomato Genetic Diversity

How does this VARiability ALLow us to infer Genes Exist & Traits Inherited?

Diversity generated by Mutations in a gene that change its Chemical Sequence & Slightly ALters its function

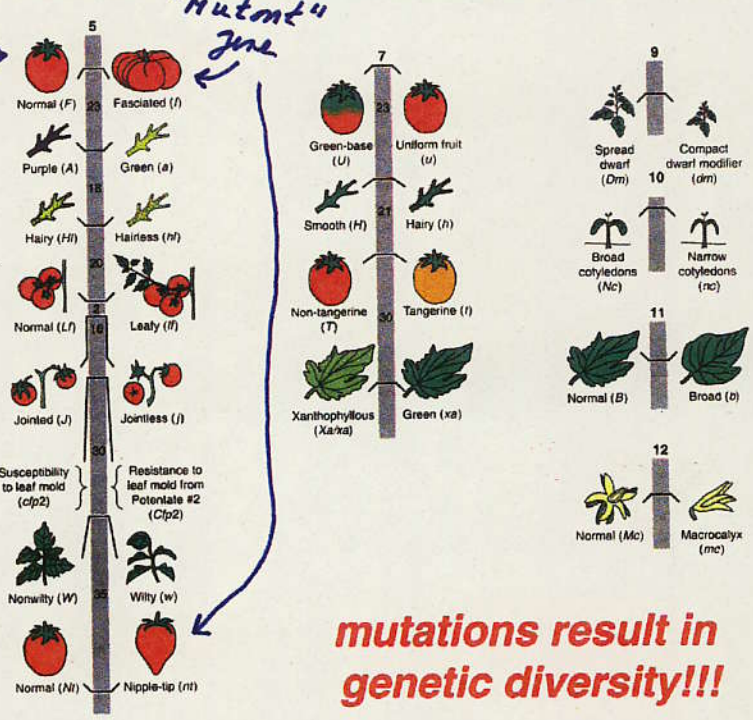
Alleles → Genetic Diversity

Alternative Forms of the Same Gene Lead to Genetic Diversity

"normal" gene

"Mutant" gene

alleles

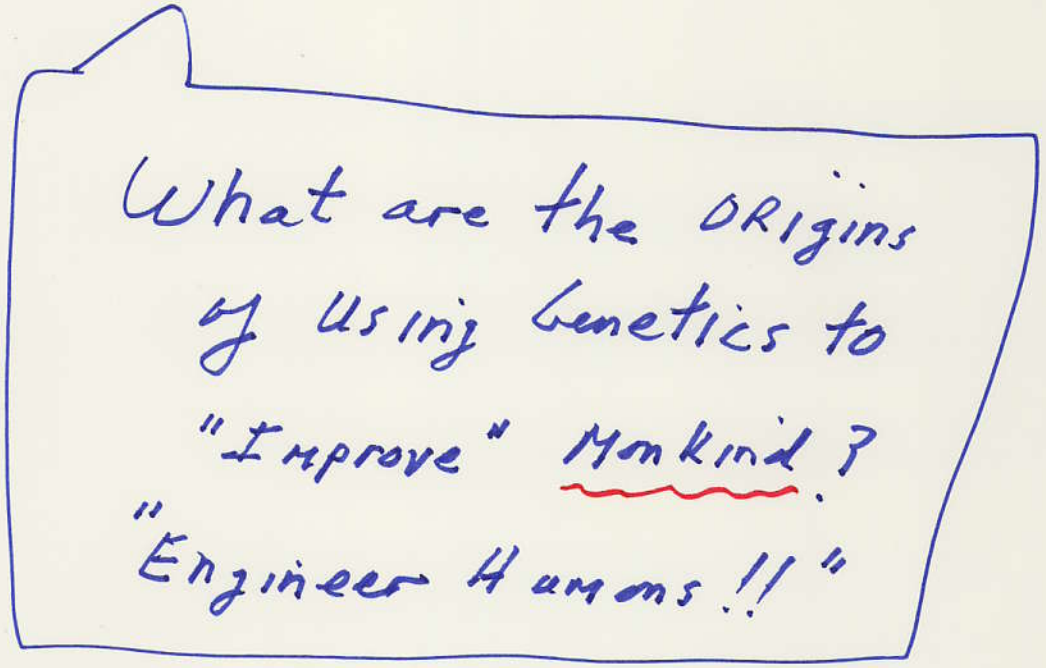


12 Chromosomes
Different Genes

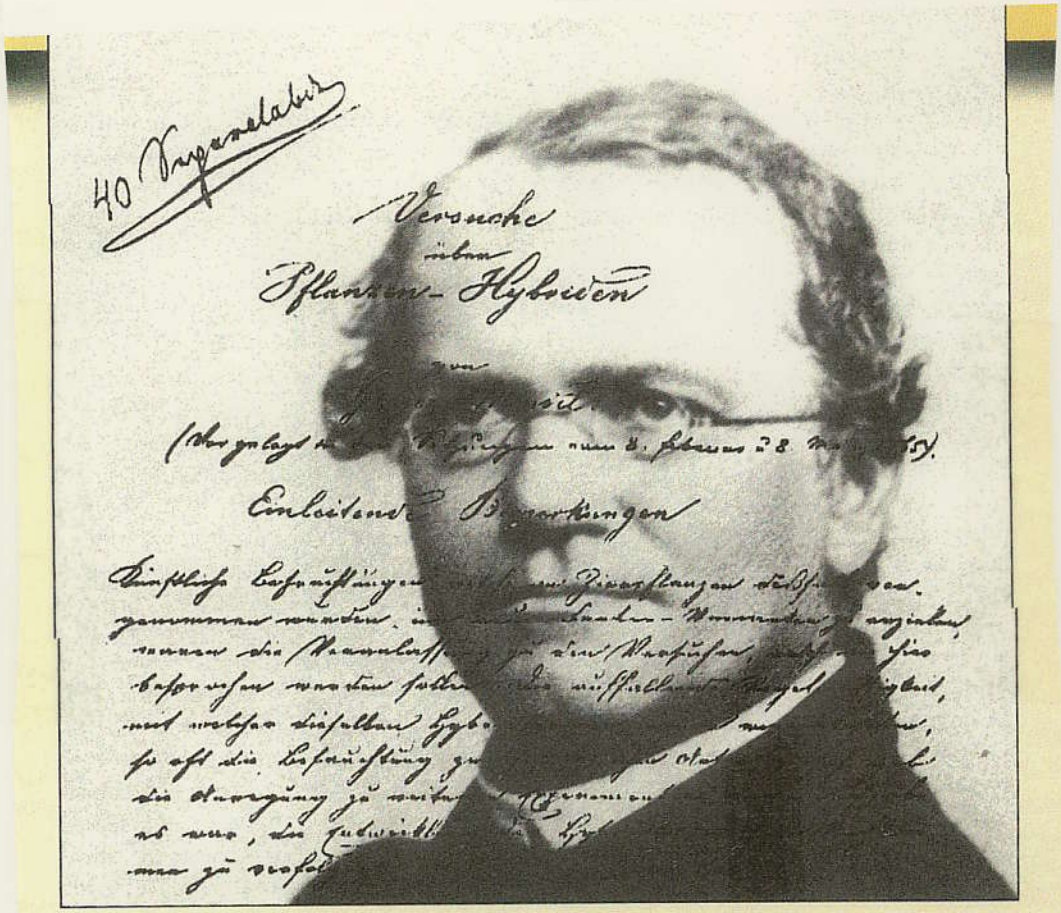
mutations result in genetic diversity!!!

What is the Relationship Between the Mutant & Normal Gene?

This Also the BASIS of Genetic Variability in all ORGANISMS - INCLUDING HUMANS & the "raw Material" FOR DNA testing!


What are the ORIgins
of Using Genetics to
"Improve" Mankind?
"Engineer Humans!!"

Genetics was Re-discovered only 100 years Ago!



Front page of Mendel's paper superimposed on a portrait of Mendel.

Mendelism: The Basic Principles of Inheritance

1866 - Re-discovered in 1902 by William Bateson who wrote Book on Mendelism - Principles of Dominance, Segregation, & Independent Assortment in 1909. Independently discovered by Correns, DeVries, & Tschermak in 1900.

1909 - Johaussen first used the term gene

INBORN ERRORS OF METABOLISM

TABLE 9-3 Common Inherited Human Diseases

Disease	Molecular and Cellular Defect	Incidence
AUTOSOMAL RECESSIVE		
Sickle-cell anemia	Abnormal hemoglobin causes deformation of red blood cells, which can become lodged in capillaries; also confers resistance to malaria.	1/625 of sub-Saharan African origin
Cystic fibrosis	Defective chloride channel (CFTR) in epithelial cells leads to excessive mucus in lungs.	1/2500 of European origin
Phenylketonuria (PKU)	Defective enzyme in phenylalanine metabolism (tyrosine hydroxylase) results in excess phenylalanine, leading to mental retardation, unless restricted by diet.	1/10,000 of European origin
Tay-Sachs disease	Defective hexosaminidase enzyme leads to accumulation of excess sphingolipids in the lysosomes of neurons, impairing neural development.	1/1000 Eastern Europe Jews
AUTOSOMAL DOMINANT		
Huntington's disease	Defective neural protein (huntingtin) may assemble into aggregates causing damage to neural tissue.	1/10,000 of European origin
Hypercholesterolemia	Defective LDL receptor leads to excessive cholesterol in blood and early heart attacks.	1/122 French Canadian
X-LINKED RECESSIVE		
Duchenne muscular dystrophy (DMD)	Defective cytoskeletal protein dystrophin leads to impaired muscle function.	1/3500 males
Hemophilia A	Defective blood clotting factor VIII leads to uncontrolled bleeding.	1–2/10,000 males

Archibald GARROD – 1902
Alkaptonuria

GARROD — SOME HUMAN DISEASES CAN BE DUE TO INHERITED DEFECTS IN METABOLISM

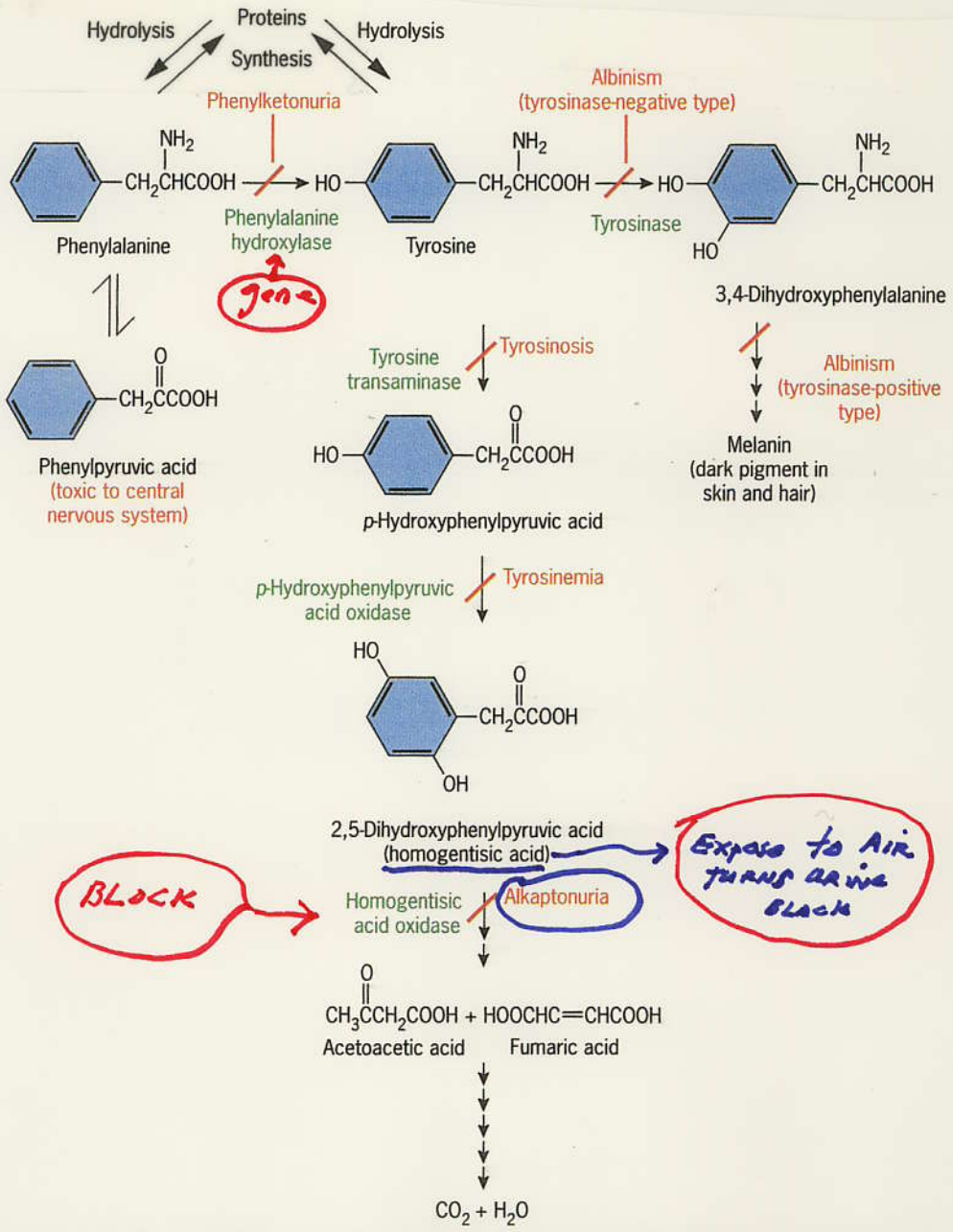


Figure 14.10 Inherited human disorders with defects in phenylalanine-tyrosine metabolism: phenylketonuria, tyrosinosis, tyrosinemia, alkaptonuria, and albinism. All five disorders are caused by autosomal recessive mutations. The mutations, which result in the synthesis of inactive enzymes, block phenylalanine-tyrosine metabolism at the steps indicated.

REVOLUTIONARY AT TIME — GENETICS AFFECTS HUMAN DISEASE!

And Attempts Have Been Made to "Select" out "Bad" Genes in Man.....

Eugenics → Directed Genetic Change in Man

FRANCIS GALTON ~1902

1. Positive - Add "good" genes
2. Negative - Remove "bad" genes (Can this ever be done completely?)

Question

By: Preventing individuals from having children (negative)

OR

Encouraging individuals with the "CORRECT" traits to have children (positive .... or is it??) OR using Gene therapy/Enhancement in the future!??

Question

Don't we all do this to a certain extent?

ARE there "GOOD" & "BAD" Genes?

BUCK VS. BELL

better "left behind in the cast-off junk of ignorant efforts, with which the past is filled."[41]

By the outbreak of the First World War, sterilization laws were in such dispute as to have been de facto suspended in their operation in a number of states. The courts had also declared unconstitutional not only the stringent Iowa statute but less sweeping measures in six other states. Advocates of eugenic sterilization, frustrated at the legal impasse, wanted to take the issue to the Supreme Court. In Virginia, eugenicists helped draw up a sterilization statute, passed by the legislature in March 1924, that was designed to meet the constitutional objections. The opportunity to press a test case arose that June, when a seventeen-year-old girl named Carrie Buck, who seemed definable as a "moral imbecile," was committed to the Virginia Colony for Epileptics and Feebleminded, in Lynchburg.[42]

Carrie's mother, Emma, had lived at the Colony since 1920 and was also certified to be feebleminded. Carrie herself had conceived a child out of wedlock, and shortly before her commitment, she gave birth to a daughter, Vivian. Carrie was given the Stanford revision of the Binet-Simon I.Q. test and was found to have a mental age of nine years, well within Henry Goddard's definition of "moron." Carrie's mother was found to have a mental age of slightly under eight years. Thus, according to these results, there was mental deficiency in two successive generations. If Vivian could be shown to be feebleminded too, Carrie would be a perfect subject for a test of the Virginia sterilization statute. In September 1924, the Colony's board of directors ordered Carrie Buck sterilized, and a court-appointed guardian initiated legal proceedings by appealing the order in a suit on [illegible]e's behalf against the superintendent of the Colony, Albert S. Priddy.[43]

In preparing their case, Virginia officials consulted Harry Laughlin at the Eugenics Record Office. Laughlin examined the pedigrees of Carrie, her mother, and her daughter, and information about them given him by Colony officials, and—without ever having seen them in person—provided an expert deposition that Carrie's alleged feeblemindedness was primarily hereditary. Carrie and her forebears, Laughlin submitted, "belong to the shiftless, ignorant, and worthless class of anti-social whites of the South." At the time of Laughlin's deposition, however, there was no evidence at all that Vivian was mentally deficient. To clarify the matter, Caroline E. Wilhelm, a Red Cross worker who had placed Vivian in a foster home, was prevailed upon to examine her there. At the initial hearing, in the Circuit Court of Amherst County, she testified that there was "a look" about Vivian (who at the time of the visit was seven months old) which was "not quite normal." Evidence also came from Arthur Estabrook of the Eugenics Record Office, who had subjected Vivian to a mental test for an infant and concluded that she was below average for a child her age. In the court proceeding, Estabrook testified that the feeblemindedness in the Buck line conformed to the Mendelian laws of inheritance, and the judge upheld the sterilization order.[44]

The case—now known as *Buck* v. *Bell*, because Priddy had in the meantime died and been replaced as the defendant by the Colony's new superintendent, John H. Bell—was carried to the Virginia Supreme Court of Appeals in 1925, and the sterilization order was again upheld. In April 1927 it was argued before the United States Supreme Court. Carrie's defense counsel, I. P. Whitehead, a onetime member of the board of directors of the Colony, attacked the sterilization statute, warning that under this type of law a "reign of doctors will be inaugurated and in the name of science new classes will be added, even races may be brought within the scope of such a regulation and the worst forms of tyranny practiced." Nevertheless, the Court was persuaded not only that Carrie Buck and her mother were "feebleminded" but also—because Vivian was, too (or so all the experts said)—that the feeblemindedness was heritable. The Court, whose membership ranged in political conviction from William Howard Taft to Louis D. Brandeis, upheld the Virginia statute by a vote of eight to one. The sole dissenter was Justice Pierce Butler, a conservative, and he kept his minority opinion to himself. The decision declared that sterilization on eugenic grounds was within the police power of the state, that it provided due process of law, and that it did not constitute cruel or unusual punishment.[45]

The Court's opinion was written by Justice Oliver Wendell Holmes, an enthusiast of science as a guide to social action, who managed to find a link between eugenics and patriotism: "We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices . . . in order to prevent our being swamped with incompetence. . . . The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes." With deliberate punch Holmes asserted: "Three generations of imbeciles are enough."[46]

Eugenicists naturally rejoiced at *Buck* v. *Bell*. For some years prior to the decision, the American Eugenics Society had promoted what it thought might be a constitutional revision of the faulty sterilization statutes. Apart from procedural and technical changes, the revisions centered on making the laws eugenic rather than punitive in intent. After *Buck* v. *Bell*, what was constitutional was clear. By the end of the nineteen-twenties, sterilization laws were on the books of twenty-four states, with the South no longer a regional exception. (Though now severely restricted by federal regulation, they are still on the books of twenty-two states today.) The laws were not uniformly enforced, but Carrie Buck was sterilized soon after the Court's

decision, and officials at the Virginia Colony subjected other inmates to the procedure—a total of about a thousand in the next ten years. By the mid-thirties, some twenty thousand sterilizations had been legally performed in the United States.[47]

Buck v. *Bell* generally stimulated either favorable, cautious, or—most commonly—no editorial comment. Few if any newspapers took notice of the impact of the decision on civil liberties in the United States. The I.Q. tests used in the Buck case have long since been discredited as indicators purely of general intelligence. With regard to the allegedly hereditary nature of mental defect in the Buck line, it is of interest that Carrie's daughter Vivian went through the second grade before she died of an intestinal disorder in 1932. Her teachers reportedly considered her very bright.[48]

Buck vs. Bell

BUCK v. BELL

274 U.S. 200 (1927).

MR. JUSTICE HOLMES delivered the opinion of the Court.

This is a writ of error to review a judgment of the Supreme Court of Appeals of the state of Virginia, affirming a judgment of the Circuit Court of Amherst County, by which the defendant in error, the superintendent of the State Colony for Epileptics and Feeble Minded, was ordered to perform the operation of salpingectomy upon Carrie Buck, the plaintiff in error, for the purpose of making her sterile. The case comes here upon the contention that the statute authorizing the judgment is void under the Fourteenth Amendment as denying to the plaintiff in error due process of law and the equal protection of the laws.

Carrie Buck is a feeble minded white woman who was committed to the State Colony above mentioned in due form. She is the daughter of a feeble minded mother in the same institution, and the mother of an illegitimate feeble minded child. She was eighteen years old at the time of the trial of her case in the Circuit Court, in the latter part of 1924. An Act of Virginia, approved March 20, 1924, recites that the health of the patient and the welfare of society may be promoted in certain cases by the sterilization of mental defectives, under careful safeguard, & c.; that the sterilization may be effected in males by vasectomy and in females by salpingectomy, without serious pain or substantial danger to life; that the Commonwealth is supporting in various institutions many defective persons who if now discharged would become a menace but if incapable of procreating might be discharged with safety and become self-supporting with benefit to themselves and to society; and that experience has shown that heredity plays an important part in the transmission of insanity, imbecility, & c. The statute then enacts that whenever the superintendent of certain institutions including the above named State Colony shall be of opinion that it is for the best interests of the patients and of society that an inmate under his care should be sexually sterilized, he may have the operation performed upon any patient afflicted with hereditary forms of insanity, imbecility, & c., on complying with the very careful provisions by which the act protects the patients from possible abuse.

The superintendent first presents a petition to the special board of directors of his hospital or colony, stating the facts and the grounds for his opinion, verified by affidavit. Notice of the petition and of the time and place of the hearing in the institution is to be served upon the inmate, and also upon his guardian, and if there is no guardian the superintendent is to apply to the Circuit Court of the County to appoint one. If the inmate is a minor notice also is to be given to his parents if any with a copy of the petition. The board is to see to it that the inmate may attend the hearings if desired by him or his guardian. The evidence is all to be reduced to writing, and after the board has made its order for or against the operation, the superintendent, or the inmate, or his guardian, may appeal to the Circuit Court of the County. The Circuit Court may consider the record of the board and the evidence before it and such other admissible evidence as may be offered, and may affirm, revise, or reverse the order of the board and enter such order as it deems just. Finally any party may apply to the Supreme Court of Appeals, which, if it grants the appeal, is to hear the case upon the record of the trial in the Circuit Court and may enter such order as it thinks the

BUCK VS. BELL CONTINUED

Circuit Court should have entered. There can be no doubt that so far as procedure is concerned the rights of the patient are most carefully considered, and as every step in this case was taken in scrupulous compliance with the statute and after months of observation, there is no doubt that in that respect the plaintiff in error has had due process of law.

The attack is not upon the procedure but upon the substantive law. It seems to be contended that in no circumstances could such an order be justified. It certainly is contended that the order cannot be justified upon the existing grounds. The judgment finds the facts that have been recited and that Carrie Buck "is the probable potential parent of socially inadequate offspring, likewise afflicted, that she may be sexually sterilized without detriment to her general health and that her welfare and that of society will be promoted by her sterilization," and thereupon makes the order. In view of the general declarations of the legislature and the specific findings of the Court, obviously we cannot say as matter of law that the grounds do not exist, and if they exist they justify the result. We have seen more than once that the public welfare may call upon the best citizens for their lives. It would be strange if it could not call upon those who already sap the strength of the State for these lesser sacrifices, often not felt to be such by those concerned, in order to prevent our being swamped with incompetence. It is better for all the world, if instead of waiting to execute degenerate offspring for crime, or to let them starve for their imbecility, society can prevent those who are manifestly unfit from continuing their kind. The principle that sustains compulsory vaccination is broad enough to cover cutting the Fallopian tubes. Jacobson v. Massachusetts, 197 U.S. 11. Three generations of imbeciles are enough.

"TO PROMOTE THE PUBLIC WELFARE"

Preamble to Constitution

But, it is said, however it might be if this reasoning were applied generally, it fails when it is confined to the small number who are in the institutions named and is not applied to the multitudes outside. It is the usual last resort of constitutional arguments to point out shortcomings of this sort. But the answer is that the law does all that is needed when it does all that it can, indicates a policy, applies it to all within the lines, and seeks to bring within the lines all similarly situated so far and so fast as its means allow. Of course so far as the operations enable those who otherwise must be kept confined to be returned to the world, and thus open the asylum to others, the equality aimed at will be more nearly reached.

Judgment affirmed.

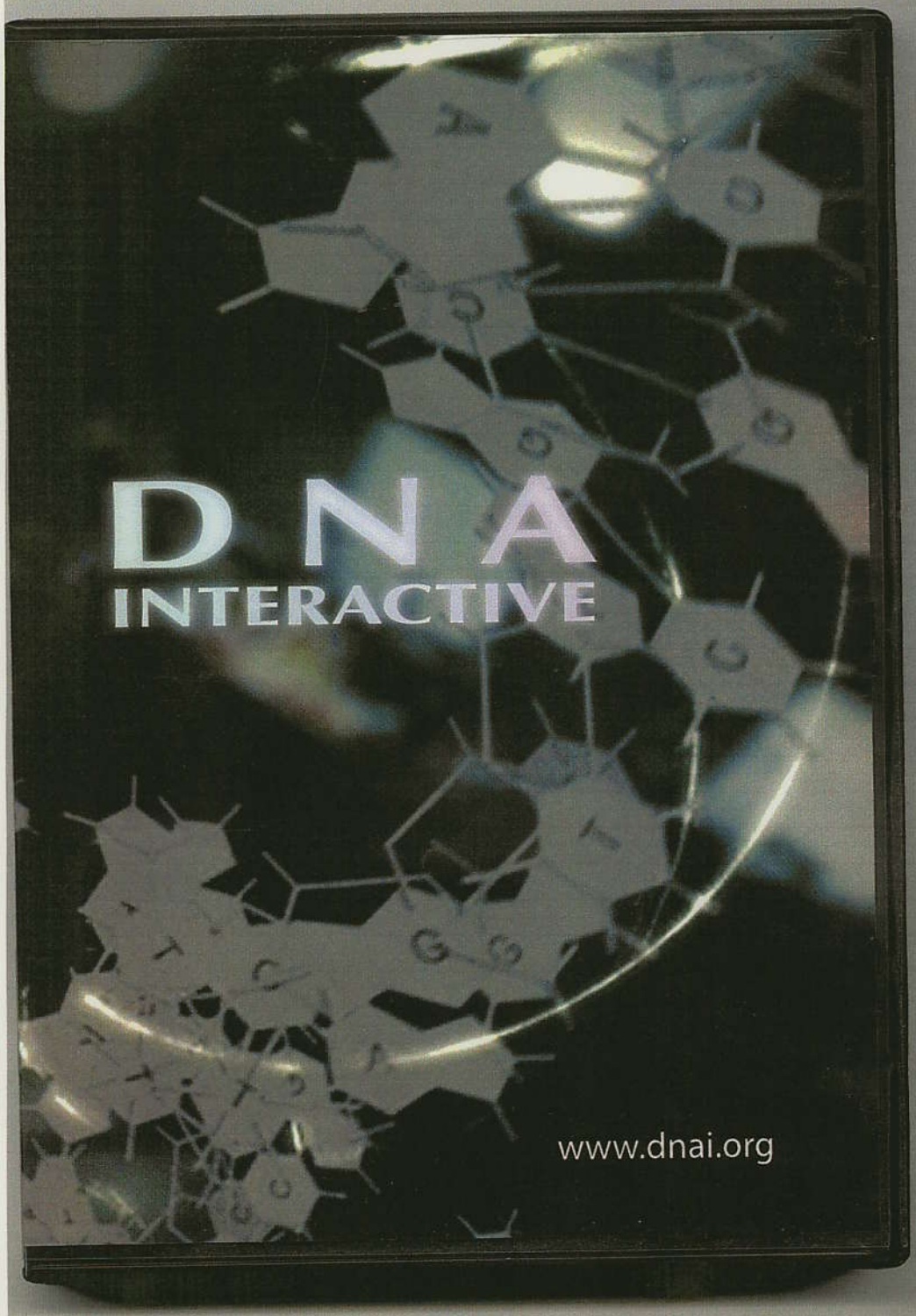
MR. JUSTICE BUTLER dissents.

What about 14th Amendment?
"Life, Liberty, & Happiness without due Process of Law"

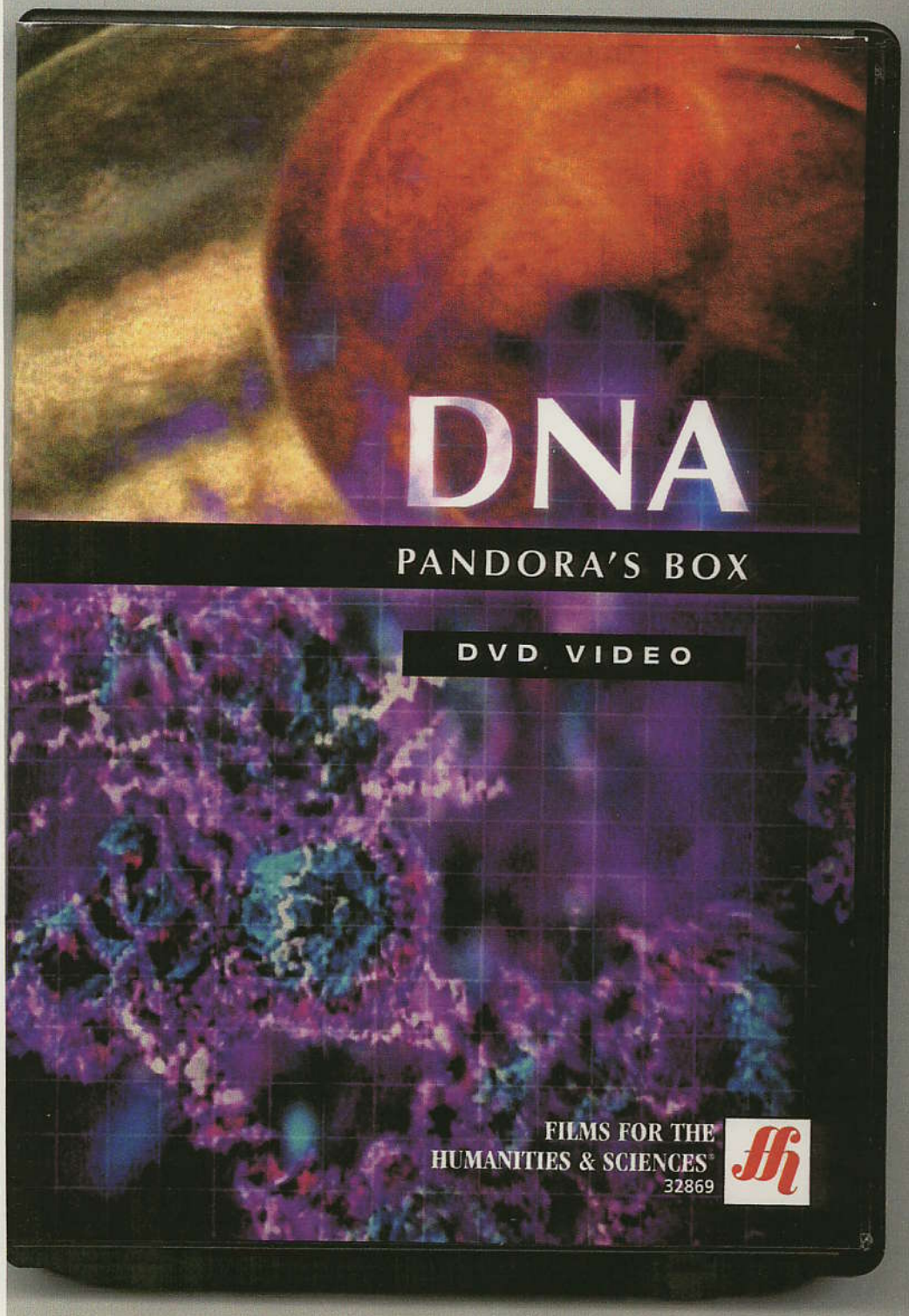
Buck vs. Bell

Themes → Ethics + Implications → Eugenics

www.dnai.org



Eugenics - Chapter 2



This is Eugenics!

21st Century Style!

EGG DONOR NEEDED

Caucasian Egg Donor Needed For Loving Family

You Must Be At Least 5' 7"
Have A 1300+ Sat Score
Possess no major family medical issues

Free Medical Screening **All Expenses Paid**

$50,000.00

For More Information
Please Email Darlene:
TomEsquire@aol.com
Of fax inquiries to: 1-619-234-8881

Hitt & Pinkerton, Attorneys at Law
(1-800-264-8828)

(14)

(12)

But don't we "all" do this.??!!

What is Genetic Engineering revisited!!

Directed Genetic Change

a. **Classical Breeding** - new gene combinations

b. **Molecular Genetic Engineering** - DNA technology

(1) Reconstructing genes
(2) Modifying genes
(3) Synthesizing genes
(4) Combining genes from different organisms
(5) Cross species barrier! Mouse genes → plants!
(6) Synthesizing whole genomes!!

Altering Genetic Makeup of an organism for:

(1) Basic Science
(2) Medicine
(3) Agriculture
(4) Environment
(5) Biology factories
(6) The Law
(7) Commerce
etc.!

LIMITATIONS OF CLASSICAL BREEDING/Engineering

(1) Limited to genes of ORGANISMS that interbreed & severe Ethical issues with "Man"

(2) Only CAN Make new gene combinations with existing genes --- genes created by "natural" mutations. CAN'T predict outcome (Kongsedenkd)

(3) CAN'T make existing genes "better" - just better combinations of existing genes — new combinations of gene forms/alternatives.

(4) Only useful for obvious traits -- one's that can be observed Visually (e.g., seed size)

(5) Time -- limited by generation time of organism to introduce "wild" forms of a gene into a crop or farm animal -- slow

e.g. — crops & domesticated animals bred over 100's & 1000's of years!

Using DNA Technology to Genetically Engineer Organisms Has Unlimited Potential

(1) Any gene from any organism can be used in any organism -- No Breeding Barrier!

(2) New Genes can be created --- Genes that produce new proteins or that work better

NEW Genetic VARIABILITY!!

(3) Existing Genes can be Switched ON in "places" they are normally off & vice versa! Gene regulation can be Altered! Gene pathways can be controlled!

(4) Speed - can happen within a generation --- very quickly (e.g., Human ADA engineering or gene therapy)

(5) Genes or Pieces of genes can be used FROM any Genome/organism - only Limited by rules of Life! & the gene's chemistry!

(6) Ability to change, alter, manipulate, control the genetic "blueprint" of any organism —

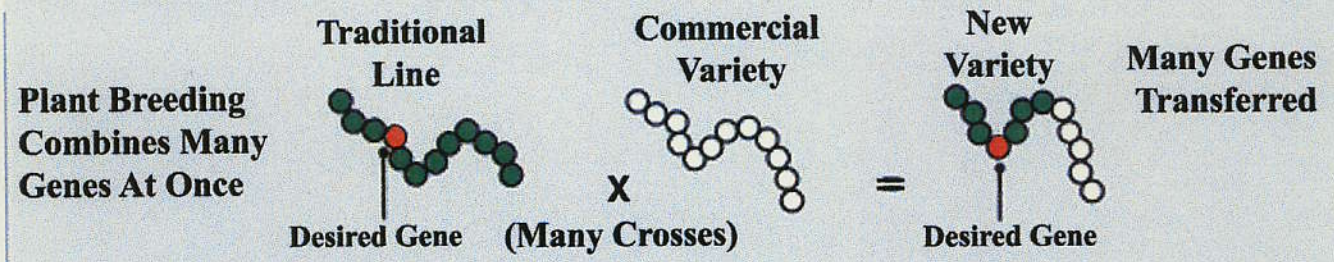
END Biological Limitation — Follow Rules of Biology!

Make better?

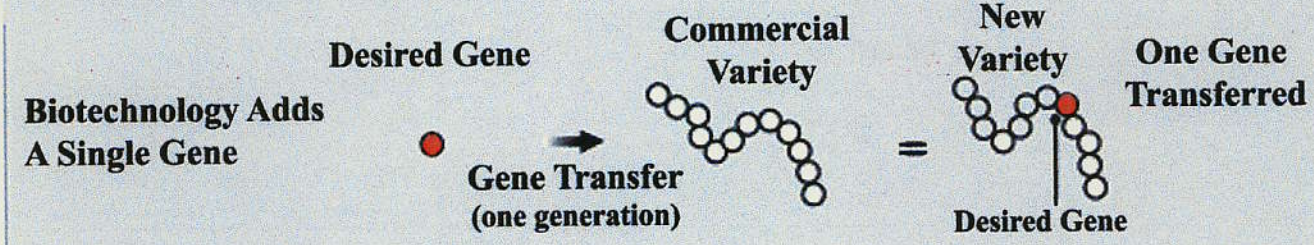
Classical Breeding combines Many Genes with unpredictable Consequences

↳ Karpechenko!

TRADITIONAL PLANT BREEDING



PLANT BIOTECHNOLOGY



Molecular Breeding / Engineering is controlled & uses one characterized Gene & Process at a time!

The ERA of Genomics will Enable us to Have ACCESS to ALL Genes of Every Living ORGANISM on the EARTH!

① TO understand BioLogy —

② TO use to Engineer New Gene combinations —

③ TO use for the benefit of Mankind (e.g., new drugs, better crops, novel industrial processes, etc.!)

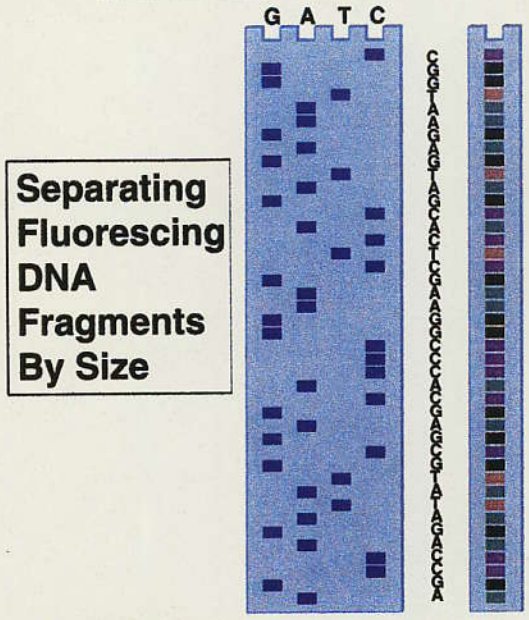
We Live in the Genomics Era – The Age of the Genome !!

Genetic Engineering gave "Birth" to this ERA !!

IT IS POSSIBLE TO ISOLATE AND SEQUENCE Every Gene in A Genome!

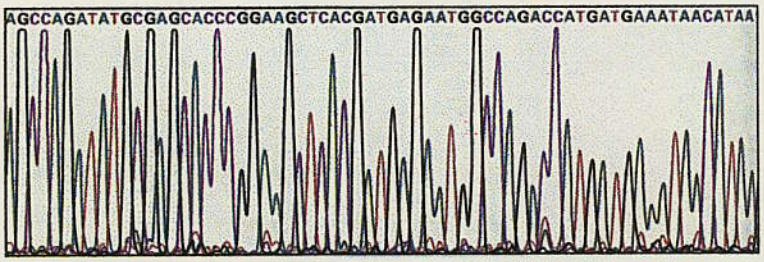
Need to clone DNA segment first

Genome Sequencing Using Computers and Robotics



Separating Fluorescing DNA Fragments By Size

Laser Detection of Fluorescing Nucleotides



Computer Visualization of DNA Sequence

Gene Chemical Sequence

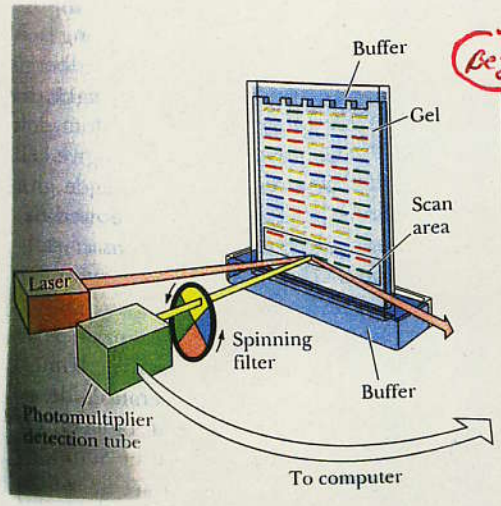
Begin → End

CCGGAAGCATAAAGTGTAAAT

(1) What makes gene unique

(2) What it does!

(3) How it works in cell!



Specific Order → Specific function!! in cell

The Genomes of all major CLASSES of ORGANISMS Have Been Sequenced
Including HUMANS!

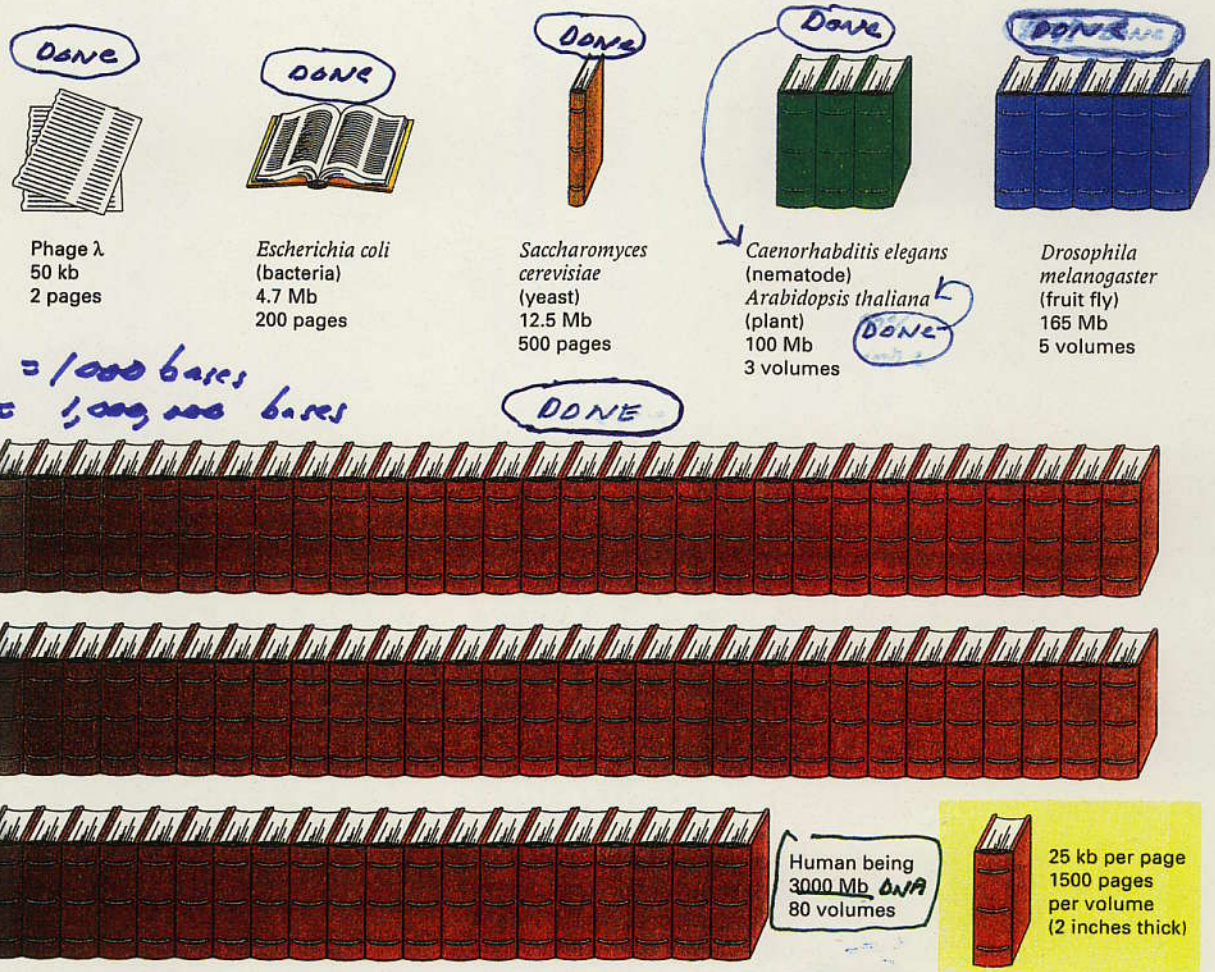


Figure 9.21
Relative sizes of genomes if they were printed at 25,000 characters per page and bound in 1500-page volumes. One volume would contain about as many characters as a telephone book 2.5 inches thick. The *E. coli* genome would require about 200 pages, yeast 500 pages, and so forth.

(+)
Chimpanzee
Rat
Chicken
Dog
Rice

MOUSE
pufferfish
Both done!!

By 2010 (or sooner) all of the genes of each major group of organisms on Earth will have been isolated, sequenced & their functions revealed!

ALL genes in these organisms have been identified – e.g., Mouse & Humans have same genes!

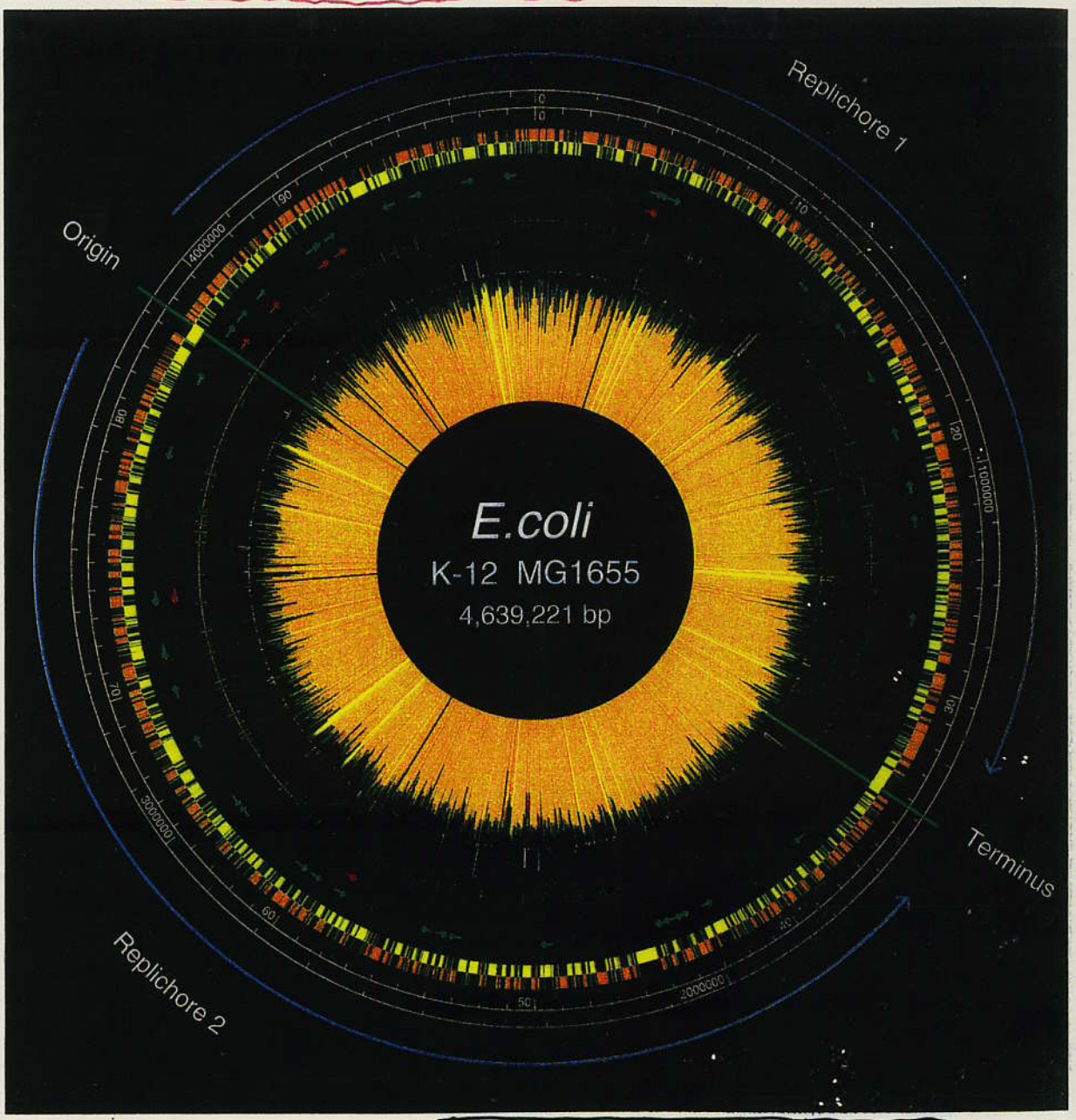
SEQUENCED GENOMES

1. Many Viruses
2. Hundreds of bacteria including E. coli & many human bacterial pathogens (180)
3. Many Molds including Yeast
4. Important plants such as Rice & Arabidopsis which is a broccoli relative
5. Many Animals including nematode, fruit fly, Mosquito, Chicken
6. Close Relatives of humans including mouse, rat, & chimpanzee, dog
7. Human

We will learn about our genetic origins & what makes us different from a Chimpanzee or Mouse — only 1% DNA difference!

The E. coli DNA Sequence
4,639,000 bpairs

Reveals all Genes & what makes this organism Unique!



FACTORY FOR Gene ENGINEERS!

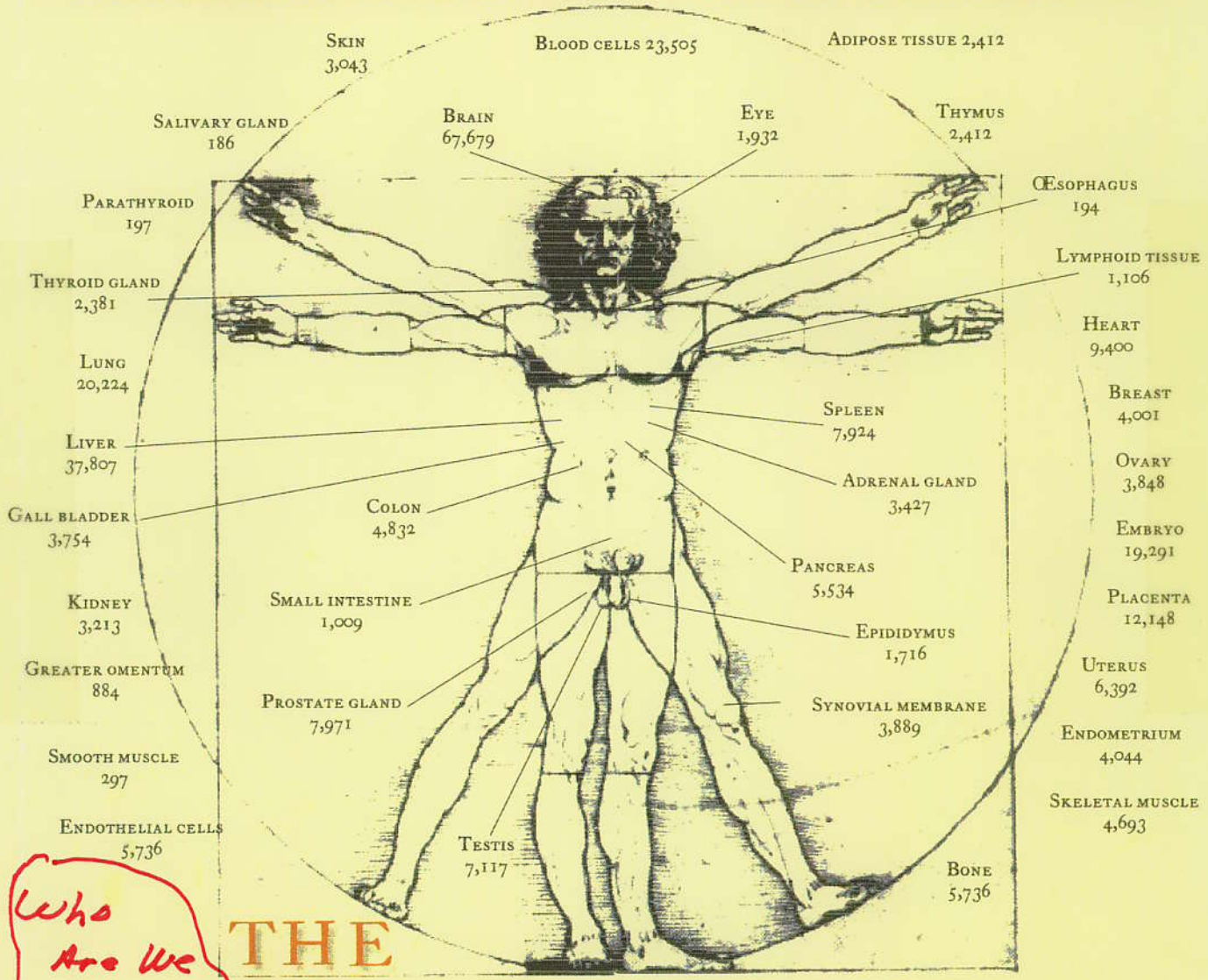
The Sequence Reveals all the genes in the E. coli cell – but Not the Function!

Figure 9.24
Diagram of the DNA sequence organization of *Escherichia coli* strain K-12. The coordinates are given in base pairs as well as in minutes on the genetic map. The coding sequences are shown as gold and yellow bars, which are transcribed in a clockwise (gold) or counterclockwise (yellow) direction. Green and red arrows denote genes for transfer RNAs or for ribosomal RNAs, respectively. The gold rays of the "sunburst" are proportional to the degree of randomness of codon usage in the coding sequences. Genes with the longest rays use the codons in the genetic code almost randomly. The origin and terminus of DNA replication are indicated. Bidirectional replication creates two "replichores." The peaks on the circle immediately outside the sunburst indicate coding sequences with high similarity to previously described bacteriophage proteins. [Courtesy of Frederick R. Blattner and Guy Plunkett III. From F. R. Blattner et al. 1997. *Science* 277: 1453.]

~ 4,000 genes!

The Human Genome Has been Sequenced!

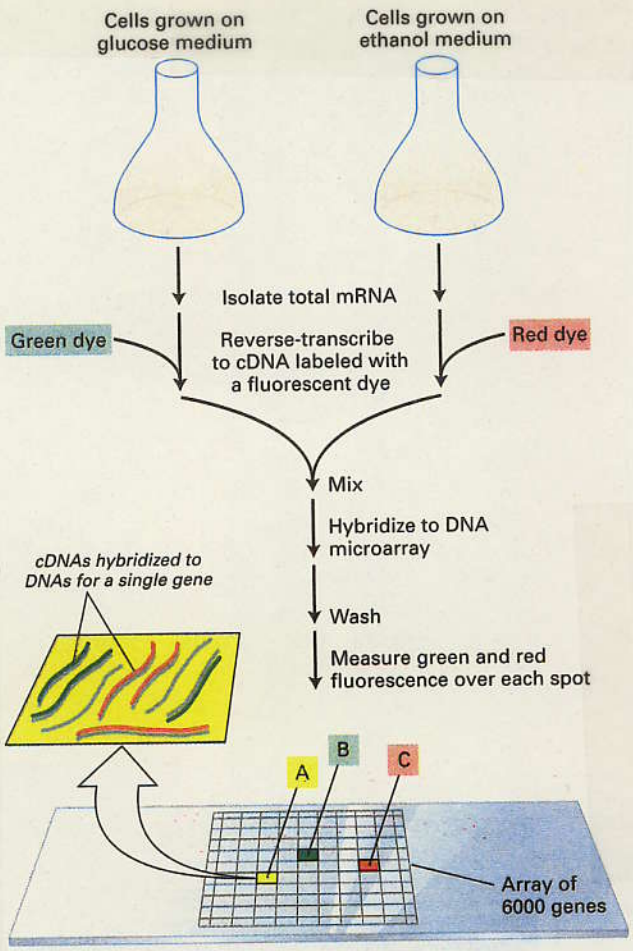
nature
INTERNATIONAL WEEKLY JOURNAL OF SCIENCE



THE genome DIRECTORY

Who Are We + Where Did We Come From?

AND ALL OF YOUR GENES CAN BE STUDIED FOR THEIR ACTIVITY IN CELLS COLLECTIVELY!



A If a spot is yellow, expression of that gene is the same in cells grown either on glucose or ethanol

B If a spot is green, expression of that gene is greater in cells grown in glucose

C If a spot is red, expression of that gene is greater in cells grown in ethanol

▲ **EXPERIMENTAL FIGURE 9-35 DNA microarray analysis can reveal differences in gene expression in yeast cells under different experimental conditions.** In this example, cDNA prepared from mRNA isolated from wild-type *Saccharomyces* cells grown on glucose or ethanol is labeled with different fluorescent dyes. A microarray composed of DNA spots representing each yeast gene is exposed to an equal mixture of the two cDNA preparations under hybridization conditions. The ratio of the intensities of red and green fluorescence over each spot, detected with a scanning confocal laser microscope, indicates the relative expression of each gene in cells grown on each of the carbon sources. Microarray analysis also is useful for detecting differences in gene expression between wild-type and mutant strains.

DNA Chip → Find which genes are active where e.g., cancer genes

- cancer genes
- heart disease genes
- obesity genes
- hypertension genes
- aging genes etc., etc.

IT's a NEW ERA of biology!

The Ultimate Outcome of Genome Projects

1. ALL the genes of Major organisms isolated & identified. Use these genes / combine them for any purpose (Medicine, Agriculture).

2. ALL of the functions of genes in the cells of Major organisms revealed. What they do to specify traits.

3. The regulatory networks or wiring that controls gene activity from "birth" to "death" revealed. How a child is formed from a fertilized egg cell!

4. The DNA Functions & Networks that direct cells to develop into complex organisms revealed our Biological destiny!!

5. The relationships Between the DNA/Genes of all organisms revealed – What makes a "man a man" and a "mouse a mouse?"

→ Immortality?

The ultimate in Genetic Engineering!
Creating "Life" FROM Synthetic Molecules

MOLECULAR BIOLOGY

Venter Cooks Up a Synthetic Genome in Record Time

Stir-and-bake genomes. Venter's (left) success in building a viral genome drew praise from DOE Secretary Abraham.

Generating a synthetic genome by whole genome assembly: ϕX174 bacteriophage from synthetic oligonucleotides

Hamilton O. Smith, Clyde A. Hutchison III†, Cynthia Pfannkoch, and J. Craig Venter‡

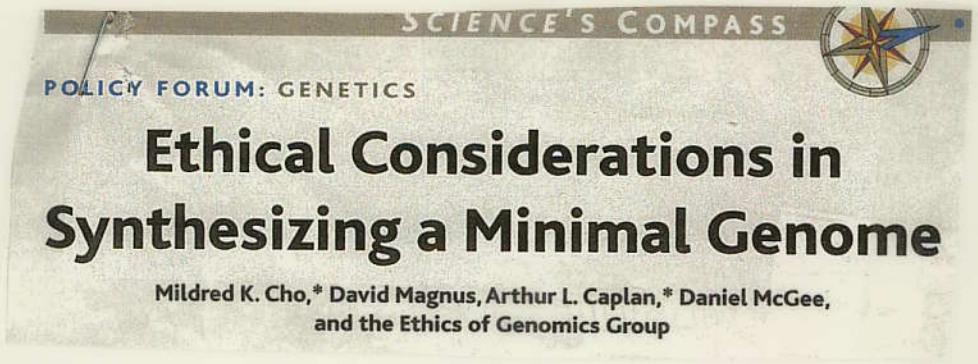
Institute for Biological Energy Alternatives, 1901 Research Boulevard, Suite 600, Rockville, MD 20850

Fig. 4. Plaques of synϕX-A. There appear to be several plaque morphologies: small plaques with sharp borders, medium-sized plaques, and large plaques with fuzzy borders.

What does this Experiment Say about Living Processes?

85

The ultimate in Genetic Engineering



"The prospect of constructing minimal and new genomes does not violate any fundamental moral precepts or boundaries, but does raise questions..."

Will it be possible to create "life" beginning with a genome sequence?

(1) Create new organisms to study critical life processes — origins of life, bacterial evolution, control of cell metabolism, etc.

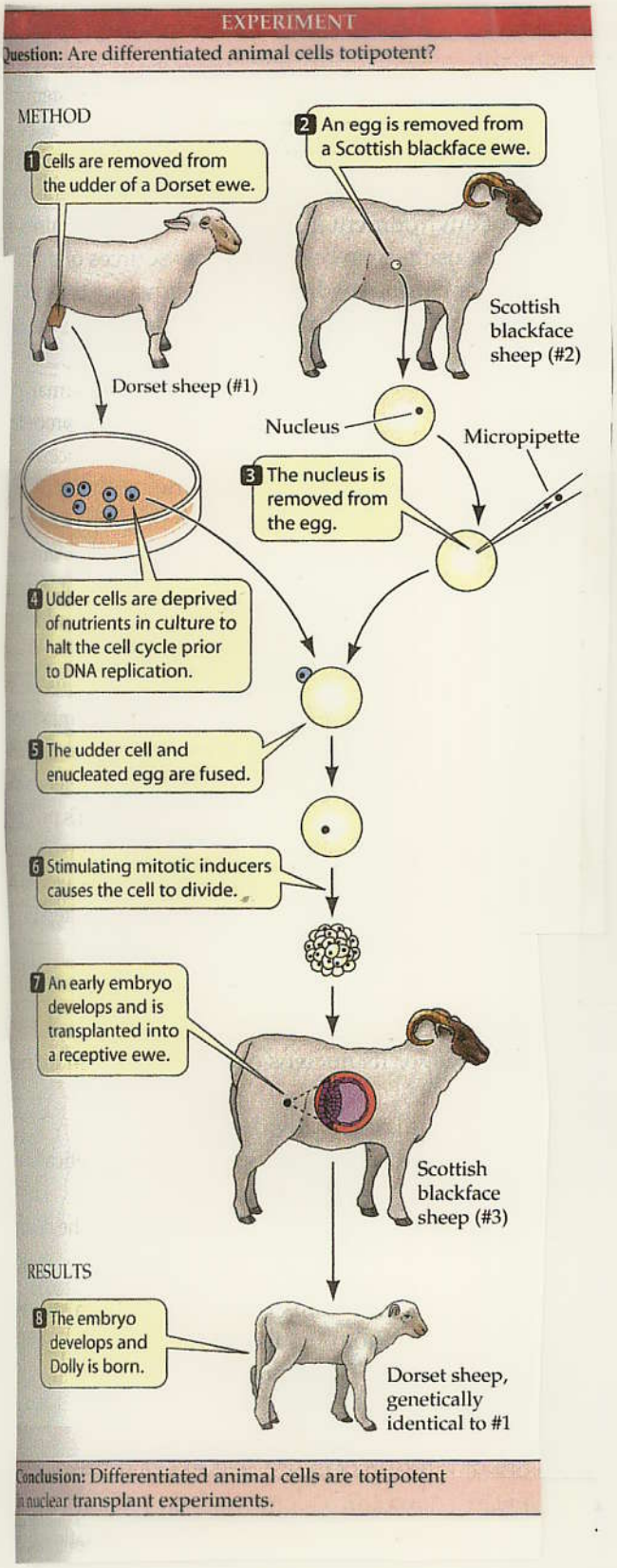
(2) Designer bacteria for specific tasks — e.g., breakdown of environmental toxins

(3) How does this experiment change our views of what life is? OR does it!?

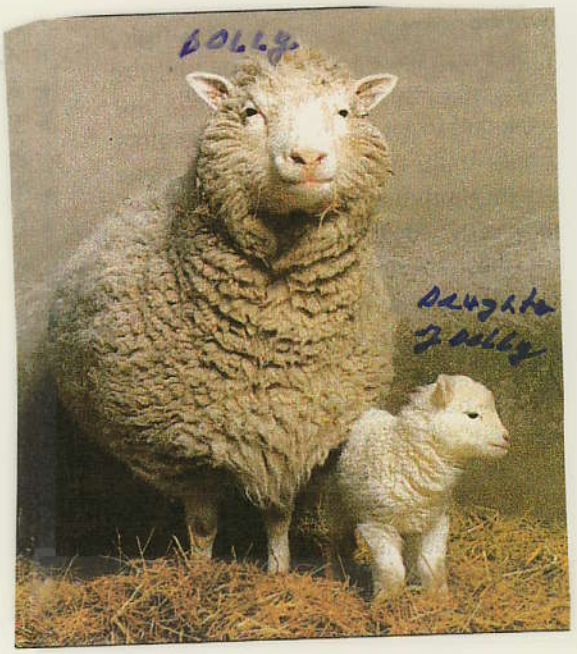
The ERA of MAMMALIAN Reproduction & Cloning combined with Genetic Engineering opens up a whole new set of possibilities


TIME
FICTION ISSUE
"CLONE ON THE RANGE"
BY DOUGLAS COUPLAND
Will There Ever
Be Another You?
A SPECIAL REPORT ON CLONING

CLONING DOLLY THE SHEEP



CAN engineer at this step!



What does this say about the genetic potential of cells?

Question

ORGANISMS THAT HAVE BEEN CLONED

1. Plants
2. Frogs
3. Mice
4. Rats
5. Sheep (Dolly)
6. Goats
7. Mules
8. Cattle
9. Horses
10. Pigs
11. Cats (cc - copy cat) - Dogs
12. Monkeys (ANDi - inserted DNA)
13. Humans ?!

Leading to Ethical Issues & new opportunities (e.g., curing human disorders, saving endangered species, etc.)

GENETICALLY ENGINEERED CLONES CAN BE MADE

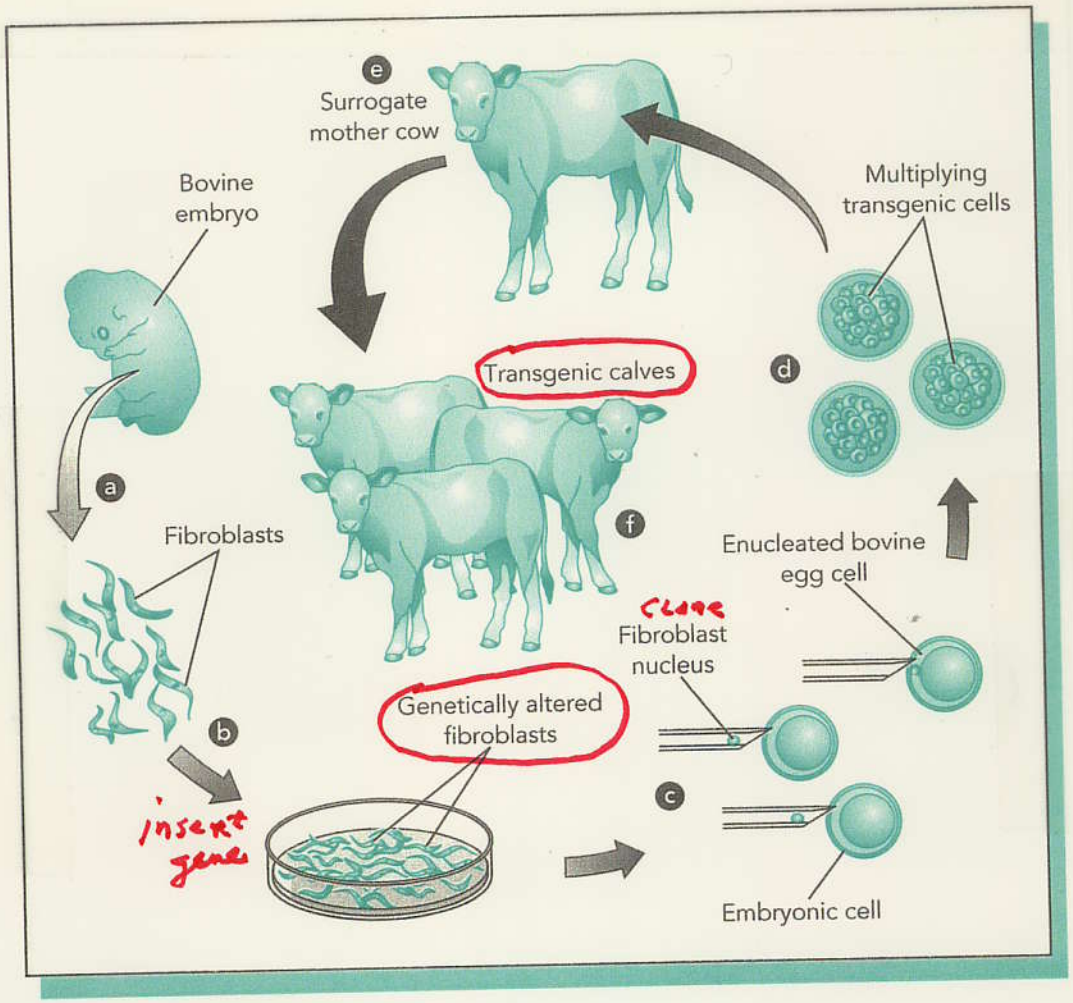


FIGURE 11.11
Transgenic cattle produced by cloning with fetal cells. (a) Fibroblasts are obtained from a fifty-five-day-old bovine fetus. The fibroblasts are totipotent muscle and tendon cells arising early in the fetal stage. (b) The fibroblasts are cultivated in nutritious medium Petri dishes and modified with foreign genes. (c) Then the nucleus, with its genetically altered DNA, is removed from the cell, and the nucleus is implanted into an egg cell lacking a nucleus. (d) The egg cell with its new nucleus is encouraged to multiply and form an embryo. (e) Embryos are implanted to surrogate mothers, and (f) some months later, transgenic calves are born. They are clones because they have originated from single cells, and they are transgenic because all their cells bear foreign genes.

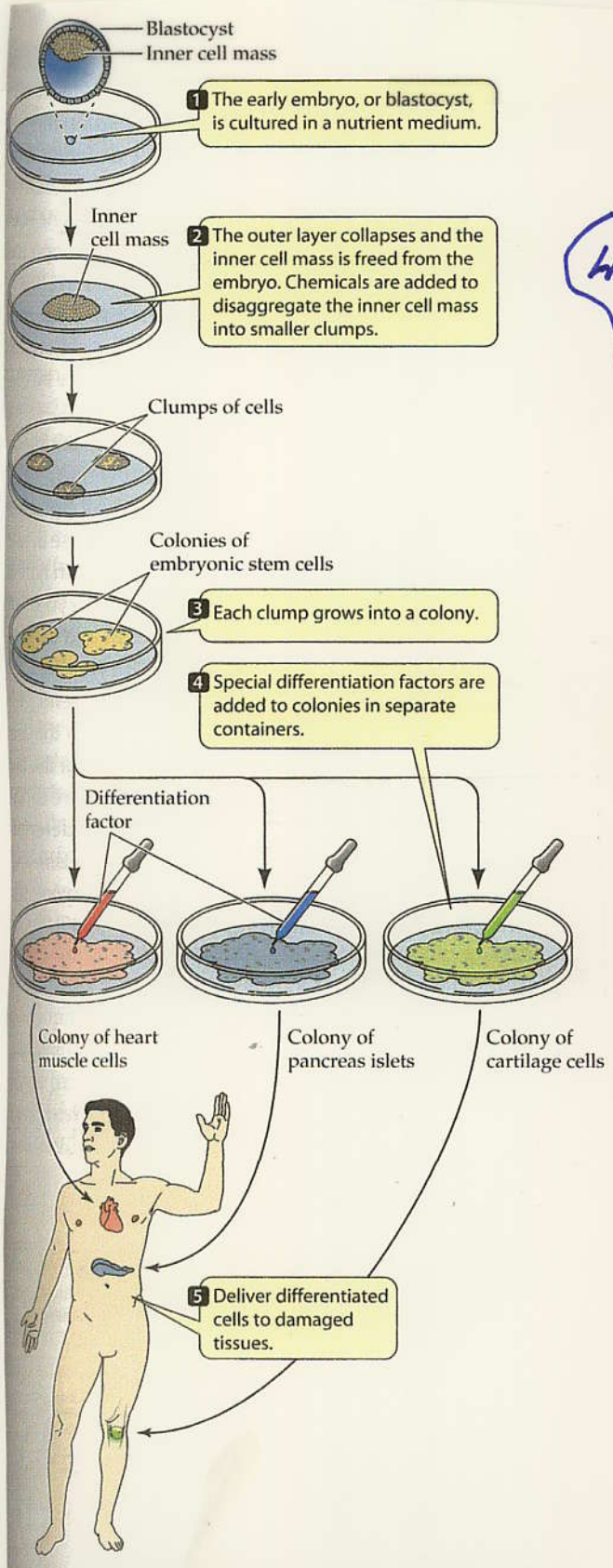
COMBINING Genetic Engineering + Mammalian cloning! Implications?

Human Stem Cells can potentially be genetically engineered!

Where do Embryos come from?

Human Stem Cells
Embryonic
Stem Cells

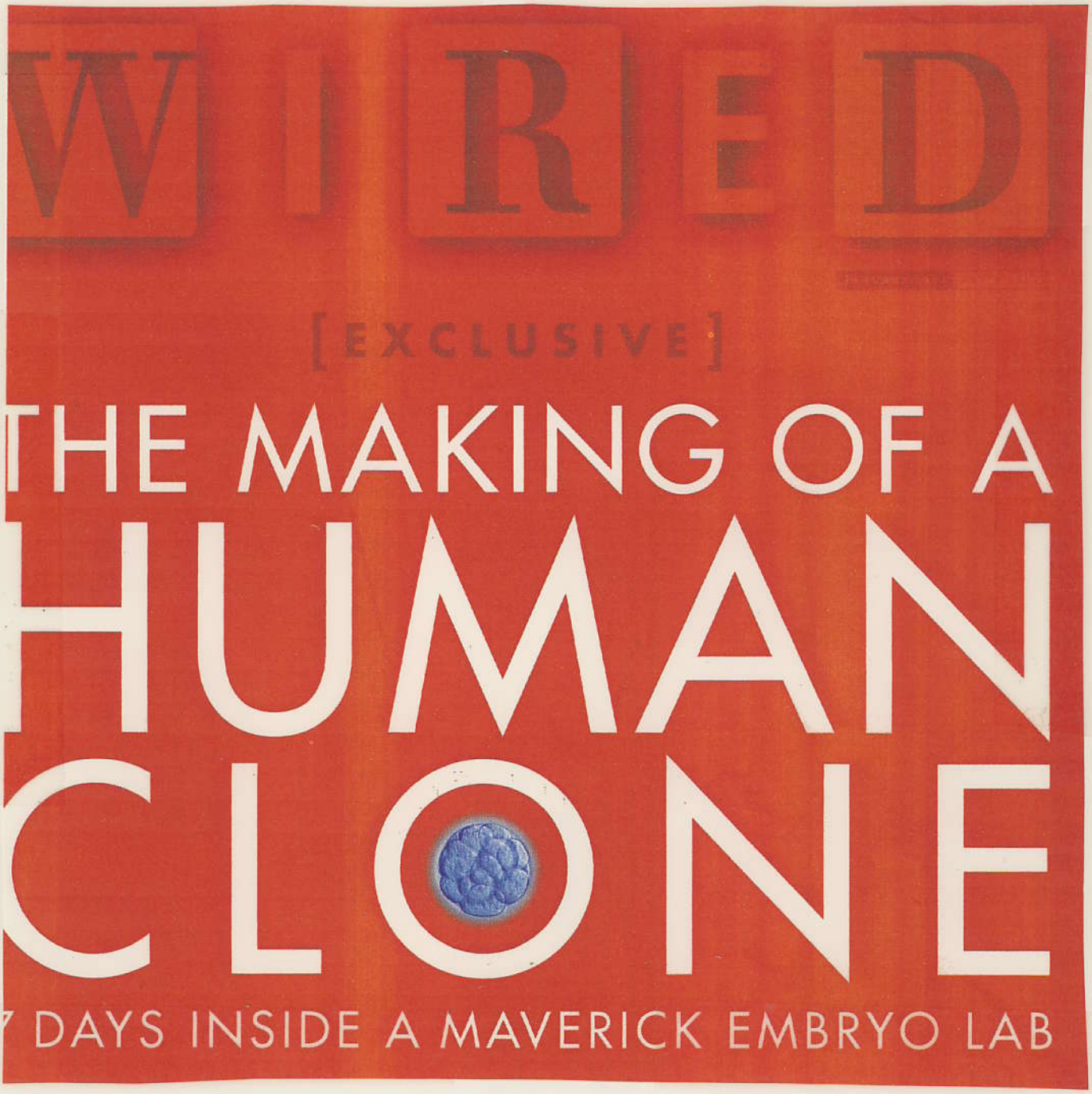
correct genetic disorder (e.g. diabetes) + replace with normal engineered pancreas!



19.6 The Potential Use of Embryonic Stem Cells in Medicine
Human embryonic stem cells can be cultured in the laboratory and induced to differentiate. Their use as transplants to replace damaged tissue is under intensive investigation.

What About Human cloning?

AND combining with Genetic Engineering!!



Embryos? Adult Human Beings?

Genetically Engineer Cloned Human Embryos?

Is a "Clone" human?

HUMAN CLONING POSSIBILITIES

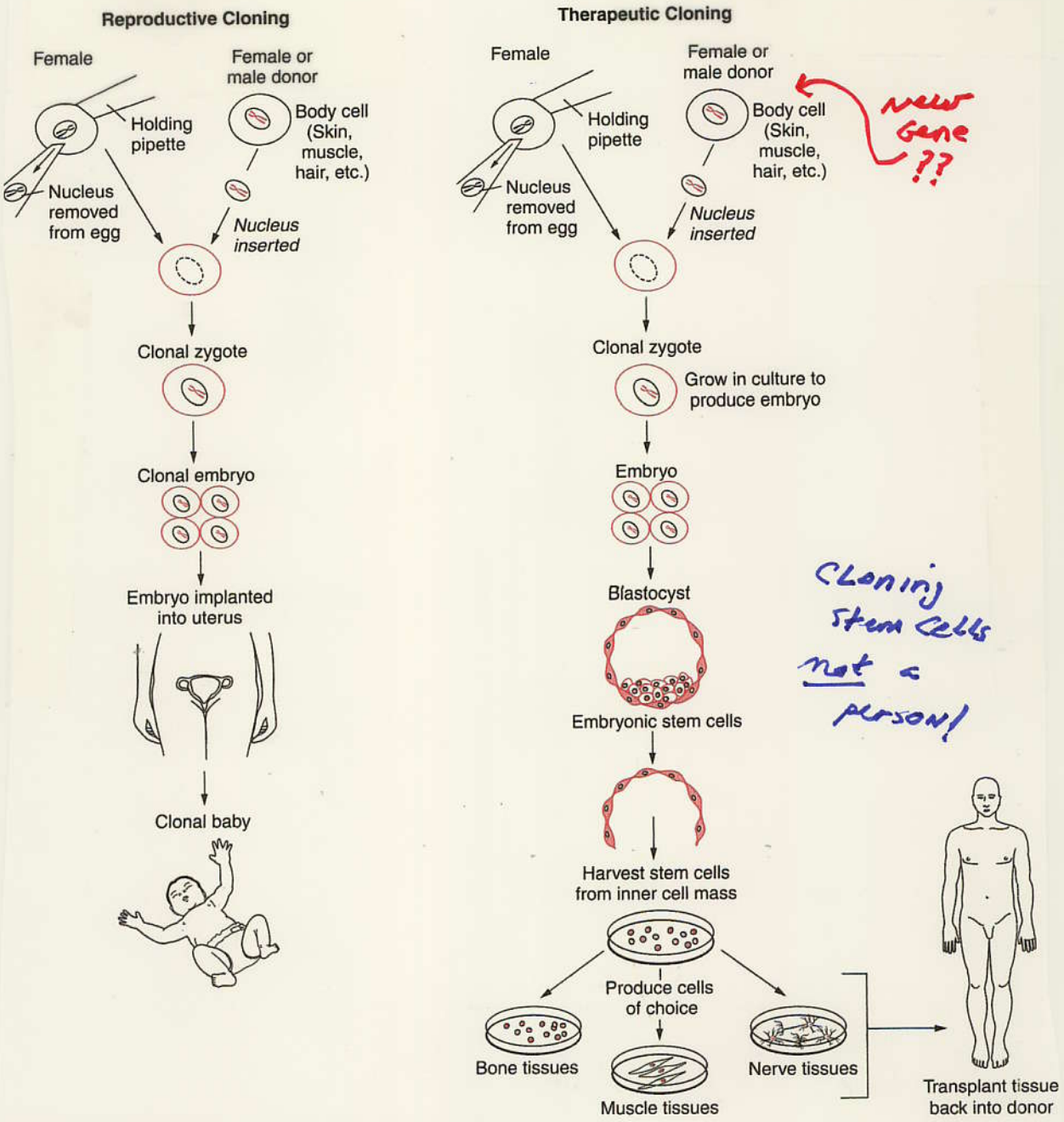


Figure 11.20 Reproductive Cloning and Therapeutic Cloning In reproductive cloning, the goal is to produce a cloned baby. In therapeutic cloning stem cells that are genetically identical to the cells taken from a patient are produced to provide patient-specific stem cell therapy.

STEM CELLS, THERAPEUTIC CLONING, & REPRODUCTIVE CLONING

TABLE 11.3 COMPARISON OF STEM CELLS, THERAPEUTIC CLONING, AND REPRODUCTIVE CLONING

	Embryonic Stem Cells	Adult Stem Cells	Therapeutic Cloning (Somatic Cell Nuclear Transfer)	Reproductive Cloning
Final or "end" product	Undifferentiated stem cells (isolated from fetal or embryonic tissue such as an embryo at the blastocyst stage) growing in culture	Undifferentiated stem cells (isolated from adult tissue such as bone marrow cells) growing in a culture dish	Undifferentiated stem cells growing in a culture dish (obtained from the person who will also serve as the recipient of these cells)	"Cloned" human
Purpose/application	Source of stem cells for research and for treating human disease conditions such as replacing diseased or injured tissue	Source of stem cells for research and for treating human disease conditions such as replacing diseased or injured tissue	Source of stem cells that are genetically matched to recipient for treating human disease conditions such as replacing diseased or injured tissue	Create, duplicate, or replace a human by producing an embryo for implantation, leading to the birth of a child
Surrogate mother required	No	No	No	Yes
Human created	No	No	No	Yes
Time frame	A few weeks of growth in culture	A few weeks of growth in culture	A few weeks of growth in culture	9 months, the duration of a normal biological pregnancy (after growth of the embryo in culture)