HC70A Winter 2006

Professor Bob Goldberg

Lecture # 2

What Are Genes?

THEMES

1. What are the function of Genes?
2. What is the scientific PROCESS - Revisited?
3. What was known about genes in 1940s?
4. Does the nucleus Contain the Genetic Material?
5. What re the properties of the Genetic Material?
6. Griffith/Avery Experiments → DNA as the Genetic Material?
7. BACTERIA & BACTERIAL GENOMES
8. Macromolecules in Cells
9. TRANSformation is universal Phenomenon - BASIS of Genetic Engineering - other BACTERIAL traits, Animals, Plants

Stop 1/24/06

10. DNA STRUCTURE
11. Genes, DNA, Chromosomes
12. Anatomy of a Gene
13. Yes - it's in the DNA - Engineering Body PLAN & Beyond!

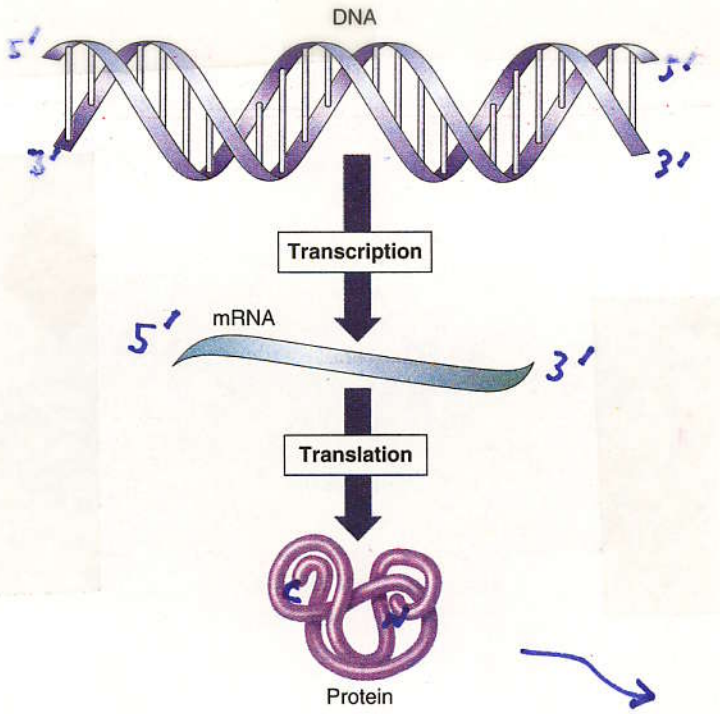
Stop 1/31/06

What Are the Functions of A Gene?

collection of Genes

Genotype

Gene



Replication (1)

Gene Action (2)

Cell Function (3)

Phenotype

FIGURE 15.5
The Central Dogma of gene expression. DNA is transcribed to make mRNA, which is translated to make a protein.

GENETIC Engineering Alters Cell Function By Changing Genotype

Design an Experiment!

HOW DEMONSTRATE THIS EXPERIMENTALLY?

Gene Action Leads to Specific Traits

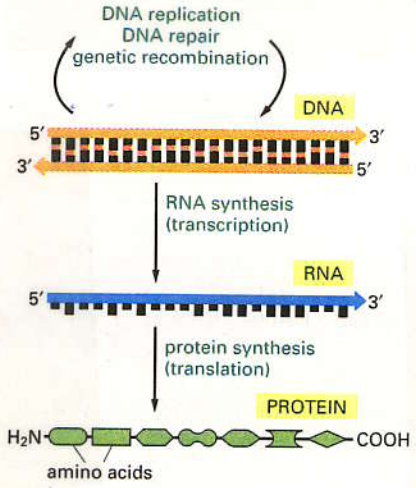
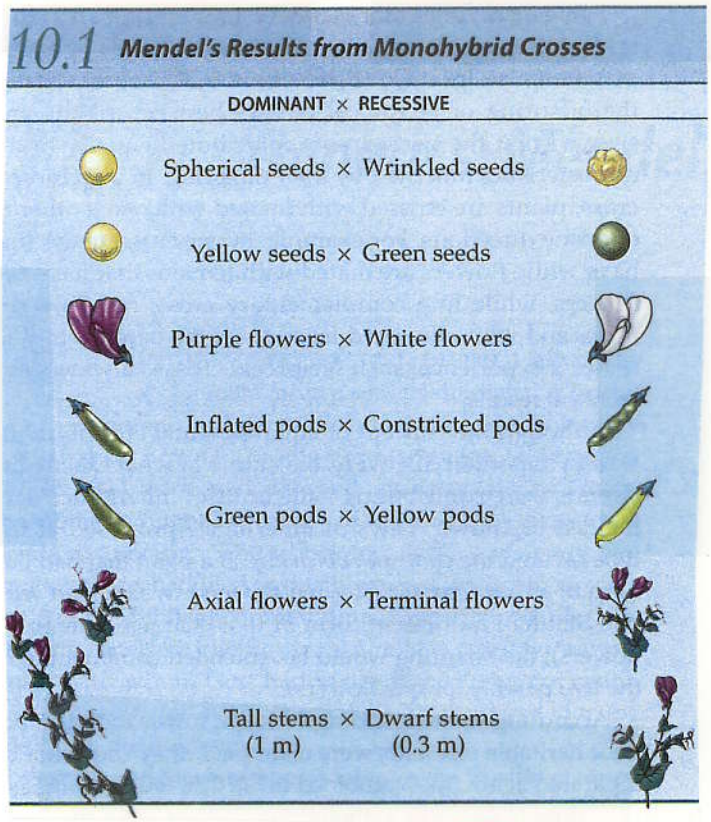


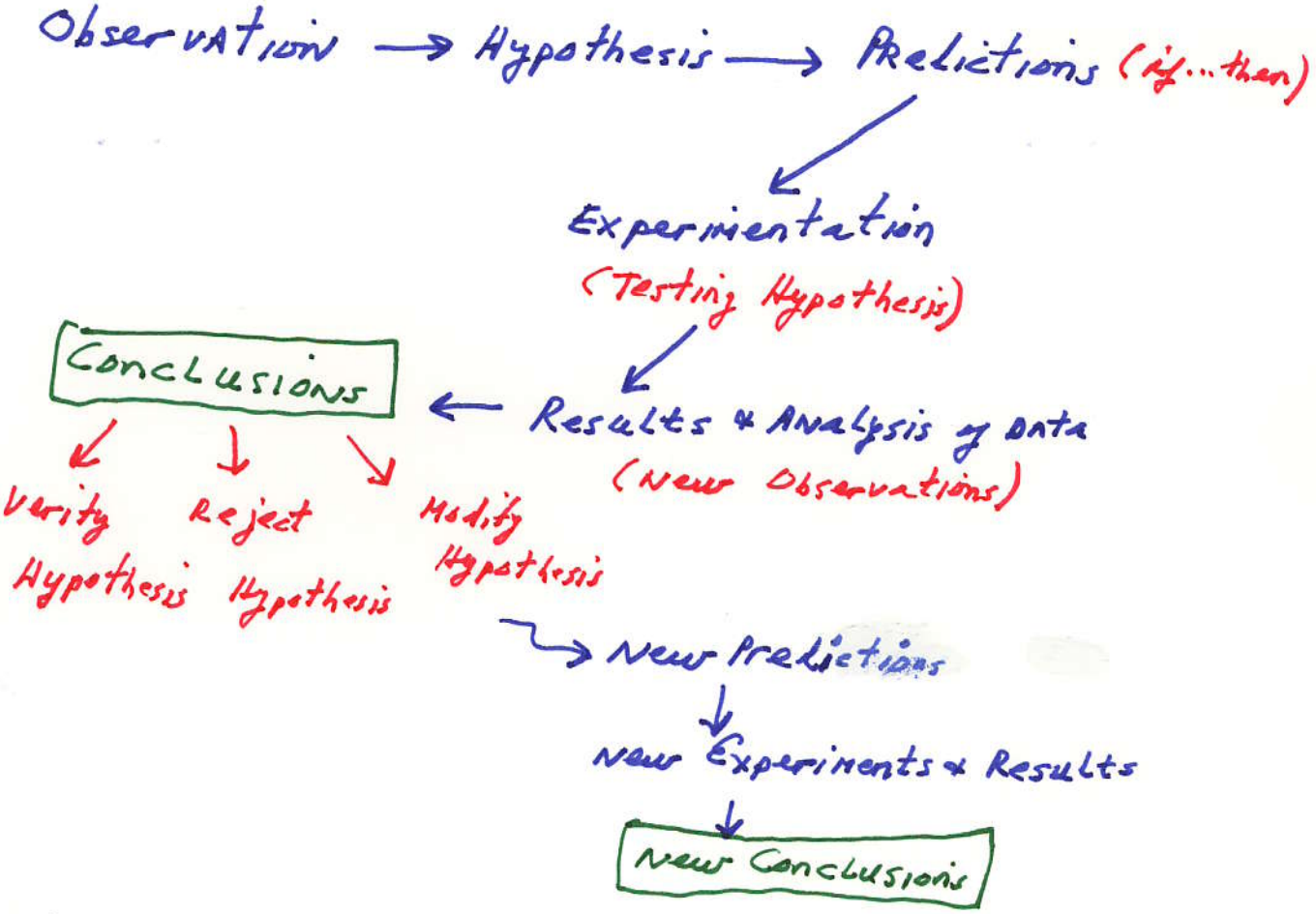
Figure 6–2 The pathway from DNA to protein. The flow of genetic information from DNA to RNA (transcription) and from RNA to protein (translation) occurs in all living cells.



Altering Genes By Mutation Leads to Genetic VARIABILITY - Different FORMS OF SAME Gene

Genetic Engineering CAN create ∅ AMOUNTS of NEW Gene VARIABILITY Not Found in "Nature"!!

How is science carried out?



Scientists look for "what did I miss" & analyze results critically. Hypotheses are Rejected - Never proved

One question always leads to another

NOT AN OPINION

What Was Known About Genes Prior to 1940s?

1. On Chromosomes
2. At Specific Location on Chromosomes
3. Directed Formation of Specific Traits
4. Could Mutate - Mutations Stable
5. Followed Mendel's Laws of Heredity
6. Probably either protein or Nucleic Acid (DNA or RNA)
   - Discrete Units → Replicate
   - → Factors

Did Not Know what the Molecule of Inheritance Was

Hammerling's Grafting Experiment Showing The Nucleus Contains Genetic Material

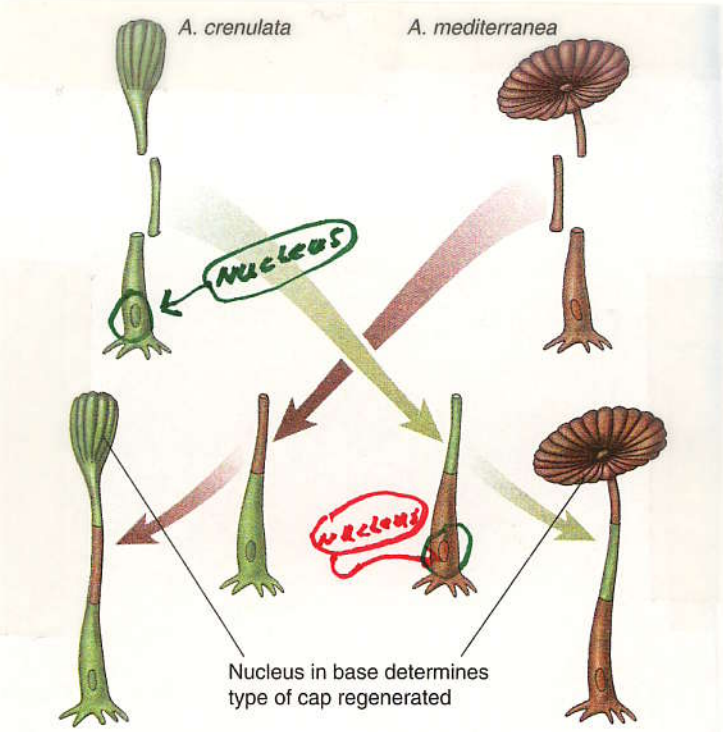


FIGURE 14.2
Hammerling's *Acetabularia* reciprocal graft experiment. Hammerling grafted a stalk of each species of *Acetabularia* onto the foot of the other species. In each case, the cap that eventually developed was dictated by the nucleus-containing foot rather than by the stalk.

1943

Hypothesis?
Predictions?

Hypothesis to Explain CAP at Top from Nucleus at Bottom?

How Test?
Predictions?

But what Molecule/Substance in the nucleus is Responsible for the Phenotype?

FROG CLONING EXPERIMENT SHOWS THAT THE NUCLEUS contains the Genetic Material TO PROGRAM all of DEVELOPMENT

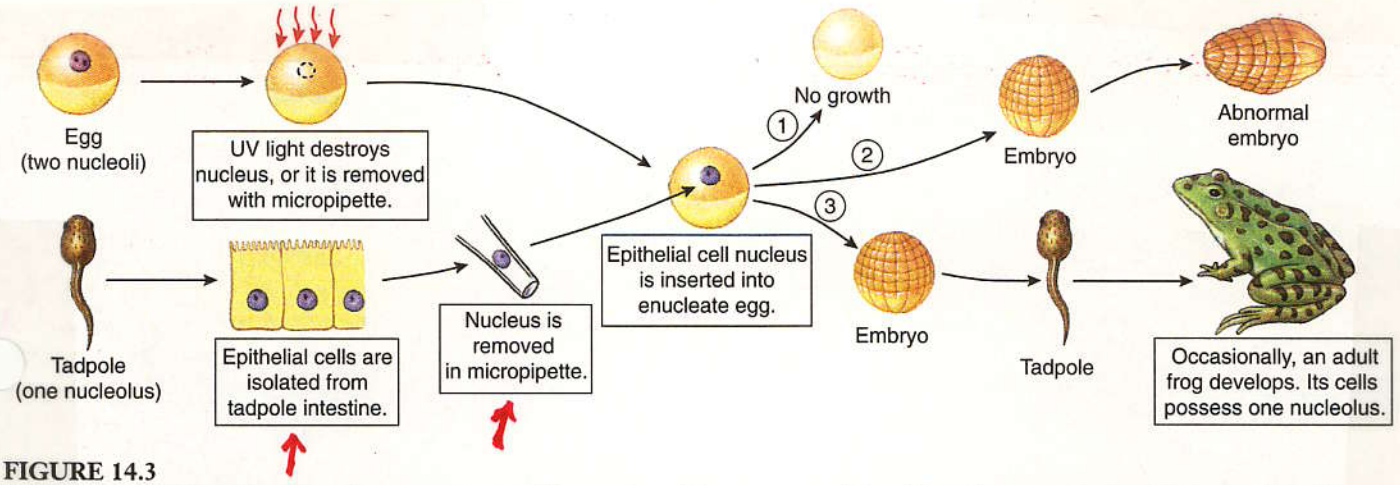


FIGURE 14.3
Briggs and King's nuclear transplant experiment. Two strains of frogs were used that differed from each other in the number of nucleoli their cells possessed. The nucleus was removed from an egg of one strain, either by sucking the egg nucleus into a micropipette or, more simply, by destroying it with ultraviolet light. A nucleus obtained from a differentiated cell of the other strain was then injected into this enucleate egg. The hybrid egg was allowed to develop. One of three results was obtained in individual experiments: (*1*) no growth occurred, perhaps reflecting damage to the egg cell during the nuclear transplant operation; (*2*) normal growth and development occurred up to an early embryo stage, but subsequent development was not normal and the embryo did not survive; and (*3*) normal growth and development occurred, eventually leading to the development of an adult frog. That frog was of the strain that contributed the nucleus and not of the strain that contributed the egg. Only a few experiments gave this third result, but they serve to clearly establish that the nucleus directs frog development.

FIRST CLONING Experiment - 1952

Briggs & King

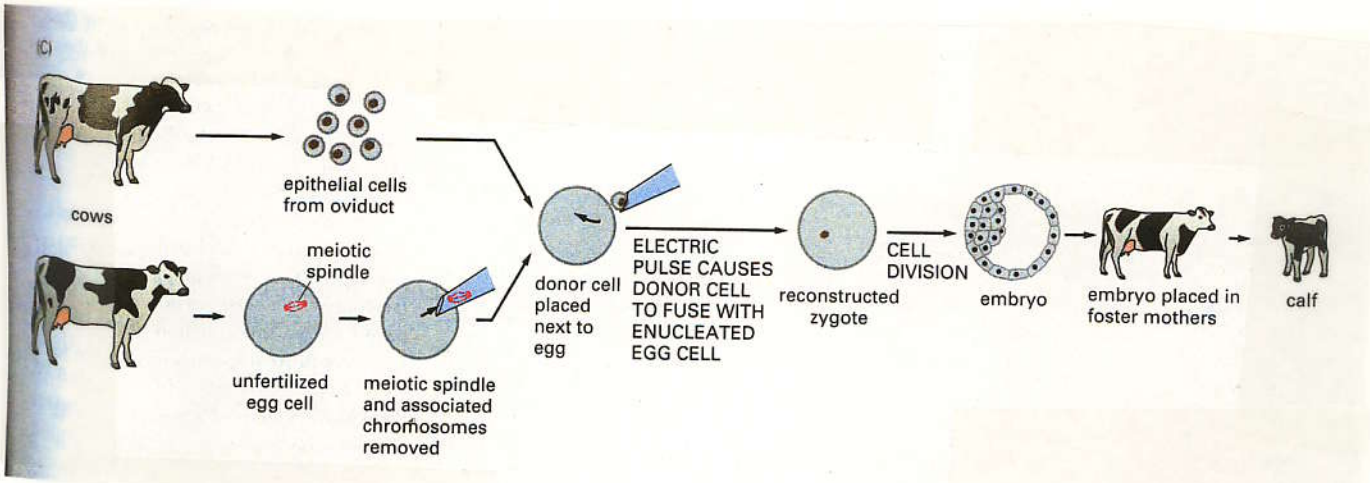
Hypothesis?

Predictions?

Approach?

Implications for Genetic Engineering?

FROG CLONING Experiment of the 1950's lead to CLONING of MAMMALS TODAY



SHOWS That The Nucleus contains ALL genes Needed TO PROGRAM ALL of MAMMAL development

But.... how WAS it shown that genes are made of DNA?

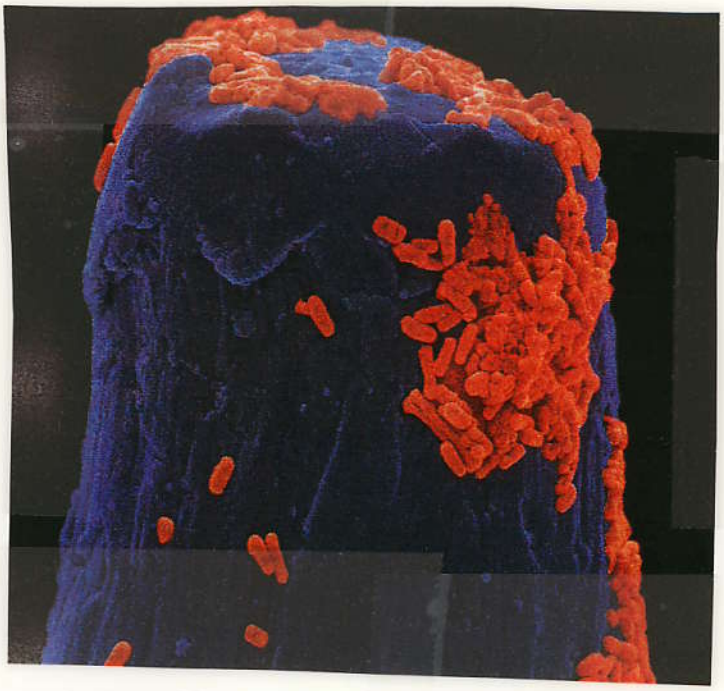
What ARE THE PROPERTIES OF A Gene?

1. Replication
2. Stability (Mutations)
3. Universality
   (a) all cells
   (b) all organisms
4. Direct cell function / Phenotype

HOW SHOW THAT DNA IS The Genetic Material?

How CAN these Properties Be tested Experimentally?
What <u>predictions</u> follow FROM These Properties

GRIFFITH'S Experiment with Pneumonia Bacteria 1927

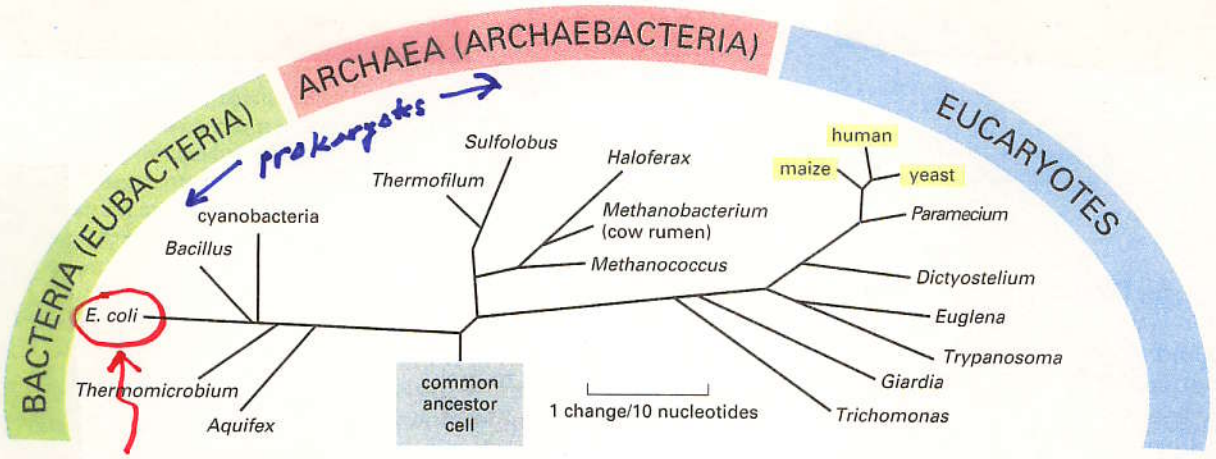


Bacteria on a pinhead!

The First Genetic Engineering Experiment - Except That WAS Not understood For Another 50 years!

Streptococcus pneumoniae (sequenced!)

BACTERIA ARE PROKARYOTIC SINGLE CELL ORGANISMS

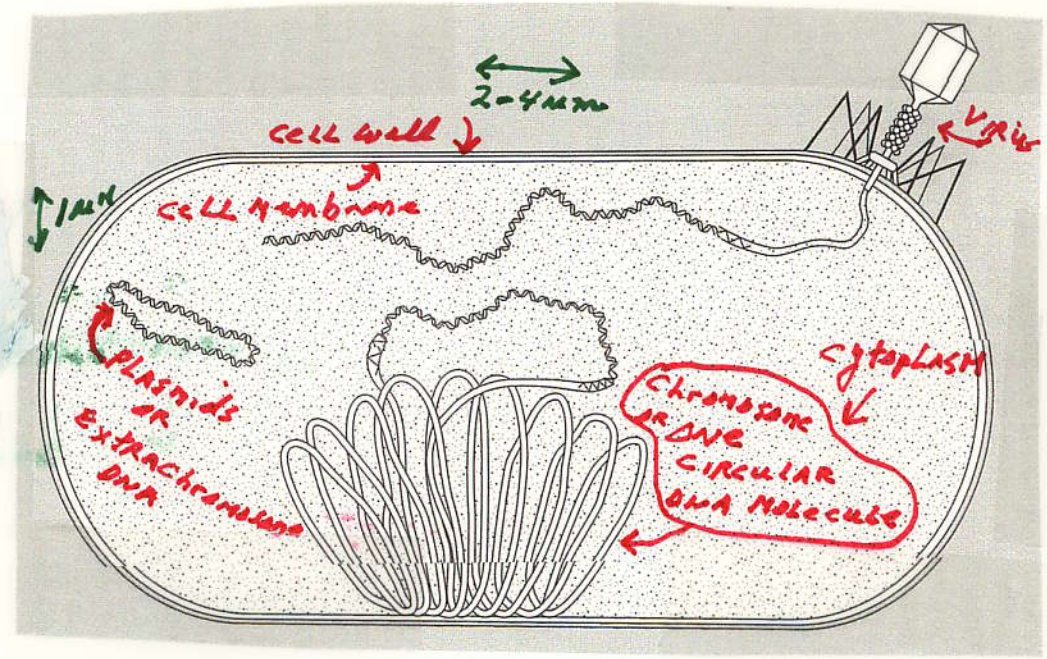


genetic engineering factories
colon bacteria

Figure 1–21 The three major divisions (domains) of the living world. Note that traditionally the word *bacteria* has been used to refer to procaryotes in general, but more recently has been redefined to refer to eubacteria specifically. Where there might be ambiguity, we use the term *eubacteria* when the narrow meaning is intended. The tree is based on comparisons of the nucleotide sequence of a ribosomal RNA subunit in the different species. The lengths of the lines represent the numbers of evolutionary changes that have occurred in this molecule in each lineage (see Figure 1–22).

How Show that these Creatures are Related? Predictions?

A "Typical" Bacterial Cell



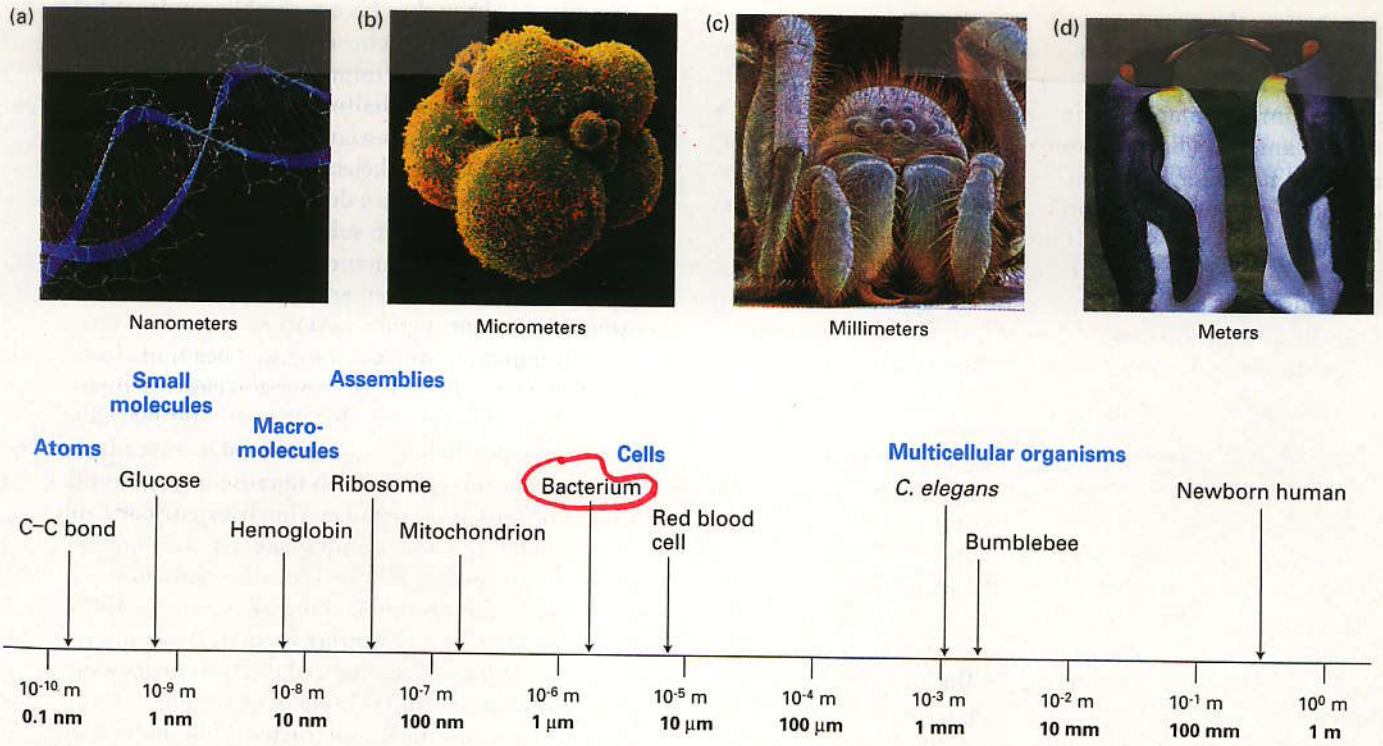
Plasmids – 2,000 – 150,000 bp (1 – 100 genes)
Chromosome – 580,000 – 5,000,000 bp (500 – 4500 genes)

E. coli DNA = ~ 1.4 mm (10^{-3} m) in circumference

Small plasmid DNA = 1.4 μm (10^{-6} m) in circumference

↳ antibiotic^R genes – "Vectors" for genetic engineering

Size Relationships Between Atoms, Molecules, Cells, & Organisms



▲ FIGURE 1-20 Biologists are interested in objects ranging in size from small molecules to the tallest trees. A sampling of biological objects aligned on a logarithmic scale. (a) The DNA double helix has a diameter of about 2 nm. (b) Eight-cell-stage human embryo three days after fertilization, about 200 μm across. (c) A wolf spider, about 15 mm across. (d) Emperor penguins are about 1 m tall. [Part (a) Will and Deni McIntyre. Part (b) Yorgas Nikas/Photo Researchers, Inc. Part (c) Gary Gaugler/Visuals Unlimited, Inc. Part (d) Hugh S. Rose/Visuals Unlimited, Inc.]

$1\,\mu m = 10^{-6}\,m$

$1\,Å = 10^{-10}\,m$

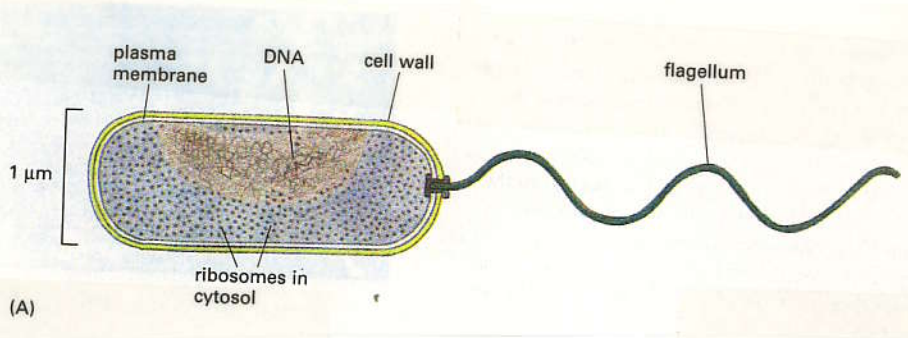
$10\,Å = 1\,nm = 1 \times 10^{-9}\,m$

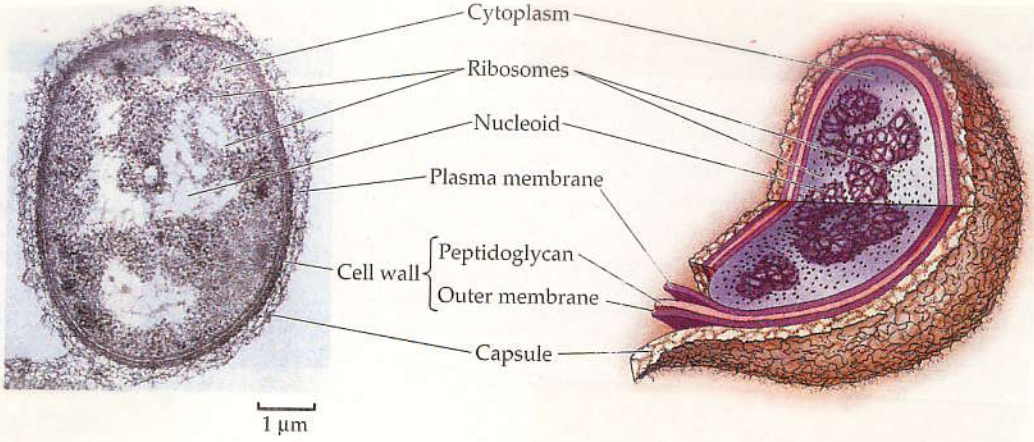
Bacteria = 2-5 μm

1 meter = 39.4 inches ~ 3 feet!

1 μm = ~4 × 10^{-5} inches!

BACTERIA CELL STRUCTURE





4.4 A Prokaryotic Cell
The bacterium *Pseudomonas aeruginosa* illustrates typical prokaryotic cell structures. The electron micrograph on the left is magnified about 80,000 times. Note the existence of several protective structures external to the plasma membrane.

BACTERIA HAVE MUCH LESS DNA & FEWER GENES THAN HIGHER ORGANISMS

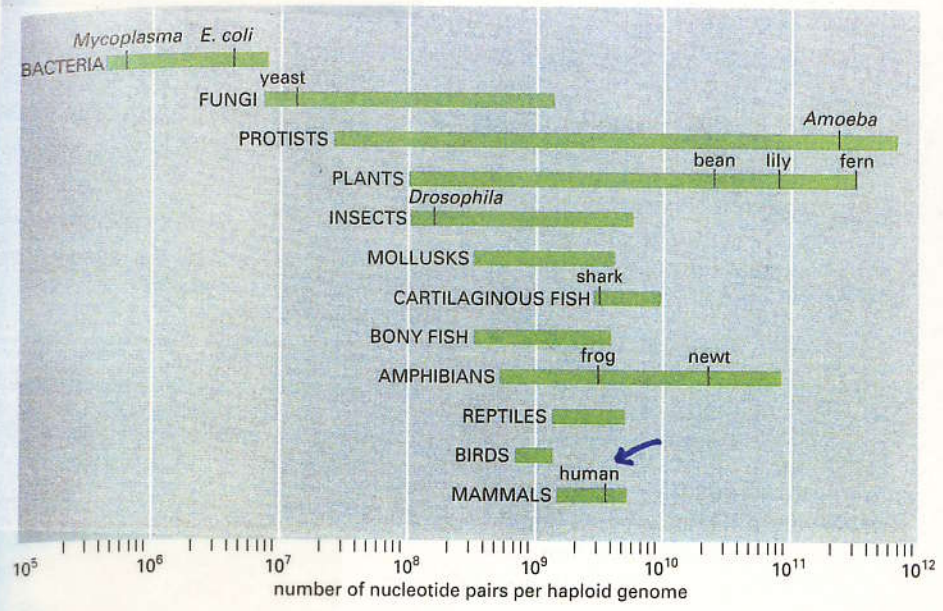


Figure 1–38 Genome sizes compared. Genome size is measured in nucleotide pairs of DNA per haploid genome, that is, per single copy of the genome. (The cells of sexually reproducing organisms such as ourselves are generally diploid: they contain two copies of the genome, one inherited from the mother, the other from the father.) Closely related organisms can vary widely in the quantity of DNA in their genomes, even though they contain similar numbers of functionally distinct genes. (Data from W.-H. Li, Molecular Evolution, pp. 380–383. Sunderland, MA: Sinauer, 1997.)

E. coli	4,600,000 bp	4300 genes
HUMANS	3,200,000,000 bp	35,000 genes

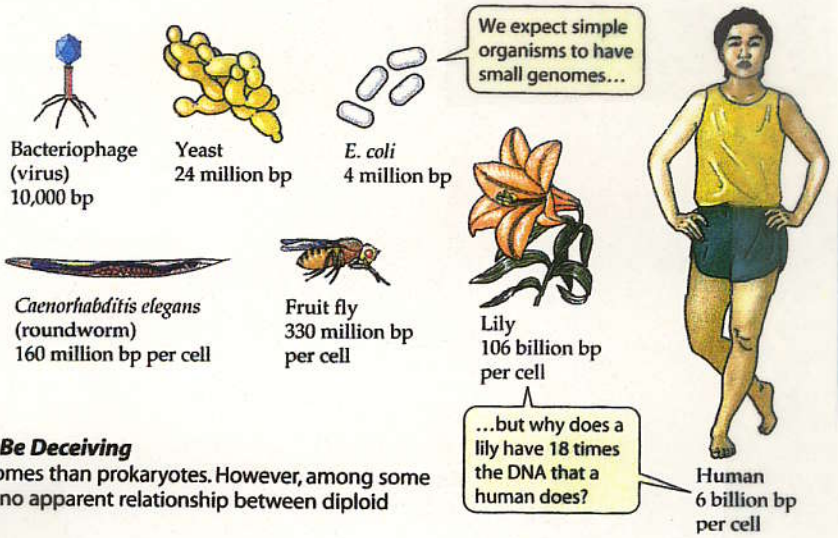
Note! HUMAN Genome ~ 1000x Larger than E. coli but only ~ 10x Larger # genes !!

Hypothesis?

How CAN some Plants Have More DNA than Humans?

Genome size & Gene Number Don't Always Correlate

Genome Size



14.1 Amounts of Genomic DNA Can Be Deceiving
Eukaryotes have more DNA in their genomes than prokaryotes. However, among some eukaryotes—especially plants—there is no apparent relationship between diploid genome size and organism complexity.

Gene # from sequencing Projects

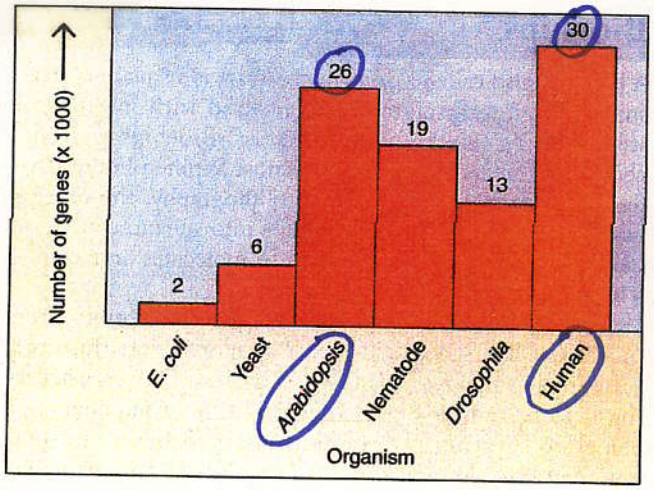


FIGURE 19.15
What the human genome is like. The human genome has an unexpectedly small number of genes, some 30,000. This is not many more than the plant *Arabidopsis*, and only a third more than nematode worms.

MANY, MANY BACTERIAL GENOMES HAVE BEEN SEQUENCED.

TABLE 1–1 Some Genomes That Have Been Completely Sequenced

SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	NUMBER OF GENES (PROTEINS)
	SEQUENCING POSSIBLE BECAUSE OF GENETIC ENGINEERING			
EUBACTERIA				
Mycoplasma genitalium	smallest genome of any known cell	human genital tract	580	468
Synechocystis sp.	photosynthetic, oxygen-generating (cyanobacterium)	lakes and streams	3573	3168
Escherichia coli	laboratory favorite	human gut	4639	4289
Helicobacter pylori	causes stomach ulcers and predisposes to stomach cancer	human stomach	1667	1590
Bacillus subtilis	bacterium	soil	4214	4099
Aquifex aeolicus	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
Mycobacterium tuberculosis	causes tuberculosis	human tissues	4447	4402
Treponema pallidum	spirochaete; causes syphilis	human tissues	1138	1041
Rickettsia prowazekii	bacterium most closely related to mitochondria; causes typhus	lice and humans (intracellular parasite)	1111	834
Thermotoga maritima	organotrophic; lives at high temperatures	hydrothermal vents	1860	1877
ARCHAEA				
Methanococcus jannaschii	lithotrophic, anaerobic, methane-producing	hydrothermal vents	1664	1750
Archaeoglobus fulgidus	lithotrophic or organotrophic, anaerobic, sulfate-reducing	hydrothermal vents	2178	2493
Aeropyrum pernix	aerobic, organotrophic hot-steam vents	coastal volcanic	669	2620
EUCARYOTES				
Saccharomyces cerevisiae (budding yeast)	minimal model eucaryote	grape skins, beer	12,069	~6300
Arabidopsis thaliana (wall cress)	model organism for flowering plants	soil and air	~142,000	~26,000
Caenorhabditis elegans (nematode worm)	simple animal with perfectly predictable development	soil	~97,000	~19,000
Drosophila melanogaster (fruit fly)	key to the genetics of animal development	rotting fruit	~137,000	~14,000
Homo sapiens (human)	most intensively studied mammal	houses	~3,200,000	~30,000

(+) Anthrax, cholera, diptheria, pneumonia, plague, leprosy, Lyme disease, syphilis, etc.

ANTHRAX!

180 as of today! 1/13/05

(+) Mouse, Rat, Chicken, Chimp, Cow

ONE OF THE MOST EXCITING AREAS OF BIOLOGY TODAY!

Bacterial Genes & Genomes Differ from Those of Higher organisms

14.1 A Comparison of Prokaryotic and Eukaryotic Genes and Genomes

CHARACTERISTIC	PROKARYOTES	EUKARYOTES
Genome size (base pairs)	10^4–10^7	10^8–10^{11}
Repeated sequences	Few	Many
Noncoding DNA within coding sequences	Rare	Common
Transcription and translation separated in cell	No	Yes
DNA segregated within a nucleus	No	Yes
DNA bound to proteins	Some	Extensive
Promoter	Yes	Yes
Enhancer/silencer	Rare	Common
Capping and tailing of mRNA	No	Yes
RNA splicing required	Rare	Common
Number of chromosomes in genome	One	Many

only in details – not overall chemical/DNA features

BACTERIA ARE HIGHLY DIVERSE CREATURES

Table 34.1 Bacteria

Major Group	Typical Examples		Key Characteristics
			ARCHAEBACTERIA
Archaebacteria	Methanogens, thermophiles, halophiles		Bacteria that are not members of the kingdom Eubacteria. Mostly anaerobic with unusual cell walls. Some produce methane. Others reduce sulfur.
			EUBACTERIA
Actinomycetes	*Streptomyces*, *Actinomyces*		Gram-positive bacteria. Form branching filaments and produce spores; often mistaken for fungi. Produce many commonly used antibiotics, including streptomycin and tetracycline. One of the most common types of soil bacteria; also common in dental plaque.
Chemoautotrophs	Sulfur bacteria, *Nitrobacter*, *Nitrosomonas*		Bacteria able to obtain their energy from inorganic chemicals. Most extract chemical energy from reduced gases such as H_2S (hydrogen sulfide), NH_3 (ammonia), and CH_4 (methane). Play a key role in the nitrogen cycle.
Cyanobacteria	*Anabaena*, *Nostoc*		A form of photosynthetic bacteria common in both marine and freshwater environments. Deeply pigmented; often responsible for "blooms" in polluted waters.
Enterobacteria	*Escherichia coli*, *Salmonella*, *Vibrio*		Gram-negative, rod-shaped bacteria. Do not form spores; usually aerobic heterotrophs; cause many important diseases, including bubonic plague and cholera.
Gliding and budding bacteria	Myxobacteria, *Chondromyces*		Gram-negative bacteria. Exhibit gliding motility by secreting slimy polysaccharides over which masses of cells glide; some groups form upright multicellular structures carrying spores called fruiting bodies.
Pseudomonads	*Pseudomonas*		Gram-negative heterotrophic rods with polar flagella. Very common form of soil bacteria; also contain many important plant pathogens.
Rickettsias and chlamydias	*Rickettsia*, *Chlamydia*		Small, gram-negative intracellular parasites. *Rickettsia* life cycle involves both mammals and arthropods such as fleas and ticks; *Rickettsia* are responsible for many fatal human diseases, including typhus (*Rickettsia prowazekii*) and Rocky Mountain spotted fever. Chlamydial infections are one of the most common sexually transmitted diseases.
Spirochaetes	*Treponema*		Long, coil-shaped cells. Common in aquatic environments; a parasitic form is responsible for the disease syphilis.

FACTORIES FOR Genetic Engineering

BACTERIA ARE AMONG THE MOST LETHAL ORGANISMS ON THE EARTH!

Table 34.2 Important Human Bacterial Diseases

Disease	Pathogen	Vector/Reservoir	Epidemiology
Anthrax	*Bacillus anthracis*	Animals, including processed skins	Bacterial infection that can be transmitted through contact or ingested. Rare except in sporadic outbreaks. May be fatal.
Botulism	*Clostridium botulinum*	Improperly prepared food	Contracted through ingestion or contact with wound. Produces acute toxic poison; can be fatal.
Chlamydia	*Chlamydia trachomatis*	Humans, STD	Urogenital infections with possible spread to eyes and respiratory tract. Occurs worldwide; increasingly common over past 20 years.
Cholera	*Vibrio cholerae*	Human feces, plankton	Causes severe diarrhea that can lead to death by dehydration; 50% peak mortality if the disease goes untreated. A major killer in times of crowding and poor sanitation; over 100,000 died in Rwanda in 1994 during a cholera outbreak.
Dental caries	*Streptococcus*	Humans	A dense collection of this bacteria on the surface of teeth leads to secretion of acids that destroy minerals in tooth enamel—sugar alone will not cause caries.
Diphtheria	*Corynebacterium diphtheriae*	Humans	Acute inflammation and lesions of mucous membranes. Spread through contact with infected individual. Vaccine available.
Gonorrhea	*Neisseria gonorrhoeae*	Humans only	STD, on the increase worldwide. Usually not fatal.
Hansen's disease (leprosy)	*Mycobacterium leprae*	Humans, feral armadillos	Chronic infection of the skin; worldwide incidence about 10–12 million, especially in Southeast Asia. Spread through contact with infected individuals.
Lyme disease	*Borrelia bergdorferi*	Ticks, deer, small rodents	Spread through bite of infected tick. Lesion followed by malaise, fever, fatigue, pain, stiff neck, and headache.
Peptic ulcers	*Helicobacter pylori*	Humans	Originally thought to be caused by stress or diet, most peptic ulcers now appear to be caused by this bacterium; good news for ulcer sufferers as it can be treated with antibiotics.
Plague	*Yersinia pestis*	Fleas of wild rodents: rats and squirrels	Killed ¼ of the population of Europe in the 14th century; endemic in wild rodent populations of the western U.S. today.
Pneumonia	*Streptococcus, Mycoplasma, Chlamydia*	Humans	Acute infection of the lungs, often fatal without treatment
Tuberculosis	*Mycobacterium tuberculosis*	Humans	An acute bacterial infection of the lungs, lymph, and meninges. Its incidence is on the rise, complicated by the development of new strains of the bacteria that are resistant to antibiotics.
Typhoid fever	*Salmonella typhi*	Humans	A systemic bacterial disease of worldwide incidence. Less than 500 cases a year are reported in the U.S. The disease is spread through contaminated water or foods (such as improperly washed fruits and vegetables). Vaccines are available for travelers.
Typhus	*Rickettsia typhi*	Lice, rat fleas, humans	Historically a major killer in times of crowding and poor sanitation; transmitted from human to human through the bite of infected lice and fleas. Typhus has a peak untreated mortality rate of 70%.

BOTOX

POTENTIAL BIOTERROR WEAPONS!

Gene engineering ??

e.g., antibiotic R anthrax!

HOW WAS DNA DEMONSTATED TO BE THE GENE?

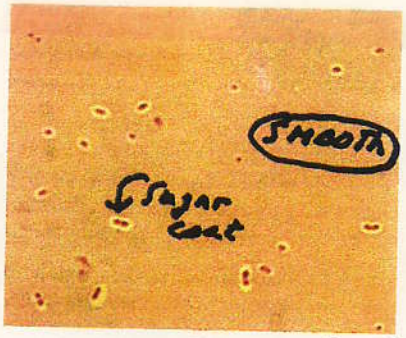
Genetic Engineering Begins!

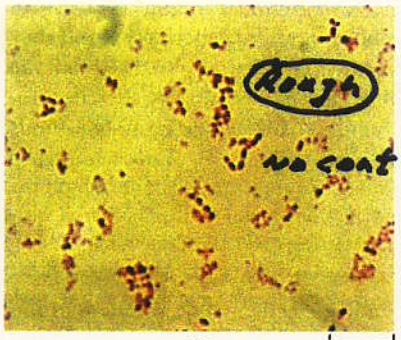
FIGURE 15.1
The unraveled chromosome of an *E. coli* bacterium. This complex tangle of DNA represents the full set of assembly instructions for the living organism *E. coli*.

IT'S ALL IN THE DNA!

1927!!

GRIFFITH'S PNEUMONIA BACTERIA EXPERIMENT





14–2 (a) *Encapsulated and* (b) *nonencapsulated forms of pneumococci. The capsule is made up of polysaccharides deposited outside the cell wall. The encapsulated form, which is resistant to phagocytosis by white blood cells, produces pneumonia; the mutant, nonencapsulated form is harmless.*

What is BASIS OF AVIRULENCE?

SMOOTH/VIRULENT STRAIN

ROUGH/AVIRULENT STRAIN

SPONTANEOUS MUTATION

~1927 GRIFFITH EXPERIMENT

Streptococcus pneumoniae – Genome Sequenced 2001 2.1 Mb 2236 genes

GRIFFITH'S DEMONSTRATION OF TRANSFORMATION

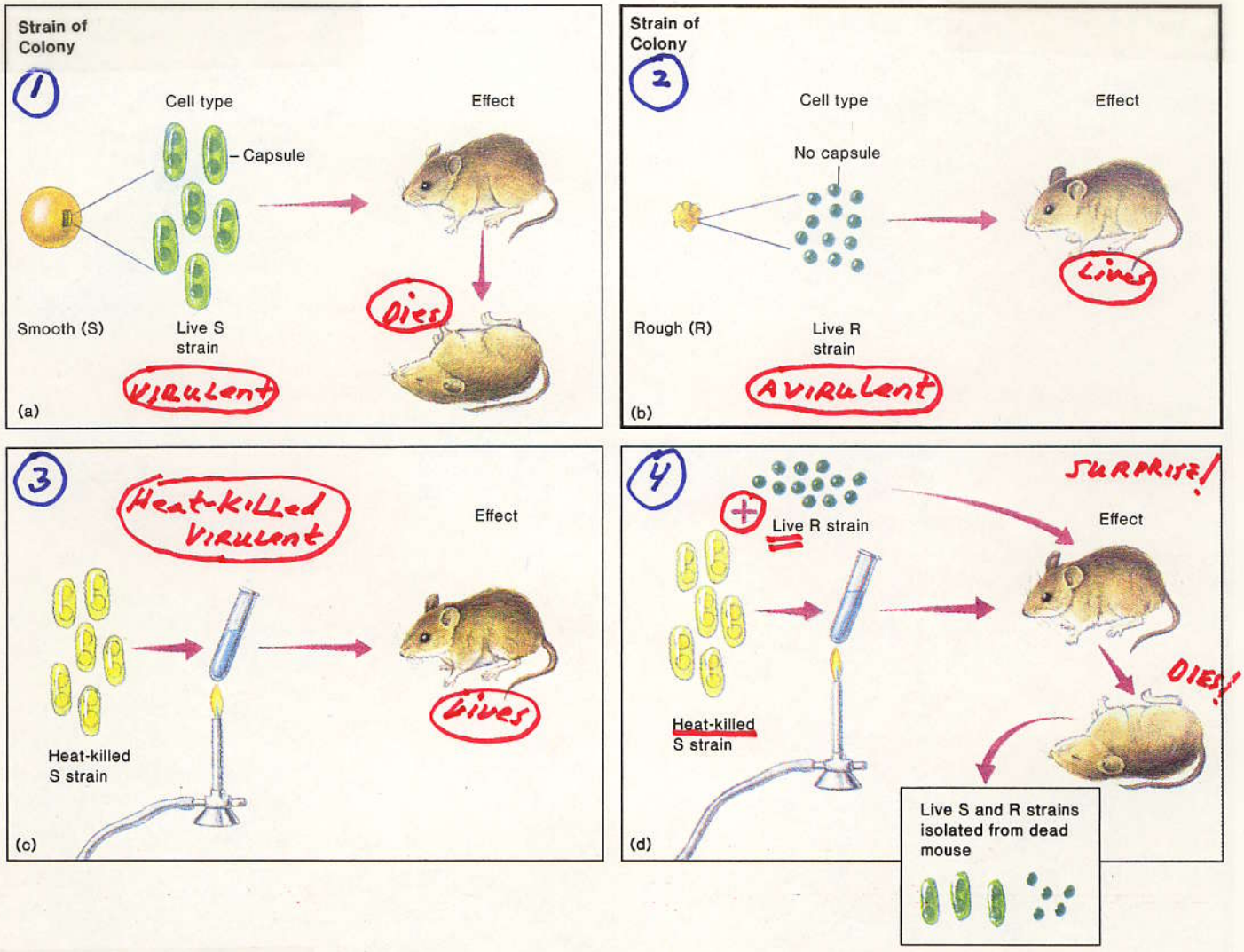
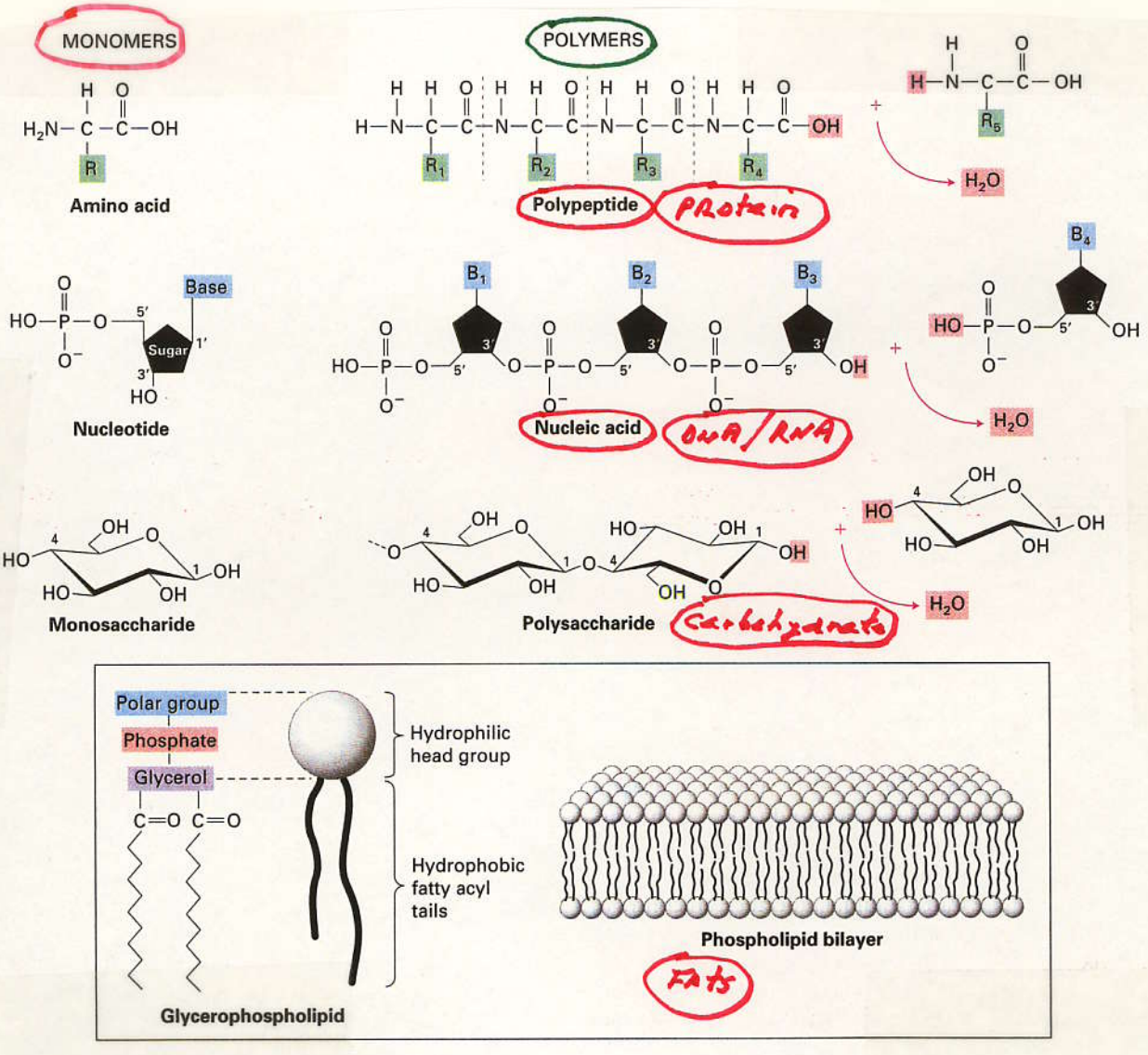


Figure 2.2 Griffith's transformation experiments. (**a**) Virulent strain S *S. pneumoniae* bacteria kill their host; (**b**) avirulent strain R bacteria cannot infect successfully, so the mouse survives; (**c**) strain S bacteria that are heat-killed can no longer infect; (**d**) a mixture of strain R and heat-killed strain S bacteria kills the mouse. The killed virulent (S) bacteria have transformed the avirulent (R) bacteria to virulent (S).

LIVE R WAS TRANSFORMED BY DEAD S!

HOW? What was the TRANSFORMING principle?

LARGE MOLECULES in CELLS HAVE different Structure



Chemistry → Biology!

What predict if DNA the Genetic Material?

LARGE MOLECULES IN ALL CELLS

Table 3.1 Macromolecules

Macromolecule	Subunit	Function	Example
PROTEINS			
Globular	Amino acids	Catalysis; transport	Hemoglobir
Structural	Amino acids	Support	Hair; silk
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
LIPIDS			
Fats	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Lecithin
Prostaglandins	Five-carbon rings with two nonpolar tails	Chemical messengers	Prostaglandin E (PGE)
Steroids	Four fused carbon rings	Membranes; hormones	Cholesterol; estrogen
Terpenes	Long carbon chains	Pigments; structural	Carotene; rubber
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells

Which is the TRANSFORMING PRINCIPLE?
and the Genetic Material?

(1) What is Predicted if DNA is the Genetic Material?

(2) How Test Hypothesis?

Los Angeles Times
latimes.com.

http://www.latimes.com/news/obituaries/la-me-mccarty8jan08,1,349784.story?coll=la-news-obituaries

OBITUARIES

Maclyn McCarty, 93; Helped Unlock the Secrets of DNA


Maclyn McCarty

By Thomas H. Maugh II
Times Staff Writer

January 8, 2005

Maclyn McCarty, the last surviving member of the trio of researchers who defied conventional wisdom by proving that our genetic blueprint is encoded in deoxyribonucleic acid — DNA — has died. He was 93.

McCarty died Sunday of congestive heart failure at a hospital in New York City, where he lived.

Surprisingly, the research team did not receive the Nobel Prize for its effort, which Nobel laureate Joshua Lederberg has called "the pivotal discovery of 20th century biology."

F the work laid the foundation for many other researchers who did receive the Nobel, beginning with James Watson a Francis Crick, who deciphered the structure of DNA only nine years after McCarty and his colleagues published their results.

Before McCarty began his work in 1941 with Oswald T. Avery and Colin M. MacLeod, all of whom were at Rockefeller University in New York City (then known as the Rockefeller Institute of Medical Research), most scientists thought genetic information was carried by proteins, long chains composed of at least 20 different amino acids.

DNA, which contained only four distinct chemical compounds called bases, was believed to be too simple to carry the complex information necessary for building even a bacterium, much less a human. Avery, MacLeod and McCarty put the lie to that argument.

The stage was set for their work in 1928 when British microbiologist Frederick Griffith discovered what was then called the "transforming principle." Griffith was studying two closely related strains of the bacterium *Streptococcus pneumoniae*. One of the strains, called S, killed mice when it infected them. The second strain, called R, did not.

Griffith found that when he mixed chemicals from the S strain with living R bacteria, the treated bacteria became the lethal S strain. Griffith called the chemicals the transforming principle, but we now recognize that he was transferring genes from the S strain to the R strain.

Avery and MacLeod began trying to identify what it was in the mixture of chemicals that produced the change. When MacLeod left Rockefeller in 1941, McCarty started working with Avery to finish solving the puzzle.

E use the rudimentary chemical techniques of the period would not allow them to isolate the transforming principle directly, they took a different approach. First, they took an enzyme that destroyed proteins and added it to the

15a

transforming principle. The R strains still became S, so proteins clearly did not carry genetic information.

Next, they used enzymes that destroyed ribonucleic acid — RNA — which a few scientists thought might carry genetic information. Again, R strains still became S. Eliminating proteins and RNA took more than a decade and led them to suspect that DNA, the only major component left, was the key molecule.

When McCarty joined the team, he isolated an enzyme that degraded DNA, the first such enzyme known. When they added this enzyme to the transforming principle, all its activity was destroyed. Hence, DNA carries genetic information. The three finally published their conclusion in February 1944, opening the door to the age of biotechnology.

McCarty was born June 9, 1911, in South Bend, Ind., where his father was an executive with the Studebaker Corp. The family moved frequently because of his father's job, and McCarty later attributed his inquiring mind to the diversity of people and places he encountered.

He studied biochemistry at Stanford, then got his medical degree at Johns Hopkins University, specializing in pediatrics. New antibiotics were coming into use during this period, and McCarty was one of the first physicians to save a child from a usually lethal streptococcus infection using the newly developed sulfonamide drugs. The encounter sparked a lifelong interest in infectious agents.

During World War II, he did research with the Naval Medical Research Unit at Rockefeller while completing his studies of the transforming principle.

He remained at Rockefeller the rest of his life, spending most of his time studying the structure of the streptococci bacteria that cause rheumatic fever. Over the next four decades, his team identified virtually every component in the cell wall structure of the streptococci, making them one of the best-characterized disease-causing bacteria.

He received a number of major awards over the years for his research and his organizational efforts in monitoring and responding to infectious diseases internationally.

In 1994, long after Avery and MacLeod died, McCarty finally received the Albert Lasker Award for Special Achievement in Medical Science, a prize some call the American Nobel.

McCarty recounted his research in his 1985 book, "The Transforming Principle: Discovering That Genes Are Made of DNA." He did not particularly lament that the team had not received a Nobel for its work, but he expressed disappointment that Watson and Crick had not cited the work in their 1953 paper describing DNA's structure.

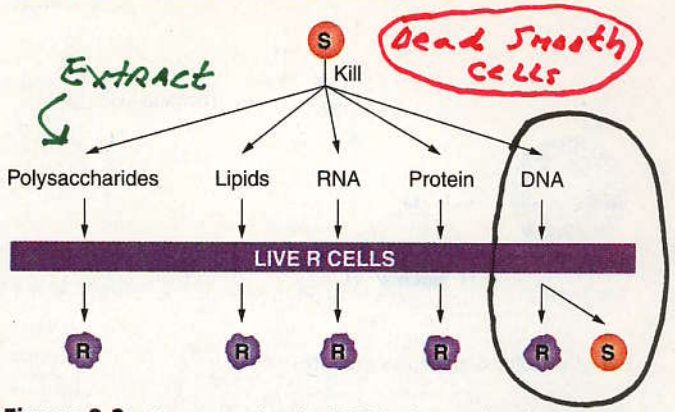
In 2003, Watson formally apologized for the omission. In his defense, Watson noted that by 1953, the idea of DNA carrying genetic information had become so widely accepted that it didn't seem necessary to acknowledge the earlier work.

McCarty is survived by his second wife, the former Marjorie Fried; sons Richard E. and Colin Avery; daughter Dale Dinunzio; eight grandchildren and five great-grandchildren.

FIRST "NAKED" DNA TRANSFORMATION OR Genetic Engineering Experiment!

Avery, McCleod, & McCarty Experiment SHOWING DNA is the Genetic Material

MESSAGE
The demonstration that DNA is the transforming principle was the first demonstration that genes are composed of DNA.



Add to Live Rough Cells →

Figure 8-2 Demonstration that DNA is the transforming agent. DNA is the only agent that produces smooth (S) colonies when added to live rough (R) cells.

1. Hypothesis?
2. Predictions?
3. Experiment?
4. Results?
5. Conclusions?

DNA from Dead Smooth/Virulent cells CAN TRANSFORM Live/Avirulent cells → LIVE VIRULENT CELLS

∴ DNA taken up by Live Smooth cells & CAUSES TRANSFORMATION

GRIFFITH & AVERY's Experiments Showing DNA is the Genetic Material

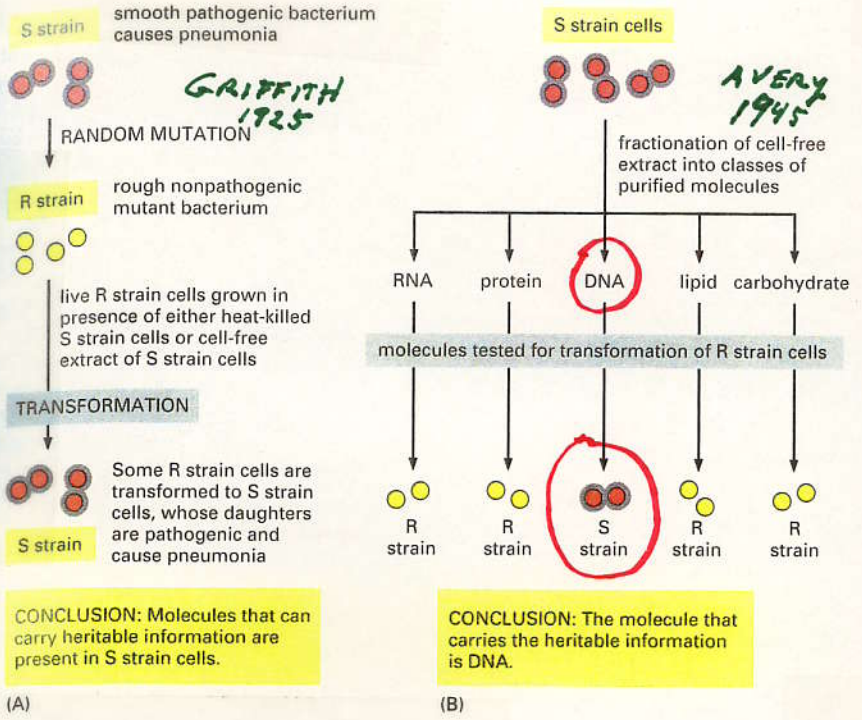


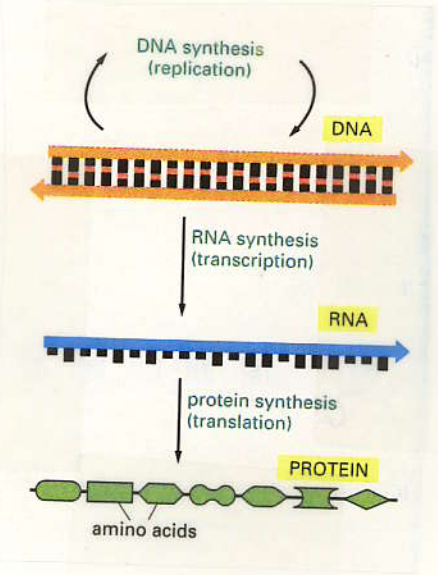
Figure 4–2 Experimental demonstration that DNA is the genetic material. These experiments, carried out in the 1940s, showed that adding purified DNA to a bacterium changed its properties and that this change was faithfully passed on to subsequent generations. Two closely related strains of the bacterium *Streptococcus pneumoniae* differ from each other in both their appearance under the microscope and their pathogenicity. One strain appears smooth (S) and causes death when injected into mice, and the other appears rough (R) and is nonlethal. (A) This experiment shows that a substance present in the S strain can change (or transform) the R strain into the S strain and that this change is inherited by subsequent generations of bacteria. (B) This experiment, in which the R strain has been incubated with various classes of biological molecules obtained from the S strain, identifies the substance as DNA.

Hypothesis?
Predictions?
Experiment to test!

Watson + Crick

HOW DID AVERY'S EXPERIMENT VERIFY THE HYPOTHESIS THAT DNA IS THE GENE?

Predictions	Results
Replication	yes
Phenotype	yes
Stable	yes



CELL PROCESSES

S DNA Taken up by R cells

S "gene"

TRANSCRIPTION

S "RNA"

TRANSLATION

S "protein"

Smooth / virulent cell

Phenotype

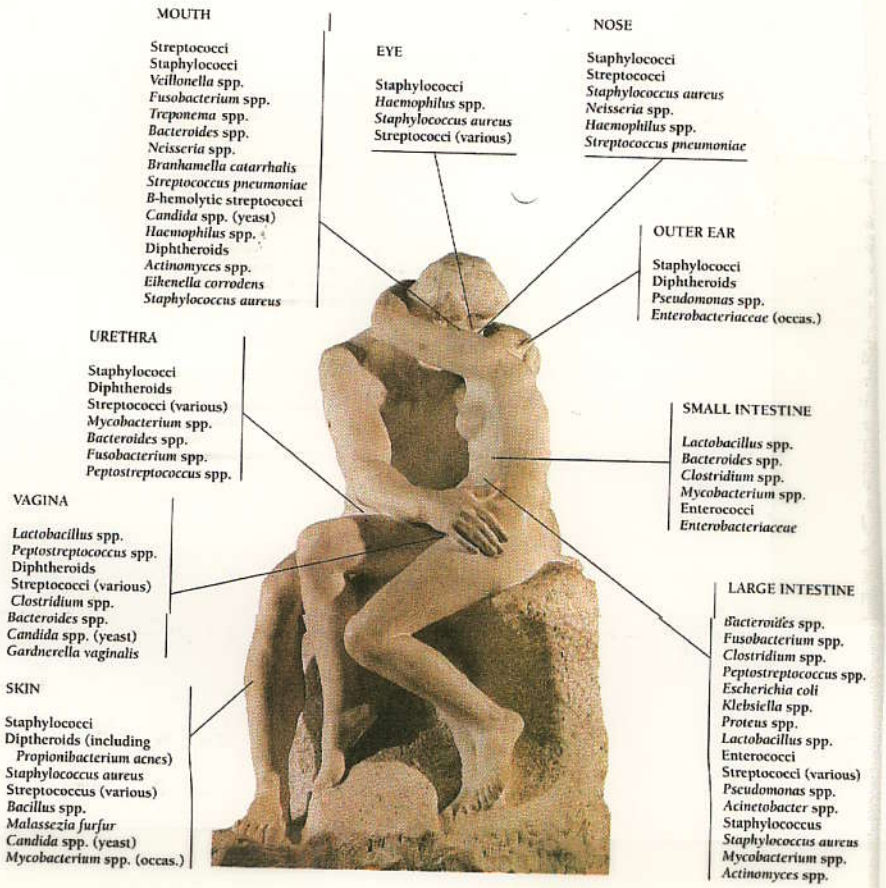
TRANSFORMATION used as a Genetic Engineering Process to Present Day!

TRANSFORMATION ? Ability of a cell phenotype to be changed / transformed by DNA!

ORIGIN OF TERM FROM GRIFFITH'S 1920's EXPERIMENT!

CAN BACTERIA BE TRANSFORMED WITH OTHER GENES/TRAITS?

Figure 20-3 **Microorganisms that normally inhabit the human body.** All of the microorganisms listed here live—usually harmoniously—on the surfaces and in the interiors of human bodies. *Candida albicans*, commonly known as yeast, is a fungus that lives on the skin and in the mouth and vagina. *Candida* is, of course, a eukaryote, not a prokaryote. *(Erich Lessing/Art Resource)*



What are Antibiotics?

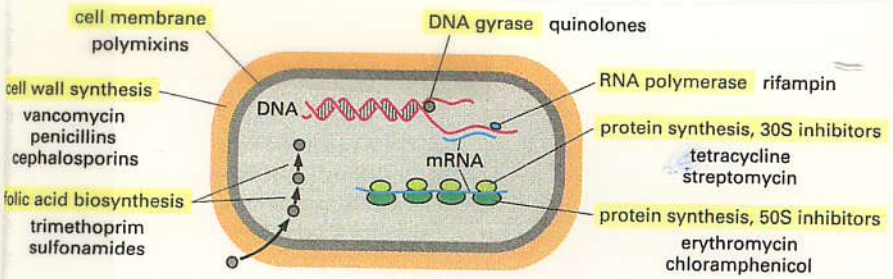
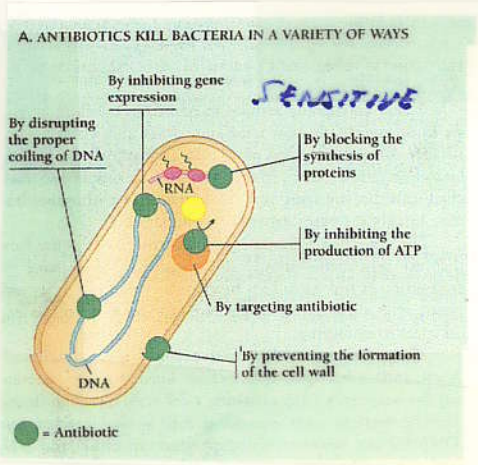


Figure 25–8 Antibiotic targets. Despite the large number of antibiotics available, they have a narrow range of targets, which are highlighted in *yellow*. A few representative antibiotics in each class are listed. All antibiotics used to treat human infections fall into one of these categories. The vast majority inhibit either bacterial protein synthesis or bacterial cell wall synthesis.



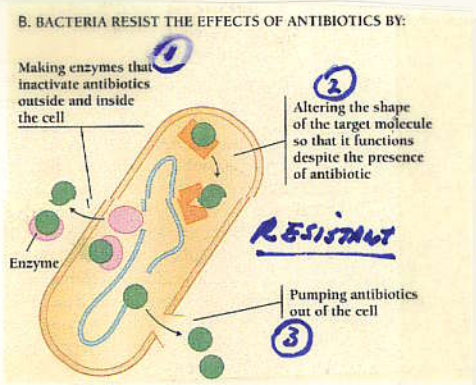


Figure 20-5 How does it work? A. Every antibiotic has a distinctive way of preventing bacteria from reproducing. B. Bacteria have different ways of resisting the effects of antibiotics.

TARGET
1. Cell Wall Synthesis
2. DNA Replication
3. Gene Activity

OR Vital cell Processes!

Antibiotic Resistance is Encoded by Genes on Xtra chromosomal DNA called PLASMIDS

Made by fungi + other bacteria!

The FIRST Genetic Engineering Experiment used Antibiotic Resistance

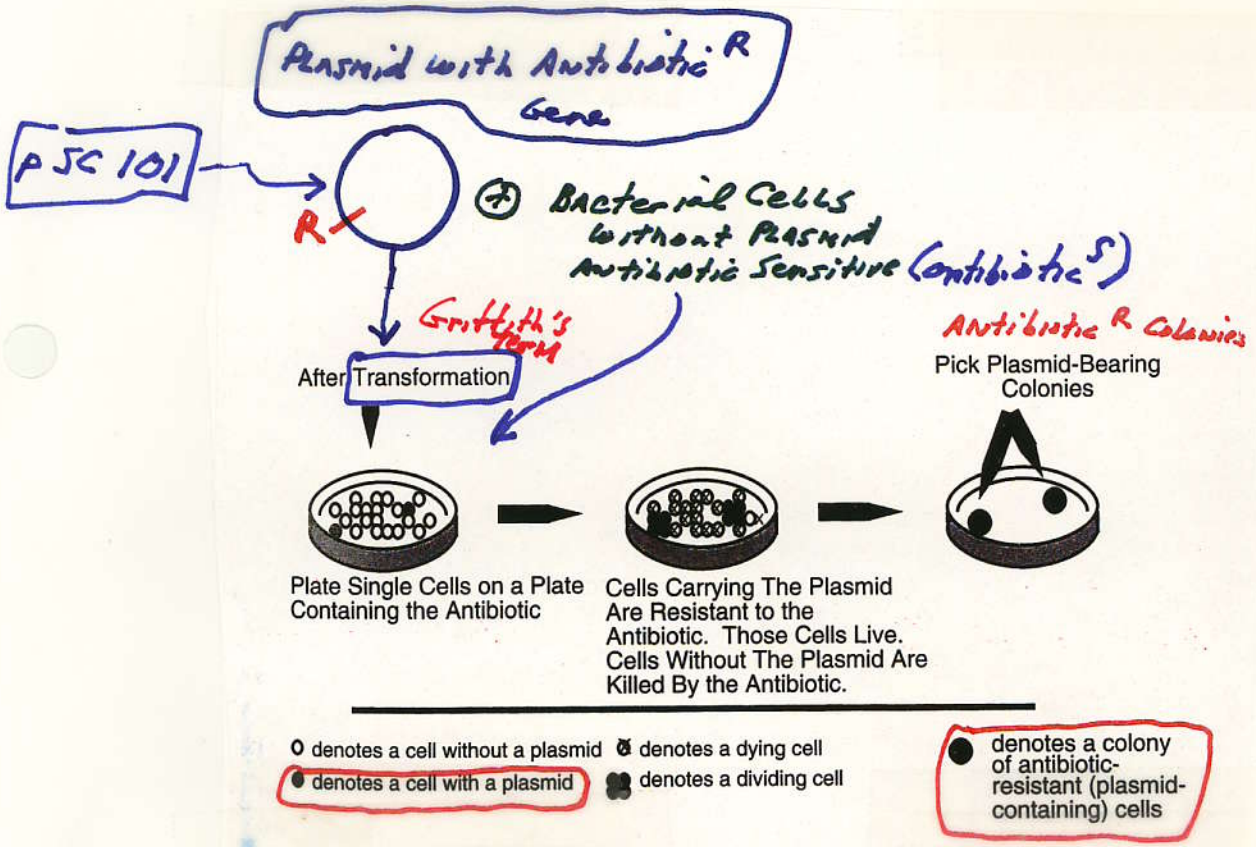


FIGURE 12.3 The process of transformation.

DNA^R → S → $^{S^R}$ → Antibiotic^R Phenotype!

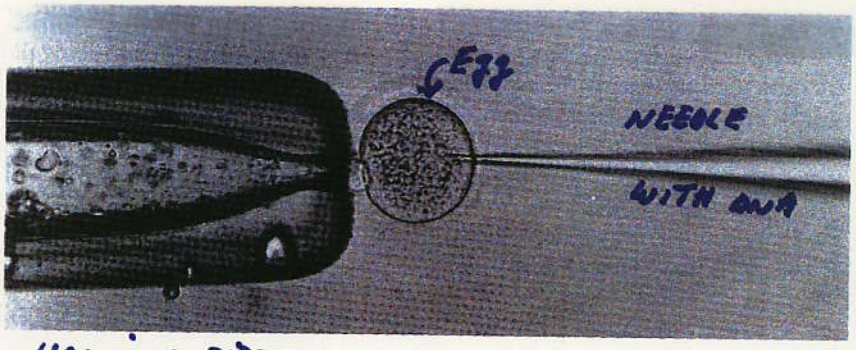
Antibiotic^R DNA + Antibiotic^S CELLS

TRANSFORMATION → Antibiotic^R cells

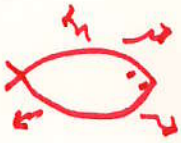
Stanley Cohen & Herb Boyer → 1973

HOW SHOW DNA Genetic Material?

CAN Higher Organisms BE TRANSFORMED?
Genetically Engineered?



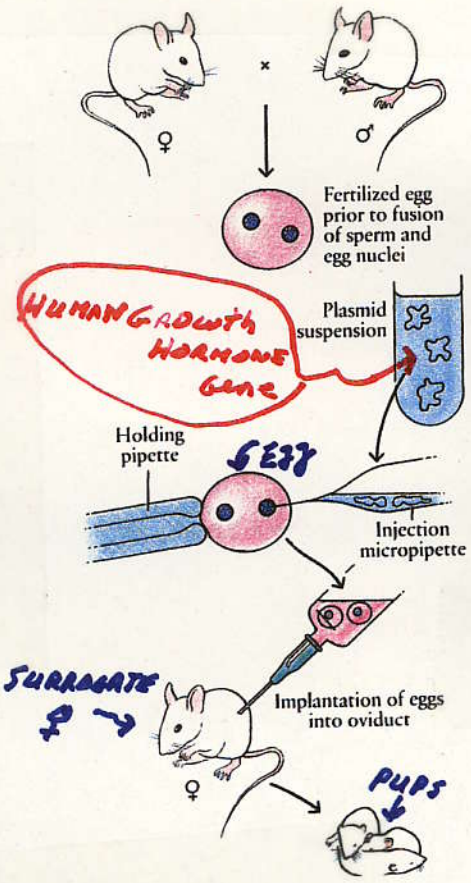
HOLDING PIPET (b)

Recall GLO Fish  Experiment!

GLO Fly
GLO Mouse
GLO Plant !!
GLO Monkey

DNA → Specifies TRAIT
↳ Replicates

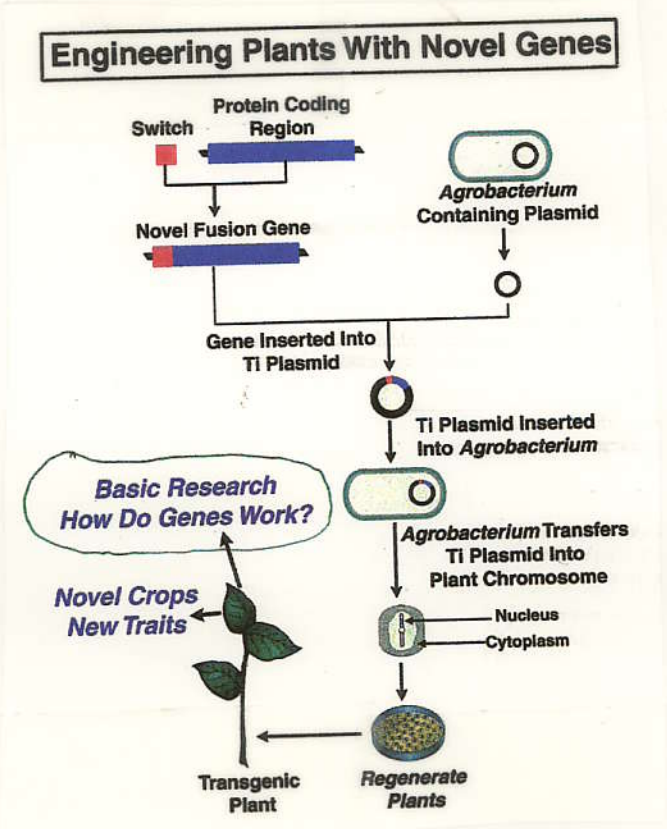
THE MAKING OF A MIGHTY MOUSE!



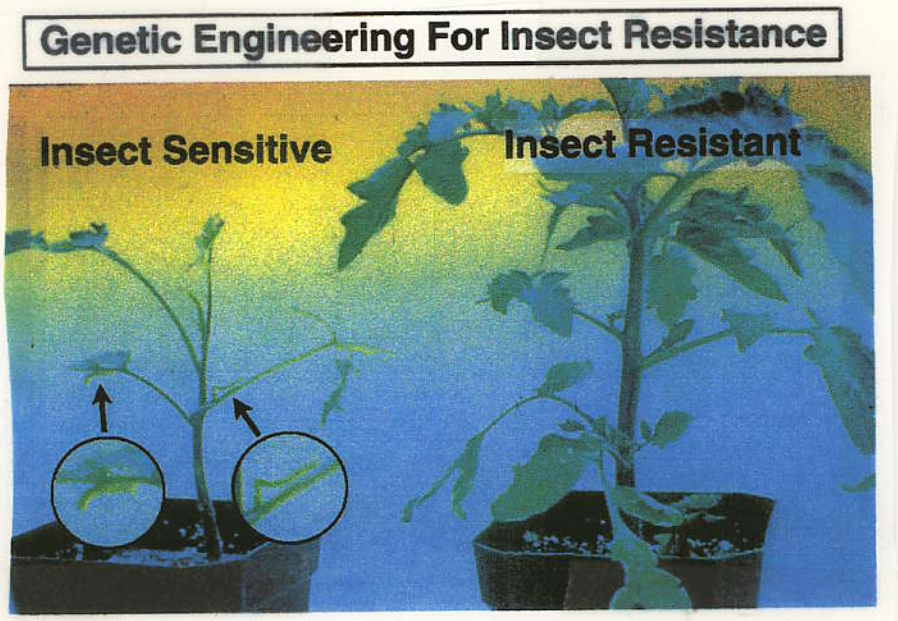
DNA → Growth Hormone → Mighty Mouse Phenotype

Yo! It's all in the DNA

CAN PLANTS BE Genetically Engineered OR TRANSFORMED WITH DNA?



The MAKING OF AN Insect Resistant PLANT



Bacteria Insect (R) Gene / DNA → PLANT cells → PLANT (I)

∴ DNA is the genetic material of all organisms

Bacteria → Animals + PLANTS

DEMONSTRATIONS

Bacteria "Cloning"

Gel Electrophoresis

NATURAL PROCESSES!

Genetic Engineering / TRANSFORMATION Involves INCORPORATING Engineered DNA or Genes Into Different ORGANISMS

genotype

phenotype

Engineered Gene MUST

1. Enter Target Cell
2. Use Target Cell Machinary enzymes to become Part of Chromosome
3. Replicate with target cell Chromosome
4. Use Target Cell Protein Synthesis Machinary to make a New Protein → Phenotype trait!

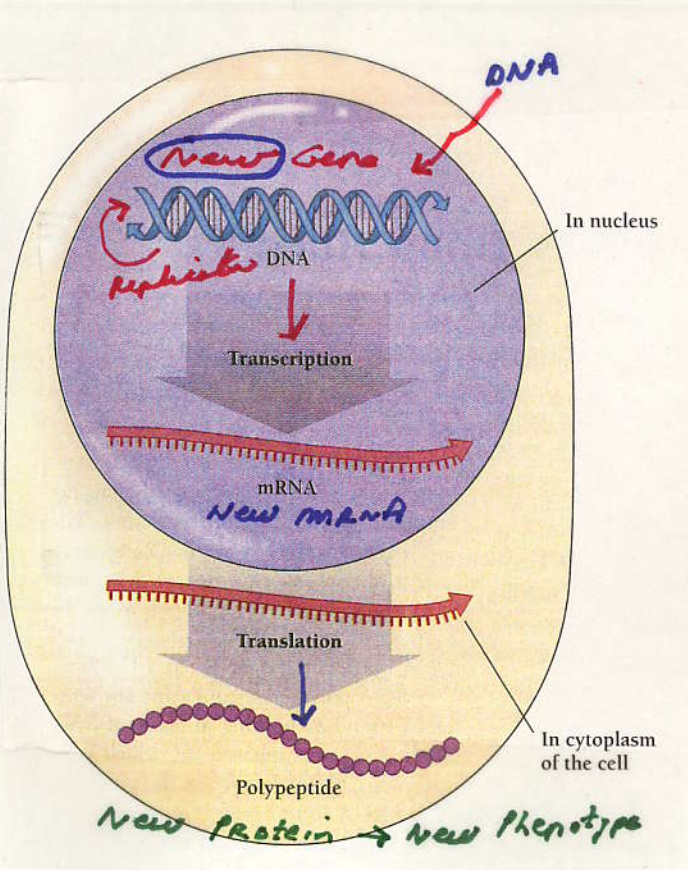
Engineered Gene Can Be

1. From Same Organism
2. From Different Organism
3. From a Combination of organisms stitched together by genetic engineering

Gene Engineering Shows that Gene Processes Are Universal!

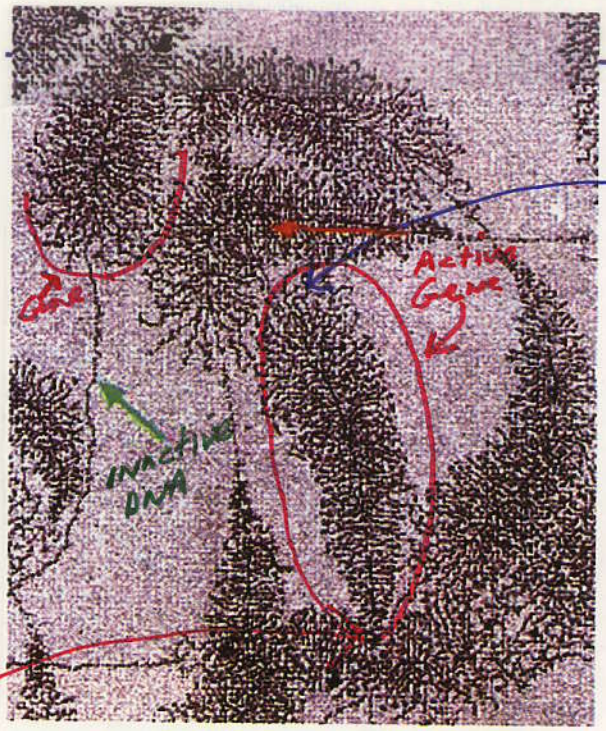
JUST Like the GloGene Experiments!!!

Genetic Engineering Does not Involve Any "Hocus Pocus"



IT's ALL in the DNA & CELL PROCESSES - ultimate in "Organic" Biology

What are Genes?

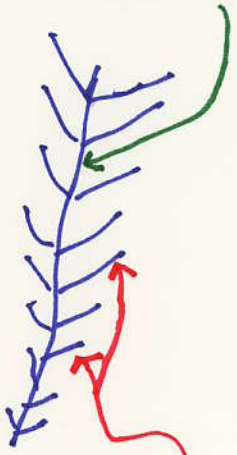


Electron micrograph of DNA (green arrow) being transcribed into RNA (red arrow). [O. L. Miller, Jr., and Barbara R. Beatty, Oak Ridge National Laboratory.]

Beginning

Visualization of a Gene in Action

What is this?



What are these ?

How Test?

What is a Gene?

Begin 5'

```
CCCTGTGGAGCCACACCCTAGGGTTGGCCA
ATCTACTCCCAGGAGCAGGGAGGGCAGGAG
CCAGGGCTGGGCATAAAAGTCAGGGCAGAG
CCATCTATTGCTTACATTTGCTTCTGACAC
AACTGTGTTCACTAGCAACTCAAACAGACA
CCATGGTGCACCTGACTCCTGAGGAGAAGT
CTGCCGTTACTGCCCTGTGGGGCAAGGTGA
ACGTGGATGAAGTTGGTGGTGAGGCCCTGG
GCAGGTTGGTATCAAGGTTACAAGACAGGT
TTAAGGAGACCAATAGAAACTGGGCATGTG
GAGACAGAGAAGACTCTTGGGTTTCTGATA
GGCACTGACTCTCTCTGCCTATTGGTCTAT
TTTCCCACCCTTAGGCTGCTGGTGGTCTAC
CCTTGGACCCAGAGGTTCTTTGAGTCCTTT
GGGGATCTGTCCACTCCTGATGCTGTTATG
GGCAACCCTAAGGTGAAGGCTCATGGCAAG
AAAGTGCTCGGTGCCTTTAGTGATGGCCTG
GCTCACCTGGACAACCTCAAGGGCACCTTT
GCCACACTGAGTGAGCTGCACTGTGACAAG
CTGCACGTGGATCCTGAGAACTTCAGGGTG
AGTCTATGGGACCCTTGATGTTTTCTTTCC
CCTTCTTTTCTATGGTTAAGTTCATGTCAT
AGGAAGGGGAGAAGTAACAGGGTACAGTTT
AGAATGGGAAACAGACGAATGATTGCATCA
GTGTGGAAGTCTCAGGATCGTTTTAGTTTC
TTTTATTTGCTGTTCATAACAATTGTTTTC
TTTTGTTTAATTCTTGCTTTCTTTTTTTTT
CTTCTCCGCAATTTTTACTATTATACTTAA
TGCCTTAACATTGTGTATAACAAAAGGAAA
TATCTCTGAGATACATTAAGTAACTTAAAA
AAAAACTTTACACAGTCTGCCTAGTACATT
ACTATTTGGAATATATGTGTGCTTATTTGC
ATATTCATAATCTCCCTACTTTATTTTCTT
TTATTTTTAATTGATACATAATCATTATAC
ATATTTATGGGTTAAAGTGTAATGTTTTAA
TATGTGTACACATATTGACCAAATCAGGGT
AATTTTGCATTTGTAATTTTAAAAAATGCT
TTCTTCTTTTAATATACTTTTTTGTTTATC
TTATTTCTAATACTTTCCCTAATCTCTTTC
TTTCAGGGCAATAATGATACAATGTATCAT
GCCTCTTTGCACCATTCTAAAGAATAACAG
TGATAATTTCTGGGTTAAGGCAATAGCAAT
ATTTCTGCATATAAATATTTCTGCATATAA
ATTGTAACTGATGTAAGAGGTTTCATATTG
CTAATAGCAGCTACAATCCAGCTACCATTC
TGCTTTTATTTTATGGTTGGGATAAGGCTG
GATTATTCTGAGTCCAAGCTAGGCCCTTTT
GCTAATCATGTTCATACCTCTTATCTTCCT
CCCACAGCTCCTGGGCAACGTGCTGGTCTG
TGTGCTGGCCCATCACTTTGGCAAAGAATT
CACCCCACCAGTGCAGGCTGCCTATCAGAA
AGTGGTGGCTGGTGTGGCTAATGCCCTGGC
CCACAAGTATCACTAAGCTCGCTTTCTTGC
TGTCCAATTTCTATTAAAGGTTCCTTTGTT
CCCTAAGTCCAACTACTAAACTGGGGGATA
TTATGAAGGGCCTTGAGCATCTGGATTCTG
CCTAATAAAAAACATTTATTTTCATTGCAA
TGATGTATTTAAATTATTTCTGAATATTTT
ACTAAAAAGGGAATGTGGGAGGTCAGTGCA
TTTAAAACATAAAGAAATGATGAGCTGTTC
AAACCTTGGGAAAATACACTATATCTTAAA
CTCCATGAAAGAAGGTGAGGCTGCAACCAG
CTAATGCACATTGGCAACAGCCCCTGATGC
CTATGCCTTATTCATCCCTCAGAAAAGGAT
TCTTGTAGAGGCTTGATTTGCAGGTTAAAG
TTTTGCTATGCTGTATTTTACATTACTTAT
TGTTTTAGCTGTCCTCATGAATGTCTTTTC
```

End 3'

Sequence or order of Nucleotides coding DNA strand

The β-globin Gene

Blood protein carries Oxygen to ALL cells from Lungs → Energy

A gene is a unique sequence of Nucleotides specifying A function

SEQUENCE = BIOLOGY!

What if Sequence changed?

SEQUENCE ↓ FUNCTION

Relative to coding OR Sense STRAND of Gene

Genes + Genomes Differ
Because the Sequence
of DNA Differs

DNA Sequence

Beginning → End → Biological Uniqueness

5' 3'

If you know the DNA Sequence, you can
Engineer Anything! / Even Make
New Genes + Genomes!

DNA and Genes Consist of Nucleotides Joined By Bonds

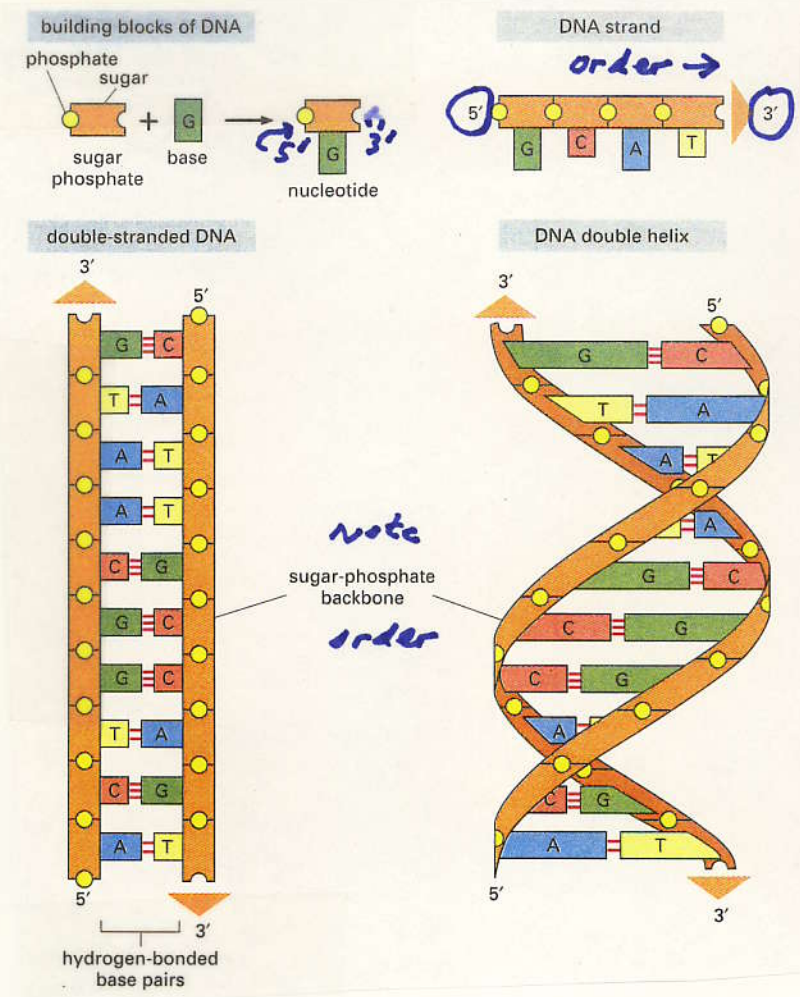


Figure 4–3 DNA and its building blocks. DNA is made of four types of nucleotides, which are linked covalently into a polynucleotide chain (a DNA strand) with a sugar-phosphate backbo from which the bases (A, C, G, and T) extend. A DNA molecule is composed two DNA strands held together by hydrogen bonds between the paired ba The *arrowheads* at the ends of the DNA strands indicate the polarities of the tw strands, which run antiparallel to each other in the DNA molecule. In the diagram at the bottom left of the figure, the DNA molecule is shown straightene out; in reality, it is twisted into a double helix, as shown on the right. For details, see Figure 4–5.

① A Nucleotide = Sugar + base + phosphate

② Nucleotides are Linked IN ORDER 5′→3′ by Phosphodiester Bonds

A Review

NUCLEOTIDES HAVE POLARITY

5'P Beginning →

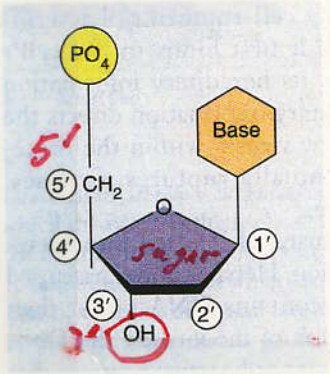


FIGURE 14.7
Numbering the carbon atoms in a nucleotide. The carbon atoms in the sugar of the nucleotide are numbered 1′ to 5′, proceeding clockwise from the oxygen atom. The "prime" symbol (′) indicates that the carbon belongs to the sugar rather than the base.

3'OH End →

BASED ON what is bonded to Sugar

The Sugar is the Hub !!

ORder of DNA defined by nucleotide
↳ DNA Sequence
↳ Biology

NUCLEOTIDES ARE JOINED by Phosphodiester Bonds

5' ORDER

B_1
↓
B_2

3'

Defined by sugars!!

Specified by Bases!

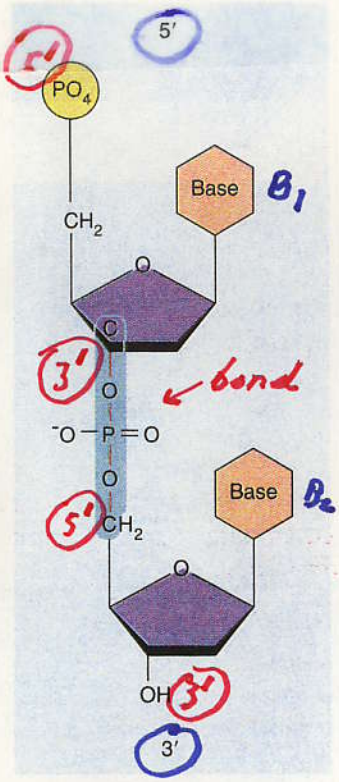


FIGURE 14.8
A phosphodiester bond.

The order is specified by the nucleotides which join 5'→3'

Basis of all Genetics & Genetic Engineering

Order = Biology!

ORDER IS MAINTAINED DURING REPLICATION

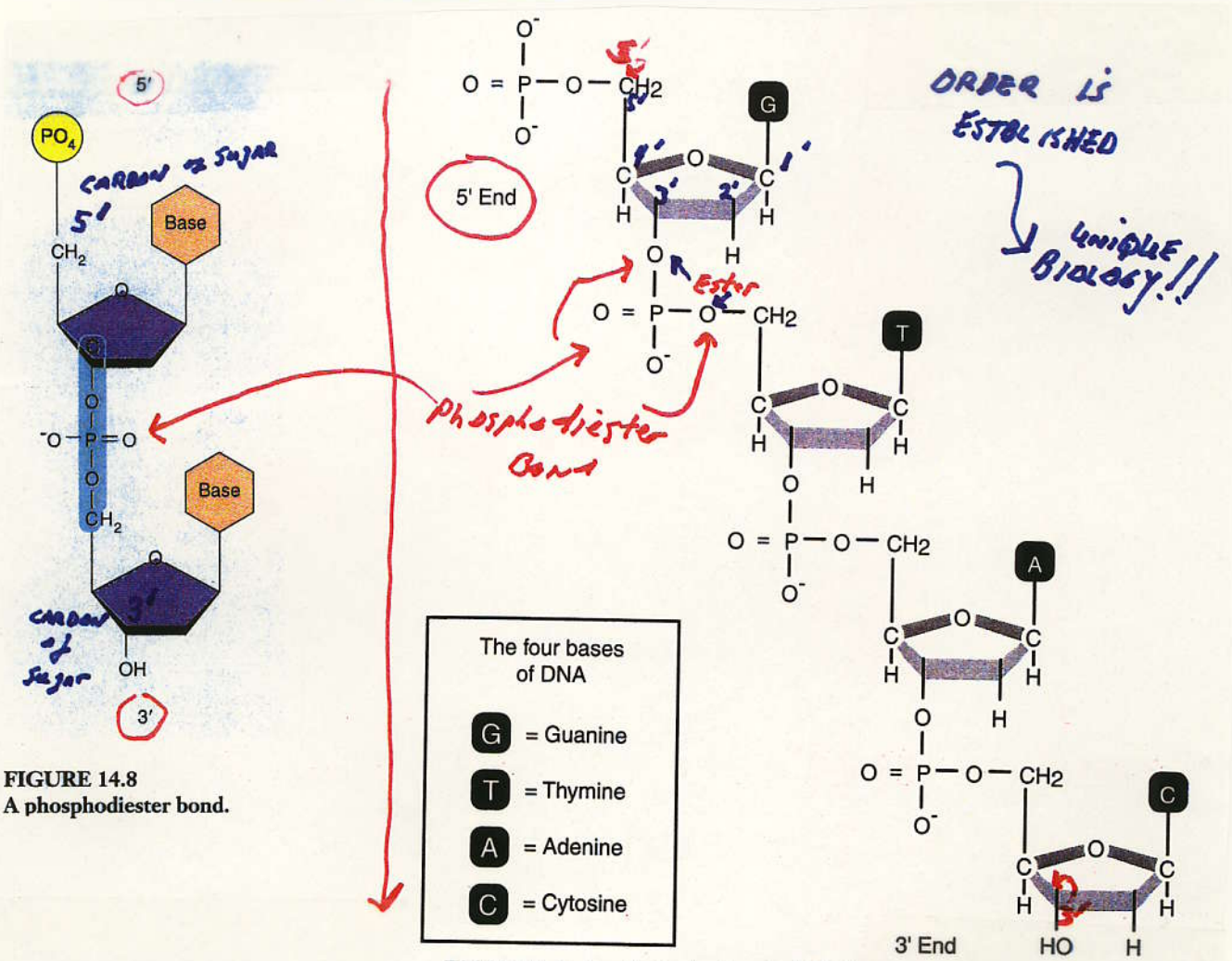


FIGURE 14.8
A phosphodiester bond.

FIGURE 3.1 A single strand of DNA composed of four nucleotides.

BASIS OF A CELL generating the same cell!

U Replaces T in RNA

ribose replaces deoxyribose

There Are FOUR Nucleotides in DNA

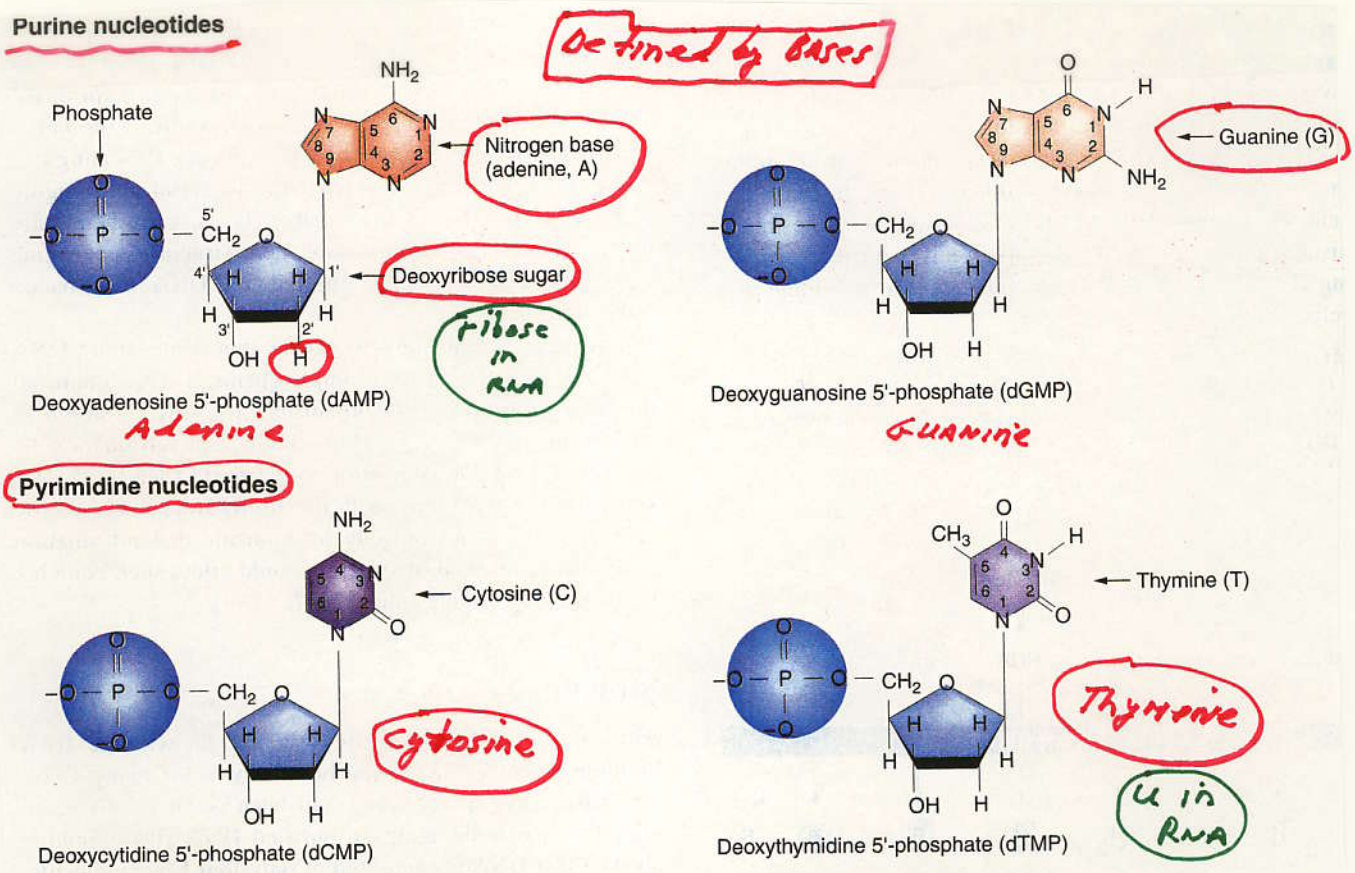
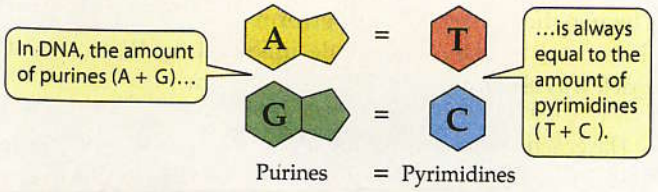


Figure 8-4 Chemical structure of the four nucleotides (two with purine bases and two with pyrimidine bases) that are the fundamental building blocks of DNA. The sugar is called *deoxyribose* because it is a variation of a common sugar, ribose, that has one more oxygen atom.

Chemistry → Biology
Know order of Bases → DO anything!

Purines = Pyrimidines in DNA
Chargaff's Rules

A = T
G = C



11.5 Chargaff's Rule
The total abundances of purines and pyrimidines are equal in DNA.

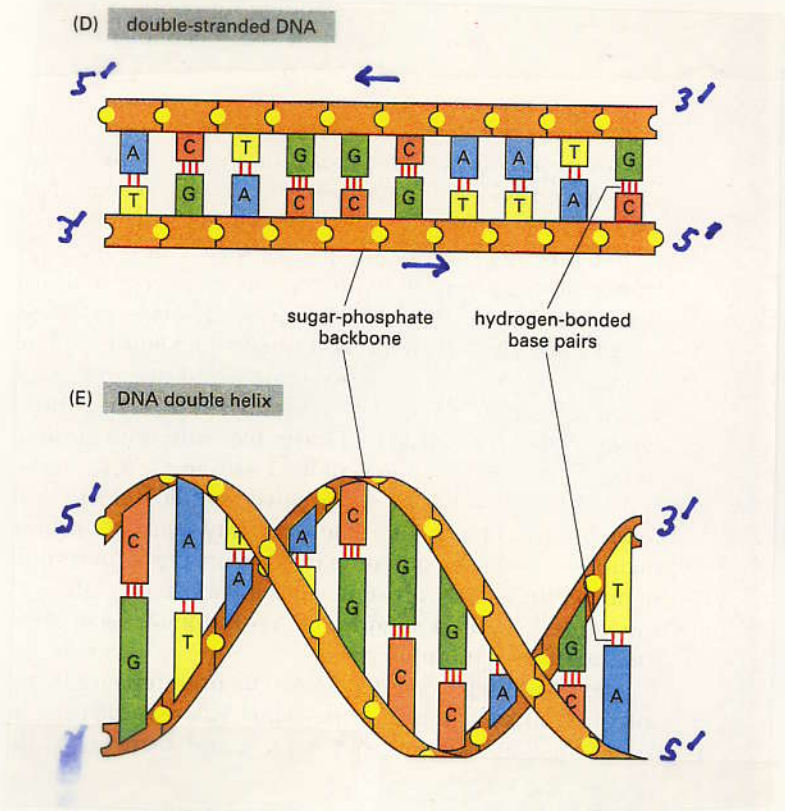
11.1 Percentages of Bases in the DNA of Some Well-Studied Species

DNA ORIGIN	AMOUNT OF BASE (PERCENTAGE OF TOTAL DNA) A	T	G	C
Human (*Homo sapiens*)	31.0	31.5	19.1	18.4
Corn (*Zea mays*)	25.6	25.3	24.5	24.6
Fruit fly (*Drosophila melanogaster*)	27.3	27.6	22.5	22.5
Bacterium (*Escherichia coli*)	26.1	23.9	24.9	25.1

What would you predict for a single strand of DNA?

Chargaff's Rules!

DNA IS A DOUBLE HELIX OF TWO COMPLEMENTARY CHAINS OF DNA WOUND AROUND EACH OTHER



1. Complementary strands
2. A = T, G ≡ C (H-bonds)
3. Sequence of strands differs
4. Bases to interior
5. phosphate/sugar backbone
6. STRANDS in opposite direction only way chains fit together

WATSON & CRICK 1953

ONLY WAY MOLECULE "FITS" TOGETHER!

SEQUENCE OF ONE CHAIN AUTOMATICALLY SPECIFIES SEQUENCE OF COMPLEMENTARY CHAIN

BASIS OF GENETICS!

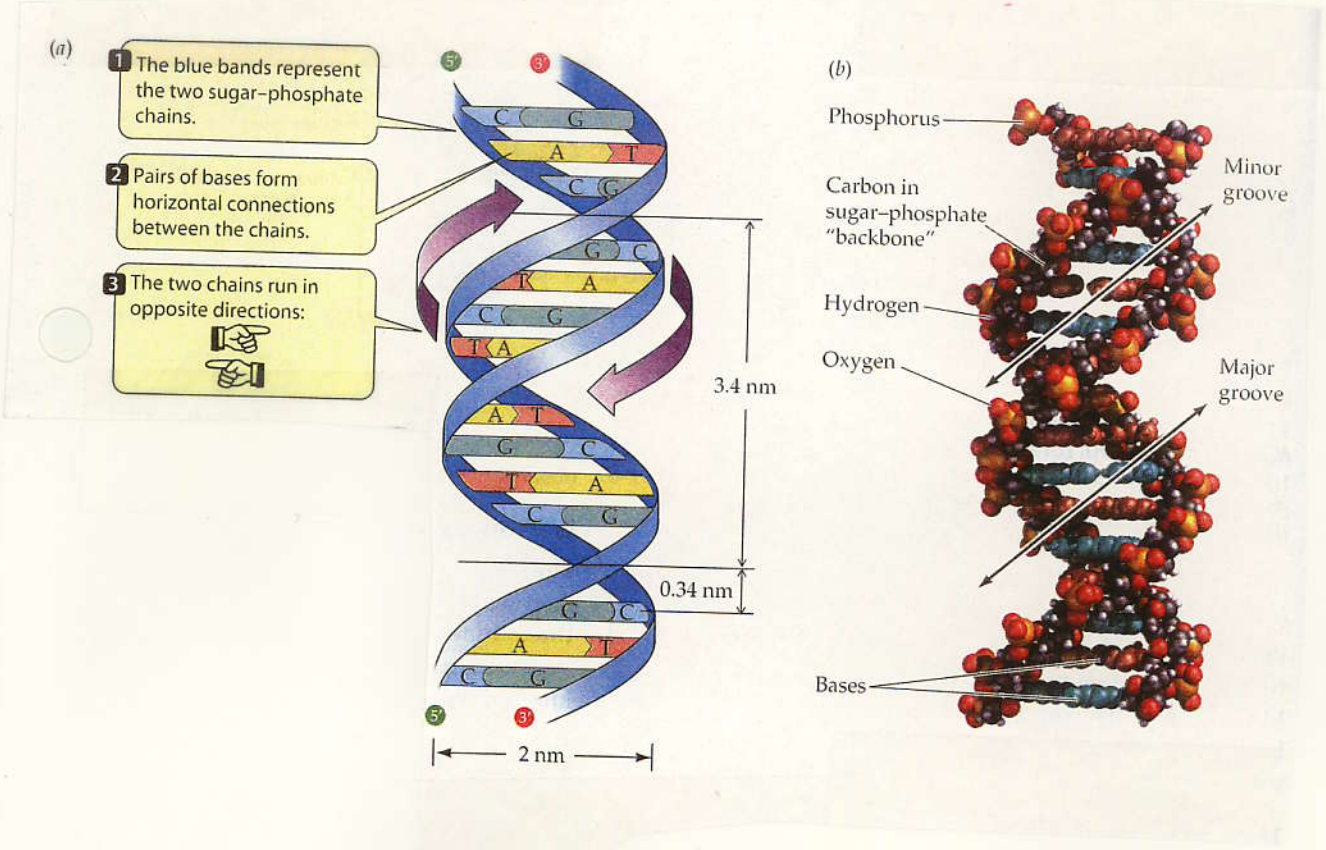
Properties of DNA

1. Four different nucleotides
2. Nucleotides linked by Phosphodiester Bonds
3. Nucleotides linked in order 5'→3'
4. Two chains complementary in antiparallel direction
   5' ⟹ 3'
   3' ⟸ 5'
   sequence differs * only way bases fit in "middle"
5. Bases in interior stacked & bonded by H-bonds – complementary "rungs" on "ladder"
6. Backbone – sugar-/phosphate bonds
7. No constraint on sequence $4^n = n$ #sequences
8. DNA has dimensions:
   - 20Å diameter
   - 3.4Å/bp
   - 10bp/turn

   Know #bp ∴ know length!
9. order → Biology

FROM X-Ray Diffraction Pictures

The Double Helix



READ BOOK/TEXT BY SAME NAME!

A Chromosome Contains ONE (or two!) continuous DNA Molecule

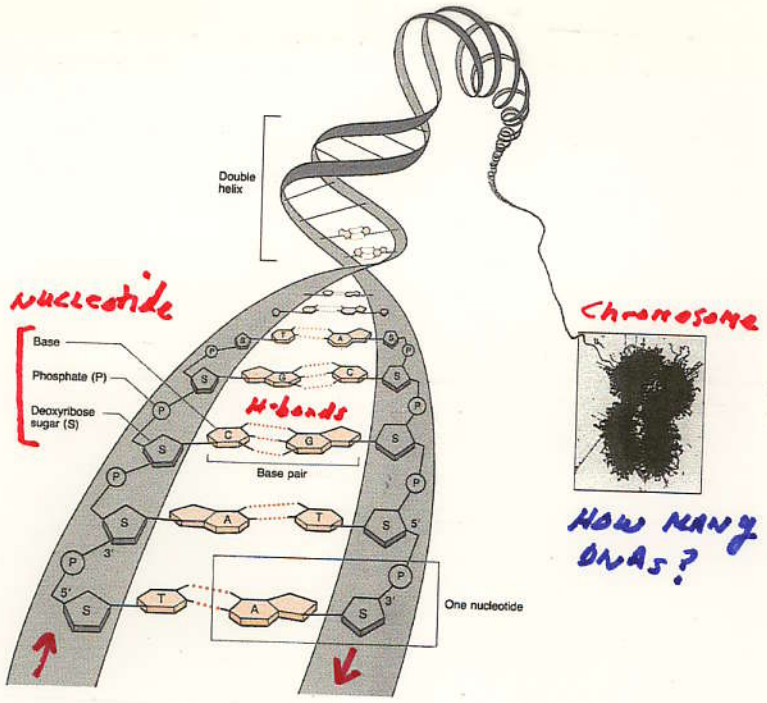


Figure 2.5 The arrangement and association of nucleotides in the DNA double helix.

DNA in Higher Organisms is Linear!
DNA in Bacteria is Circular!

The Circular E. coli Chromosome
One DNA Circle

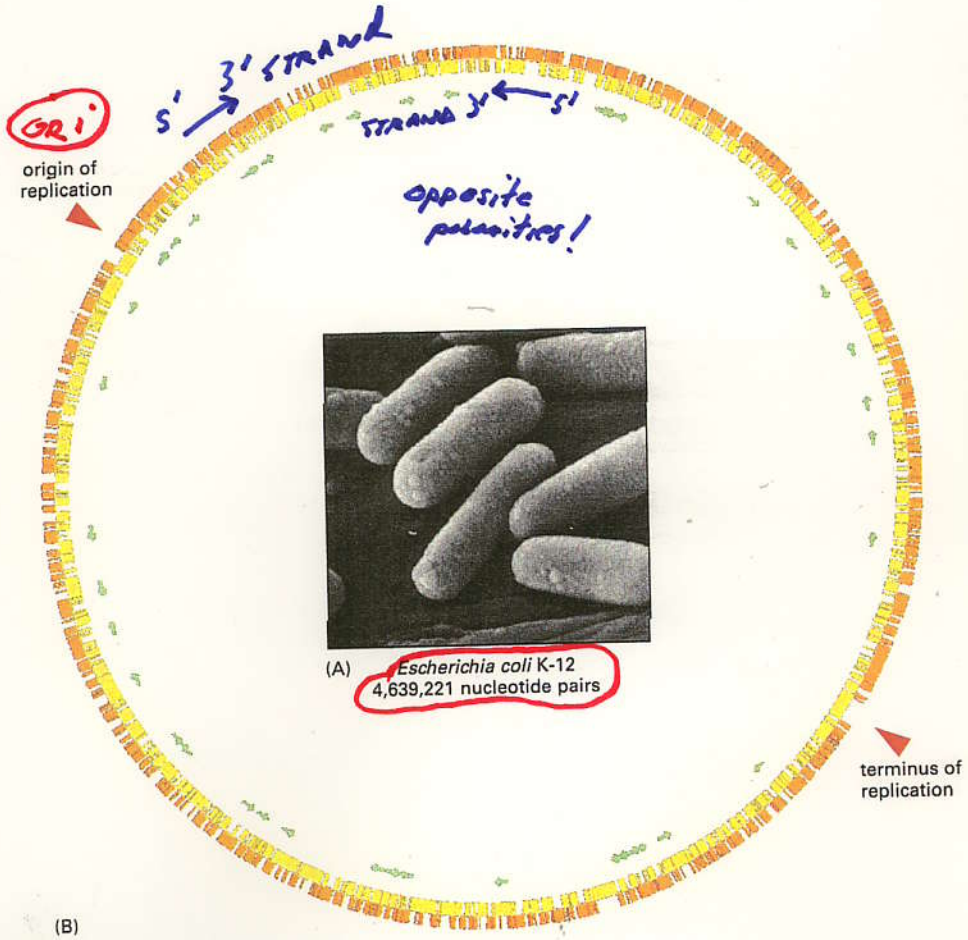
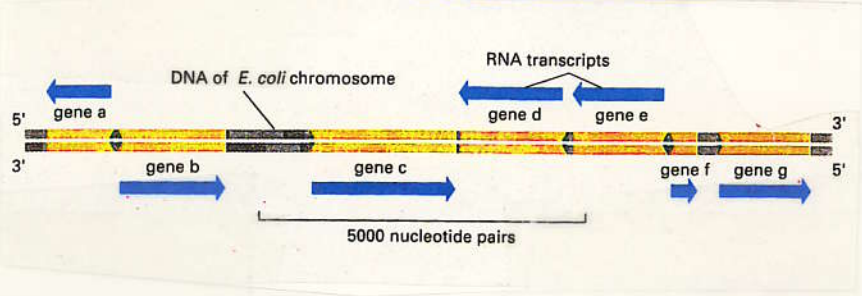


Figure 1–30 The genome of *E. coli*. (A) A cluster of *E. coli* cells. (B) A diagram of the *E. coli* genome of 4,639,221 nucleotide pairs (for *E. coli* strain K-12). The diagram is circular because the DNA of *E. coli*, like that of other prokaryotes, forms a single, closed loop. Protein-coding genes are shown as *yellow* or *orange bars*, depending on the DNA strand from which they are transcribed; genes encoding only RNA molecules are indicated by *green arrows*. Some genes are transcribed from one strand of the DNA double helix (*in a clockwise direction in this diagram*), others from the other strand (counterclockwise). (A, courtesy of Tony Brain and the Science Photo Library; B, after F. R. Blattner et al., *Science* 277:1453–1462, 1997. © AAAS.)

A Chromosome contains MANY Genes That Reside at Specific Positions And have unique functions

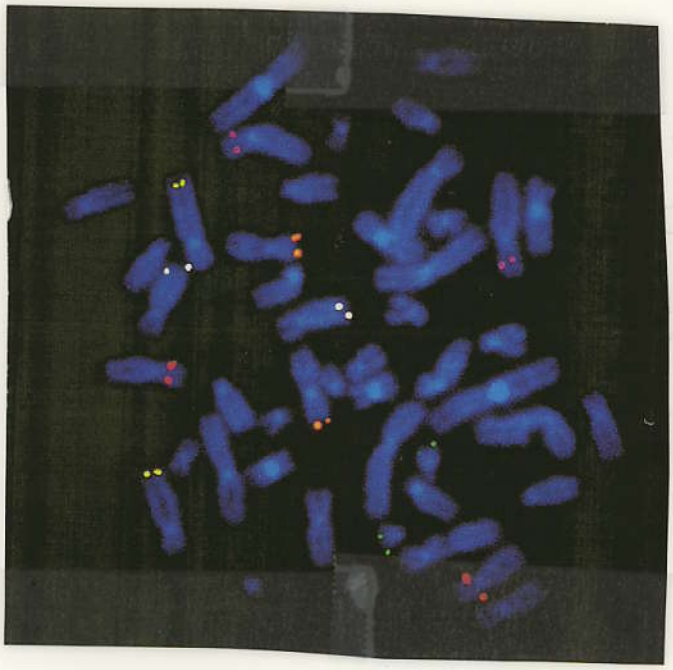


What defines the gene position?

Because DNA consists of two strands genes CAN be transcribed from either strand but only one/gene!

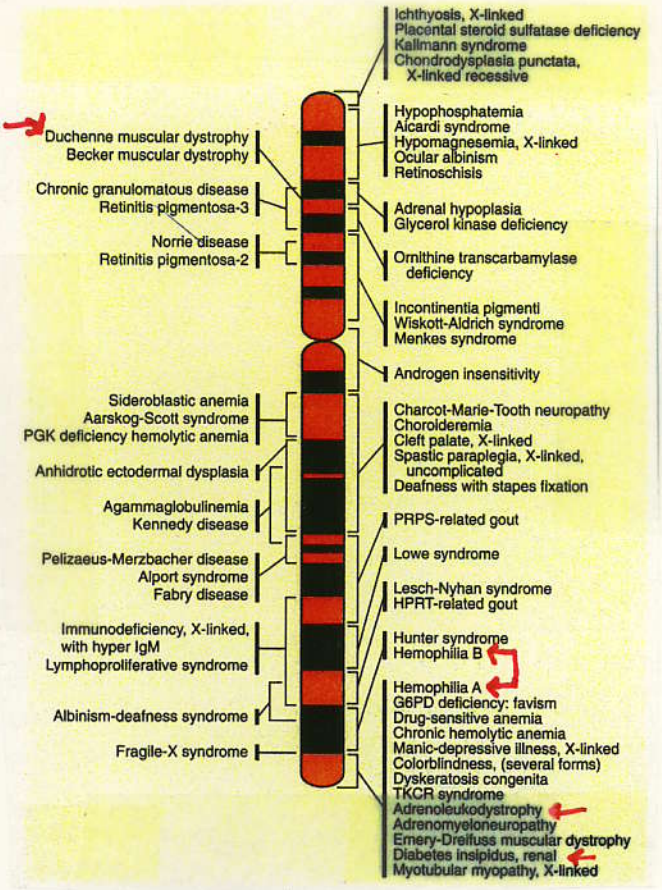
How do you know when one gene starts & the other ends?

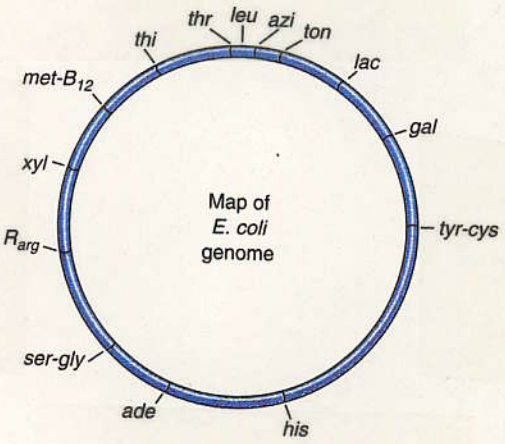
Genes Reside at Specific Positions or Loci



Gene Position = Locus = UNIQUE DNA Sequence

Genes reside at specific locations





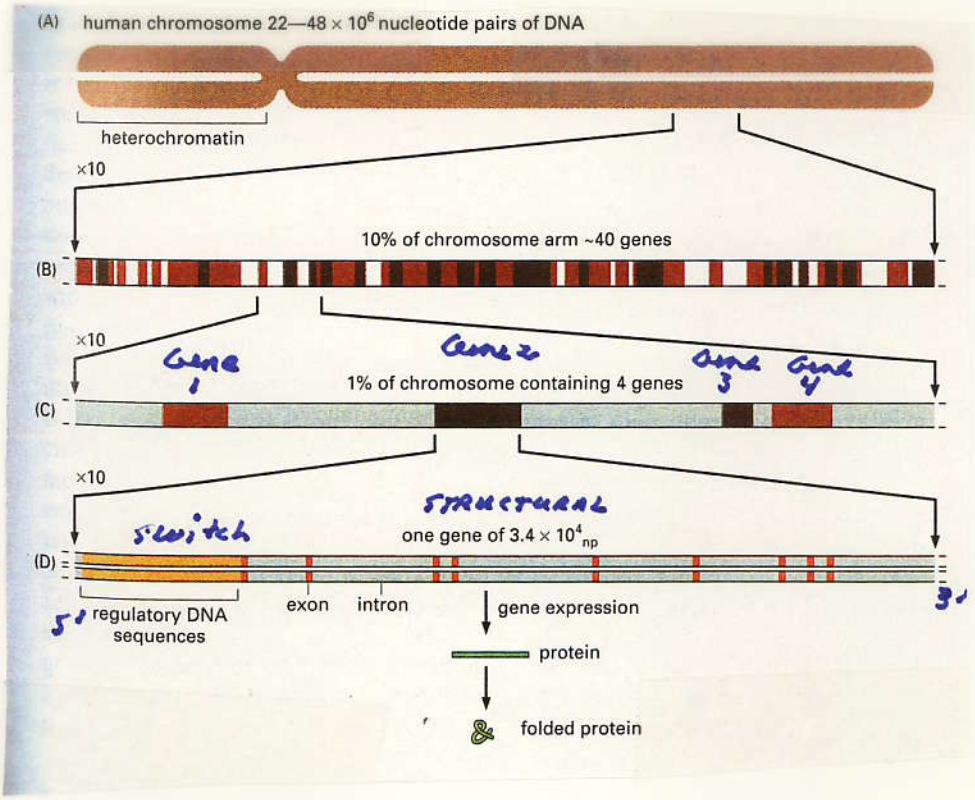
CIRCULAR DNA
How know?

Linear DNA
How know?

note BANDS - What are these?

How know Gene Positions? Chromosome #?

ORGANIZATION OF GENES ON HUMAN CHROMOSOME 22



Chromosome 22 A "Small" one!

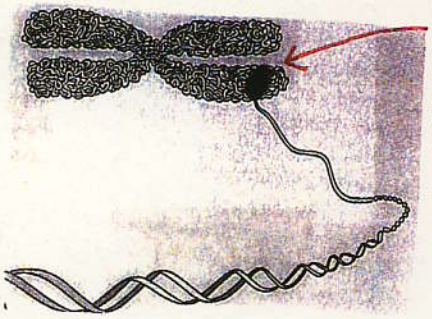
one Large Gene!

Genes Are Defined/Precise Regions of DNA

Genes Act As Individual units?

How Know? Globin Experiment! Genetic Engineering Anti (R)

A Chromosome Contains Many Genes



Position of Genes 1, 2, & 3 in Chromosome

Discrete Units!

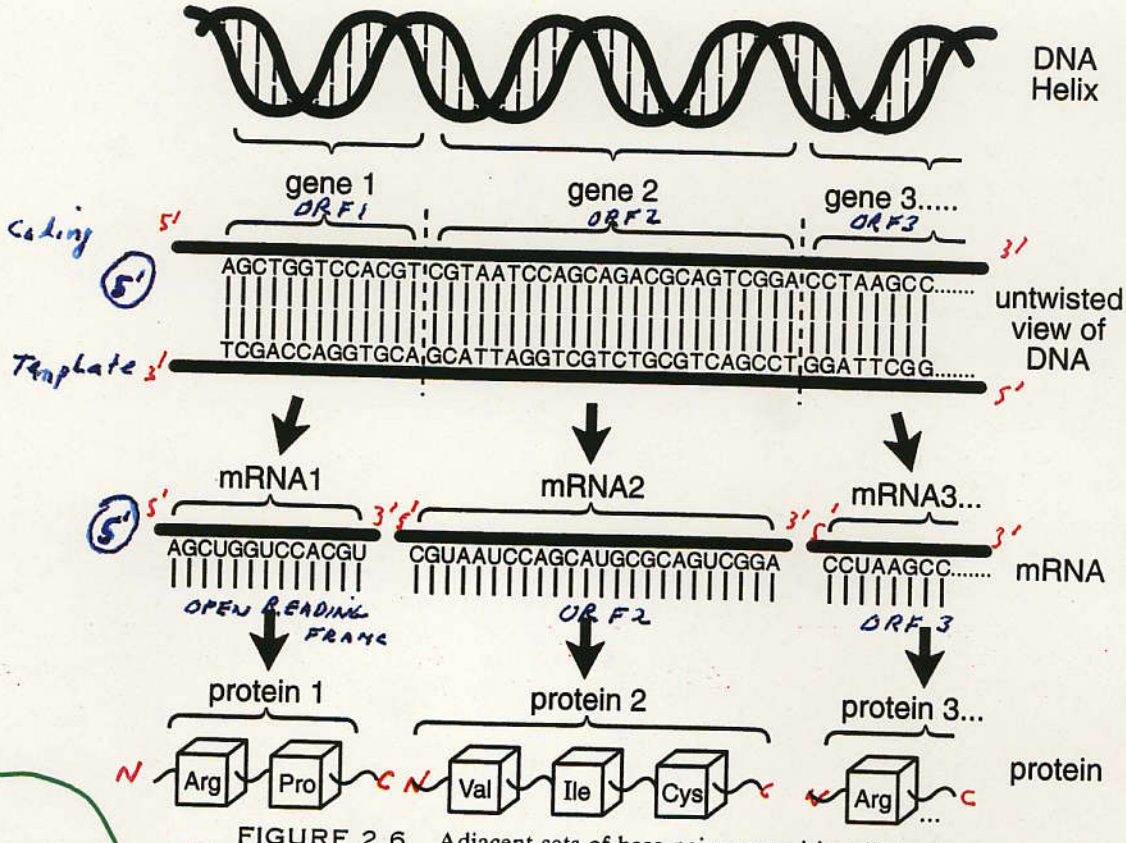
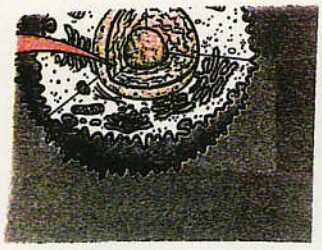


FIGURE 2.6 Adjacent sets of base pairs comprising different genes.

VERY IMPORTANT CONCEPT



Central Dogma

∴ Genes → Functions in Cells via Proteins

Cells duplicate & stay the SAME → DNA Replication

Notice – Each gene, mRNA, & protein has a unique order/Sequence of Monomeric Units

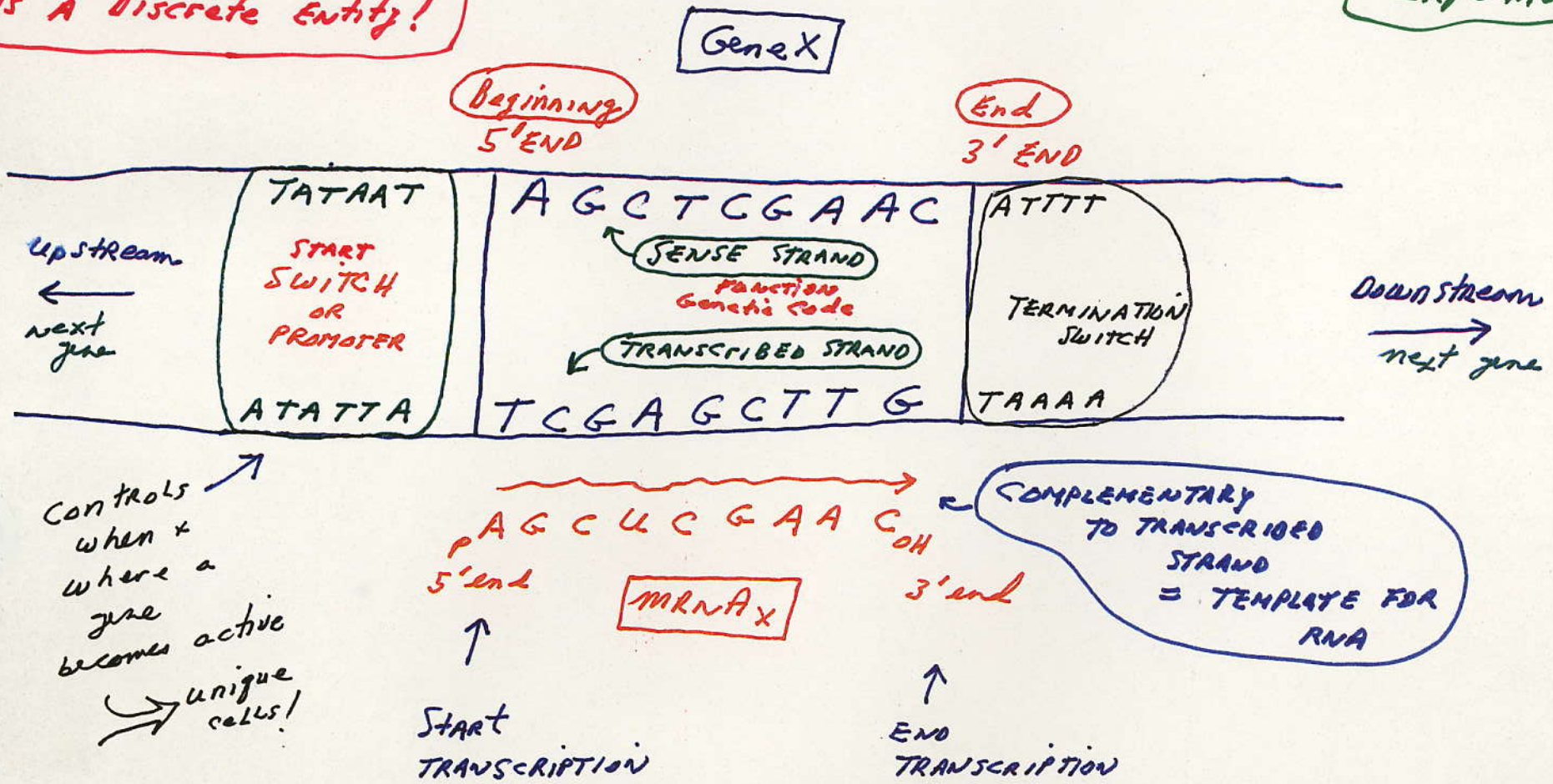
COLINEARITY BETWEEN GENESEQUENCE AND PROTEIN SEQUENCE

GENE is a SPECIFIC UNIT of DNA & Functions AS A Discrete Entity!

A Simple Gene = A DOUBLE HELIX

ONLY ONE STRAND TRANSCRIBED

GloFish Experiment



NOTICE! Specific Sequences specify Beginning & End of Gene & CONTROL ITS ACTIVITY!

NOTICE: mRNA Sequence = SEQUENCE OF SENSE STRAND

A "Simple" Gene Reviewed

1. Sense STRAND = Genetic Code
2. Sense STRAND = 5'→3' Direction (all DNA sequences specified 5'→3')
3. Anti-Sense STRAND = Complement of Sense Strand & is TRANSCRIBED STRAND
4. mRNA = SAME SEQUENCE AS SENSE STRAND & Complementary to Anti-Sense Strand
5. mRNA = 5'→3'
6. Switch TURNS Gene ON – NOT TRANSCRIBED BUT UPSTREAM OF CODING REGION

Genes Function As Independent units – Design Experiment to Show!

"Everything" Follows the Double Helix & its Rules – Anti-parallel Chains & Complementary Base Pairing!

Control Switches Are Unique DNA Sequences & CAN be Cloned!

AND USED TO Re-ENGINEER ORGANISMS!! Switches ACT independently of gene!!

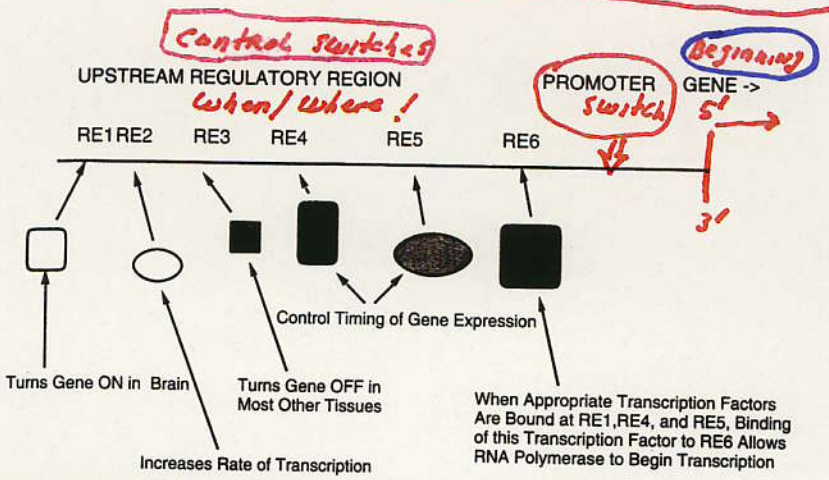


FIGURE 3.13 Enhancers and transcription factors in eukaryotic cells. A schematic diagram of the upstream regulatory region for a brain specific transcript is provided.

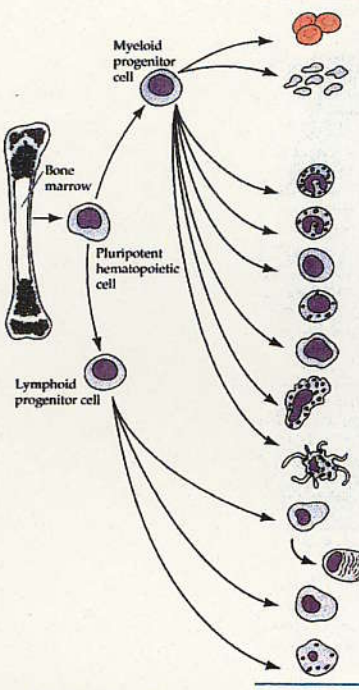
Each Switch = Unique DNA Sequence!

Genome Projects Reveal BOTH the Genes & the Logic that controls them!

RULE! SEQUENCE → BIOLOGY!!

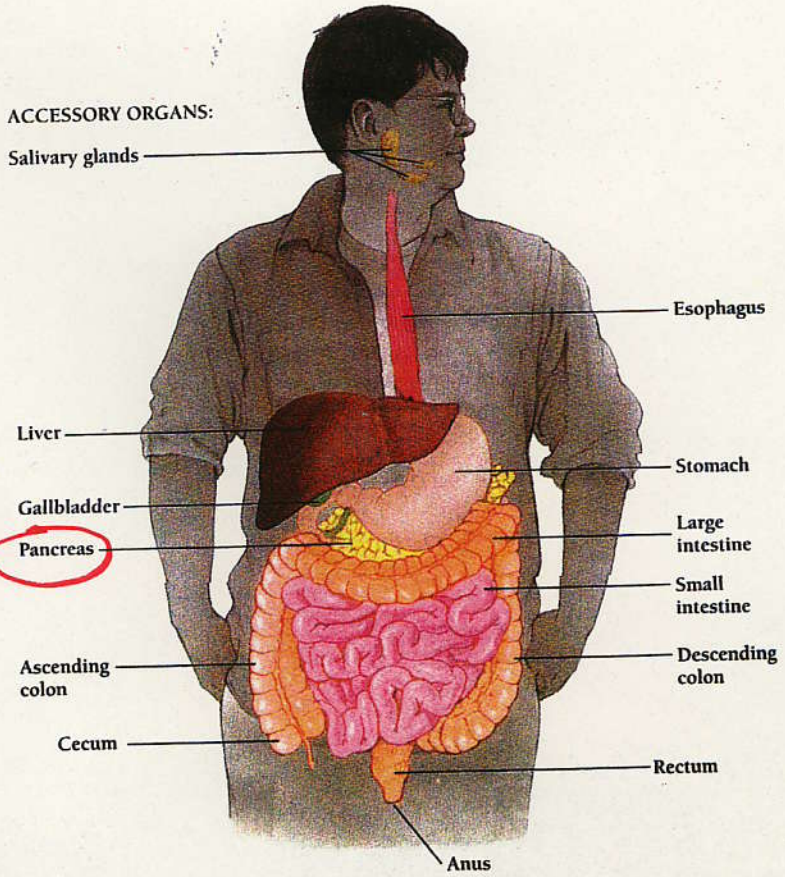
NO "HOCUS POCUS"
YO! IT's in the DNA!

SWITCHES CONTROL WHERE + WHEN A GENE IS ACTIVE → UNIQUE FUNCTIONS → UNIQUE CELLS!



TYPE OF CELL	FUNCTION
Red blood cells (erythrocytes)	Transport oxygen and carbon dioxide
Platelets (cell fragments without nuclei)	Initiate blood clotting
White blood cells (leukocytes)	
PHAGOCYTES	
Basophils	Release histamine; may promote the development of T cells
Eosinophils	Kill antibody-coated parasites
Neutrophils	Phagocytize antibody-coated pathogens
Mast cells	Release histamine when they are damaged
Monocytes	Develop into macrophages
Macrophages	Engulf and digest microorganisms; activate T cells
Dendritic cells	Present antigens to T cells
LYMPHOCYTES	
B cells	Differentiate to form antibody-producing cells and memory cells
Plasma cells	Secrete antibodies
T cells	Kill virus-infected cells; regulate activities of other white blood cells
Natural killer cells	Attack and lyse virus-infected or cancerous body cells

19.2 Blood Cells
Pluripotent stem cells in the bone marrow can differentiate into red blood cells, platelets, and the various types of white blood cells.



Insulin Gene →

THE GENE AND SWITCHES ARE UNIQUE DNA SEQUENCES

They CAN be Cloned & "Shuffled" & Engineered

① CREATING **new** Genes that have no counterparts in nature ⟹ Genetic Engineering

② These new genes CAN be transcribed in NewCell types (switch change) &/or organisms &/or Both (e.g., human genes in plant leaves)

→ human gene + plant reg switch

③ ALL genes are regulated & controlled by Switches. The Genome Projects reveal both the genes & the switches & Wiring together of all switches in gene

→ Program of life from birth to death

Yo! It's in the Sequences!!

An Eye of a fly can be Produced at other PLACES on the Fly's Body by Genetic Engineering

1. CONTROL Genes Activate Switches of other Genes
2. These genes can Specify Proteins that tell Cells to develop into complex organs (e.g., eye!)

∴ genes that do the "work" need to connect to genes that control them → regulatory circuits / logic

CAN USE Switches to Engineer where / when Gene Active in an organism → Controls ON/OFF

18–25 *The red-eyed fruit fly at the right is the offspring of the brown-eyed fly at the left.* Drosophila *transposons bearing a gene for red eyes were injected into the brown-eyed fly when it was an early embryo. Transposons with the gene for red eyes were incorporated into chromosomes of the cells that ultimately formed its gametes. The gene for red eyes was therefore passed on to its offspring.*

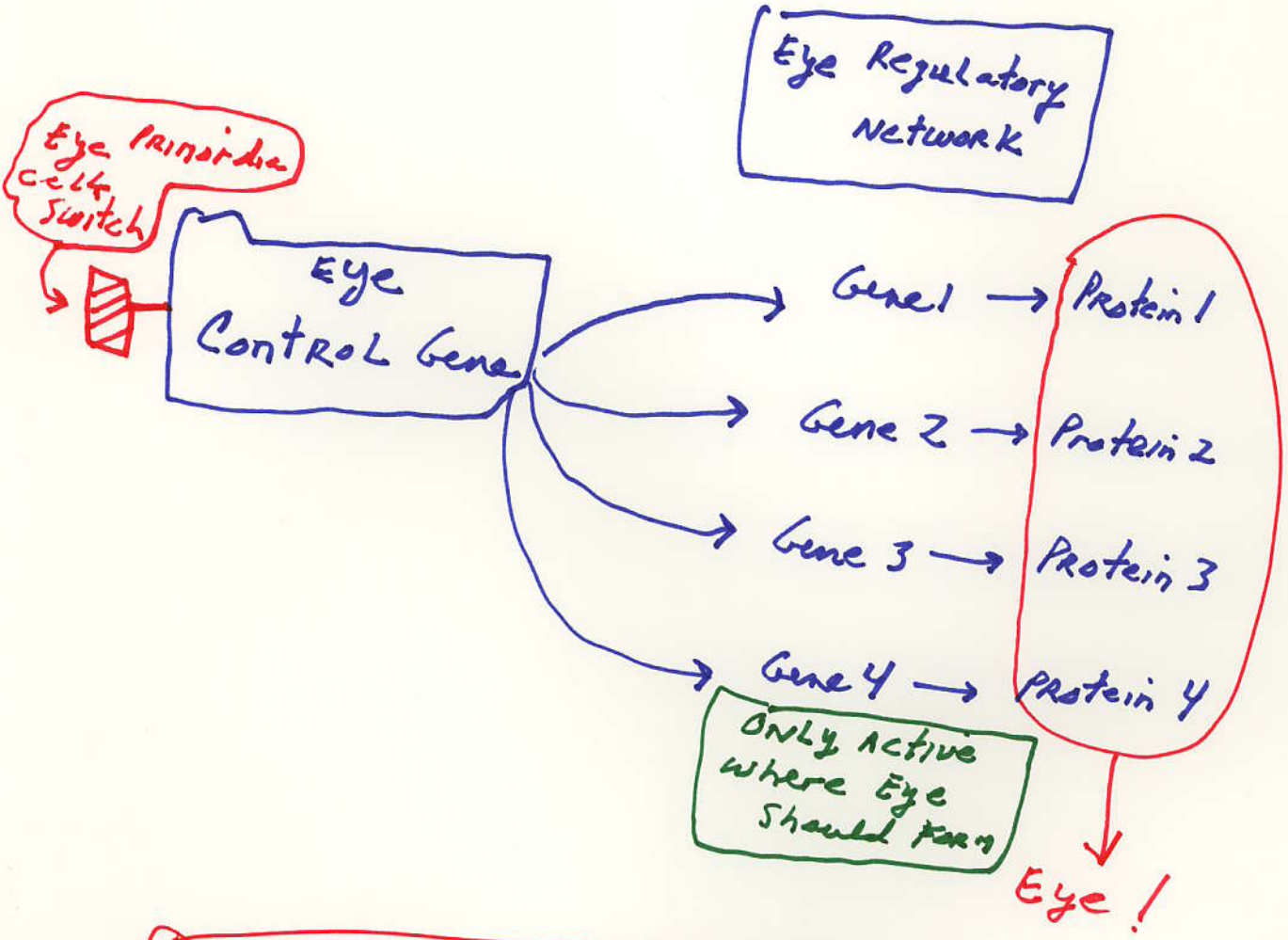
Use the Appropriate Switch with a Master Control Gene that Switches on other Switches to activate genes needed to make an eye!

Another Example is the SRY Male Gene it is A control gene that Activates other Genes!

XX mouse + SRY Gene → XY ♂ Mouse!

CD

EYE REGULATORY NETWORK



What Happens if Switch Changed?

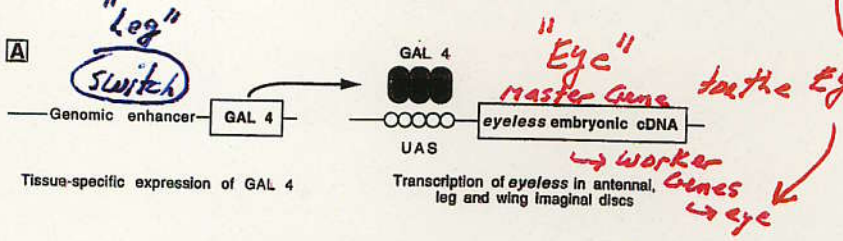
Age of Developmental Engineering is Beginning

This is the ultimate outcome of the Genome Projects! Unraveling our Developmental Gene Networks!

New Genes → Master Genes → Direct Cells → Organs

ALL in the DNA Sequence

Engineered Master Gene to Be Activated in Different Body Parts



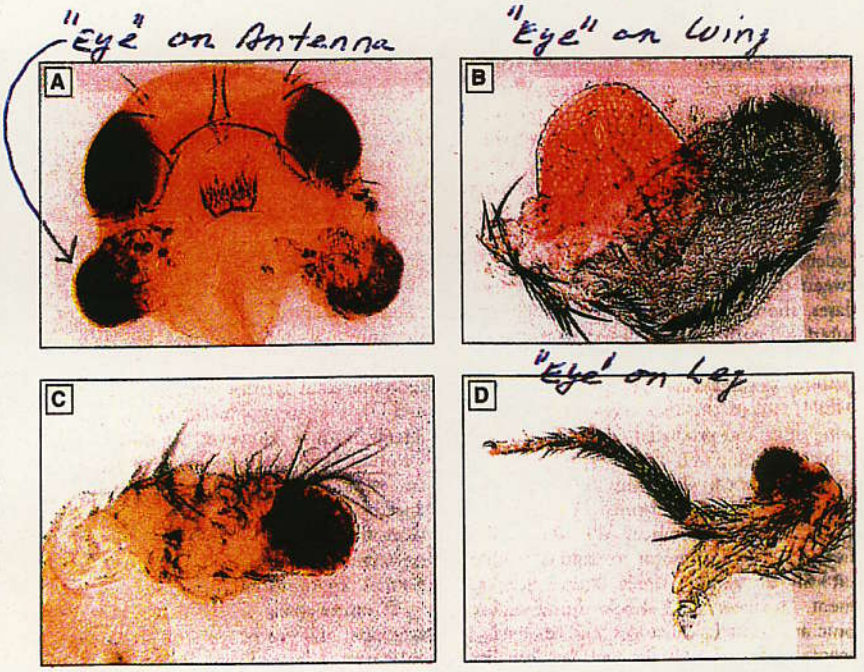


Fig. 2. GAL4 driven ectopic expression of *ey* induces the formation of eye structures in various tissues. The sites at which ectopic eyes form correspond to the regions in the imaginal discs, in which GAL4 is expressed as assayed by the activation of a *lacZ* reporter construct (Fig. 1, B, C, and D). The ectopic eye structures show ommatidial arrays, interommatidial bristles, and red pigmentation (*29*). **(A)** Cuticle of an adult head in which both antennae formed eye structures. **(B)** Dissected wing with a large outgrowth of eye tissue. The ectopic eye contains about 350 facets. Many interommatidial bristles are also apparent. The normal eye contains approximately 800 ommatidia. The wing is reduced in size. The anterior margin with its characteristic triple row of bristles occupies most of the circumference, whereas the more posterior structures are absent and replaced by eye tissue. The characteristic venation pattern of the wing is disturbed by the formation of the ectopic eye structures. **(C)** Dissected antenna in which most of the third antennal segment is replaced by eye structures. **(D)** Dissected middle leg with an eye-outgrowth on the base of the tibia.

BIG IMPLICATIONS

SHOWS function of eyeless gene

Where does this lead to? organ growth in culture?

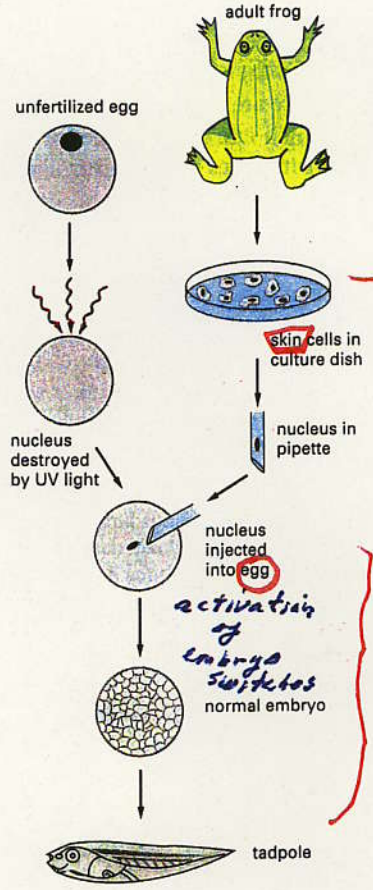
Transplants? organ design? organism design?

CLONING AN ANIMAL FROM a DIFFERENTIATED CELL NUCLEUS SHOWS THAT Gene Switches contain....

"The Logic" FOR all of Life is contained in the Genome!

Prediction?

Experiment?



What is Hypothesis Being tested?

Skin cells express specific genes due to their skin cell switches

Development of an organism from a fertilized egg requires all switches of genes to work at correct times to allow animal to form!

∴ all genes + switches present in skin cell!!

THE LOGIC TO PROGRAM ALL OF development!

If the Logic of how switches are connected is understood → Life can be programmed!

100 years into the future

(1) If the Entire Human Genome is Sequenced?

(2) If the Function/Proteins of all Genes are Known

(3) If all the Switches are identified & How they Go on & off from birth to death

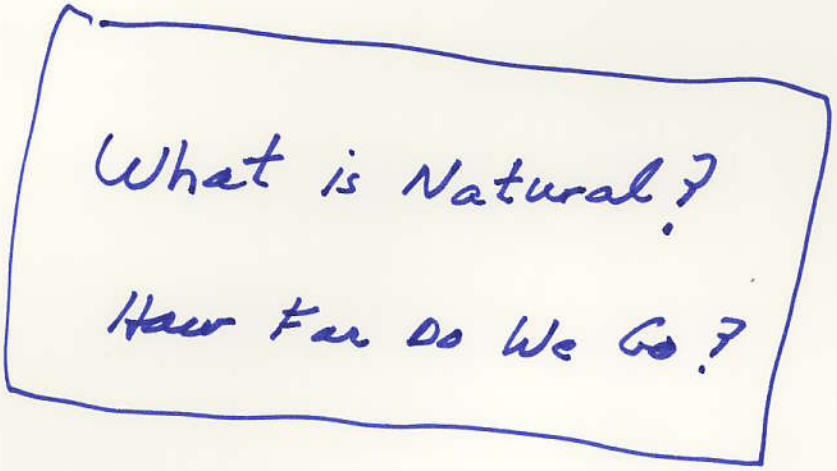
(4) If we understand how genes are Choreographed & all the Sequences that program them

What does the future Hold?

We will Know at the DNA Level What Biological Information Programs Life to Death?

What does this Mean for the future of Humanity?

Remember – Mendel's Laws were only re-discovered 100 years ago & look what we can do & know!


What is Natural?
How Far Do We Go?