



DNA  
Genetic Code of Life



Entire Genetic Code  
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues  
and Future Consequences



Plants of Tomorrow

# HC70A Winter 2008 Genetic Engineering in Medicine, Agriculture, and Law Professor Bob Goldberg

## Lecture 2 What Are Genes & How Do They Work-Part One



DNA  
Genetic Code of Life



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of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues  
and Future Consequences



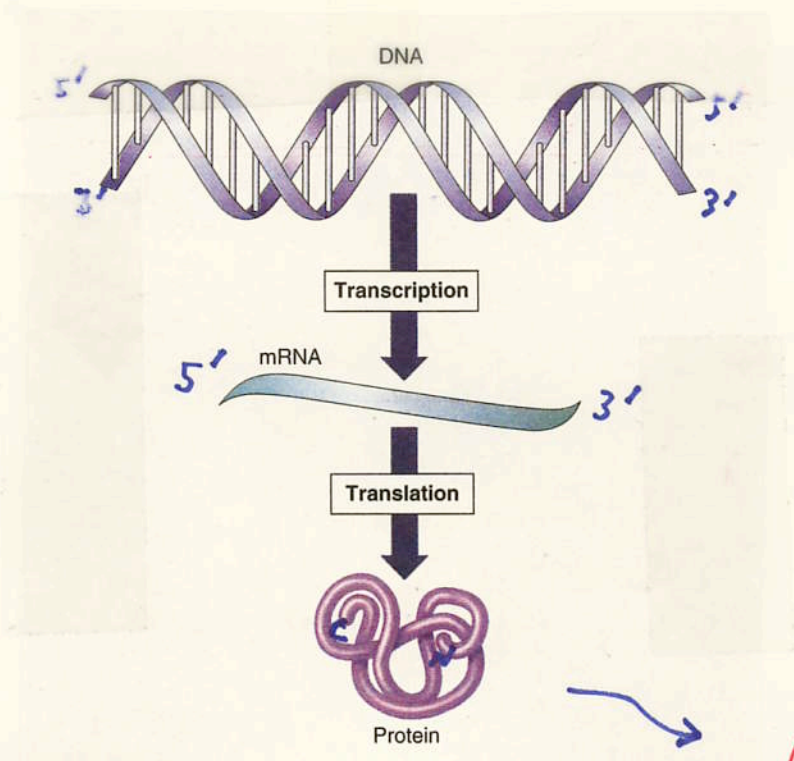
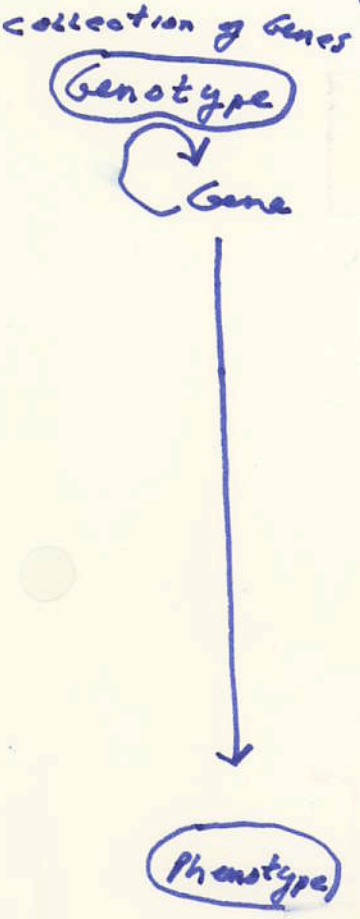
Plants of Tomorrow

## THEMES

1. What is the Function of a Gene?
2. What are the Properties of Genes?
3. What is the Evidence That DNA is the Genetic Material (Griffith and Avery Experiments)?
4. Is Transformation Universal?
5. What is the Structure of DNA?
6. What is the Structure of a Chromosome?
7. What is the Anatomy of a Gene?
8. What is the Colinearity Between Genes & Proteins (how does DNA→protein)?
9. How Do Switches Work to Control Gene Activity?
10. What Are the Possibilities For Manipulating Genes in the Future?



**What Are the Functions of A Gene?**



Replication ①

Gene Action ②

Cell Function ③

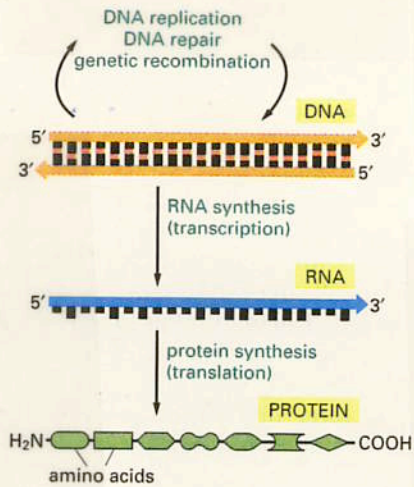
FIGURE 15.5 The Central Dogma of gene expression. DNA is transcribed to make mRNA, which is translated to make a protein.

GENETIC ENGINEERING ALTERS CELL FUNCTION BY CHANGING GENOTYPE

HOW DEMONSTRATE THIS EXPERIMENTALLY?















Design AN Experiment!

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.

**10.1 Mendel's Results from Monohybrid Crosses**

DOMINANT × RECESSIVE	
 Spherical seeds ×  Wrinkled seeds	 Yellow seeds ×  Green seeds
 Purple flowers ×  White flowers	 Inflated pods ×  Constricted pods
 Green pods ×  Yellow pods	 Axial flowers ×  Terminal flowers
 Tall stems (1 m) ×  Dwarf stems (0.3 m)	

Alleles!

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"!!

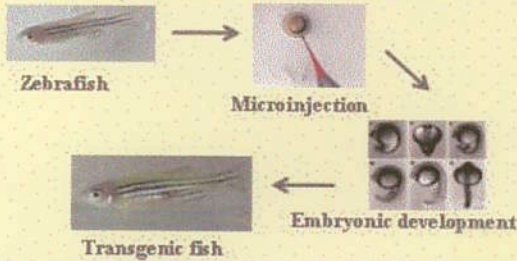


# HOW DOES THE GLOFish Experiment SHOW THAT GENES DIRECT THE PRODUCTION OF TRAITS?

Fluorescent transgenic zebrafish were developed by a research team, led by Dr. Z. Cong, in Department of Biological Sciences, National University of Singapore.

**Fig. 1.** The basic procedure to produce transgenic fish. Briefly, fluorescent color genes, originally isolated from a jellyfish and a sea anemone, were microinjected into zebrafish eggs and these foreign genes later become a part of the genetic make-up of injected zebrafish. Thus the fluorescent color acquired by these transgenic zebrafish can be stably transmitted to all future generations. This technology can also be applied to other ornamental fish species.

## General Procedure of Generation of Transgenic fish

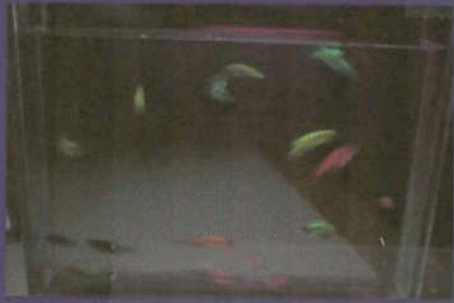


RFP DNA (gene)



**Fig. 2.** Florescent transgenic zebrafish in a rainbow array (top to bottom): Red, rfp fish; Orange, rfp/gfp fish; Yellow, yfp fish; Green, gfp fish; and Wild Type fish. The picture on the far left was taken under a daylight and the picture on the left in the dark with a uv light.

rfp - red fluorescent protein  
yfp - yellow fluorescent protein  
gfp - green fluorescent protein



**Fig. 3.** Swimming fluorescent transgenic zebrafish under the daylight (top) and in the dark (bottom, with a uv light)

## 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 Predictions Follow FROM These Properties

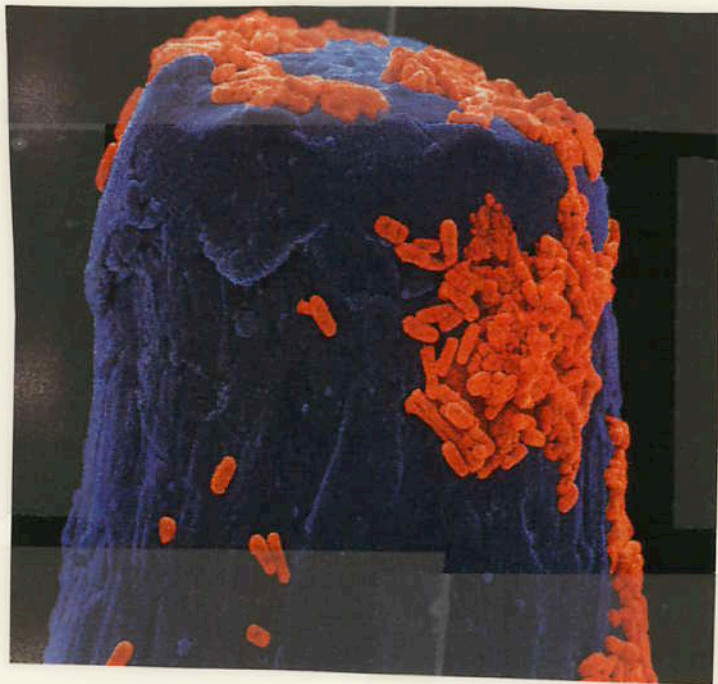
In the 1930s & 1940s Genes Were Thought to be:

- a. DNA
- b. Proteins
- c. Unidentified Cellular Molecular
- d. RNA



GRIFFITH'S Experiment With  
PNEUMONIA Bacteria

1927



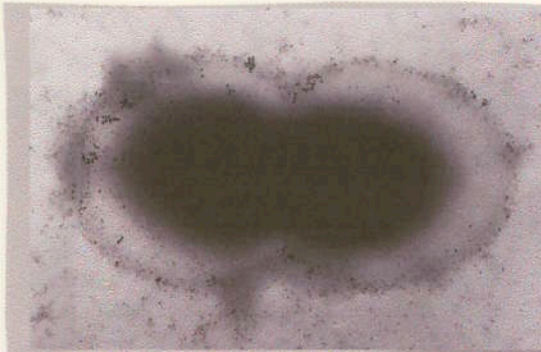
Bacteria  
on  
a pinhead!

The First Genetic Engineering Experiment - Except  
That Was Not Understood For  
Another 50 years!

*Streptococcus pneumoniae*  
(sequenced!)



*STREPTOCOCCUS pneumoniae* is A  
KILLER BACTERIA !!

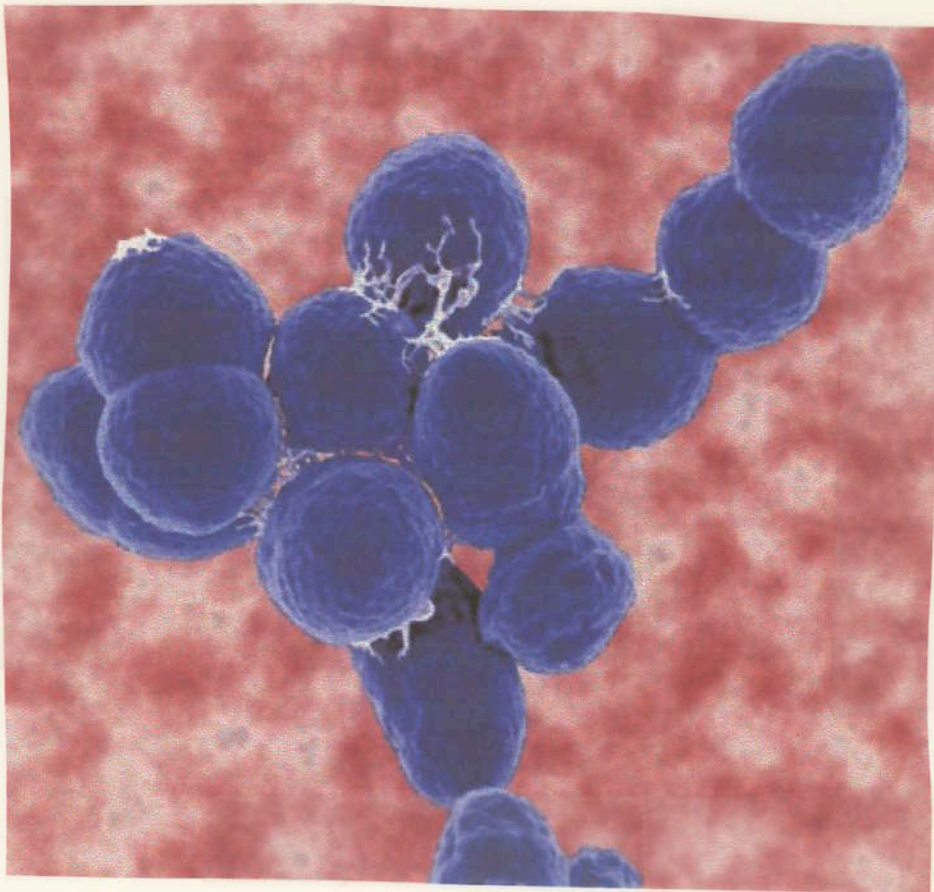


*Streptococcus pneumoniae*

Genome Diversity Project

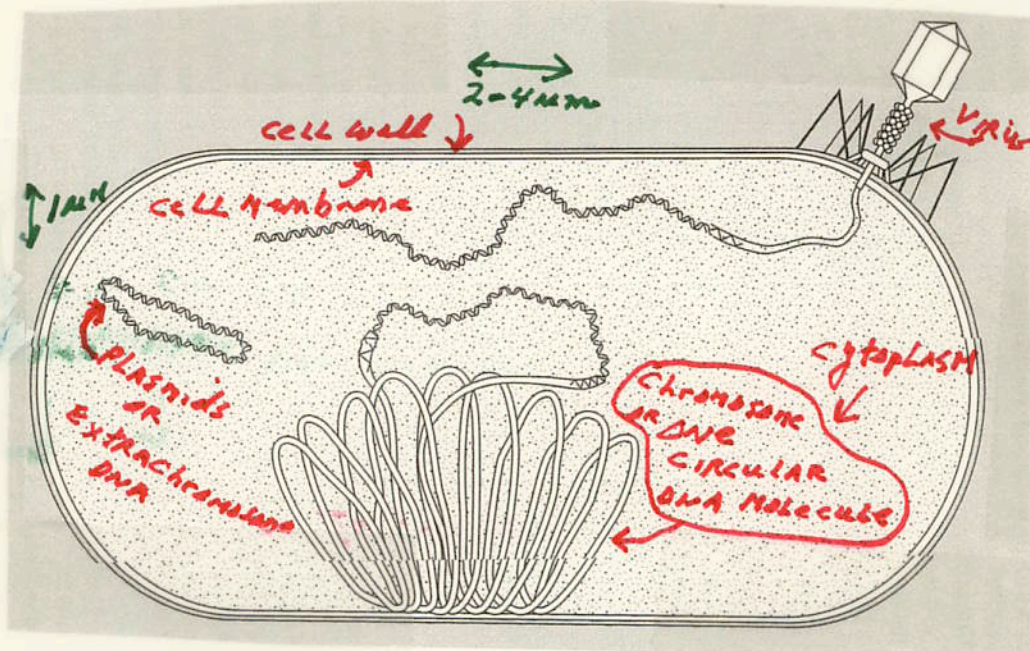
3.65 Million/yr

Worldwide there are over 10,000 deaths per day due to pneumococcal infections.





# A "Typical" Bacterial Cell



PLASMIDS - 2,000 - 150,000 bp (1-100 genes)

CHROMOSOME - 500,000 - 5,000,000 bp (500-4500 genes)

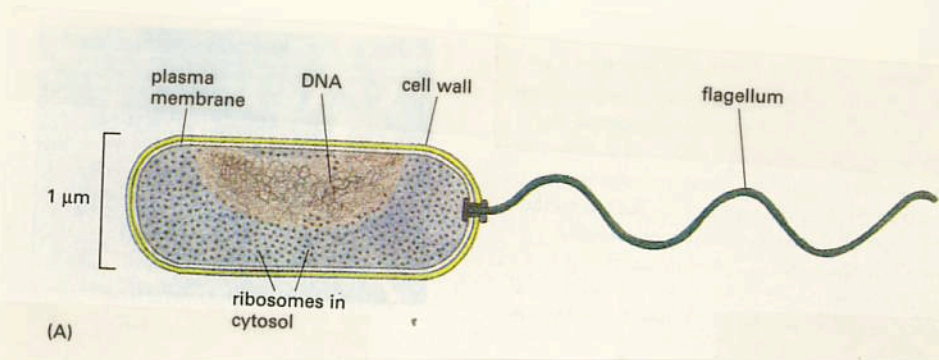
*E. coli* DNA = ~ 1.4 mm ( $10^{-3}$  m) in circumference

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

→ Antibiotic<sup>R</sup> genes - "Vectors" for Genetic Engineering

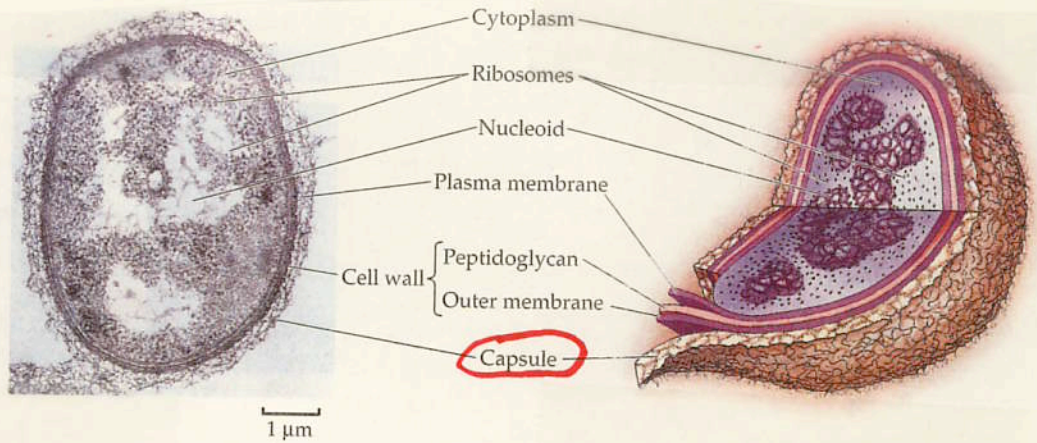
$$1 \mu\text{m} = 3.94 \times 10^{-5} \text{ inch}$$

# BACTERIA CELL STRUCTURE



## 4.4 A Prokaryotic Cell

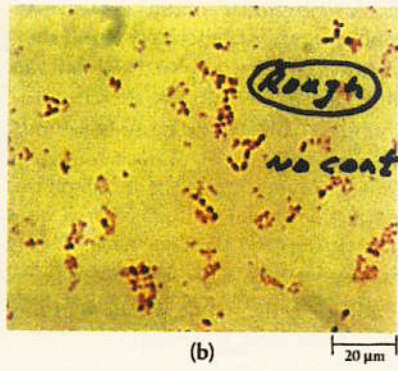
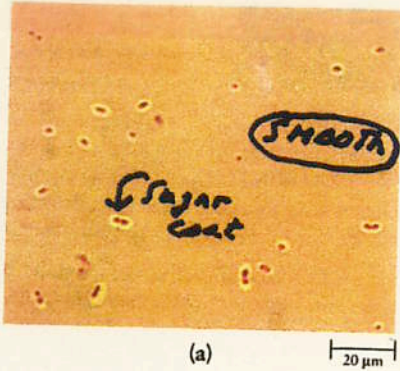
The bacterium *Pseudomonas aeruginosa* illustrates typical prokaryotic cell structures. The electron micrograph on the left is magnified about 80,000 times. Note the existence of several protective structures external to the plasma membrane.





1927!!

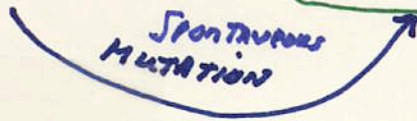
GRIFFITH'S PNEUMONIA BACTERIA Experiment



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.

SMOOTH/VIRULENT STRAIN

ROUGH/AVIRULENT STRAIN



What is BASIS OF AVIRULENCE?



Streptococcus pneumoniae -

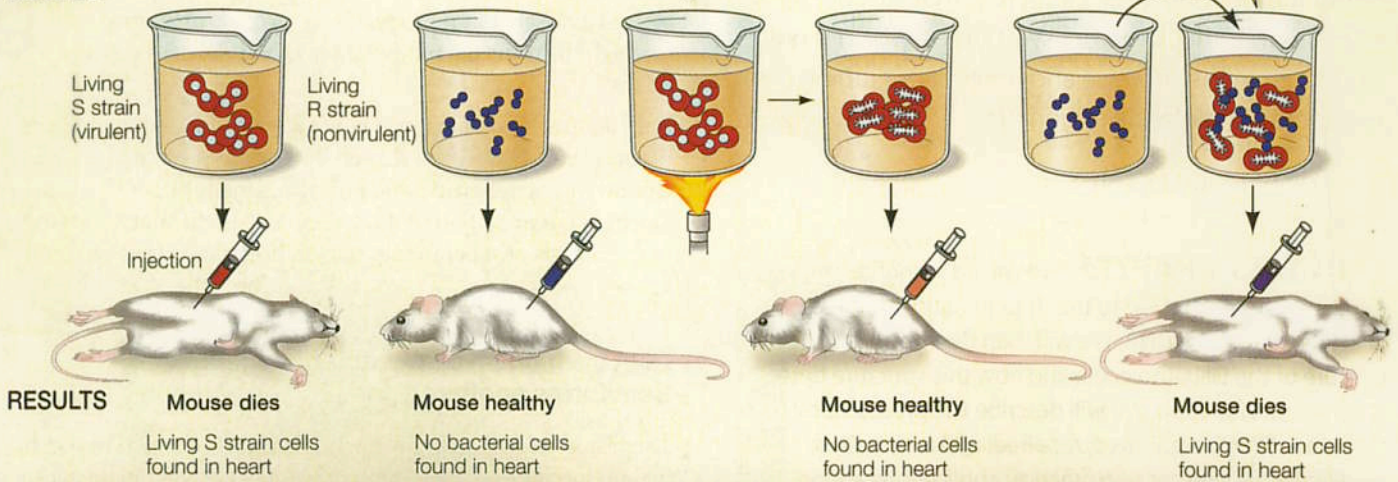
Genome Sequenced 2001 2.1 Mb 2236 genes

# GRIFFITH'S DEMONSTRATION OF TRANSFORMATION

## EXPERIMENT

**HYPOTHESIS:** Material in dead bacterial cells can genetically transform living bacterial cells.

### METHOD



**CONCLUSION:** A chemical substance from one cell is capable of genetically transforming another cell.

LIVE ROUGH WAS TRANSFORMED BY DEAD S CELLS!

HOW?

What WAS THE TRANSFORMING principle?

HYPOTHESIS?



WHAT MOLECULE(S) in THE SMOOTH CELL COULD BE THE TRANSFORMING PRINCIPLE?

LARGE MOLECULES in ALL CELLS

Table 3.1 Macromolecules

Macromolecule	Subunit	Function	Example
<b>PROTEINS</b>			
Globular	Amino acids	Catalysis; transport	Hemoglobin
Structural	Amino acids	Support	Hair; silk
<b>NUCLEIC ACIDS</b>			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
<b>LIPIDS</b>			
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
<b>CARBOHYDRATES</b>			
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?



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.

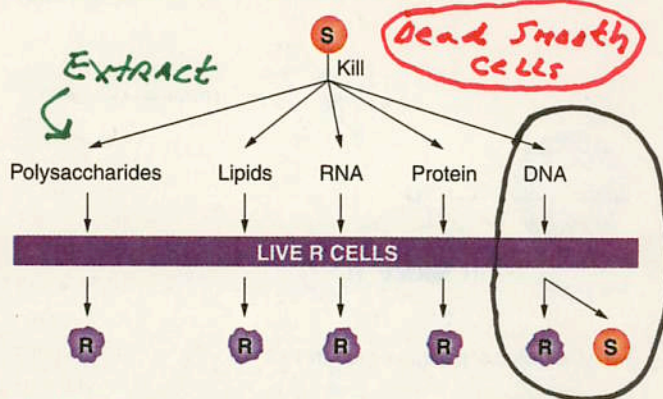


Figure 8-2 Demonstration that DNA is the transforming agent. DNA is the only agent that produces smooth (S) colonies when added to live rough (R) cells.

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

Add to Live Rough Cells →

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

∴ DNA taken up by Live Smooth cells & CAUSES TRANSFORMATION

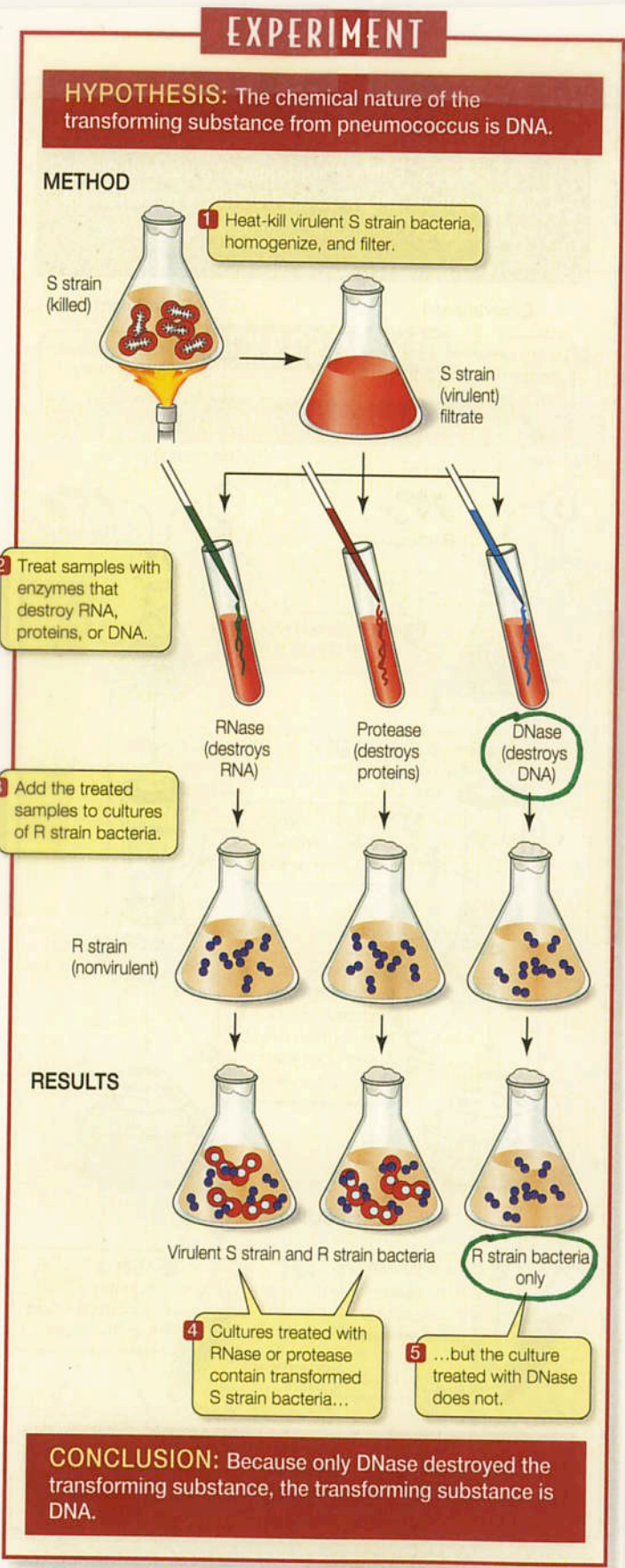
The Avery et al., Experiment Showed Conclusively That DNA is the Genetic Material?

- a. Yes
- b. No

DOES THAT EXPERIMENT  
SHOW CONCLUSIVELY  
THAT DNA IS THE  
GENETIC MATERIAL?



**Avery et al. Experiment - DNA IS THE Genetic MATERIAL!!**

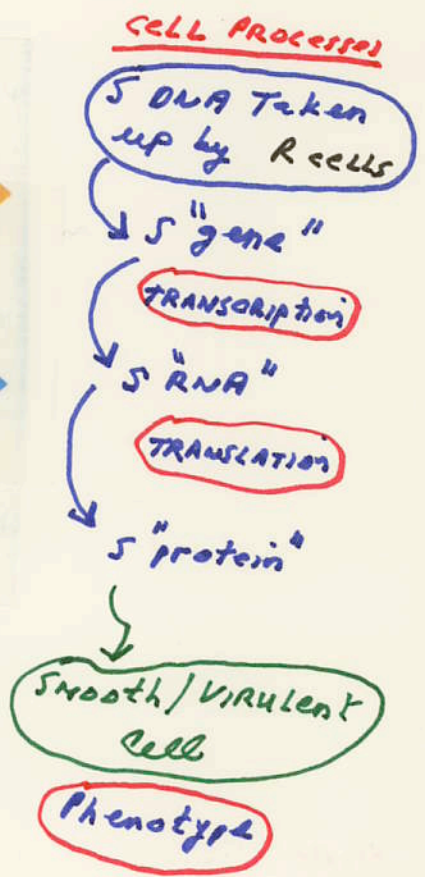
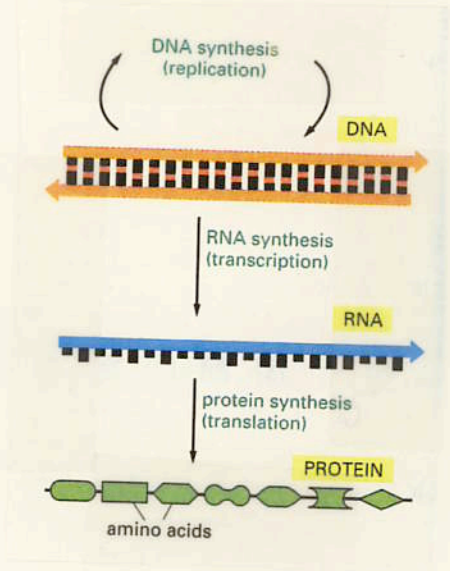


**NOTE:**  
 DESTROYING DNA PREVENTS R CELLS FROM BEING TRANSFORMED TO S CELLS!

**11.2 Genetic Transformation by DNA** Experiments by Avery, MacLeod, and McCarty showed that DNA from virulent S strain pneumococci was responsible for transformation in Griffith's experiments (see Figure 11.1).

How did Avery's Experiment Verify the Hypothesis That DNA is the Gene?

<u>Predictions</u>	<u>Results</u>
Replication	Yes
Phenotype	yes
Stable	yes



TRANSFORMATION used as a Genetic Engineering Process to Present Day!

TRANSFORMATION?

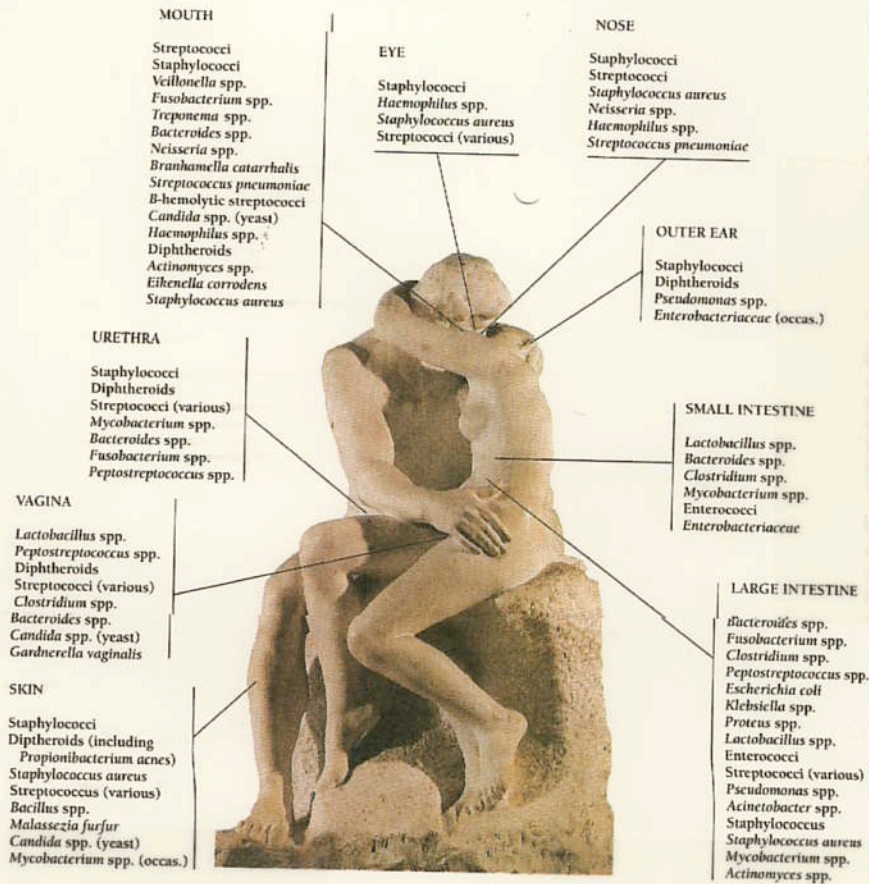
Ability of a cell phenotype to be changed/transformed by DNA!

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

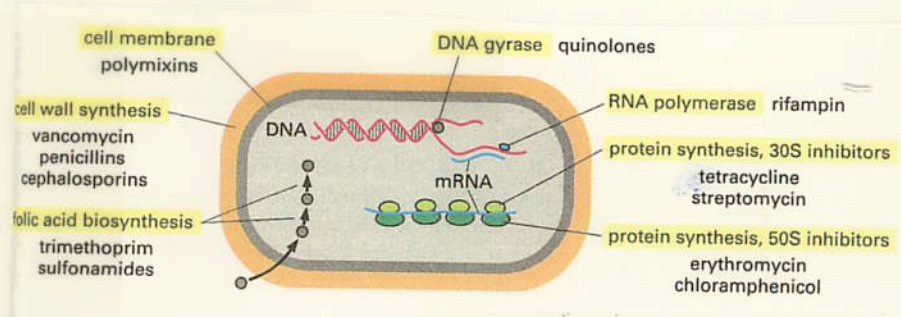


CAN BACTERIA BE TRANSFORMED WITH OTHER GENES/TRAITS?

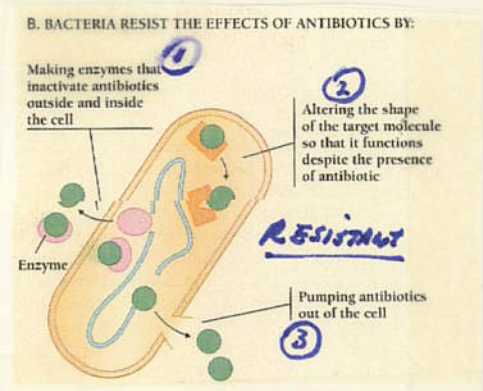
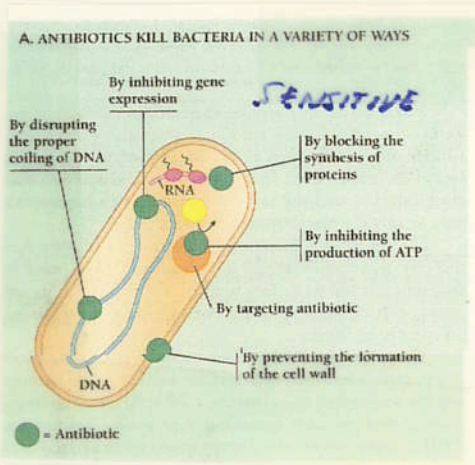
**Figure 20-3** Microorganisms that normally inhabit the human body. All of the microorganisms listed here live—usually harmoniously—on the surfaces and in the interiors of human bodies. *Candida albicans*, commonly known as yeast, is a fungus that lives on the skin and in the mouth and vagina. *Candida* 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!

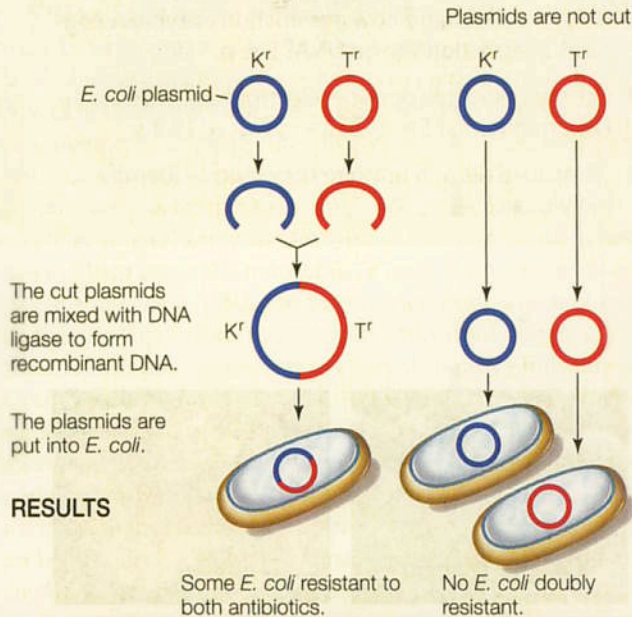


BACTERIA CAN BE TRANSFORMED  
WITH ANTIBIOTIC RESISTANCE GENES  
AND OTHER GENES - NO RESTRICTION

## EXPERIMENT

**HYPOTHESIS:** Biologically functional recombinant chromosomes can be made in the laboratory.

**METHOD** *E. coli* plasmids carrying a gene for resistance to either the antibiotic kanamycin or tetracycline are cut with a restriction enzyme.

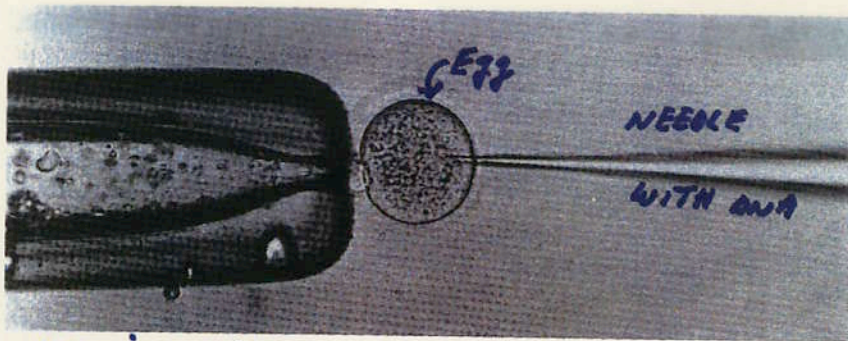


**CONCLUSION:** Two DNA fragments with different genes can be joined to make a recombinant DNA molecule, and the resulting DNA is functional.

**16.7 Recombinant DNA** Stanley Cohen and Herbert Boyer performed the first experiment in which two different DNA sequences were combined in the laboratory to make a new, functional DNA molecule. **FURTHER RESEARCH:** Only one cell in 10,000 took up the plasmid in the experiment. The spontaneous mutation rate to  $T^r$  or  $K^r$  is one cell in  $10^6$ . How would you distinguish between genetic transformation and spontaneous mutation in this experiment?

ALL ORGANISMS CAN BE TRANSFORMED  
GENETICALLY WITH DNA!

CAN Higher Organisms BE TRANSFORMED?  
Genetically Engineered?



HOLDING PIPET

(b)

Recall GLO Fish Experiment!  
GLO Fly  
GLO Mouse  
GLO PLANT !!  
GLO MONKEY

DNA → Specifics TRAIT  
↳ Replicates



NATURAL PROCESSES!

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

Engineered Gene  
MUST

- genotype
- ↓
- ① Enter Target Cell
  - ② Use Target Cell Machinery  
Enzymes to become part of  
Chromosome
  - ③ Replicate with target cell  
Chromosome
  - ④ Use target cell Protein  
Synthesis Machinery to make  
a new protein → phenotype  
trait!
- phenotype

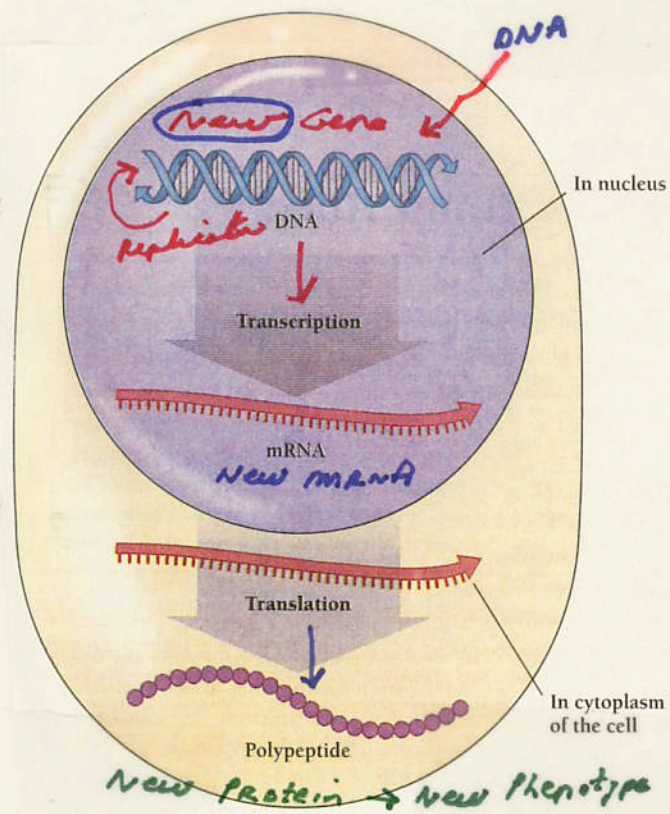
Engineered Gene  
Can Be

- 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

CRITICAL POINT!!!!



# What is a Gene?

## The $\beta$ -globin Gene

Blood protein carries  
Oxygen to ALL cells  
From Lungs  $\rightarrow$  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

CCCTGTGGAGCCACACCCCTAGGGTTGGCCA  
ATCTACTCCCAGGAGCAGGGAGGGCAGGAG  
CCAGGGCTGGGCATAAAAGTCAGGGCAGAG  
CCATCTATTGCTTACATTTGCTTCTGACAC  
AACTGTGTTACTAGCAACTCAACAGACA  
CCATGGTGCACCTGACTCCTGAGGAGAAGT  
CTGCCGTTACTGCCCTGTGGGGCAAGGTGA  
ACGTGGATGAAGTTGGTGGTGAAGCCCTGG  
GCAGGTTGGTATCAAGGTTACAAGACAGGT  
TTAAGGAGACCAATAGAAACTGGGCATGTG  
GAGACAGAGAAGACTCTTGGGTTTCTGATA  
GGCACTGACTCTCTGCTATTTGGTCTAT  
TTCCACCCCTTAGGCTGCTGGTGGTCTAC  
CCTTGGACCCAGAGGTTCTTTGAGTCCTTT  
GGGGATCTGTCCACTCCTGATGCTGTTATG  
GGCAACCCTAAGGTGAAGGCTCATGGCAAG  
AAAGTCTCGGTGCCTTTAGTGATGGCCTG  
GCTCACCTGGACAACCTCAAGGGCACCTTT  
GCCACTGAGTGAGCTGACTGTGACAAAG  
CTGCACGTGGATCCTGAGAAGTTCAGGGTG  
AGTCTATGGGACCCCTGATGTTTCTTTCC  
CCTTCTTTTCTATGGTTAAGTTCATGTCAT  
AGGAAGGGGAGAAGTAACAGGGTACAGTT  
AGAATGGGAAACAGACGAATGATGATCA  
GTGGGAAGTCTCAGGATCGTTTAGTTTC  
TTTTATTGCTGTTCAACAATGTTTTTC  
TTTTGTTAATCTTGCTTTCTTTTTTTT  
CTTCTCCGCAATTTTACTATTATACTTAA  
TGCCTTAACATTGTGTATAACAAAAGGAAA  
TATCTGAGATACATTAAGTAAGTAAAA  
AAAAACTTTACACAGTCTGCCTAGTACATT  
ACTATTTGGAATATATGTGTCTTATTGTC  
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ATATTTATGGGTTAAAGTGAATGTTTAA  
TATGTGTACACATATTGACCAAAACAGGGT  
AATTTGCAATTTGTAATTTAAAAAATGCT  
TTCTTCTTTAATATACTTTTTTGTTTATC  
TTATTTCTAATACTTTCCCTAATCTCTTTC  
TTTCAGGGCAATAATGATACAATGATCAT  
GCCTCTTTGCACCATTCTAAGAATAACAG  
TGATAATTTCTGGGTTAAGGCAATAGCAAT  
ATTTCTGCATATAAATATTTCTGCATATA  
ATTGTAAGTGTGTAAGAGGTTTCATATTG  
CTAATAGCAGCTACAATCCAGCTACCATT  
TGCTTTTATTTATGGTGGGATAAGGCTG  
GATTATCTGAGTCCAAGCTAGGCCCTTTT  
GCTAATCATGTTTACACTCTTATCTTCT  
CCCACAGCTCCTGGGCAAGTGTGGTCTG  
TGTGCTGGCCCATCACTTTGGCAAAGAAAT  
CACCCACAGTGCAGGCTGCCTATCAGAA  
AGTGGTGGCTGGTGGCTAATGCCCTGGC  
CCACAAGTACTACTAAGCTCGCTTTCTTGC  
TGTCCAATTTCTATTAAGGTTCCCTTTGTT  
CCCTAAGTCCAATACTAACTGGGGATA  
TTATGAAGGGCCTTGAGCATCTGATTCTG  
CCTAATAAAAAACATTTATTTTATTGCAA  
TGATGTATTTAAATTTTCTGAATATTT  
ACTAAAAAGGGAATGTGGGAGGTCAGTGCA  
TTTAAACATAAAGAAATGATGAGCTGTT  
AAACCTTGGGAAAATACACTATATCTTAAA  
CTCCATGAAAGAAGGTGAGGCTGCAACCAG  
CTAATGCACATTTGGCAACAGCCCTGATGC  
CTATGCCTTATCATCCCTCAGAAAAGGAT  
TCTTGTAGAGGCTTGAATTTGCAGGTTAAAG  
TTTTGCTATGCTGATTTTACATTACTTAT  
TGTTTTAGCTGCTCATGAATGCTTTTC

Begin

5'

Sequence  
or  
order  
of  
nucleotides  
CODING  
DNA  
STRAND

End 3'

Genes + Genomes Differ  
Because the Sequence  
of DNA differs

DNA Sequence

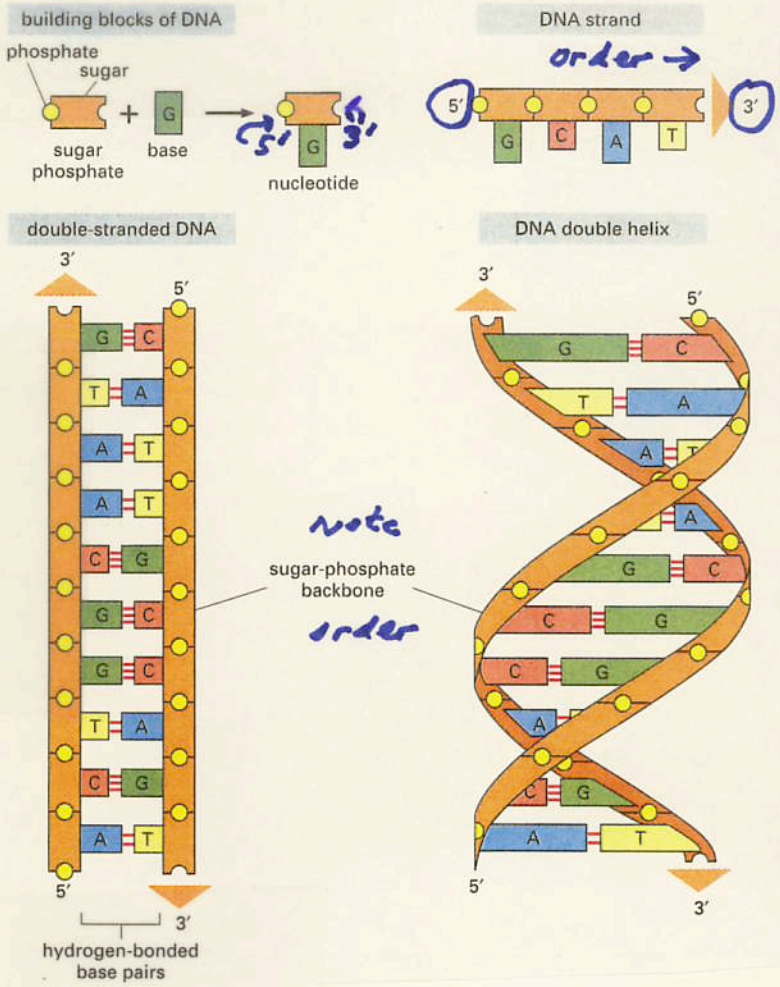
Beginning → End  
5' 3'

→ Biological Uniqueness

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 backbone from which the bases (A, C, G, and T) extend. A DNA molecule is composed of two DNA strands held together by hydrogen bonds between the paired bases. The arrowheads at the ends of the DNA strands indicate the polarities of the two 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 straightened 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
- ③ Two strands of DNA are **complementary** & have different sequences!

A Review

# NUCLEOTIDES HAVE POLARITY

ORDER = FUNCTION!

5' P  
Beginning →

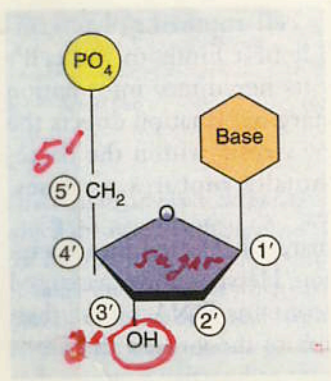


FIGURE 14.7  
Numbering the carbon atoms in a nucleotide. The carbon atoms in the sugar of the nucleotide are numbered 1' to 5', proceeding clockwise from the oxygen atom. The "prime" symbol (') indicates that the carbon belongs to the sugar rather than the base.

3' OH  
End →

BASED ON what is bonded to sugar

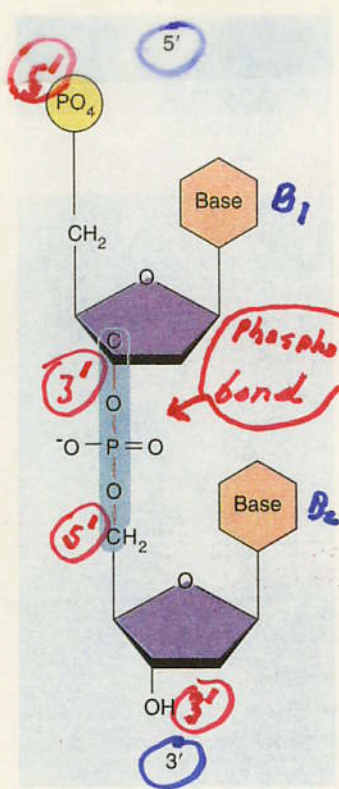
The sugar is the Hub !!

Order of DNA defined by nucleotide  
↳ DNA Sequence  
↳ Biology



NUCLEOTIDES ARE JOINED by Phosphodiester Bonds

5' ORDER  
 ↓  
 B<sub>1</sub>  
 ↓  
 B<sub>2</sub>  
 ↓  
 3'  
 Defined by Sugars!!  
 Specified by Bases!



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

Phosphodiester bond

Basis of all Genetics + Genetic Engineering

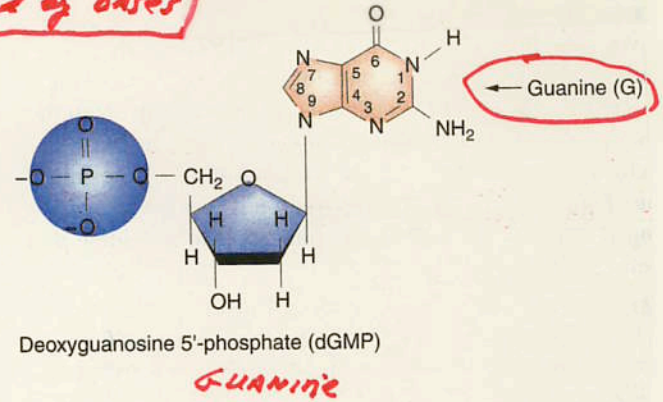
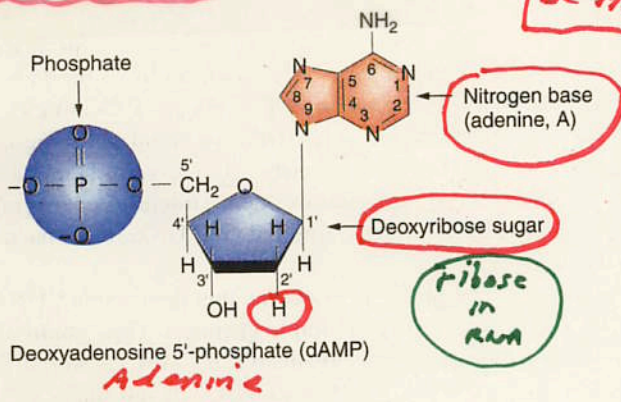
Order = Biology!  
 ORDER IS MAINTAINED DURING REPLICATION!

FIGURE 14.8 A phosphodiester bond.

There Are FOUR Nucleotides in DNA

Purine nucleotides

Defined by bases



Pyrimidine nucleotides

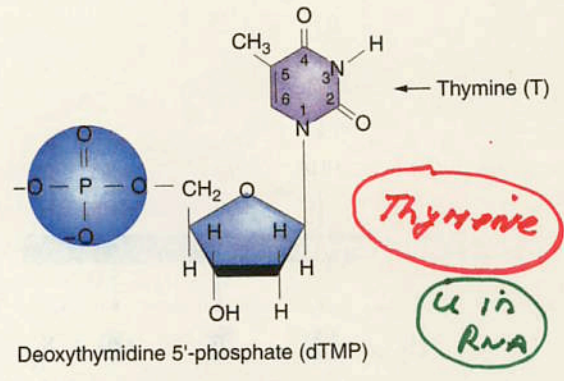
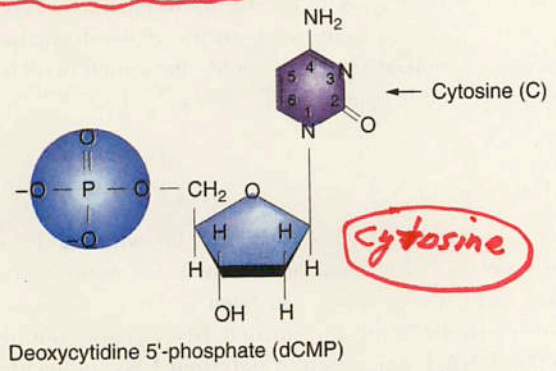


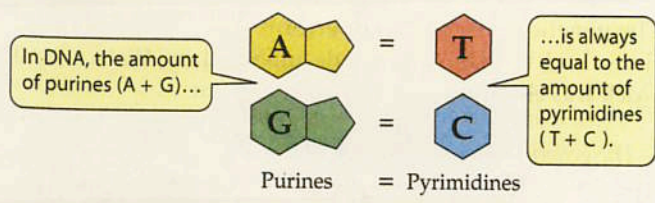
Figure 8-4 Chemical structure of the four nucleotides (two with purine bases and two with pyrimidine bases) that are the fundamental building blocks of DNA. The sugar is called deoxyribose because it is a variation of a common sugar, ribose, that has one more oxygen atom.

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**

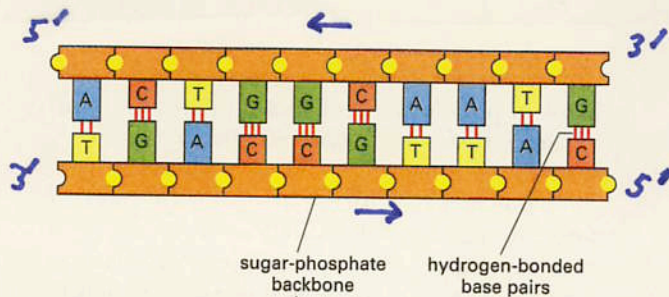
DNA ORIGIN	AMOUNT OF BASE (PERCENTAGE OF TOTAL DNA)			
	A	T	G	C
Human ( <i>Homo sapiens</i> )	31.0	31.5	19.1	18.4
Corn ( <i>Zea mays</i> )	25.6	25.3	24.5	24.6
Fruit fly ( <i>Drosophila melanogaster</i> )	27.3	27.6	22.5	22.5
Bacterium ( <i>Escherichia coli</i> )	26.1	23.9	24.9	25.1

What would you predict for a single strand of DNA?

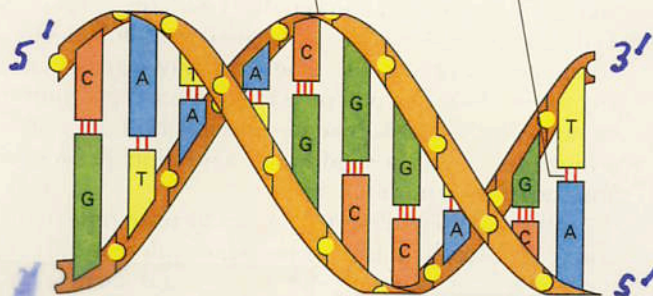
Chargaff's Rules!

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

(D) double-stranded DNA



(E) DNA double helix



- 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  
$$\begin{array}{ccc} 5' & \rightleftarrows & 3' \\ 3' & \leftleftarrows & 5' \end{array}$$

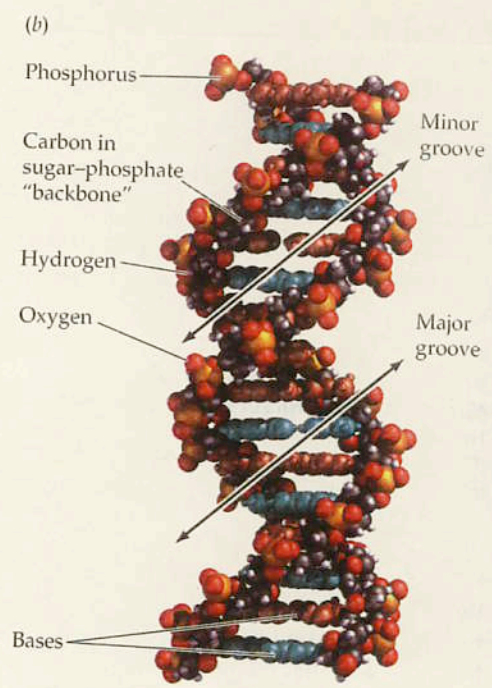
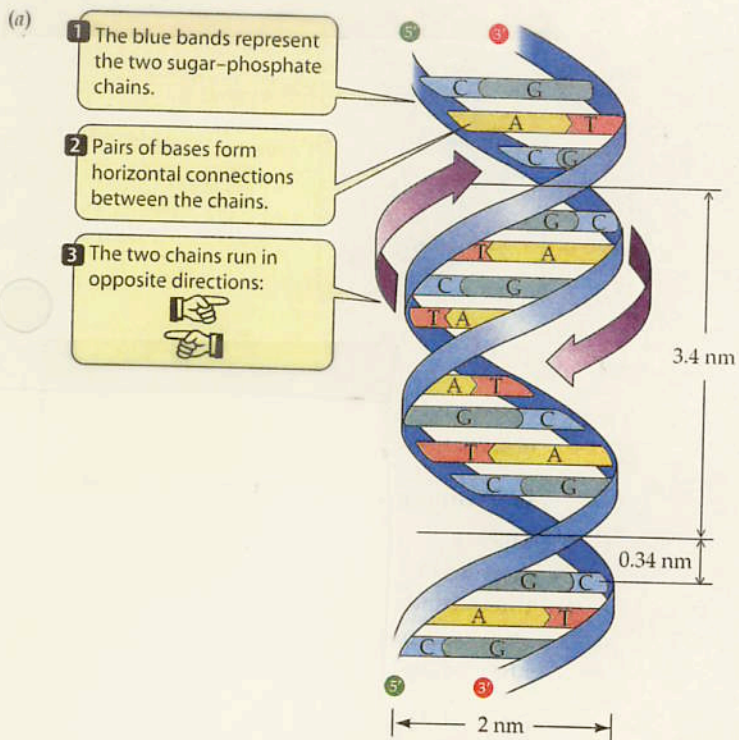
sequence differs \* only way bases fit in "middle"
- ⑤ Bases in interior stacked & bonded by H-bonds - complementary "rungs" on "ladder"
- ⑥ Backbone - sugar-phosphate bonds
- ⑦ No constraint on sequence  $4^n = n$  # sequences
- ⑦ DNA has dimensions: 

20Å diameter
3.4Å/bp
10bp/turn

Know # bp  
∴  
know length!
- ⑧ order → Biology

FROM X-Ray Diffraction Pictures

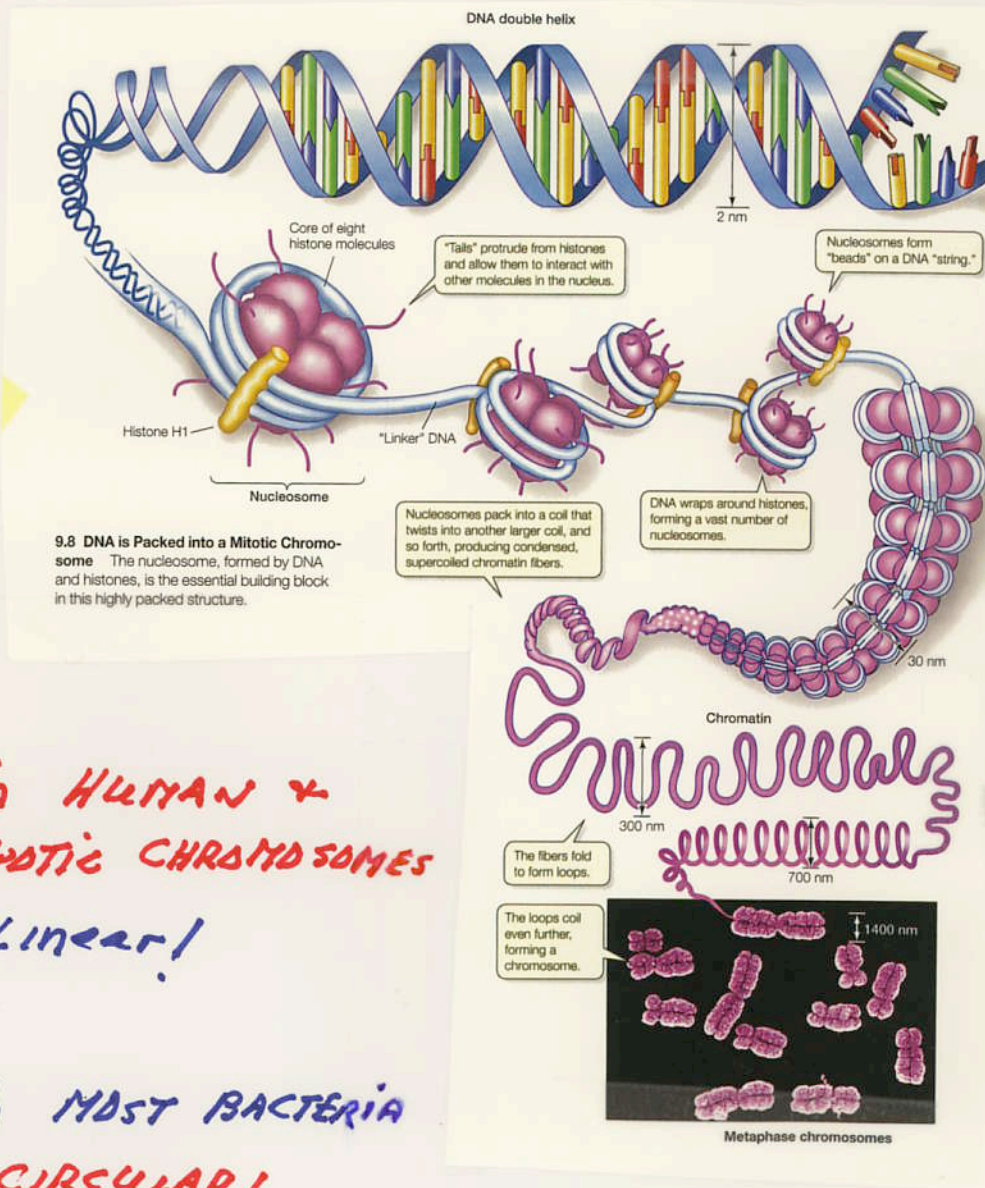
# The Double Helix



READ BOOK/TEXT BY SAME NAME!



A CHROMOSOME CONTAINS ONE (OR TWO!!)  
CONTINUOUS DNA MOLECULE



DNA in HUMAN &  
 EUKARYOTIC CHROMOSOMES  
 is LINEAR!

DNA in MOST BACTERIA  
 is CIRCULAR!

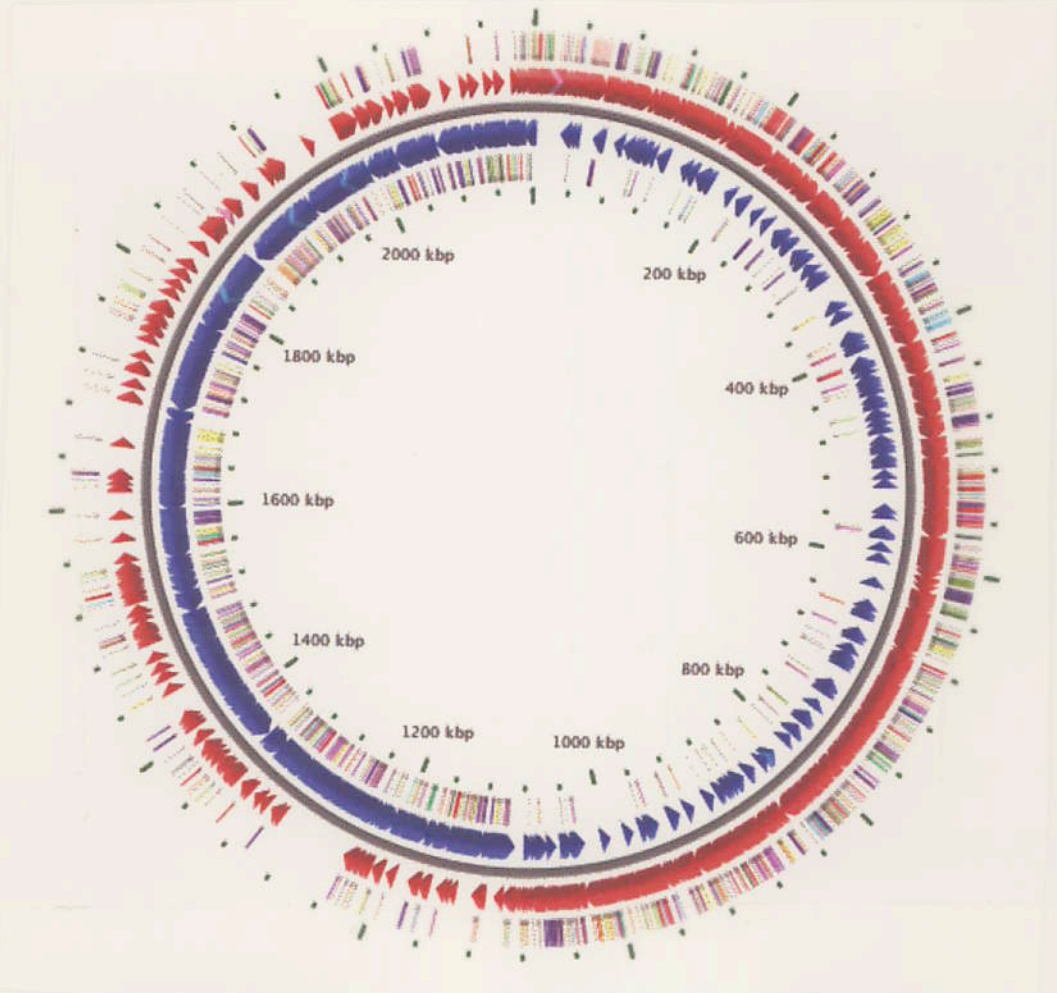
The CIRCULAR *E. coli* Chromosome  
ONE DNA Circle



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.)

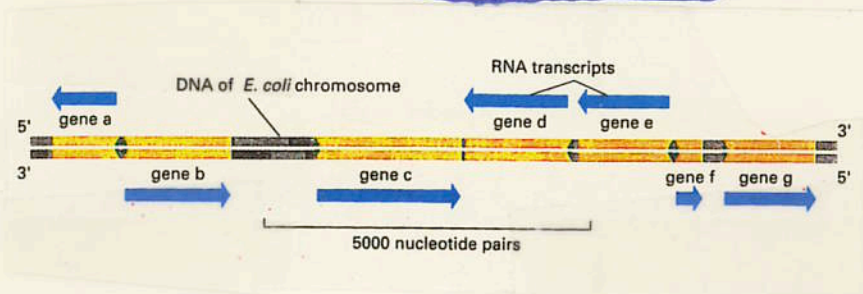


THE CHROMOSOME OF STREPTOCOCCUS  
pneumoniae is ALSO CIRCULAR!



2,160,837 bp  
2,164 genes

A CHROMOSOME CONTAINS MANY GENES  
That Reside at Specific Positions  
And have unique  
FUNCTIONS



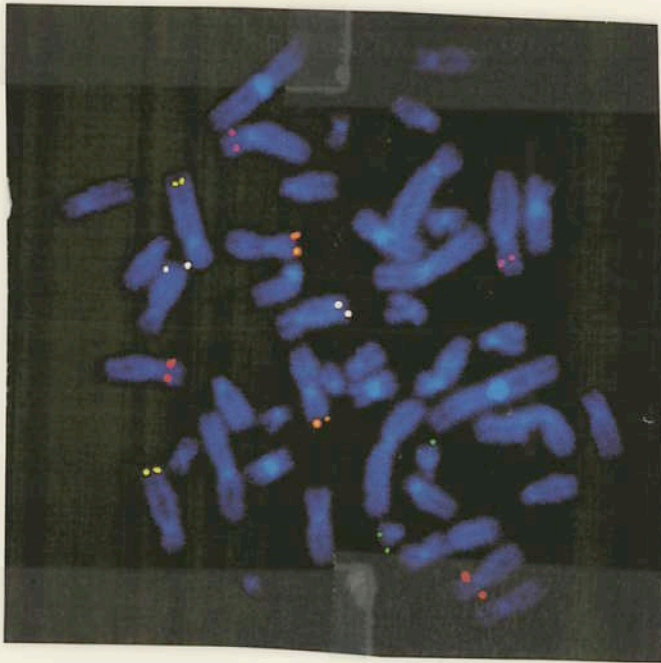
What  
defines the  
gene  
position?

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?

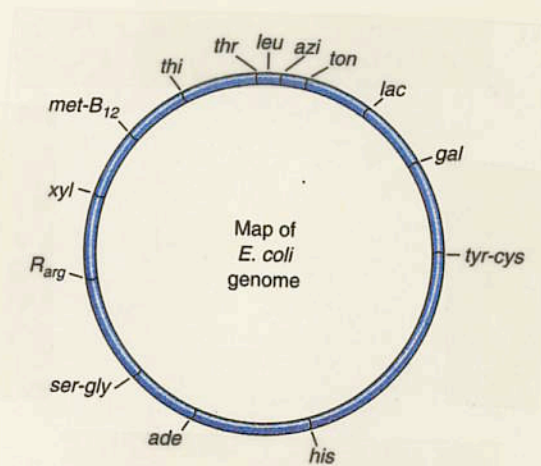
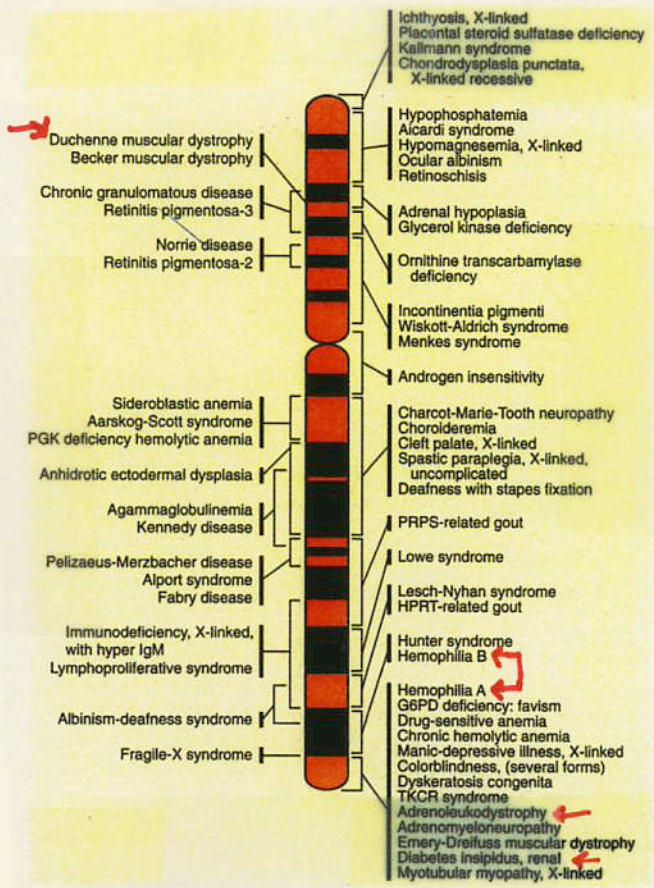


Genes Reside at Specific Positions  
or **Loci**



Gene Position = LOCUS = UNIQUE  
DNA Sequence

**Genes Reside at Specific Locations**



Circular DNA  
How know?

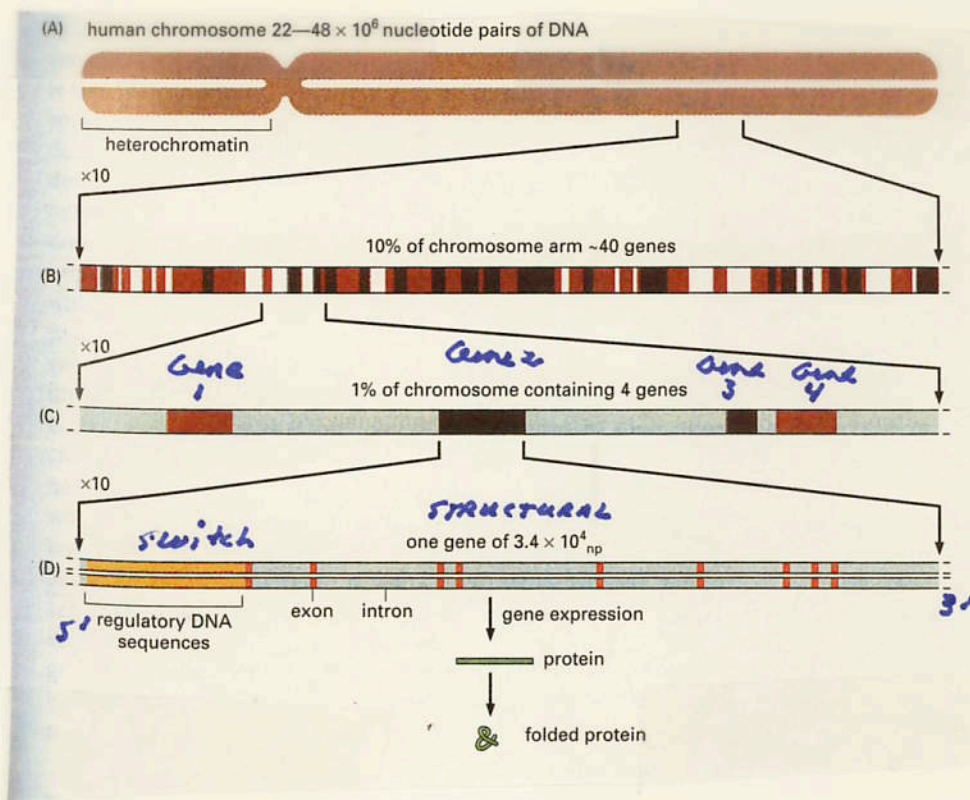
Linear DNA  
How know?

**Note Bands - What are these?**

How know Gene Positions? Chromosome #?



# ORGANIZATION OF GENES ON HUMAN CHROMOSOME 22



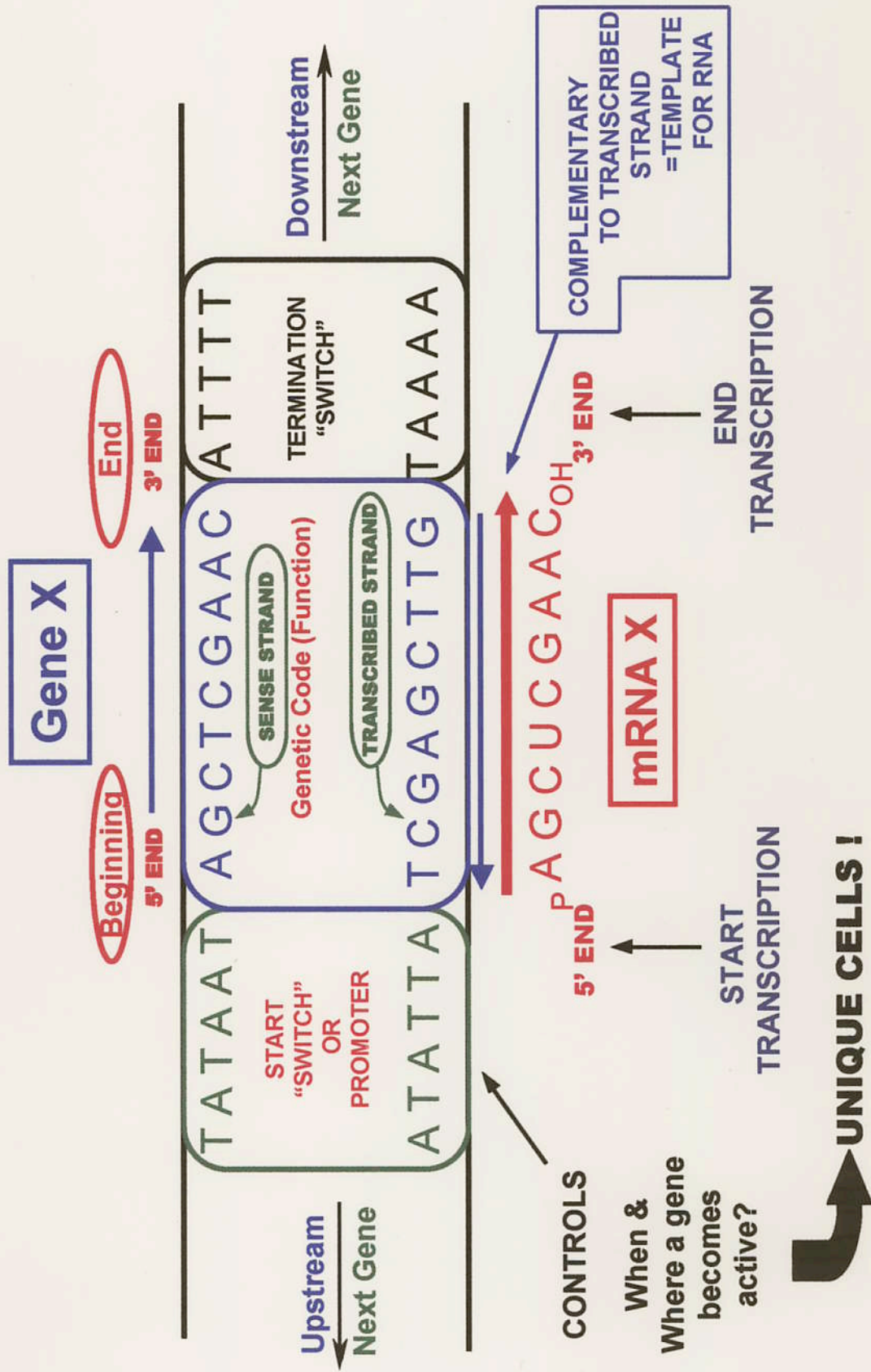
Chromosome 22  
A "small" one!

one large gene!

Genes are defined/precise regions of DNA

Genes Act as individual units?  
How know? Glatfish Experiment!  
Genetic Engineering Anti<sup>®</sup>

**A Gene is a Specific DNA Sequence That Directs the Expression of a Unique Trait**



Note: mRNA Sequence = Sense Strand Sequence



## A "Simple" Gene Reviewed

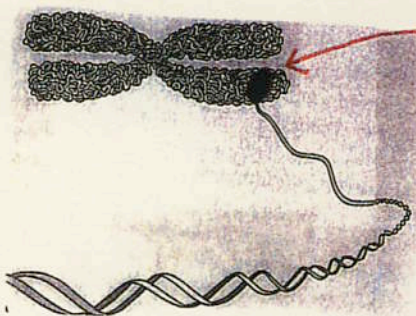
- ① Sense STRAND = Genetic code
- ② Sense STRAND = 5' → 3' direction (all DNA sequences specified 5' → 3')
- ③ Anti-Sense STRAND = Complement of Sense STRAND & is TRANSCRIBED STRAND
- ④ mRNA = SAME SEQUENCE AS SENSE STRAND & Complementary to Anti-Sense STRAND
- ⑤ mRNA = 5' → 3'
- ⑥ Switch TURNS GENE 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 Chassis & Complementary Base Pairing!

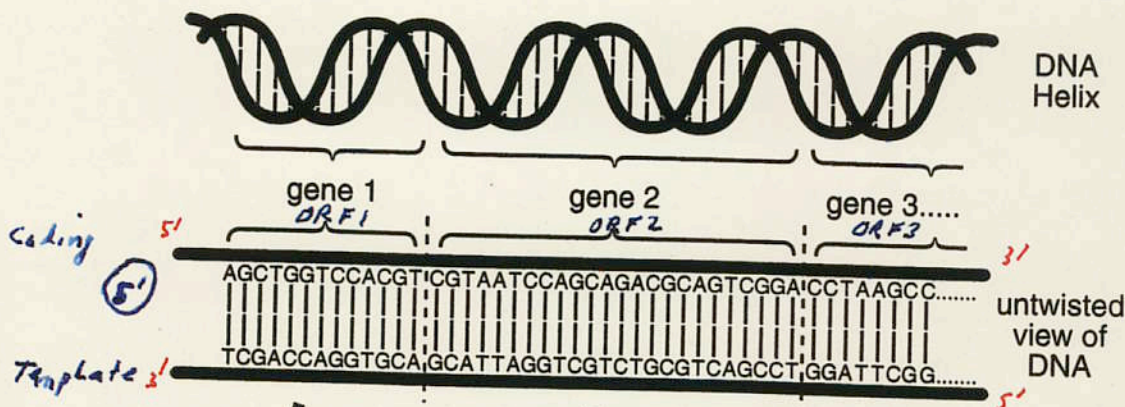


A Chromosome Contains Many Genes



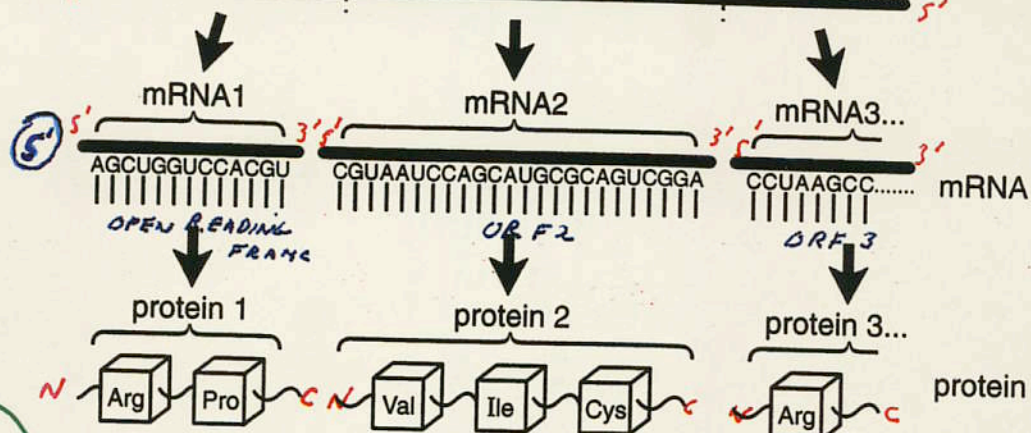
Position of Genes 1, 2, & 3 in Chromosome

Discrete Units!



What delineates each gene?

Notice Sequence of each gene



5'

Note Sequence of each protein

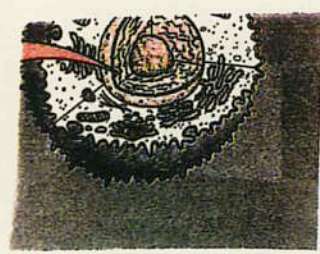
FIGURE 2.6 Adjacent sets of base pairs comprising different genes.

Function 1

Function 2

Function 3

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 GENE SEQUENCE AND PROTEIN SEQUENCE



Control Switches are  
 unique DNA  
 Sequences  
 &  
 CAN BE CLONED!

AND USED TO Re-Engineer Organisms!!  
 Switches ACT independently of gene!!

Regulatory  
 proteins  
 TURN Genes  
 on & off  
 ① SRY gene  
 ② eye gene

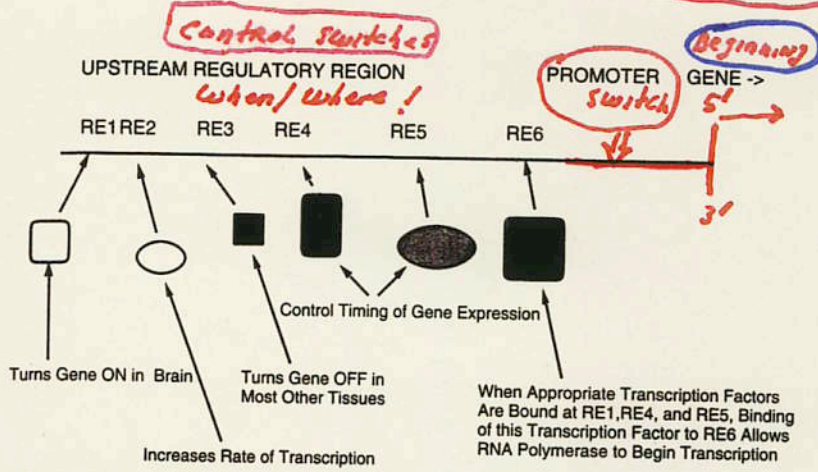


FIGURE 3.13 Enhancers and transcription factors in eukaryotic cells. A schematic diagram of the upstream regulatory region for a brain specific transcript is provided.

Each Switch = Unique DNA Sequence!

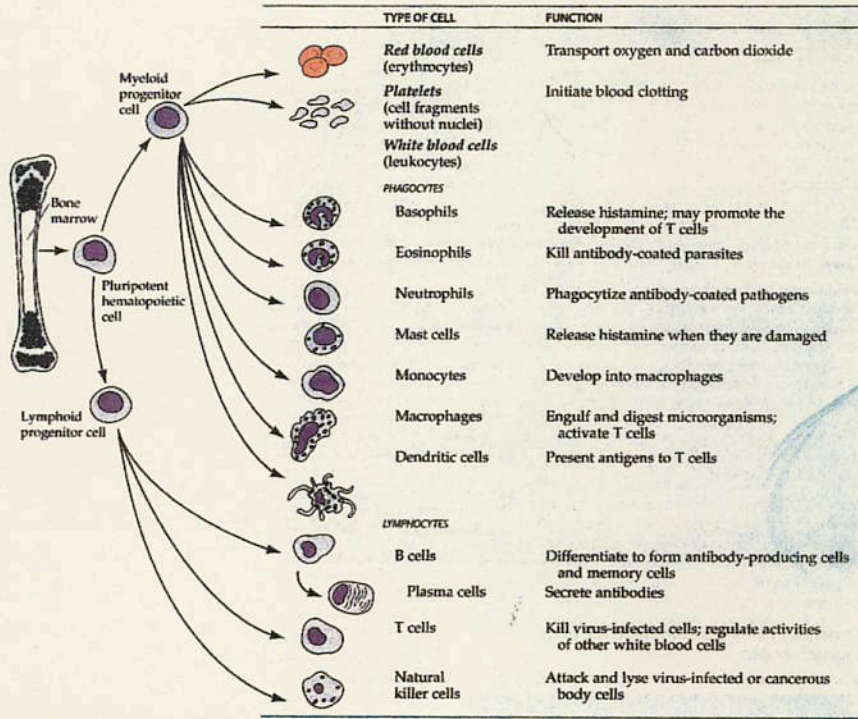
Genome Projects Reveal BOTH  
 the Gene & the Logic that  
 Controls them!

RULE! SEQUENCE → BIOLOGY!!

NO "HOCUS FOCUS"  
 YO! IT'S IN THE DNA!



**SWITCHES CONTROL WHERE & WHEN A GENE IS ACTIVE → UNIQUE FUNCTIONS → UNIQUE 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.

**ACCESSORY ORGANS:**

Salivary glands

Liver

Gallbladder

Pancreas

Ascending colon

Cecum

Esophagus

Stomach

Large intestine

Small intestine

Descending colon

Rectum

Anus

*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  $\Rightarrow$  Genetic Engineering

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

→ human gene (+) plant leaf 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!!



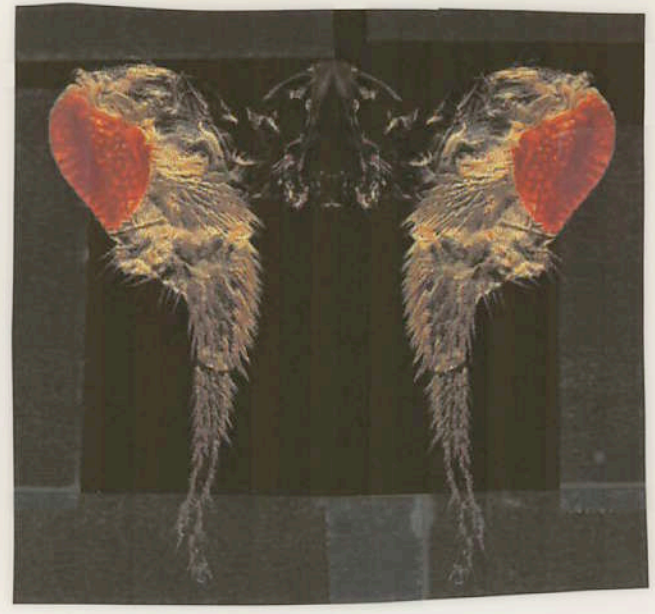
AN EYE GENE CAN BE EXPRESSED  
in OTHER BODY REGIONS  
BY ENGINEERING its switch



eye gene

Replace  
eye gene  
switch  
with  
leg gene  
switch  
by  
Genetic  
Engineering

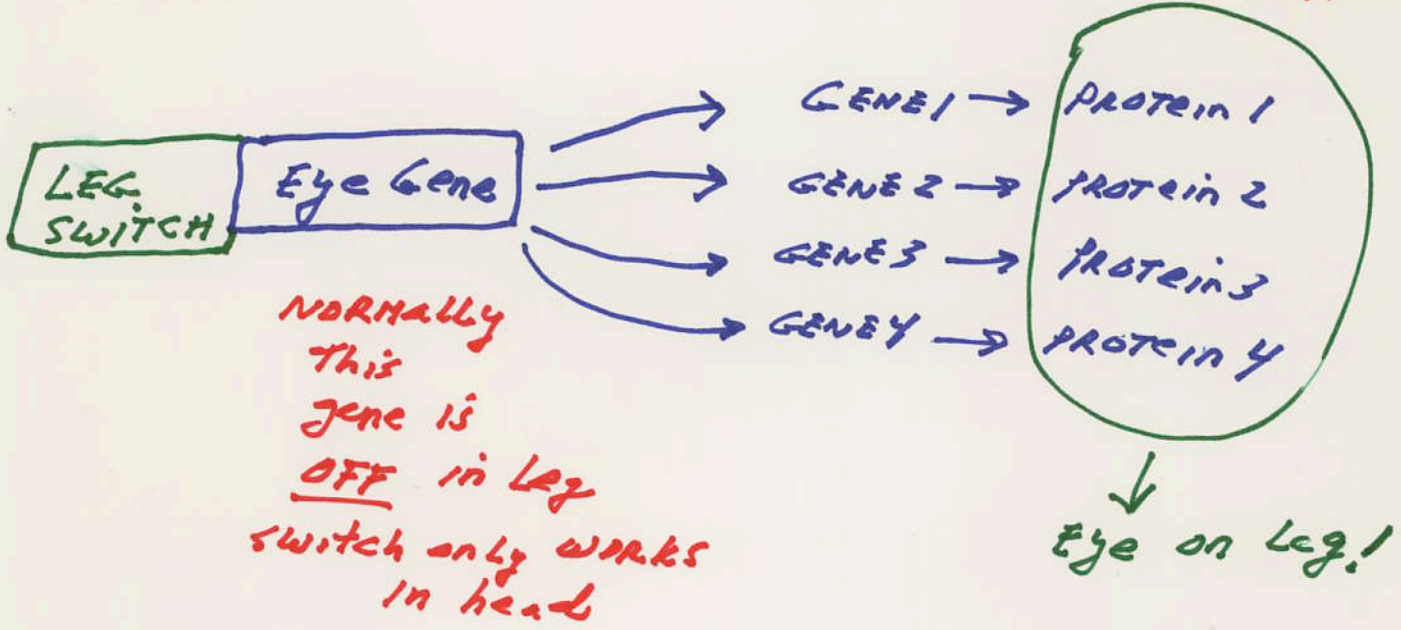
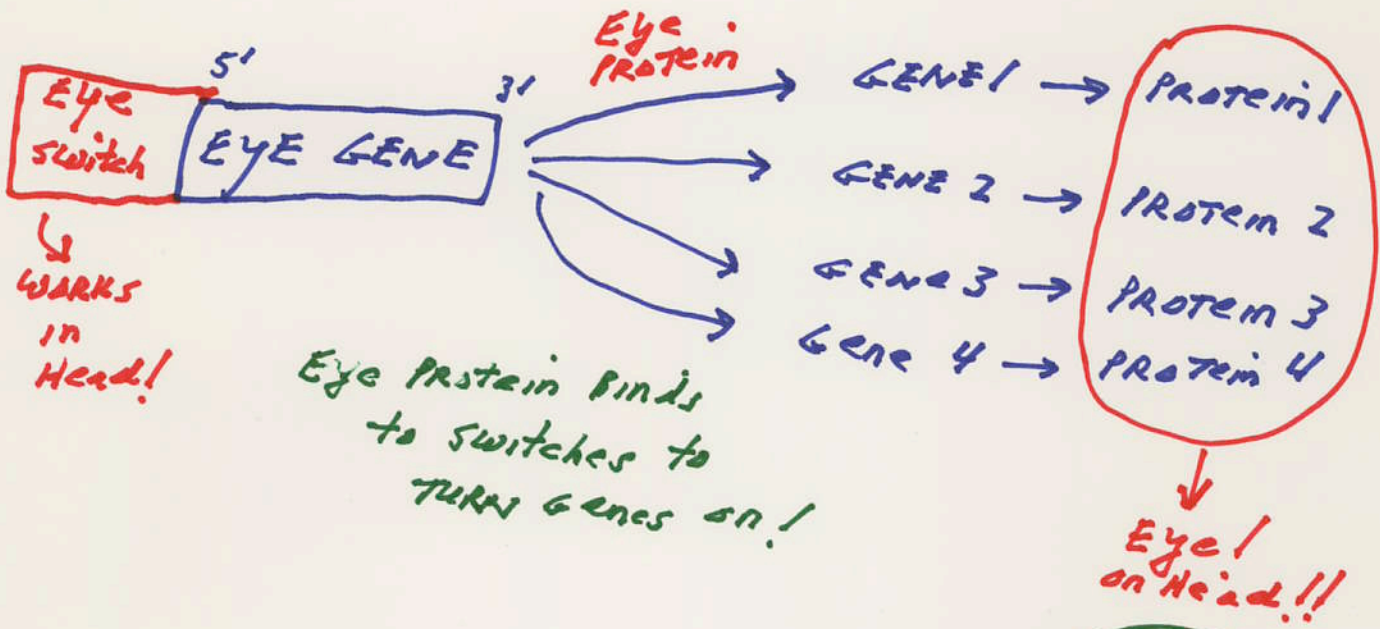
eye gene  
+  
leg switch



∴  
Active in  
Leg!!!

# Eye Regulatory Network

CONTROL GENES LIKE THE EYE GENE CONTROL THE ACTIVITY OF OTHER GENES!





## 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?



If We Know (1) the Entire Genome Sequence of an Organism (e.g. humans), Including Genes and Switches (2) What Protein and Process Every Gene Specifies and (3) When, Where, and How Every Gene Is Turned On and Off in Development (i.e., the genetic logic from birth to death) Is There Any Biological Limit to What Can Be Done Using Genetic Engineering?

- a. Yes
- b. No