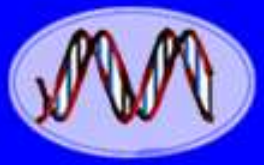


DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria

DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

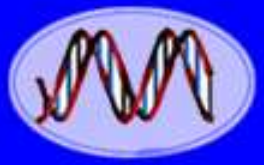
HC70A & SAS70A Winter 2011
Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg & John Harada

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

UCLA

UCDAVIS
UNIVERSITY OF CALIFORNIA



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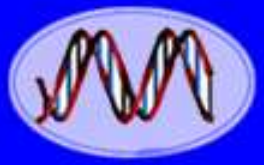
PREVIOUS TWO LECTURES

- Age of DNA
- Genetic Engineering Origins
- What Can Be Done With Genetic Engineering?
- Classical vs. Molecular Genetic Engineering
- Demonstrations
  - Spooling DNA
  - Bacterial "Cloning"
  - Gel Electrophoresis
  - Classical Genetic Engineering



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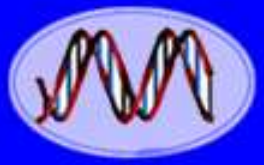
THEMES FOR TODAY'S LECTURE
Gene Structure & Function
Part One

- What is the Function of a Gene?
- What are the Properties of Genes?
- What is the Evidence That DNA is the Genetic Material (Griffith and Avery Experiments)?
- Is Transformation Universal?
- What is the Structure of DNA?
- What is the Structure of a Chromosome?
- What is the Anatomy of a Gene?

1. What is the Colinearity Between Genes & Proteins (how does DNA→protein)?
2. How Do Switches Work to Control Gene Activity?
3. What Are the Possibilities For Manipulating Genes in the Future?



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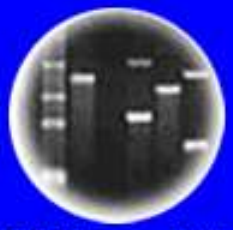


DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

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?

If DNA is the Genetic Material, THEN What……?

The Spanish Flu Pandemic - 1918 to 1920

It is estimated that anywhere from 20 to 100 million people were killed worldwide,or the approximate equivalent of one third of the population of Europe, more than double the number killed in World War I. This extraordinary toll resulted from a high death rate of up to 50%.

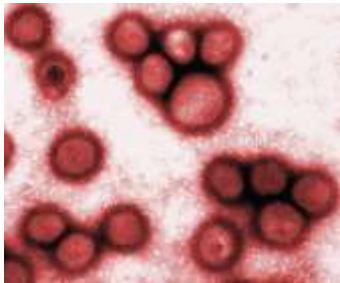
Characterization of the 1918 "Spanish" influenza virus neuraminidase gene PNAS June 6, 2000

Ann H. Reid,* Thomas G. Fanning, Thomas A. Janczewski, and Jeffery K. Taubenberger

Researchers detect deadly Spanish flu genes

A team of researchers in Japan and the United States have determined the causative genes for the Spanish flu that reportedly claimed the lives of some 40 million people around the world in 1918. PNAS January, 2009

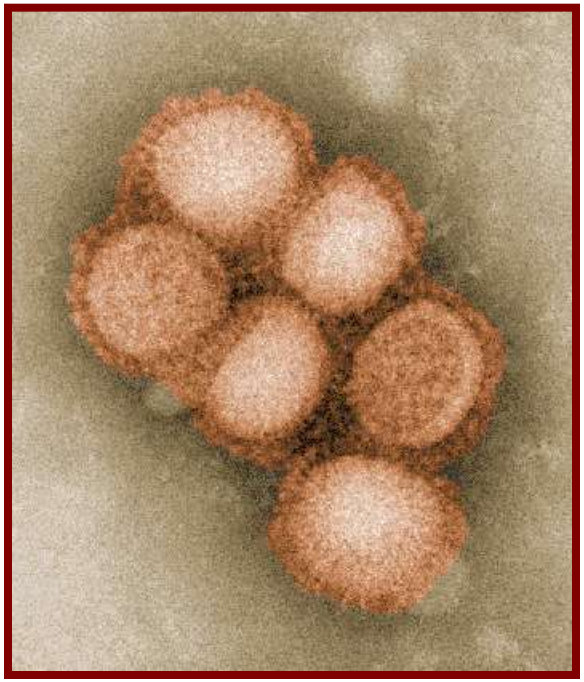
By Sequencing the Virus Genome From Victims Dead For 80 Years & Synthesizing the "Original" Flu Virus By Genetic Engineering



How Many People Died Worldwide During the 2009 H1N1 Pandemic?

a. 130
b. 1,300
c. 13,000
d. 130,000
e. 1,300,000

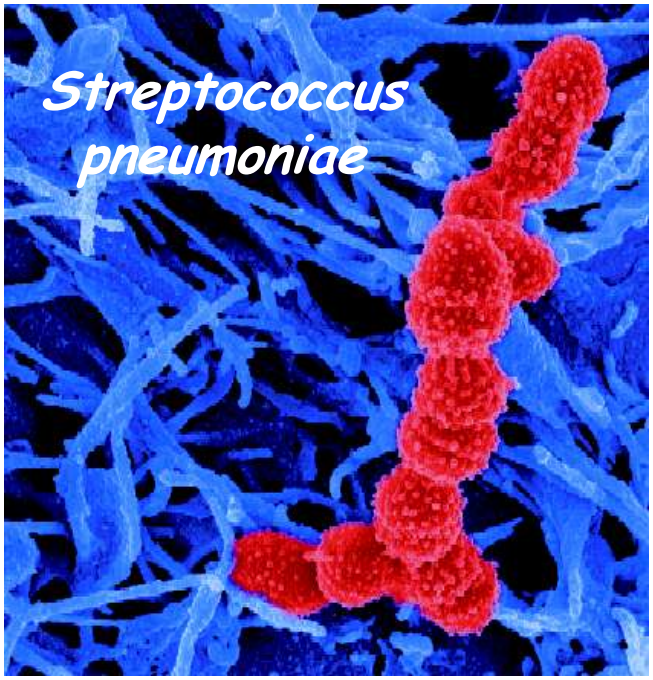
H1N1 Virus



January 29, 1922 - New York City

PNEUMONIA KILLS 990 IN CITY SINCE JAN. 1; Forty-Eight Die in Twenty-Four Hours, Four Fewer Than on Previous Day. 387 INFLUENZA CASES Six More Deaths Reported, but Copeland Sees Chief Danger in First-Named Disease.

Bacterial Pneumonia Was Also a "Killer" at This Time!



And still is…1,000,000 Deaths/Year TODAY! Mostly Children

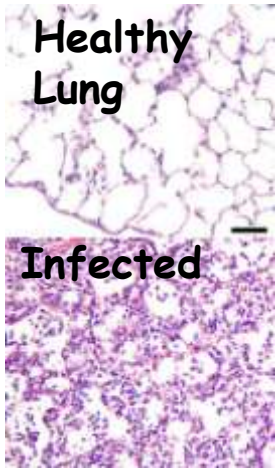
Major Causes of Death

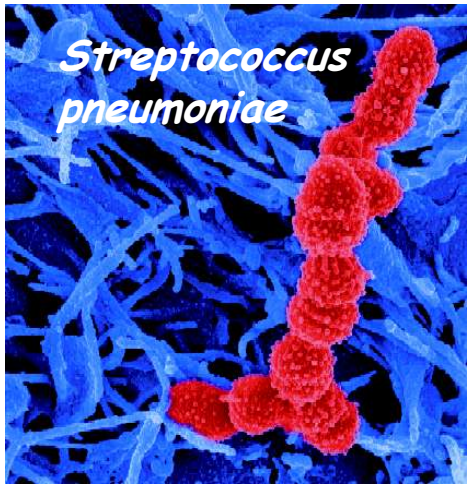
1920	2002
1. Typhoid Fever	1. Heart Disease
2. Malaria	2. Infectious & Parasitic Diseases
3. Small Pox (virus)	3. Cancer
4. Measles	4. Stroke
5. Scarlet Fever	5. Respiratory Diseases
6. Whooping Cough	6. Unintended Injuries (e.g., Cars)
7. Diphtheria	7. HIV/AIDS
8. Flu	8. Digestive Diseases
9. Mumps	9. Diarrheal Diseases
10. Cholera	10. Intentional Injuries (Murder, War, etc.)
Note: *All of these diseases are treatable or preventable with antibiotics or vaccines!!!!*	

Frederick Griffith & The Transforming Principle

The First Genetic Engineering Experiment

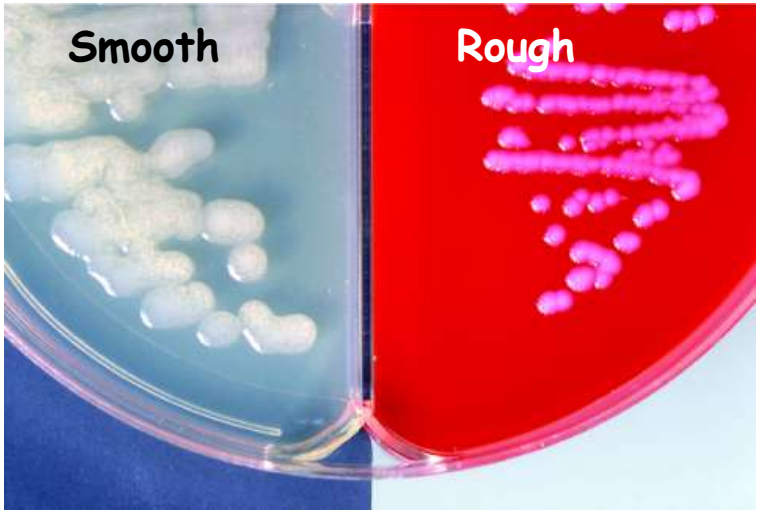
QuickTime™ and a
decompressor
are needed to see this picture.



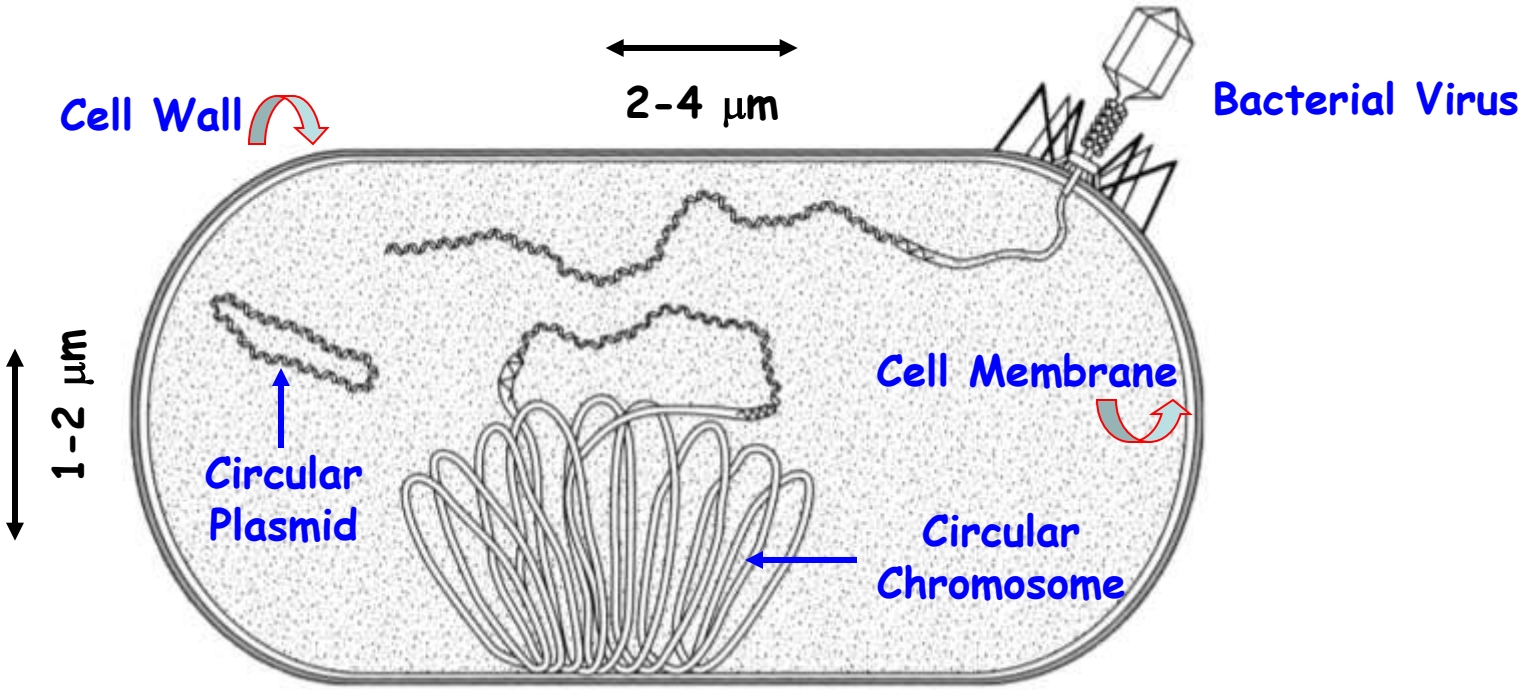


1879-1941

Invented the Word "Transformation"
Not Understood For Another 50 Years



A Typical Bacterial Cell



Plasmids: 2,000-150,000 bp (1-100 genes)
Chromosome: 500,000-5,000,000 bp (500-5,000 genes)

Plasmid DNA: ~1.4 μm (10^{-6} m) in circumference (Genetic Engineering Vectors)
Chromosome: ~ 1.4 mm (10^{-3} m) in circumference

1 μm = 3.94×10^{-5} inches

Bacterial Genome Projects Have Provided Remarkable Insight Into Bacterial Genomes and Cell Functions

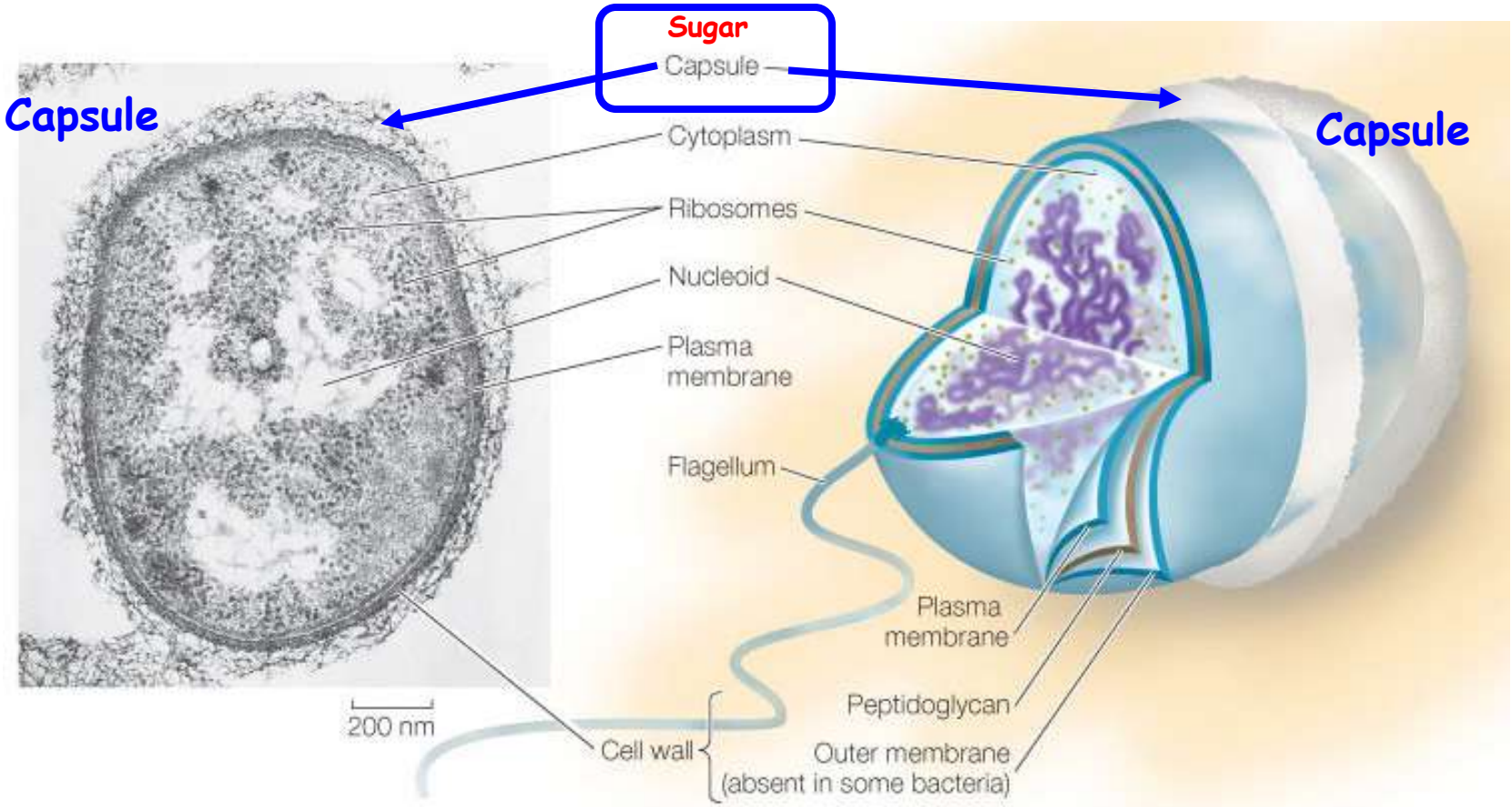
Table 1–1 Some Genomes That Have Been Completely Sequenced

SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	ESTIMATED NUMBER OF GENES CODING FOR PROTEINS
BACTERIA				
Mycoplasma genitalium	has one of the smallest of all known cell genomes	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 anthracis	causes anthrax	soil	5227	5634
Aquifex aeolicus	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
Streptomyces coelicolor	source of antibiotics; giant genome	soil	8667	7825
Treponema pallidum	spirochete; 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 very high temperatures	hydrothermal vents	1860	1877

1400 Bacterial Genomes Have Been Sequenced to Date (January, 2011)

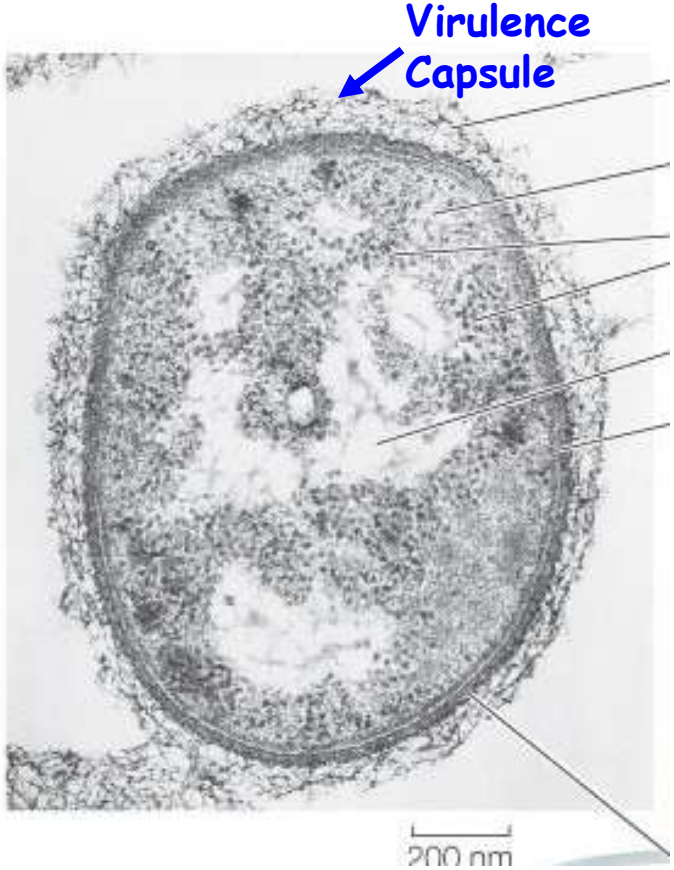
Table 1-1 (part 1 of 2) *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

Streptococcus pneumoniae



The Sugar Capsule Protects the Bacteria From Mammalian Host Antibodies

Streptococcus pneumoniae Genome Has Been Sequenced!

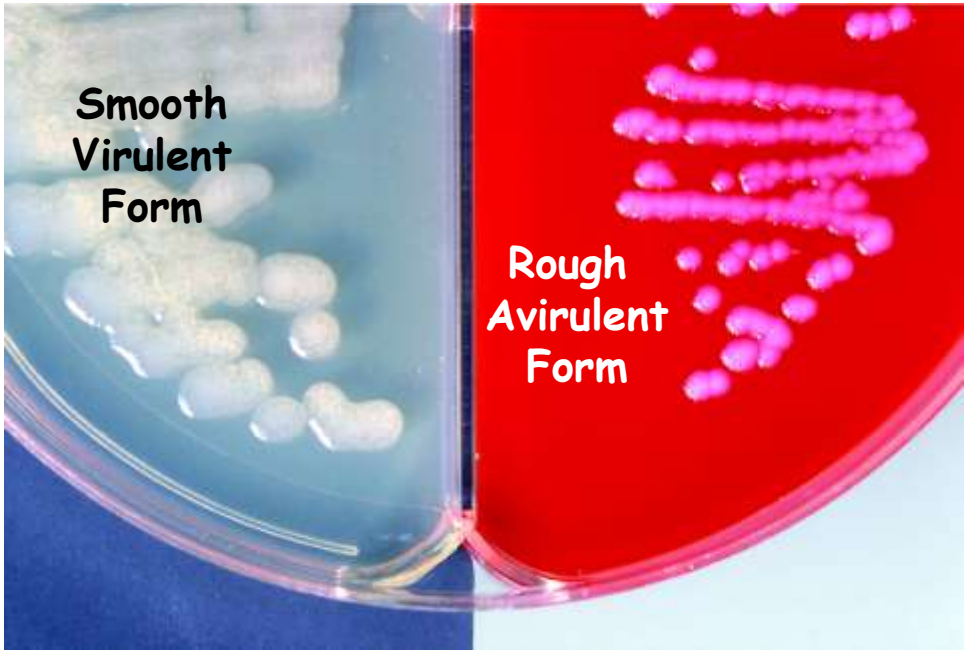


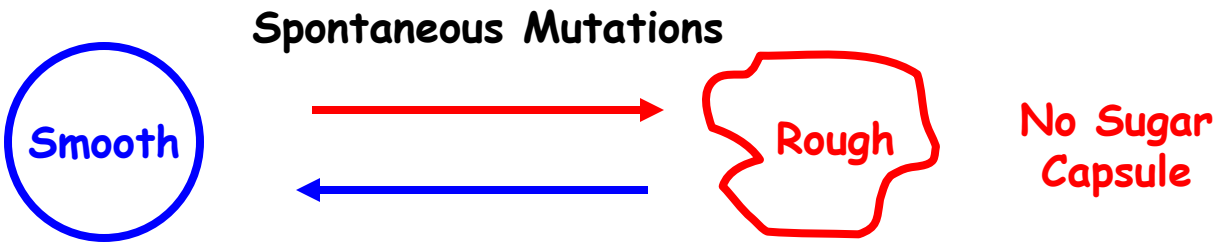
Note Genes on BOTH DNA Strands!

2,046,115 bp and 1,987 Genes

J. Bacteriology
2001

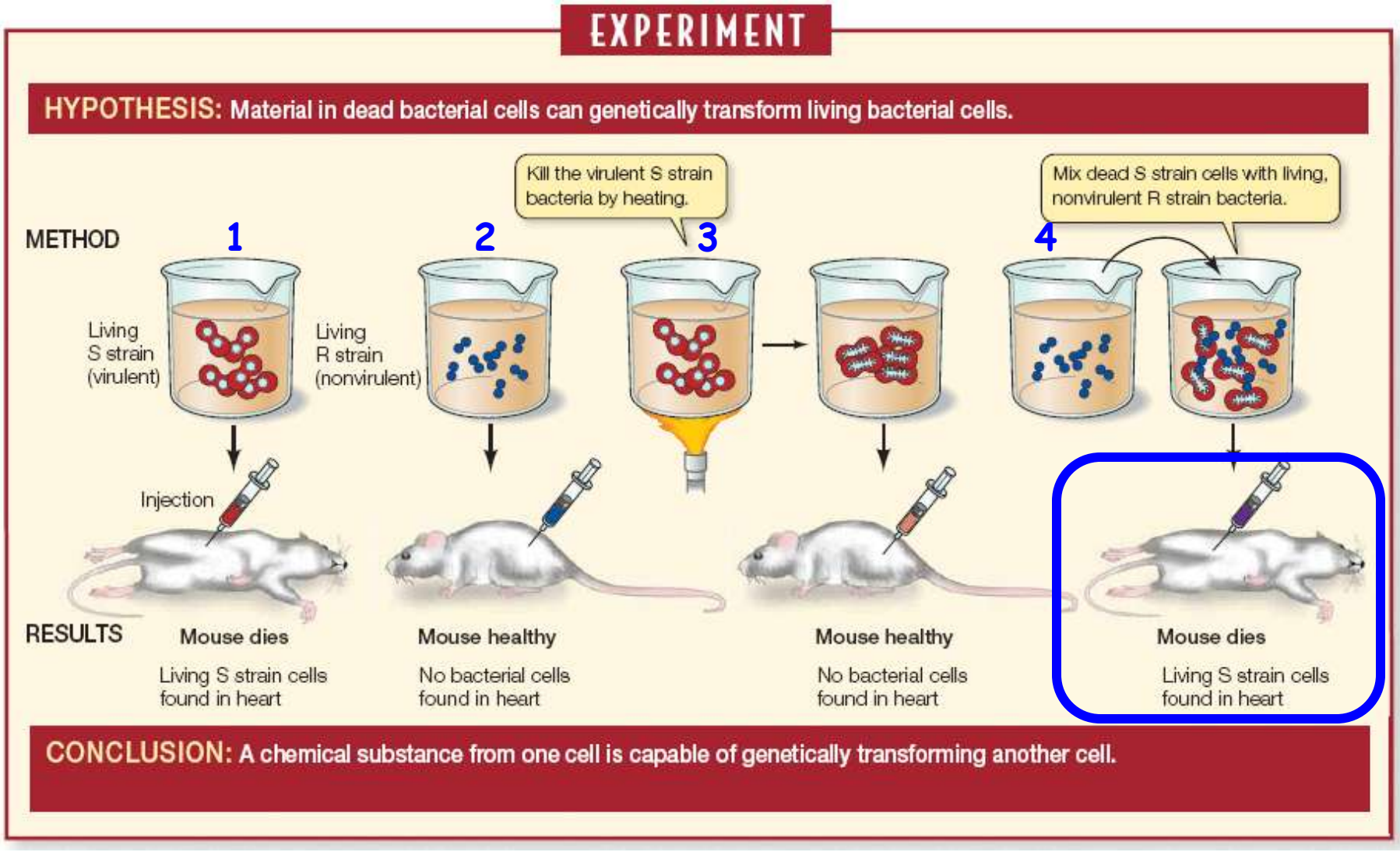
The Griffith Experiment
With Smooth and Rough Pneumonia Bacteria





J. Hygiene, 1928

The Griffiths Experiment (1928)



LIVE Rough Cells TRANSFORMED by DEAD Smooth Cells!!!

HOW? What Was the Transforming Principle? Hypothesis?

Griffiths, 1928, J. of Hygiene, 28 (2), 113-157

VOLUME XXVII JANUARY, 1928 No. 2

THE SIGNIFICANCE OF PNEUMOCOCCAL TYPES.

BY FRED. GRIFFITH, M.B.

(*A Medical Officer of the Ministry of Health.*)

(*From the Ministry's Pathological Laboratory.*)

Inoculation experiments with heated virulent Type I culture and attenuated R strains of Types I and II.

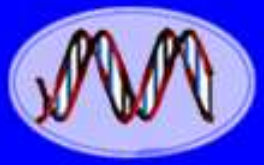
Conversion of R Type II into S Type I. In the experiment in Table VII two out of eight mice injected with heated virulent Type I culture together with an attenuated R culture derived from Type II died of pneumococcal septicaemia and yielded pure S colonies of Type I from the blood; plates from the lesions at the seat of inoculation showed a mixture of R and S colonies.

Table VII.

Killed S pneumococci	Living R pneumococci	No. of mouse	Result	Type of culture obtained from mouse
Type I heated 2 hours at 60° C. Dose = deposit of 50 c.c. of broth culture	None	641	Killed 5 days	None
	,,	642	,, 6 ,,	,,
	,,	643	,, 6 ,,	,,
	,,	644	,, 6 ,,	,,
As above	R 4, Type II. Dose = 0·25 c.c. of blood broth culture	645	Died 3 days	S colonies, Type I
		646	Killed 5 ,,	R cols. from local lesion
		647	,, 6 ,,	,, ,,
		648	,, 6 ,,	,, ,,
As above	R 4, Type II, grown in the heated Type I deposit. Dose = 0·36 c.c.	649	Killed 5 days	R cols. from local lesion
		650	Died 4 ,,	S colonies, Type I
		651	Killed 6 ,,	None
		652	,, 6 ,,	One R colony

Note: R Strain II Transformed into Smooth Strain I

Significance?



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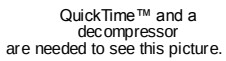
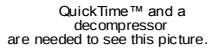
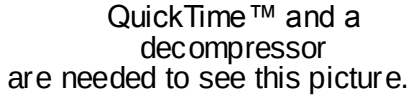
Change of Rough II Strain to Smooth I Strain Indicates that the Change is Due to Mutation or "Something" Else

a. Mutation
b. "Something" Else

What Was The Transforming Principle?
Experiments of Avery, McCleod, & McCarty
Fast Forward to the 1940s!



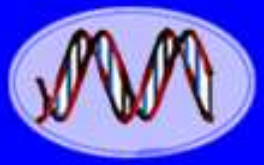




DNA is the Genetic Material!

One of the Major Reasons Watson and Crick Considered DNA As the Genetic Material In Order to Solve DNA Structure

***J. Exp. Med.*,1944**



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STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES

OSWALD T. AVERY, COLIN M. MACLEOD, AND MACLYN MCCARTY

J. Of Experimental Medicine,79 (2), 137-158 (1944)

STUDIES ON THE CHEMICAL NATURE OF THE SUBSTANCE INDUCING TRANSFORMATION OF PNEUMOCOCCAL TYPES

INDUCTION OF TRANSFORMATION BY A DESOXYRIBONUCLEIC ACID FRACTION ISOLATED FROM PNEUMOCOCCUS TYPE III

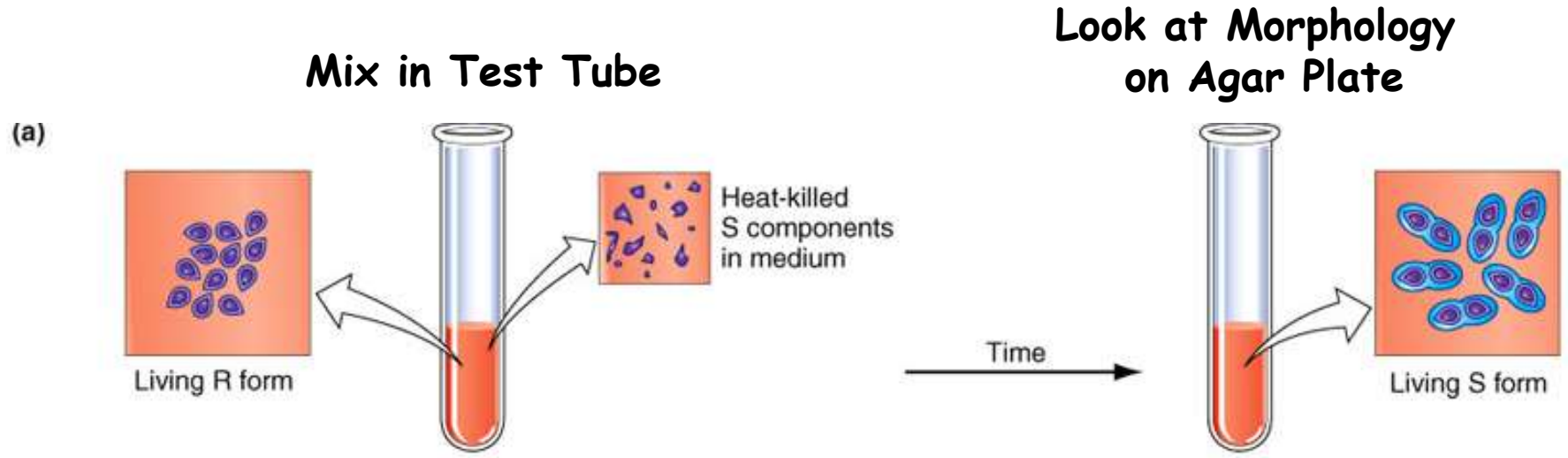
BY OSWALD T. AVERY, M.D., COLIN M. MACLEOD, M.D., AND MACLYN MCCARTY,* M.D.

Avery et al.Questions?

1. Does the Transforming Principle Come From the Mouse or Bacteria?
2. If From the Bacteria -- What Component?
3. How Devise Techniques to Determine What is the Transforming Principle?
   a) Transformation in Test Tube
   b) Isolation of Macromolecules
   c) Isolation of Enzymes (e.g., DNase, RNase)

Design Experiments To Show!!!

Does the Transforming Principle Come From the Mouse or Bacteria?



Hypothesis? Predictions? Experiment?

What Are the Major Chemical Components of a Bacterial Cell?
What Could Be the Transforming Principle?

1. What is Predicted if DNA is the Genetic Material?

2. How Test Hypothesis?

Table 2–2 The Approximate Chemical Composition of a Bacterial Cell

	PERCENT OF TOTAL CELL WEIGHT	NUMBER OF TYPES OF EACH MOLECULE
Water	70	1
Inorganic ions	1	20
Sugars and precursors	1	250
Amino acids and precursors	0.4	100
Nucleotides and precursors	0.4	100
Fatty acids and precursors	1	50
Other small molecules	0.2	~300
Macromolecules (proteins, nucleic acids, and polysaccharides)	26	~3000

Macromolecules

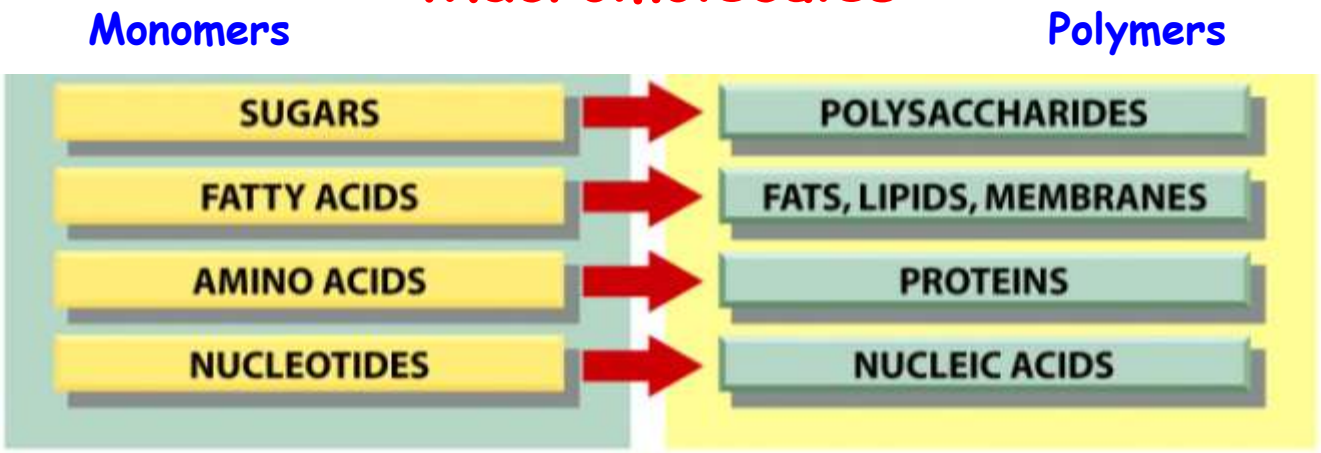


Table 2-2 *Molecular Biology of the Cell* (© Garland Science 2008)

Macromolecules and Their Cellular Functions

TABLE 3.1	Macromolecules		
Macromolecule	**Subunit**	**Function**	**Example**
CARBOHYDRATES	Sugar Virulence Capsule		
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Plant cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
PROTEINS			
Functional	Amino acids	Catalysis; transport	Hemoglobin
Structural	Amino acids	Support	Hair; silk
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	Phosphatidylcholine
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 support	Carotene; rubber

Testing Macromolecules For Transforming Activity

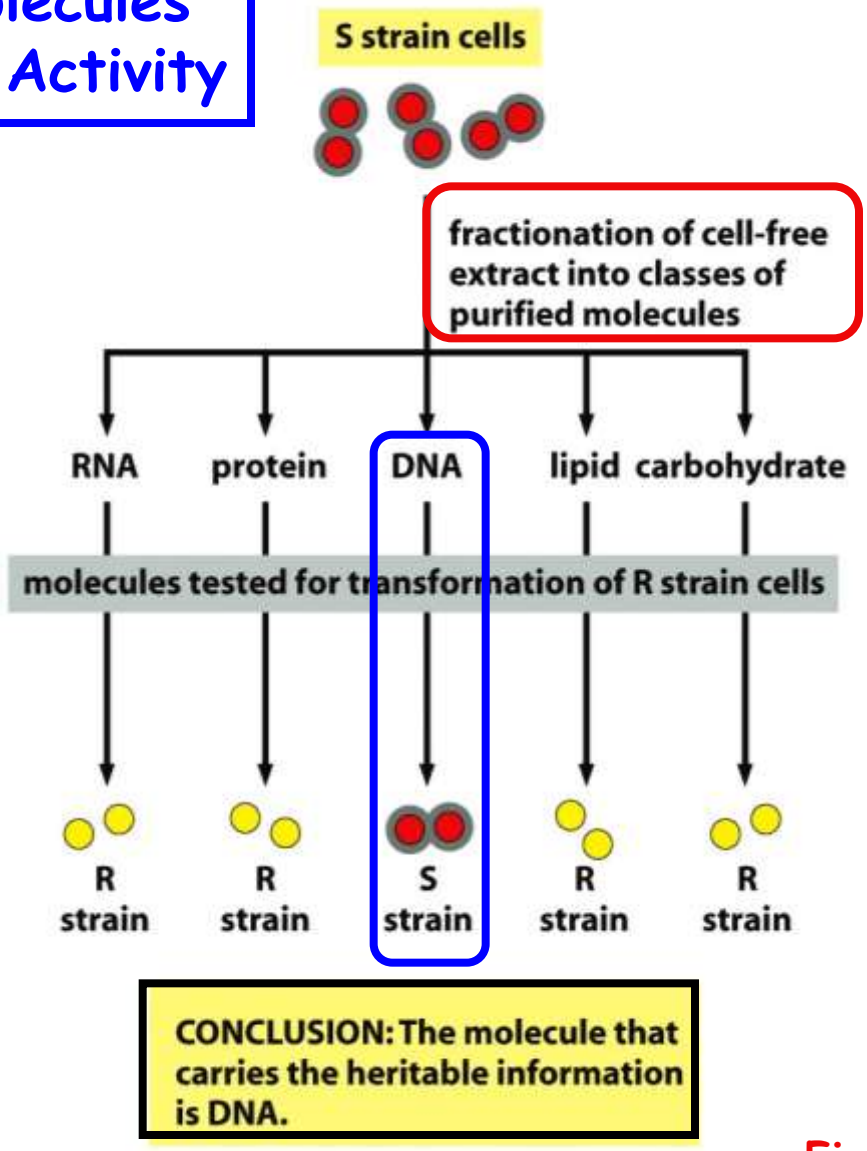


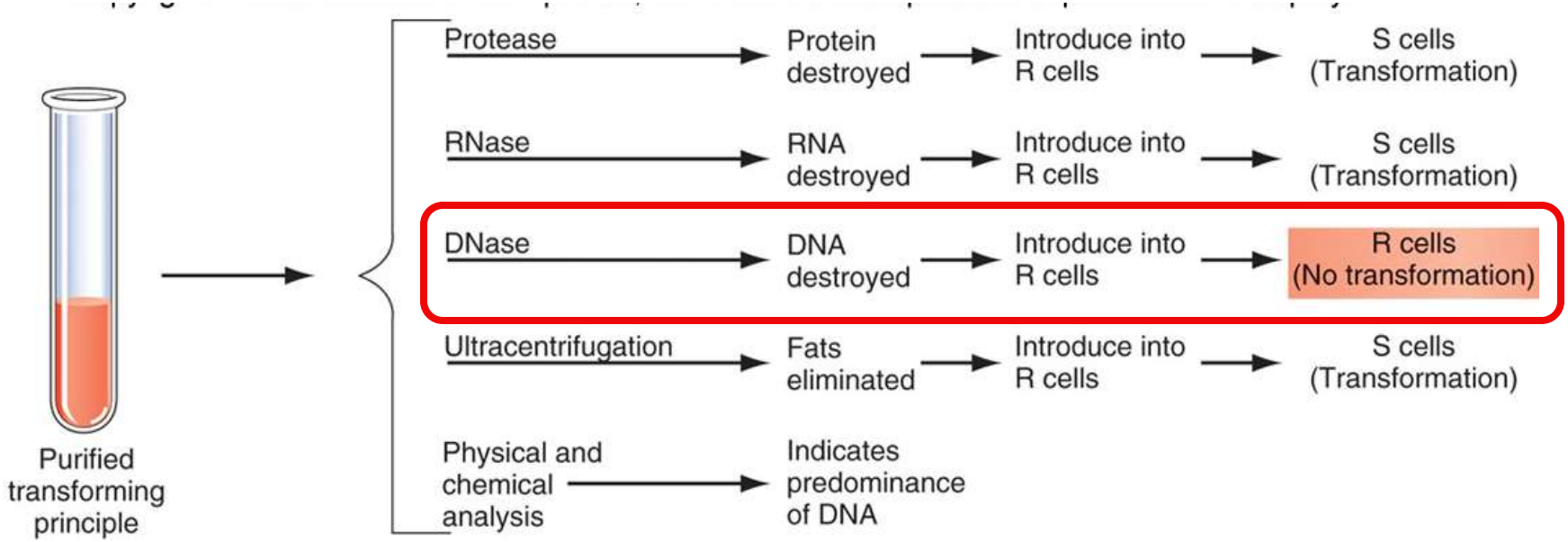
Figure 4-2 *Molecular Biology of the Cell* (© Garland Science 2008)

First Transformation Experiment With Purified Molecules!!

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

a. Yes
b. No

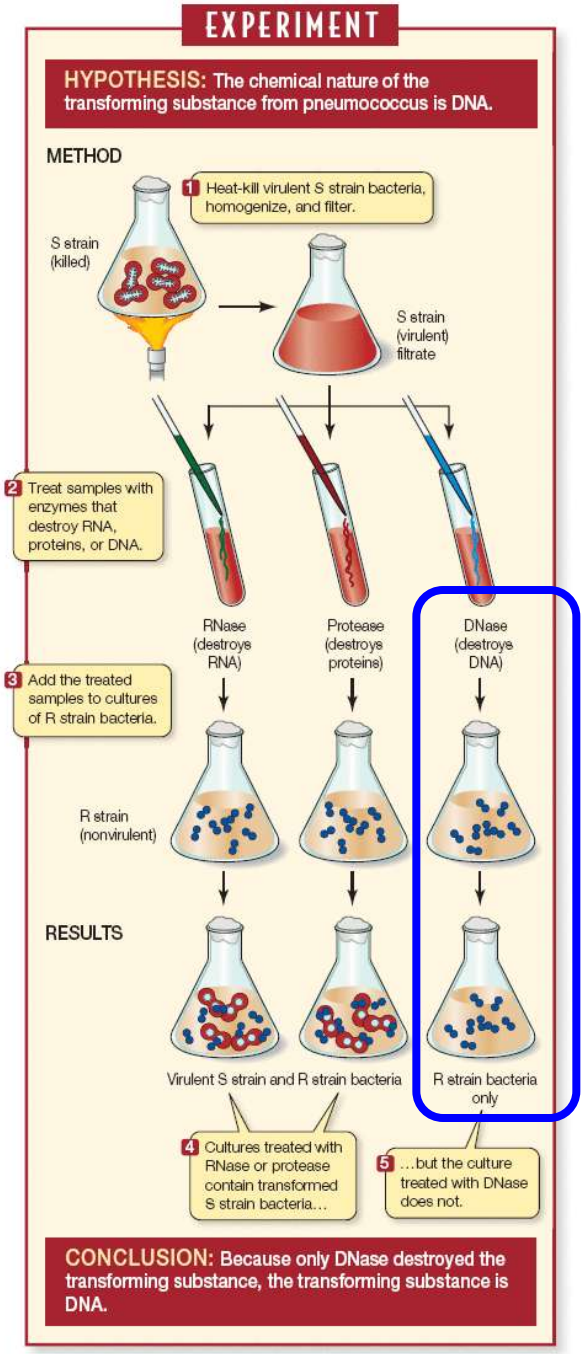
THE Critical Experiment by Avery et al.Showing That DNA IS THE Genetic Material



When DNase Destroyed DNA There Was No Transformation & Only Rough Cells Were Found in the Culture

If Smooth DNA Not Present, Rough Cells Cannot Be Transformed Into Smooth Cells!

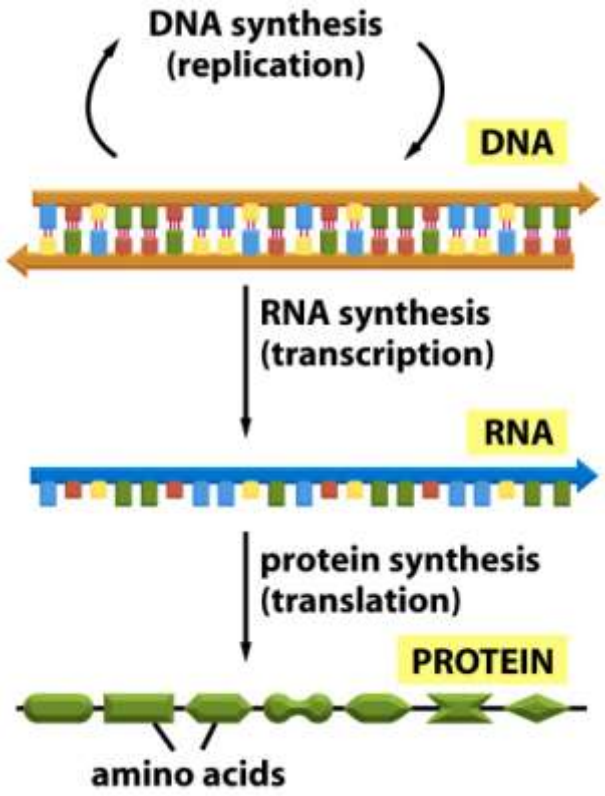
THE Critical Experiment by Avery et al. Showing That DNA Is the Genetic Material



When DNase Destroyed DNA There Was No Transformation & Only Rough Cells Were Found In Culture

How Did Avery et al. Experiments Verify the Hypothesis That DNA is the Genetic Material

Predictions	Results
Replication	Yes
Phenotype	Yes
Stable	Yes



Cell Processes

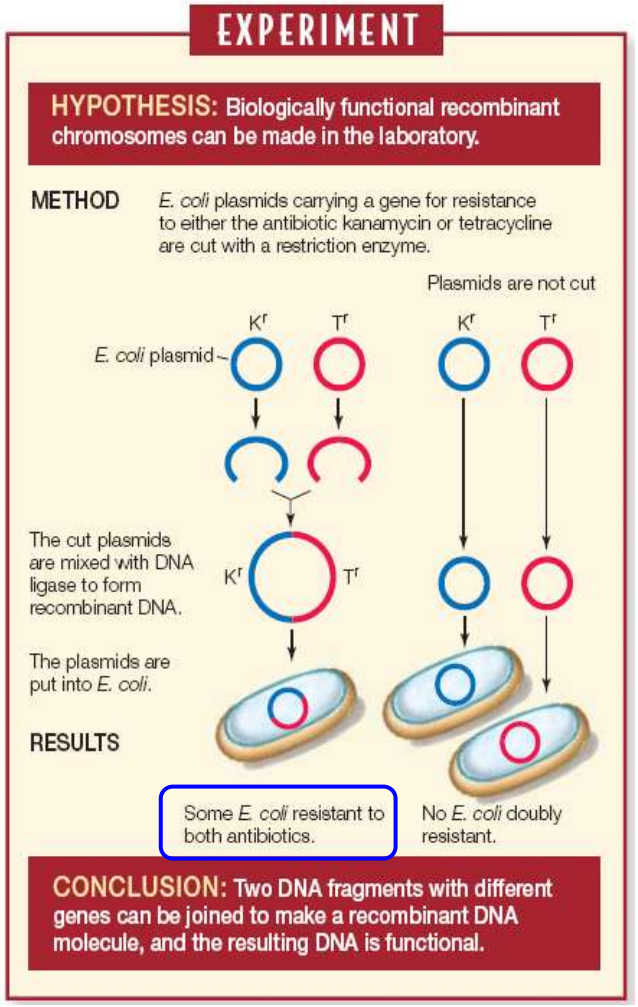
1. S DNA Taken Up By R-Cells
2. S Gene Transcribed Into S mRNA
3. S mRNA Translated Into Smooth Protein
4. Smooth Protein Helps Construct Sugar Capsule and Protects Bacteria From Antibodies ∴Cells Virulent

Transformation is a Basic Genetic Engineering Process Today!

Transformation=Ability of Cell Phenotype To Be Changed by DNA!

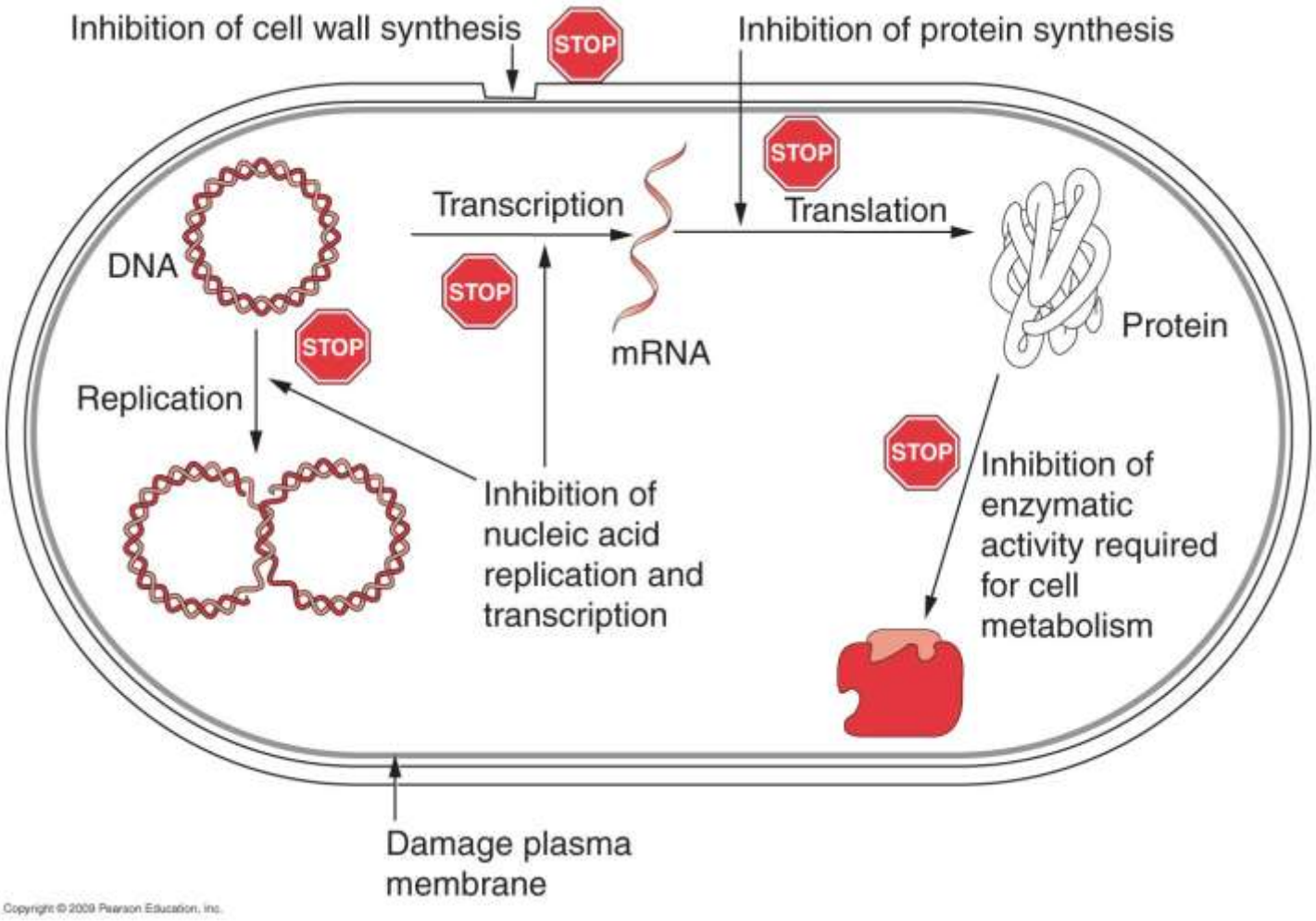
Can Bacteria Be Transformed With Other Genes/Traits?

Cohen & Boyer Experiment That "Invented" Genetic Engineering



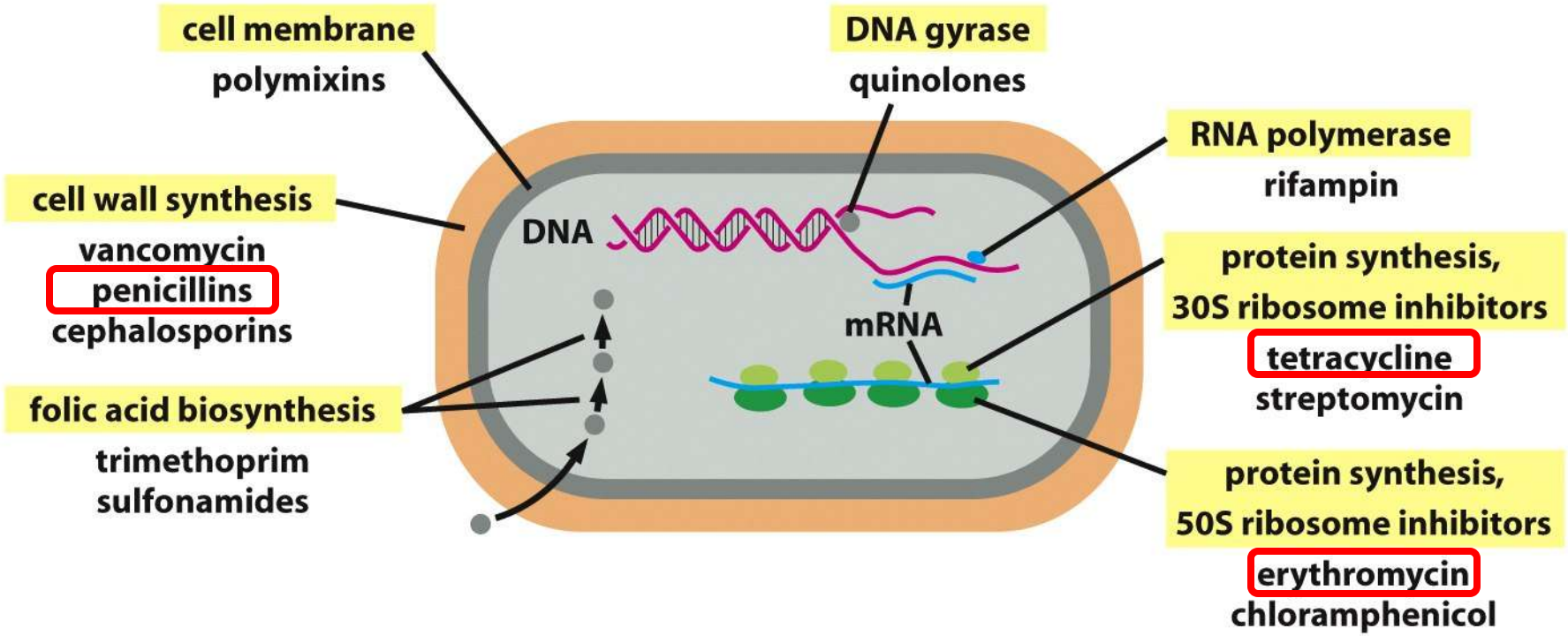
Because the Transforming Principle is DNA
Any Gene Can Be Transformed (e.g., Antibiotic^{R} to Antibiotic^{S})

How Do Antibiotics Kill Bacterial Cells?

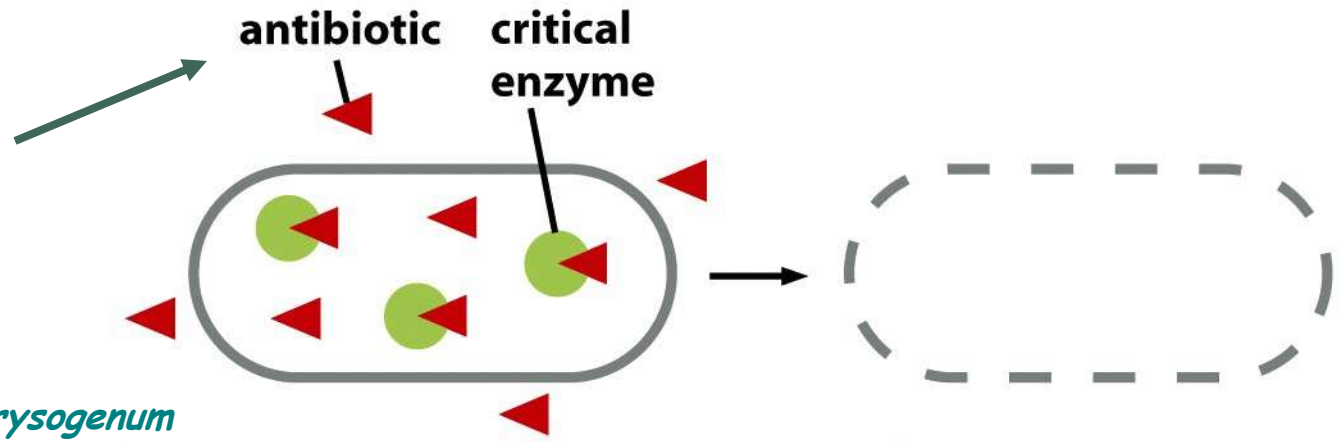


By Inhibiting Basic Microbial Cell Processes

Selected Antibiotics and Their Cell Targets

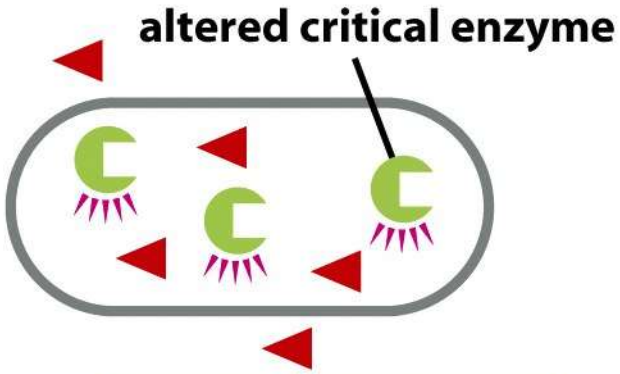


How Do Bacterial Plasmid Antibiotic Resistance Genes Work?



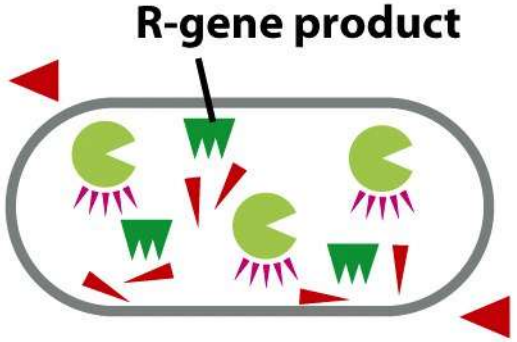
Penicillin chrysogenum

(A) antibiotic kills wild-type bacterium



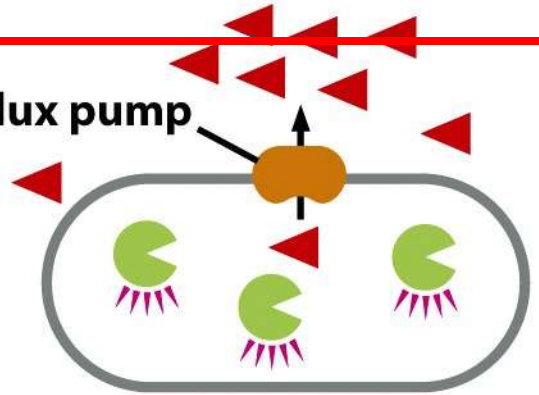
(B) antibiotic resistance

Bacterial Enzyme Alters Target Enzyme So Antibiotic Can't Affect It



(C) antibiotic resistance

Bacterial Protein Alters Antibiotic Making it Inactive

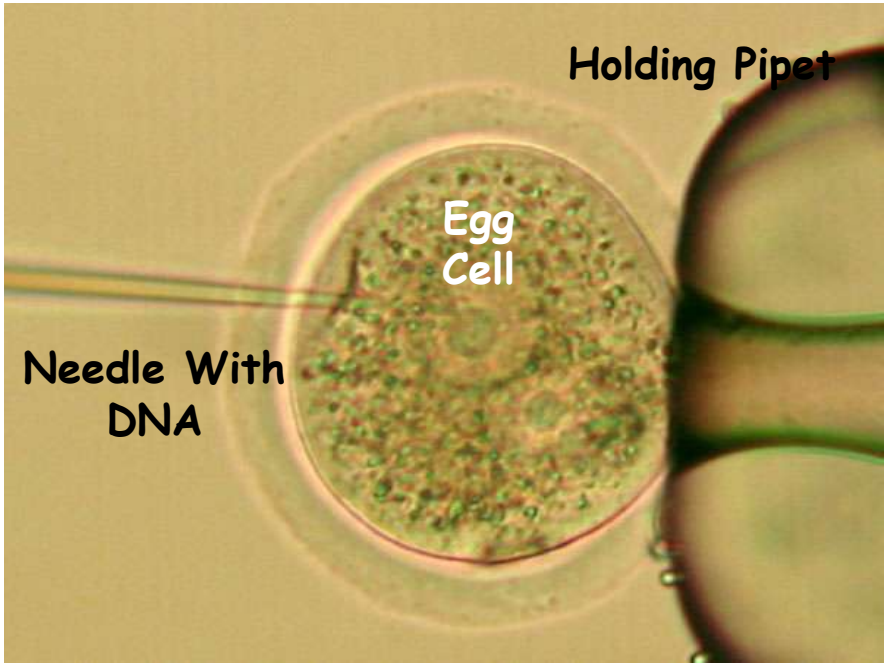


(D) antibiotic resistance

Bacterial Protein Pumps Antibiotic Out of Cell

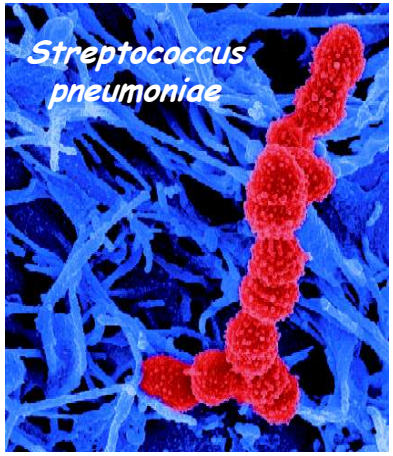
Engineering "Mighty Mouse" With a Rat Growth Hormone Gene

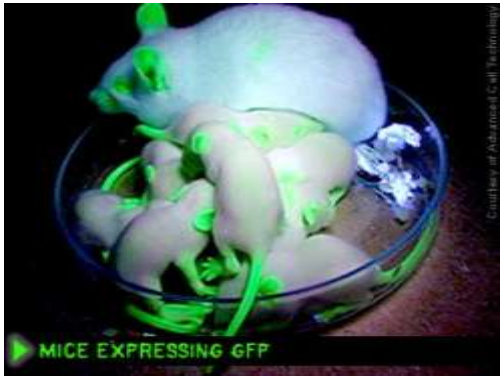
How Does This Experiment Show That DNA is the Genetic Material?



DNA → Specifies a Trait & Replicates

All Organisms Can Be Transformed!!
Genetic Engineering Has Come a Long Way Since Griffiths Experiments in 1928!!





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 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!

Engineered Gene CAN BE

1. From Same Organism
2. From Different Organism
3. From a Combination of Organisms stitched together by Genetic Engineering

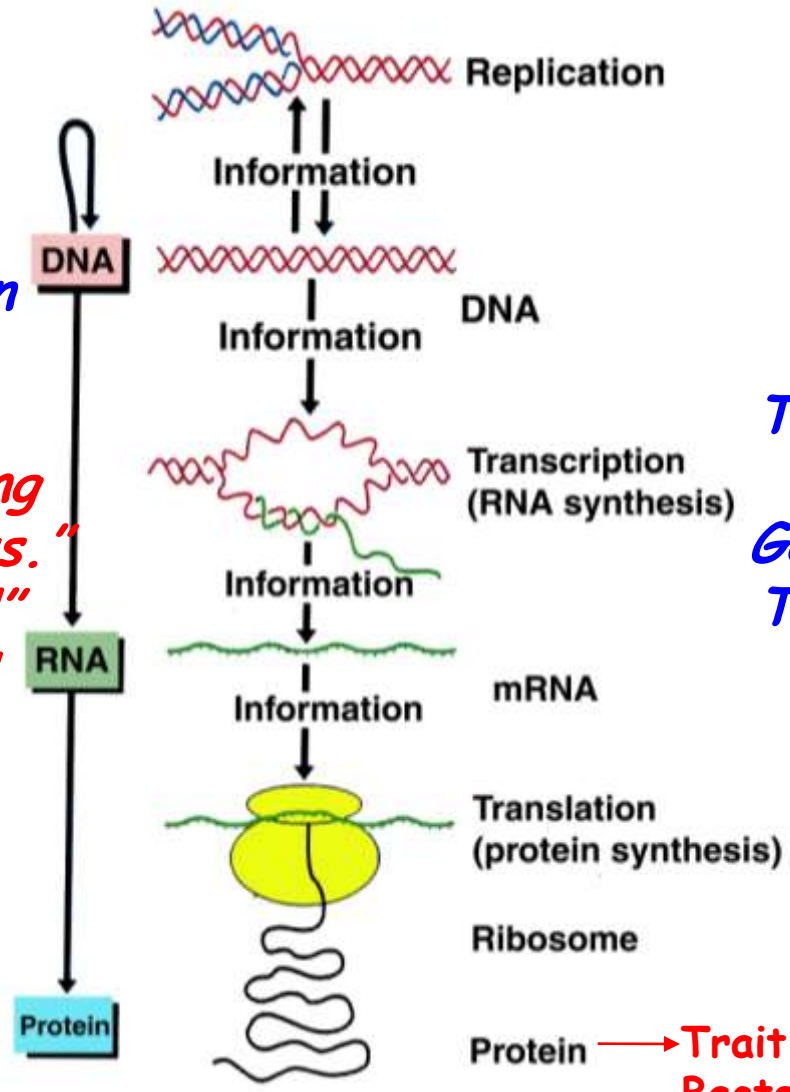
Gene Engineering Shows that Gene Processes Are Universal!!!

Just Like The GlowGene Experiments!!!

Transformation of Cells With DNA Uses Normal Cellular Processes to Produce a New Phenotype

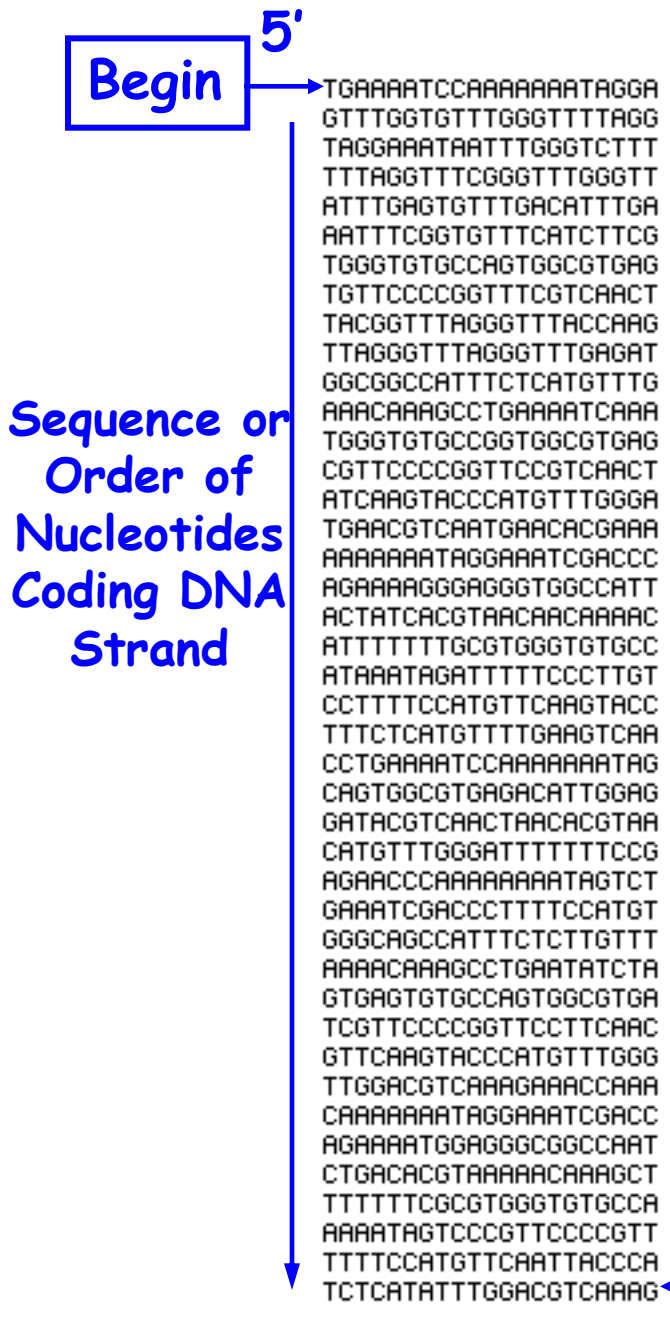
Can Intervene in This Process in Cells

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



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

What is A Gene?



The β-globin Gene

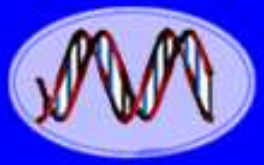
Blood Protein Carries Oxygen to All Genes From Lungs ⇨ Energy

A Gene is a <u>Unique Sequence</u> of Nucleotides Specifying a Function

DNA Sequence = Biology!
What If Sequence Changed?

SEQUENCE → FUNCTION

Relative to Coding or Sense Strand of Gene



DNA
Genetic Code of Life

Entire Genetic Code
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and Future Consequences

Plants of Tomorrow

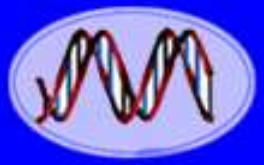
Genes & Genomes Differ Because the Sequence of DNA Differs

DNA Sequence
Beginning → End
5' 3'

→ Biological Uniqueness

If You Know the DNA Sequence, You Can Engineer Anything! Even Make New Genes & Genome!

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome



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Unnatural Genes Used to Replace Missing DNA Keep Cells Alive

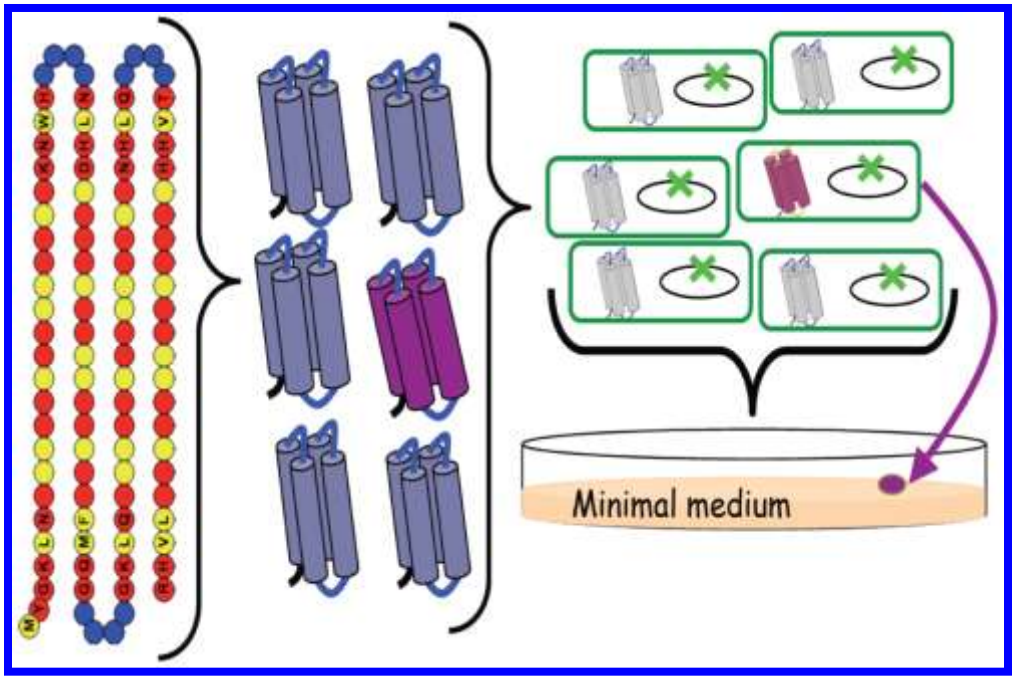
In another step for synthetic biology, genes designed in the lab and not seen in nature have been used by researchers to rescue bacterial cells from death

OPEN ACCESS Freely available online

PLoS one

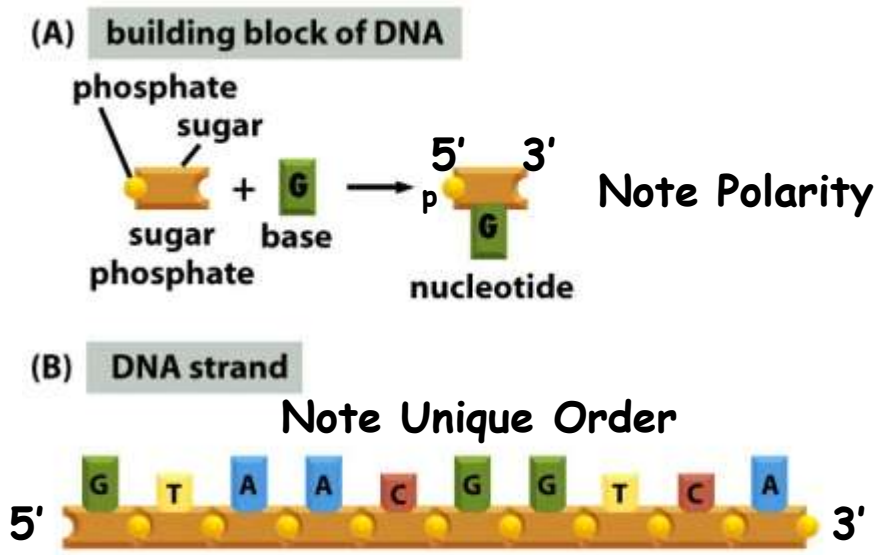
De Novo Designed Proteins from a Library of Artificial Sequences Function in *Escherichia Coli* and Enable Cell Growth

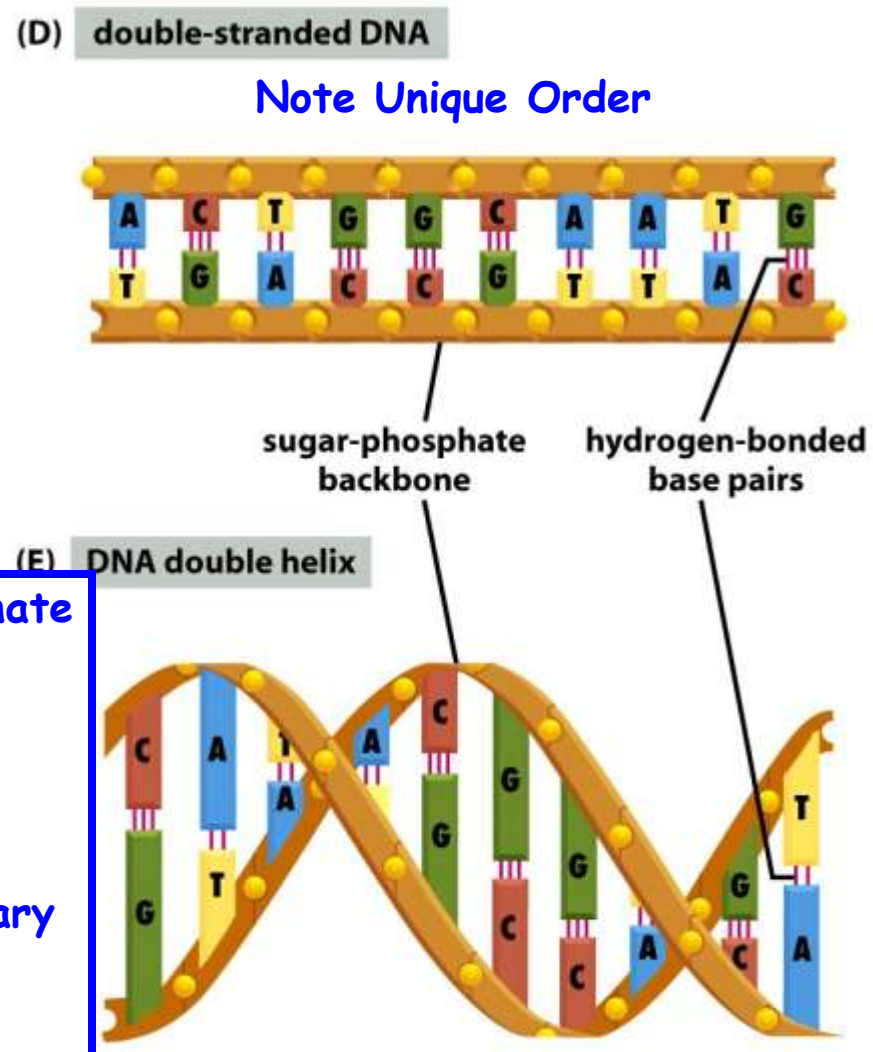
Synthetic Gene & Protein →



Evolution At Work

DNA and Genes Consist of Nucleotides Joined By Bonds

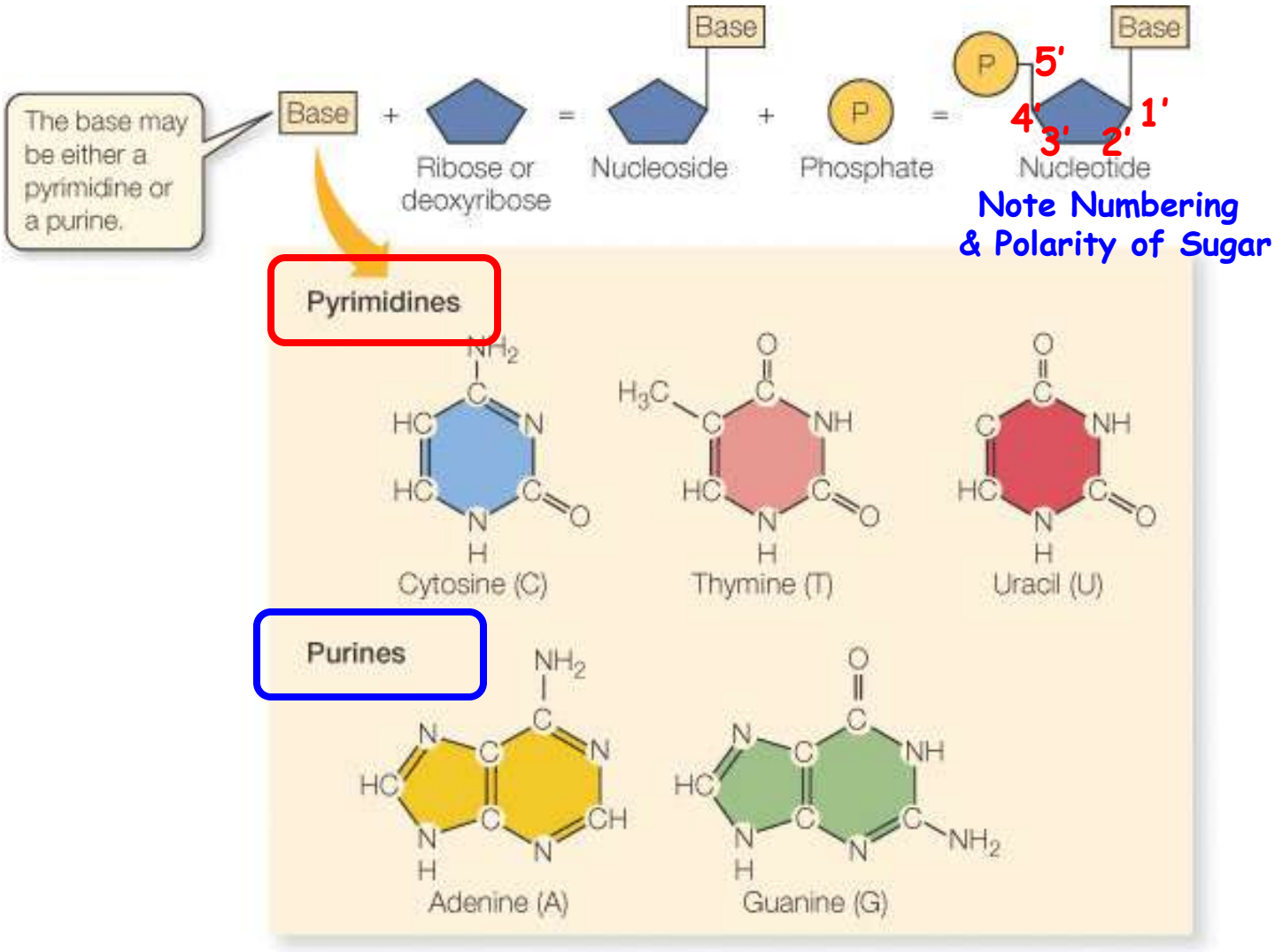




1. A Nucleotide = Sugar + Base + Phosphate
2. Nucleotides Are Linked In Order By 5′ to 3′ Phosphodiester Bonds
3. Two Strands of DNA Are Complementary And Have Different Sequences!

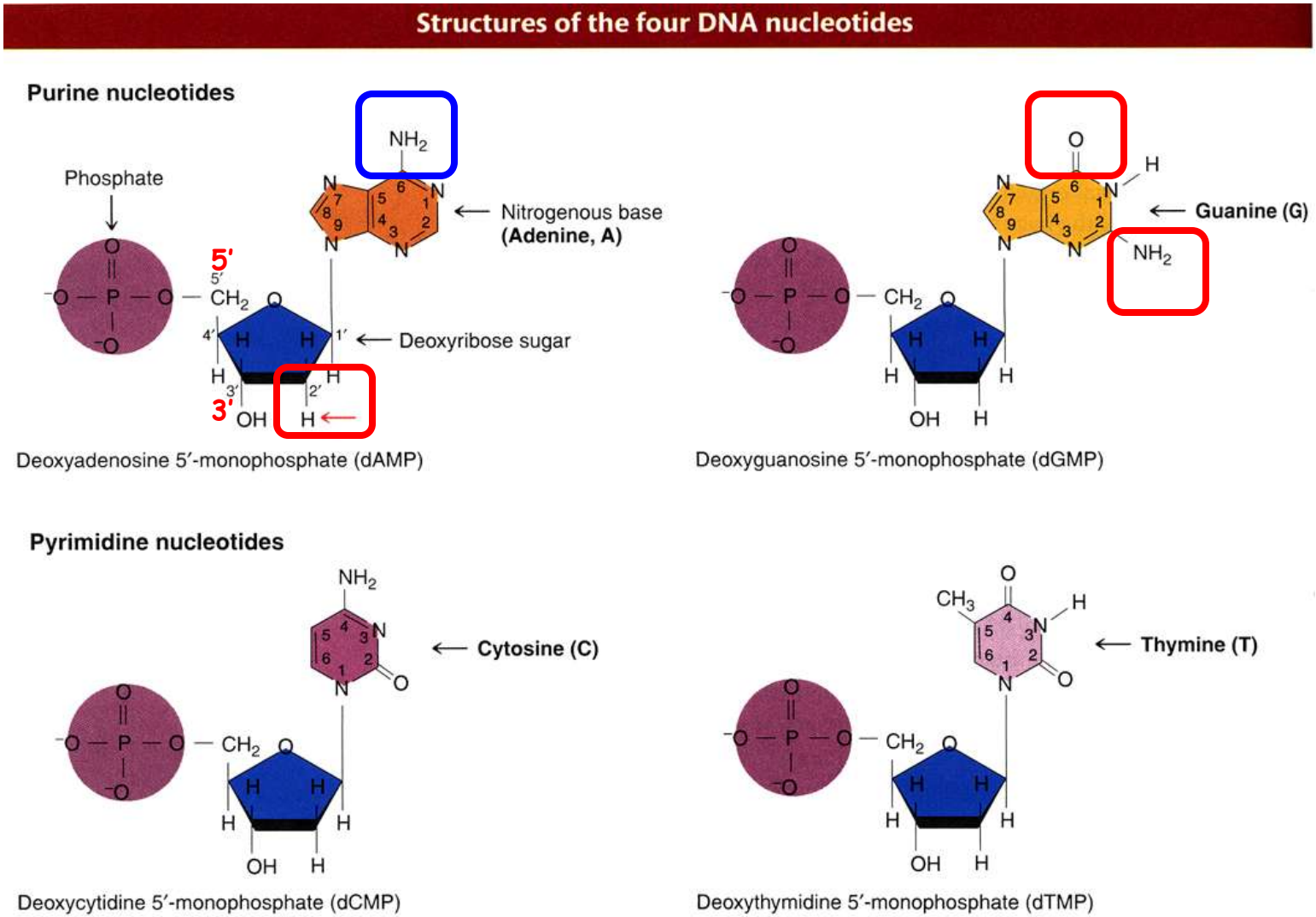
Figure 1-2 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

There Are Four Different Nucleotides in DNA

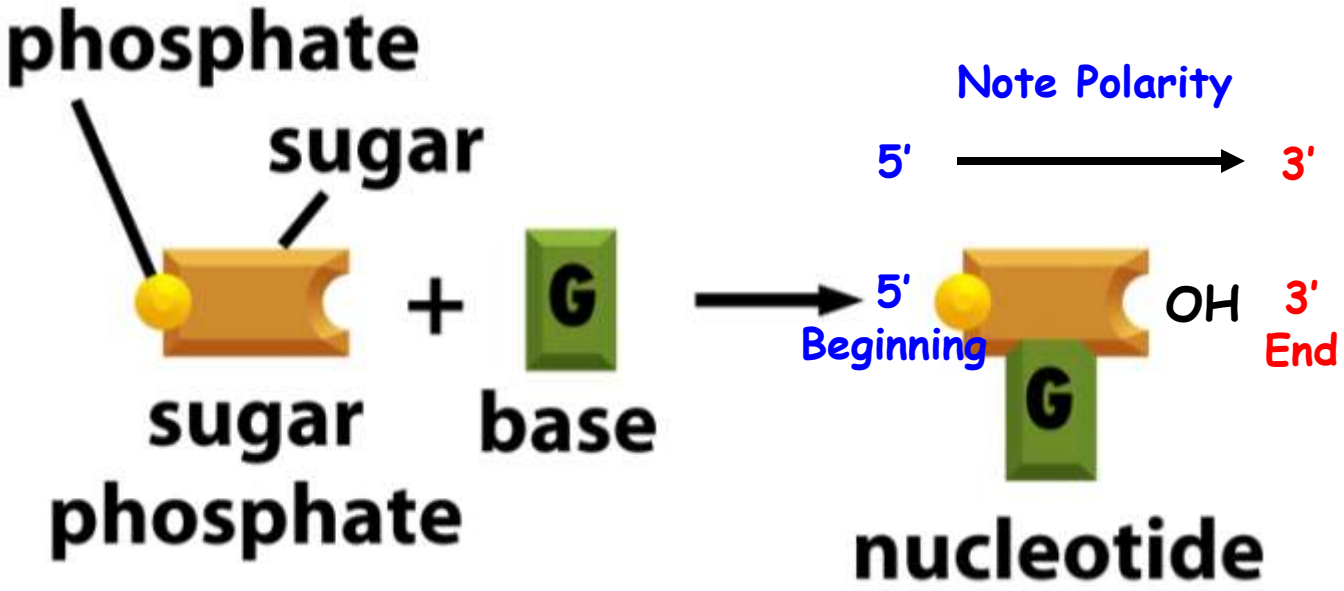


Note Chemical Differences in Bases -- Chemistry Leads to Biology!!

The Chemical Structure of Four Nucleotides Differs Because of Differences in the Bases



Nucleotides Have Polarity
Based on What is Bonded to the Five-Carbon Sugar
Phosphate on 5'Carbon and OH on 3'Carbon



The Sugar is the HUB

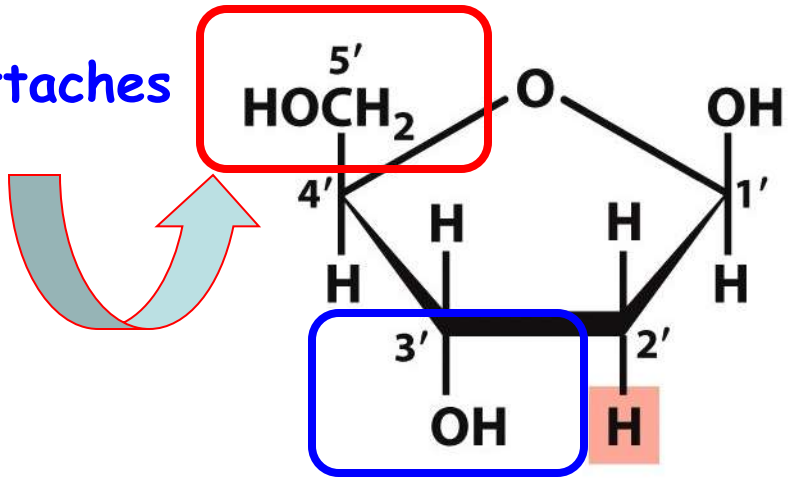
DNA Sequence Defined By Nucleotide Order

DNA Sequence = Functional Uniqueness = Biology

Figure 1-2a *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

Note Structure and Polarity of Deoxyribose Sugar

Phosphate Attaches



2-Deoxyribose

Nucleotides Are Joined By 5′ to 3′ Phosphodiester Bonds

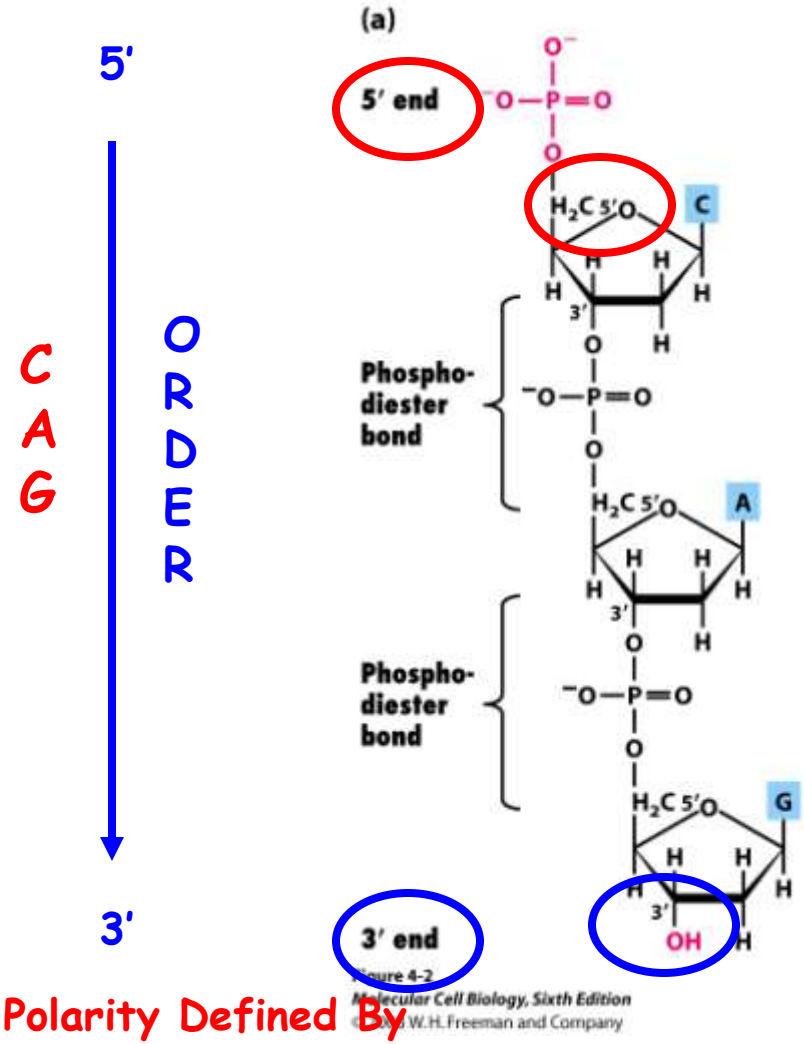


Figure 4-2
Molecular Cell Biology, Sixth Edition
© 2008 W.H. Freeman and Company

Short-Hand Notation

1. The Order is Specified by the Nucleotides That Join 5′ to 3′
2. This is the Basis For All of Biology
3. Order is Maintained During DNA Replication
4. Basis of All Genetic Engineering

Polarity Defined By
Sugars & Order Specified By Bases

Clues to the Double Helix-Chargaff's Rules
Purines = Pyrimidines

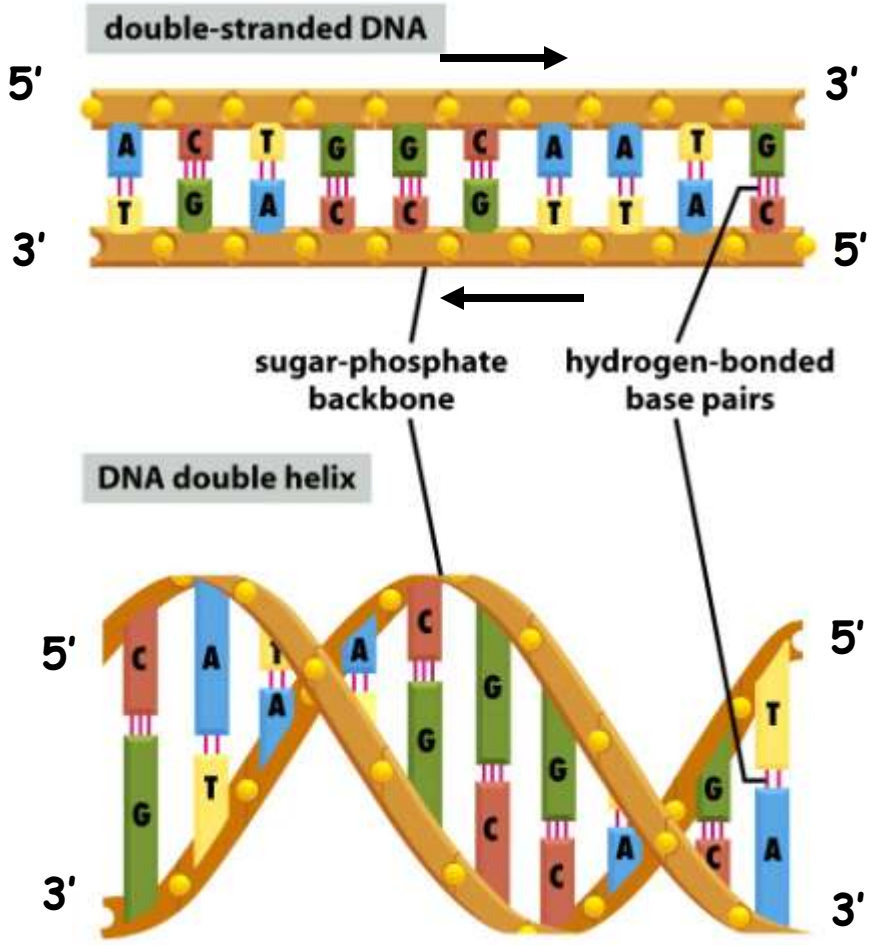
TABLE 6.1 Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms

	Percentage of Base in DNA				Ratios	
Organism	*A*	*T*	*G*	*C*	*A:T*	*G:C*
Staphylococcus afermentams	12.8	12.9	36.9	37.5	0.99	0.99
Escherichia coli	26.0	23.9	24.9	25.2	1.09	0.99
Yeast	31.3	32.9	18.7	17.1	0.95	1.09
*Caenorhabditis elegans**	31.2	29.1	19.3	20.5	1.07	0.96
*Arabadopsis thaliana**	29.1	29.7	20.5	20.7	0.98	0.99
Drosophila melanogaster	27.3	27.6	22.5	22.5	0.99	1.00
Honeybee	34.4	33.0	16.2	16.4	1.04	0.99
Mus musculus (mouse)	29.2	29.4	21.7	19.7	0.99	1.10
Human (liver)	30.7	31.2	19.3	18.8	0.98	1.03

*Data for *C. elegans* and *A. thaliana* are based on those for close relative organisms.
Note that even though the level of any one nucleotide is different in different organisms, the amount of A always approximately equals the amount of T, and the level of G is always similar to that of C. Moreover, as you can calculate for yourself, the total amount of purines (A plus G) nearly always equals the total amount of pyrimidines (C plus T).

What Would You Predict For a Single-Stranded DNA?

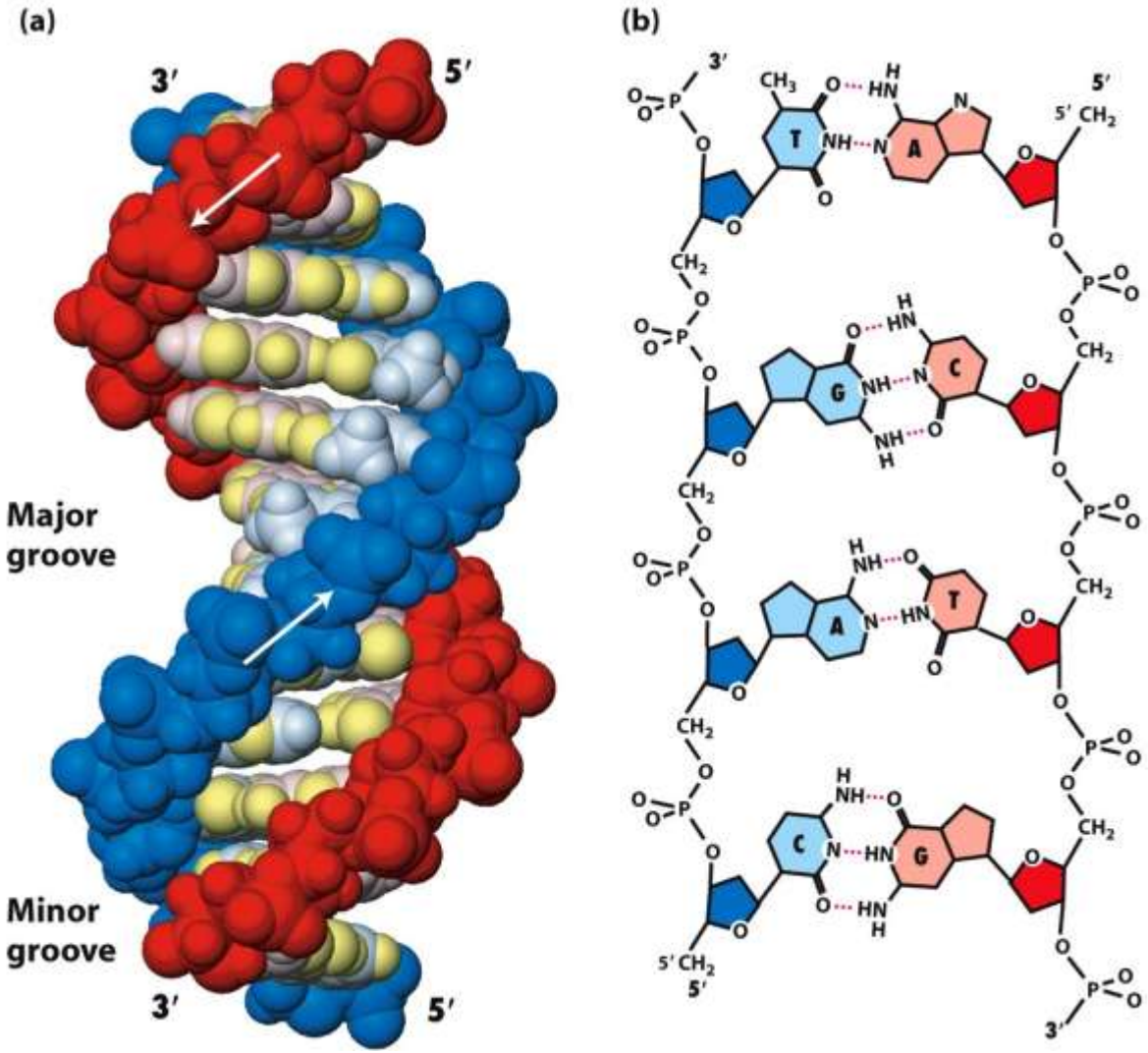
DNA is a Double Helix of Two Complementary Chains of DNA Wound Around Each Other



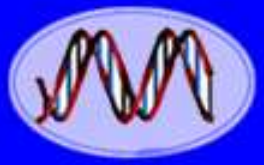
1. Complementary Strands
2. A=T and G=C
3. Sequence of Strands Differ
4. Bases to Interior
5. Phosphate-Sugar Backbone on Exterior
6. DNA Strands in Opposite Direction (Only Way Helix Fits)
7. Sequence of One Chain Automatically Specifies Sequence of Complementary Chain (Basis of Replication!)

Watson and Crick, Nature, 1953

The Double Helix



Read Book by Same Name!



DNA
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Entire Genetic Code of a Bacteria

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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

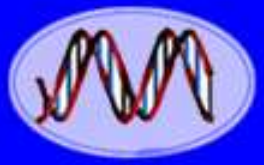
   5′ ⟶ 3′
   3′ ⟵ 5′

   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:

   From X-Ray Diffraction Pictures → Know # bp → Know length!

   - 20Å diameter
   - 3.4Å/bp
   - 10bp/turn
9. Order → Biology



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Sciencexpress Research Article

A Bacterium That Can Grow by Using Arsenic Instead of Phosphorus Science, December 2, 2010

December 2, 2010

Subsisting on Arsenic, a Microbe May Redefine Life

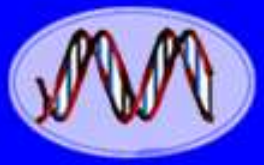
By DENNIS OVERBYE New York Times, December 2, 2010

The newfound bacteria thrives in the arsenic-rich waters of Mono Lake in California.

33
As

15
P

33
As



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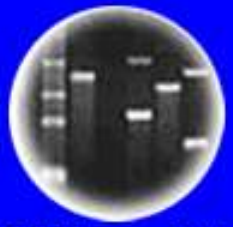

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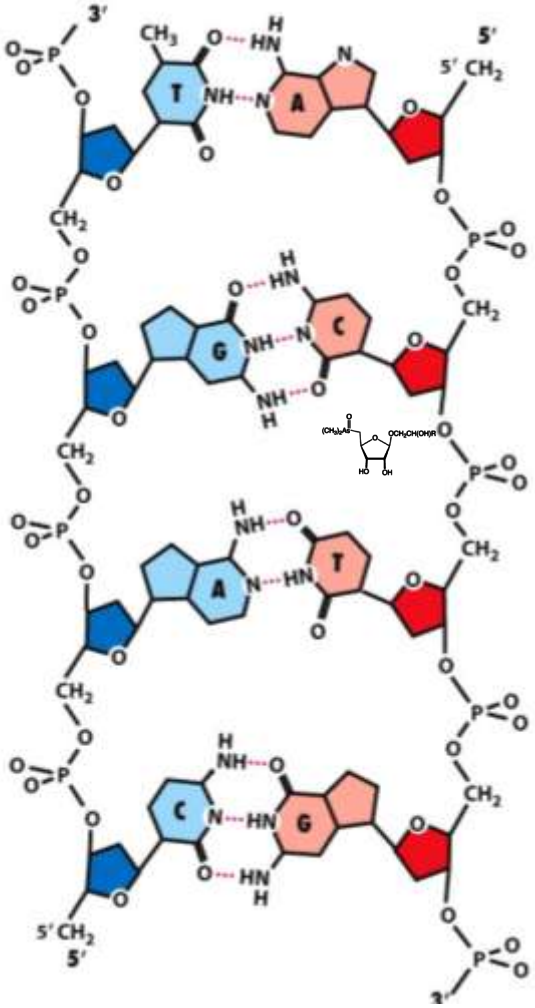
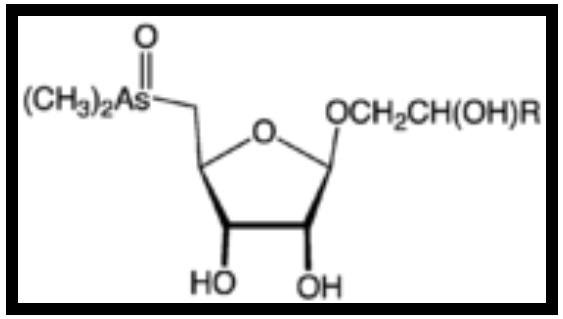
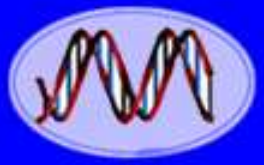
The Mysterious Case of Arsenic DNA



Arsenic

Arsenic





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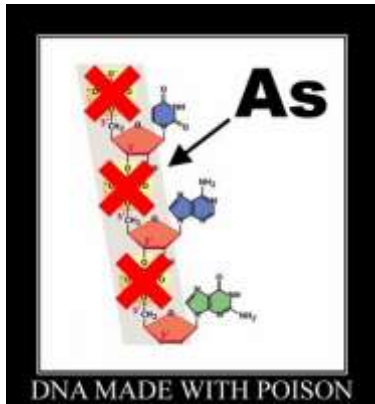
Does Growing Bacteria on Arsenic and Showing that Radioactive Arsenic is Associated With a DNA Fraction of the Cell Demonstrate Unambiguously That the Nucleotides in the Double Helix are Bound Together by Bonds Containing Arsenic?

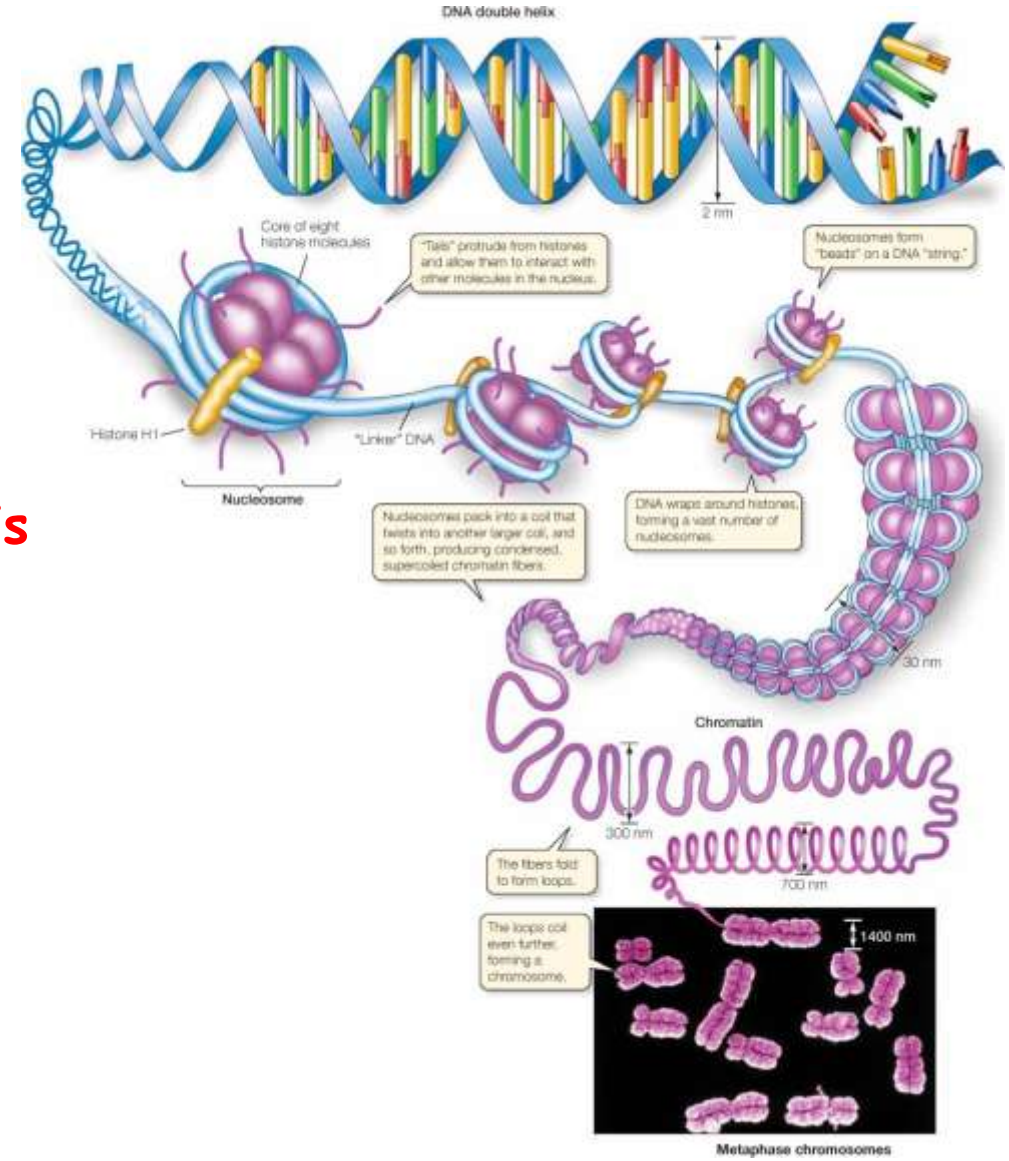
a. Yes
b. No

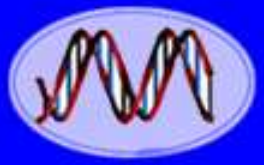


A Chromosome Contains One (or Two!!) Continuous DNA Molecule(s)

DNA in Human & Eukaryotic Chromosomes is Linear!

DNA in Most Bacteria is Circular!





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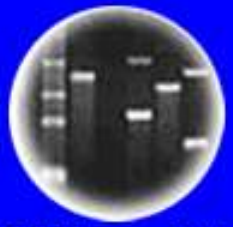

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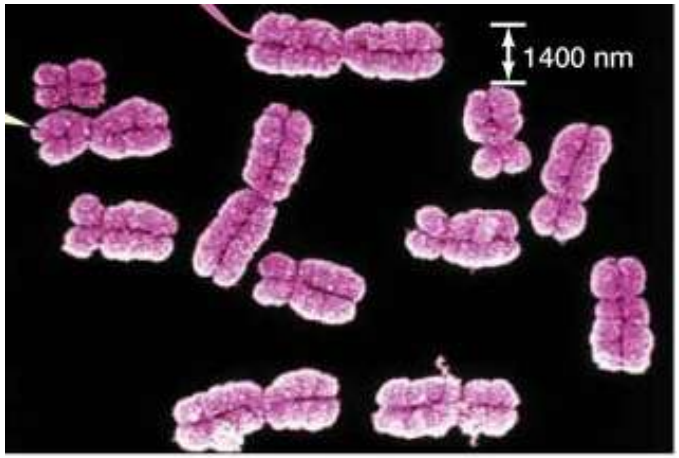
Each of These Chromosomes Contains One or Two DNA Molecules?



a. one
b. two

The Circular *E. Coli* Chromosome
One DNA Circle

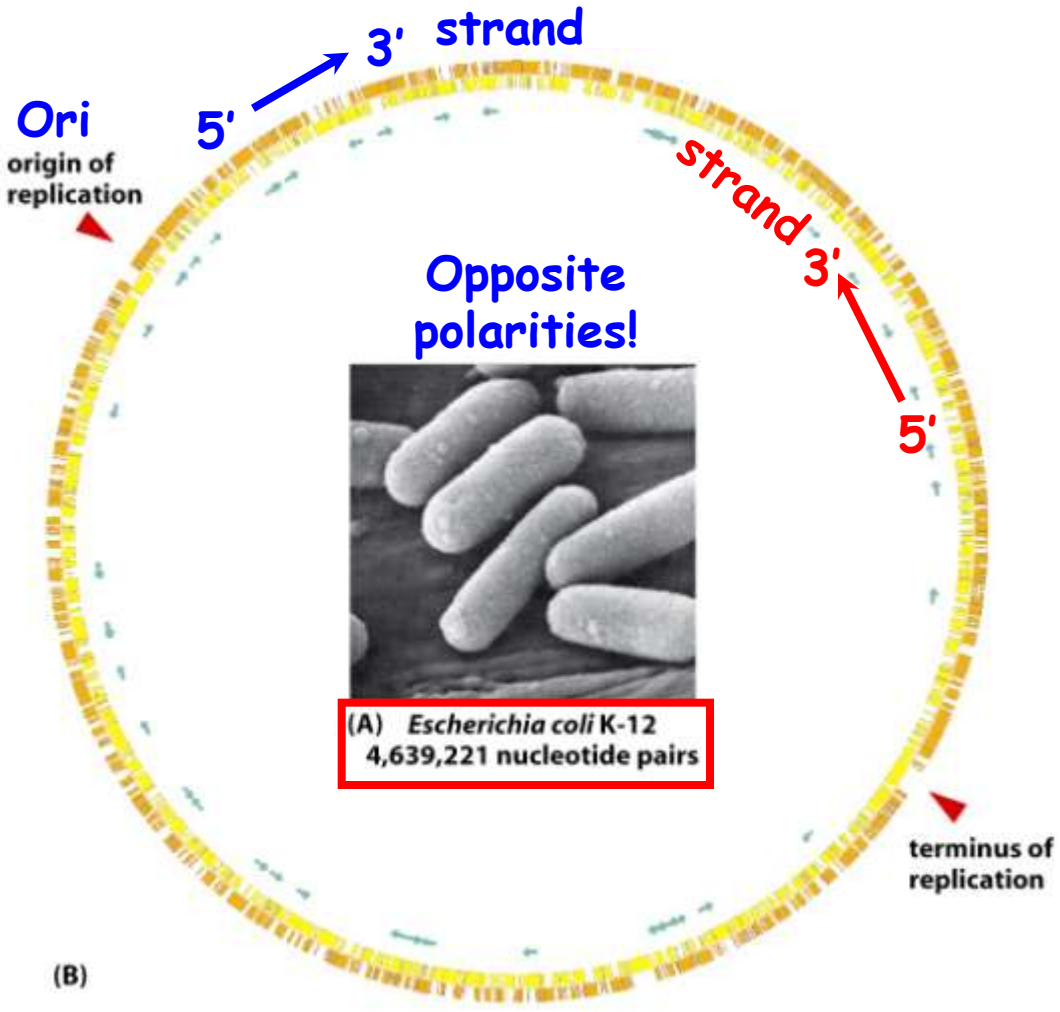
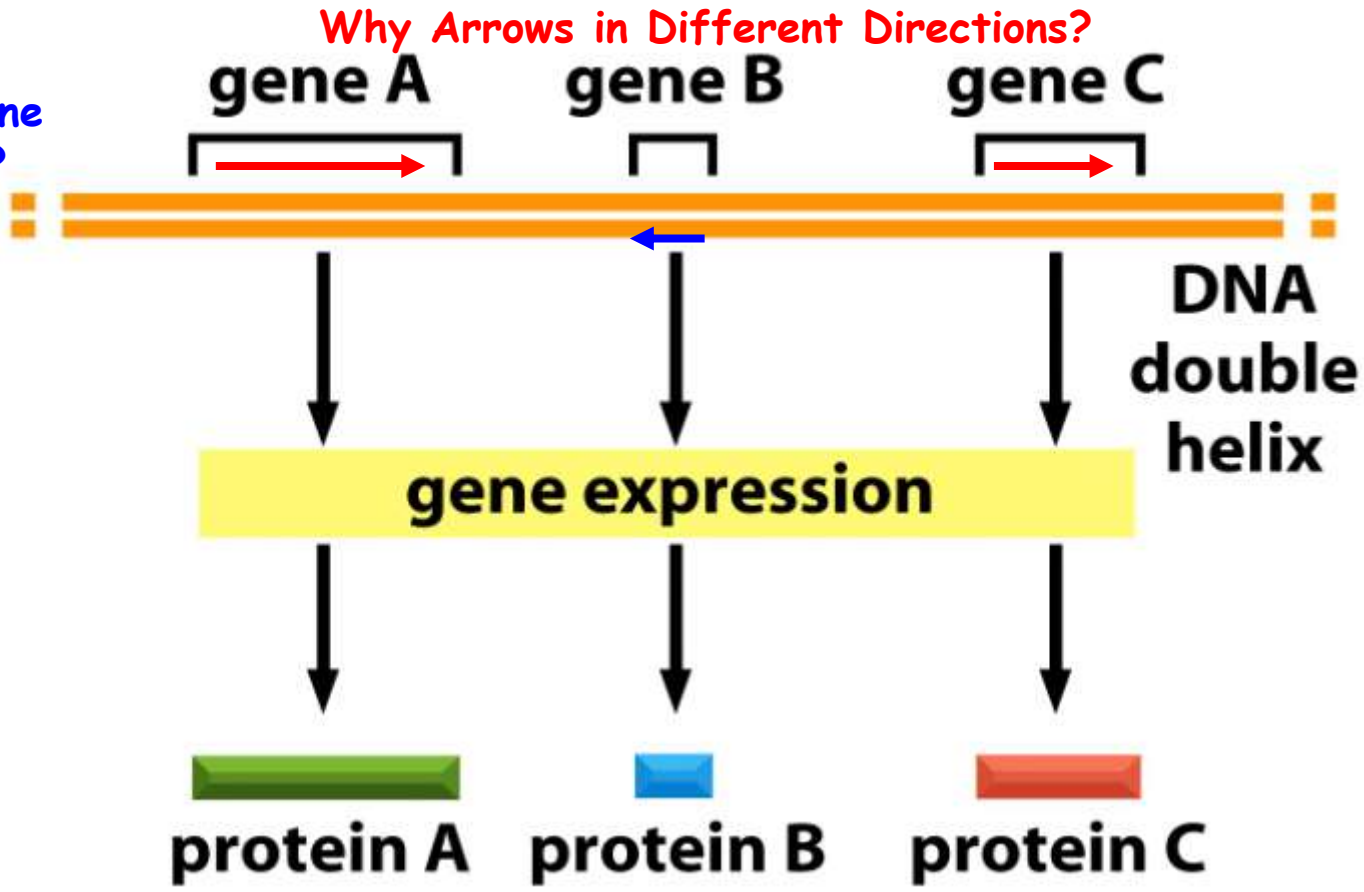


Figure 1-29 *Molecular Biology of the Cell*, Fifth Edition (© Garland Science 2008)

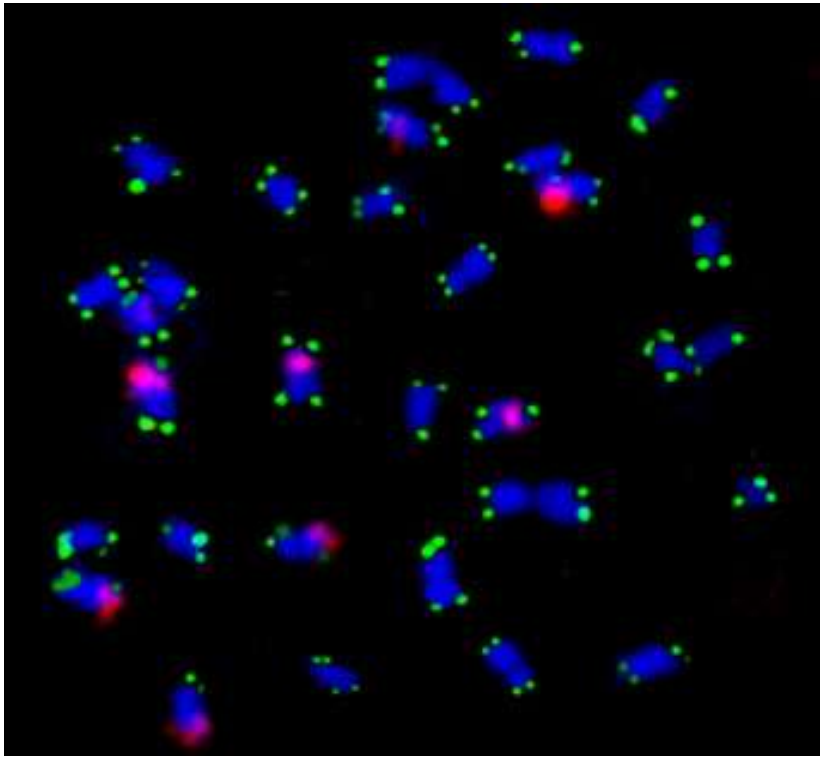
A Chromosome Contains Many Genes That Reside at Specific Positions and Have Unique Functions

What Defines Gene Positions?



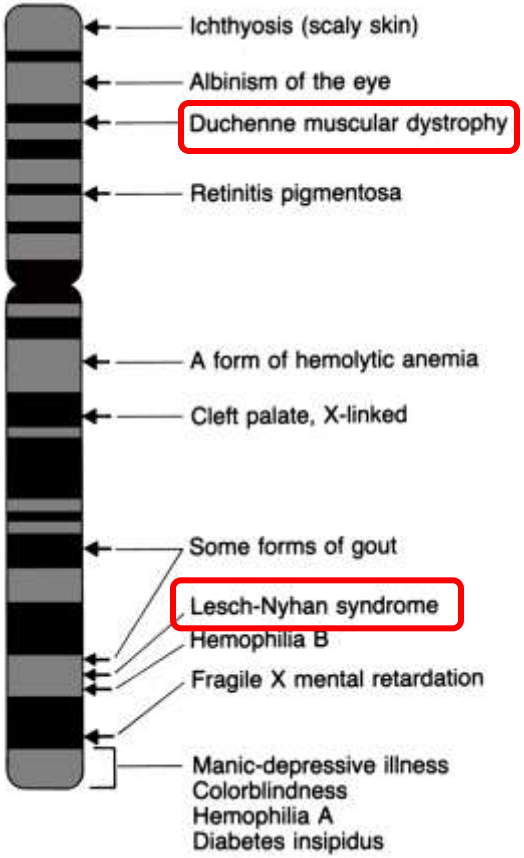
Because DNA Contains Two Strands--Genes Can Be Transcribed From Either Strand--But Only One Per Gene

Genes Reside at Specific Positions or Loci

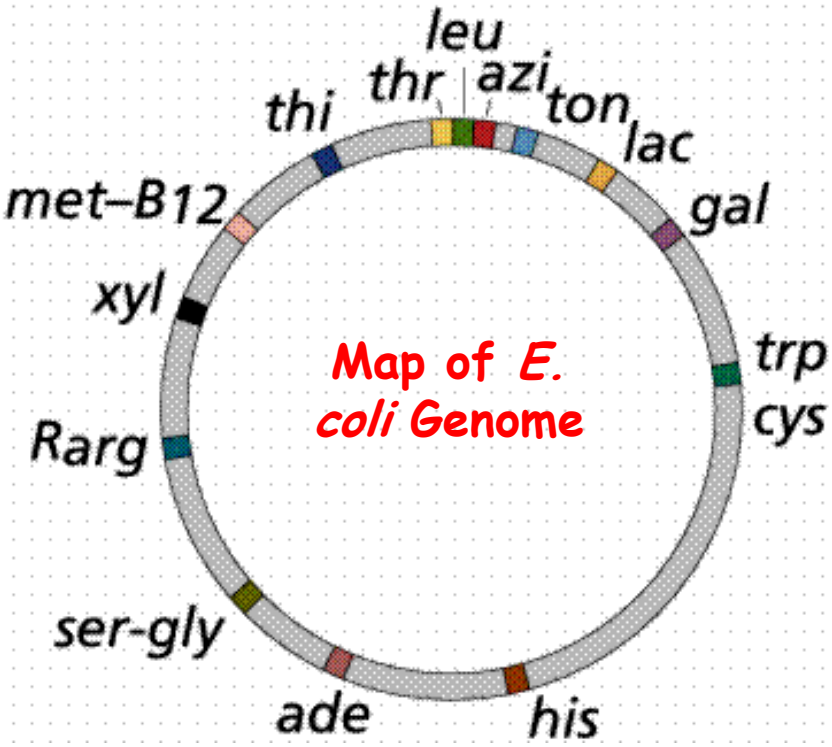


Gene Position = Locus = Unique DNA Sequence

Genes Reside at Specific Locations



Linear DNA
How Know?



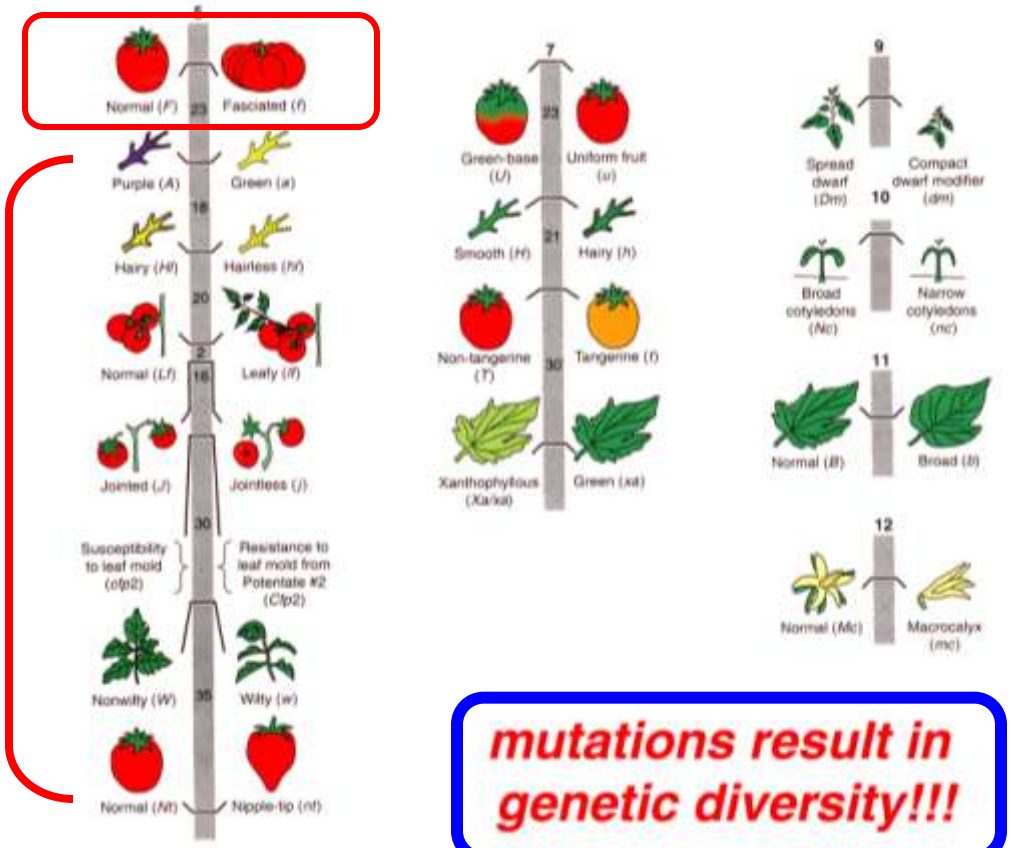
Circular DNA
How Know?

- Note Marker Bands - What are these?
- How Know Gene Positions? Chromosome Number?

Alleles Reside at the Same Position on a Chromosome

Alleles

Different Genes

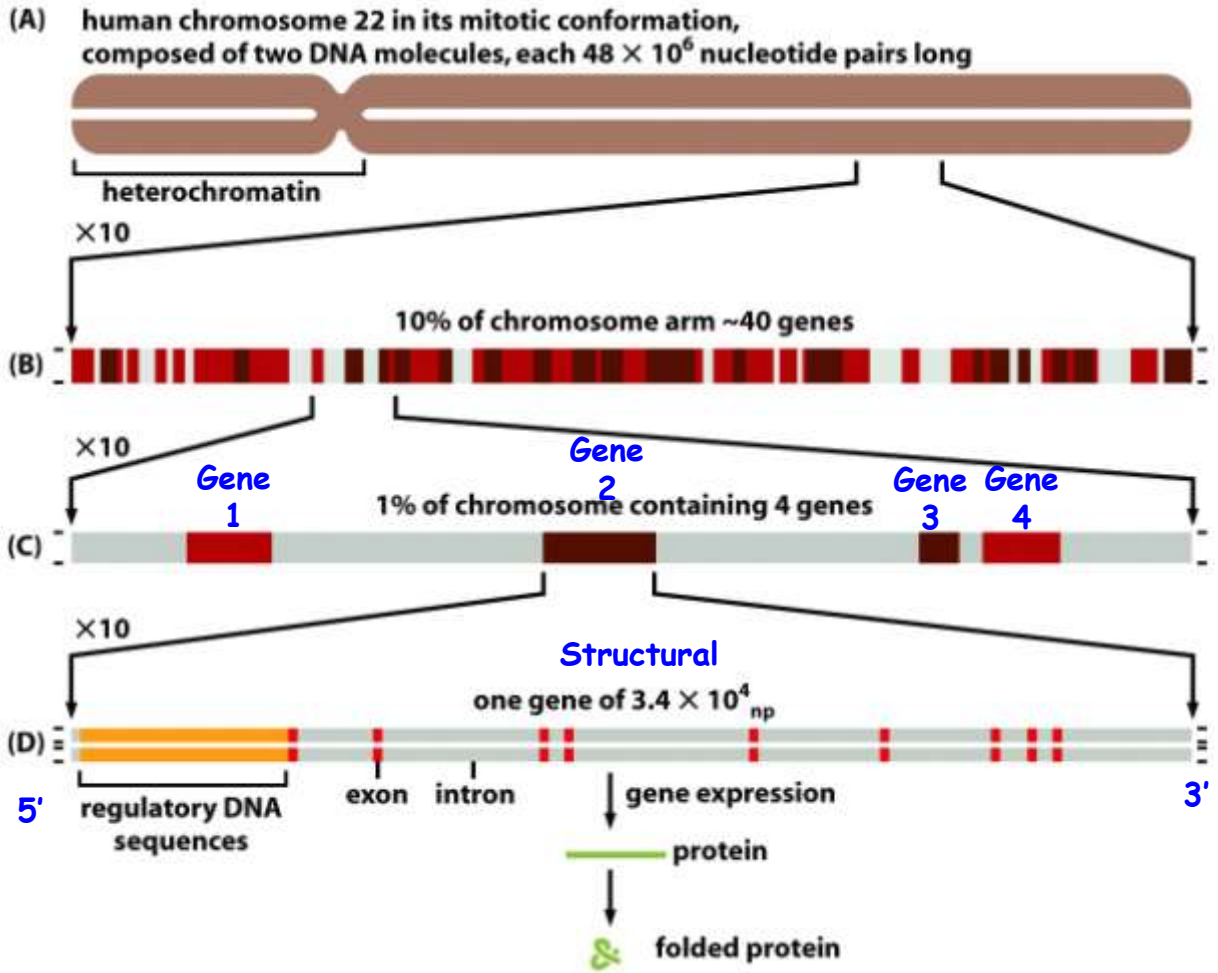


Gene Engineering Can Generate New Forms of Alleles of a Gene and, therefore, Results in More Genetic Diversity

mutations result in genetic diversity!!!

Alleles Are <u>Different Forms of the Same Gene</u> That Arise By Mutation & Can be Made in a Laboratory By Modern Genetic Engineering!

Organization of Genes on Human Chromosome 22



Genes Are Defined/Precise Regions of DNA

One Large Gene!

Genes Act As Individual Units?

How Know? GloFish Experiment! Genetic Engineering Antibiotic^R

Figure 4-15 *Molecular Biology of the Cell* (© Garland Science 2008)

A Conceptualized Gene

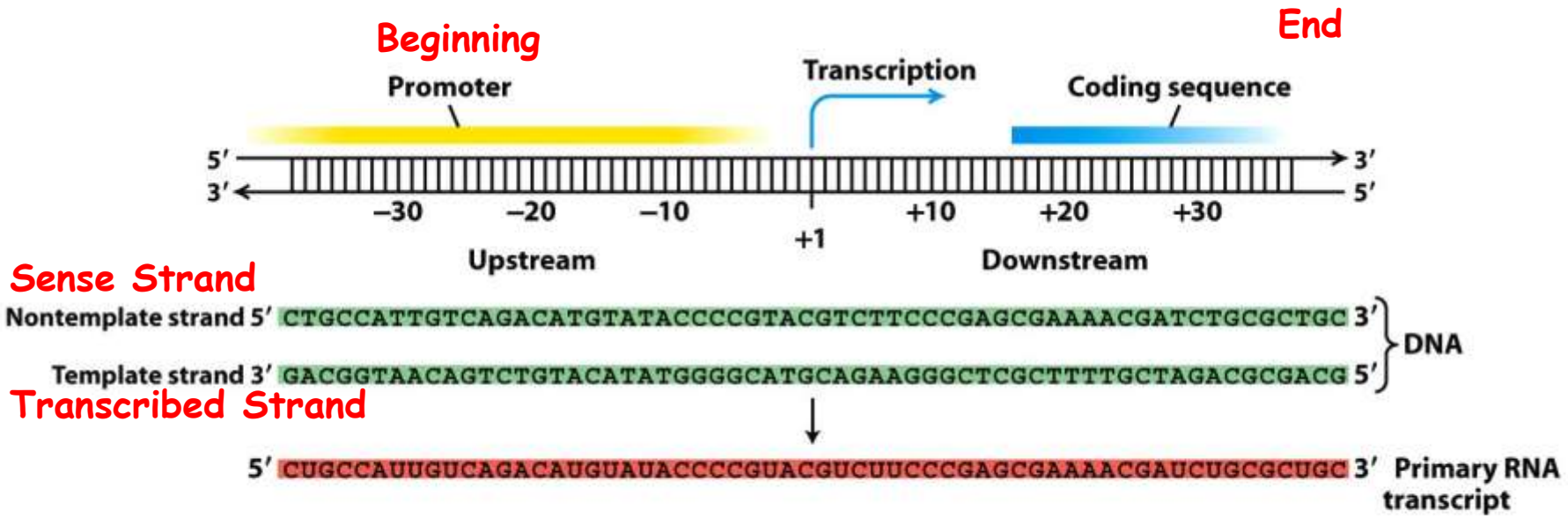
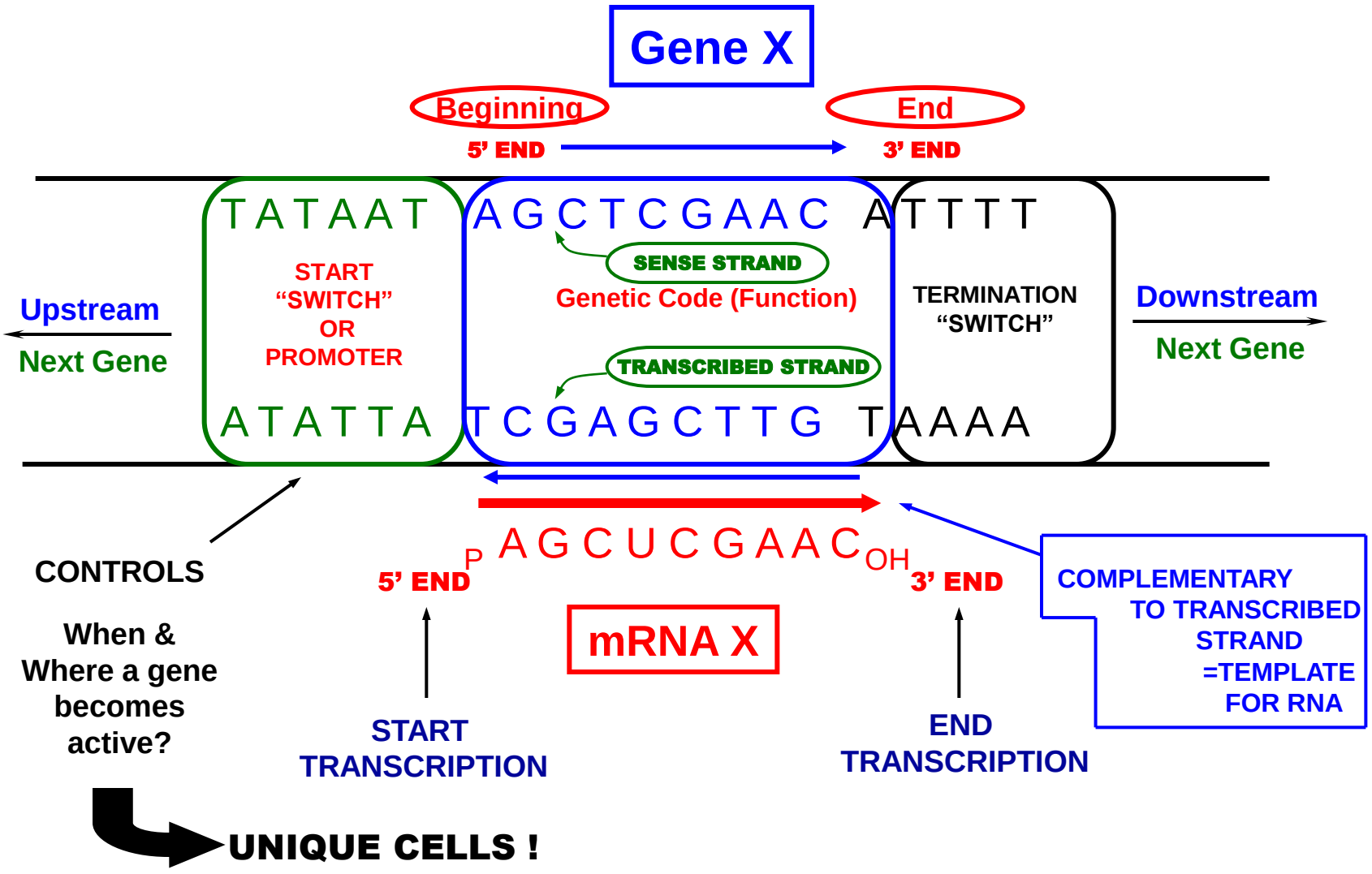


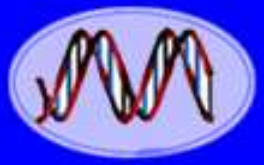
Figure 4-10b
Molecular Cell Biology, Sixth Edition

Recall -- *"Making Proteins in Recombinant Bacteria"* Article by Gilbert

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



Note: mRNA Sequence = Sense Strand Sequence



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A "Simple" Gene Reviewed

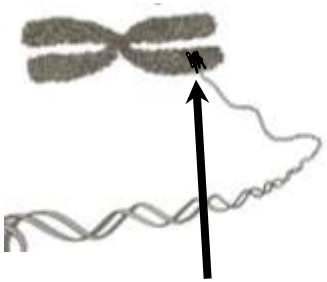
1. Sense Strand = Genetic Code
2. Sense Strand = 5′ → 3′ Direction (all DNA sequences specified 5′ → 3′)
3. AntiSense Strand = Complement of Sense Strand & is Transcribed Strand
4. mRNA = Same Sequence As Sense Strand & Complementary to AntiSense Strand
5. mRNA = 5′ → 3′
6. Switch Turns Gene On - Not 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!

A Chromosome Contains Many Genes Operating Independently

Evidence?



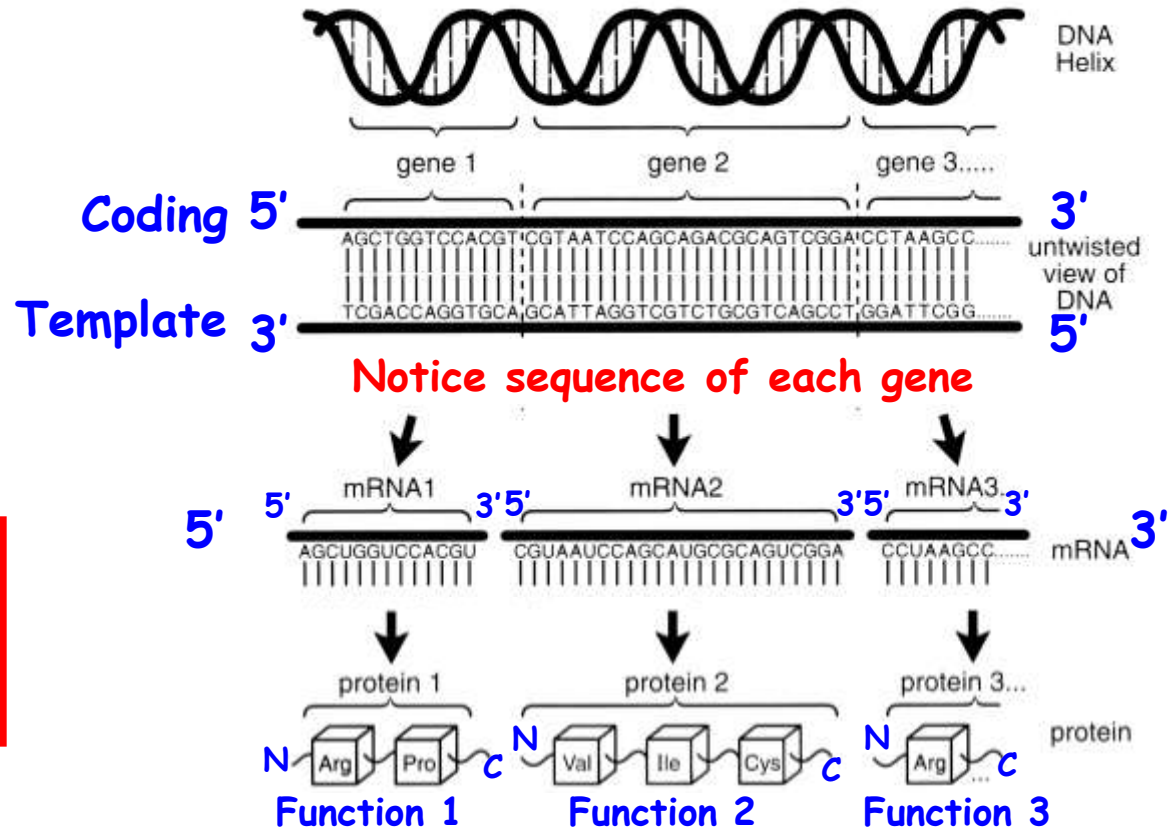
Position of Genes 1, 2, & 3 in chromosome

Discrete Units!

Notice- Each gene, mRNA, & protein has a unique order/sequence of monomeric units

Central Dogma
∴Genes -> Functions in Cells via Proteins
Cells duplicate & stay the same -> DNA replication

What delineates each gene?



Note sequence of each protein

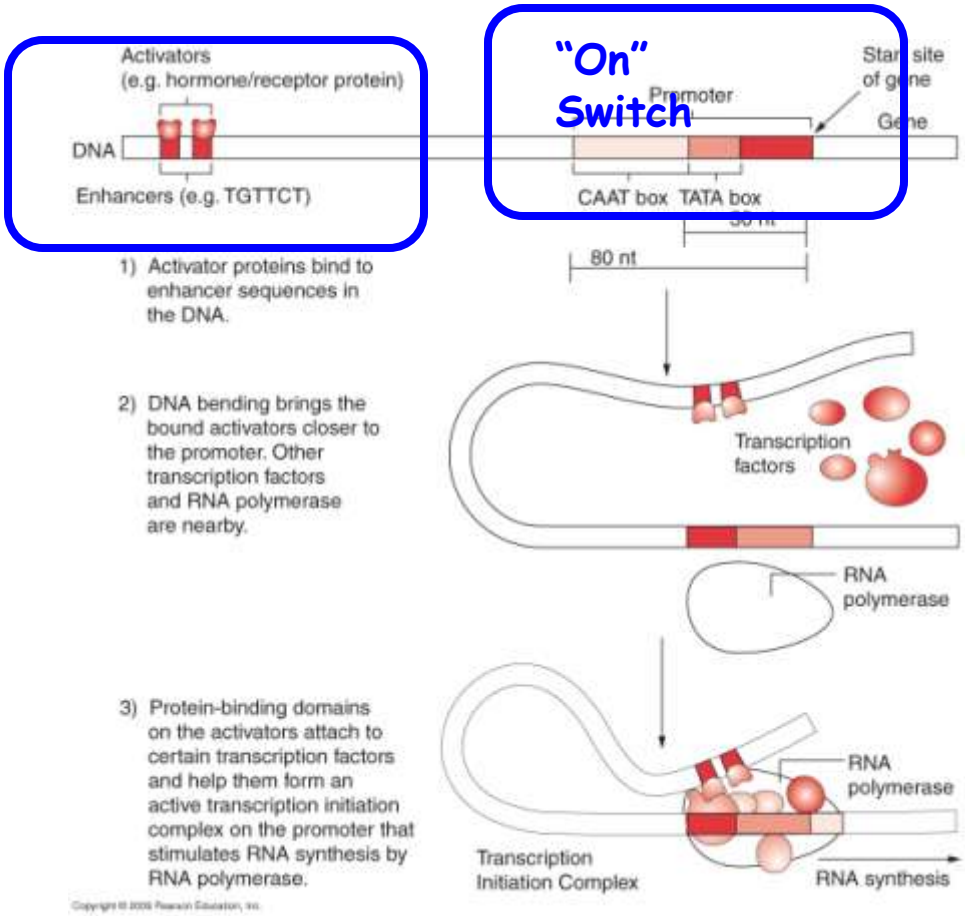
VERY IMPORTANT CONCEPT!

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!!

"Control" Switch



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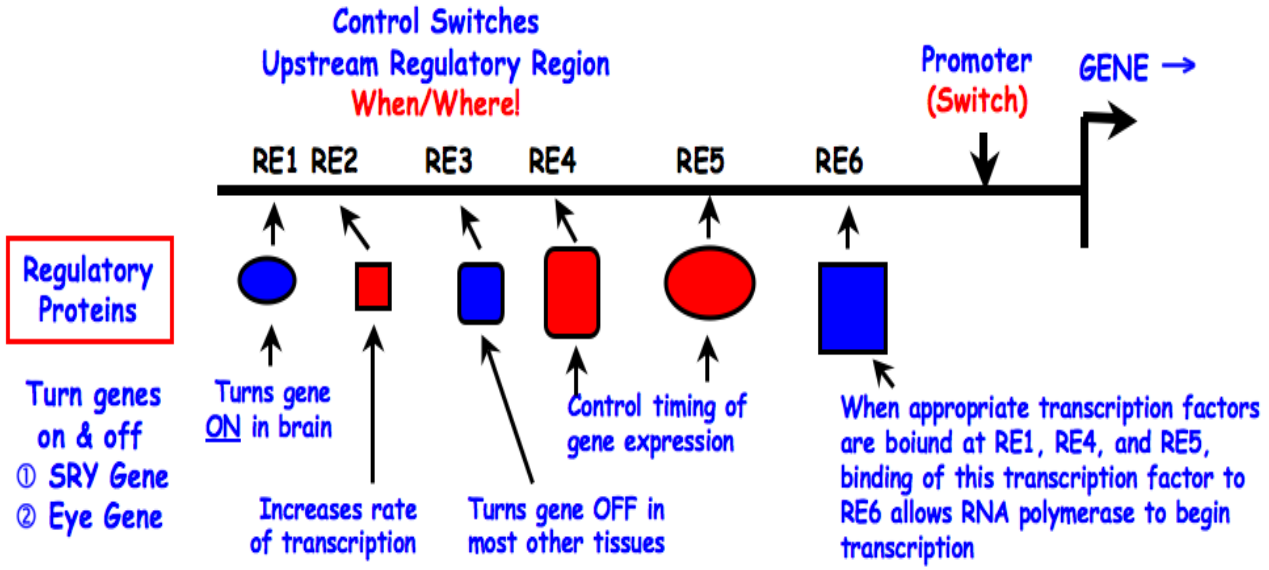


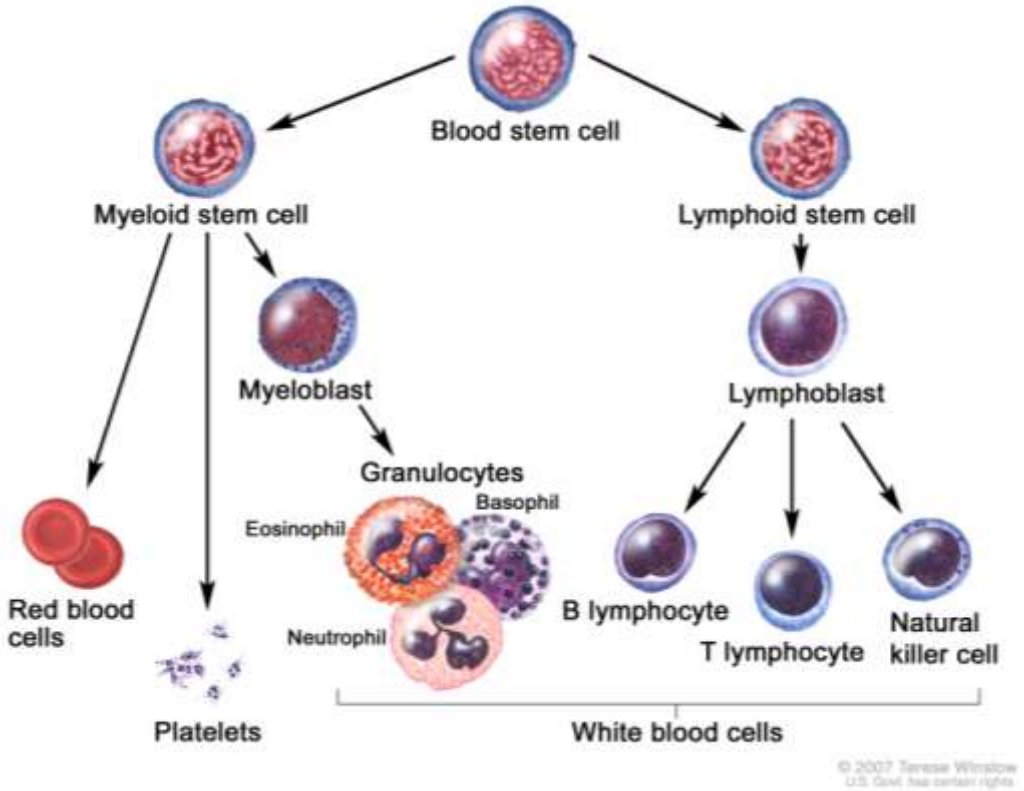
Genome Projects Reveal Both the Genes & the Logic that Controls them!

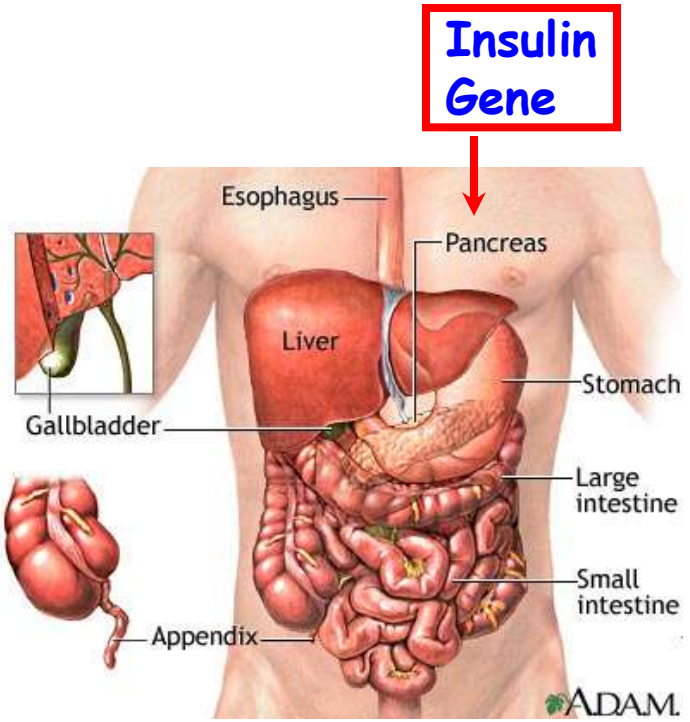
Each Switch = Unique DNA Sequence

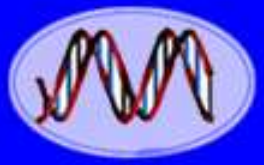
RULE: Sequence → Biology!!

No "Hocus Pocus" Yo! It's in the DNA!

Switches Control Where & When A Gene Is Active → Unique Functions → Unique Cells







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THE GENE AND SWITCHES ARE UNIQUE DNA SEQUENCES

1. They Can Be Cloned & "Shuffled" & Engineered Creating New Genes That Have No Counterparts in Nature. ⇨ **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)

   ⇩

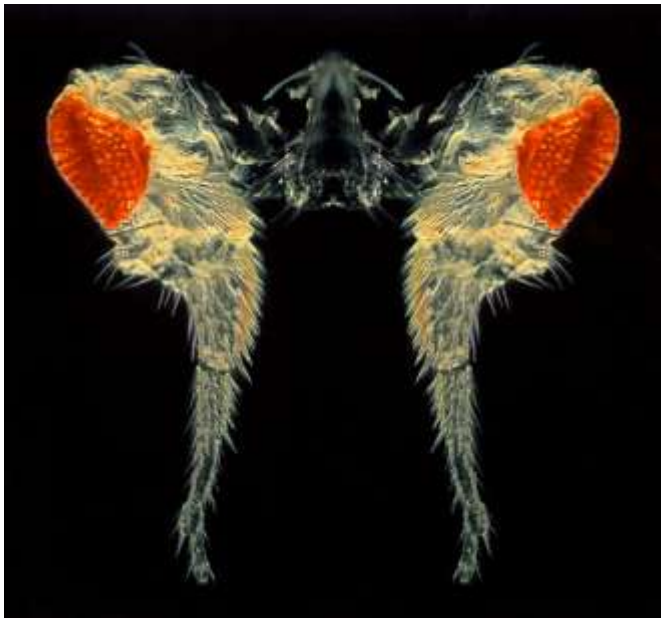
   Human Genes + Plant Leaf Switch
3. All Genes are Regulated & Controlled by Switches. Genome Projects Reveal Both The Genes & The Switches & Wiring Together of All Switches in Gene. ⇨ Program of Life From Birth to Death

Yo! It's in the Sequences!!

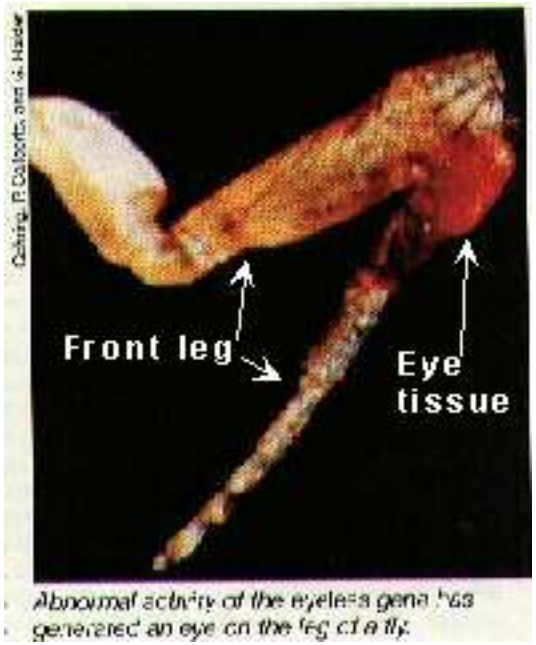
The Eye Gene Can Be Expressed in Different Parts of the Fly by Engineering the Eye Switch

Eye Gene

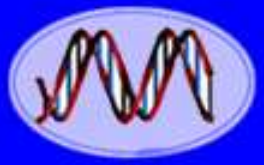
Replace the Head Switch With the Leg Switch by Genetic Engineering



Eye Gene
+
Leg Switch



Abnormal activity of the eyeless gene has generated an eye on the leg of a fly.



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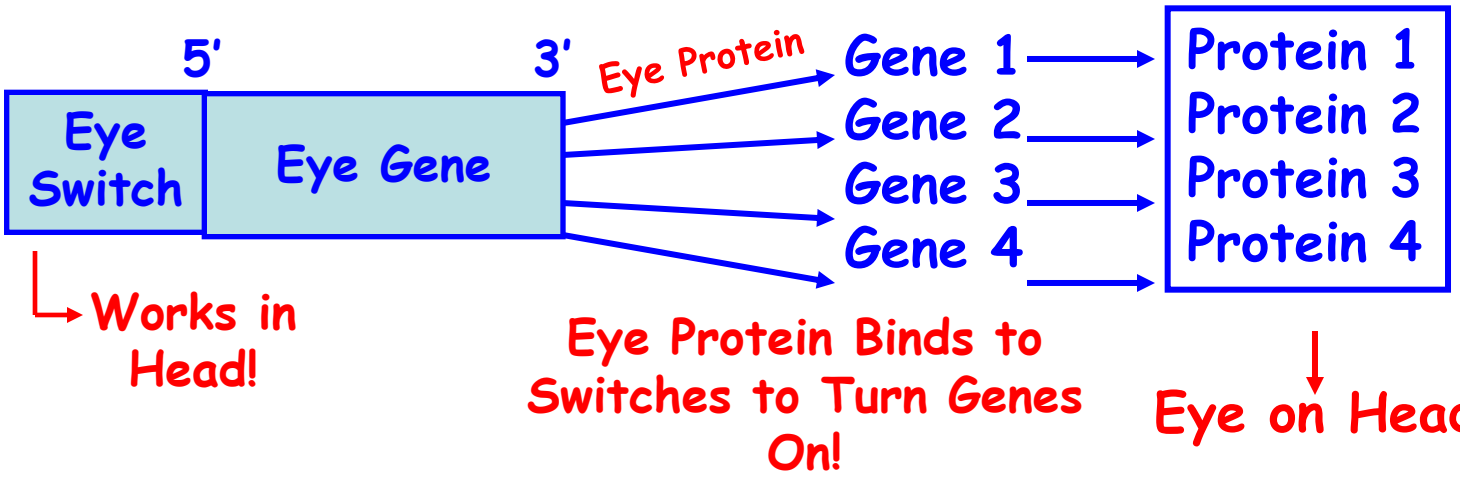
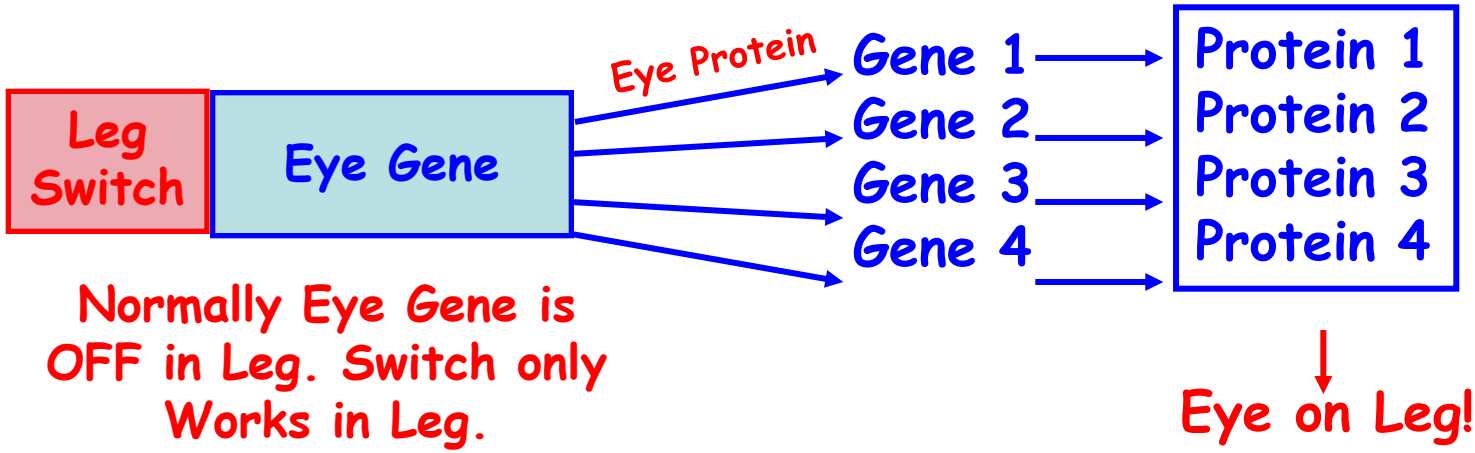
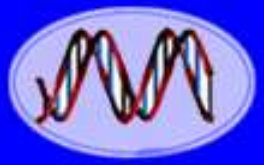
Eye Regulatory Network

Control Genes Like The Eye Gene Control The Activity of Other Genes!







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Ultimate Goal:To Dissect Genetic Regulatory Networks Programming Human Development From Birth to Death!

QuickTime™ and a
decompressor
are needed to see this picture.

Genetic Networks Programming Early Sea Urchin Development

QuickTime™ and a
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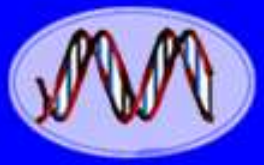

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100 Years Into The Future

1. If the Entire Human Genome is Sequenced?
2. If the Function/Protein 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 Law Were Only Rediscovered 100 Years Ago & Look What We Can Do & Now!