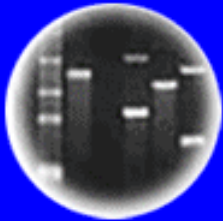


DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

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

Professors Bob Goldberg,
Channapatna Prakash, & John Harada

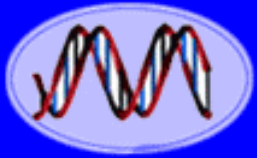
Lecture 3 What Are Genes & How Do They Work: Part One

UCLA



UC DAVIS
UNIVERSITY OF CALIFORNIA

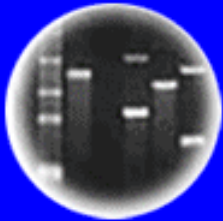
PREVIOUS TWO LECTURES



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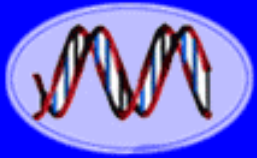


Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

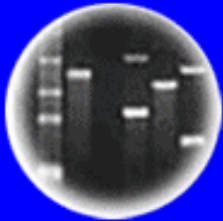
- Age of DNA
- Genetic Engineering Origins
- What Can Be Done With Genetic Engineering?
- Classical vs. Molecular Genetic Engineering
- **Demonstrations**
 - Spooling DNA
 - Vegetables - Classic Genetic Engineering



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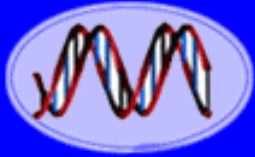
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THEMES FOR TODAY'S LECTURE

Gene Structure & Function

Part One (Text Chapter 2)

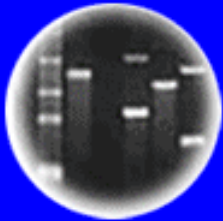
- What is the Function of a Gene?
- What are the Properties of Genes?
- What is the Evidence That DNA is the Genetic Material (Griffith and Avery Experiments)?
- Is Transformation Universal?
- What is the Structure of DNA?
- What is the Structure of a Chromosome?
- What is the Colinearity Between Genes & Proteins (how does DNA→protein)?
- How Do We Know That Genes Function Independently of One Another?
- What is the Anatomy of a Gene?
- How Do Switches Work to Control Gene Activity?
- What Are the Possibilities For Manipulating Genes in the Future?
- **Demonstration:** "Bacterial Cloning"



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

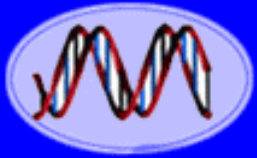
WHAT ARE THE PROPERTIES OF A GENE?

1. Replication
2. Stability (Mutations)
3. Universality
 - a) All Cells
 - b) All Organisms
4. Direct Cell Function/Phenotype

Design an Experiment to Show
That DNA is The Genetic
Material?

- How Can These Properties Be Tested Experimentally?
- What Predictions Follow From These Properties?

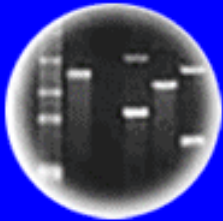
If DNA is the Genetic Material, THEN What.....?



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



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Reminder: Science is a Process!

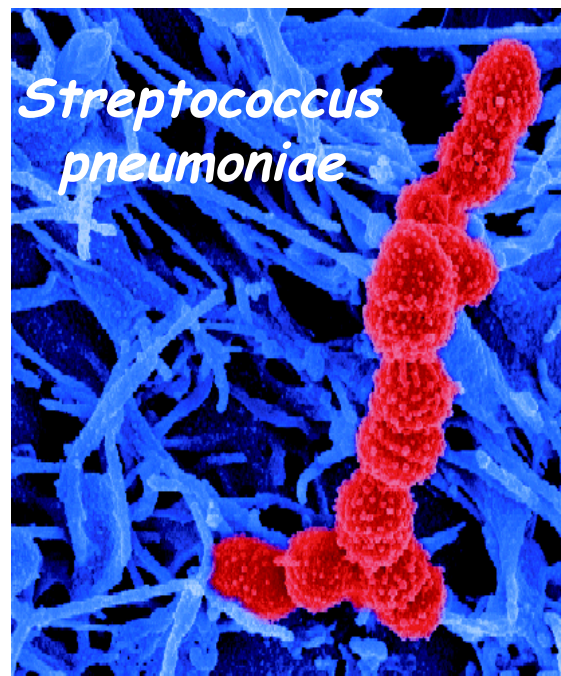
- What are the Observations?
- What is Your Hypothesis to Explain the Observations?
- What are the Predictions?
 - How Test Hypothesis?
- What are the Experimental Data?
 - Have the Data Been Verified & Peer Reviewed?

Evidence That DNA Is the Genetic Material Starts With Pneumonia

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.
January 29, 1922 - New York City

Spanish Flu (viral) Was also "Killer" at This Time!

INFLUENZA
FREQUENTLY COMPLICATED WITH
PNEUMONIA
IS PREVALENT AT THIS TIME THROUGHOUT AMERICA.
THIS THEATRE IS CO-OPERATING WITH THE DEPARTMENT OF HEALTH.
YOU MUST DO THE SAME
IF YOU HAVE A COLD AND ARE COUGHING AND SNEEZING, DO NOT ENTER THIS THEATRE
GO HOME AND GO TO BED UNTIL YOU ARE WELL.
Coughing, Sneezing or Spitting Will Not Be Permitted In The Theatre. In case you must cough or sneeze, do so in your own handkerchief, and if the coughing or sneezing persists leave the theatre at once.
This Theatre has agreed to cooperate with the Department Of Health in disseminating the truth about Influenza, and thus serve a great educational purpose.
HELP US TO KEEP CHICAGO THE HEALTHIEST CITY IN THE WORLD
JOHN DILL ROBERTSON
COMMISSIONER OF HEALTH



Spanish Influenza has endangered the prosecution of the WAR in Europe.
There are 1500 cases in the Navy Yard
30 deaths have already resulted
SPITTING SPREADS SPANISH INFLUENZA DONT SPIT

Epidemic Closing
Order Is Sweeping
The State Board of Health orders closing schools, theatres, churches, saloons, etc., in an effort to prevent a further spread of the Spanish Influenza epidemic, is a sweeping one. All clubs must close, including bowling alleys and pool rooms. No society, club or organization meeting can be held, not even at homes.

Spanish Flu Killed 50-100 million people world-wide from 1918 to 1920 - Most From Secondary Bacterial Infections

The Spanish Flu Pandemic - 1918 to 1920

It is estimated that anywhere from **50 to 100 million** people were killed world wide - 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%.

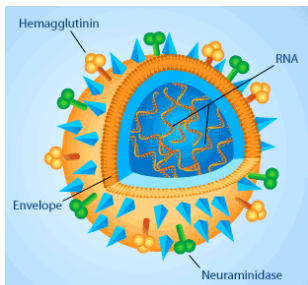
Characterization of the 1918 “Spanish” influenza virus neuraminidase gene

PNAS June 6, 2000

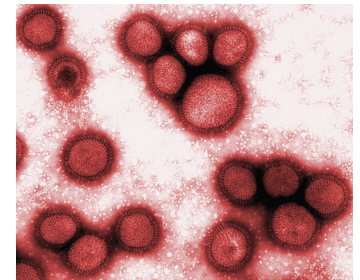
Ann H. Reid,* Thomas G. Fanning, Thomas A. Janczewski, and Jeffery K. Taubenberger

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



Major Causes of Death in USA

1920 (CDC)

1. Pneumonia
2. Heart Disease
3. Tuberculosis
4. Stroke
5. Kidney Disease
6. Cancer
7. Unintentional Accidents (excluding cars)
8. Diarrhea, Enteritis, Intestinal Lesions
9. Premature Birth
10. Maternal Death Giving Birth

Note: Based on 1.1 M Deaths (1,300 per 100,000). Child Mortality = 100 per 1,000

2011 (CDC)

1. Heart Disease
2. Cancer
3. Chronic Respiratory Diseases (e.g., Emphysema & Bronchitis)
4. Stroke
5. Unintentional Accidents (e.g., Cars)
6. Alzheimer's Disease
7. Diabetes
8. Kidney Disease
9. Influenza & Pneumonia
10. Intentional Self Harm (Suicide)
11. Septicemia (Bacteria)

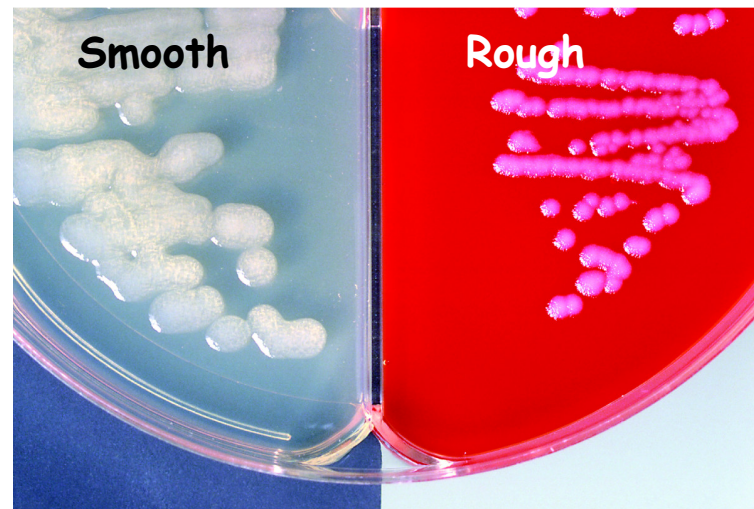
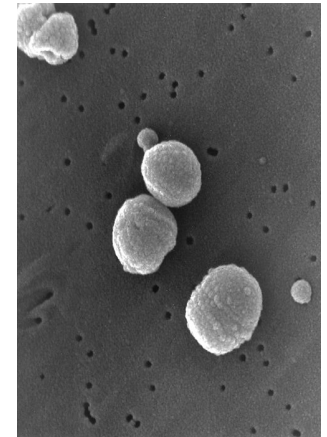
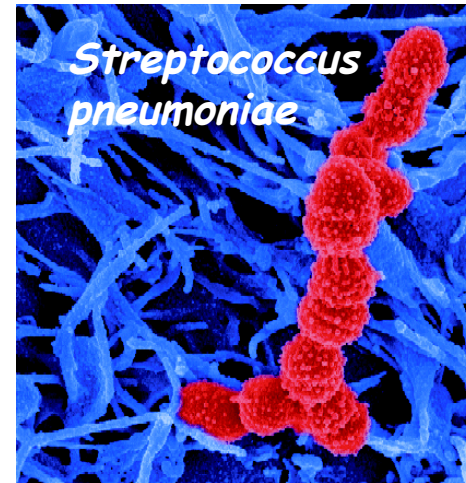
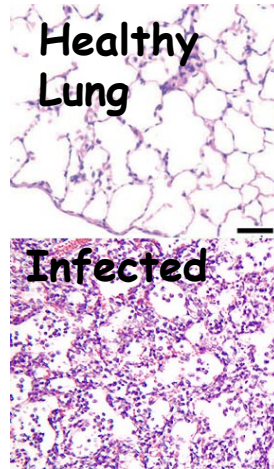
Note: Based on 2.5M Deaths (741 per 100,000). Child Mortality 6 per 1,000

Frederick Griffith & The Transforming Principle

The First Genetic Engineering Experiment (unintentional!)

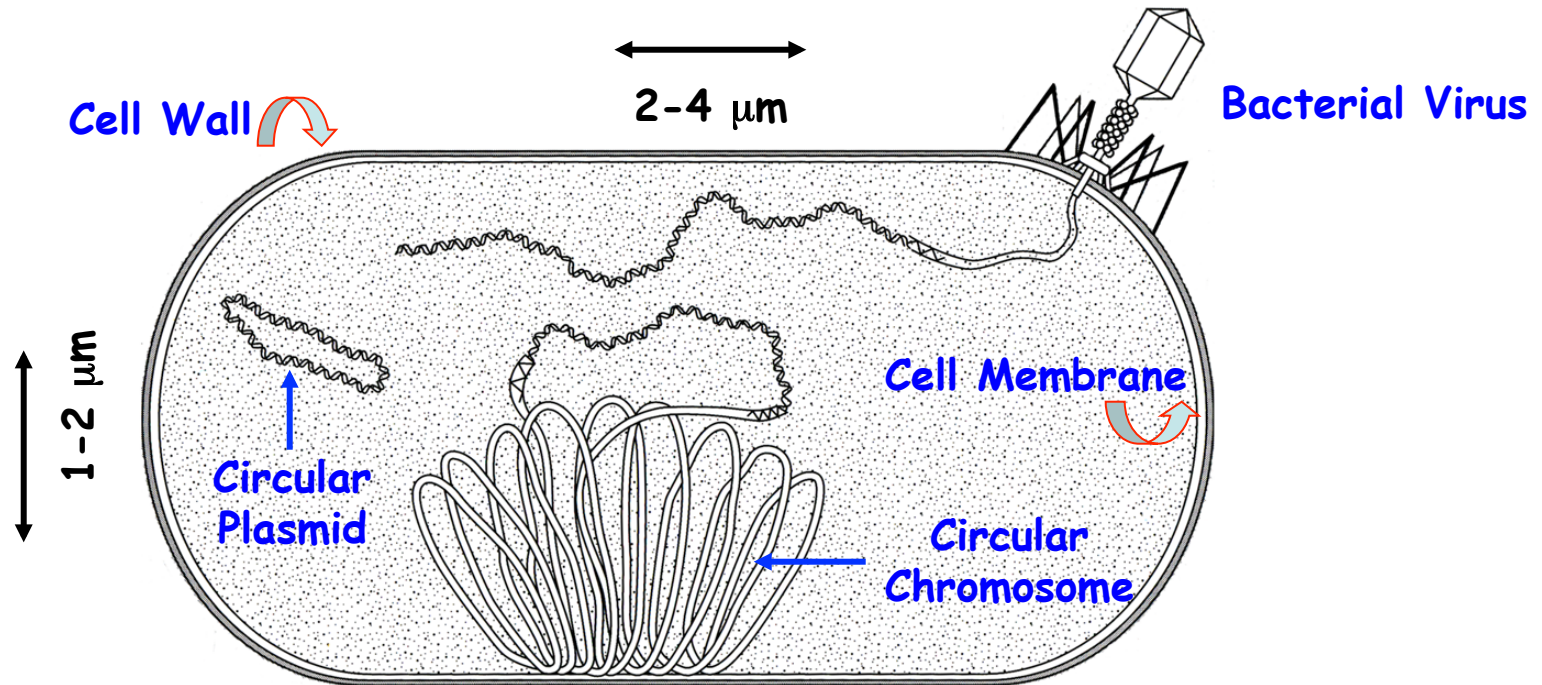


1879-1941



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: $\sim 1.4 \mu\text{m}$ (10^{-6} m) in circumference (Genetic Engineering Vectors)
Chromosome: ~ 1.4 mm (10^{-3} m) in circumference

1 μm = 3.94×10^{-5} inches

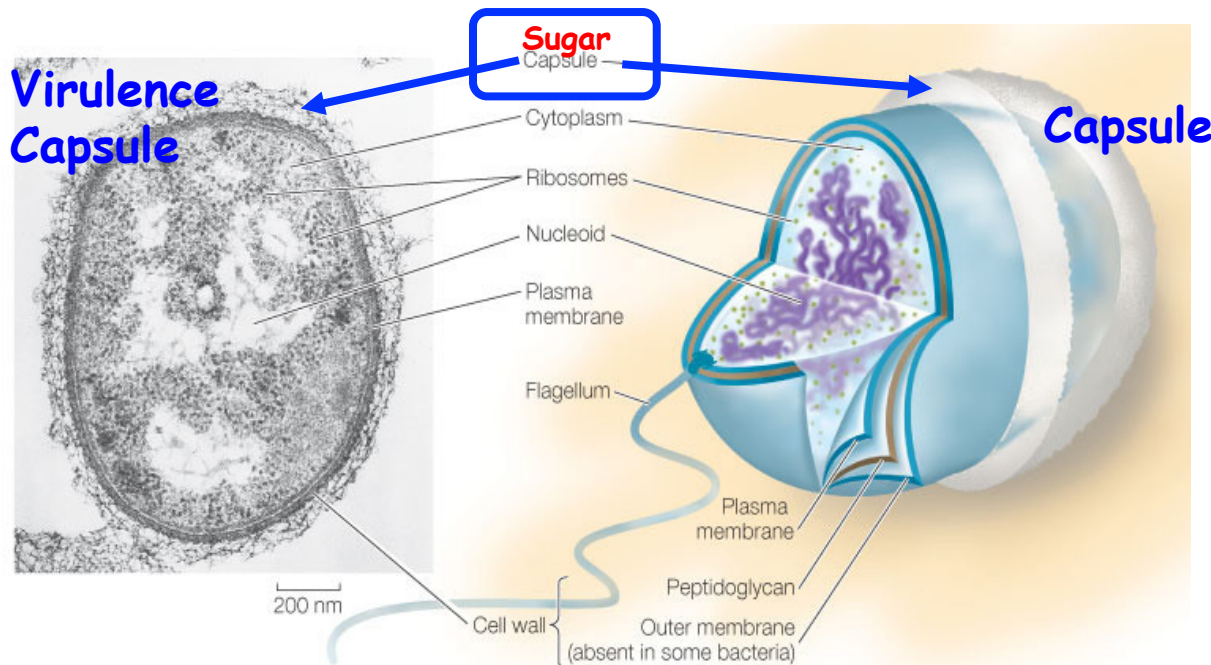
Bacterial Genome Projects Have Provided Remarkable Insight Into Bacterial Genomes and Cell Functions

Table 1–1 Some Genomes That Have Been Completely Sequenced

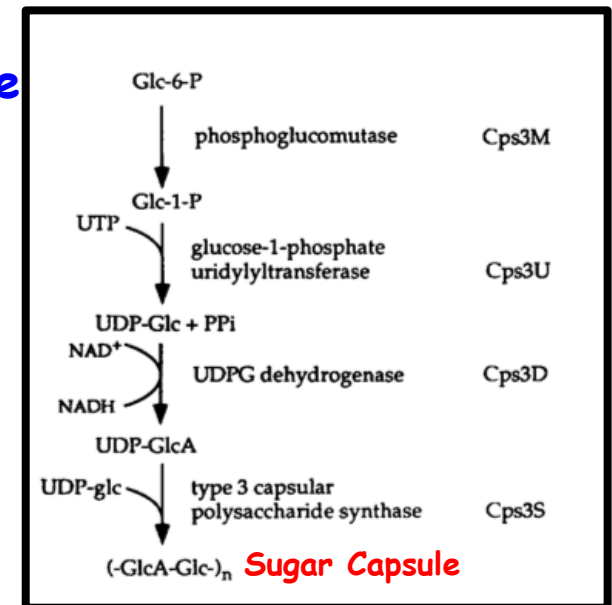
SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	ESTIMATED NUMBER OF GENES CODING FOR PROTEINS
BACTERIA				400 to 8,000 Genes
<i>Mycoplasma genitalium</i>	has one of the smallest of all known cell genomes	human genital tract	580 <i>Made Synthetically!</i>	468
<i>Synechocystis</i> sp.	photosynthetic, oxygen-generating (cyanobacterium)	lakes and streams	3573	3168
<i>Escherichia coli</i>	laboratory favorite	human gut	4639	4289
<i>Helicobacter pylori</i>	causes stomach ulcers and predisposes to stomach cancer	human stomach	1667	1590
<i>Bacillus anthracis</i>	causes anthrax	soil	5227	5634
<i>Aquifex aeolicus</i>	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
<i>Streptomyces coelicolor</i>	source of antibiotics; giant genome	soil	8667	7825
<i>Treponema pallidum</i>	spirochete; causes syphilis	human tissues	1138	1041
<i>Rickettsia prowazekii</i>	bacterium most closely related to mitochondria; causes typhus	lice and humans (intracellular parasite)	1111	834
<i>Thermotoga maritima</i>	organotrophic; lives at very high temperatures	hydrothermal vents	1860	1877

3,758 Bacterial Genomes Have Been Sequenced to Date (January, 2013)

Streptococcus pneumoniae



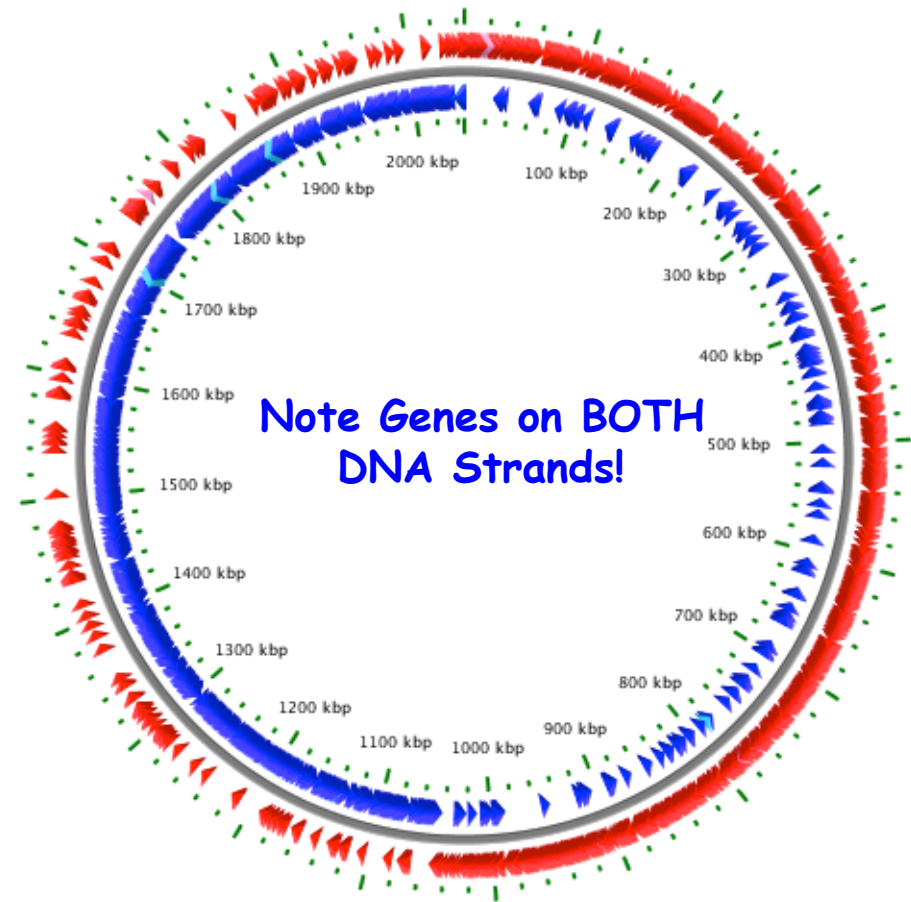
Capsule Biosynthesis



J. Exp. Med. 181, 973, 1995

The Sugar Capsule Protects the Bacteria From Mammalian Host Antibodies
Capsule = Virulence No Capsule = Avirulence

Streptococcus pneumoniae Genome Has Been Sequenced!



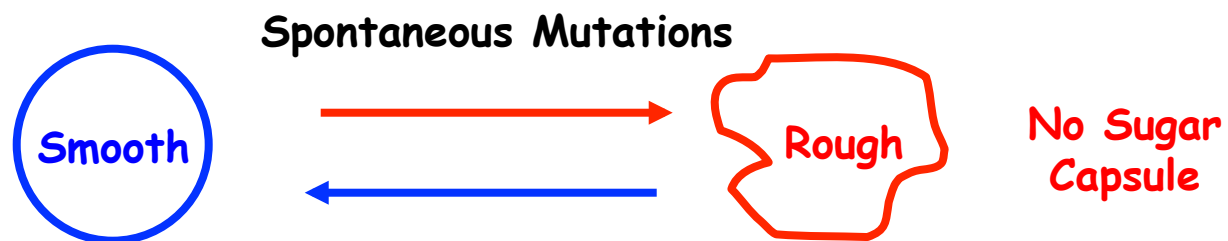
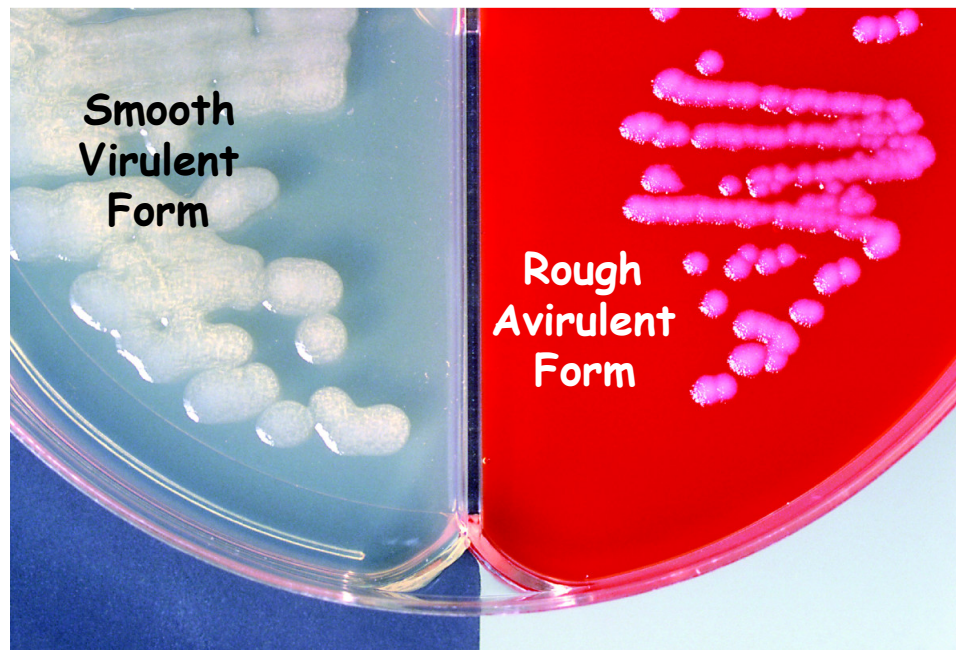
2,046,115 bp and 1,987 Genes

Four Genes Specify Capsule Formation

What Happens If One of These Genes Is Mutated?

J. Bacteriology
2001

The Griffith Experiment With Smooth and Rough Pneumonia Bacteria



J. Hygiene, 1928

The Griffiths Experiment (1928)

EXPERIMENT

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

MIX LIVE ROUGH & DEAD SMOOTH CELLS

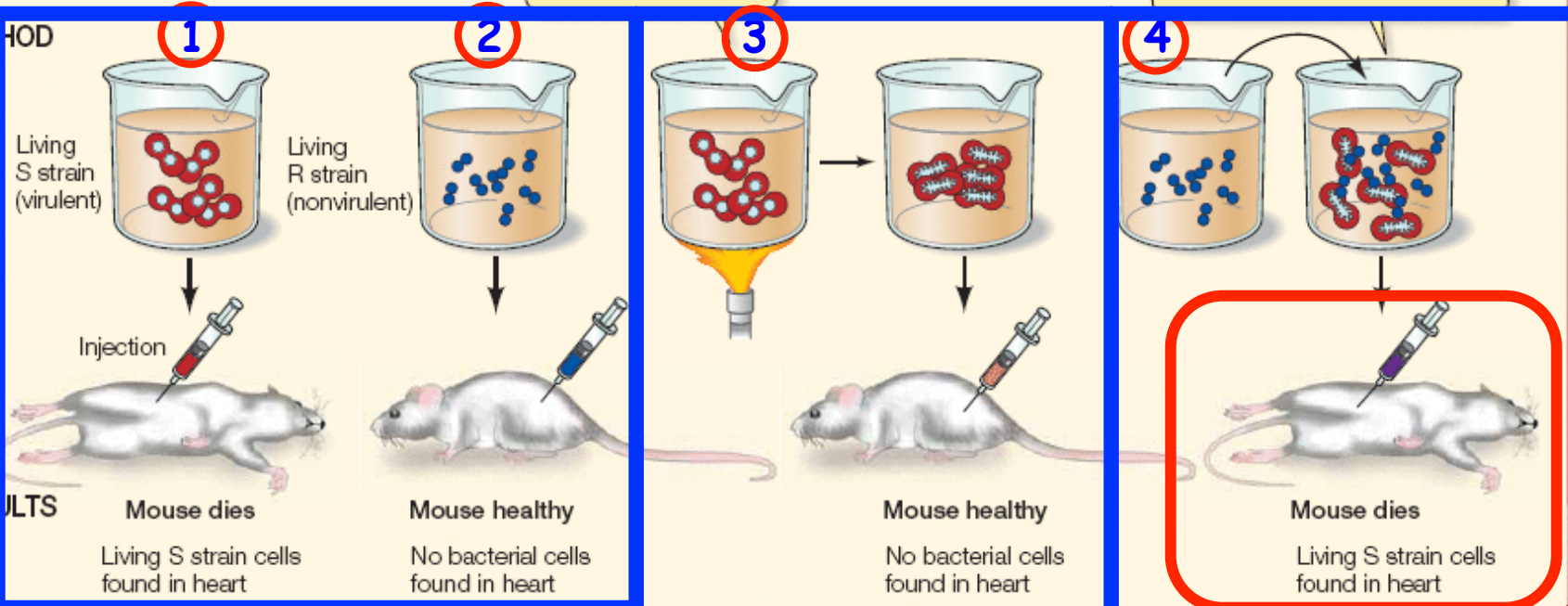
CONTROLS

Kill the virulent S strain bacteria by heating.

BOILING KILLS SMOOTH CELLS

Mix dead S strain cells with living, nonvirulent R strain bacteria.

METHOD



RESULTS

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

MOUSE DIES - SMOOTH CELLS FOUND IN HEART

**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.

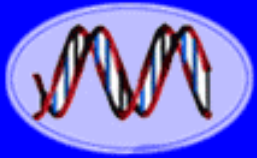
Conversion of R Type II into S Type I. In the experiment in Table VII two out of eight mice injected with heated virulent Type I culture together with an attenuated R culture derived from Type II died of pneumococcal septicaemia and yielded pure S colonies of Type I from the blood; plates from the lesions 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
As above	R 4, Type II, grown in the heated Type I deposit. Dose = 0.36 c.c.	647	" 6 "	" "
		648	" 6 "	" "
	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

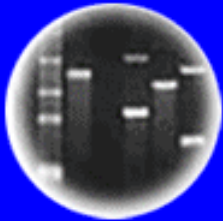
Significance?



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Cloning: Ethical Issues
and Future Consequences

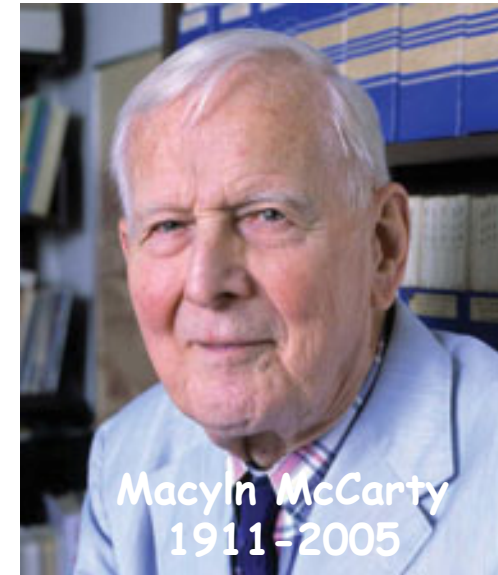
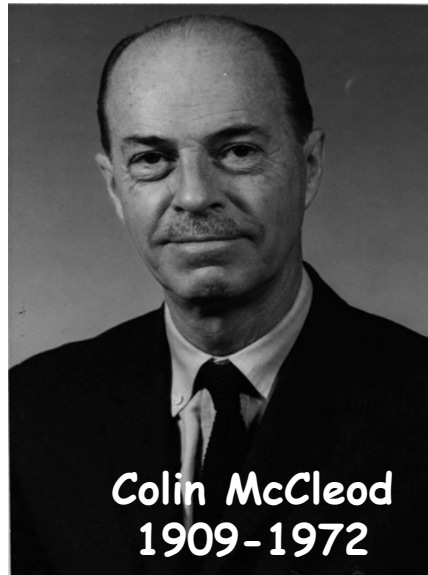
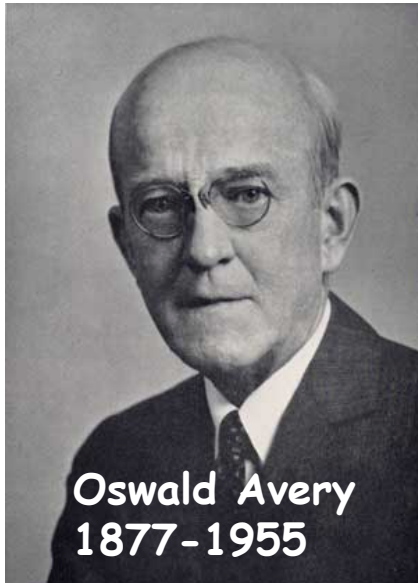


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Change of Rough II Strain to Smooth I Strain Indicates that the Change is Due to Mutation or “Something” Else

- a. Mutation
- b. “Something” Else

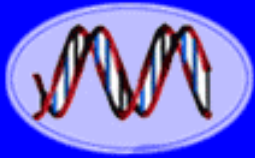
What Was The Transforming Principle? Experiments of Avery, McCleod, & McCarty Fast Forward to the 1940s!



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

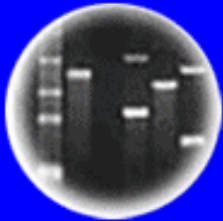
J. Exp. Med., 1944



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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

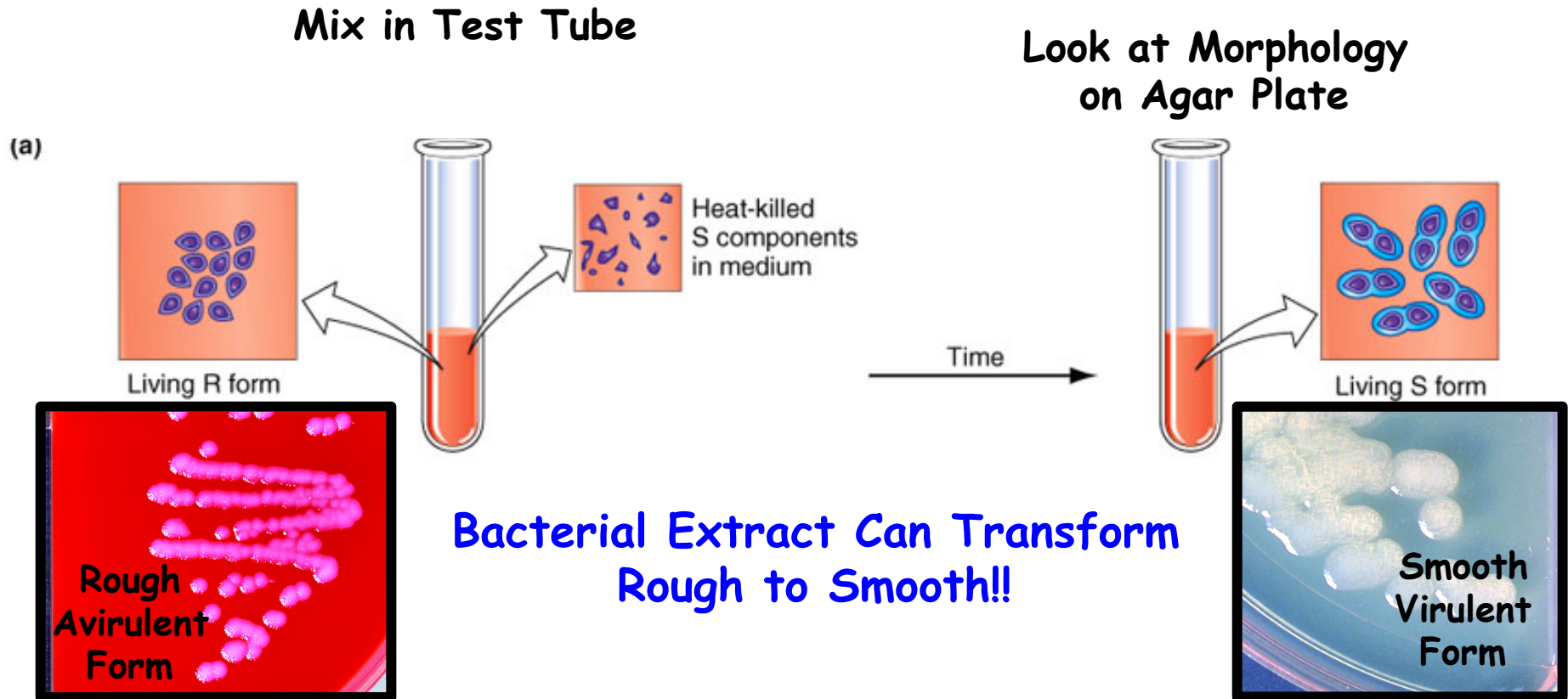
By OSWALD T. AVERY, M.D., COLIN M. MacLEOD, M.D., AND
MACLYN McCARTY,* M.D.

Avery et al. Questions?

1. Does the Transforming Principle Come From the Mouse or Bacteria?
2. If From the Bacteria -- What Substance?
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?

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

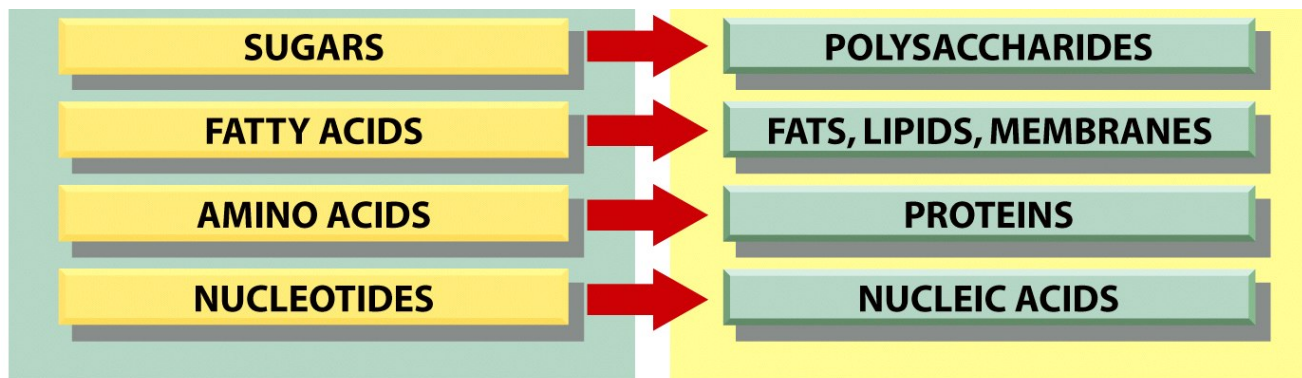
1. What is Predicted if DNA is the Genetic Material?

2. How Test Hypothesis?

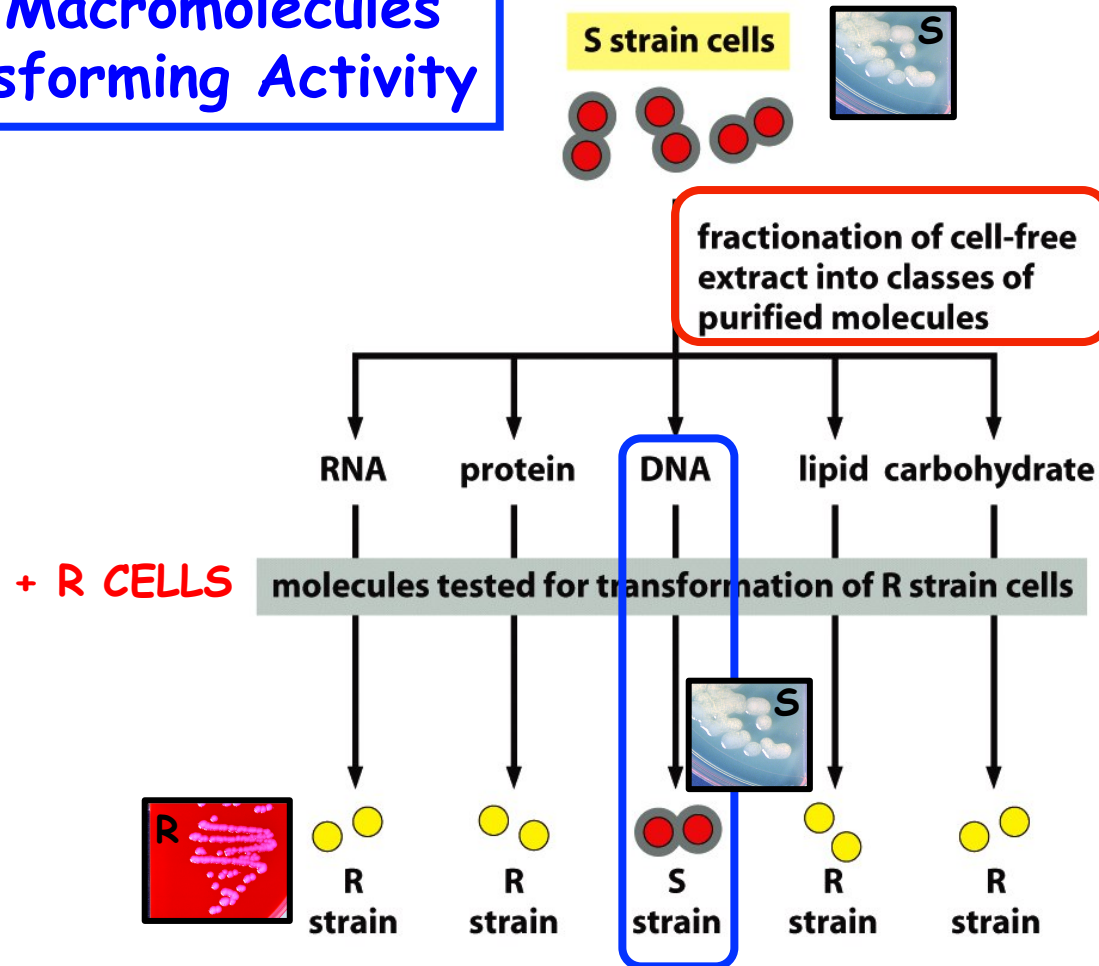
Macromolecules

Monomers

Polymers



Testing Macromolecules For Transforming Activity



CONCLUSION: The molecule that carries the heritable information is DNA.

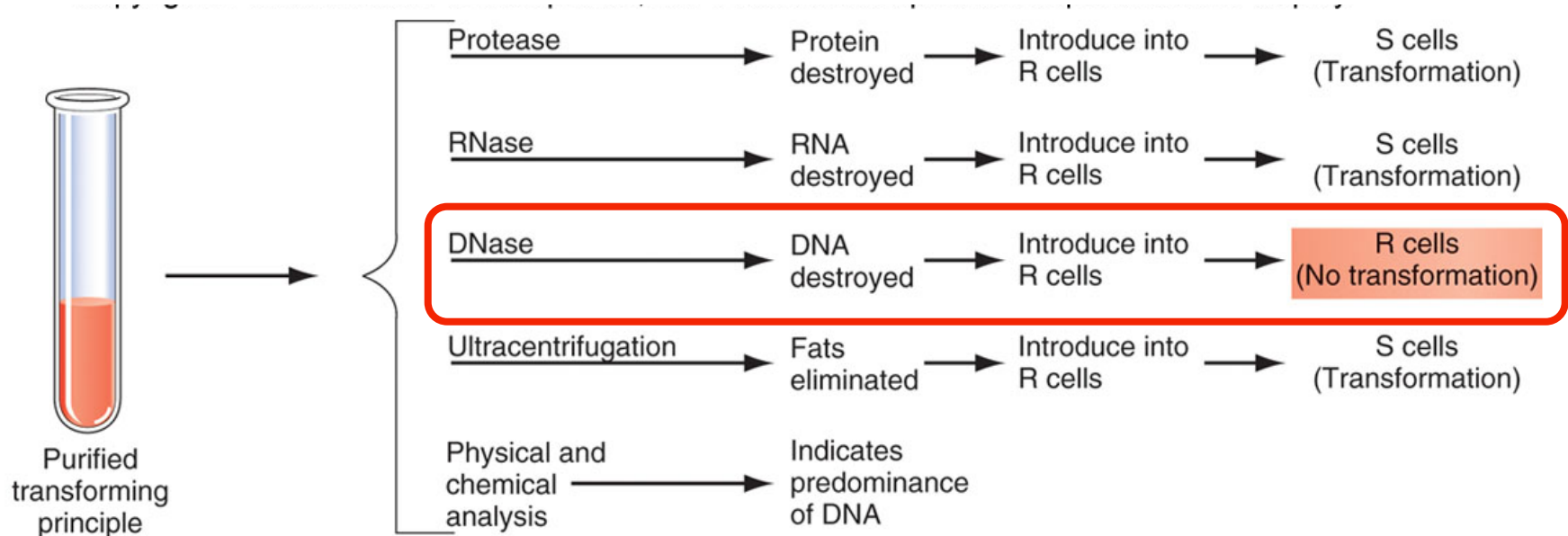
First Transformation Experiment With Purified Molecules!!

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

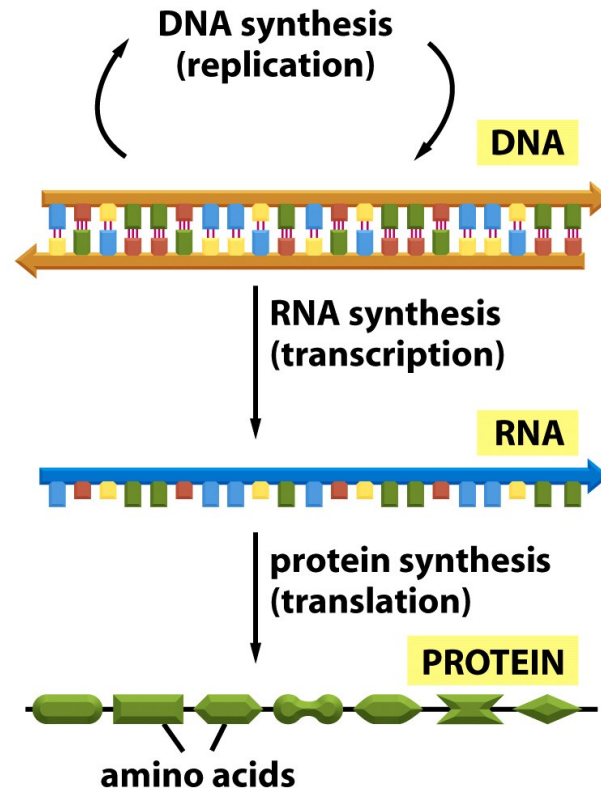


When DNase Destroyed DNA There Was No Transformation & Only Rough Cells Were Found in the Culture

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

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

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



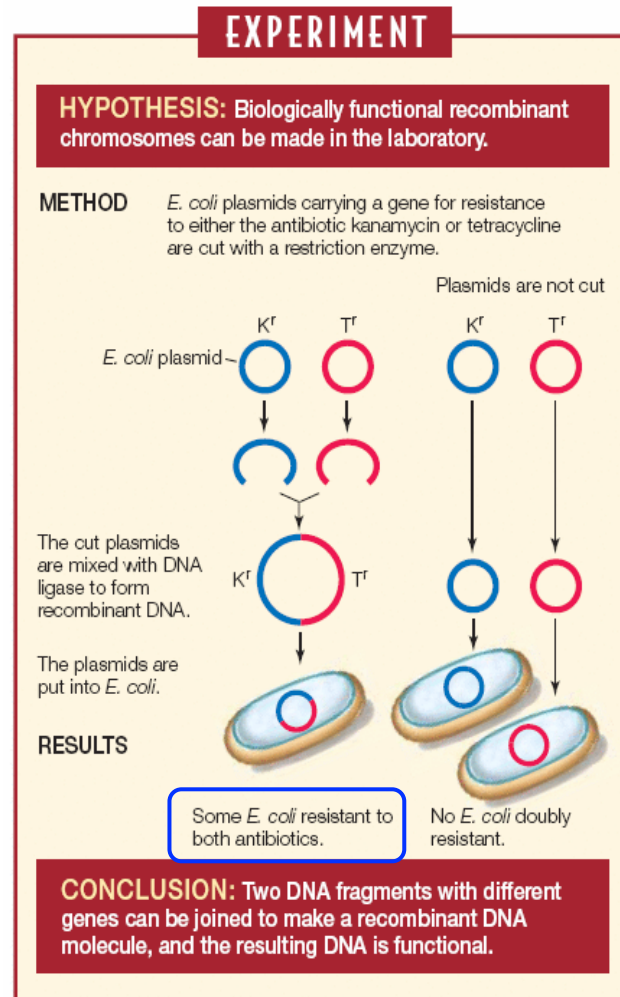
Cell Processes

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 and Traits?

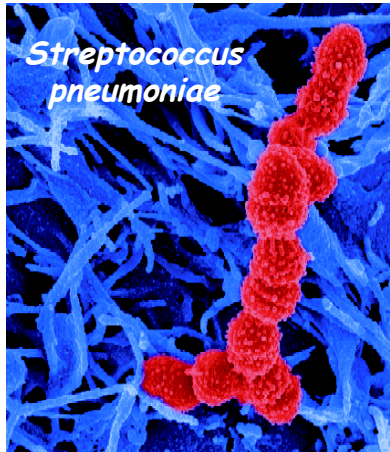
Cohen & Boyer Experiment That “Invented” Genetic Engineering



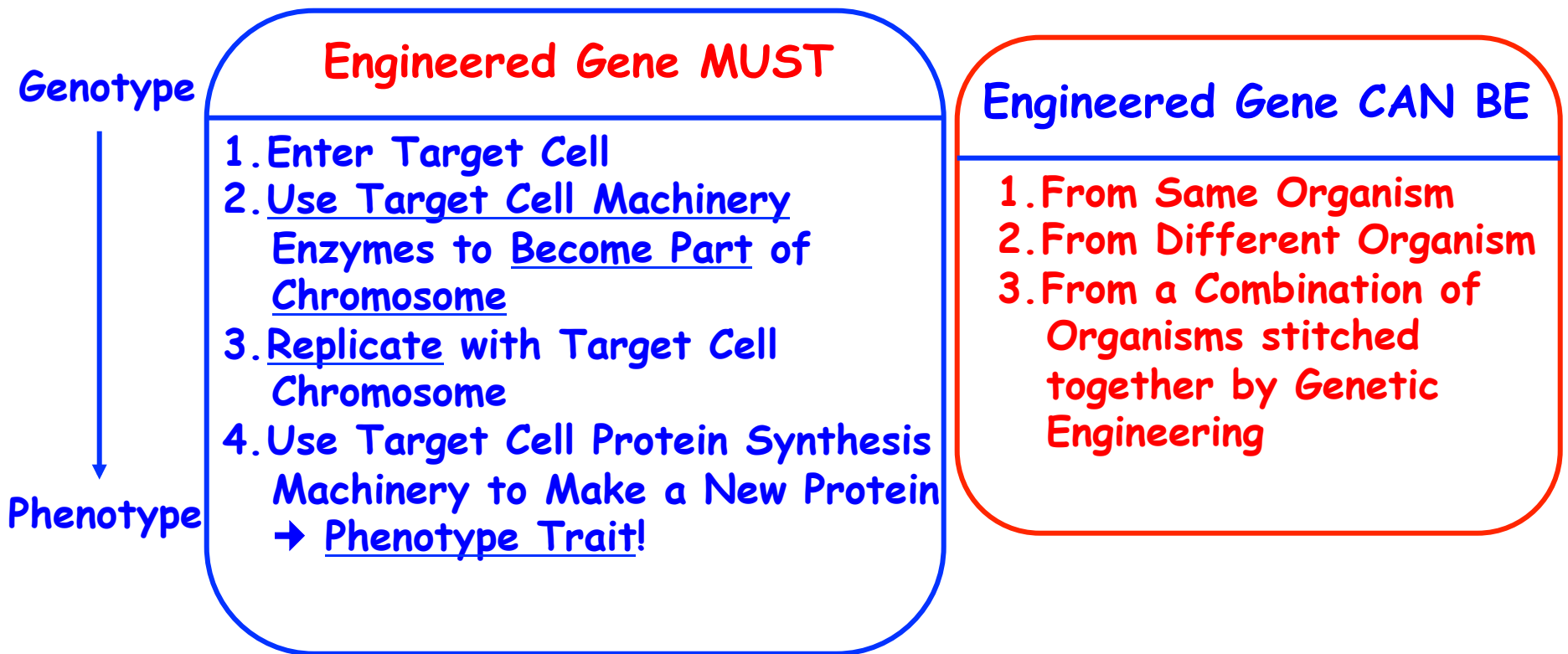
Because the Transforming Principle is DNA
Any Gene Can Be Transformed (e.g., Antibiotic^R to Antibiotic^S)

All Organisms Can Be Transformed!!

Genetic Engineering Has Come a Long Way Since Griffiths Experiments in 1928!!



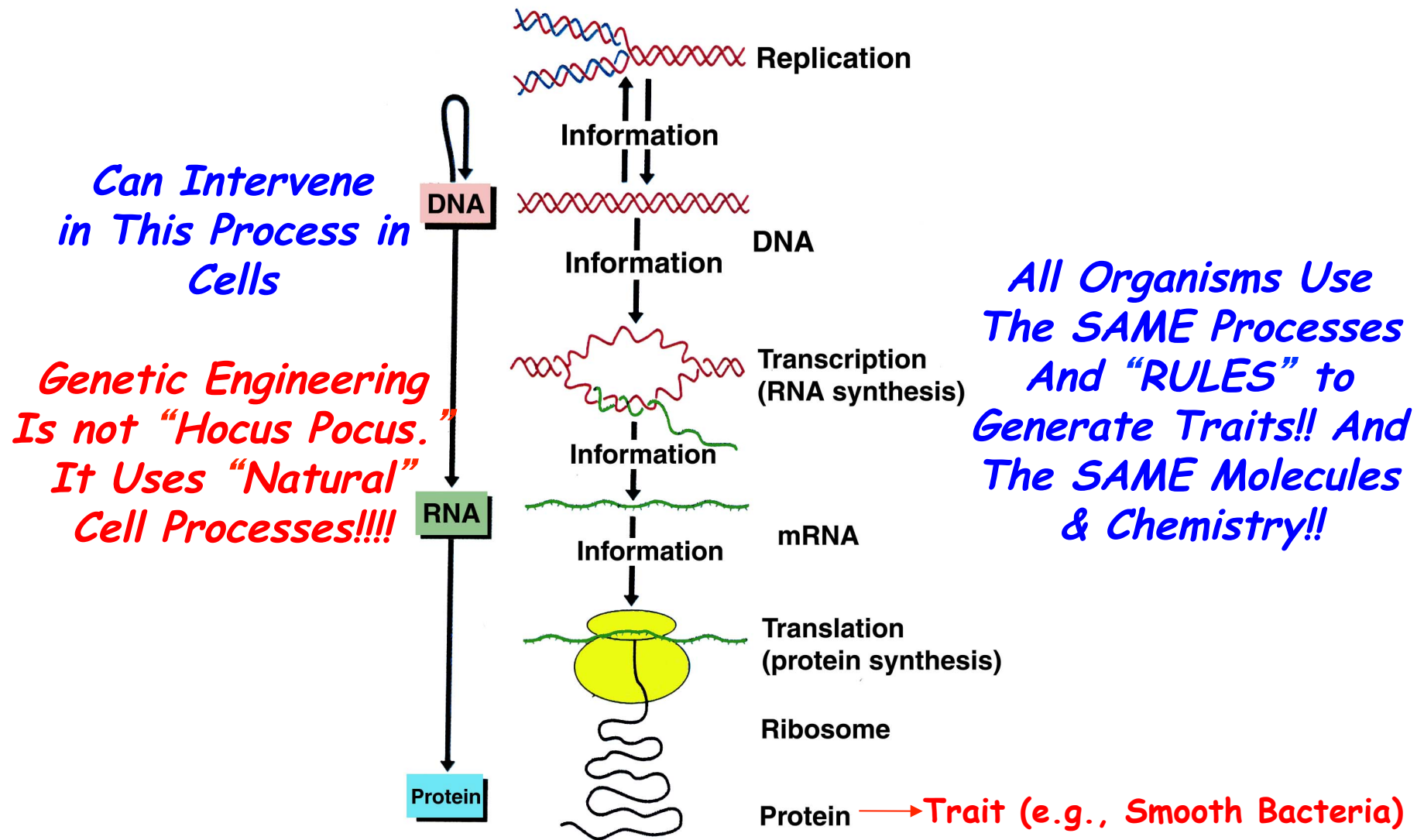
Genetic Engineering/Transformation Involves Incorporating Engineered DNA or Genes Into Different Organisms



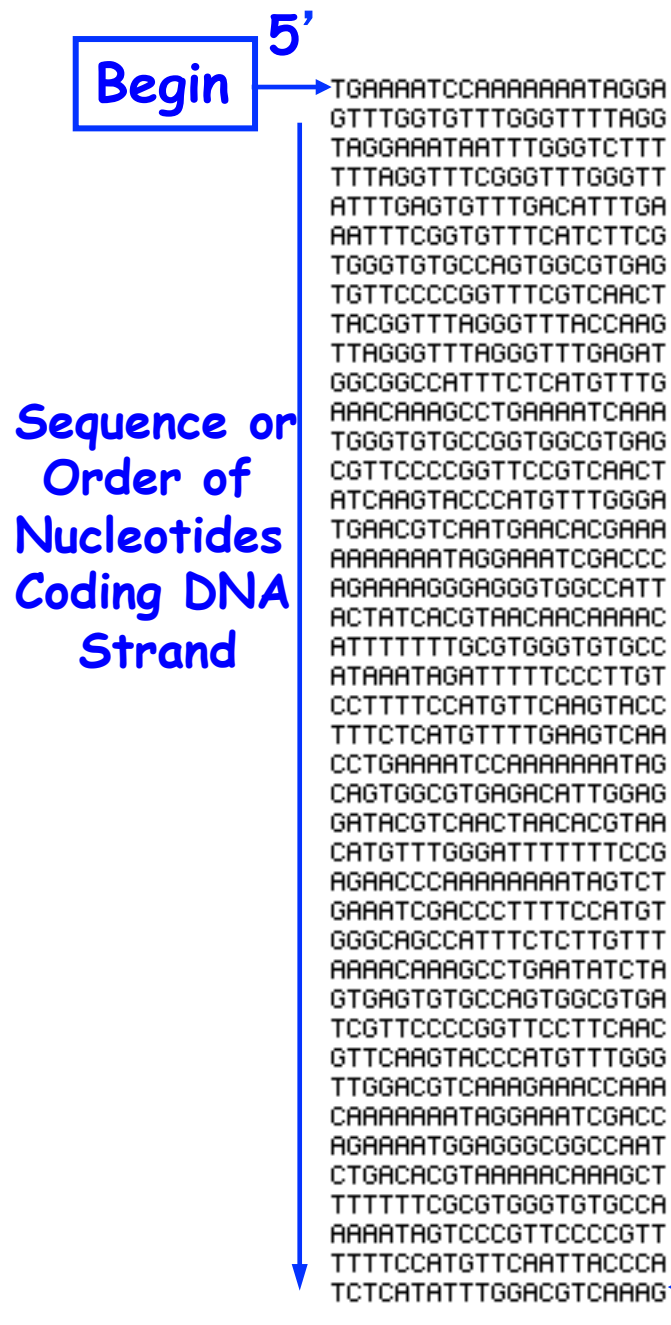
Gene Engineering Shows that Gene Processes Are Universal!!!

Just Like The GlowGene Experiments!!!

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



What is A Gene?



The β -globin Gene

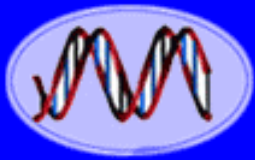
Blood Protein Carries Oxygen to
All Genes From Lungs \Rightarrow Energy

A Gene is a Unique Sequence of
Nucleotides Specifying a Function

DNA Sequence = Biology!
What If Sequence Changed?

SEQUENCE \rightarrow FUNCTION

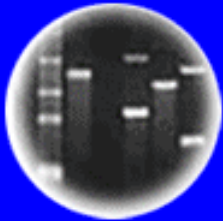
Relative to Coding or
Sense Strand of Gene



DNA
Genetic Code of Life



Entire Genetic Code
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DNA Fingerprinting

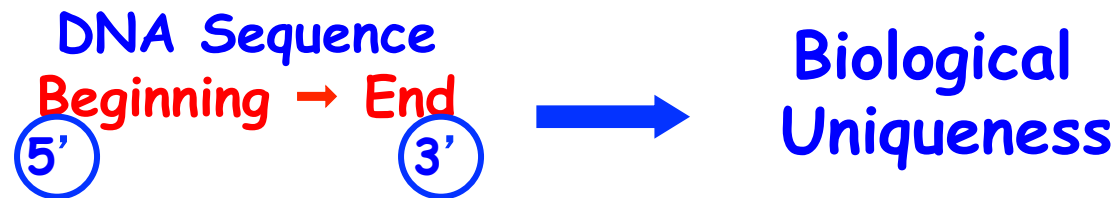


Cloning: Ethical Issues
and Future Consequences



Plants of Tomorrow

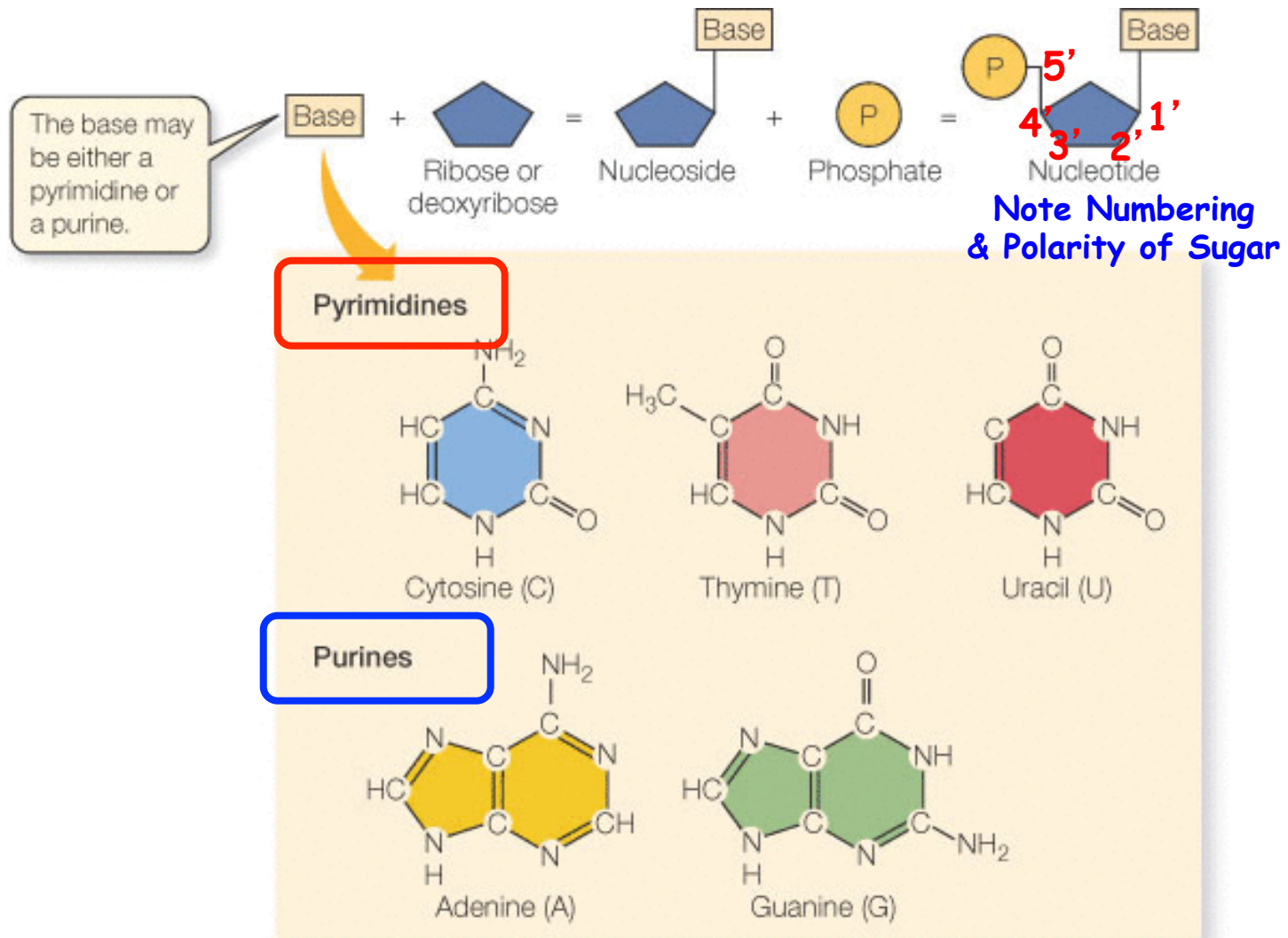
Genes & Genomes Differ Because the Sequence of DNA Differs



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**

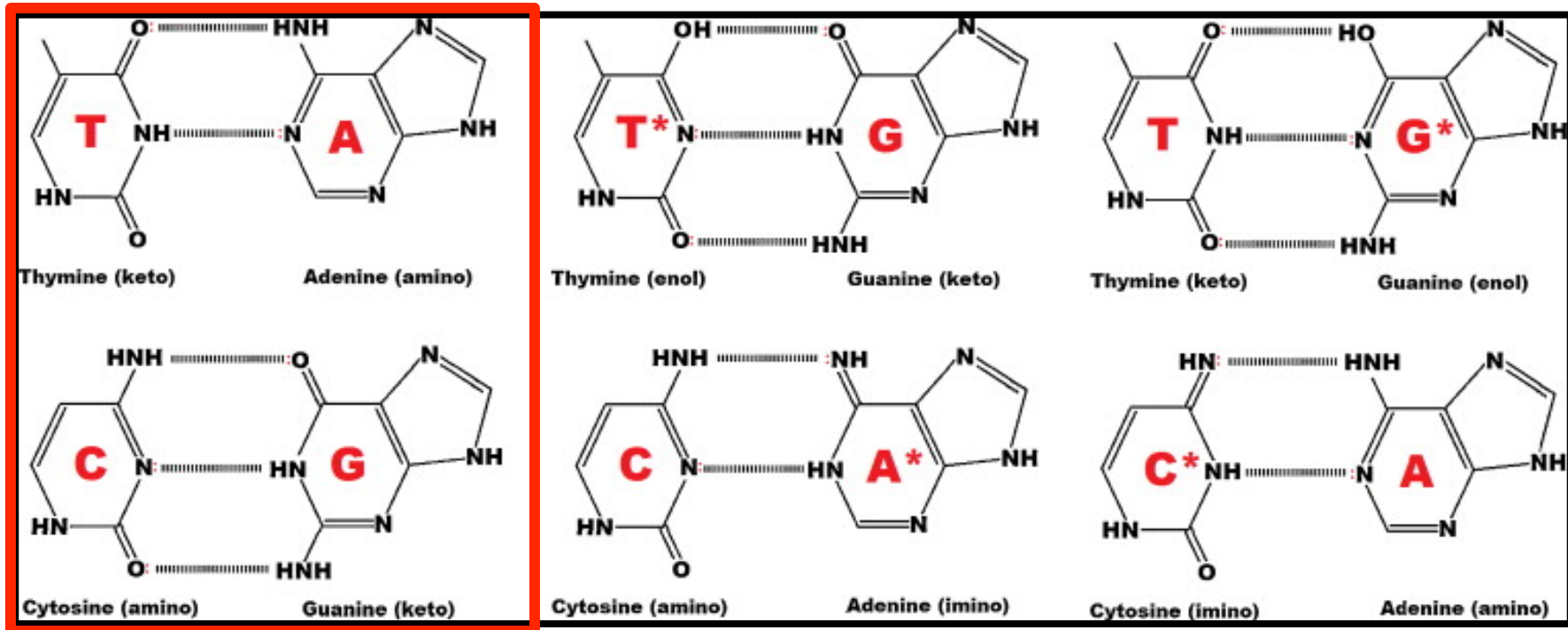
There Are Four Different Nucleotides in DNA



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

TAUTOMERS CHANGE BASE PAIRING RULES

Normal Forms - Keto & Amino

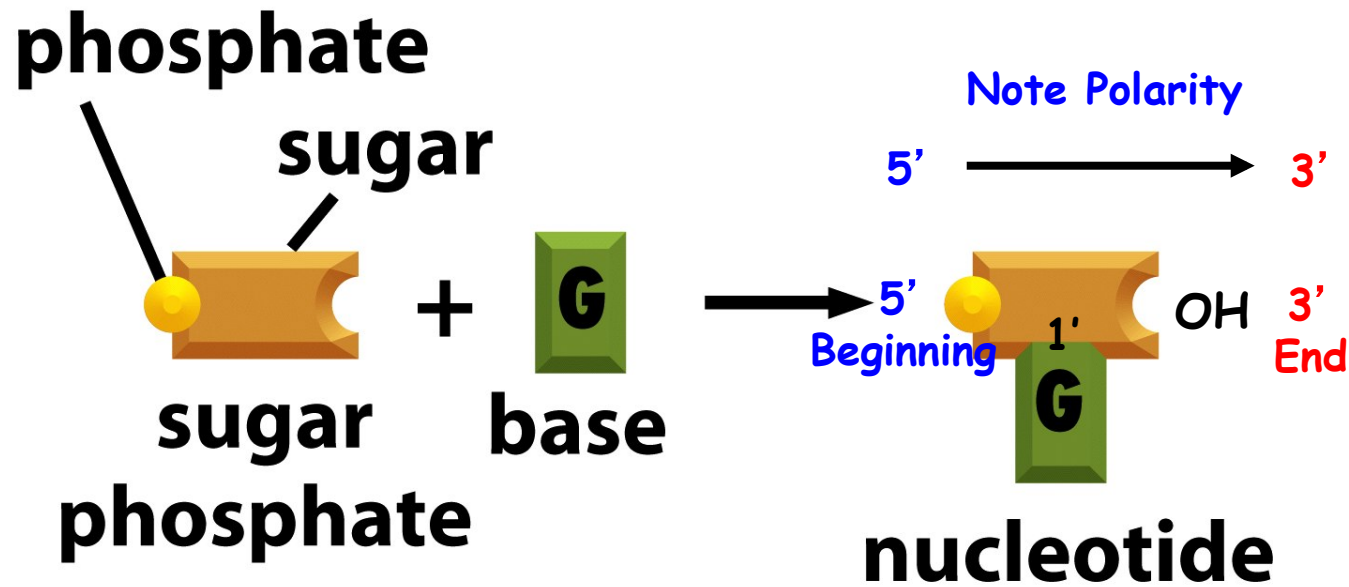


And Lead To Mistakes in DNA
Replication & Mutations --
Chemistry Leads to Biology!!



Nucleotides Have Polarity

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

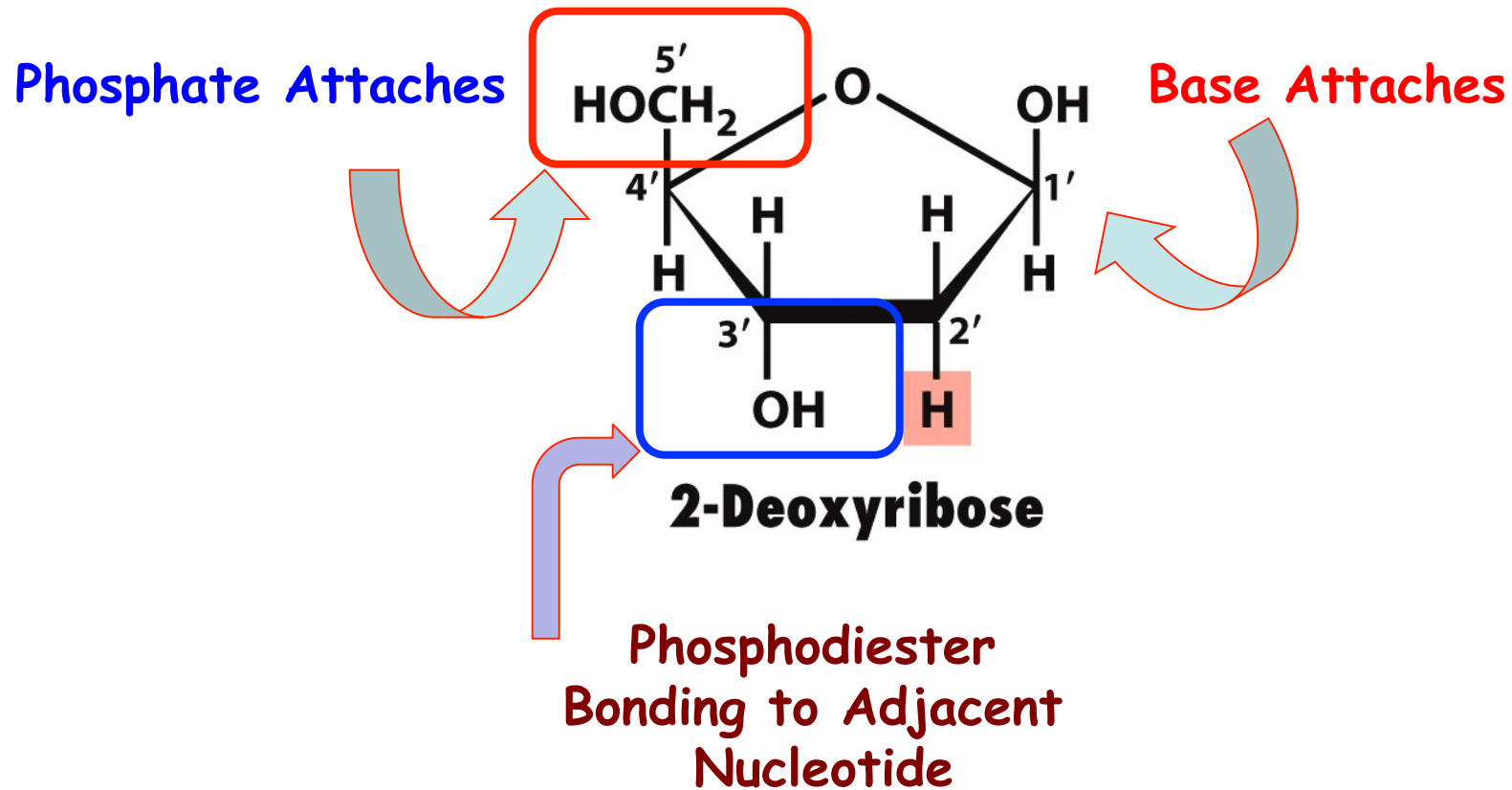


The Sugar is the HUB

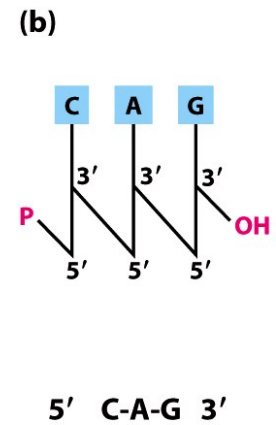
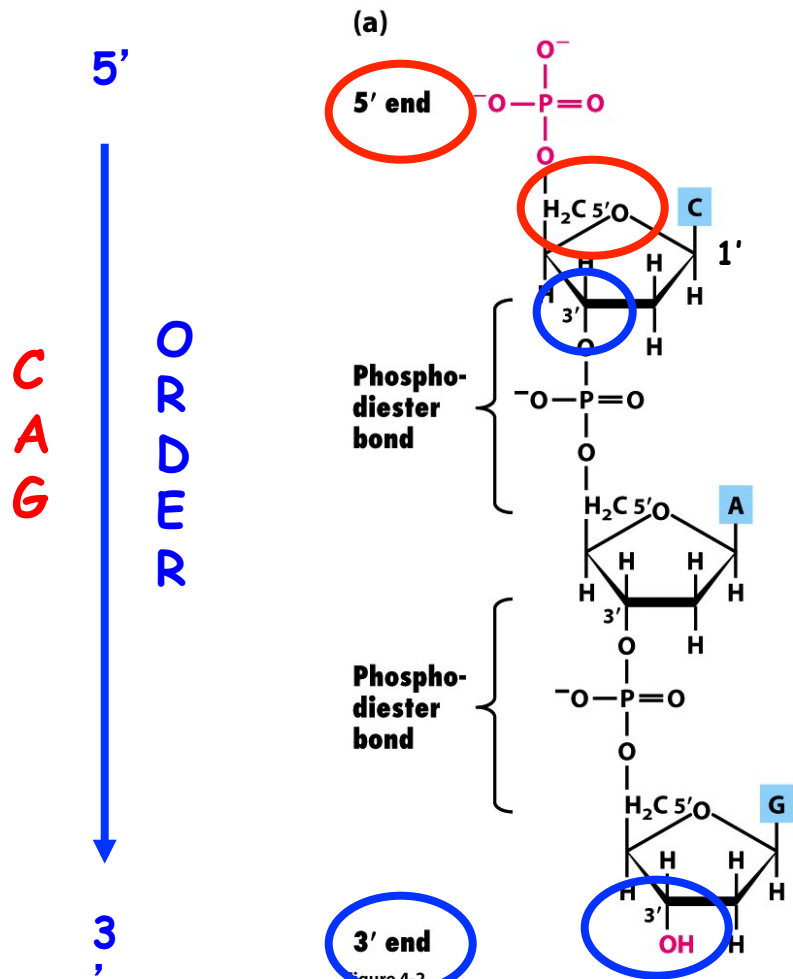
DNA Sequence Defined By Nucleotide Order

DNA Sequence = Functional Uniqueness = Biology

Note Structure and Polarity of Deoxyribose Sugar



Nucleotides Are Joined By 5' to 3' Phosphodiester Bonds



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

Figure 4-2
Molecular Cell Biology, Sixth Edition
© 2003 W.H. Freeman and Company

Clues to the Double Helix-Chargaff's Rules

Purines = Pyrimidines

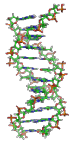
TABLE 6.1 Chargaff's Data on Nucleotide Base Composition in the DNA of Various Organisms

Organism	Percentage of Base in DNA				Ratios	
	A	T	G	C	A:T	G:C
<i>Staphylococcus afermentams</i>	12.8	12.9	36.9	37.5	0.99	0.99
<i>Escherichia coli</i>	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
<i>Caenorhabditis elegans</i> *	31.2	29.1	19.3	20.5	1.07	0.96
<i>Arabidopsis thaliana</i> *	29.1	29.7	20.5	20.7	0.98	0.99
<i>Drosophila melanogaster</i>	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
<i>Mus musculus</i> (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

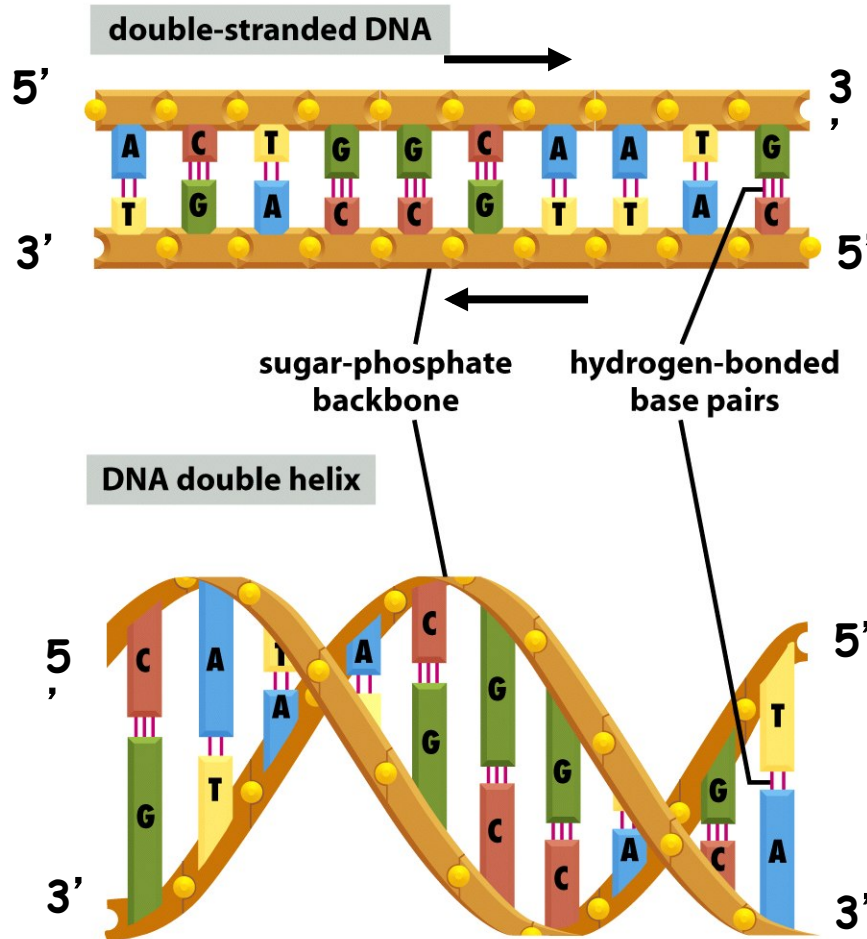
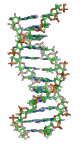
*Data for *C. elegans* and *A. thaliana* are based on those for close relative organisms.

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?

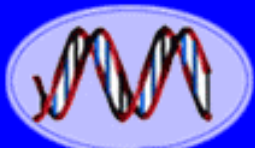


DNA is a Double Helix of Two Complementary Chains of DNA Wound Around Each Other



Watson and Crick, Nature, 1953

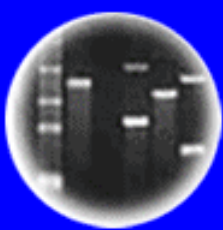
1. Complementary Strands
2. A=T and G=C (Four Bases)
3. Sequence of Strands Differ
4. Bases to Interior
5. Phosphate-Sugar Backbone on Exterior
6. DNA Strands in Opposite Direction (Only Way Helix Fits)
7. Sequence of One Chain Automatically Specifies Sequence of Complementary Chain (Basis of Replication!)
8. No Constraint on Sequence ($4^n = n \text{ # sequences}$)
9. DNA has dimensions (Know # bp
Know Length: 20Å diameter, 3.4Å/bp, 10bp/turn)
10. Sequence = Biology



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



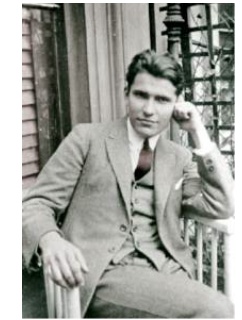
DNA Fingerprinting



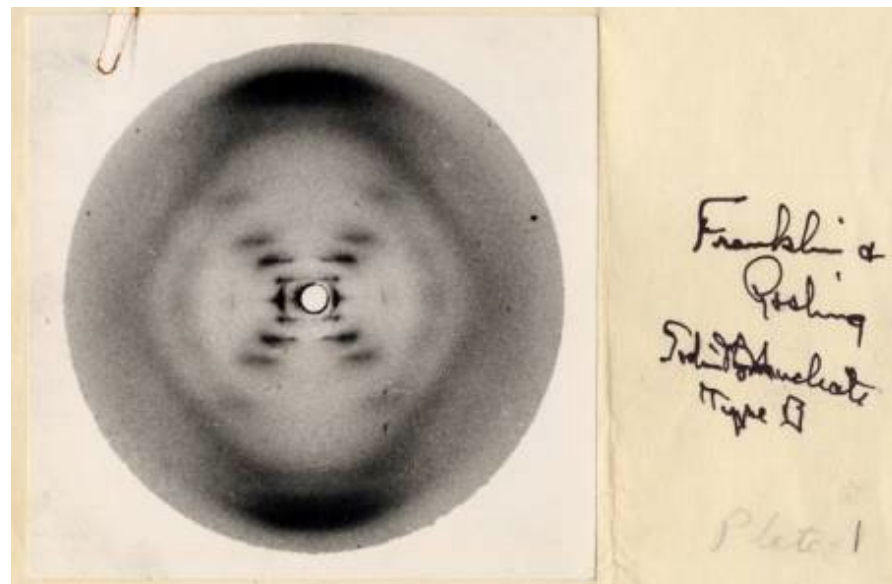
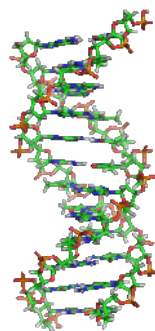
Cloning: Ethical Issues
and Future Consequences



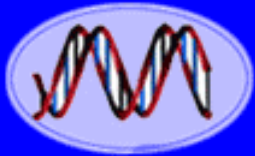
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Reflections on The "Race For the Double Helix" Film



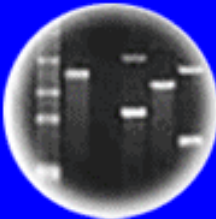




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Entire Genetic Code
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DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



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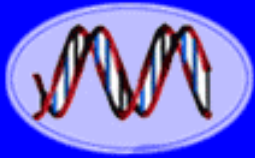
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

Nature, April 25, 1953

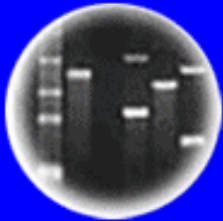
We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on inter-atomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at



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GENETICAL IMPLICATIONS OF THE STRUCTURE OF DEOXYRIBONUCLEIC ACID

By J. D. WATSON and F. H. C. CRICK

Medical Research Council Unit for the Study of the
Molecular Structure of Biological Systems, Cavendish

Laboratory, Cambridge Nature, May 30, 1953

No. 4361 May 30, 1953

N A T U

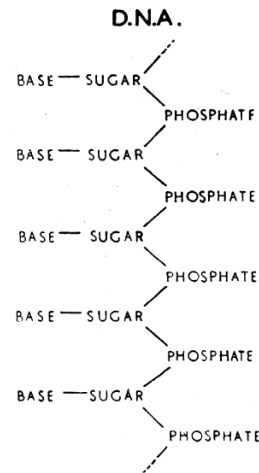


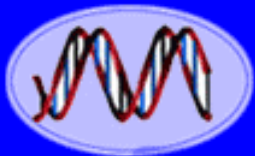
Fig. 1. Chemical formula of a single chain of deoxyribonucleic acid

Fig. 2. This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

Our model suggests possible explanations for a number of other phenomena. For example, spontaneous mutation may be due to a base occasionally occurring in one of its less likely tautomeric forms. Again, the pairing between homologous chromosomes at meiosis may depend on pairing between specific bases. We shall discuss these ideas in detail elsewhere.

For the moment, the general scheme we have proposed for the reproduction of deoxyribonucleic acid must be regarded as speculative. Even if it is correct, it is clear from what we have said that much remains to be discovered before the picture of genetic duplication can be described in detail. What are the polynucleotide precursors? What makes the pair of chains unwind and separate? What is the precise role of the protein? Is the chromosome one long pair of deoxyribonucleic acid chains, or does it consist of patches of the acid joined together by protein?

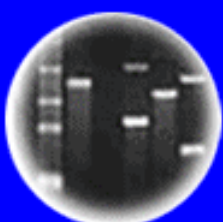
Despite these uncertainties we feel that our proposed structure for deoxyribonucleic acid may help to solve one of the fundamental biological problems—the molecular basis of the template needed for genetic replication. The hypothesis we are suggesting is that the template is the pattern of bases formed by one chain of the deoxyribonucleic acid and that the gene contains a complementary pair of such templates.



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DNA Fingerprinting



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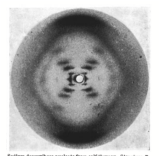
Plants of Tomorrow

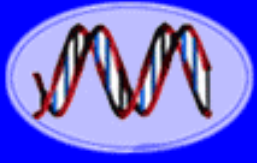
Molecular Structure of Deoxypentose Nucleic Acids

M. H. F. WILKINS
Medical Research Council Biophysics
Research Unit,
A. R. STOKES
H. R. WILSON
Wheatstone Physics Laboratory,
King's College, London. *Nature*, April 25, 1953
April 2.

Molecular Configuration in Sodium Thymonucleate

ROSALIND E. FRANKLIN*
R. G. GOSLING
Wheatstone Physics Laboratory,
King's College, London. *Nature*, April 25, 1953
April 2.

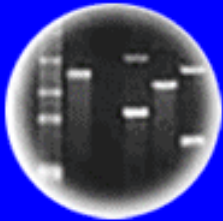




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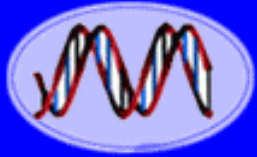


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If You Were on the Nobel Prize Committee,
Who Would Be Your Choice(s) For Being
Awarded the Nobel Prize For Discovering the
Structure of DNA?

- a. Watson
- b. Crick
- c. Wilkins
- d. Franklin
- e. Gosling
- f. Chargaff

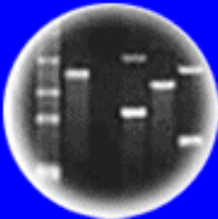
Note: Nobel Prize Rules Allow Only Three
People To Share a Prize



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of a Bacteria



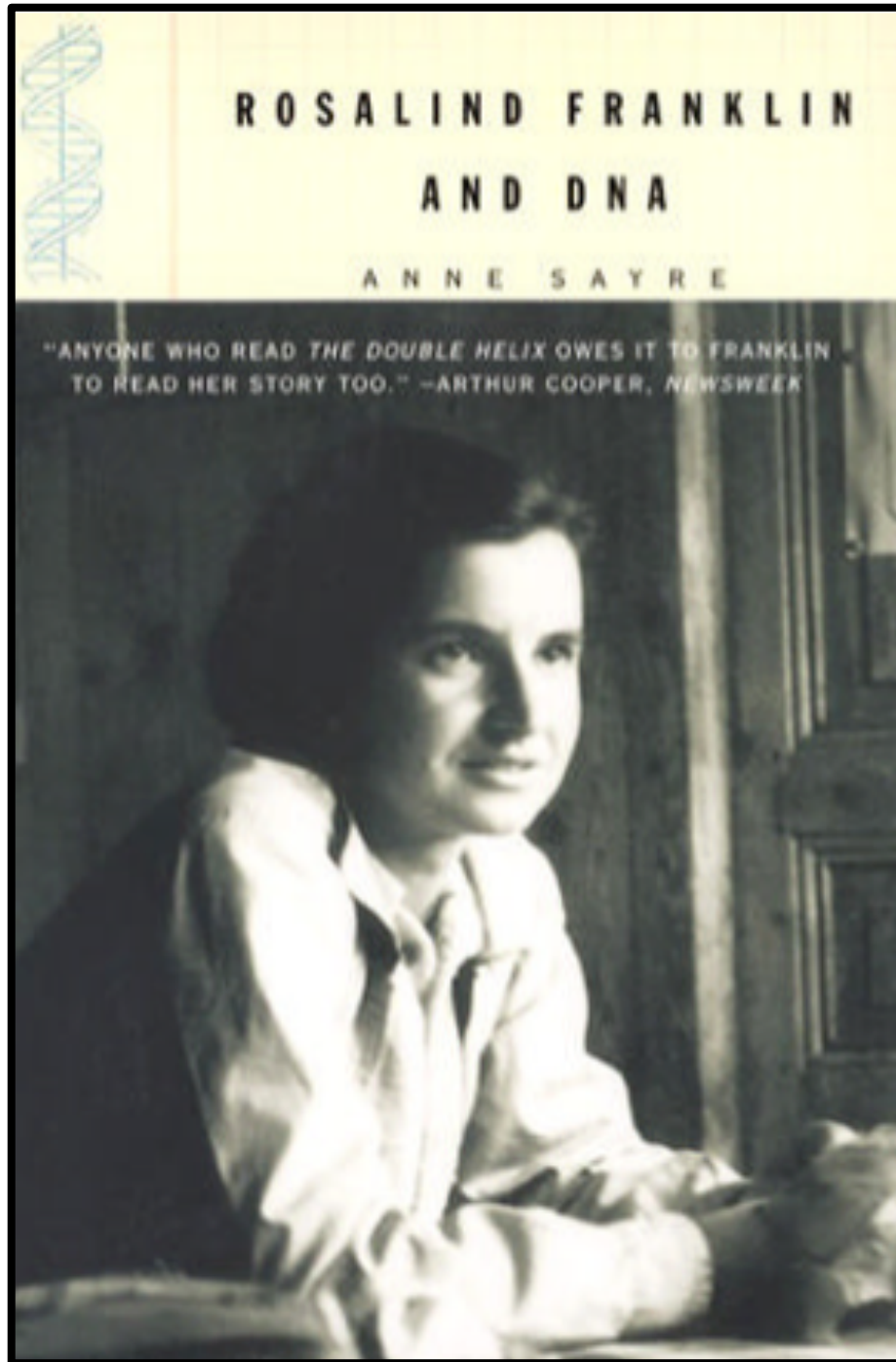
DNA Fingerprinting



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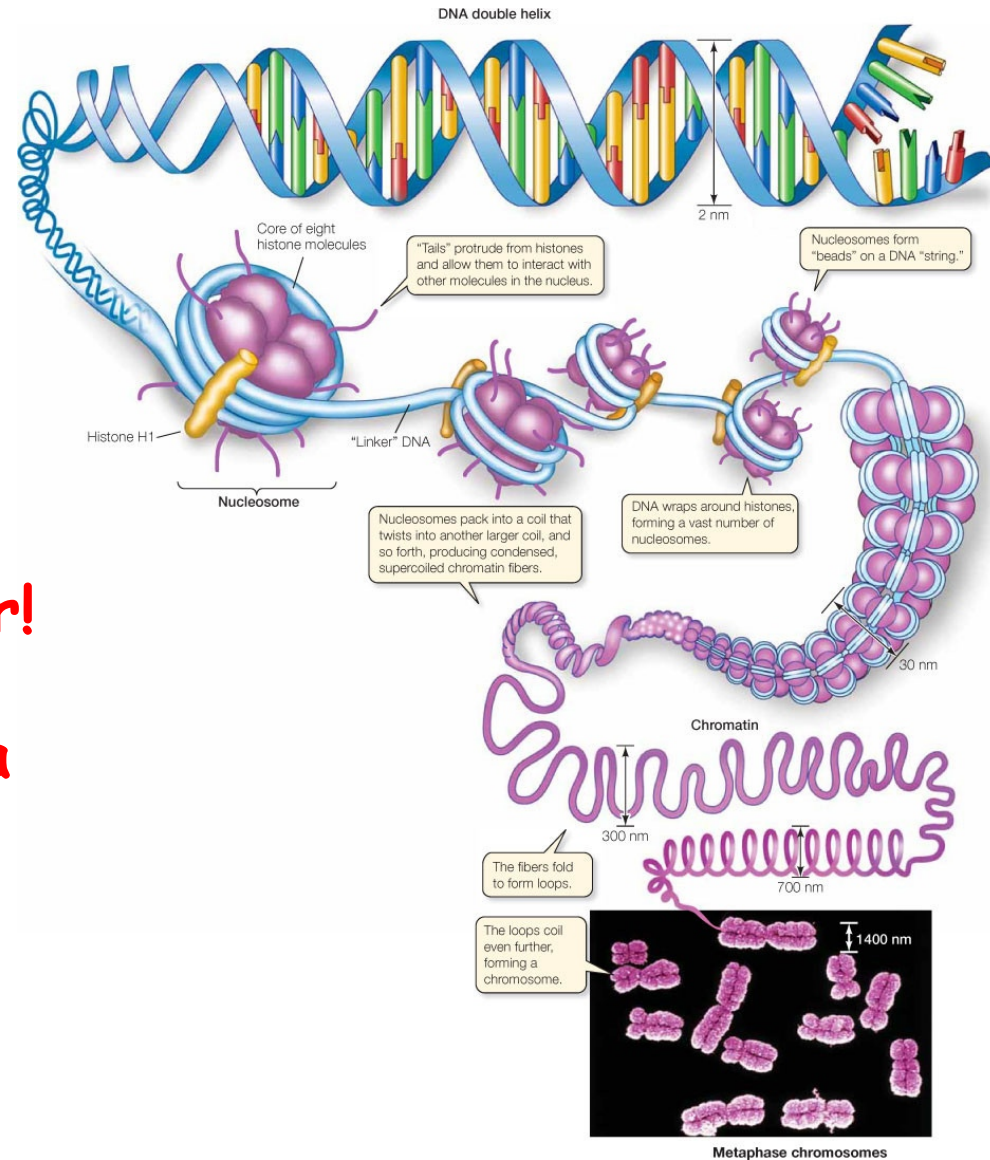
ROSALIND FRANKLIN
AND DNA

ANNE SAYRE

"ANYONE WHO READ *THE DOUBLE HELIX* OWES IT TO FRANKLIN
TO READ HER STORY TOO." —ARTHUR COOPER, *NEWSWEEK*

ISBN
3933-32044-8
1975

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

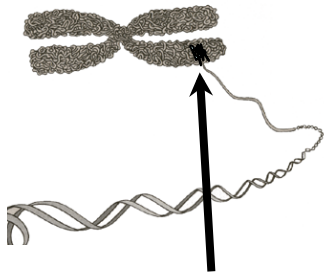


DNA in Human & Eukaryotic Chromosomes is Linear!

DNA in Most Bacteria is Circular!

A Chromosome Contains Many Genes Operating Independently

What is the Evidence?



Position of Genes
1, 2, & 3 in
chromosome

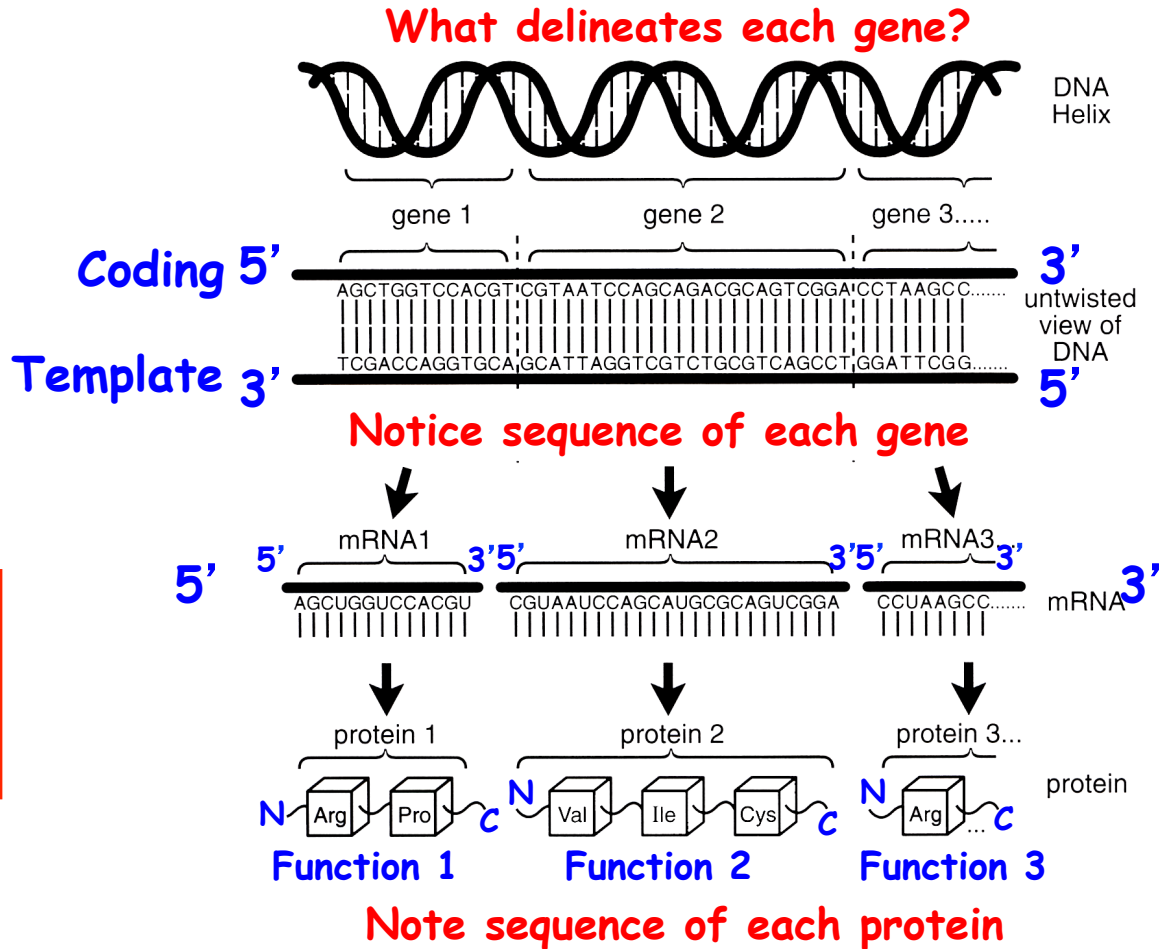
Discrete Units!

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

Central Dogma

∴ Genes → Functions in Cells
via Proteins

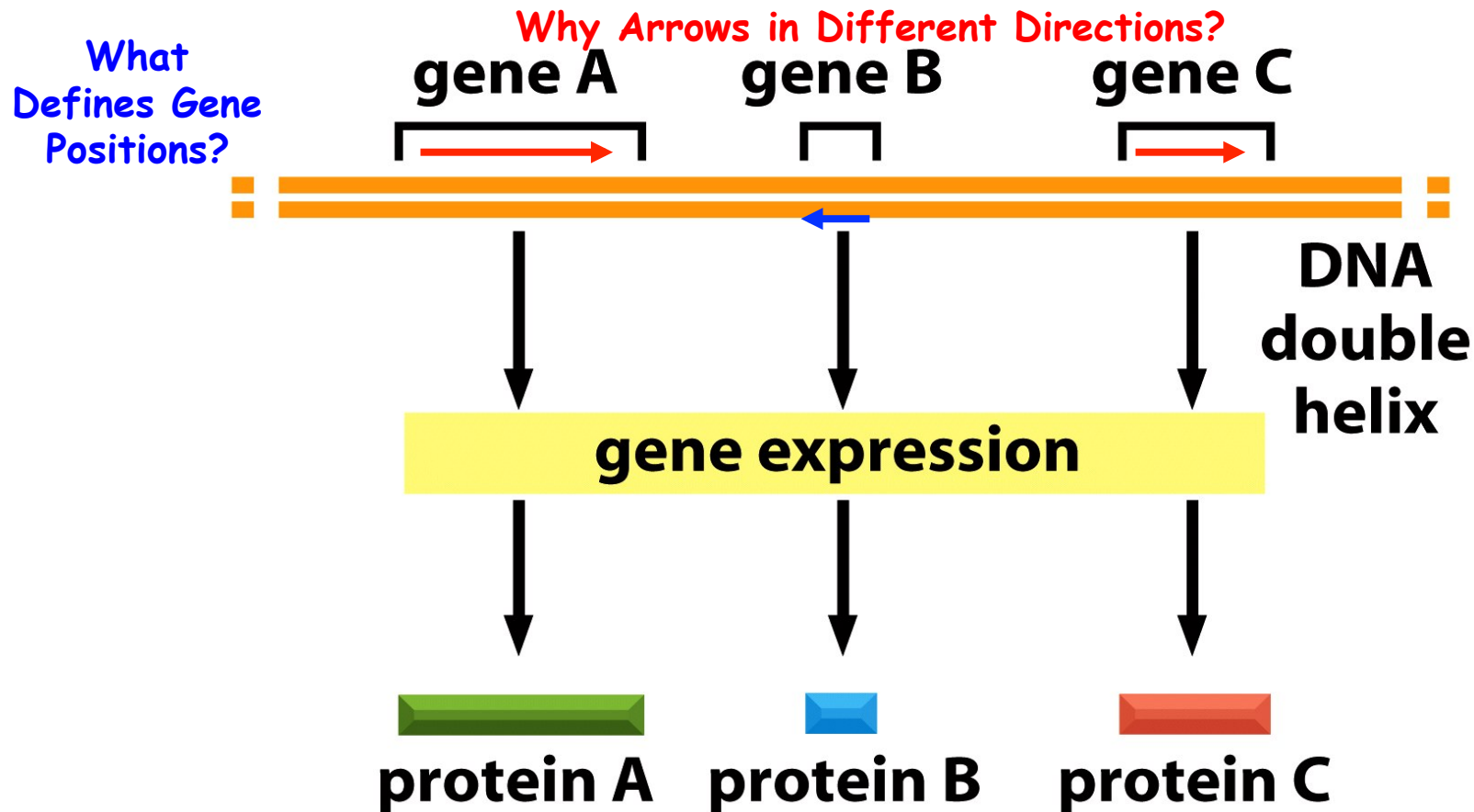
Cells duplicate & stay the same
→ DNA replication



VERY IMPORTANT CONCEPT!

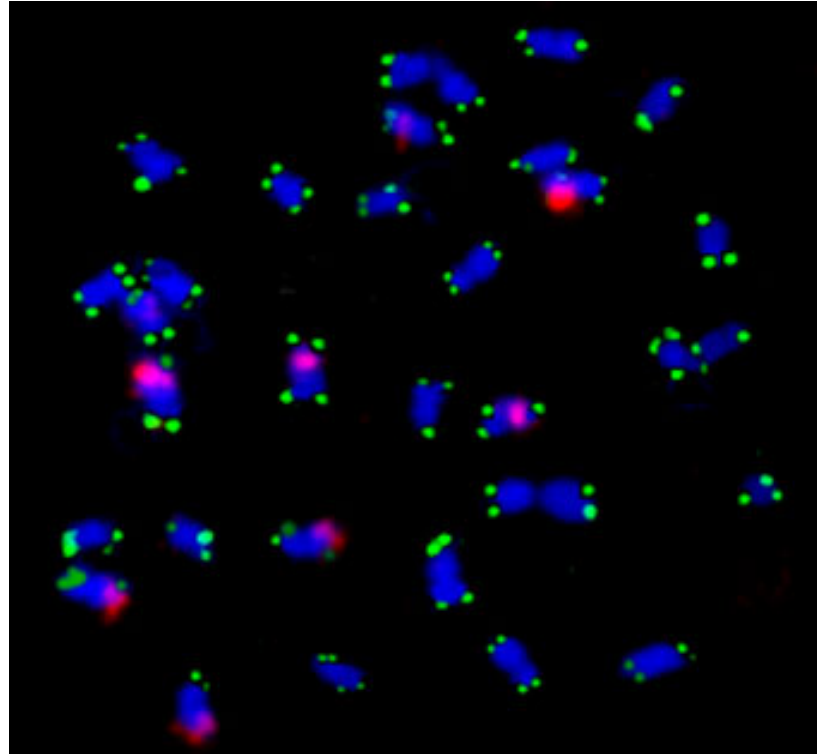
COLINEARITY BETWEEN GENE SEQUENCE AND PROTEIN SEQUENCE

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



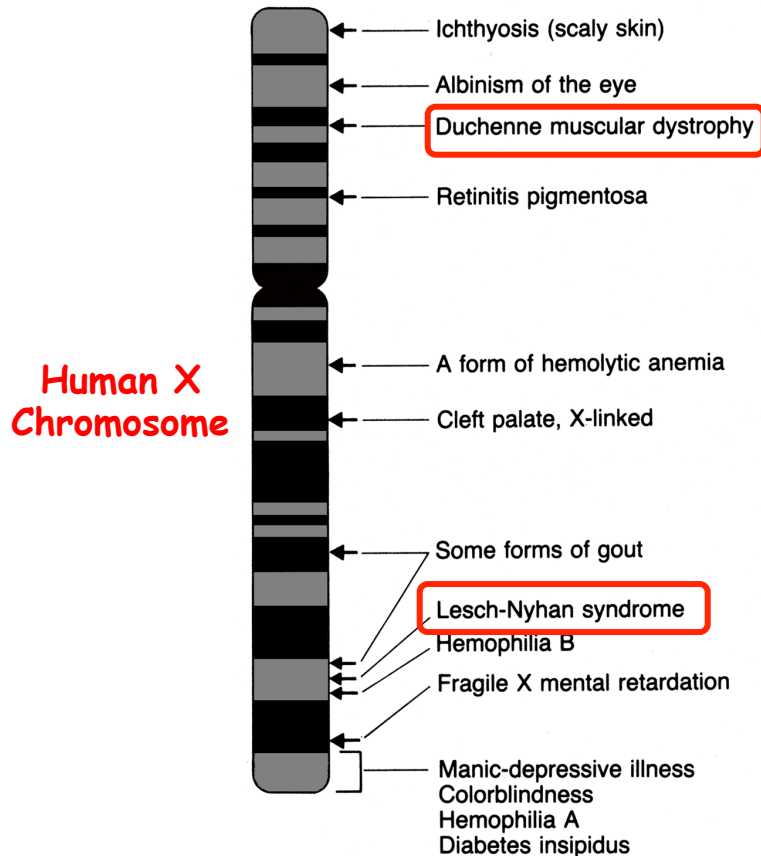
Because DNA Contains Two Strands--Genes Can Be Transcribed From Either Strand--But Only One Per Gene

Genes Reside at Specific Positions or **Loci**

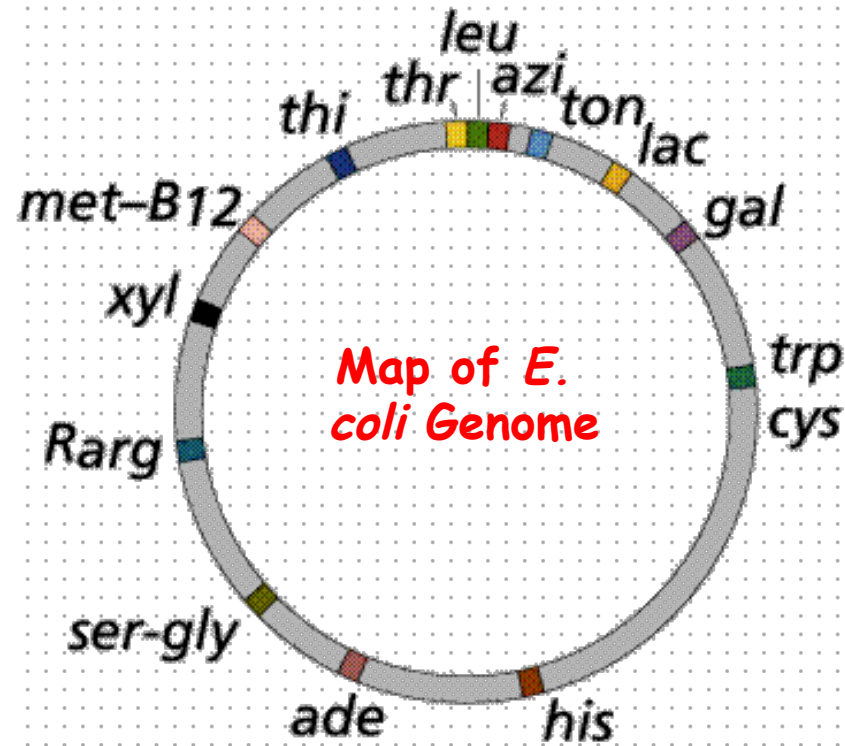


Gene Position = Locus = Unique DNA
Sequence

Genes Reside at Specific Locations That Can Be Mapped



Linear DNA
How Know?



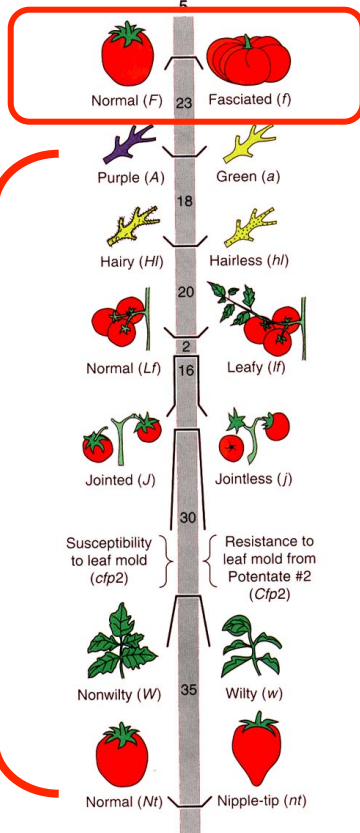
Circular DNA
How Know?

- Note **Marker Bands** - What are these? How are they useful?
- How Determine Gene Positions? Chromosome Number?

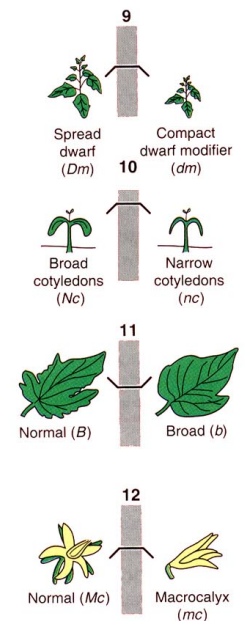
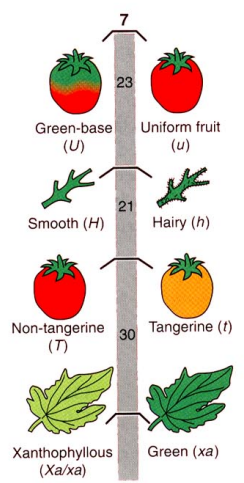
Alleles Reside at the Same Position on a Chromosome

Allele Phenotypes Specify Markers For Each Gene Location!

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!!!

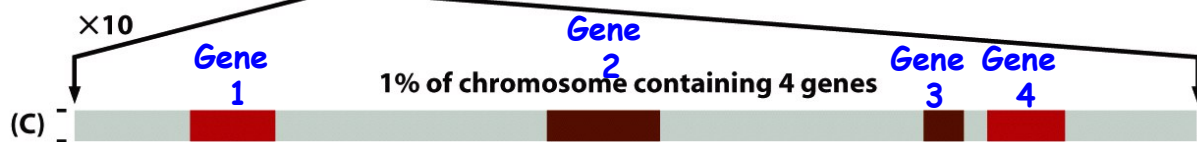
Alleles Are Different Forms of the Same Gene That Arise By Mutation & Can be Made in a Laboratory By Modern Genetic Engineering!

Organization of Genes on Human Chromosome 22

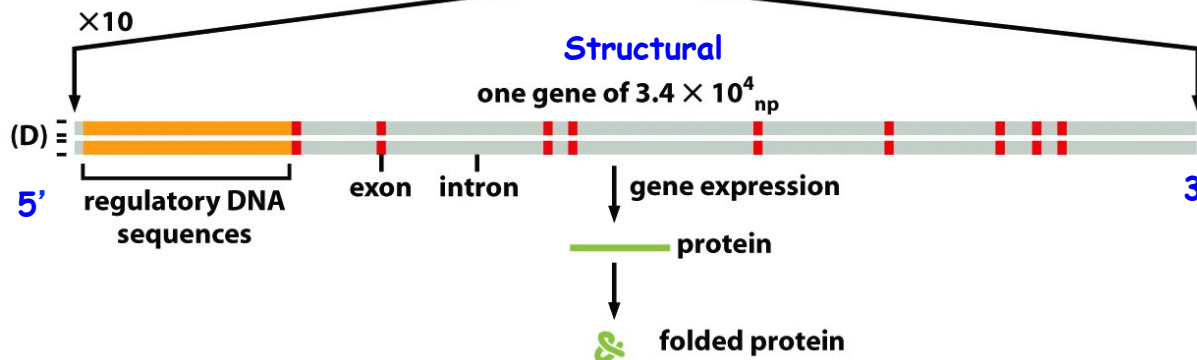
(A) human chromosome 22 in its mitotic conformation, composed of two DNA molecules, each 48×10^6 nucleotide pairs long



250 genes



Genes Are Defined/
Precise Regions of
DNA



One Large Gene!

Genes Act As Individual Units?
How Know? GloFish Experiment! Genetic Engineering Antibiotic^R

A Conceptualized Gene

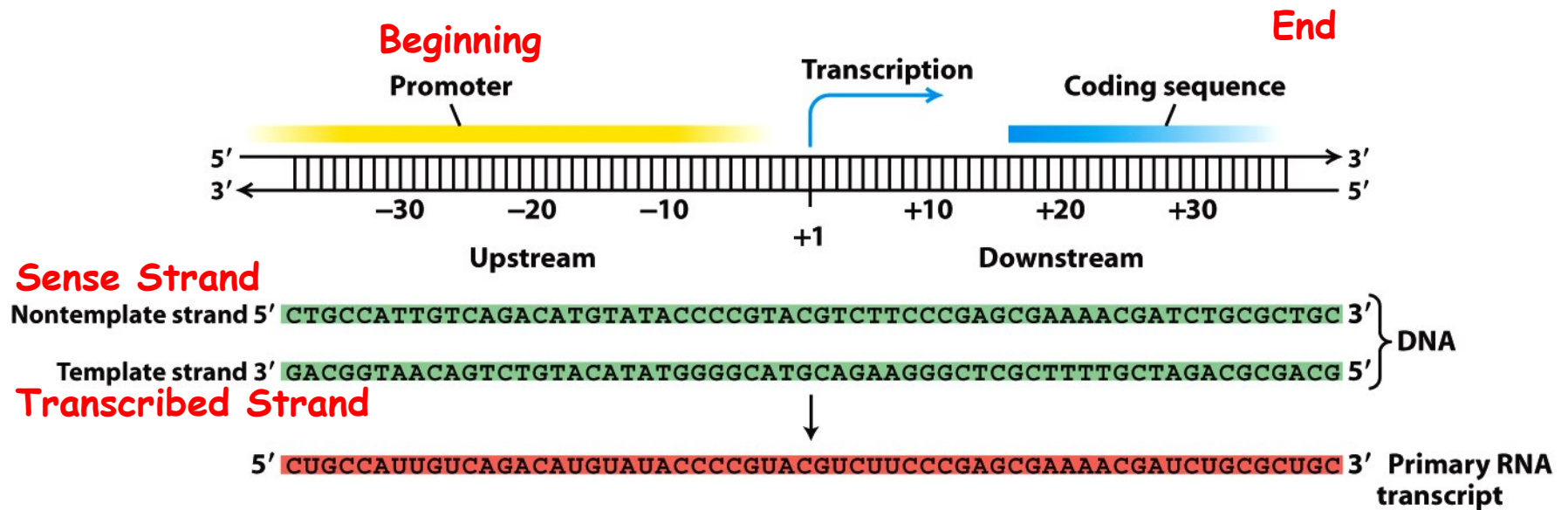
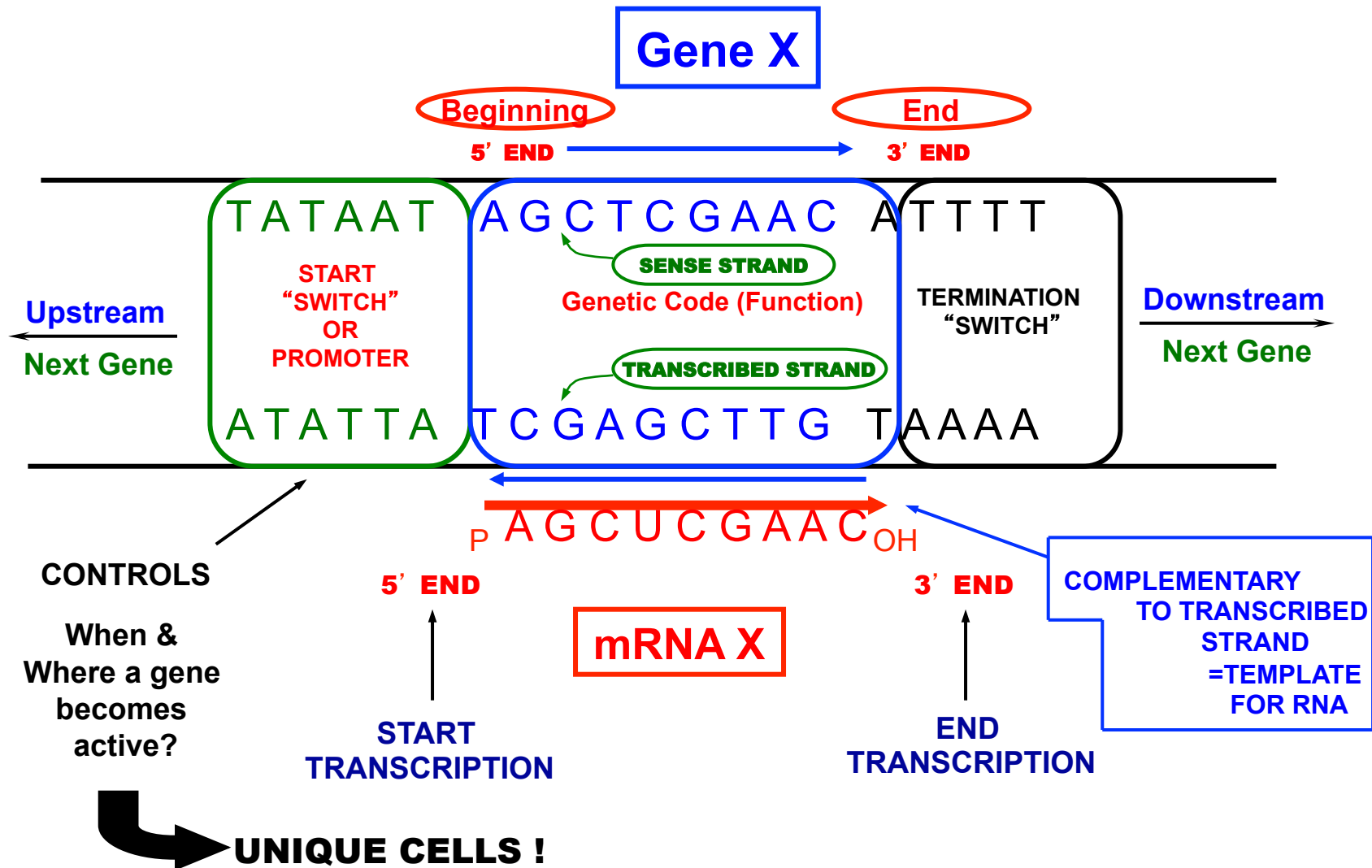


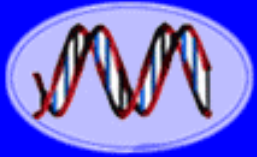
Figure 4-10b
Molecular Cell Biology, Sixth Edition
 © 2008 W. H. Freeman and Company

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

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



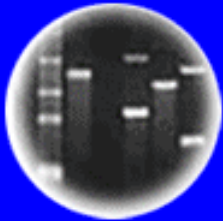
Note: mRNA Sequence = Sense Strand Sequence



DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



Cloning: Ethical Issues
and Future Consequences



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A “Simple” Gene Reviewed

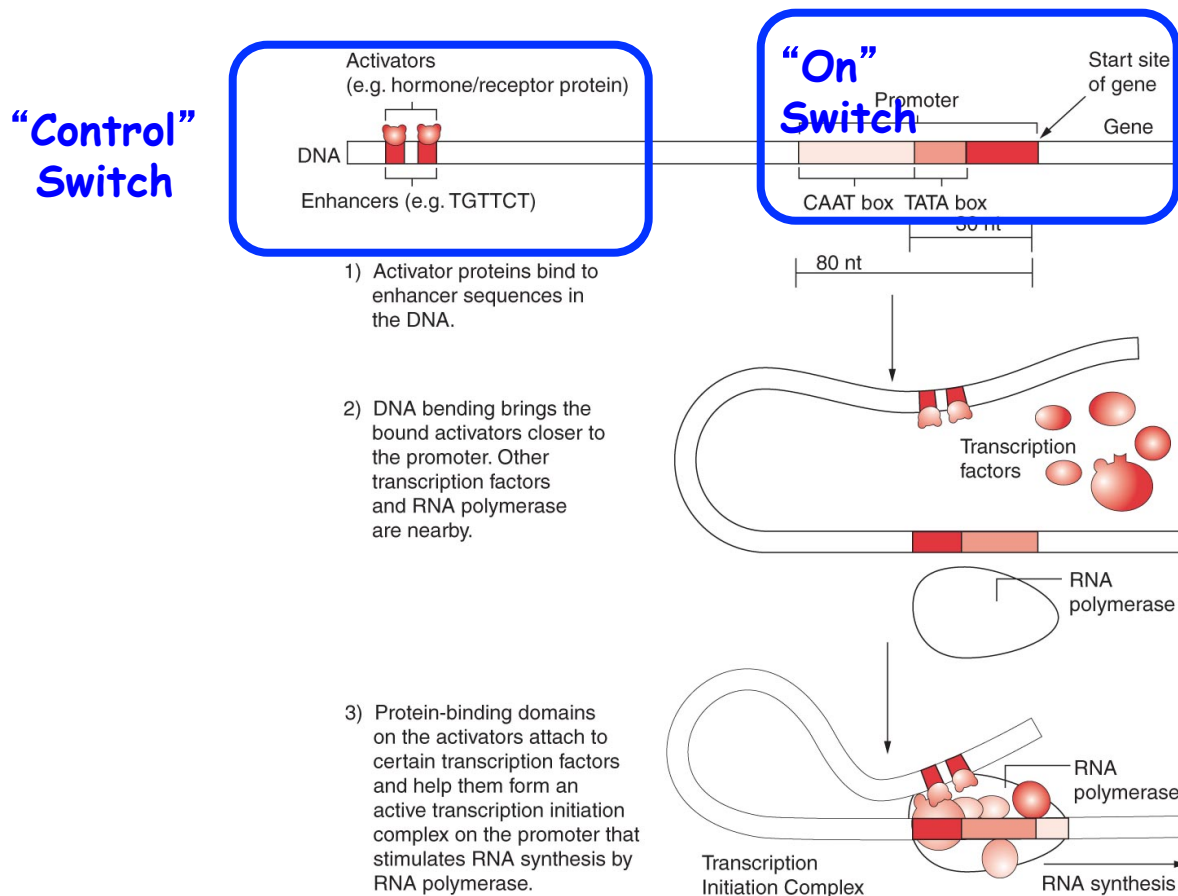
1. Sense Strand = Genetic Code
2. Sense Strand = 5' → 3' Direction (all DNA sequences specified 5' → 3')
3. AntiSense Strand = Complement of Sense Strand & is Transcribed Strand
4. mRNA = Same Sequence As Sense Strand & Complementary to AntiSense Strand
5. mRNA = 5' → 3'
6. Switch Turns Gene On - Not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

Genes Function As Independent Units! How Know? Design Experiment to Show!

“Everything” Follows the Double Helix & Its Rules - Anti-parallel Chains & Complementary Base Pairing!

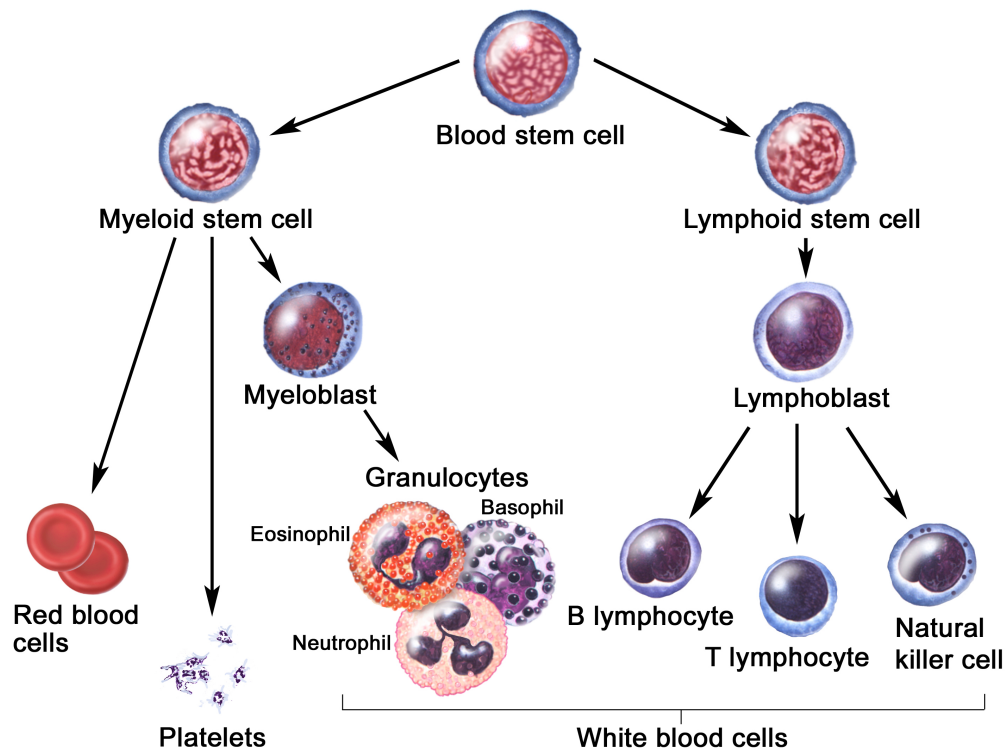
Control Switches Are Unique DNA Sequences & Can Be Cloned

**AND used to Re-Engineer Organisms!!
Switches Act Independently of Gene!!**

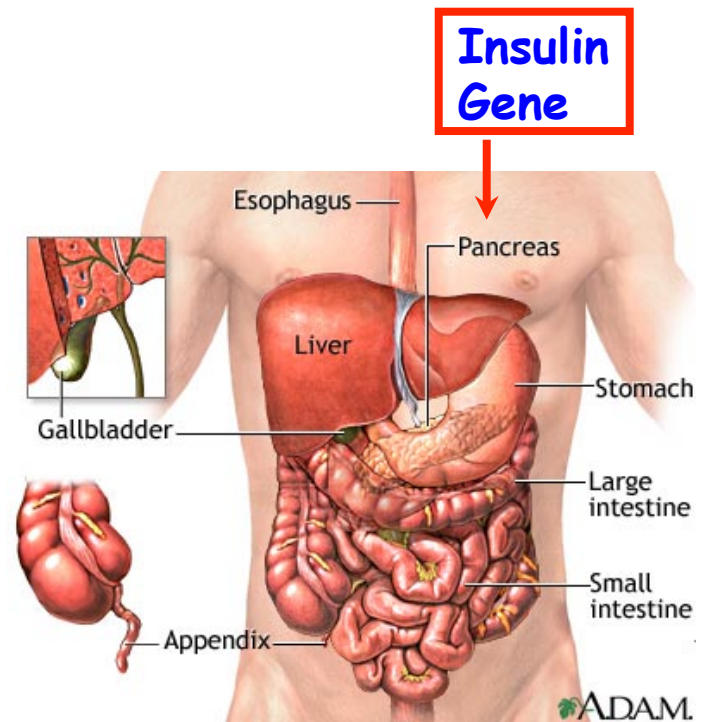


1. Each Switch Has a Unique DNA Sequence
2. Genome Projects Reveal Genes & Logic Controlled by the Switches
3. Sequence = Biology
4. No Hocus Pocus
5. Yo! It's in the DNA!!

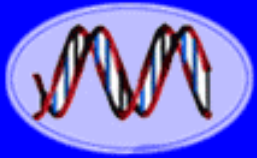
Switches Control Where & When A Gene Is Active → Unique Functions → Unique Cells



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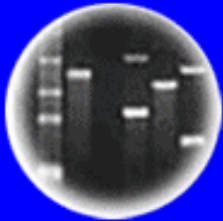
ADAM



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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

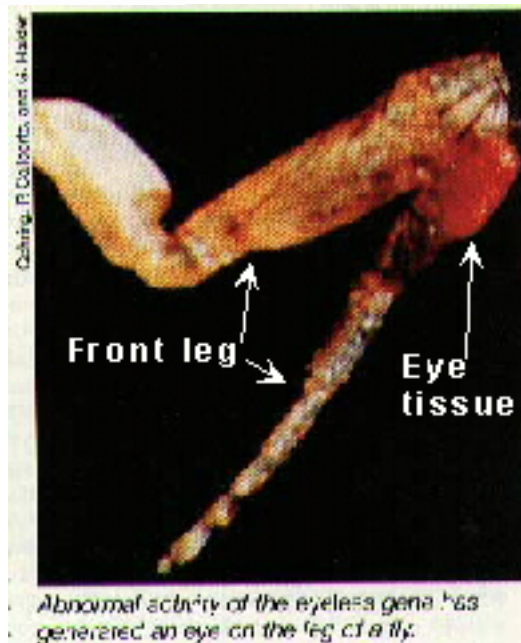
Eye Gene



Replace the Head Switch With the Leg Switch by Genetic Engineering

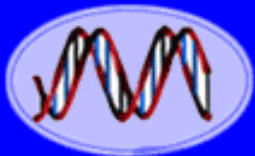
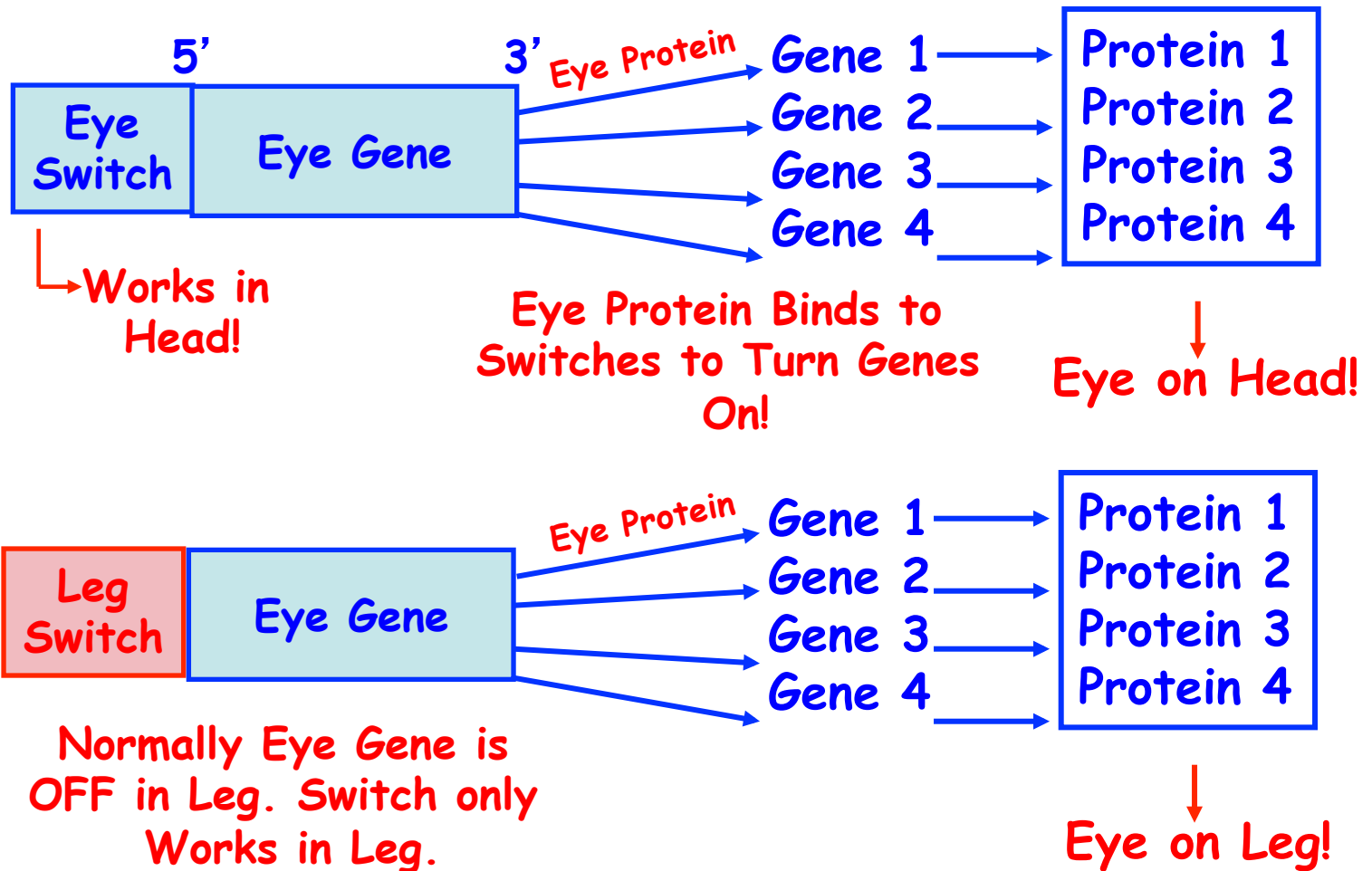


Eye Gene
+
Leg Switch



Eye Regulatory Network

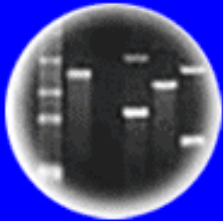
Control Genes Like The Eye Gene Control The Activity of Other Genes!



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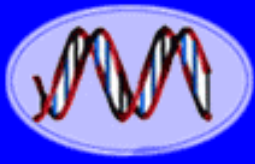
DNA Fingerprinting



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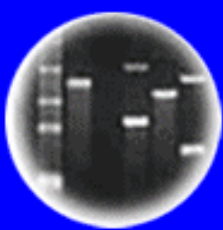
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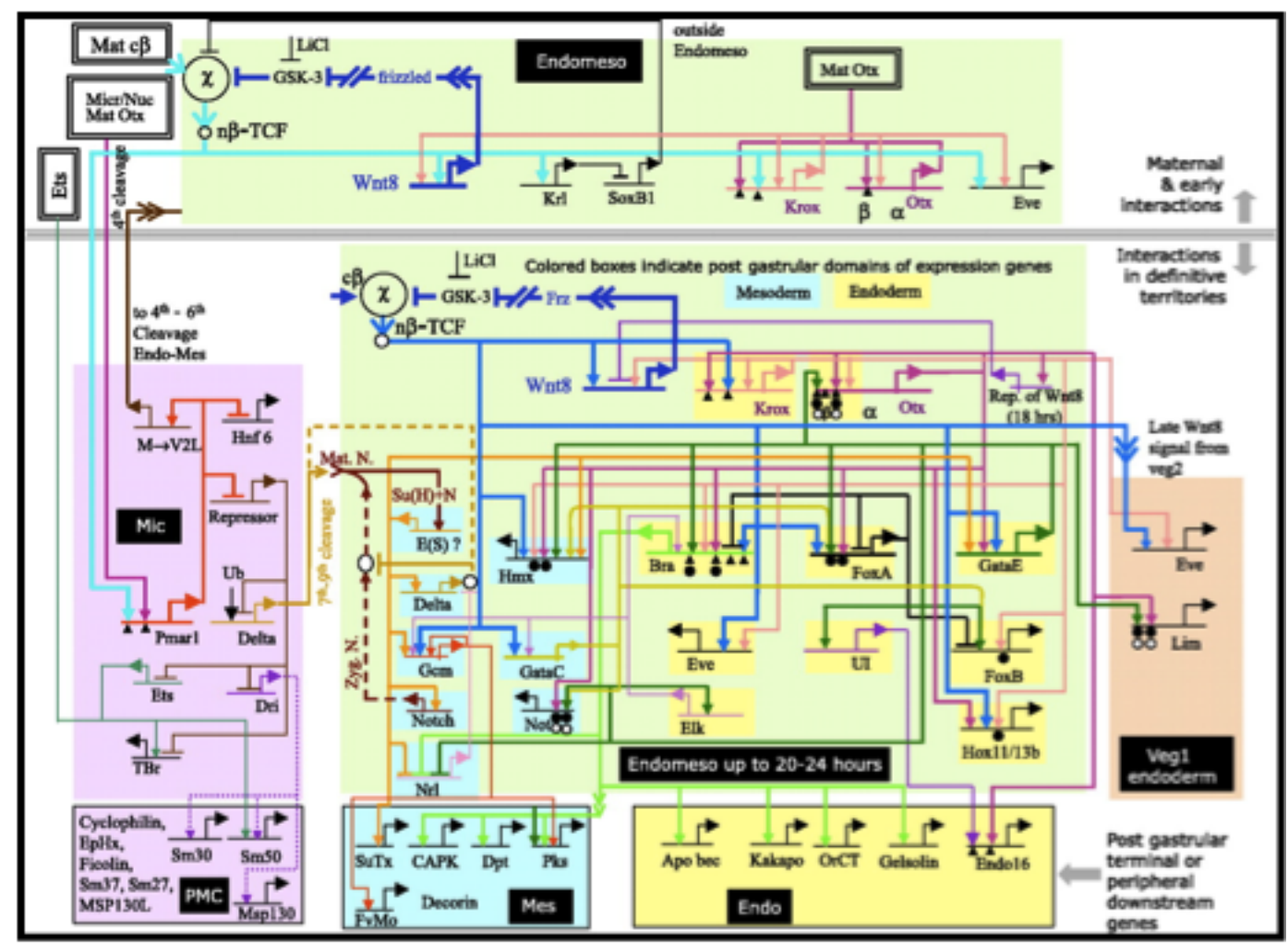


Cloning: Ethical Issues
and Future Consequences

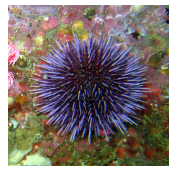
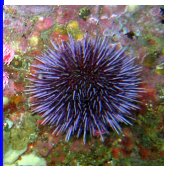


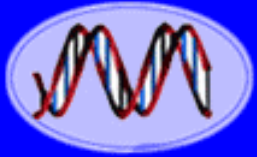
Plants of Tomorrow

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



Genetic Networks Programming Early Sea Urchin Development

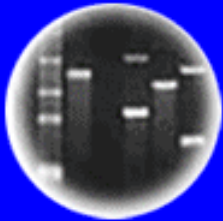




DNA
Genetic Code of Life



Entire Genetic Code
of a Bacteria



DNA Fingerprinting



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Plants of Tomorrow

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!