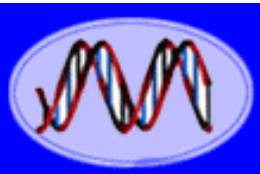
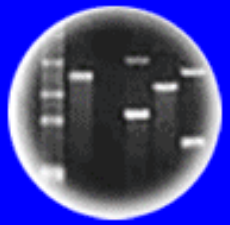


DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

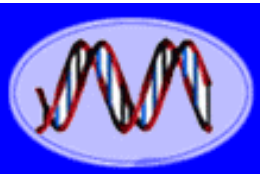
HC70A & SAS70A Winter 2011
Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg & John Harada

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

UCLA

UCDAVIS
UNIVERSITY OF CALIFORNIA



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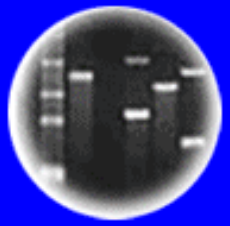

DNA Fingerprinting

Cloning: Ethical Issues
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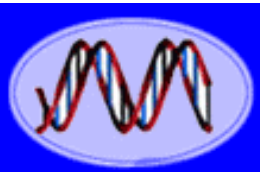
THEMES

1. What is the Function of a Gene-Review?
2. How Are Genes Regulated - Switched On & Off?
3. How Does DNA Replication Occur?
4. What is the Polymerase Chain Reaction (PCR) and How is PCR used?
5. How Do Mutations Occur?
6. How Can Pedigrees Be Used To Follow the Inheritance of Mutant Genes?
7. How Do Mutations Change Phenotypes?
8. What is the Colinearity Between Genes & Proteins (how does DNA→protein)?
9. What Is the Genetic Code?
10. How Do Gene Expression Processes Differ in Eukaryotes & Prokaryotes?
11. How Can Splicing Cause One Gene To Specify Several Different Proteins?
12. Yo!-It's in the DNA Sequences- What Are the Implications For Genetic Engineering?



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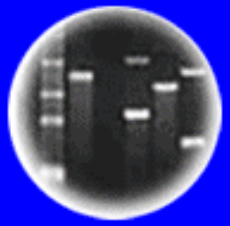

DNA Fingerprinting

Cloning: Ethical Issues
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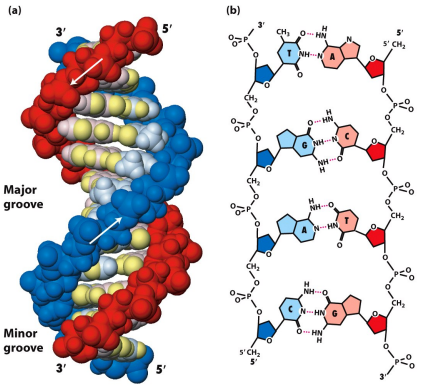
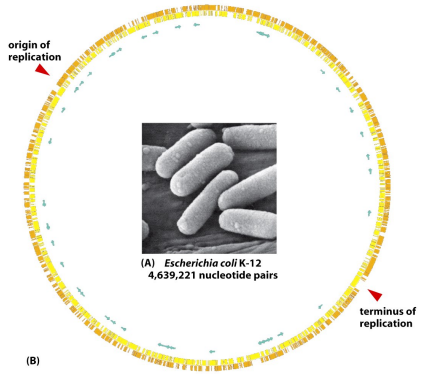
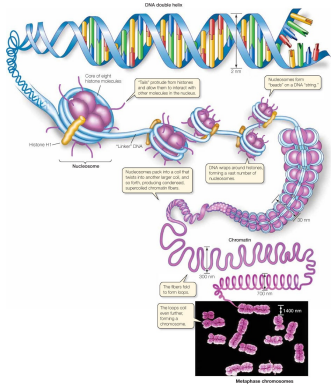
Last Tuesday's Lecture: What Are Genes & How Do They Function - Part One

1. What Are the Functions of Genes?
2. What Is Gene & Genetic Diversity
3. What is the Evidence For DNA Being the Genetic Material
   a) Griffith & Avery et al. Experiments
   b) Modern Genetic Engineering Experiments
4. Structure of DNA
5. Genes & Chromosomes in Prokaryotes & Eukaryotes
6. What is the Anatomy of a Simple Gene?







A Conceptualized Gene

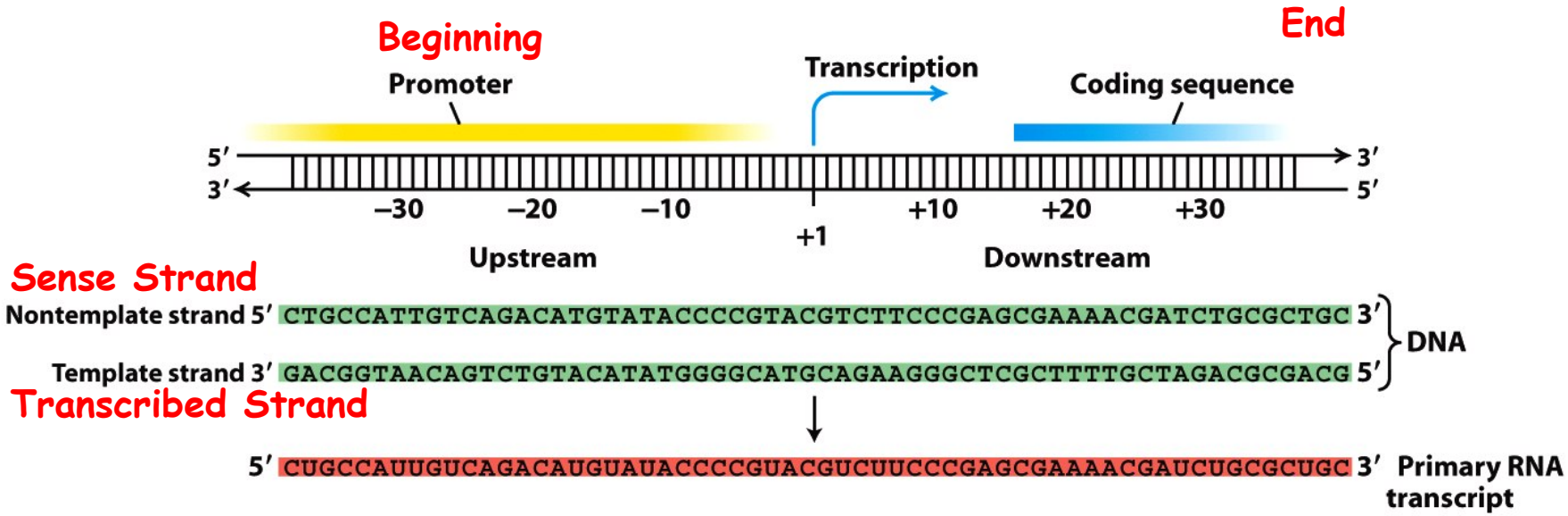
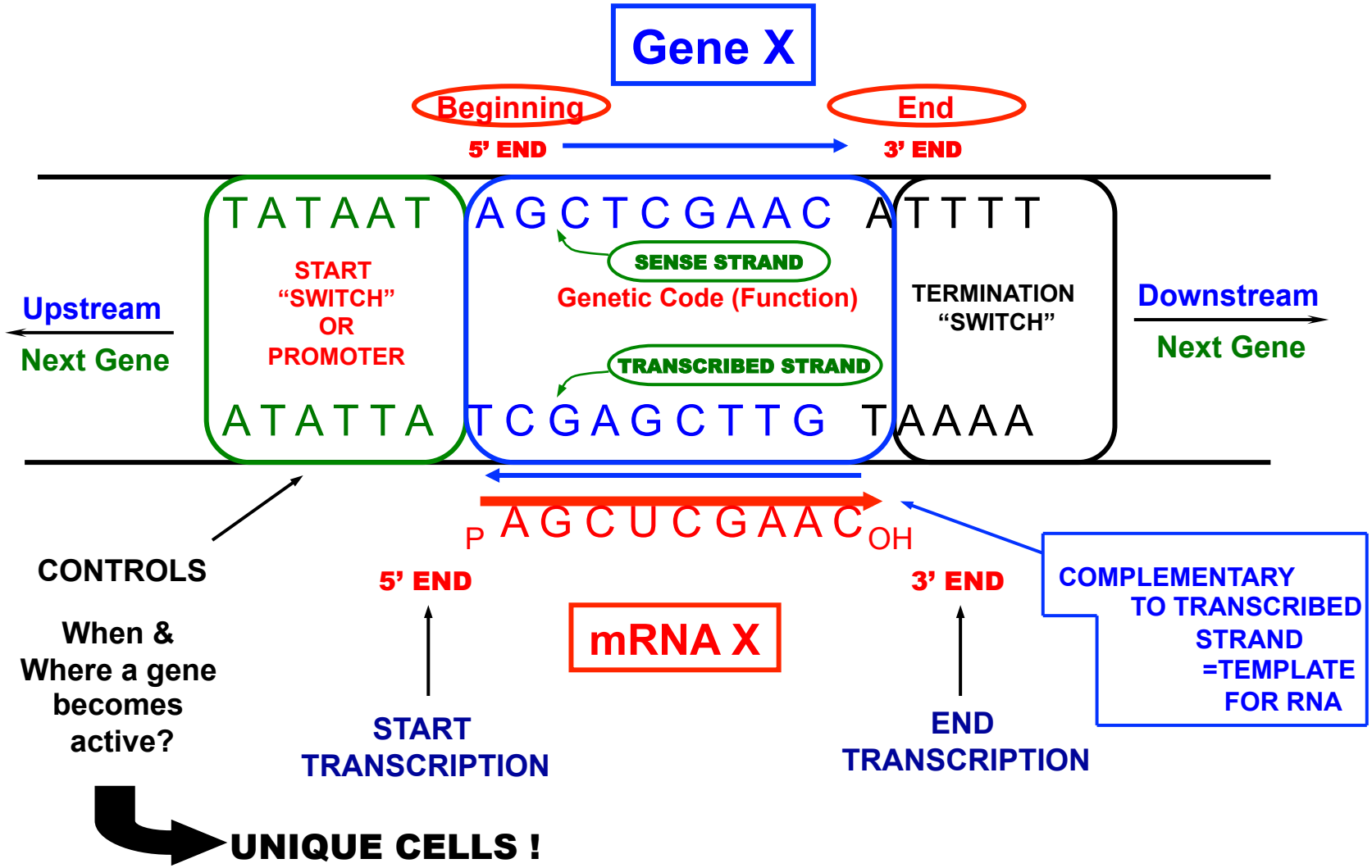
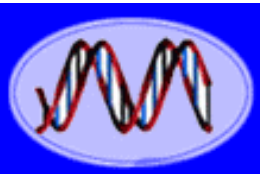


Figure 4-10b
Molecular Cell Biology, Sixth Edition

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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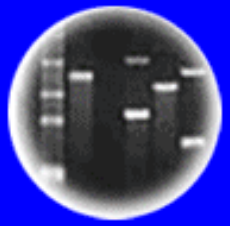

DNA Fingerprinting

Cloning: Ethical Issues
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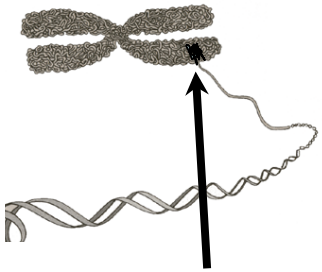
A "Simple" Gene Reviewed

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 That Work As Individual Units

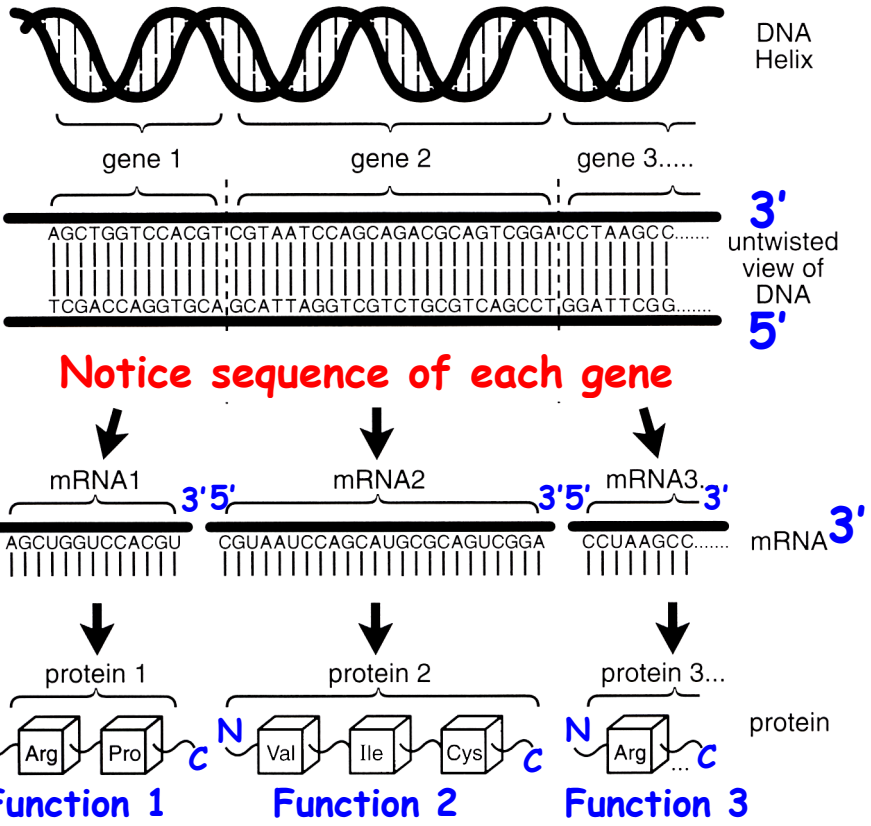


Position of Genes 1, 2, & 3 in chromosome

Discrete Units!

Evidence?

What delineates each gene?



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

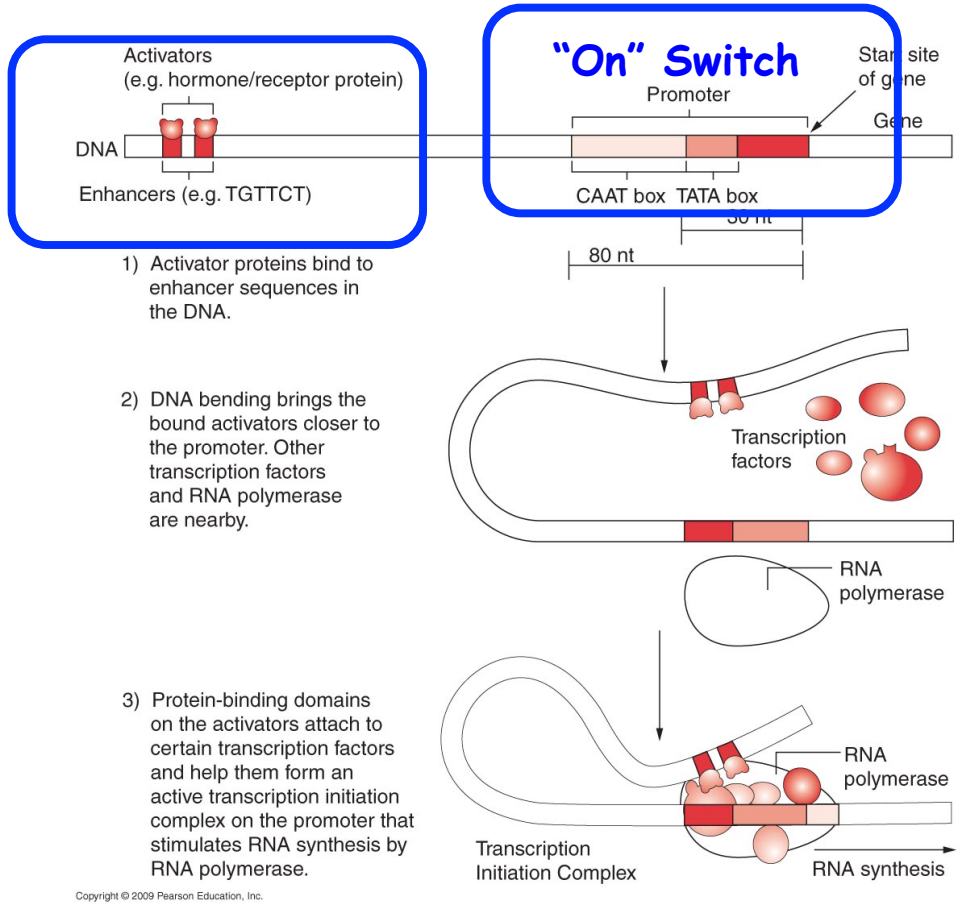
Central Dogma
∴Genes -> Functions in Cells via Proteins
Cells duplicate & stay the same -> DNA replication

VERY IMPORTANT CONCEPT!
<u>COLINEARITY</u> 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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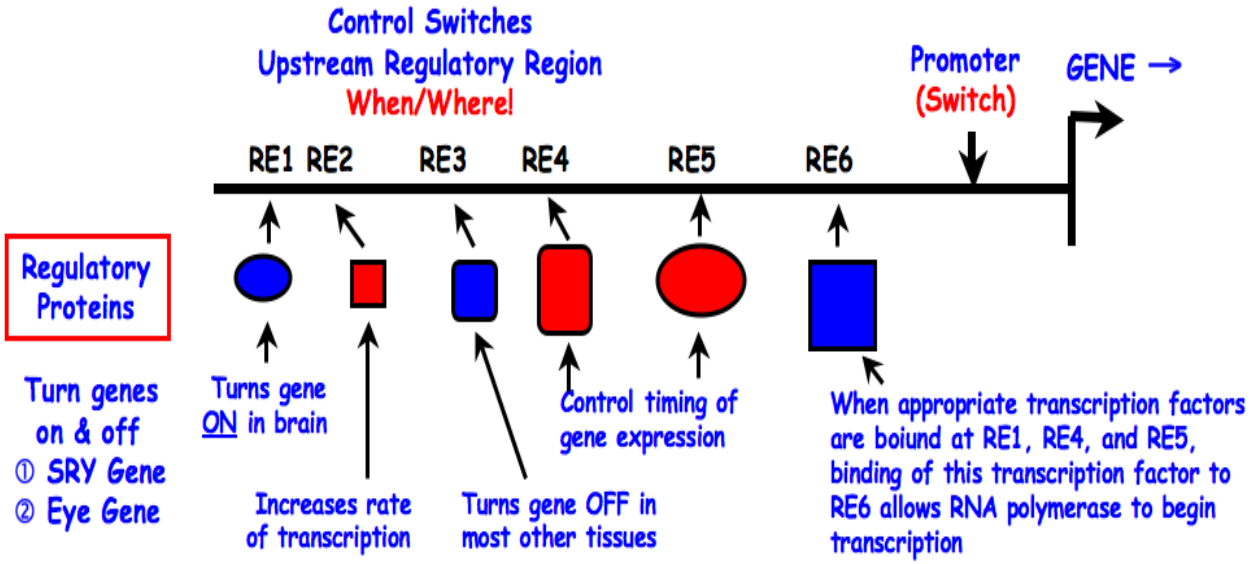


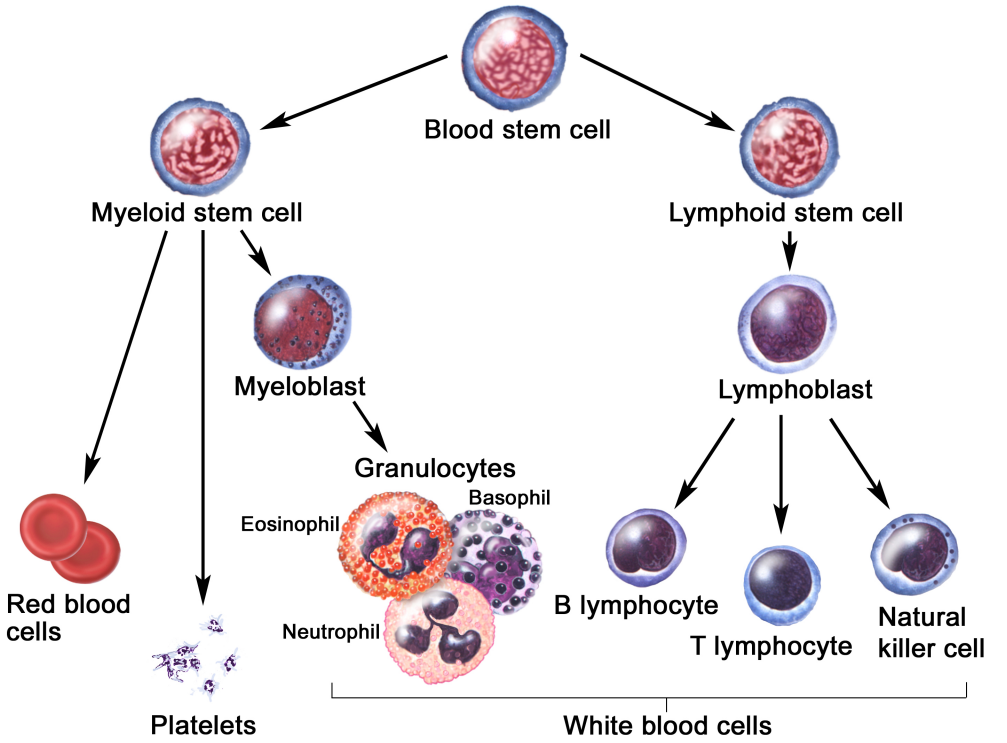
Genome Projects Reveal Both the Genes & the Logic that Controls them!

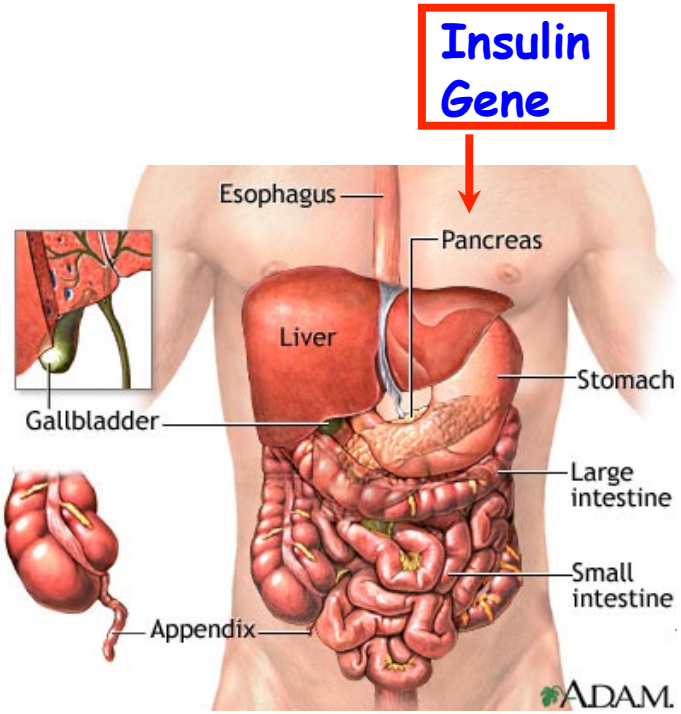
Each Switch = Unique DNA Sequence

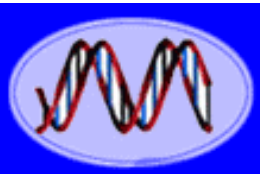
RULE: Sequence → Biology!!

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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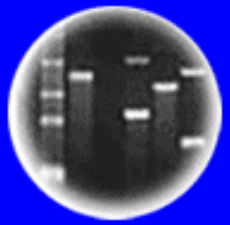

DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

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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

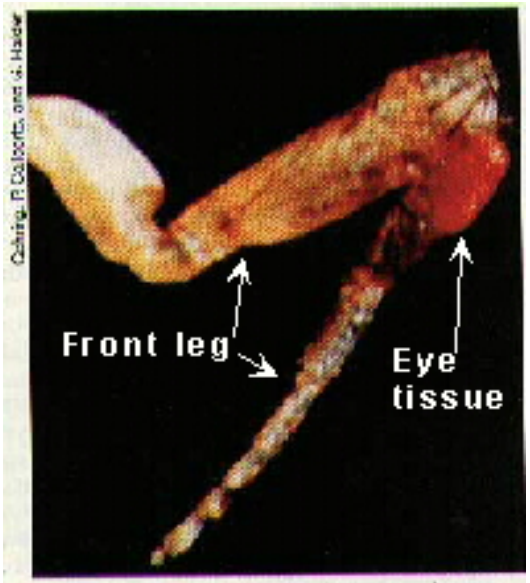
Yo! It's in the Sequences!!

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

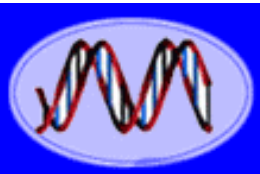
Eye Gene

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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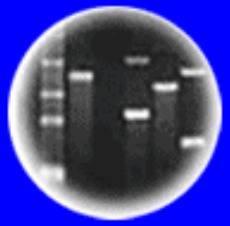

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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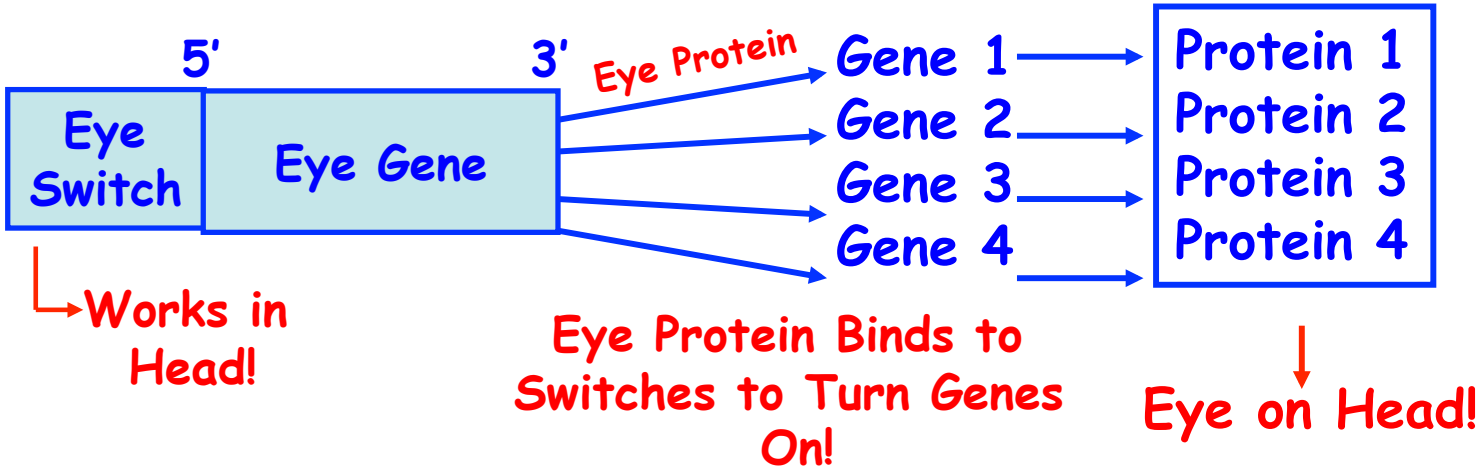
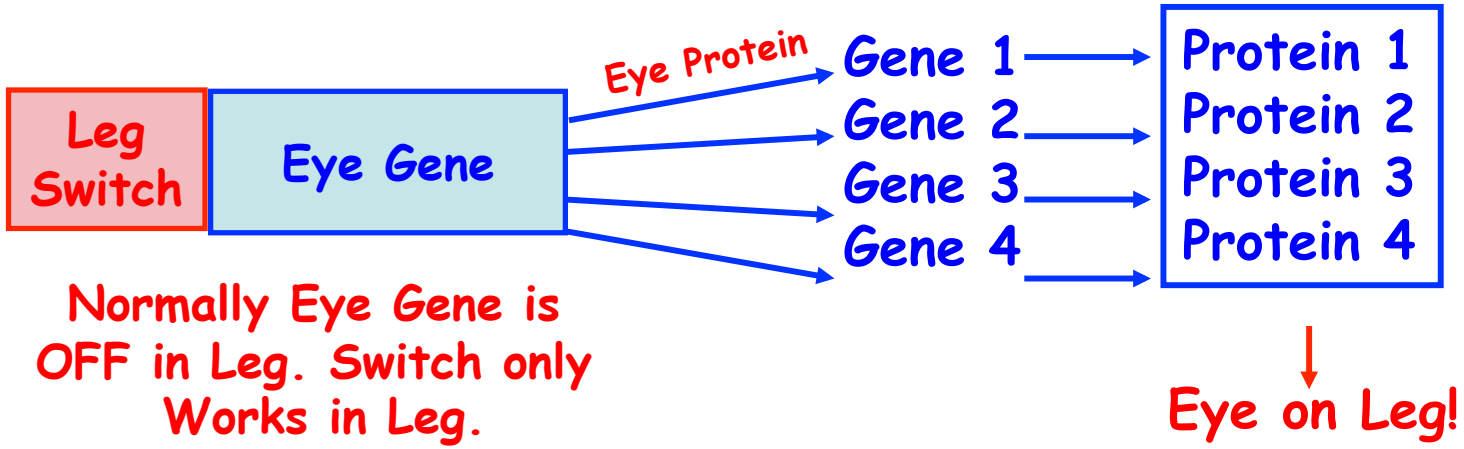
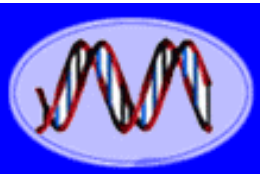
Eye Regulatory Network

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







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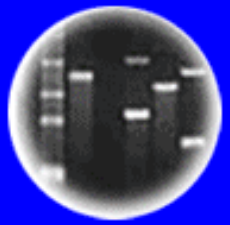

DNA Fingerprinting

Cloning: Ethical Issues
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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?

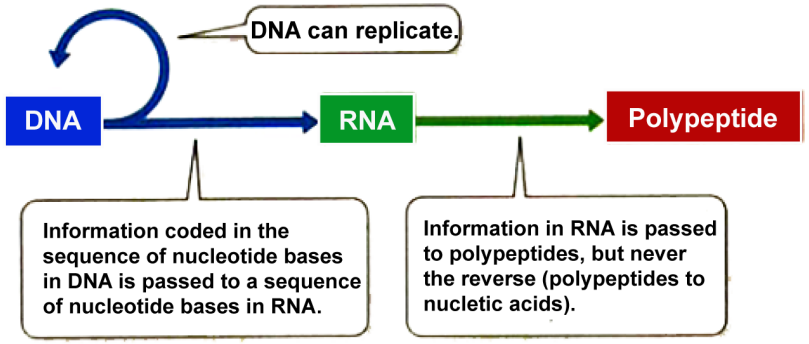
We Will Know at the DNA Level What Biological Information Programs Life to Death!

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!

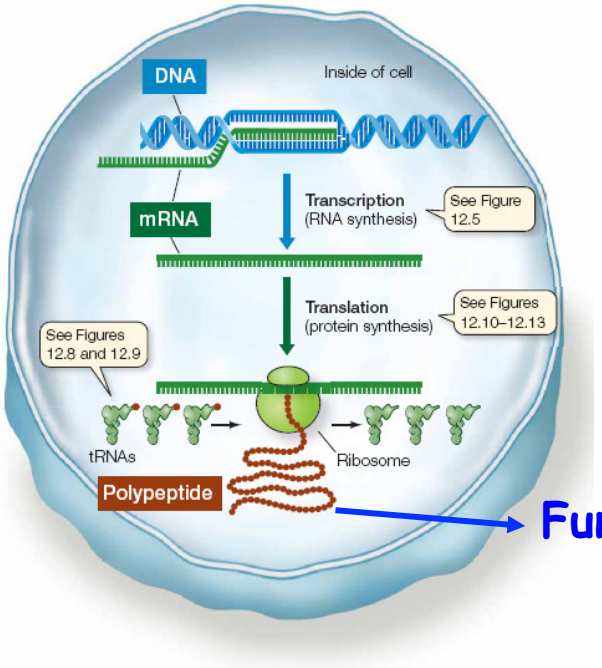
How Do Genes Work-A Review

① Replication



② Gene Activity to Function & Phenotype

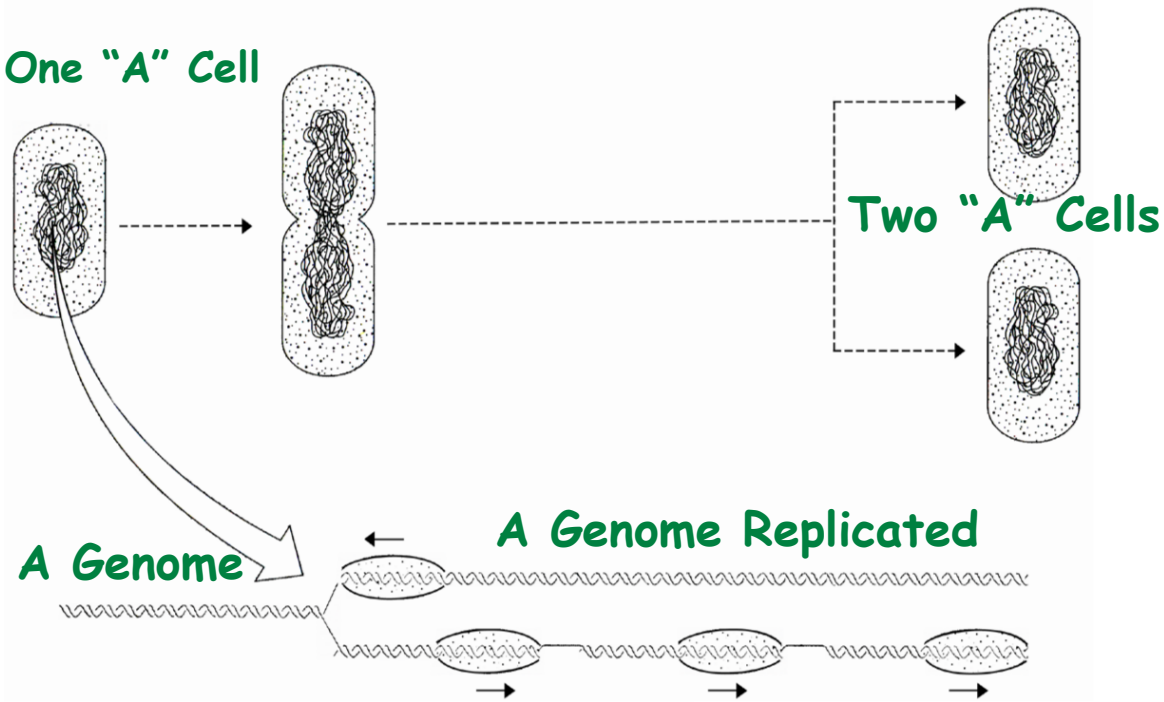
Gene Activity → Protein → Function → Phenotype (Trait)



Function →

A Gene is NOT Expressed Unless A Functional Protein Produced!

How Are Genes Replicated Each Cell Generation?

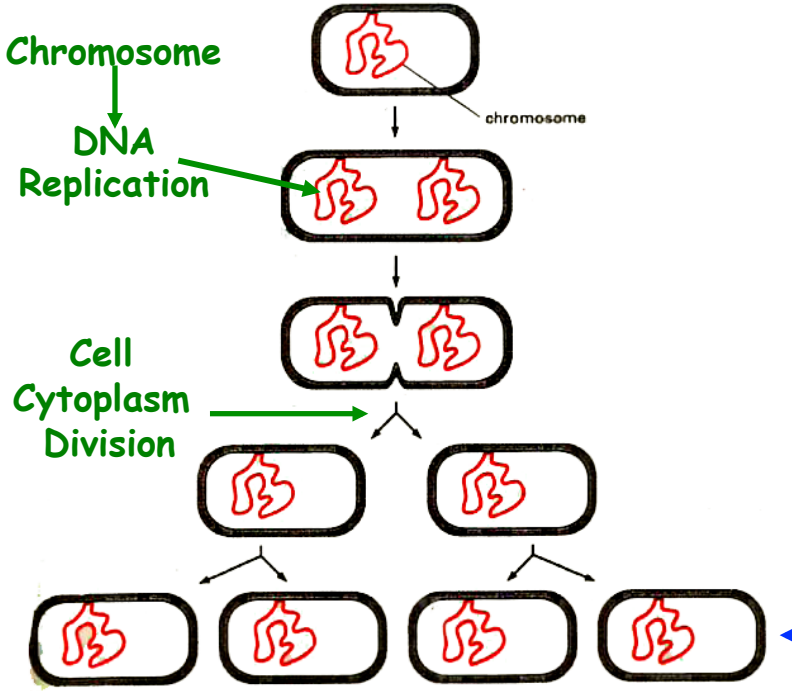


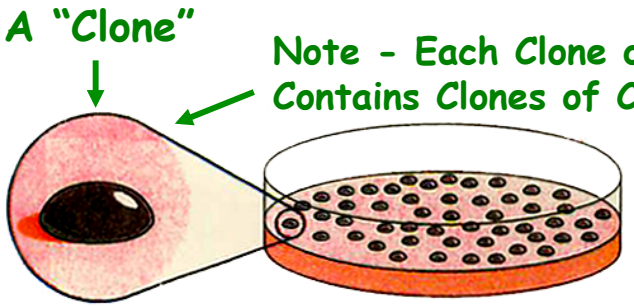
How is The DNA Sequence Copied/ Replicated Each Cell Division?

Pass on Genes to Next Generation Precisely?

BASIC OF LIFE!

Genes Are Replicated During Each Cell Division





Clones

A Bacterial Colony Contains Many Copies of Same Cell, or Clones, Which are Genetically Identical!

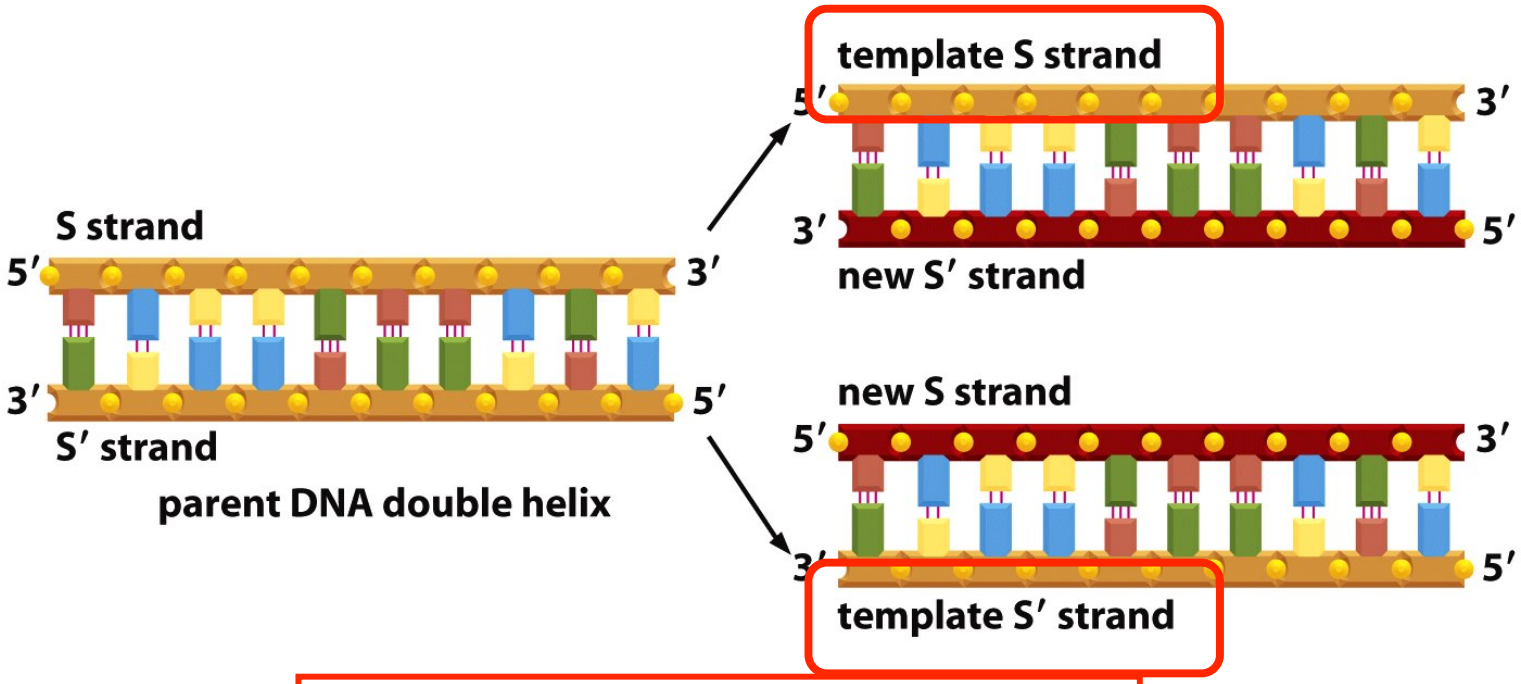
Each Daughter Cell Contains The Same Collection of Genes

Clones!

Major Properties of Genetic Material

Replication & Stability

The Sequence of Each DNA Strand Must Be Maintained Division After Division

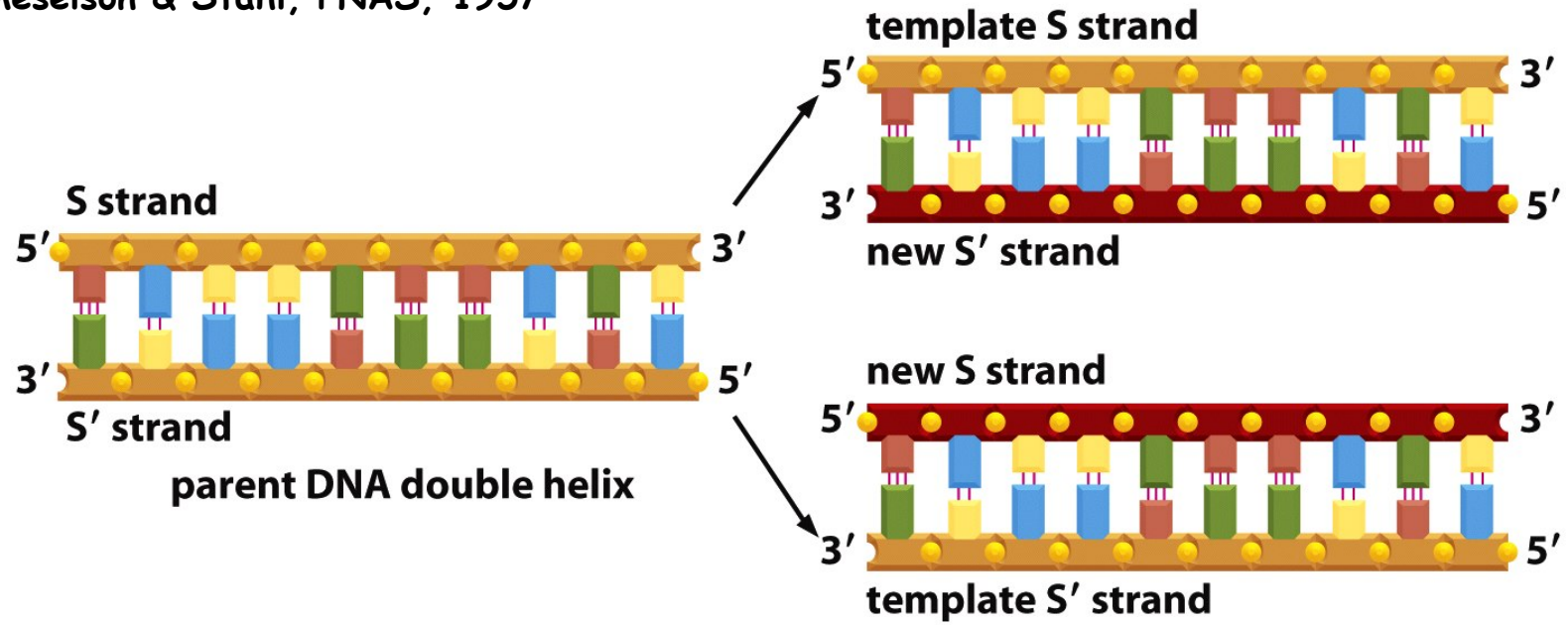


How Does This Occur?
Property of The DNA Molecule

Note → SEQUENCE & POLARITY

DNA Replication Occurs Semi-Conservatively

Meselson & Stahl, PNAS, 1957



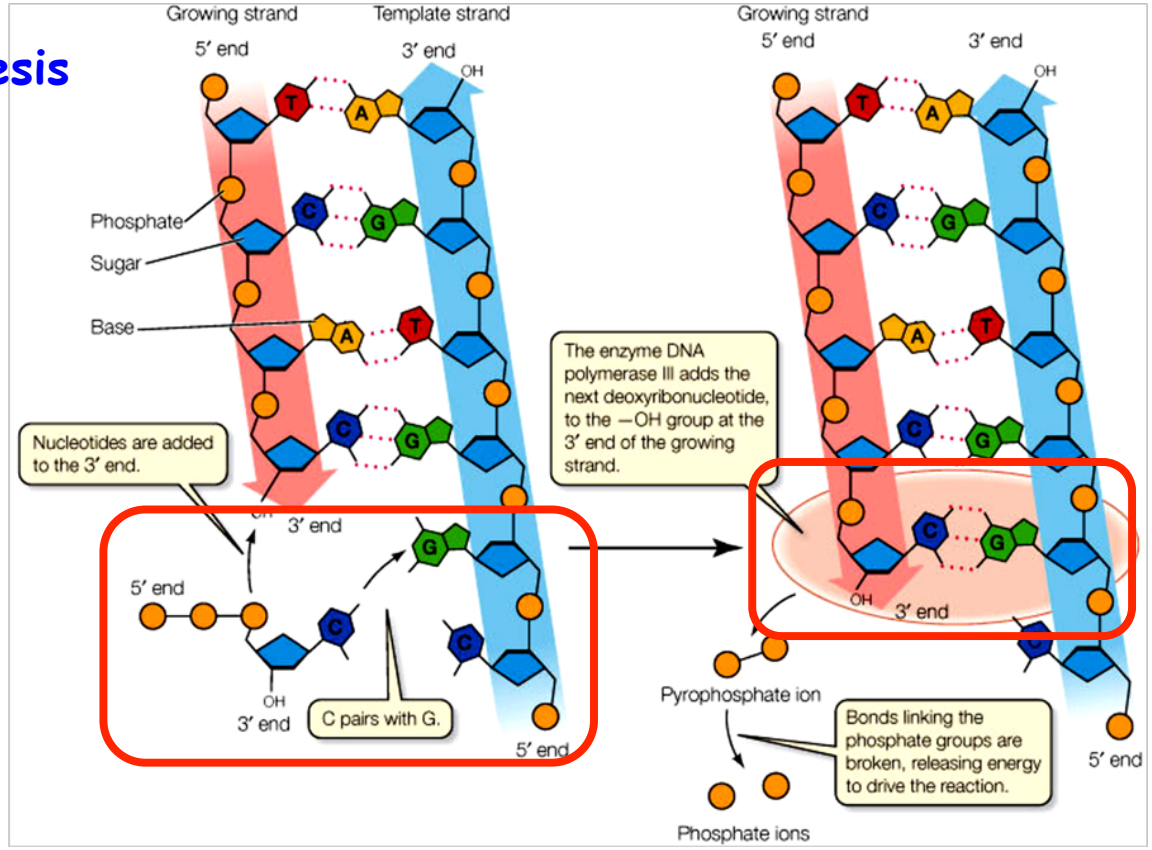
1. DNA Structure Allows DNA Sequence to Be Maintained by Complementary Base Pairing
2. Each Strand Serves as a Template for the Synthesis of a Complementary Strand
3. New DNA Molecules are Precise Copies of Parental DNA - Each Containing One Newly Synthesized Complementary Strand

DNA Sequence of One Strand is A Template For The New Strand

Synthesis

5′

3′



Sequence is Specified by Complementary Bases

Note: 5′ (P) & 3′ (OH)

5′ to 3′ Polarity Specifies Sequence

The DNA Sequence is Maintained Generation To Generation

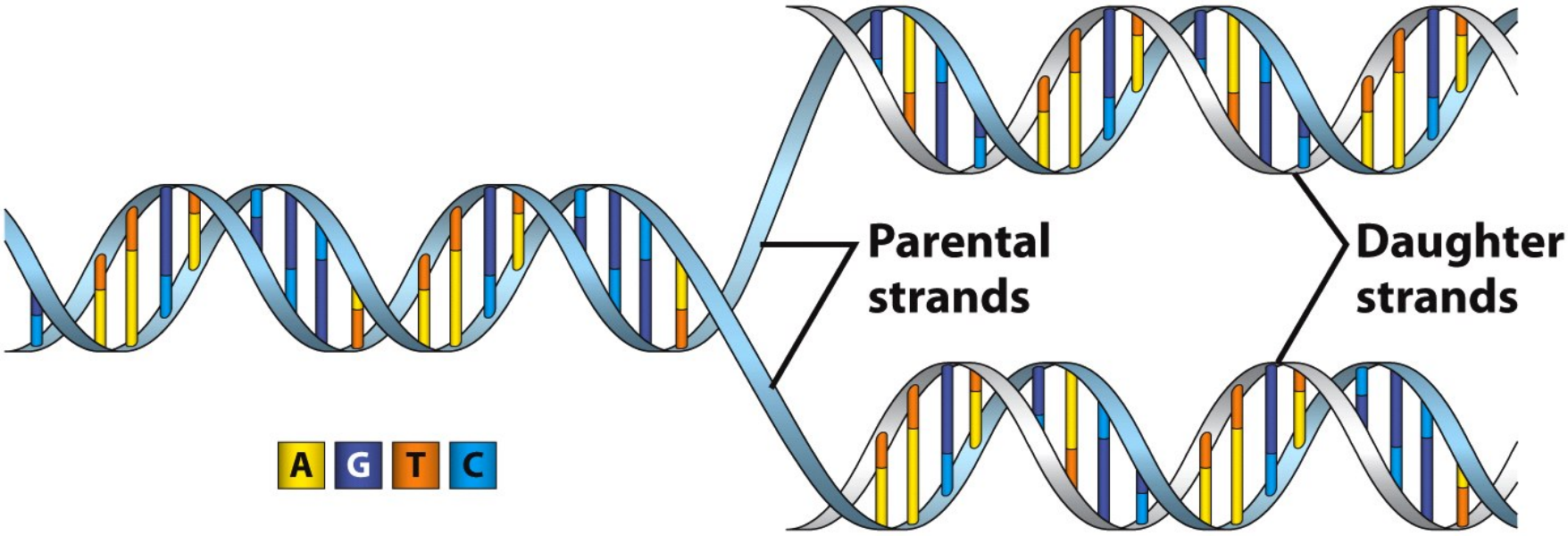
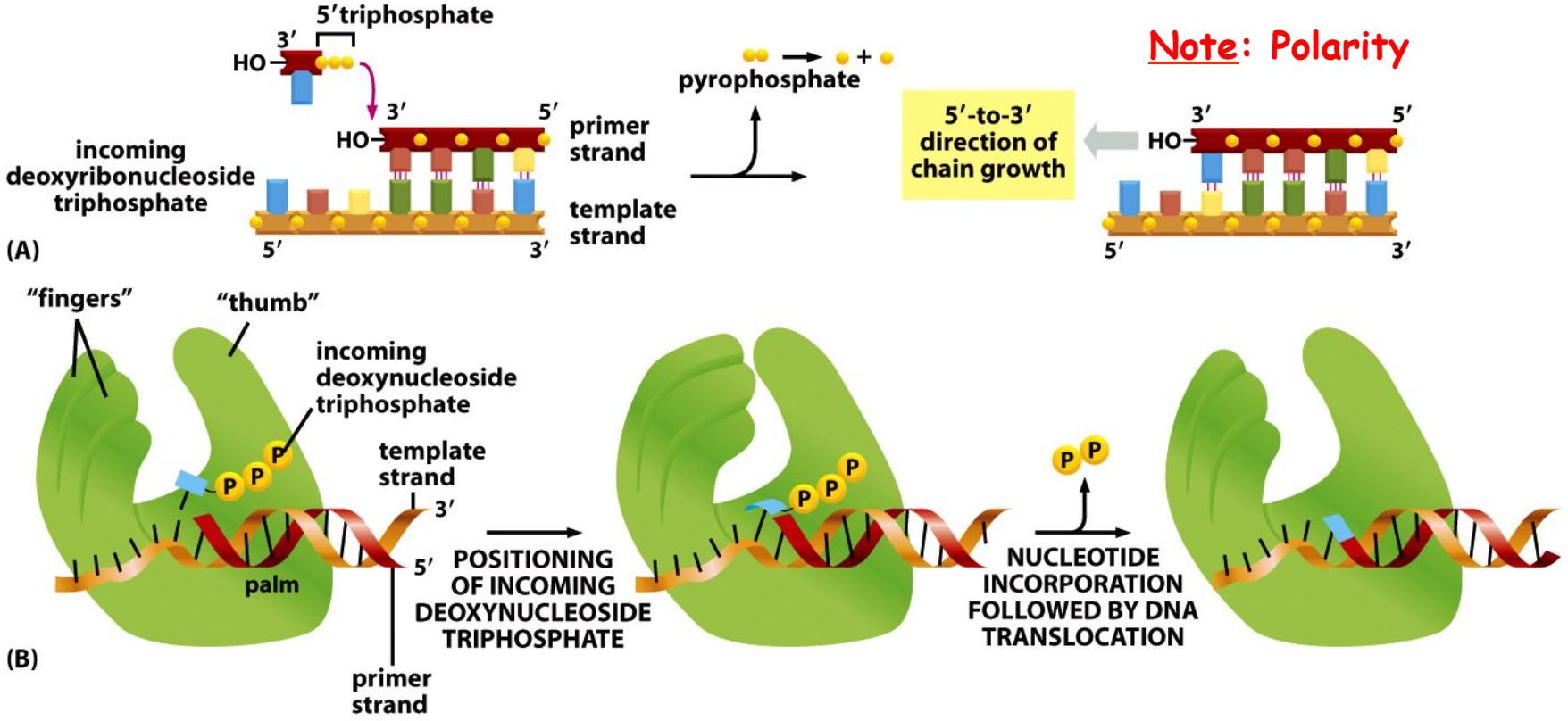


Figure 1-10
Molecular Cell Biology, Sixth Edition

The DNA Sequence "Lives" Forever!

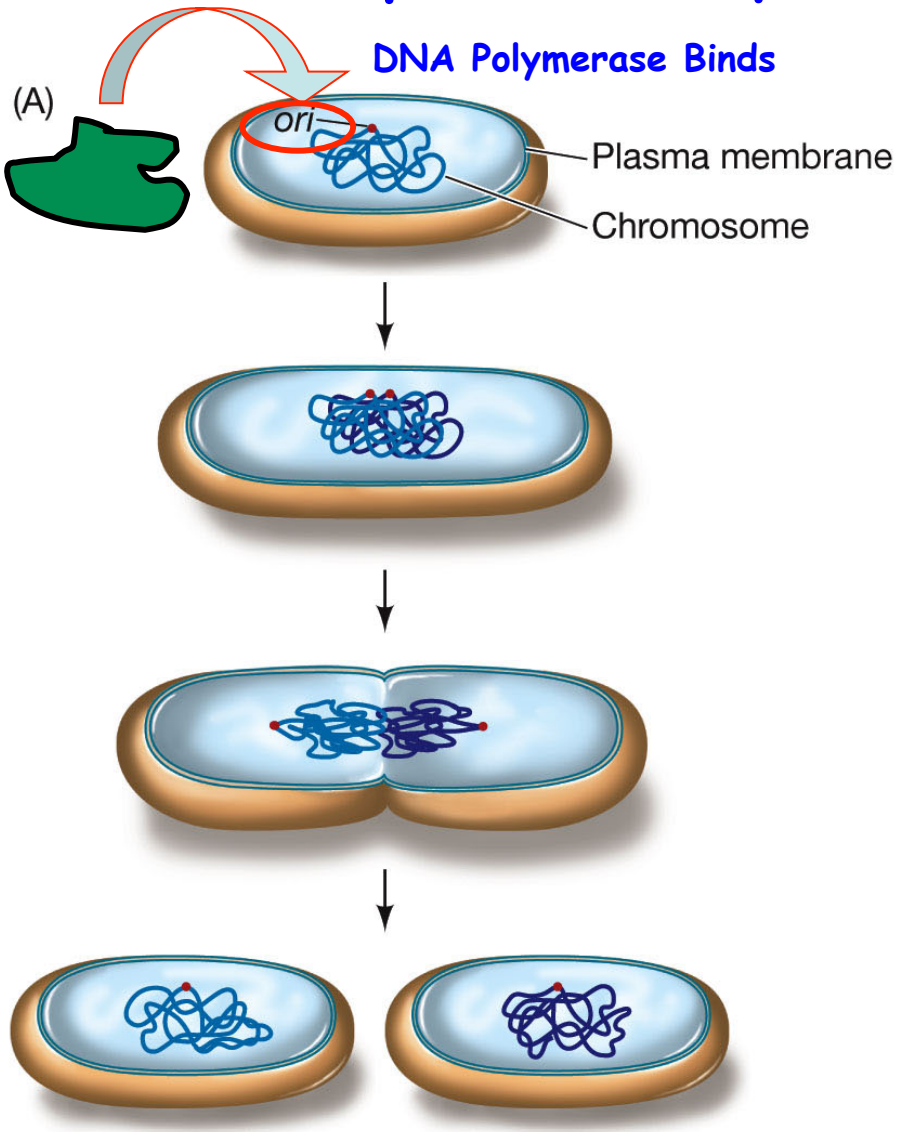
DNA Replication Requires An Enzyme - DNA Polymerase

Note: Nucleotide, Primer, & Template



1. DNA Polymerase Catalyzes 3′-5′ Phosphodiester Bonds & Copies the Template
2. DNA Replication Needs a Primer, Template, DNA Polymerase,& Nucleotides

DNA Replication Requires An Origin of Replication



Two IDENTICAL Cells - Phenotypically & Genotypically - From One

(b)

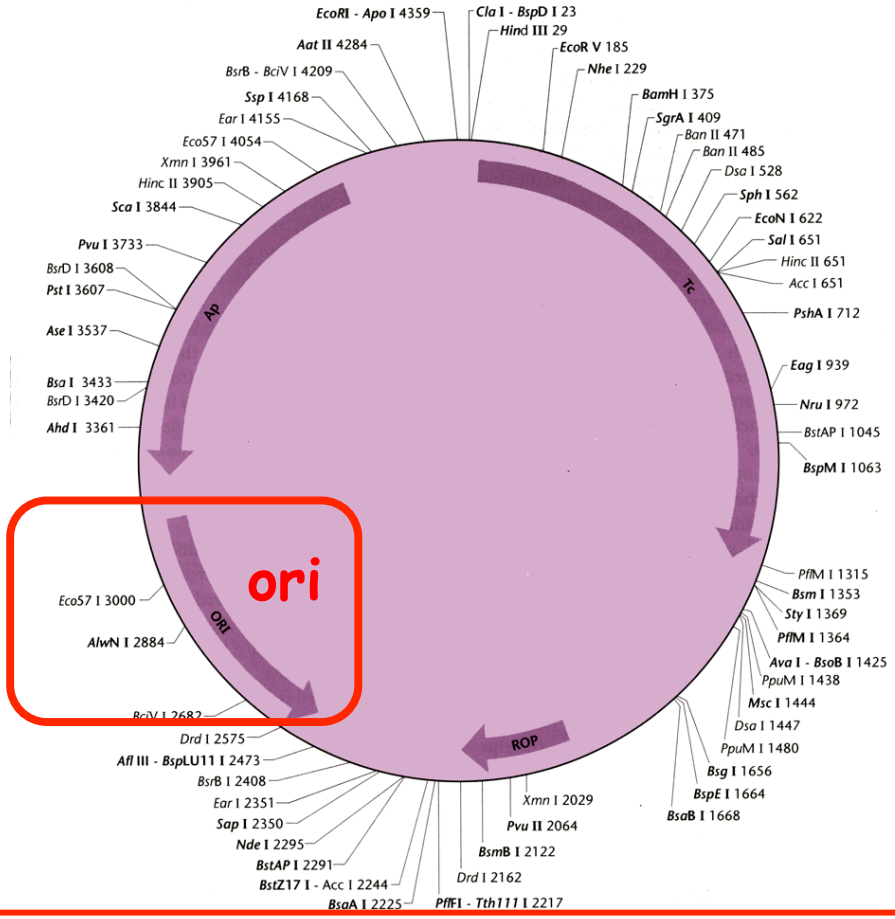
DNA Replication Also Requires:

1. Template
2. Nucleotides
3. DNA Polymerase (Machine)
4. "Primer" to Start Replication

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 9.2 Prokaryotic Cell Division

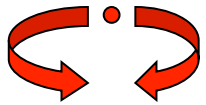
Ori

DNA Replication Starts at The Origin of Replication



DNA Replication is Bidirectional From the Ori!!!

Ori



Hypothesis For Two Direction Synthesis?

DNA Polymerase Binds to The Origin of Replication (Ori) to Begin DNA Synthesis

How Control Division?

DNA Replication Moves Bidirectionally From Origin

Genetic Engineering Concept

Foreign DNA Segments Use Ori of Chromosomes/ DNA They are Inserted Into

e.g., bacteria insect resistance gene uses plant ori

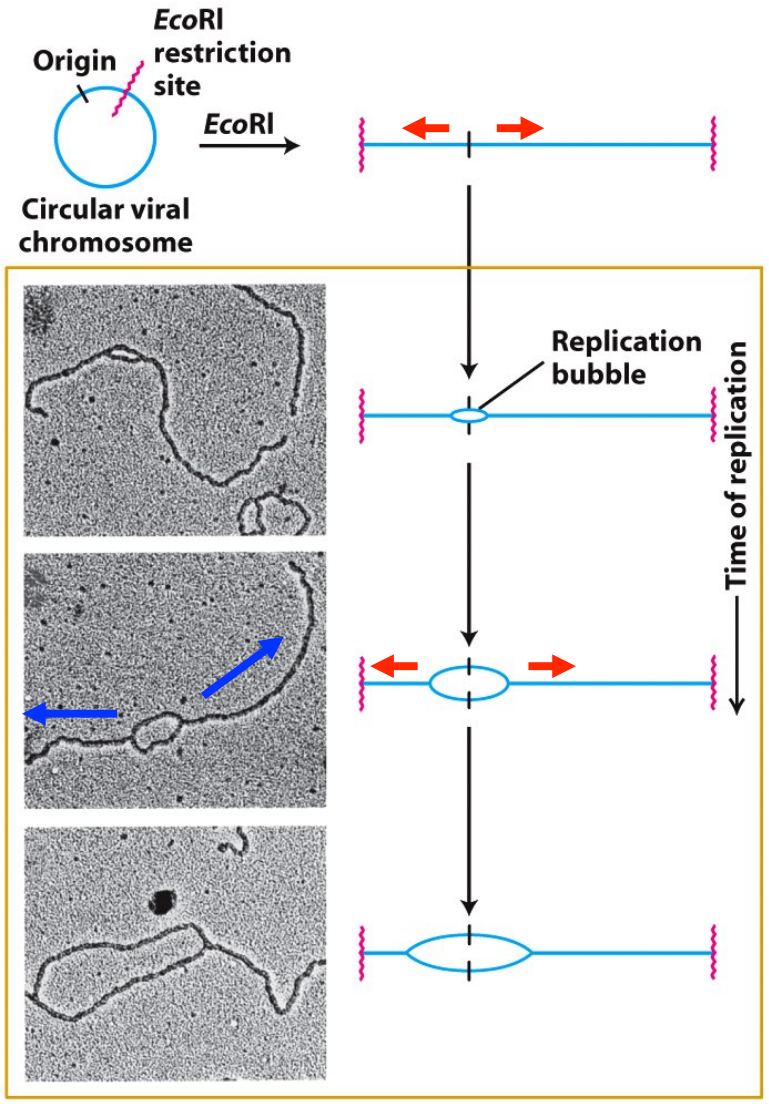
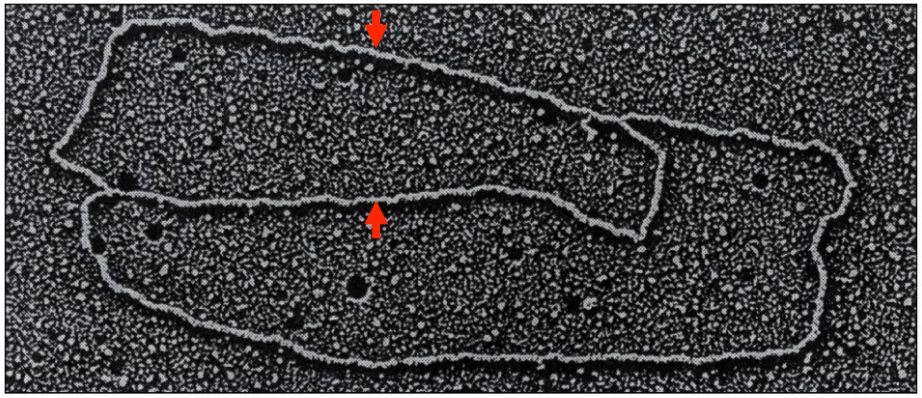
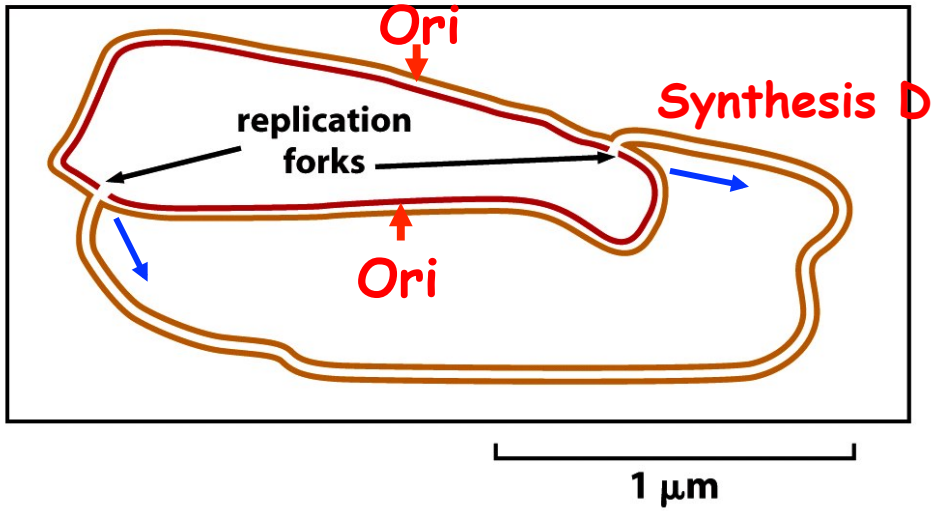


Figure 4-32
Molecular Cell Biology, Sixth Edition

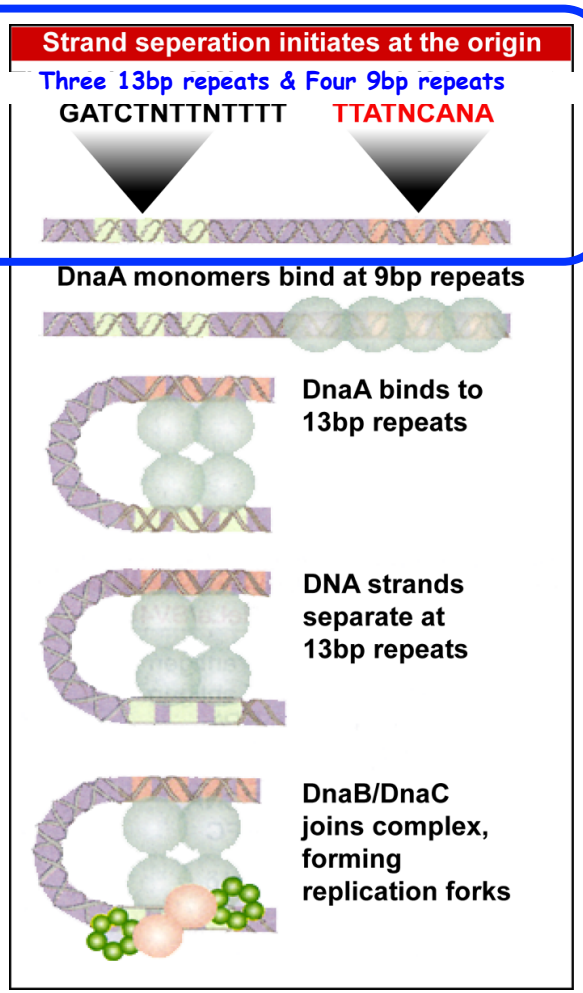
DNA in The Process of Being Replicated

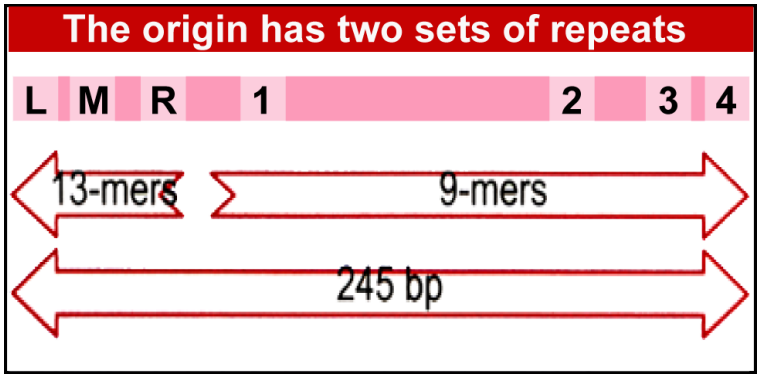




Hypothesis For Bidirectional
DNA Synthesis?

The Origin of Replication is a Specific Sequence



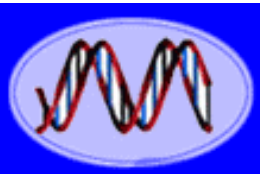


1. How Clone An Origin of Replication?

2. Specific Sequence - What Does This Mean For Genetic Engineering?

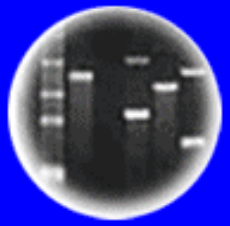
3. What is The Significance For Genetic Engineering?

4. Can Replicating "Chromosomes" Be Made?



DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



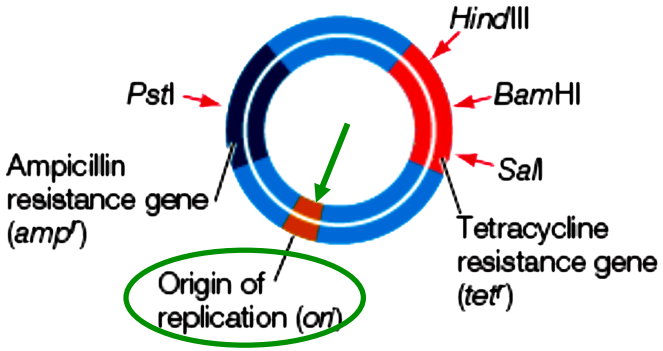
DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Vectors Are Needed To Replicate Genes In Specific Cells

(A) Plasmid pBR322
Host: *E. coli*



↓ **Recognition Site for Restriction Enzymes**

1. Ori is a specific sequence
2. Ori is Genome & Organism Specific
3. DNA Polymerases are Specific For Each Organism Therefore need correct Ori to Replicate Gene in a Specific Organism!

Note → Need Bacterial Ori to clone human gene in bacteria. Need human Ori ro replicate a bacterial gene in human cells.

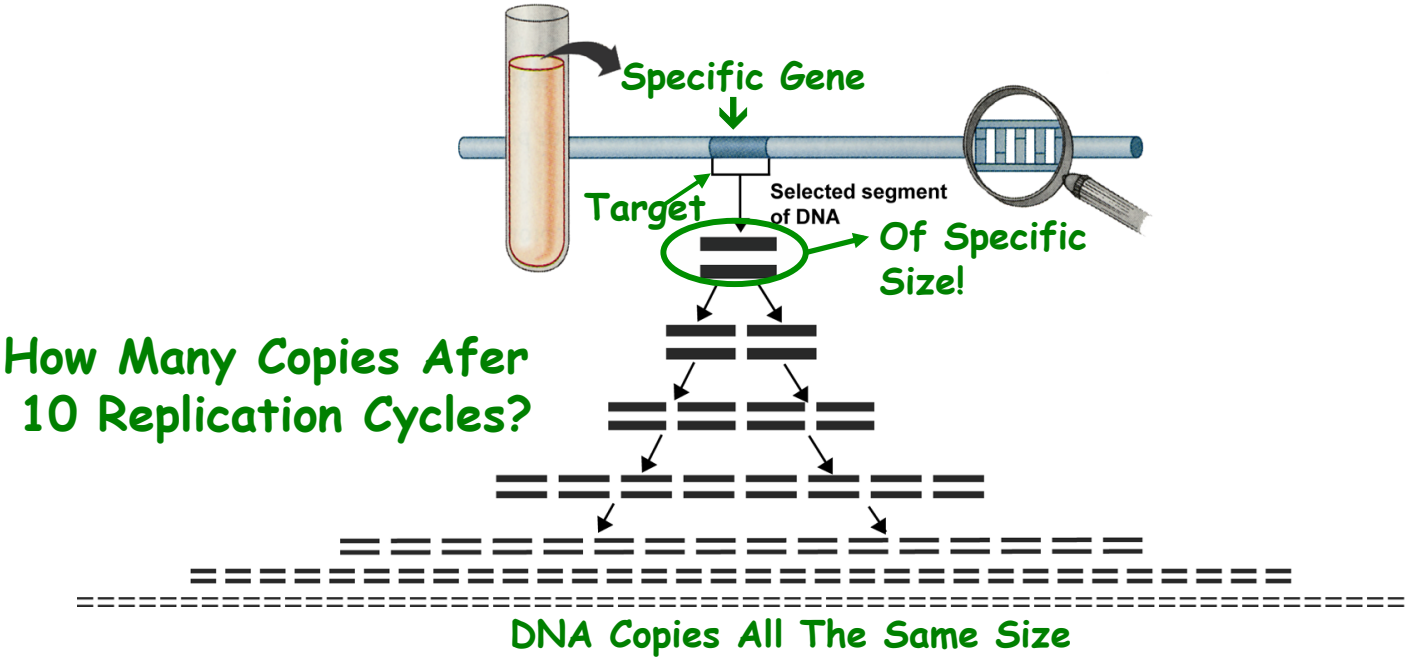
Yo! It's in the Sequence= Function

∴ Vectors can be Engineered!

Ori's can be cloned/synthesized!

MODULAR!!

The Polymerase Chain Reaction or PCR is A Molecular Xerox Machine



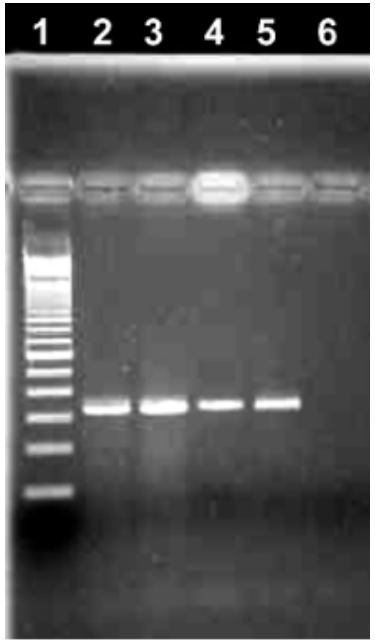
1. PCR Has Revolutionized DNA Analysis!

<u>Specific</u> DNA Sequences/Genes Can Be "Copied" Directly From "Tiny" Amount of DNA!

2. No Cloning Needed!

3. But Need Sequence! ⇨ Have to Clone "Gene" First

Using Gel Electrophoresis to Visualize PCR Products



Specific Diagnostic DNA Band Unique to DNA Sequence Being Amplified

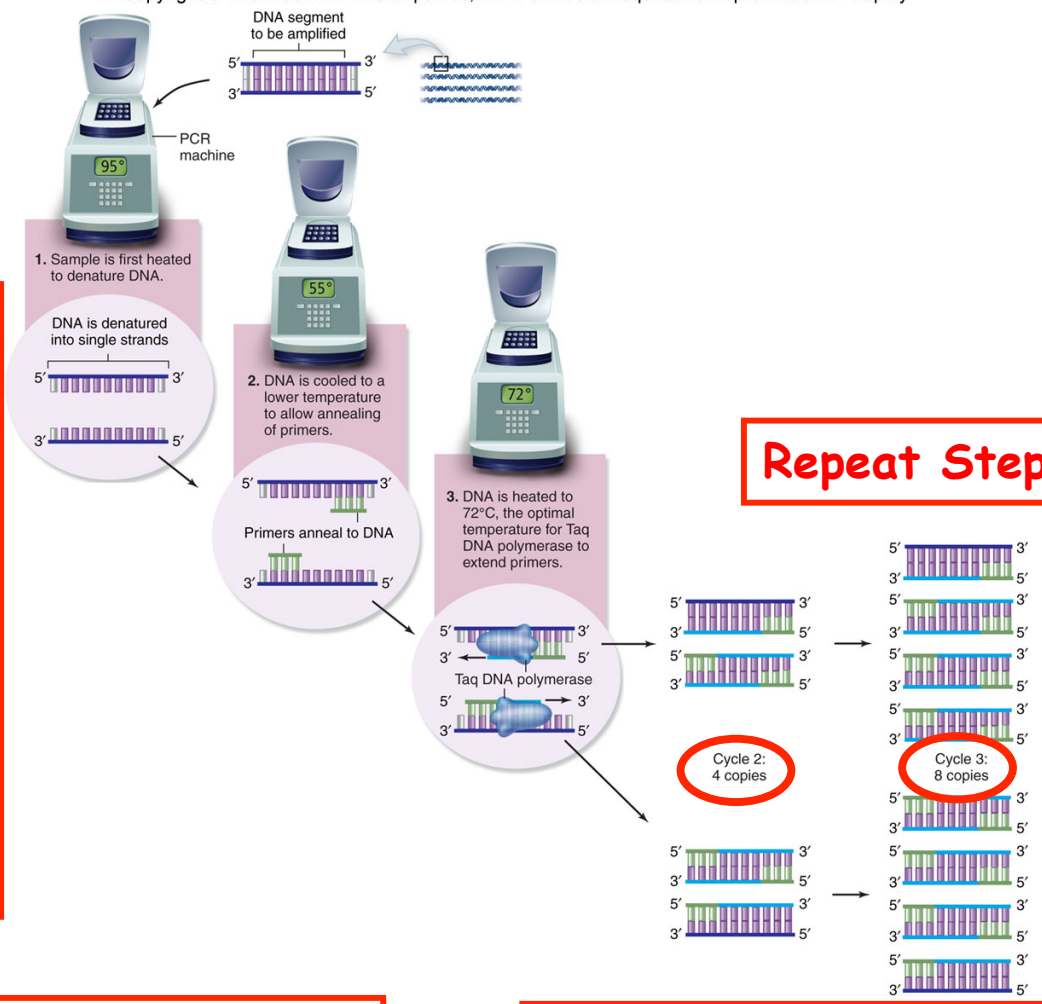
← Target-Specific Band Diagnostic For Specific DNA Sequence

Can Amplify One DNA Sequence From An Entire Genome!!!

PCR is A Cyclical Process of DNA Replication

Requires

1. Template
2. Primers
3. Knowledge of Specific Sequence
4. Nucleotides
5. Heat-Stable DNA Polymerase
6. Cycler



Repeat Steps or Cycle

2^n Molecules of DNA where n = Number of Cycles

Diagnostic For Amplified DNA Sequence → DNA Fragments All The Same Size Primer-Sequence-Primer

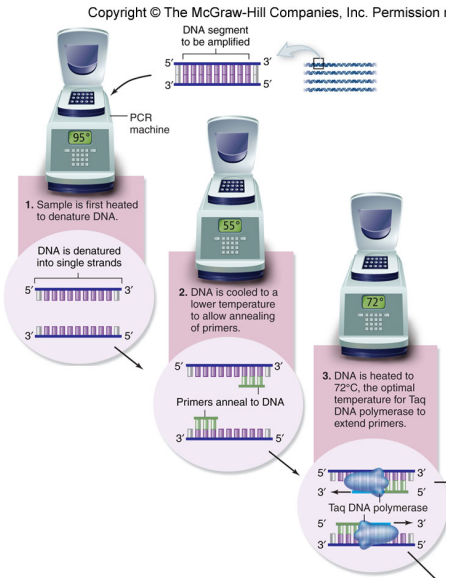
Requirements For PCR

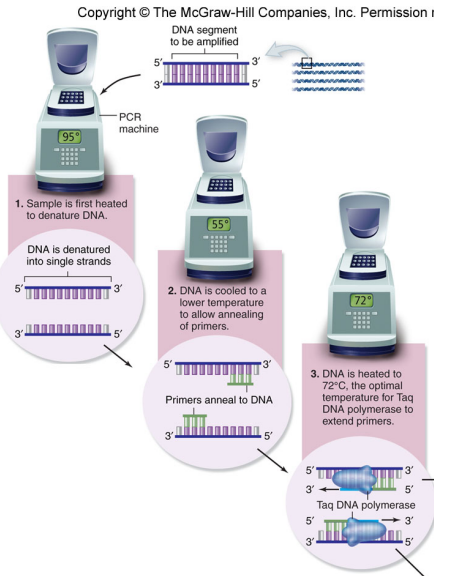
1. Knowledge of a Specific Sequence to Amplify (e.g.,insulin gene)
   a) Must Have First Cloned & Sequenced DNA of Interest the "Old-fashioned Way"
2. Primers That Recognize Specific DNA Sequences & Initiate DNA Synthesis & DNA Polymerase Binding To Template
3. Template (e.g., DNA From Human Cheek Cell)
4. Heat-Stable DNA Polymerase
5. Nucleotides
6. Thermoprogrammer/Cycler To Heat & Cool DNA in Cycles- Separating DNA Strands, Allowing Primers To Bind Complementary Sequences (Anneal), & Permiting New dsDNA Molecules to Form

It's All in the DNA Sequences -- Know Sequence & Can Synthesize an Infinite Amount of Specific DNA Sequences. It know Takes One Hour To Do What Used to Take YEARS!

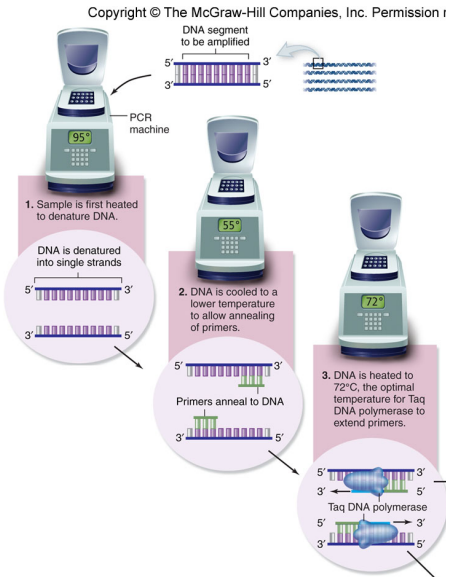
PCR Has Made DNA Cloning and Recombinant DNA Technology Obsolete?

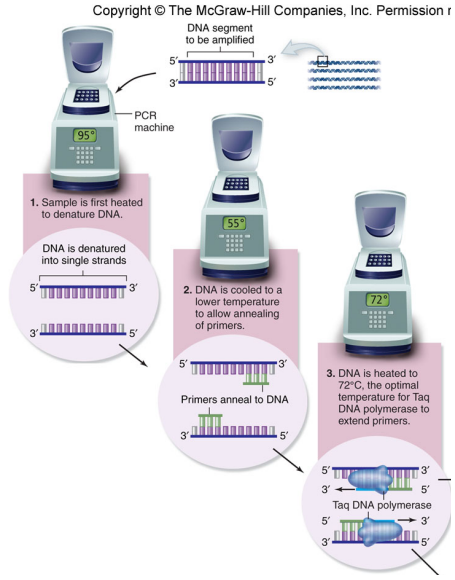
a. Yes
b. No

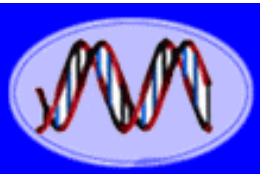




Examples of PCR Applications

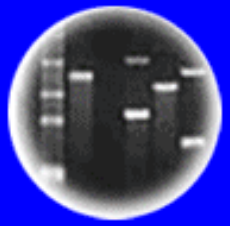






DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



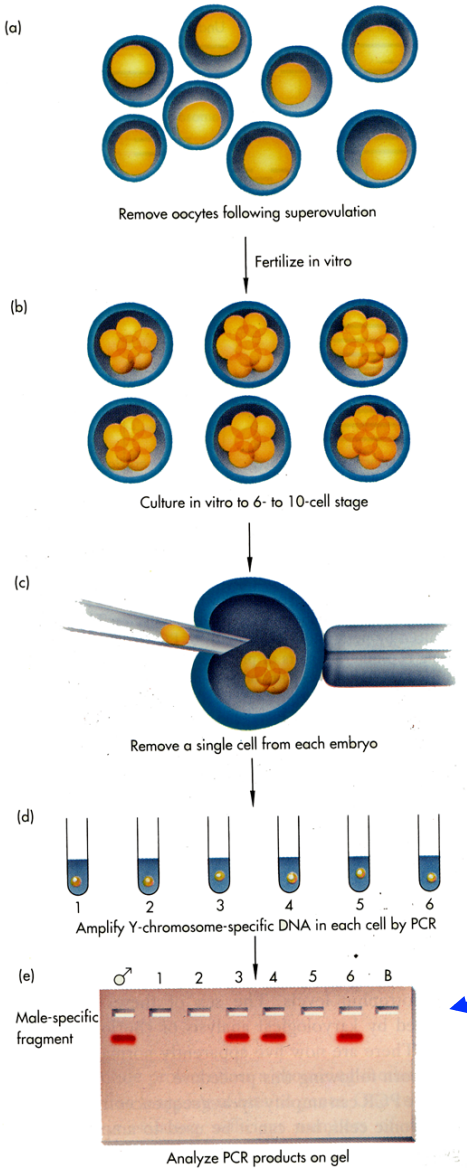
DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

PCR Can Be Used To Analyze Gene in A Single Embryo Cell

PGS
Pre-Implantation Genetic Screening



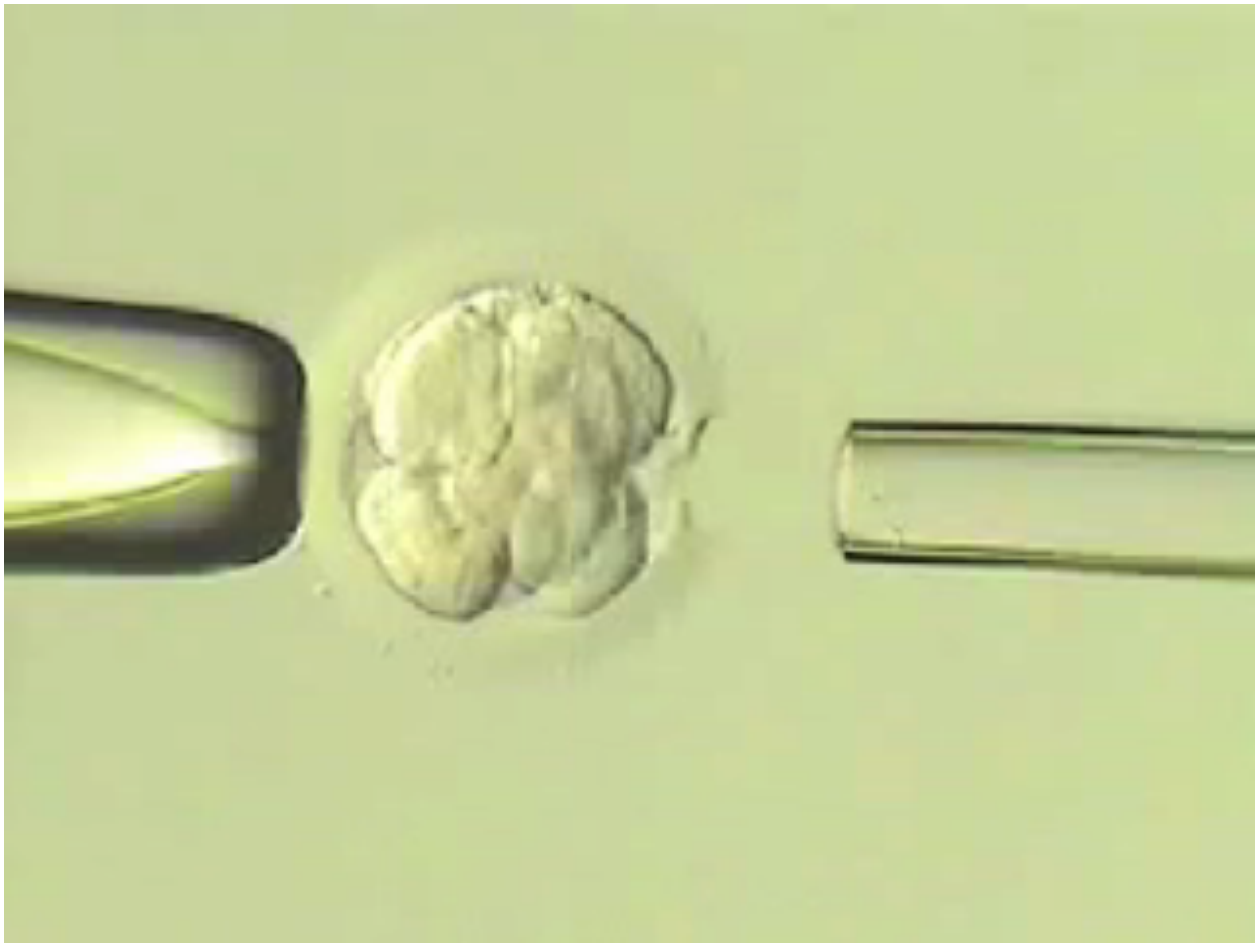
What is The Implication of This Procedure Considering That The Human Genome Has Been Sequenced?

Sex Determination in 8-cell Embryo!

Parents Should Be Allowed To Use PGS To Test Their Embryos For Any Gene and Select Those With the Combination They Want to Become Their Child?

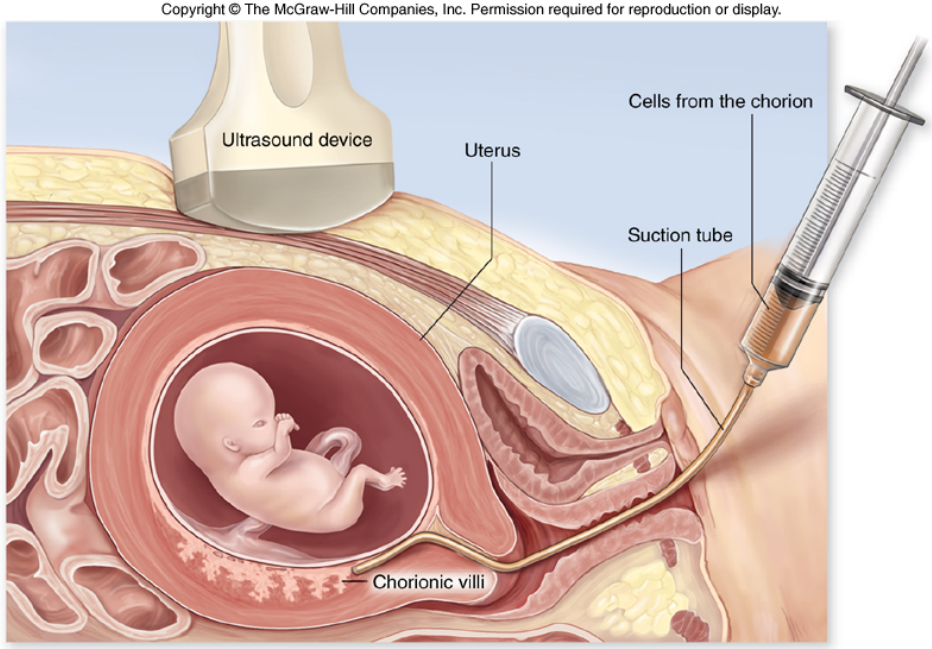
a. Yes
b. No

Determining the Genetic Identity of a Human Embryo Before Implantation!



Prenatal Genetic Diagnosis (PGD)

PCR Can Be Used To Analyze Genes During Pregnancy



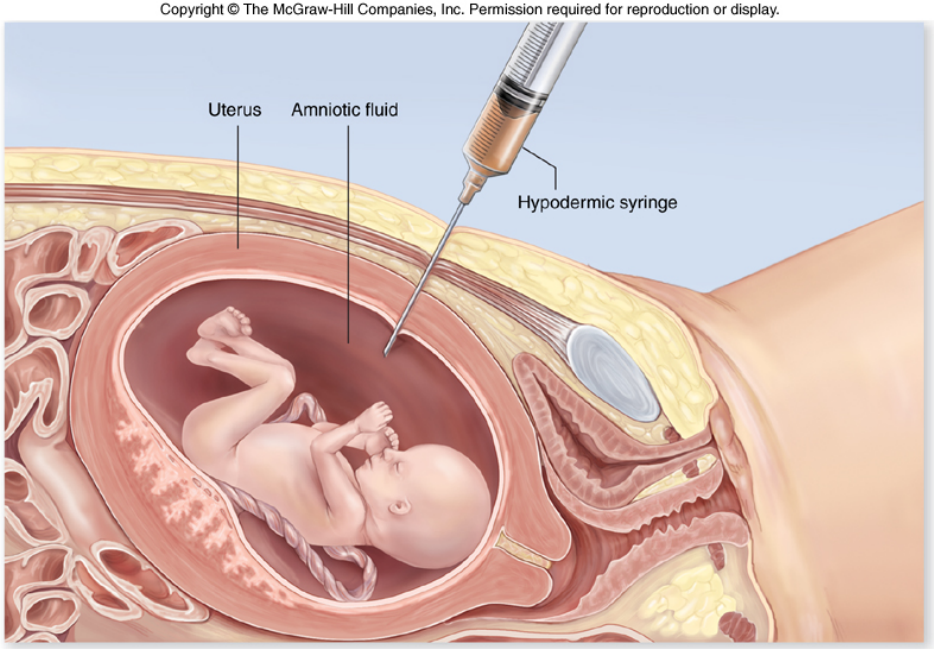
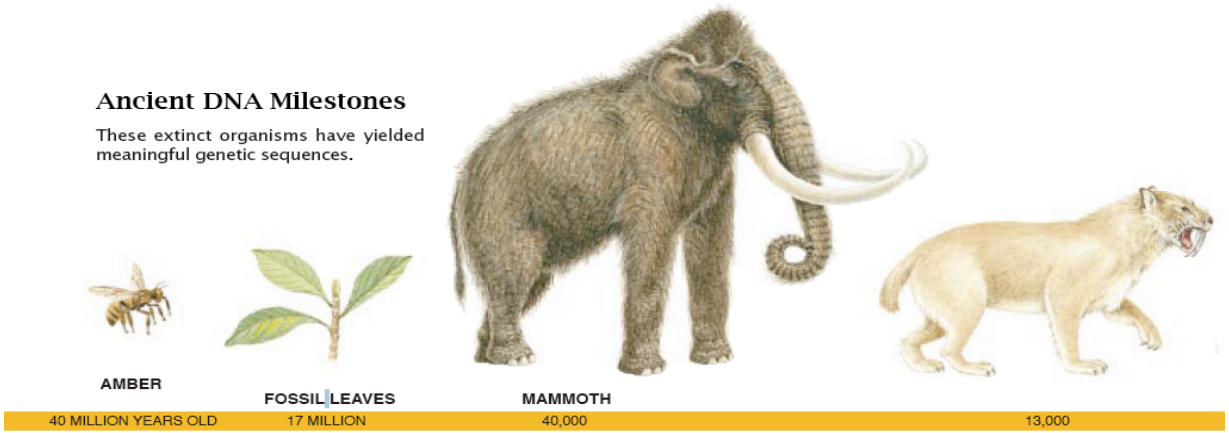
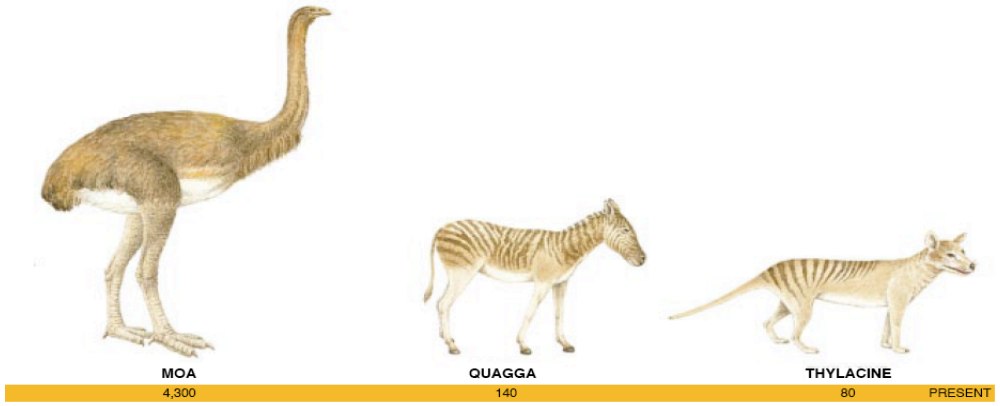


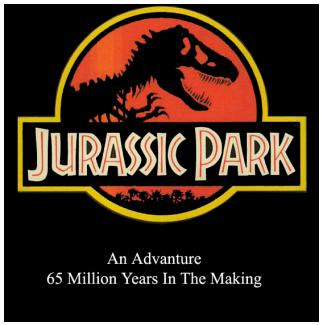
TABLE 13.2 Some Important Genetic Disorders

Disorder	Symptom	Defect	Dominant/ Recessive	Frequency Among Human Births
Hemophilia	Blood fails to clot	Defective blood-clotting factor VIII	X-linked recessive	1/10,000 (Caucasian males)
Huntington disease	Brain tissue gradually deteriorates in middle age	Production of an inhibitor of brain cell metabolism	Dominant	1/24,000
Muscular dystrophy (Duchenne)	Muscles waste away	Degradation of myelin coating of nerves stimulating muscles	X-linked recessive	1/3700 (males)
Hypercholesterolemia	Excessive cholesterol levels in blood lead to heart disease	Abnormal form of cholesterol cell surface receptor	Dominant	1/500

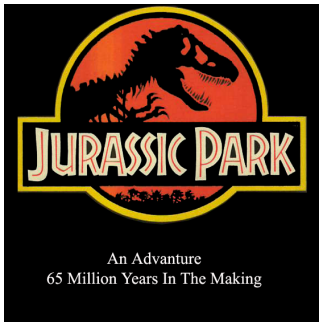
Using PCR To Detect Genes In Ancient DNA



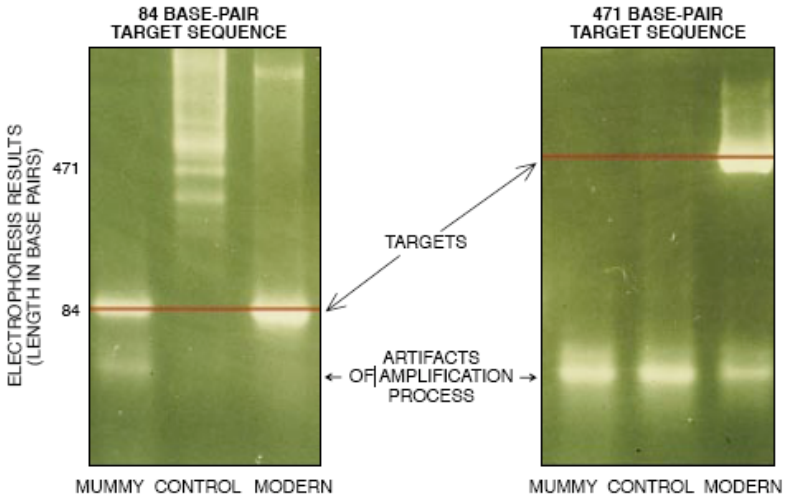




Just Need One Molecule of DNA!!



Using PCR To Detect Genes in Mummy DNA



Sequence to Determine Relationships

Using PCR to Amplify Mammoth DNA From Fossilized Hair & Sequence The Entire Genome!

Nature, November 2008

Sequencing the nuclear genome of the extinct woolly mammoth

Webb Miller[1], Daniela I. Drautz[1], Aakrosh Ratan[1], Barbara Pusey[1], Ji Qi[1], Arthur M. Lesk[1], Lynn P. Tomsho[1], Michael D. Packard[1], Fangqing Zhao[1], Andrei Sher[2]‡, Alexei Tikhonov[3], Brian Raney[4], Nick Patterson[5], Kerstin Lindblad-Toh[5], Eric S. Lander[5], James R. Knight[6], Gerard P. Irzyk[6], Karin M. Fredrikson[7], Timothy T. Harkins[7], Sharon Sheridan[7], Tom Pringle[8] & Stephan C. Schuster[1]

Using PCR to Amplify Neanderthal Bone DNA & Sequence The Entire Genome!

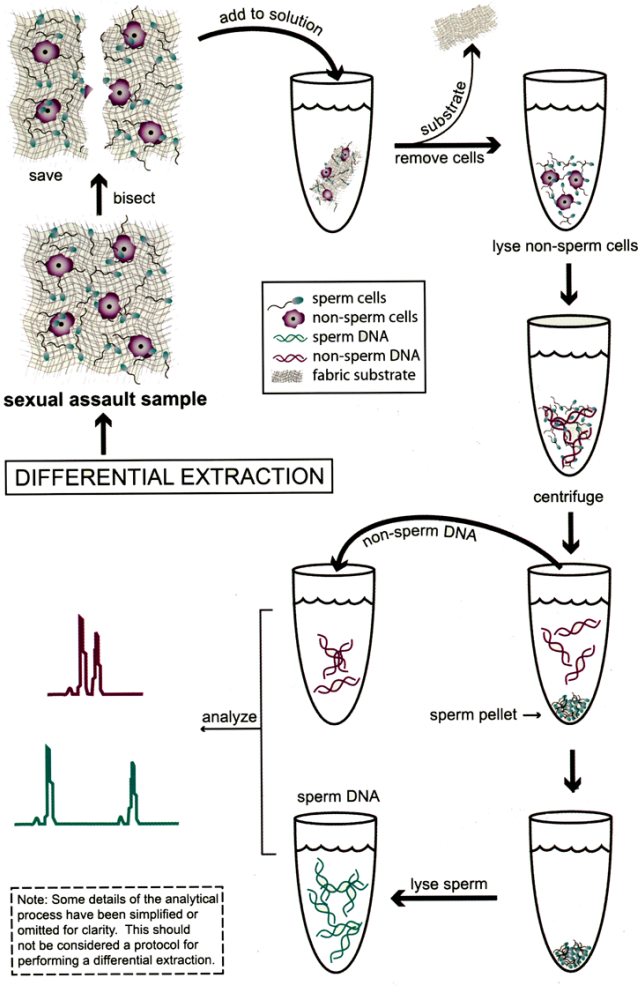
Analysis of one million base pairs of Neanderthal DNA

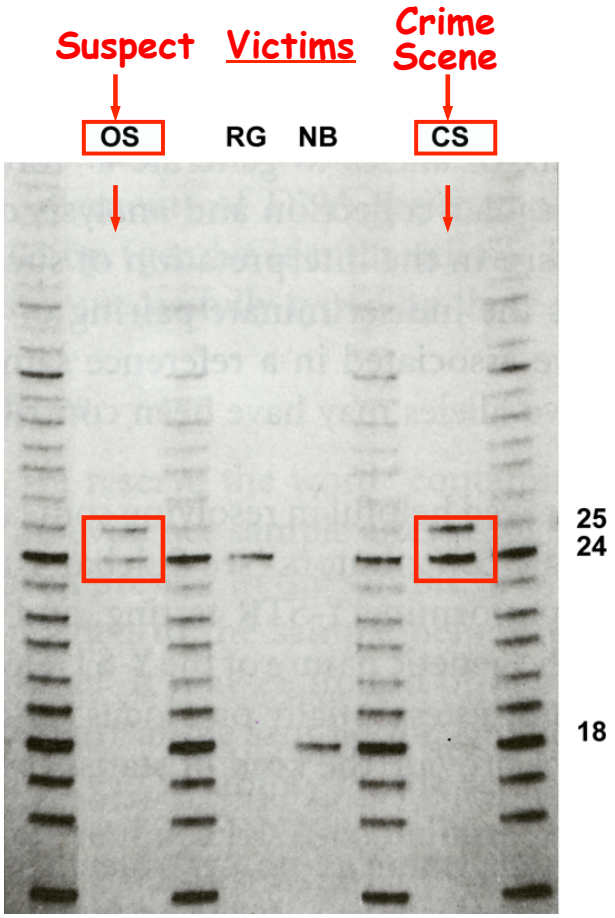
From a 45,000 Year-Old Bone

Richard E. Green[1], Johannes Krause[1], Susan E. Ptak[1], Adrian W. Briggs[1], Michael T. Ronan[2], Jan F. Simons[2], Lei Du[2], Michael Egholm[2], Jonathan M. Rothberg[2], Maja Paunovic[3]‡ & Svante Pääbo[1]

Nature, November, 2006

Using PCR in Crime Scenes



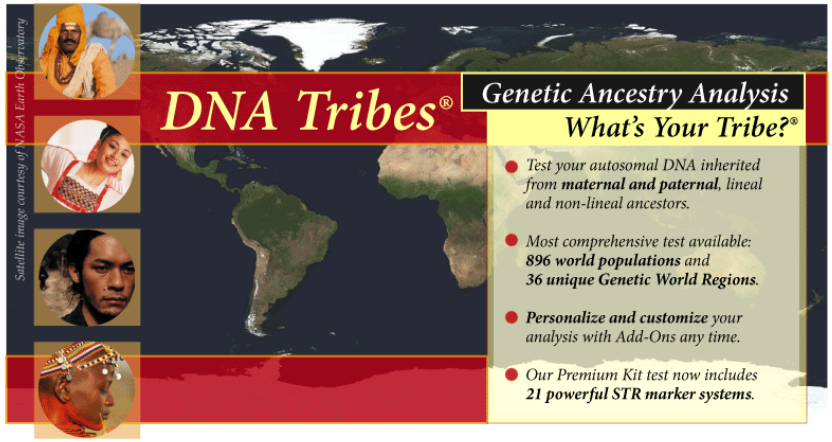


OS = Suspect
CS = Crime Scene
RG & NB = Victims

"Match" What is Probability That This Will Occur by Chance?

DNA Doesn't "Lie" !!

Using PCR To Determine an Individual's Ancestry

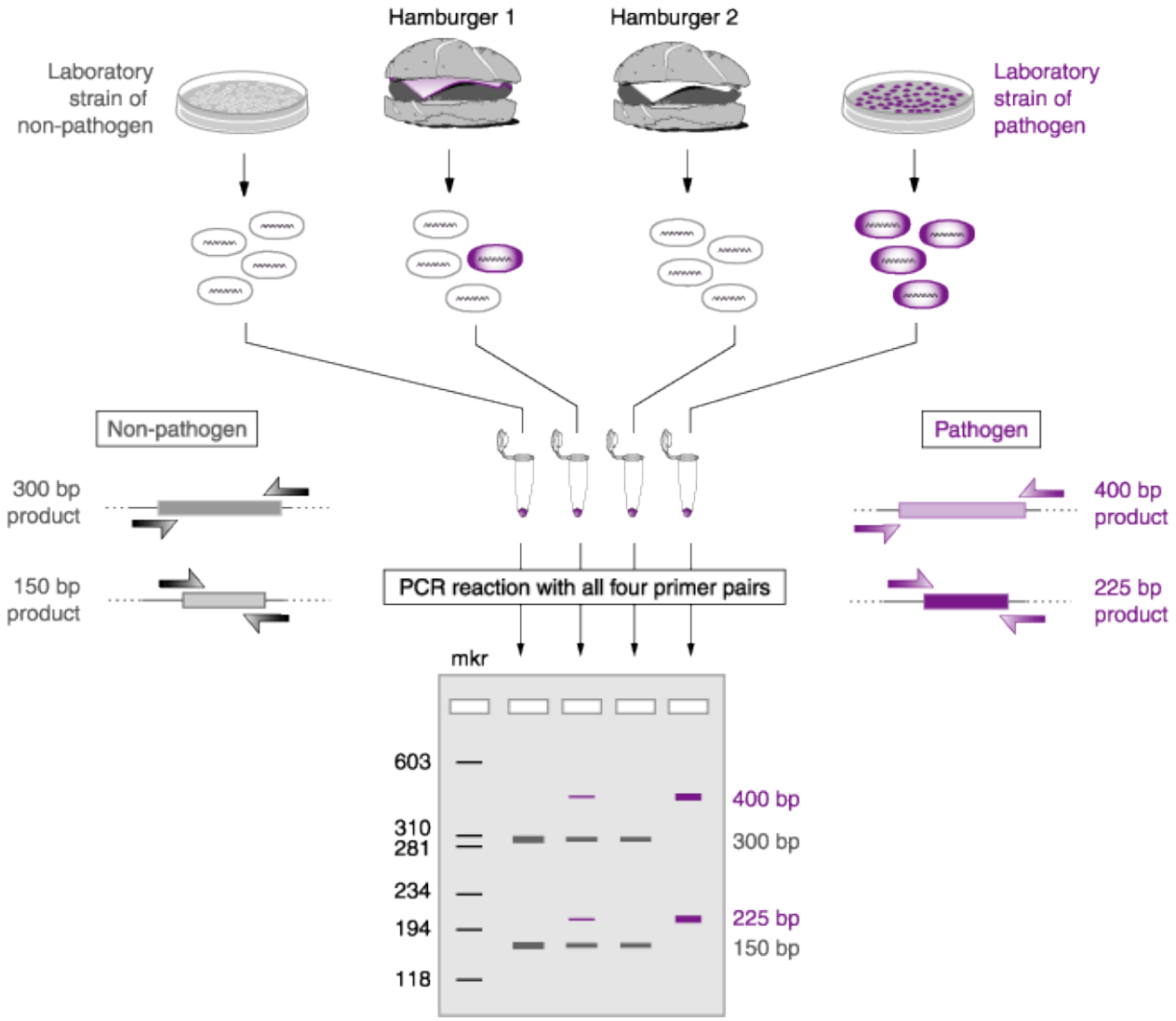


PCR Started a New Industry

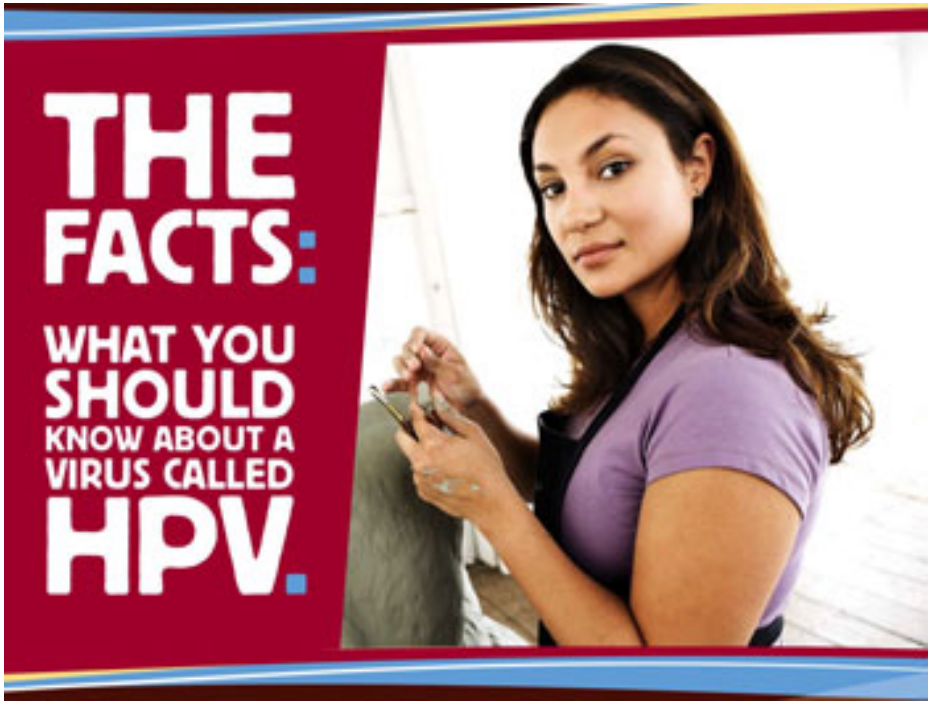
DNA can reveal ancestors' lies and secrets

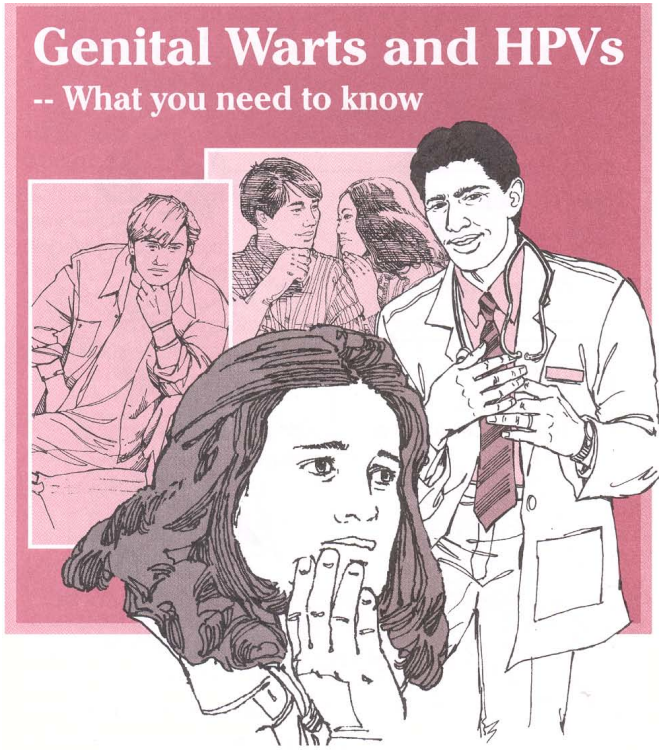
LA Times, January 18, 2009

Using PCR To Detect Food Pathogens



Using PCR To Detect Human Pathogens
(Viruses, Fungi, Bacteria)





ViroSeq™
HIV-1 Genotyping System

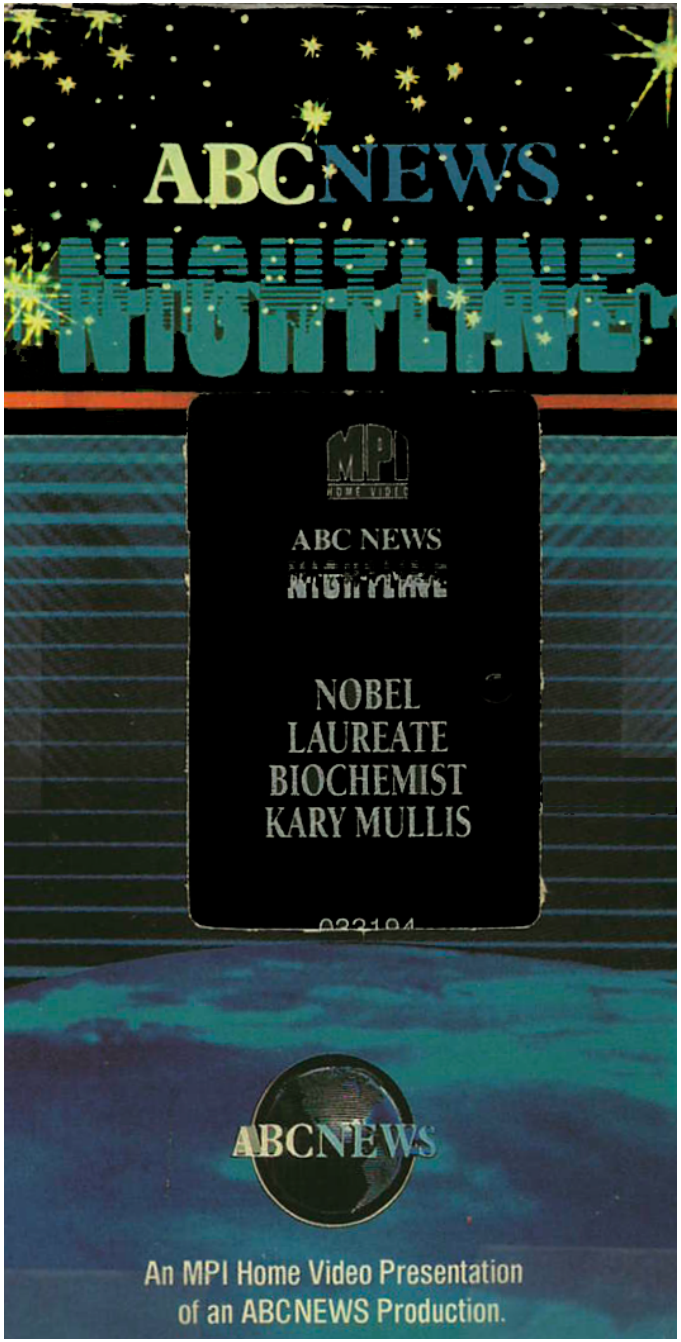
Each Genome Has Specific DNA Sequences That Can Be Used For Screening And Diagnosis Using PCR

PCR Has Many Uses, Has Changed Many Fields, and Lead To New Ones That Have Had a Big Impact On Our Lives

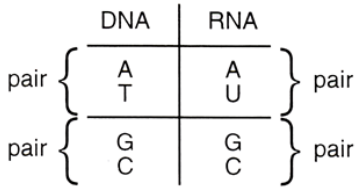
1. Amplify Any DNA Sequence, or Gene, From "Tiny" Amounts of DNA or Biological Materials IF ORIGINAL SEQUENCE KNOWN
2. Study DNA From Limited and/or Degraded Sources Such As:
    1. A Single Human Hair or Cheek Cell
    2. An Ancient Fossil (e.g., Neanderthal Bone or Mammoth Hair)
    3. An Ancient Insect Trapped in Amber
    4. Human Remains (e.g., 9/11 Victims)
    5. A Single Human Embryo Cell
    6. Contaminated Meat To Determine the Causal Organism
3. Used In:
    1. DNA Fingerprinting-Individual Identification-Genetic Disease Screening
    2. Forensics (Crime Scenes, Mass Graves, Criminal Suspects, Wrongfully Convicted)
    3. Paternity & Family Relationships (e.g., Immigration, Tracing Lost Children)
    4. Disease Diagnosis & Pathogen Identification (Humans, Animals, & Plants)
    5. Human Origins & Migrations
    6. Ancient Genome Sequences & Evolutionary Studies
    7. Specific mRNA Detection
    8. "Cloning" Specific DNA Sequences
    9. Tracing Plant & Animal Sources (e.g., Stolen Cattle, Cactus)
4. Need as Little as One Molecule of DNA & Can Replicate an ∞ Amount of Specific Sequences

Revolutionized How To Study & Manipulate DNA

March 31, 1994

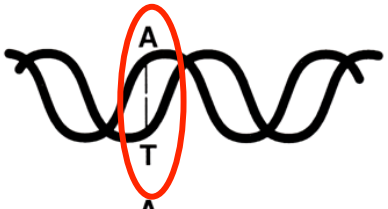


DNA Replication is Precise
But Mistakes or Mutations Can Occur!



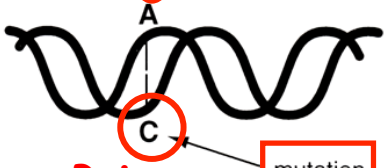
BASE PAIR RULES

Gene A



Rare Base Mismatch

Replication①



MUTATION DURING REPLICATION

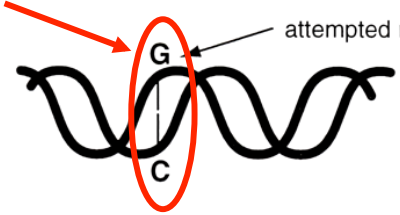
mutation

C mispairs with A

See Mutation As Change in Phenotype

New Base Pair

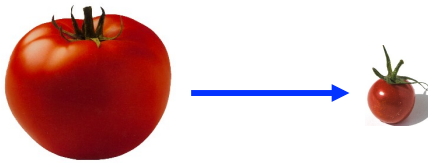
Replication②
Gene A'
Allelic Variant



RESULTING DEFECT

Change DNA Sequence From A = T to G ≡ C

∴ Change Protein Amino Acid Sequence ⇨ Alter Function!



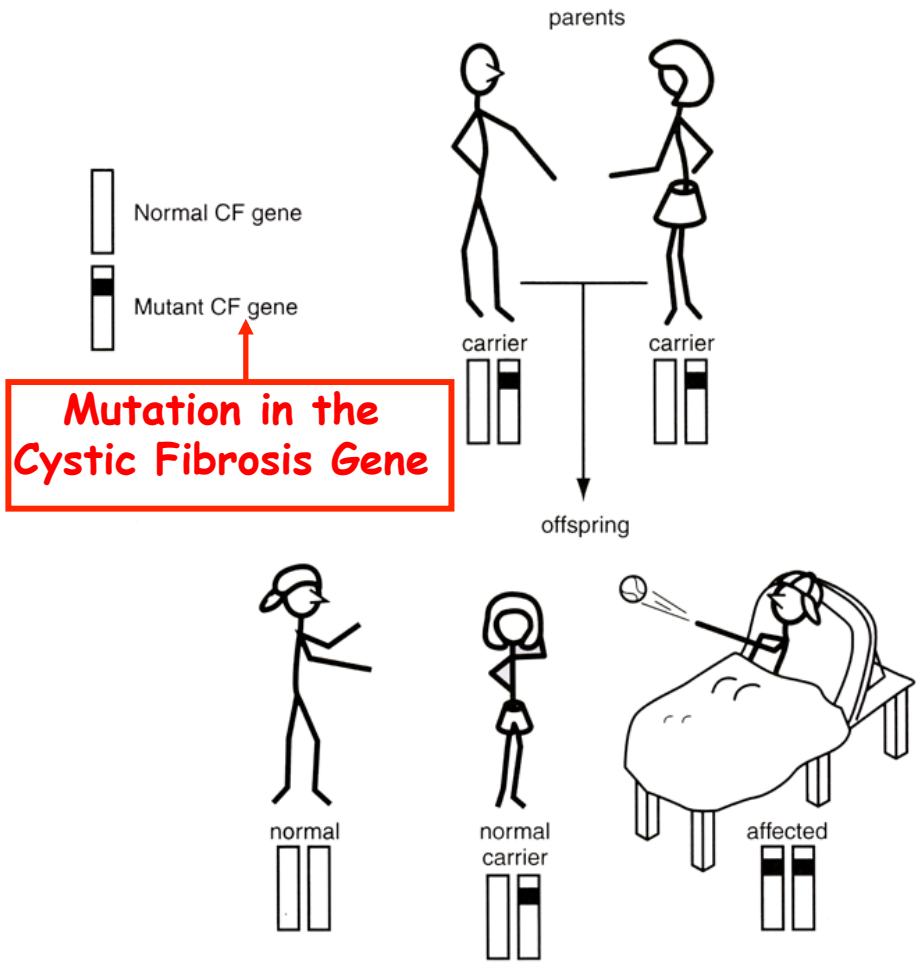
Big Tomato to Small Tomato

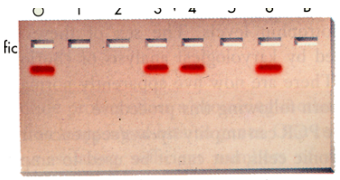
Mutation in Genes Are Rare But Are Inherited

One Gene Per Gamete

♀ + ♂

Two Genes per Somatic Cells



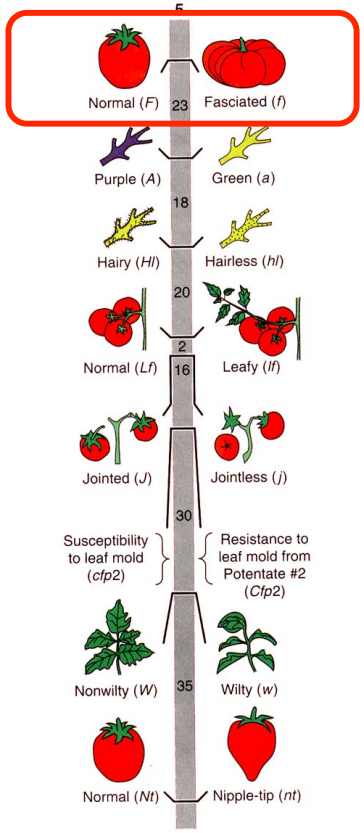


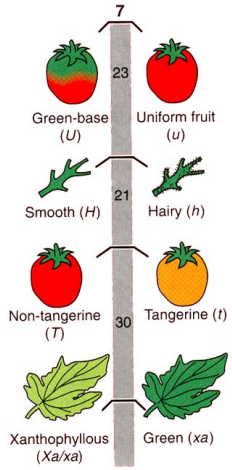
How Follow Inheritance?
What Allows Disease To Be Followed?

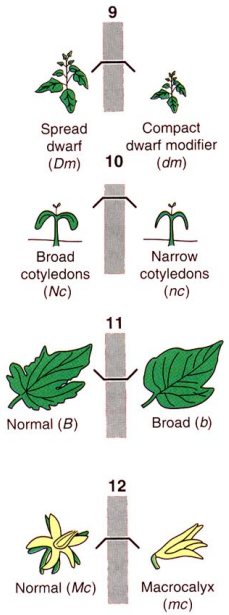
DNA Marker or Fingerprint!

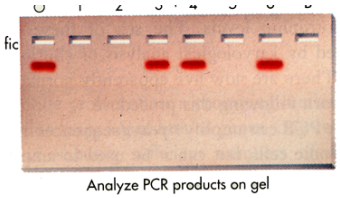
Alternative Forms of the Same Gene Lead to Genetic Diversity

Alleles









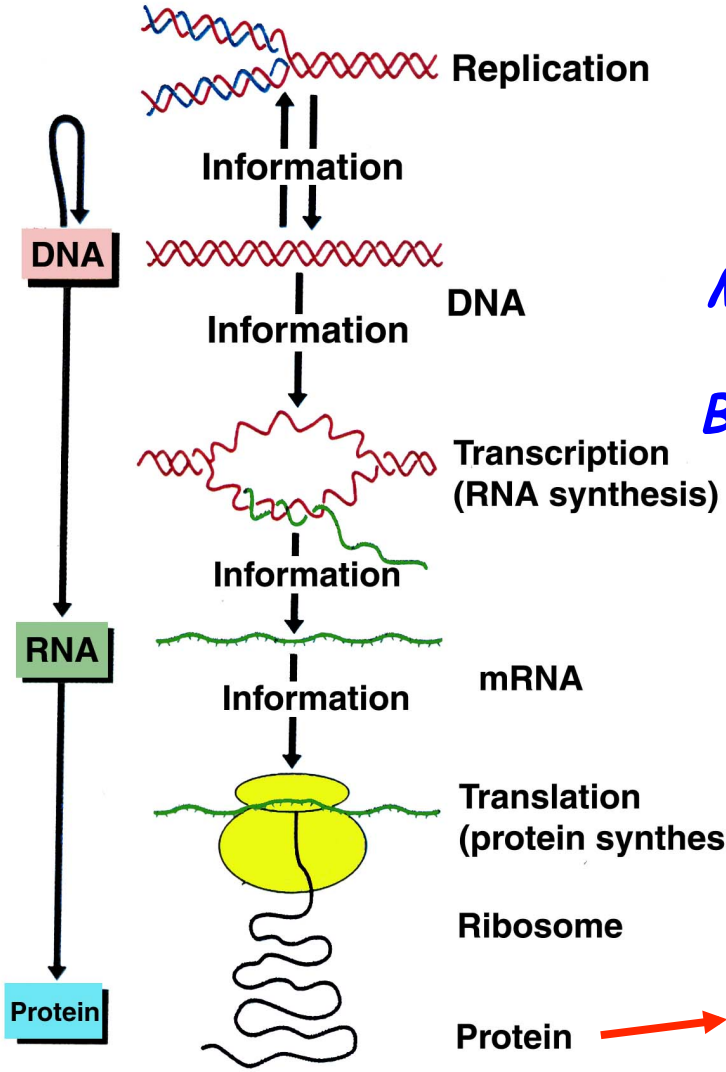
Can Follow These Traits With DNA Markers As Well

mutations result in genetic diversity!!!

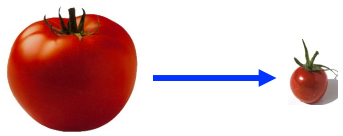
Spontaneous Mutations Give Rise To Alleles, or Different Forms of the Same Gene, And result in Small DNA Sequence Changes (e.g., SNPs or Single Nucleotide Polymorphisms)

Translating The Genetic Code Into Proteins is a Conserved Process

Mutations Are Inherited Because Altered Gene Replicates

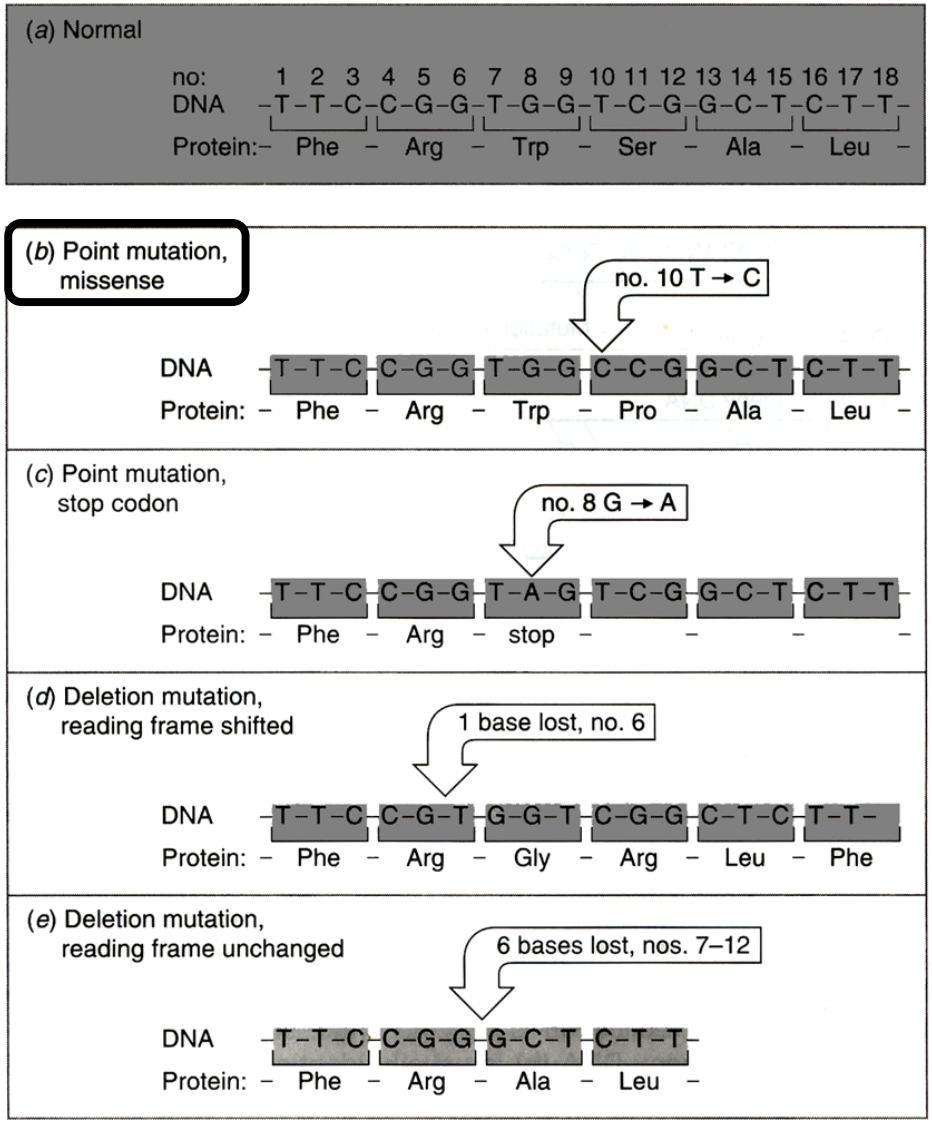


Mutations Lead To Altered Protein Because mRNA and Protein Sequence Encoded By Gene Changes



Mutations Lead to Altered Traits/Phenotype Because Protein Structure Changed

Mutations Can Occur Different Ways



1. Base-Pair Change
2. Insert or Delete Base (Indel)
3. Move Gene, or Part of Gene, to New Location (Switches Change)!

Function of Protein Lost and/or Changed

∴

Phenotype Changes

Human Genetic Disorders Occur As a Result of Mutations

TABLE 13.2 Some Important Genetic Disorders

Disorder	Symptom	Defect	Dominant/ Recessive	Frequency Among Human Births
Hemophilia	Blood fails to clot	Defective blood-clotting factor VIII	X-linked recessive	1/10,000 (Caucasian males)
Huntington disease	Brain tissue gradually deteriorates in middle age	Production of an inhibitor of brain cell metabolism	Dominant	1/24,000
Muscular dystrophy (Duchenne)	Muscles waste away	Degradation of myelin coating of nerves stimulating muscles	X-linked recessive	1/3700 (males)
Hypercholesterolemia	Excessive cholesterol levels in blood lead to heart disease	Abnormal form of cholesterol cell surface receptor	Dominant	1/500

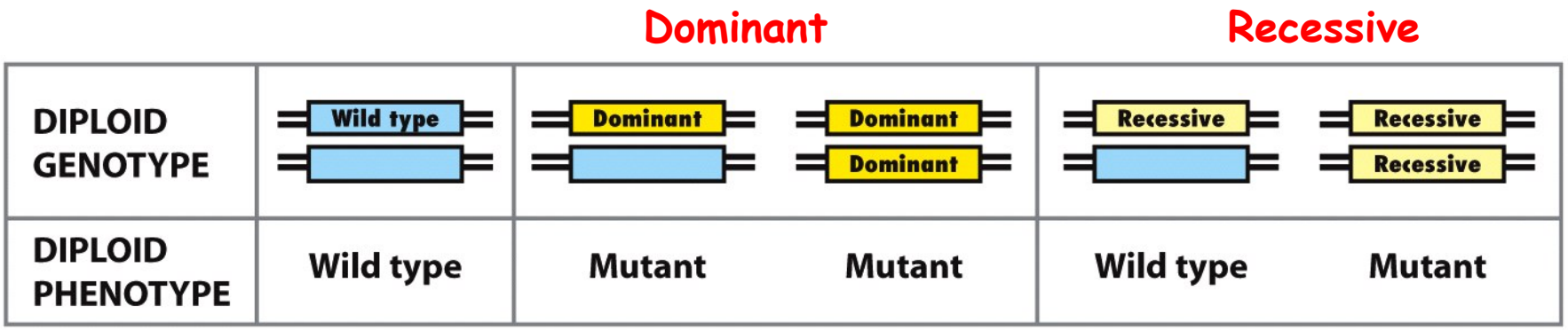
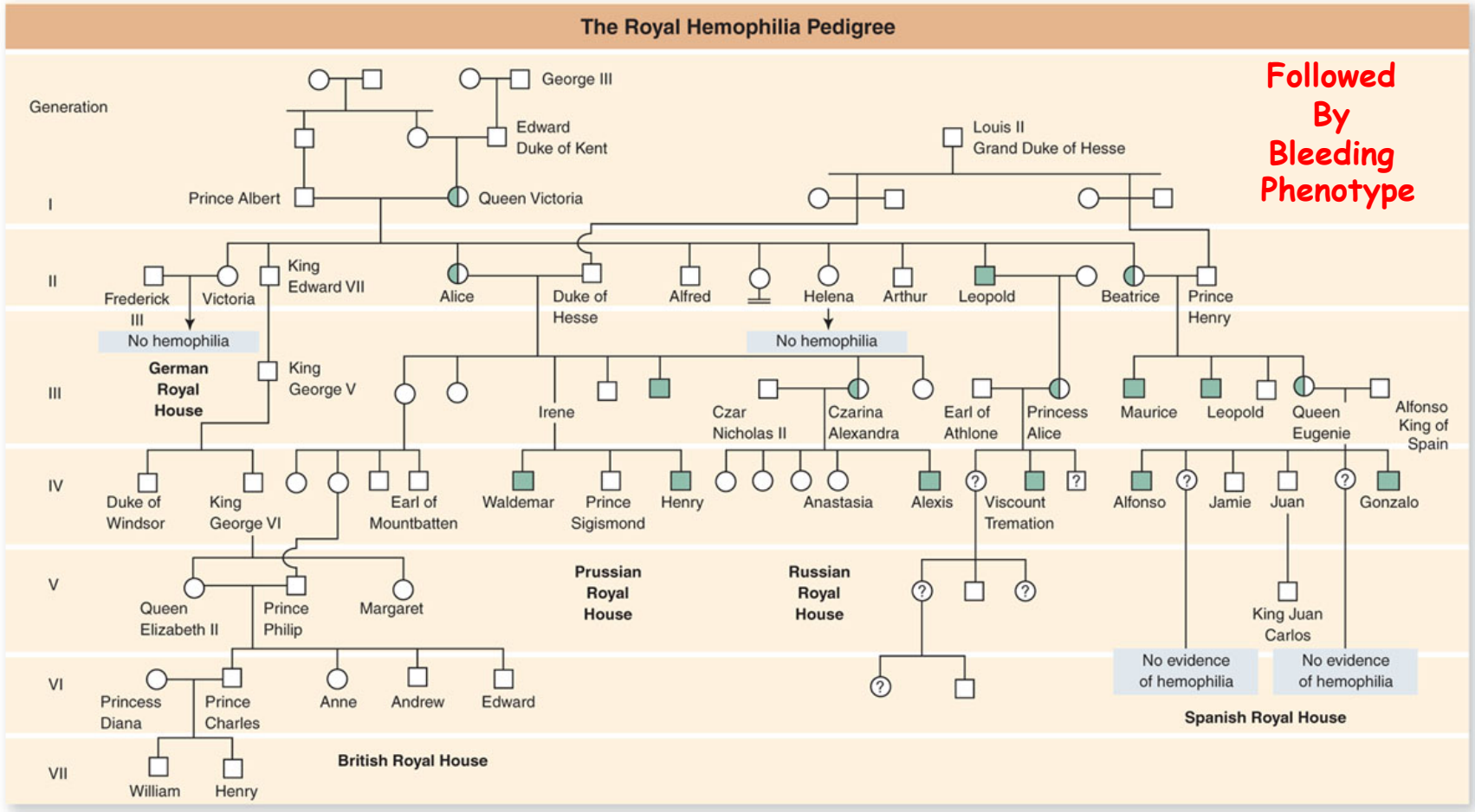


Figure 5-2
Molecular Cell Biology, Sixth Edition

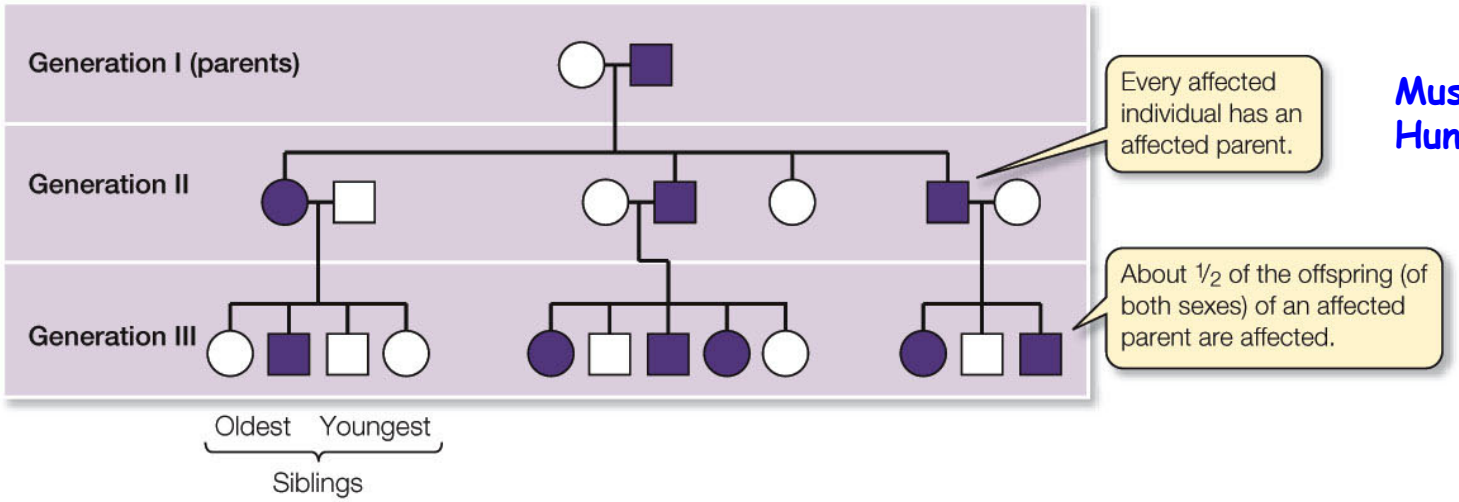
Pedigrees Can Be Used To Follow Disease Genes in Human Families



Pedigrees Can Be Used To Determine If a Trait is Dominant or Recessive

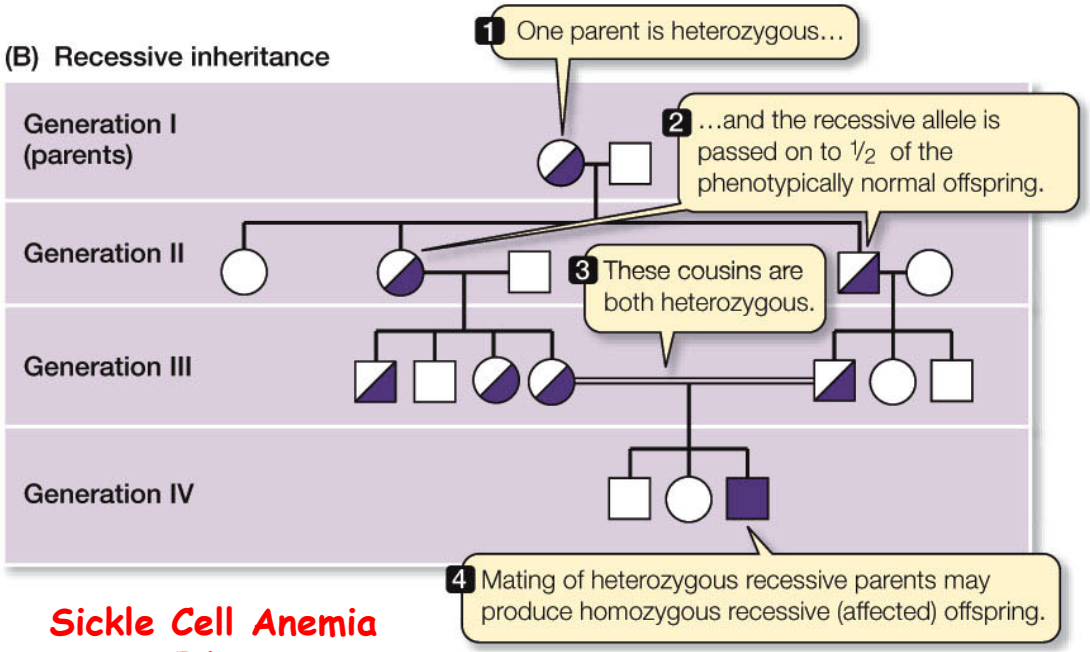
Each Type of Inheritance Predicts Specific Results in Each Generation

(A) Dominant inheritance

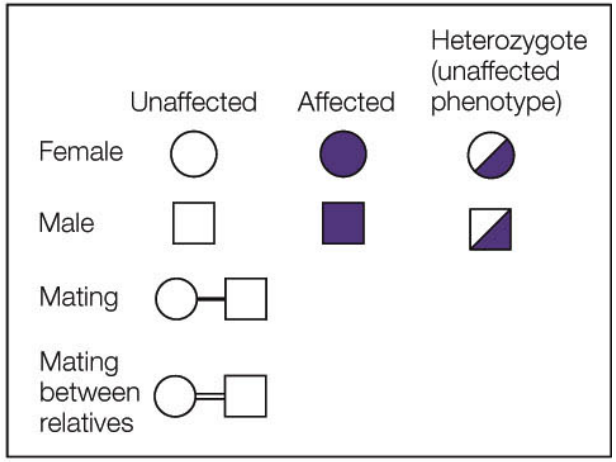


Muscular Dystrophy
Huntington Disease

(B) Recessive inheritance

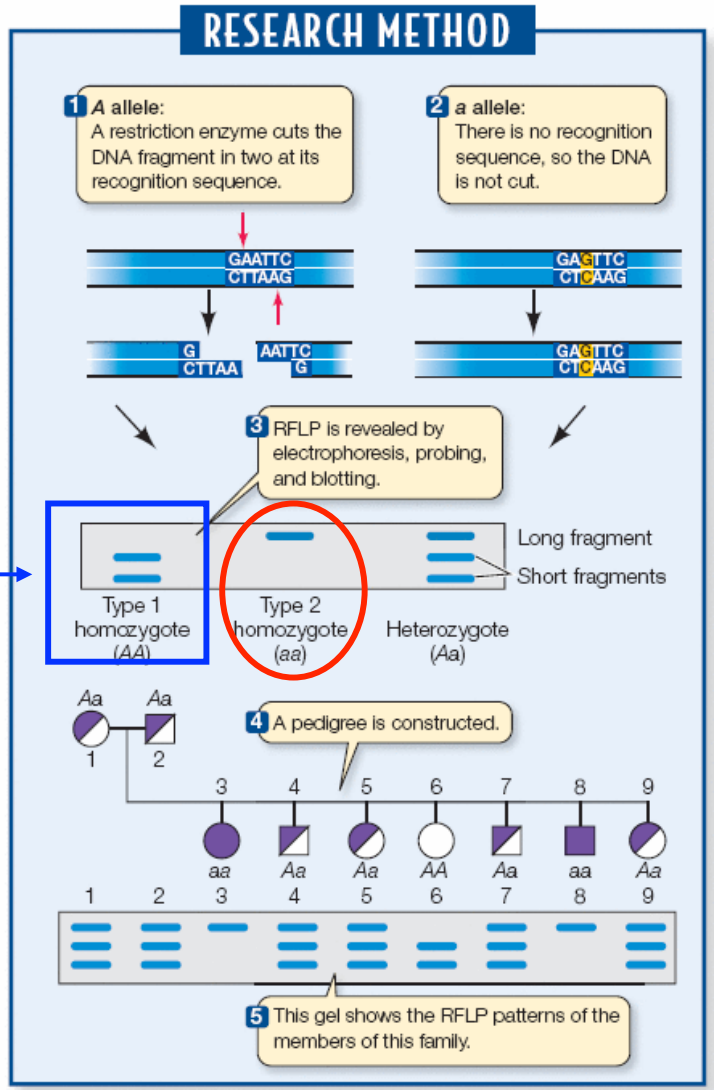


Sickle Cell Anemia
Cystic Fibrosis
Tay-Sachs Disease

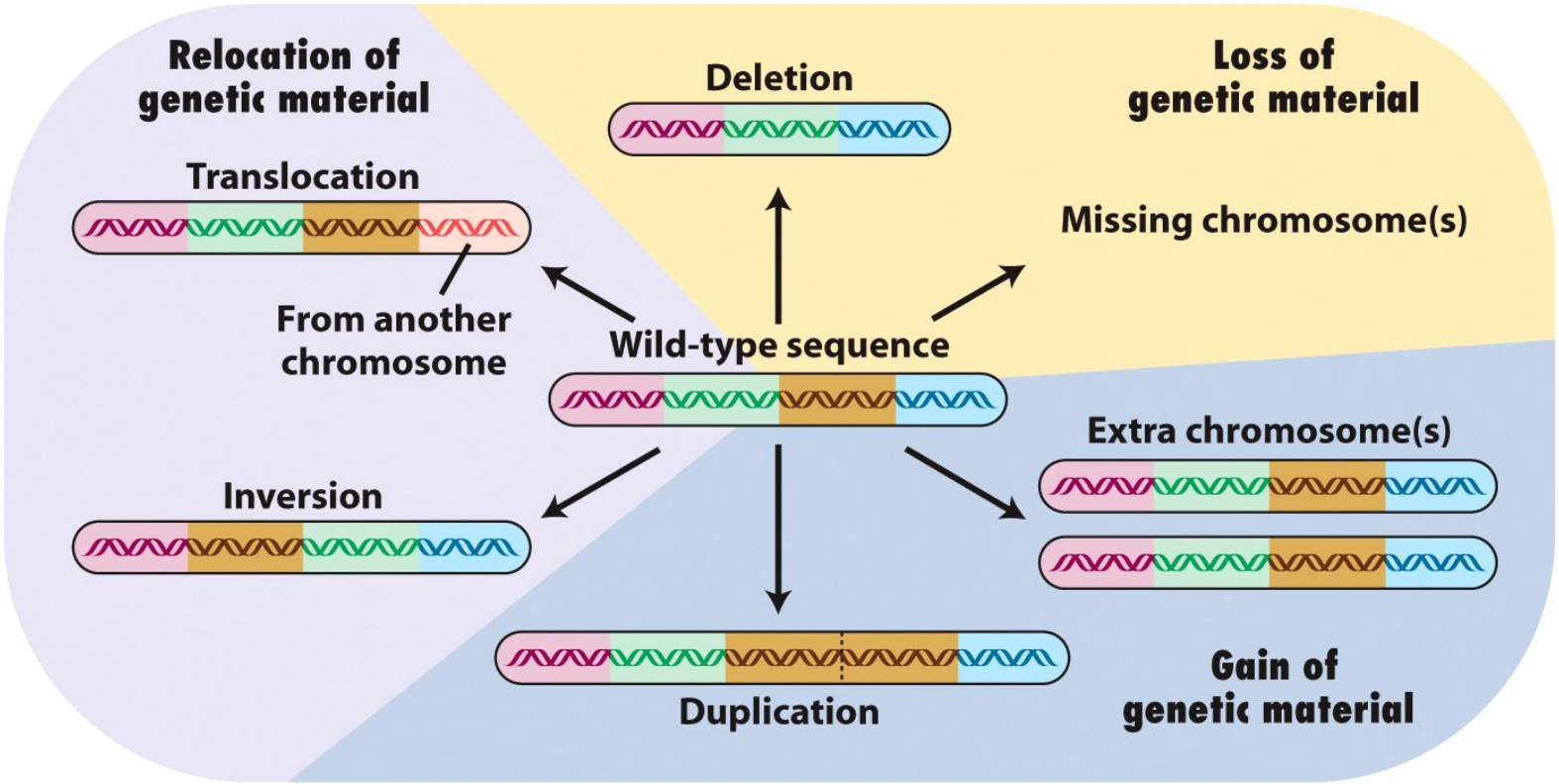


Genetic Diseases Can Be Followed in Families Using Molecular Methods (e.g., PCR)

DNA Fingerprints →



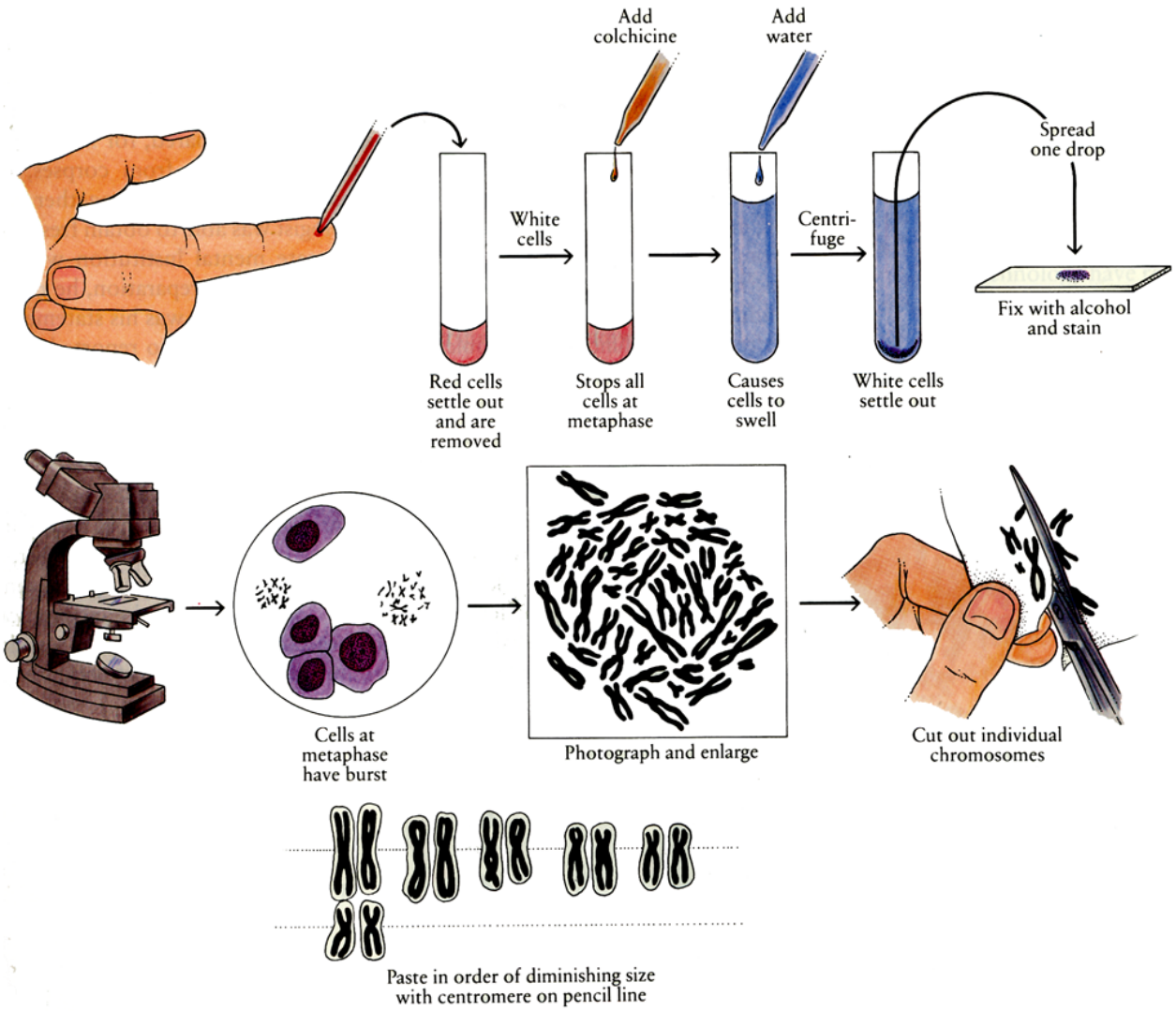
"Mutations" Can Also Occur By Large Chromosomal Changes



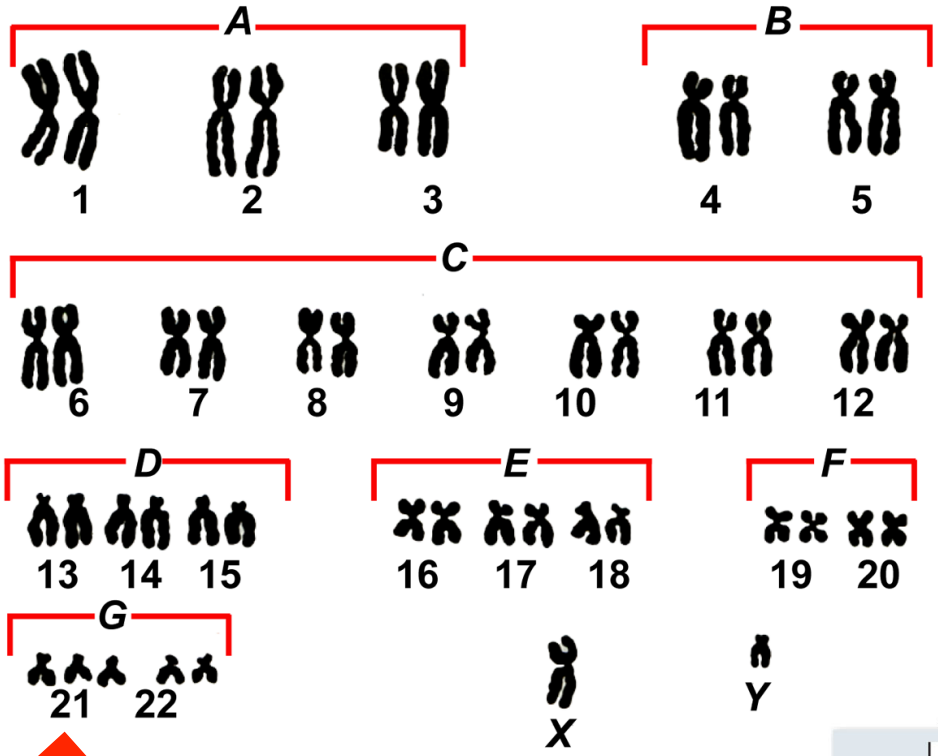
These changes affect many genes!

e.g. Down's Syndrome (3 Chromosome #21s)

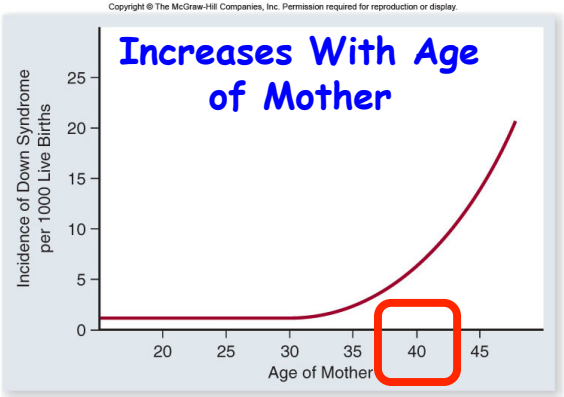
Karyotypes Can Be Used To Detect Changes in Chromosome Structure and Number



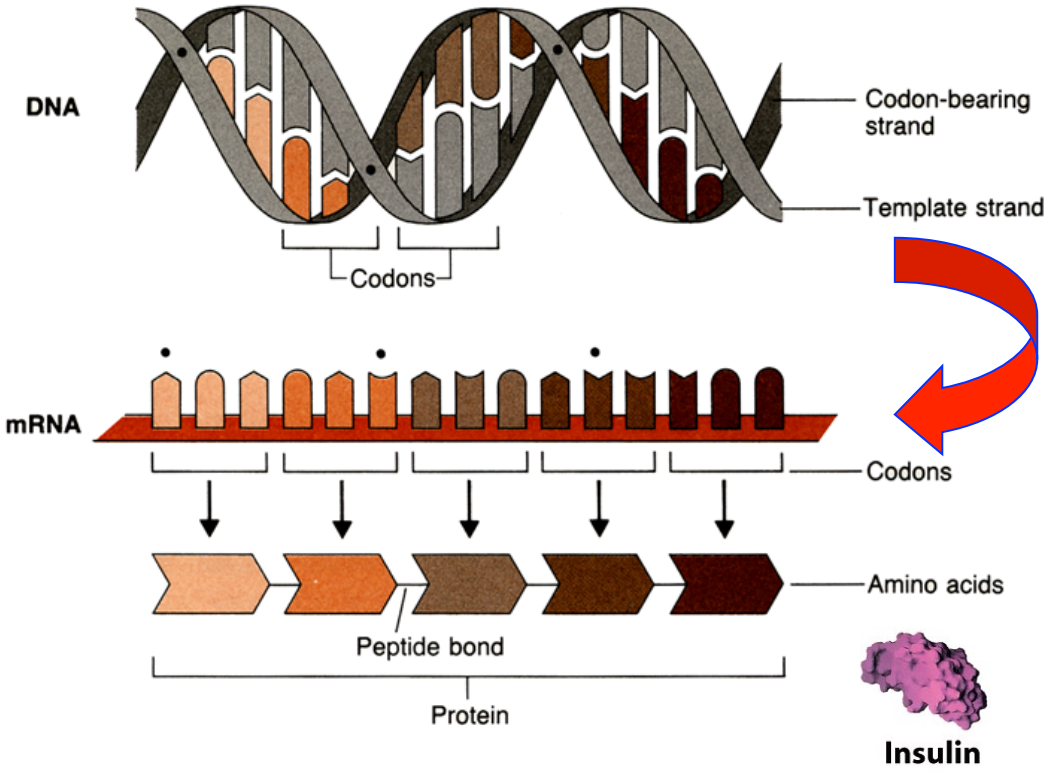
A Down's Syndrome Karyotype



Three Chromosome # 21s



How Does A Gene Lead To A Phenotype?



① mRNA Synthesized by Transcription

- Complementary to Transcribed, Non-Sense Strand
- Same Sequence As Sense Strand

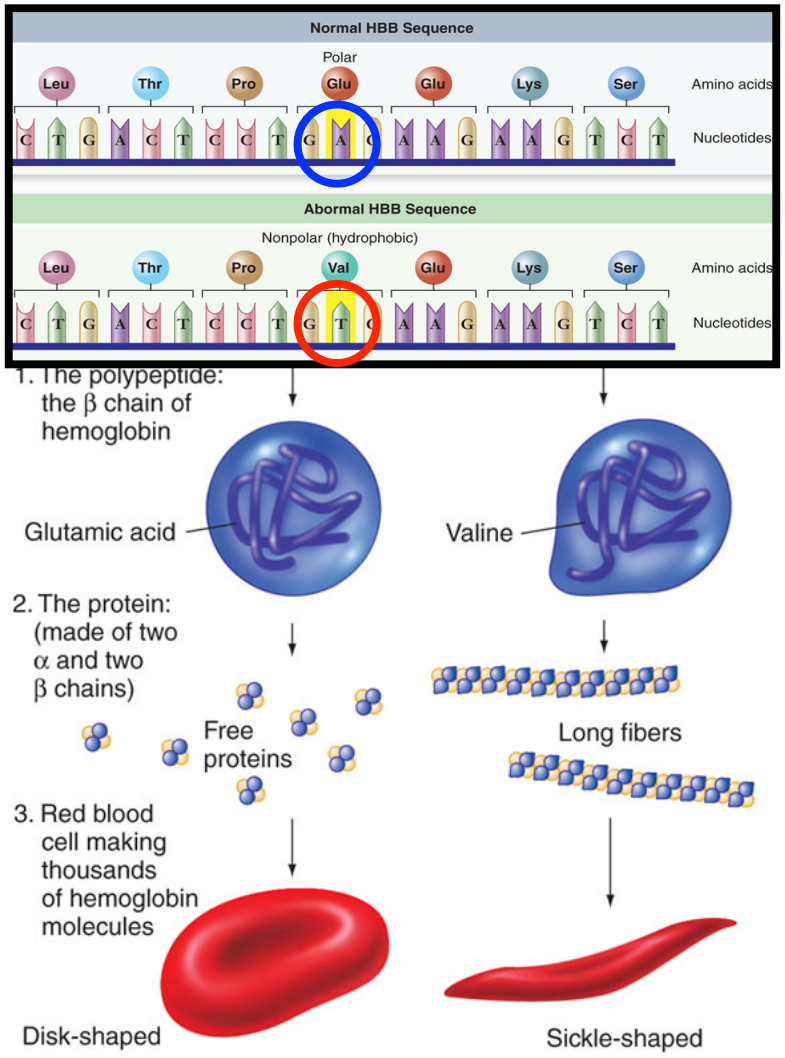
② MRNA Translated into Protein by Translation of The Genetic Code

Genetic Code on mRNA Translated to Protein Sequence

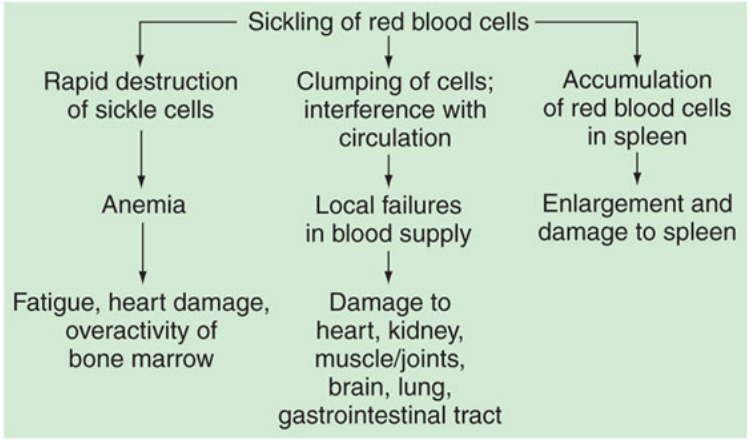
∴ Sequence of Gene
↓
Sequence of mRNA
↓
Sequence of Protein

Know Sequence
Know Protein
→ Engineer New Protein

Human Genetic Disorders Occur As A Result of Mutations



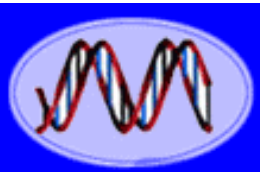
(b) Sickle-cell anemia is pleiotropic



(c) β-chain substitutions/variants

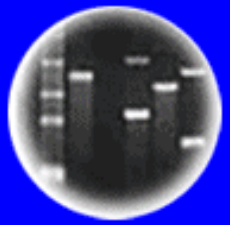
	Amino-acid position									
	1	2	3 … 6		7 … 26 … 63 … 67…125…146					
Normal (HbA)	Val	His	Leu	Glu	Glu	Glu	His	Val	Glu	His
HbS	Val	His	Leu	Val	Glu	Glu	His	Val	Glu	His
HbC	Val	His	Leu	Lys	Glu	Glu	His	Val	Glu	His
HbG San Jose	Val	His	Leu	Glu	Gly	Glu	His	Val	Glu	His
HbE	Val	His	Leu	Glu	Glu	Lys	His	Val	Glu	His
HbM Saskatoon	Val	His	Leu	Glu	Glu	Glu	Tyr	Val	Glu	His
Hb Zurich	Val	His	Leu	Glu	Glu	Glu	Arg	Val	Glu	His
HbM Milwaukee 1	Val	His	Leu	Glu	Glu	Glu	His	Glu	Glu	His
HbDβ Punjab	Val	His	Leu	Glu	Glu	Glu	His	Val	Gln	His

Sickle-Cell Anemia



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

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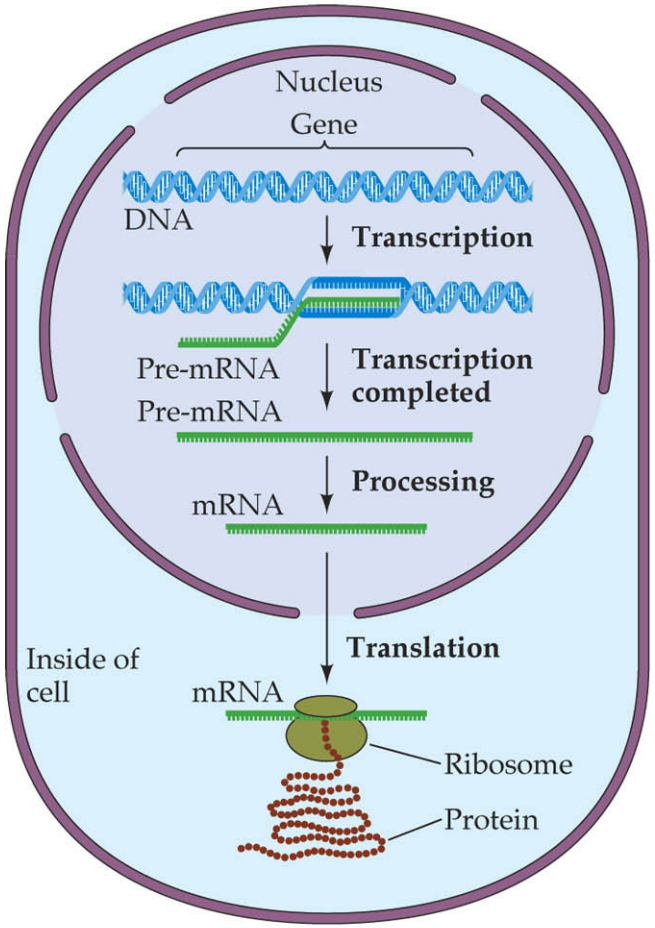
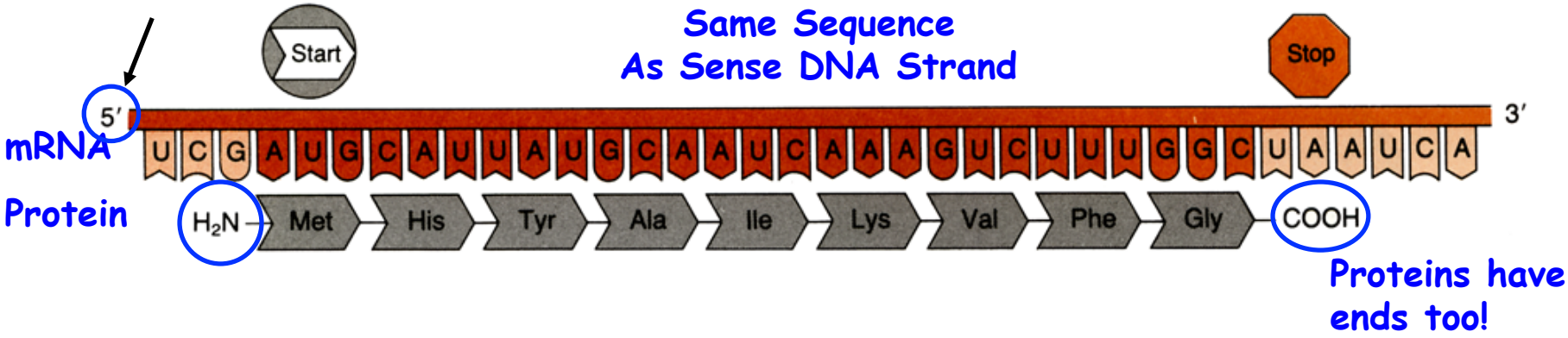
An Elaborate Cellular Machinery Requiring Thousands Of Genes is Required To Produce Proteins Encoded By Specific Genes!!



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 14.1 Eukaryotic mRNA Is Transcribed in the Nucleus but Translated in the Cytoplasm

It takes Genes to Express (and Replicate) A GENE!!!

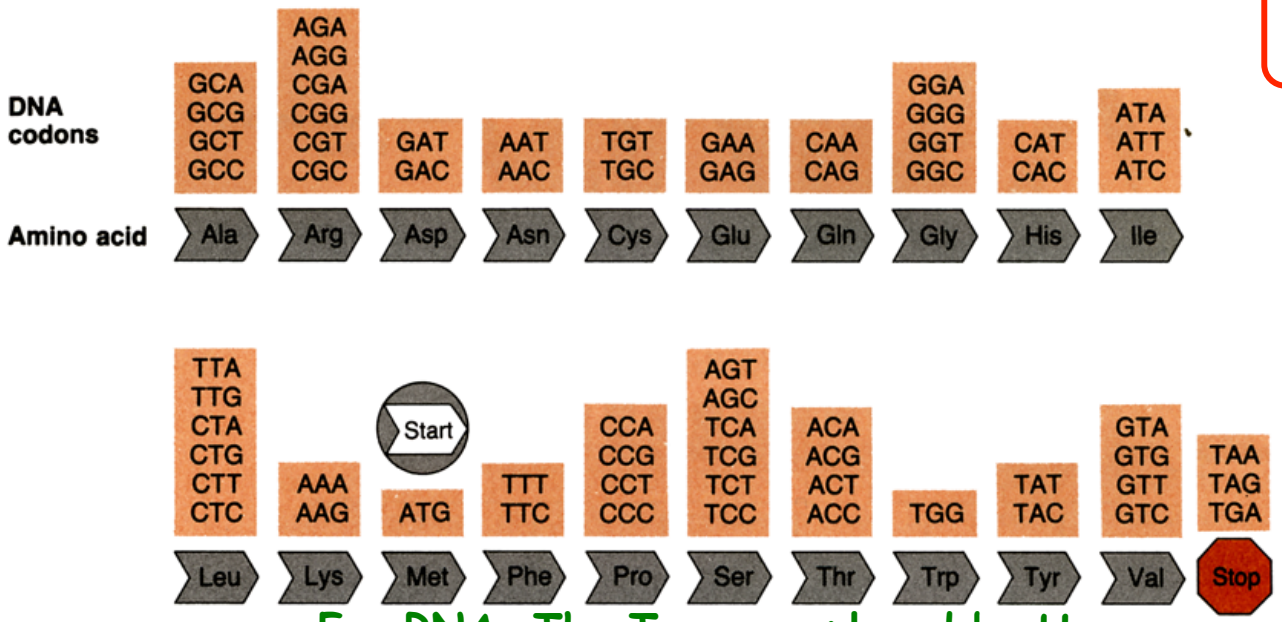
Genetic Code Allows The Sequence of Nucleotides in mRNA/ sense strand of Gene to be Translated into Sequence of Amino Acids in Proteins



Note: Sequence in mRNA (= Sense Gene Strand) is translated 5′→3′ (= beginning of sense strand to end) & Protein made in N→C direction therefore order Nts in gene = order amino acid in protein!

The Genetic Code is Universal!

How Know?



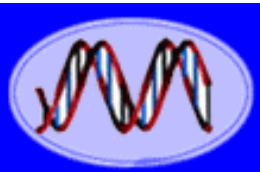
For RNA, The Ts are replaced by Us.

1. Universal
2. Triplet
3. Punctuation
4. Degenerate

Know Sequence of Gene-Know Sequence of Protein Using Genetic Code

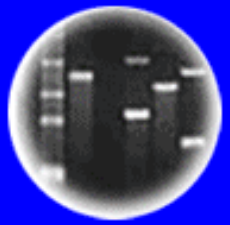
Big Implication For Genetic Engineering! Can Make Genes, Genomes & Specify Proteins Wanted! Can Express Genes From One Organism in Another!

Design An Experiment to Show Code is Universal!



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



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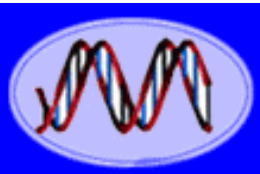
Expression of Jellyfish Green Fluorescence Protein (GFP) in Pigs Shows That Genetic Code is Universal!!



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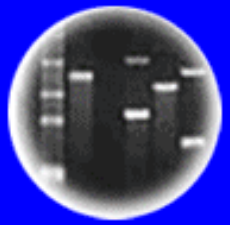

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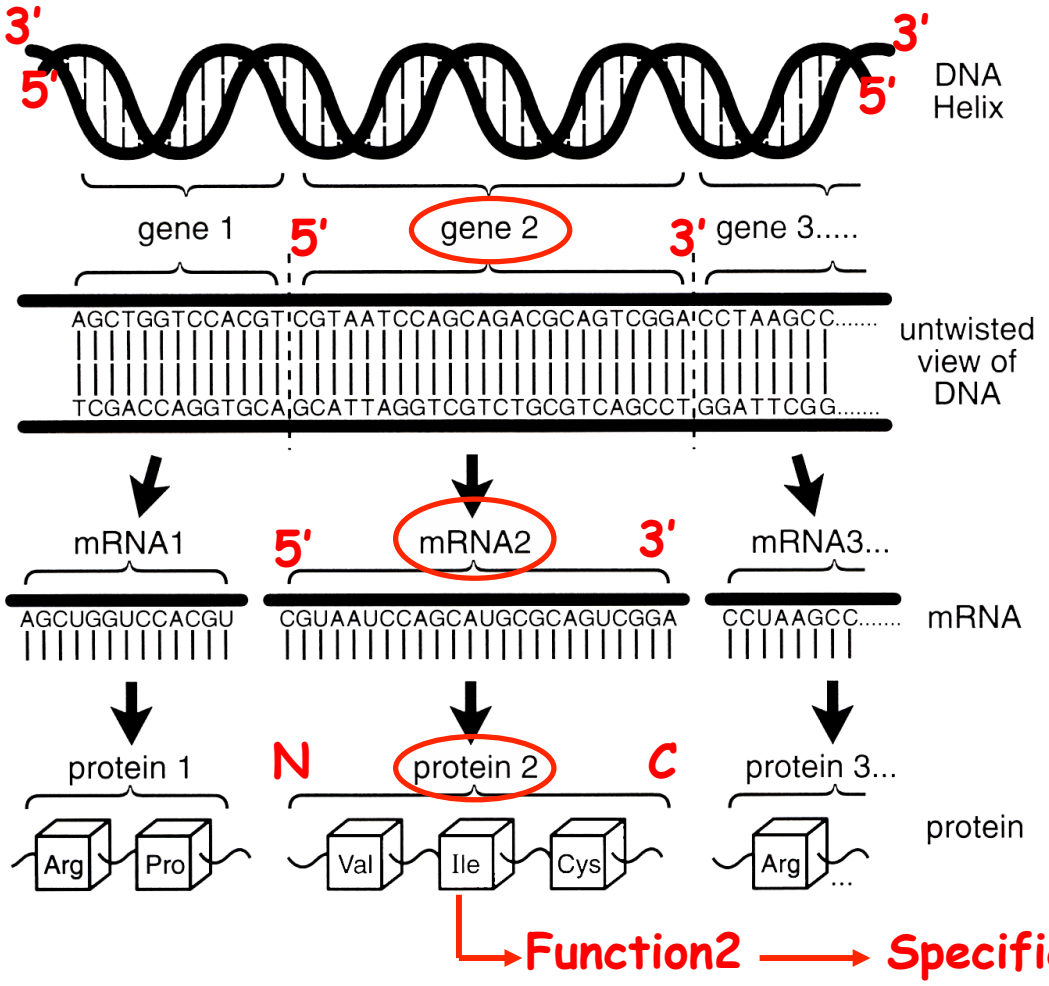
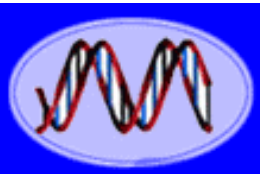
There is A Colinearity Between The DNA Sequence of A Gene & The Amino Acid Sequence of a Protein



Genes Function As Individual Units!



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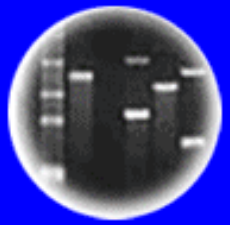

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Unique Proteins Have A Unique Composition & Order of Amino Acids & Have Unique Sizes, Shapes, & Functions

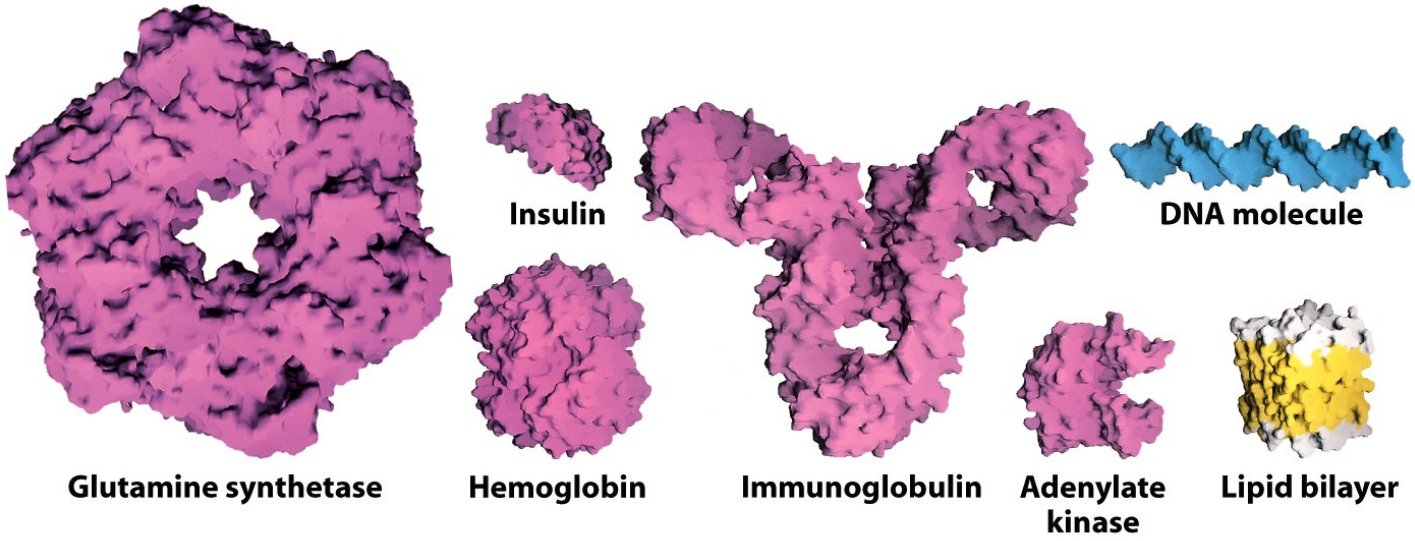
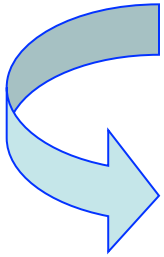
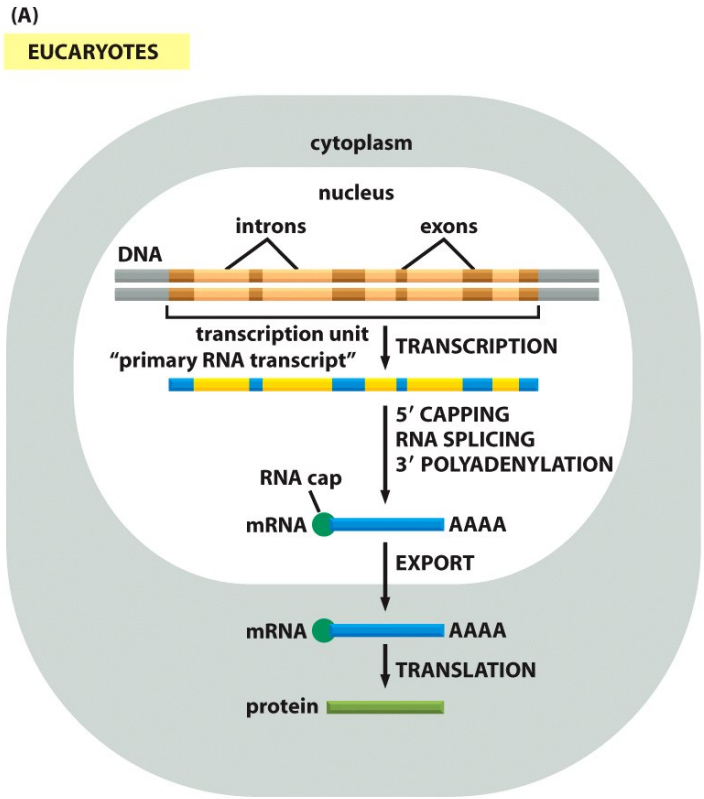


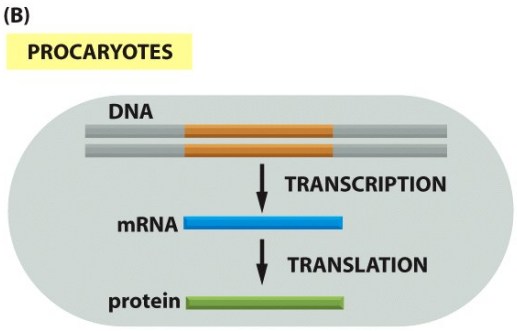
Figure 1-9
Molecular Cell Biology, Sixth Edition



Novel Cell Functions & Phenotypes

Eukaryotic and Prokaryotic Gene Expression Processes Differ Slightly

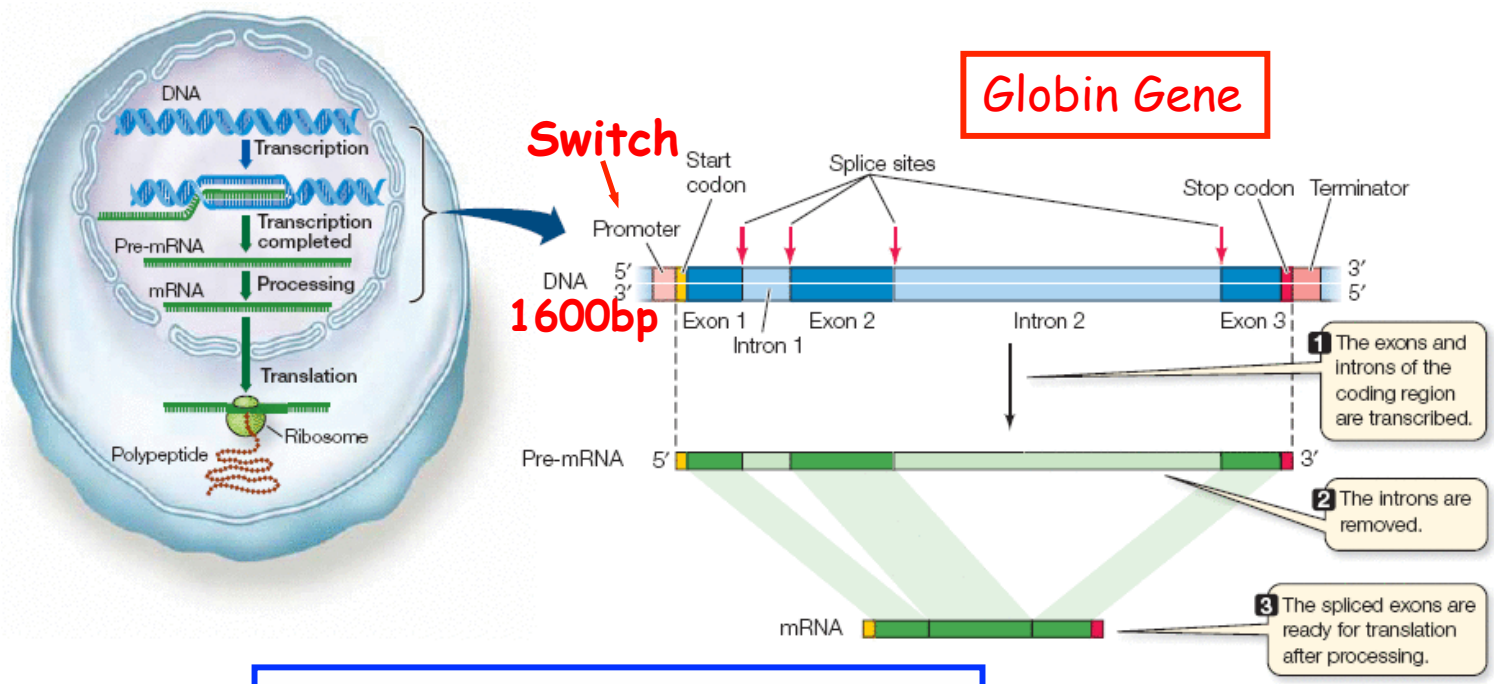




Genes Differ
Switches Differ
Genetic Code the Same
General Processes Same
Eukaryotic Gene Have Introns & Non-Coding Region in Gene!

Eukaryotic Cells Must Remove Non-Coding Region of RNA Before Genetic Code Can Be Translated Continuously!

RNA Splicing- Removing Non-Coding Sequences From Primary Transcripts & Generating Functional mRNAs



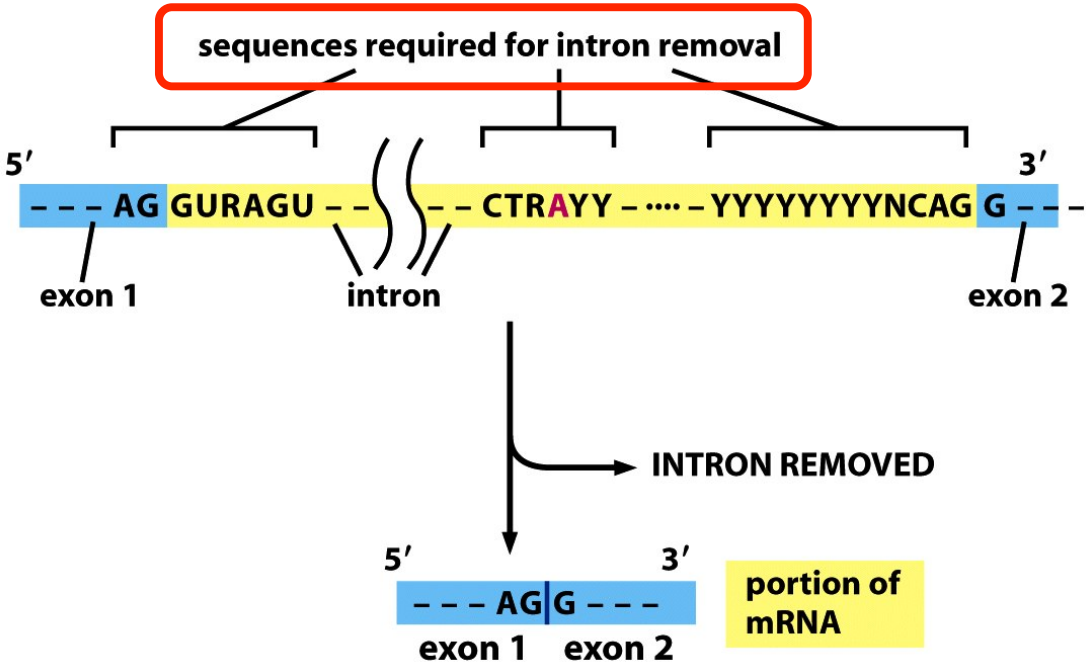
Mutations→ Blood Disorders
Where can these occur?

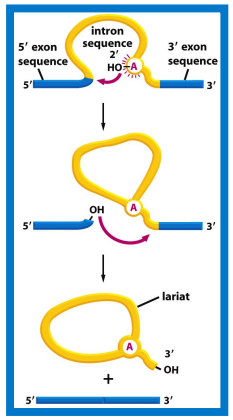
Mutations Can Occur in Coding Region, Switch, & RNA Splice Sites

→ **Mutant Phenotype**

Implications For Engineering Eukaryotic Gene in Bacterial Cell For Expression?

Yo! It's In The Sequences!

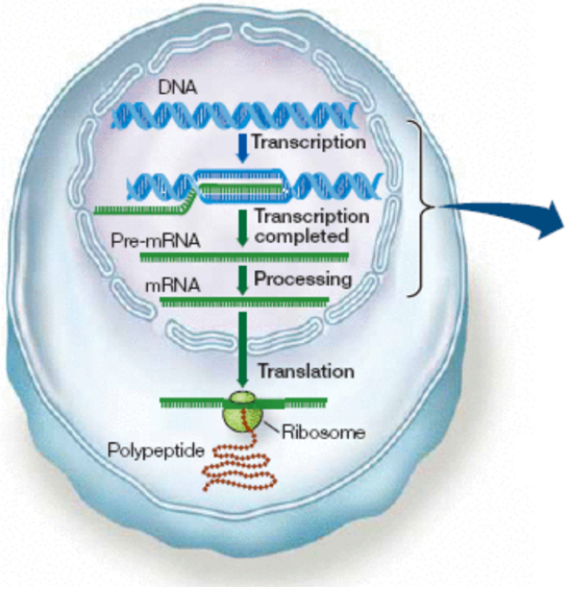




Specific Sequences Required For RNA Splicing!

What Happens If These Sequences Are Mutated in A Gene?

Alternative Splicing- One Gene → Several mRNAs & Proteins



Gene Activity in Varity of Cells, But…..!!!

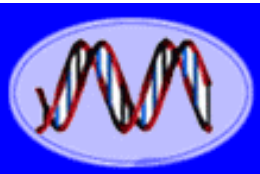
5 Different mRNAs!

Different mRNA = Different Proteins = Different Functions!

Implication- Human Genome Has Only 25,000 Genes But Can Give Rise to Many More Proteins which Are Responsible For Producing the Phenotype

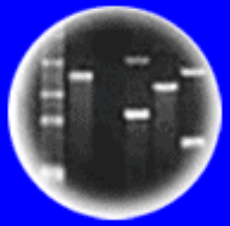
Reason Why Human Genome Can Contain Same Number of Genes as Fly and Plant Genomes!!

Implications for Genetic Engineering? Use Specific cDNA!



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues
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Implications For "Yo - Its in The DNA!!"

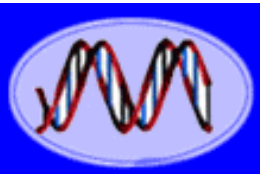
Modular Organization of Sequences

1. DNA Replication
   - Ori
2. Transcription
   - Switch/Regulator
   - Terminator
3. Processing of RNA (Eukaryotes)
   - Splicing Sites
4. Translation
   - Start
   - Stop
   - Genetic Code/Codons
5. Coding Sequence
   - Genetic Code

Modules → Anything You Want To Do Using Genetic Engineering!

The Modular Organization of Genes and Gene Finction Implies That There Are No Limits to How Genes Can Be Functionally Changed and Rearranged Using Genetic Engineering?

a. Yes
b. No



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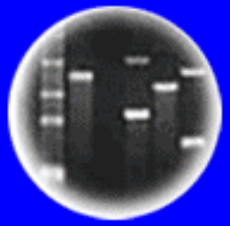

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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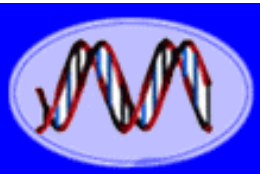
Engineering Genes Requires:

1. The Gene & Its DNA Sequences
2. A Roadmap of Where Coding Sequence & all Switches Located (Sequence, Restriction Site Map)
3. Transcription Start And Stop Switches
4. Coding Region of Gene (genetic code part)
5. Translation Start And Stop Switches
6. Kingdom-Specific Switches/ Signals

Note: The General Process of Gene→Protein is the same in ALL organisms, but the Specific Switches & Enzymes (e.g., RNA Polymerase) are Kingdom Specific

Bacteria Transcription On Switch + Human Insulin Coding Sequence + Bacteria Transcription Off Switch

→ Human Insulin in Bacteria!!



DNA
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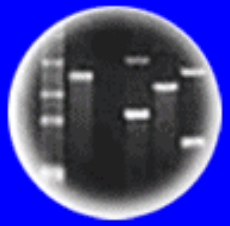

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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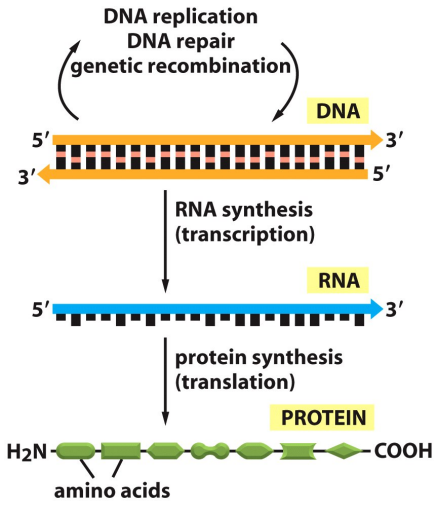
How Do Genes Work & What Are Genes In Context of…

Thinking About The Consequences of GMOs



1. What is a Gene?
2. What is the Anatomy of a gene?
3. How Does the Gene Replicate?
4. How Does the Gene Direct Synthesis of a Protein?
5. Does the Gene Work Independently of other Genes?
6. What is the Sequence & Structure of the Protein?
7. How does it work in cell?
8. Does the Protein Structure imply any Potential "Harm"?
9. Does the Gene Change the organism? Fitness?

Need Science-Based Questions & Science-Based Solutions-NOT OPINIONS!

There's NO HOCUS POCUS all hypothesis are testable!!

"Behind" All Traits!

Same Processes!