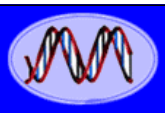
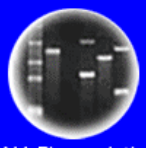


DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

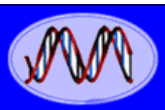
Plants of Tomorrow

HC70A, PLSS530, & SAS70A
Winter 2014
Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg,
Channapatna Prakash, & John Harada

Lecture 4
What Are Genes & How Do They Work: Part Two

UCLA TUSKEGEE UNIVERSITY UC DAVIS UNIVERSITY OF CALIFORNIA



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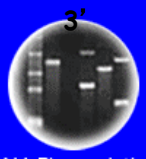

DNA Fingerprinting

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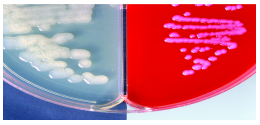
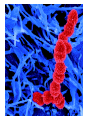
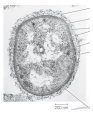
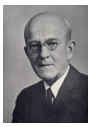
Last Tuesday's Lecture: What Are Genes & How Do They Function - Part One

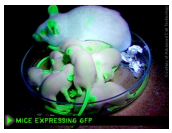
1. What Are the Properties of Genes?
   a) Replication
   b) Direct the Production of Traits
   c) Universality
   d) Stability
2. What is the Evidence For DNA Being the Genetic Material?
   a) Griffith Experiment
   b) Avery et al. Experment
   c) How Does the Avery Experiment Satisfy the Predictions of DNA as the Genetic Material?
3. Transformation Can Be Done Universally & Is the Foundation of Genetic Engineering
4. Structure of DNA
5. Demonstration
   a) Bacterial "Cloning"

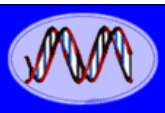












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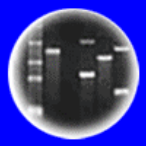

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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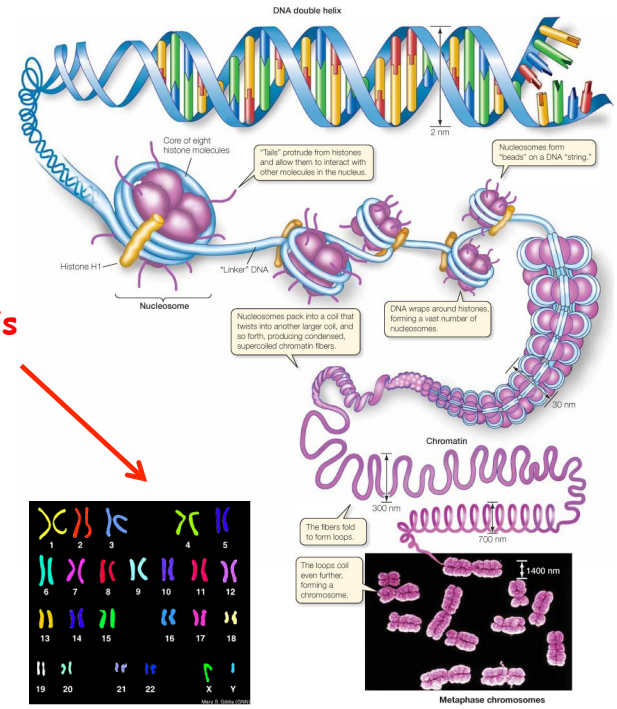
THEMES

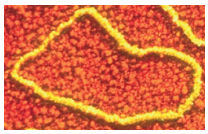
1. What is the Anatomy of a Gene?
2. How Are Genes Regulated - Switched On & Off?
3. How Does DNA Replication Occur?
4. What is the Polymerase Chain Reaction (PCR) and How is PCR used?
5. How Do Mutations Occur?
6. How Can Pedigrees Be Used To Follow the Inheritance of Mutant Genes?
7. How Do Mutations 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?

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

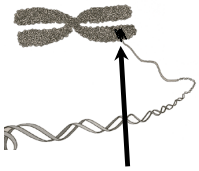
DNA in Human & Eukaryotic Chromosomes is Linear and Wrapped Around Proteins Called Histones!



DNA in Most Bacteria is Circular!



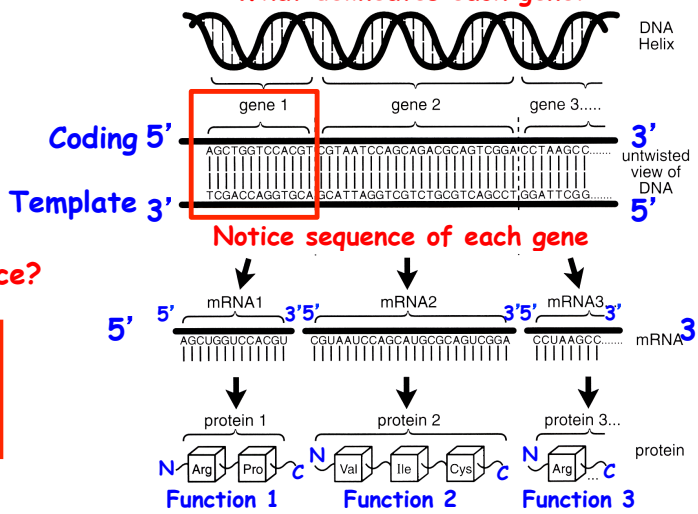
A Chromosome Contains Many Genes That Work As Individual Units (How Know?)



Position of Genes 1, 2, & 3 in chromosome

Discrete Units! Evidence?

What delineates each gene?



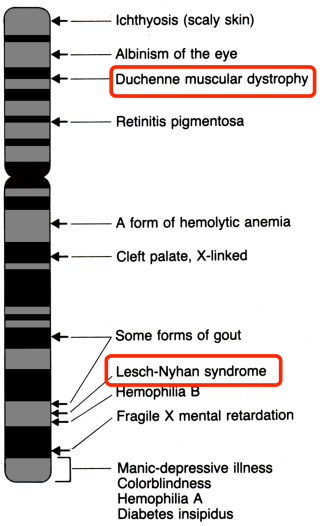
Notice- Each gene, mRNA, & protein has a unique order/ sequence of monomeric units

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

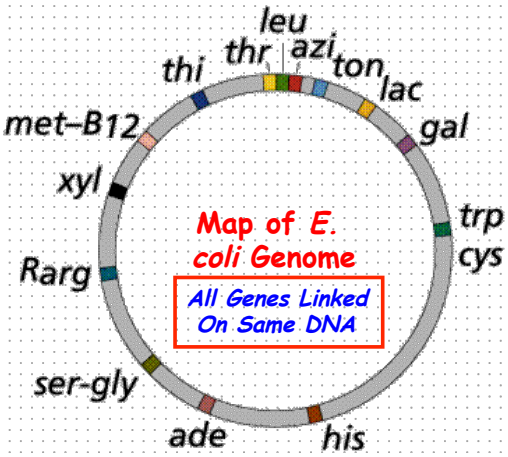
VERY IMPORTANT CONCEPT!
COLINEARITY BETWEEN GENE SEQUENCE AND PROTEIN SEQUENCE

Genes Reside at Specific Chromosomal Locations

All Genes Linked on Same Chromosome or Piece of DNA



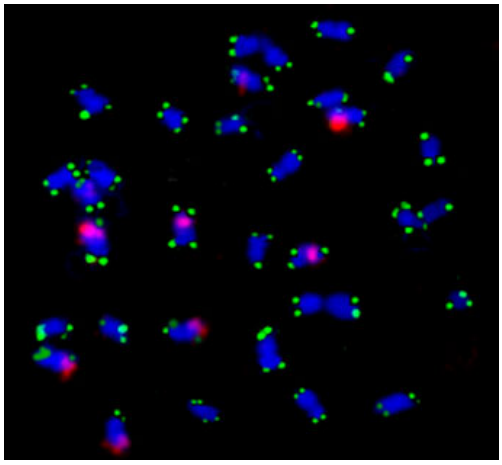
Linear DNA
How Know?



Circular DNA
How Know?

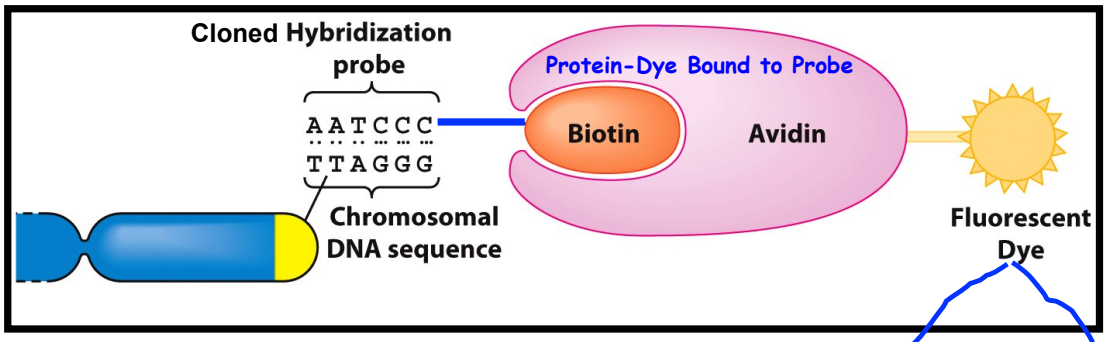
- Note Marker Bands - What are these?
- How Know Gene Positions? Chromosome Number?

Gene Loci Can Be Mapped and Visualized

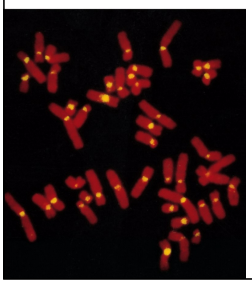


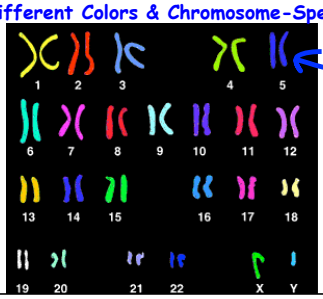
Gene Position = Locus = Unique DNA Sequence

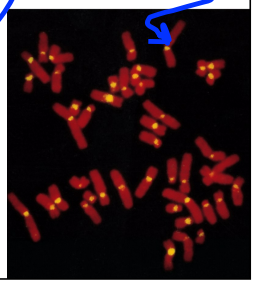
Visualization of Specific Gene Loci Using Fluorescence In Situ Hybridization (FISH)



Dyes of Different Colors & Chromosome-Specific Probes



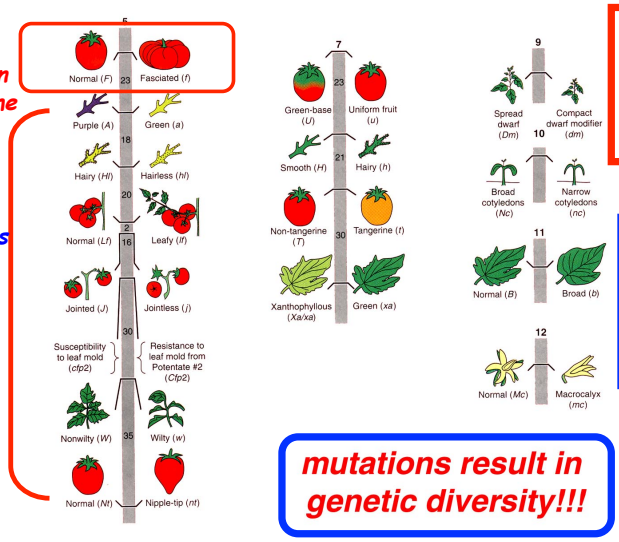




Alleles Are Different Forms of the Same Gene That Arise By Mutation & Can be Made in a Laboratory By Modern Genetic Engineering!

Different Alleles at Same Position on Chromosome (Many Alleles!)

Different Genes All Linked on One Chromosome



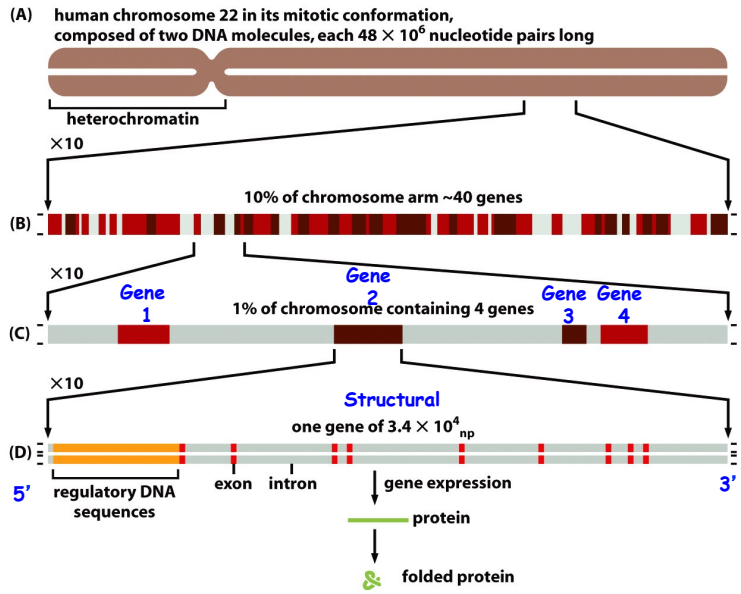
Gene Engineering Can Generate New Forms of Alleles of a Gene and, therefore, Results in More Genetic Diversity

Each Phenotype is a MARKER for the Allele & It's Position on the Chromosome Genetically!

mutations result in genetic diversity!!!

Alleles Reside at the Same Position on a Chromosome

Organization of Genes on Human Chromosome 22



Genes Are Defined/ Precise Regions of DNA

One Large Gene!

Genes Act As Individual Units?
How Know? Design an Experiment!!

A Conceptualized Gene

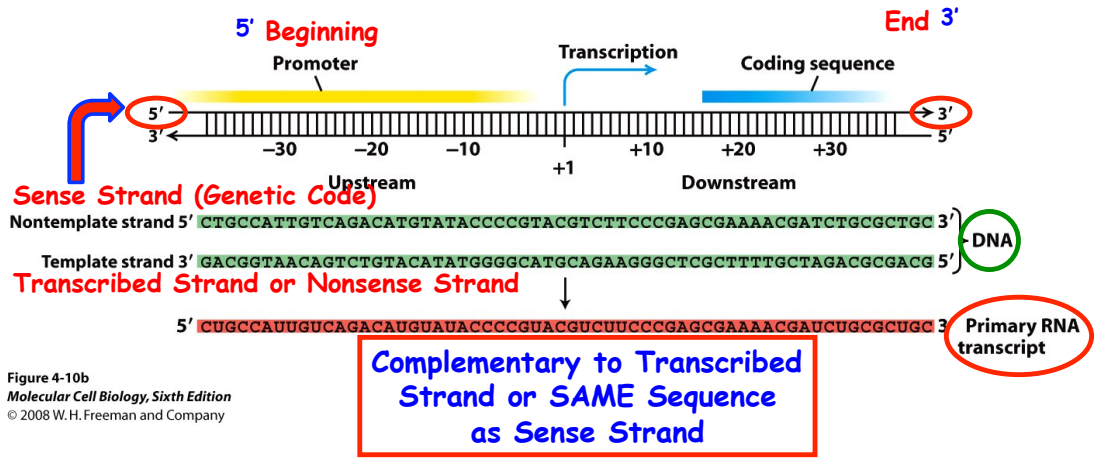
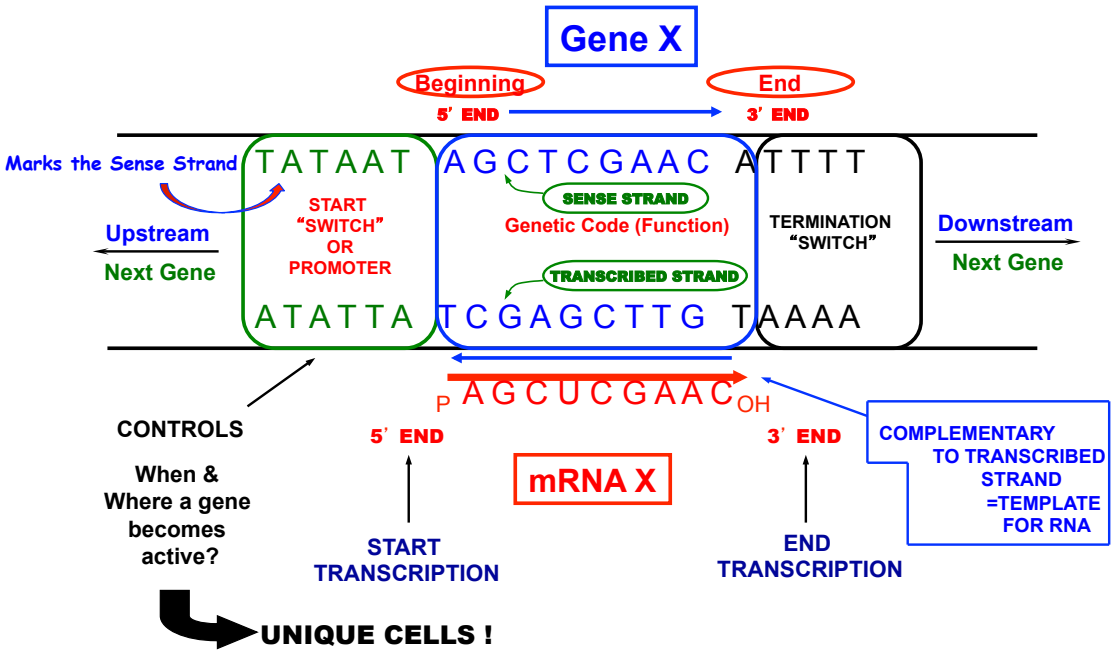


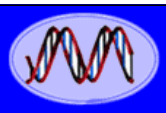
Figure 4-10b
Molecular Cell Biology, Sixth Edition

Only Know the Structure of a Gene *Because of the Invention of Recombinant DNA Technology* – Why?

The Detailed Anatomy of a Gene



Note: mRNA Sequence = Sense Strand Sequence



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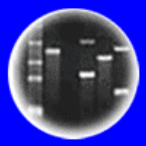
Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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"Simple" Gene Anatomy Reviewed

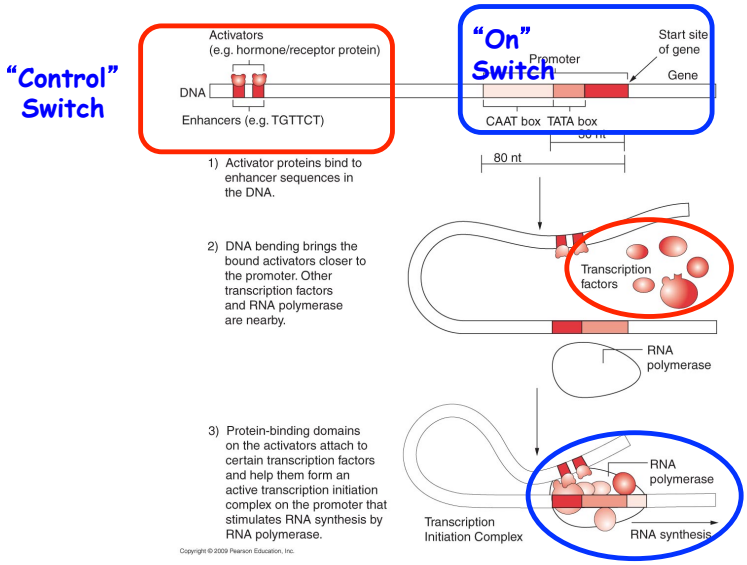
1. Sense Strand = Genetic Code
2. Sense Strand = 5' → 3' Direction (all DNA sequences specified 5' → 3')
3. Anti-Sense Strand = Complement of Sense Strand & is Transcribed Strand
4. mRNA = Same Sequence As Sense Strand & Complementary to Antisense Strand
5. mRNA = 5' → 3'
6. Switch Turns Gene On - Not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

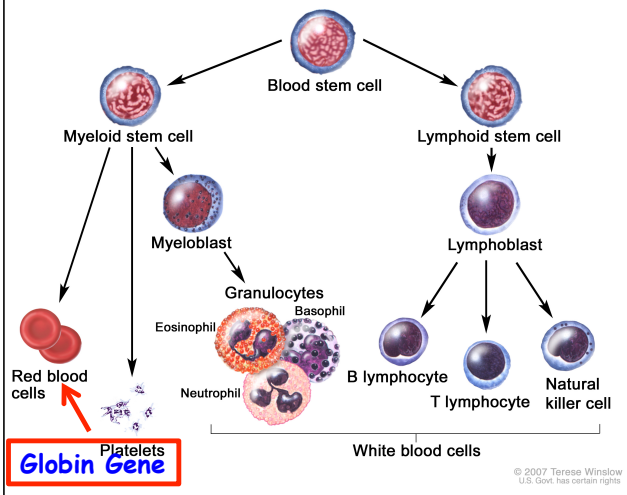
Control Switches Are Unique DNA Sequences & Can Be Cloned

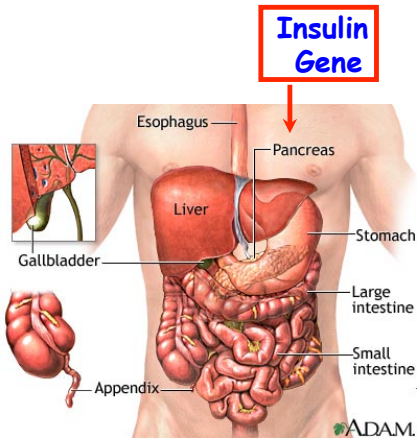
AND used to Re-Engineer Organisms!! Switches Act Independently of Gene!!



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





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.

   GFP Gene + Plant Leaf Switch
   Bacterial Switch + Human Insulin cDNA

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

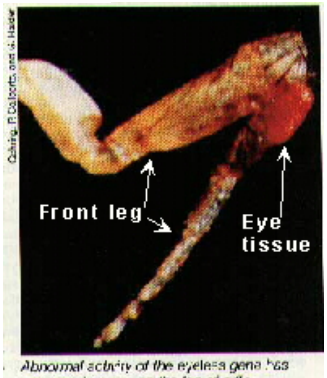
Yo! It's in the Sequences!!

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

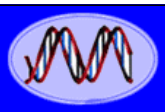
Eye Gene

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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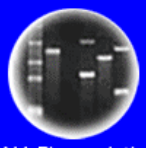

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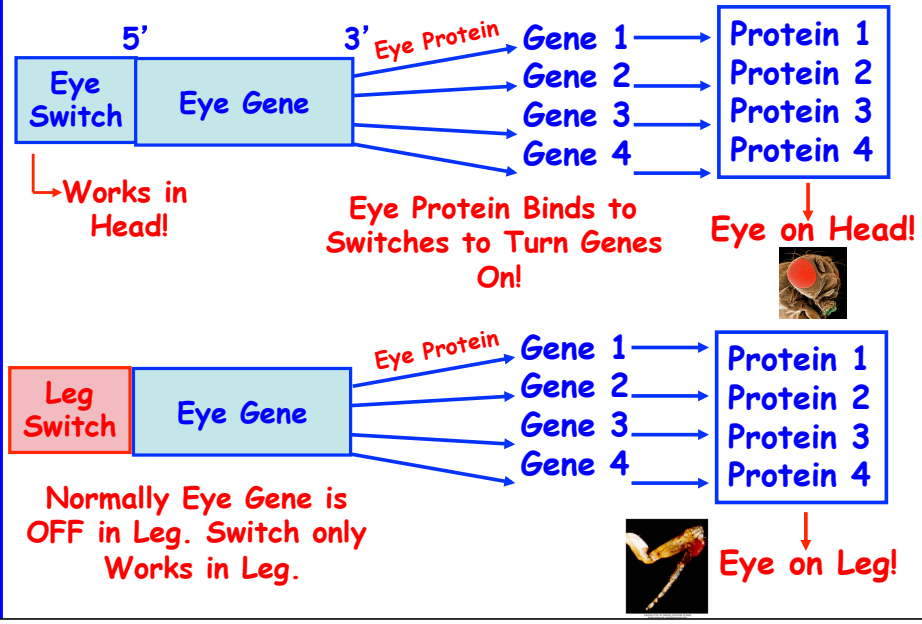
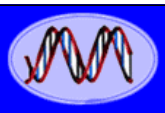
Eye Genetic Regulatory Network (GRN) – *Engineering Body Architecture*

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





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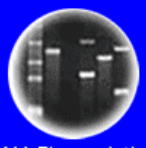

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Cloning: Ethical Issues and Future Consequences

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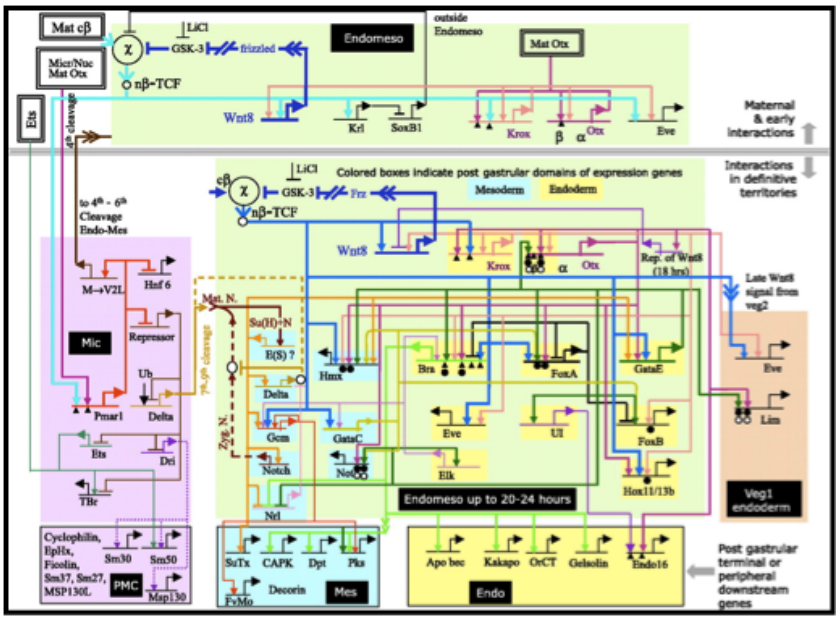
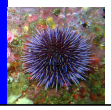
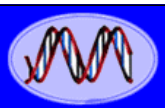
Ultimate Goal: To Dissect Genetic Regulatory Networks Programming Human Development From Birth to Death!





Genetic Networks Programming Early Sea Urchin Development



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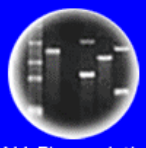

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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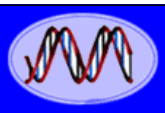
If We Understand How Genes Are Choreographed & All the Sequences That Program them

IMMORTALITY?

YES
NO



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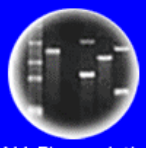

DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

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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?

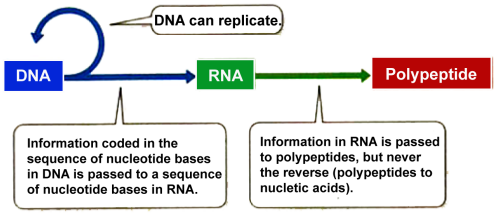
We Will Know at the DNA Level What Biological Information Programs Life to Death!

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!

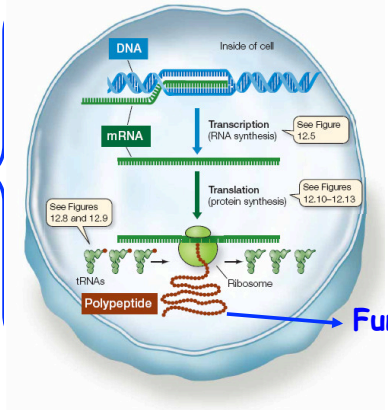
How Do Genes Work-A Review

① Replication



② Gene Activity to Function & Phenotype

Gene Activity
↓
Protein
↓
Function
↓
Phenotype (Trait)

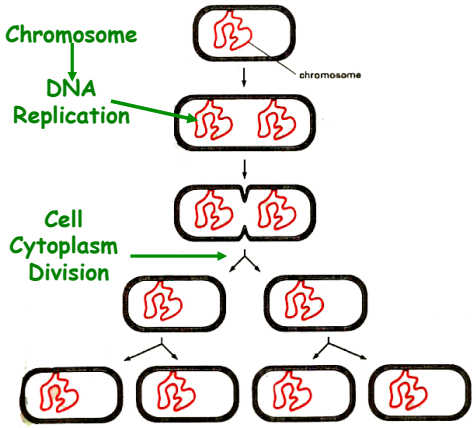


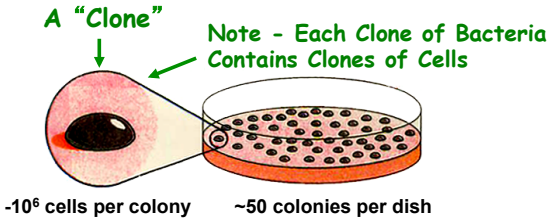
Function →

A Gene is NOT Expressed Unless A Functional Protein Produced!

1

How Are Genes Replicated Each Cell Generation? (Text Pages 40-43)





Clones

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

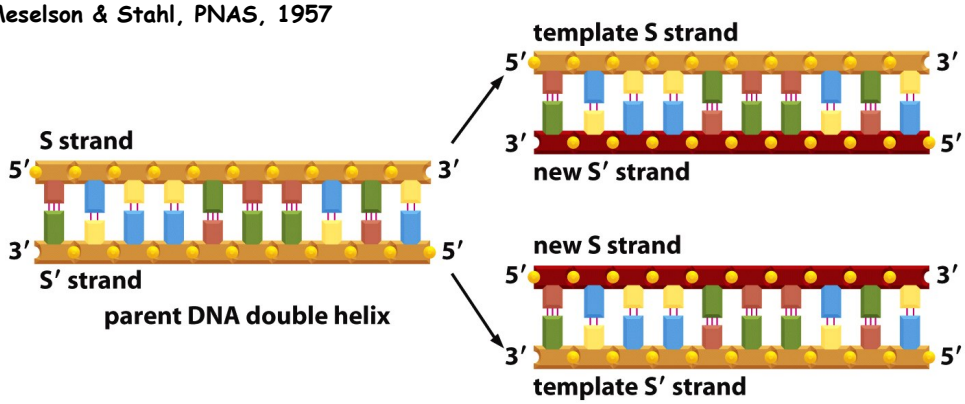
Each Daughter Cell Contains The Same Collection of Genes

Clones!

Major Properties of Genetic Material
Replication, Stability, & All Cells!!

DNA Replication Occurs Semi-Conservatively

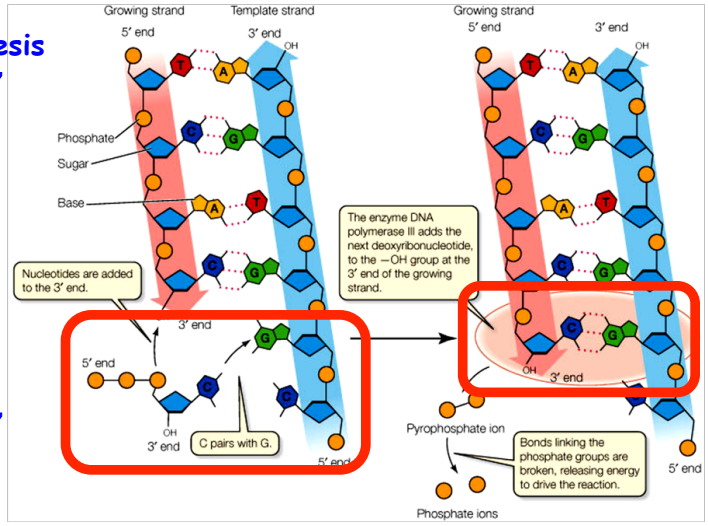
Meselson & Stahl, PNAS, 1957



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

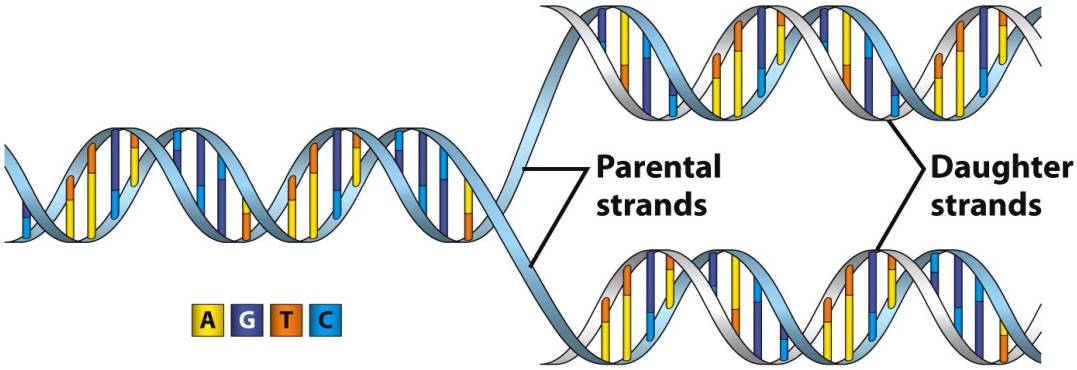
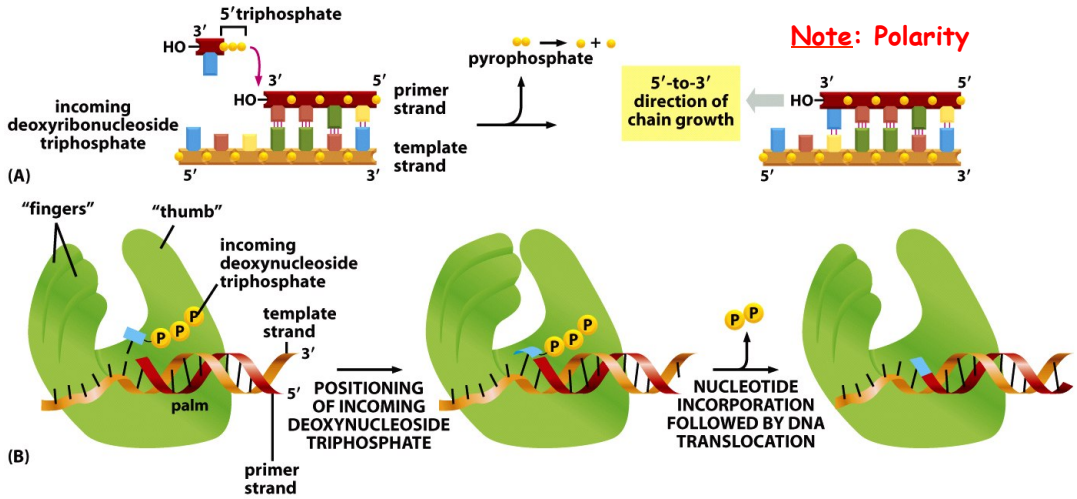


Figure 1-10
Molecular Cell Biology, Sixth Edition

The DNA Sequence "Lives" Forever!

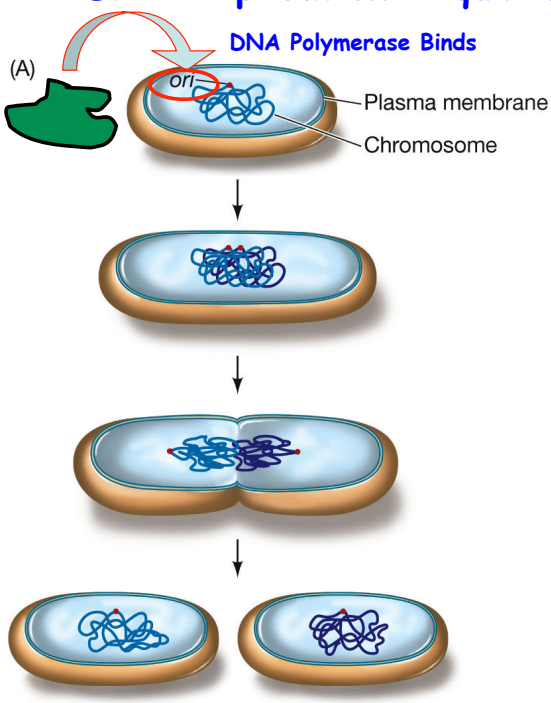
DNA Replication Requires An Enzyme - DNA Polymerase

Note: Nucleotide, Primer, & Template

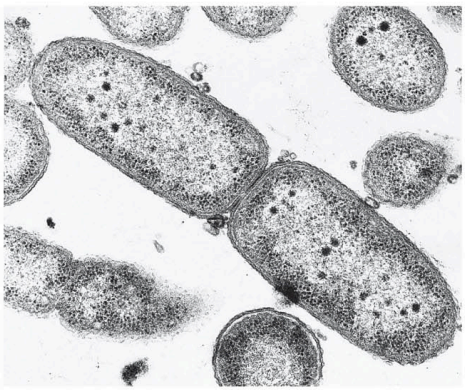


1. DNA Polymerase Catalyzes 3'-5' Phosphodiester Bonds & Copies the Template
2. DNA Replication Needs a Primer, Template, DNA Polymerase,& Nucleotides

DNA Replication Requires An Origin of Replication



Two IDENTICAL Cells - Phenotypically & Genotypically - From One



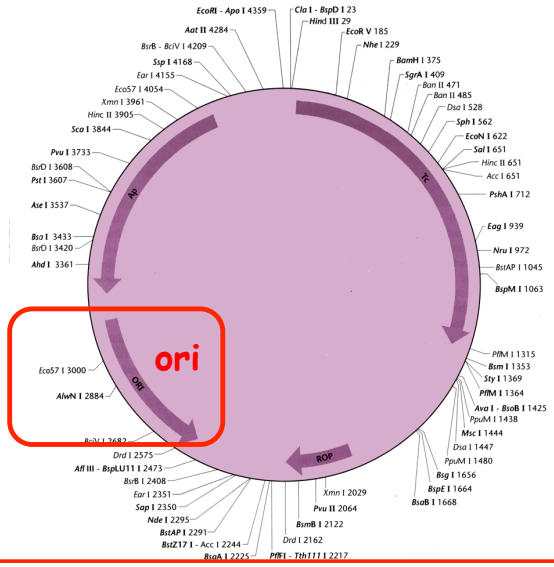
DNA Replication Also Requires:

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

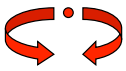
Ori

DNA Replication Starts at The Origin of Replication



DNA Replication is Bidirectional From the Ori!!!

Ori

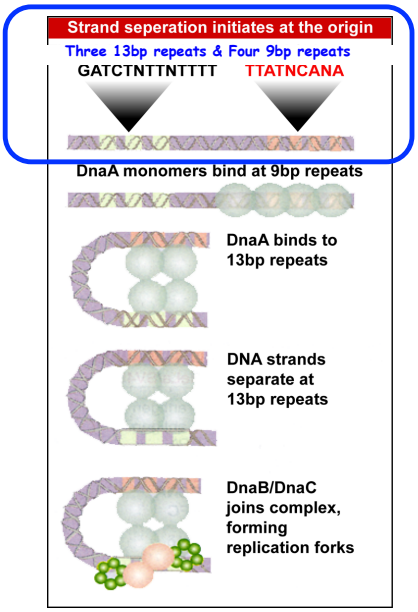


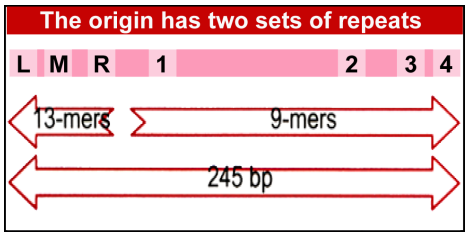
Hypothesis For Two Direction Synthesis?

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

How Control Division?

The Origin of Replication is a Specific Sequence



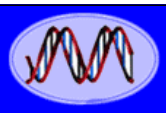


1. How Clone An Origin of Replication?

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

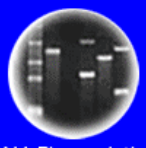
3. What is The Significance For Genetic Engineering?

4. Can Replicating "Chromosomes" Be Made?



DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

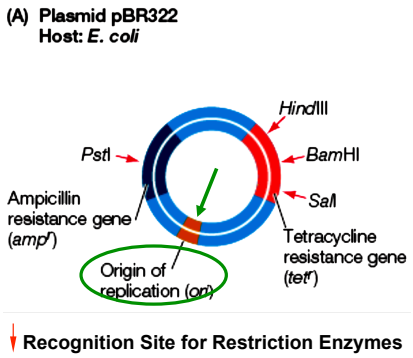


DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Vectors Are Needed To Replicate Genes In Transformed Cells



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 to replicate a bacterial gene in human cells.

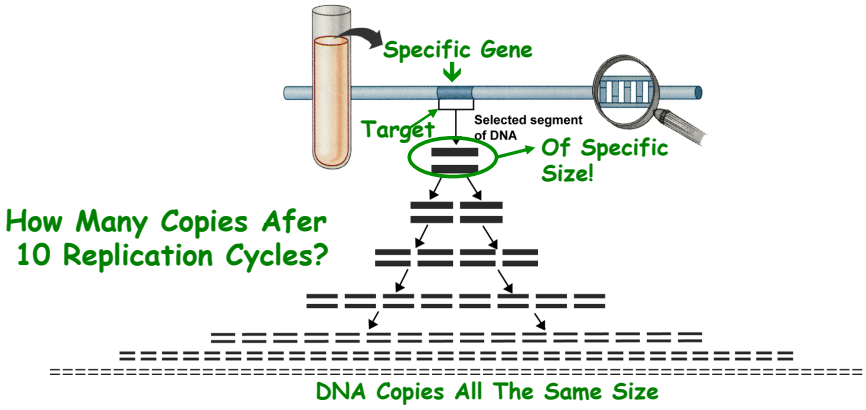
Yo! It's in the Sequence= Function

∴ Vectors can be Engineered!

Ori's can be cloned/synthesized!

MODULAR!!

The Polymerase Chain Reaction or PCR is A Molecular Xerox Machine

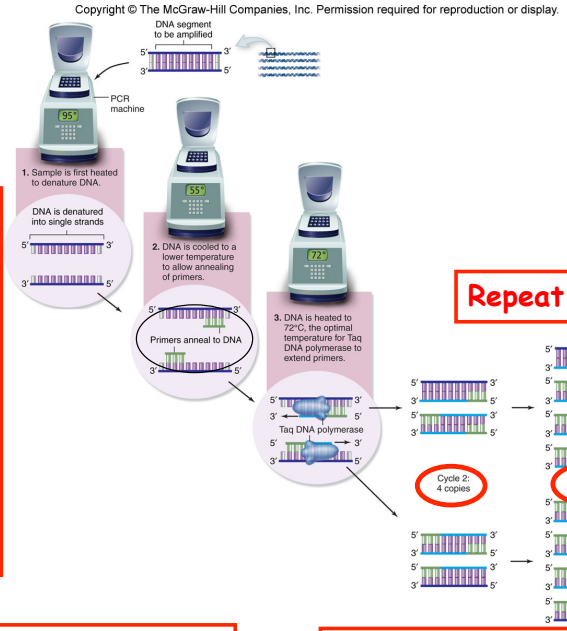


1. PCR Has Revolutionized DNA Analysis!
Specific DNA Sequences/Genes Can Be "Copied" Directly From "Tiny" Amount of DNA!

2. No Cloning Needed!

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

PCR is A Cyclical Process of DNA Replication



Requires

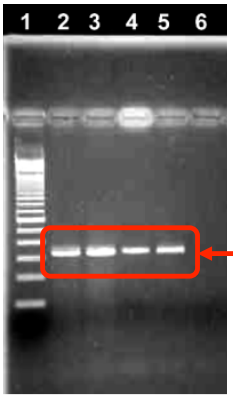
1. Template
2. Primers
3. Knowledge of Specific Sequence
4. Nucleotides
5. Heat-Stable DNA Polymerase
6. Cycler

Repeat Steps or Cycle

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

Diagnostic For Amplified DNA Sequence (Between Primers) → DNA Fragments All The Same Size Primer-Sequence-Primer

Using Gel Electrophoresis to Visualize PCR Products



Specific Diagnostic DNA Band Unique to DNA Sequence Being Amplified

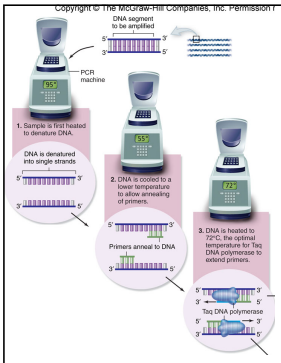
- Target-Specific Band
- Diagnostic For Specific DNA Sequence
- Band Size Unique For Specific Sequence
- Primers "Surround" the Target Sequence

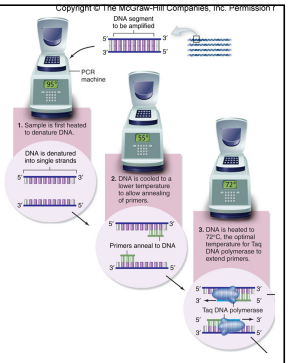
Can Amplify One DNA Sequence From An Entire Genome *or an Entire Genome*!!!

Requirements For PCR

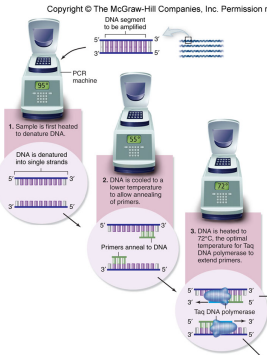
1. Knowledge of a Specific Sequence to Amplify (e.g.,insulin gene)
   a) Must Have First Cloned & Sequenced DNA of Interest the "Old-fashioned Way"
2. Primers That Recognize Specific DNA Sequences & Initiate DNA Synthesis & DNA Polymerase Binding To Template
3. Template (e.g., DNA From Human Cheek Cell)
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

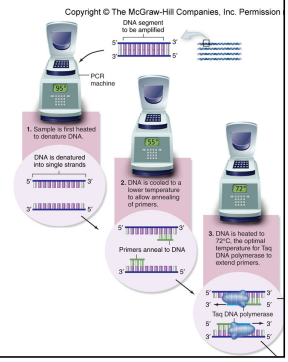
It's All in the DNA Sequences -- Know Sequence & Can Synthesize an Infinite Amount of Specific DNA Sequences.
It know Takes One Hour To Do What Used to Take YEARS!



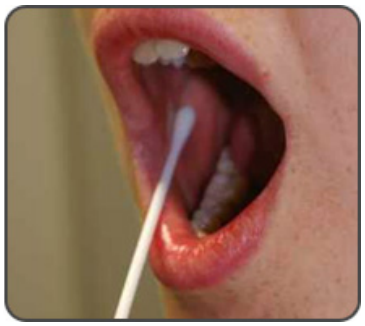


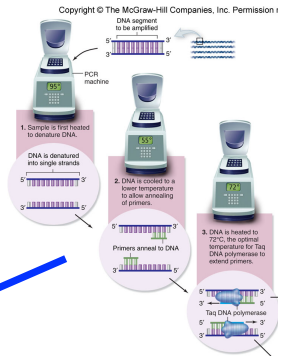
Examples of PCR Applications



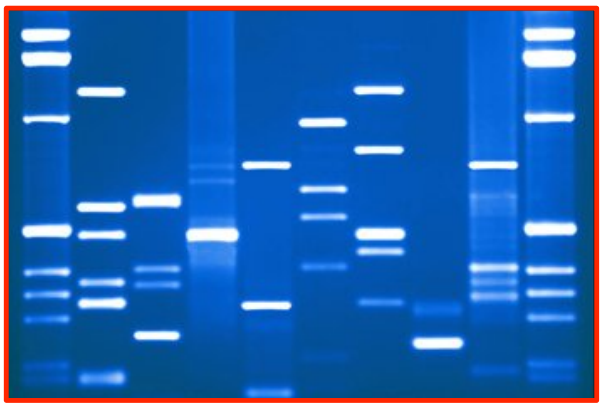


Using PCR to Determine Your DNA Fingerprint

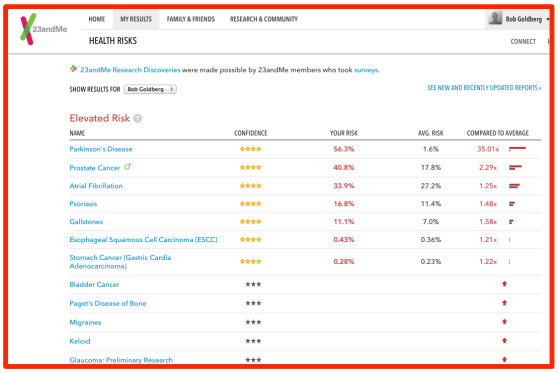


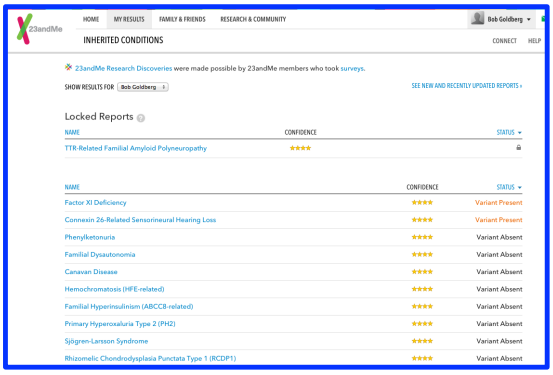


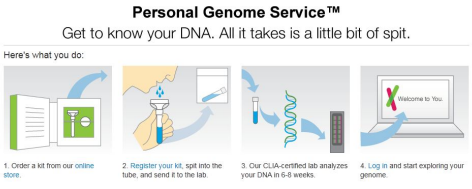
Unique Pattern of DNA Bands = Fingerprint



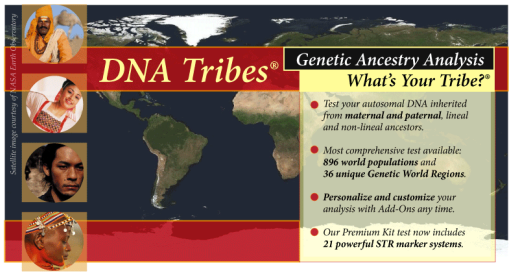
Using PCR to Determine Bobg's Genotype







Using PCR To Determine an Individual's Ancestry

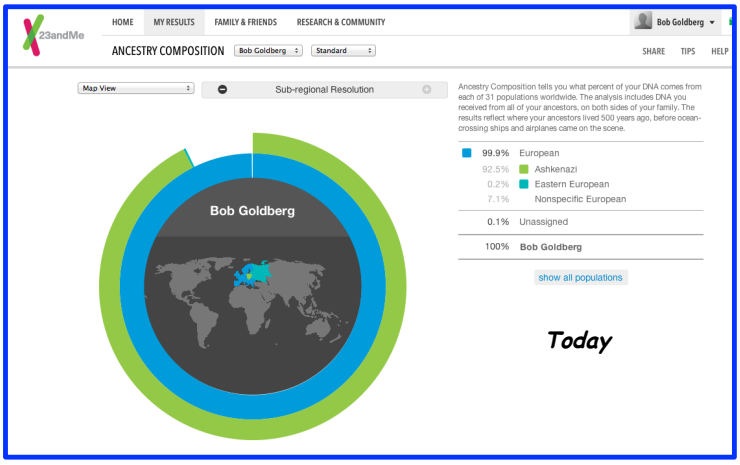


PCR Started a New Industry

DNA can reveal ancestors' lies and secrets

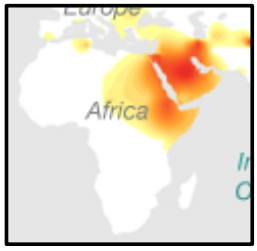
LA Times, January 18, 2009

Bobg's Ancestry

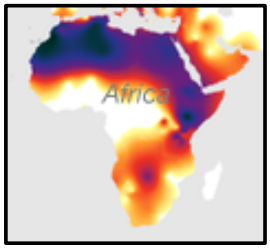


Today

♂



500 Years Ago



♀

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

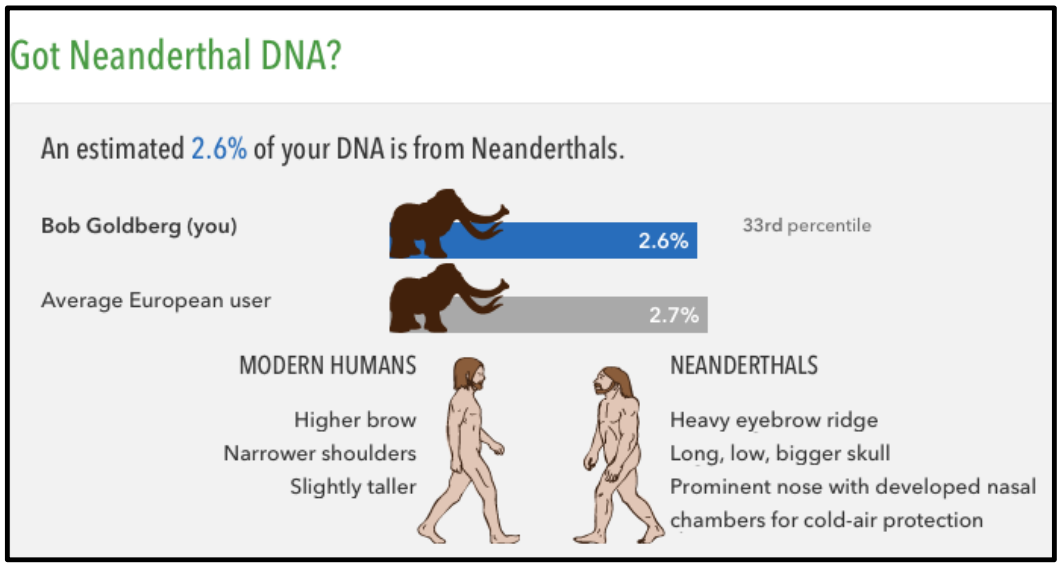
Analysis of one million base pairs of Neanderthal DNA

From a 45,000 Year-Old Bone

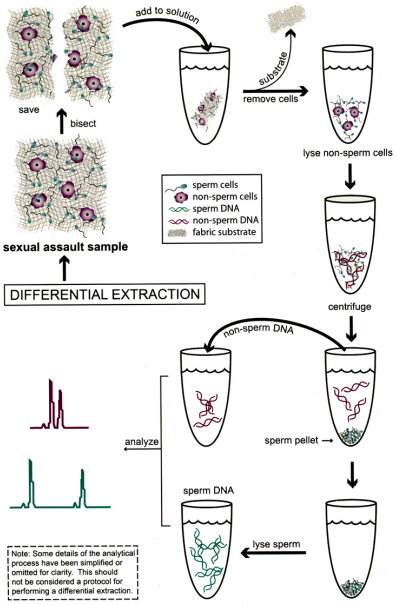
Richard E. Green[1], Johannes Krause[1], Susan E. Ptak[1], Adrian W. Briggs[1], Michael T. Ronan[2], Jan F. Simons[2], Lei Du[2], Michael Egholm[2], Jonathan M. Rothberg[2], Maja Paunovic[3]‡ & Svante Pääbo[1]

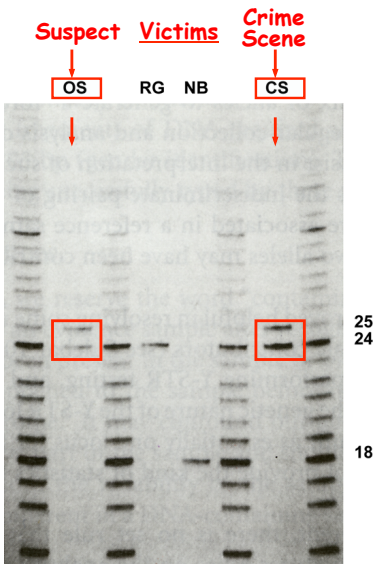
Nature, November, 2006

Bobg's Neanderthal DNA Content



Using PCR in Crime Scenes





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

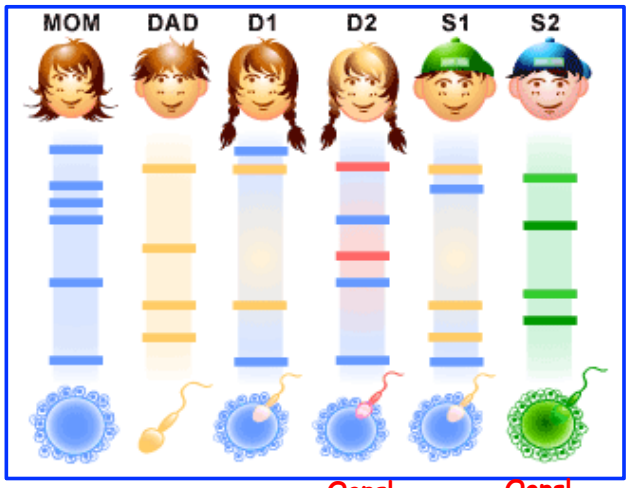
"Match" What is Probability That This Will Occur by Chance?

DNA Doesn't "Lie" !!

Using DNA Fingerprints to Identify Individuals & Genes They Don't "Lie"

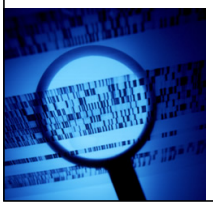
DNA Fingerprints

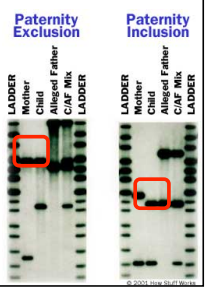
Sometimes They Reveal Unexpected Results!



Oops! Oops!

What is YOUR DNA Fingerprint?





Identifying Victims of 9/11 Using PCR and DNA Fingertinting

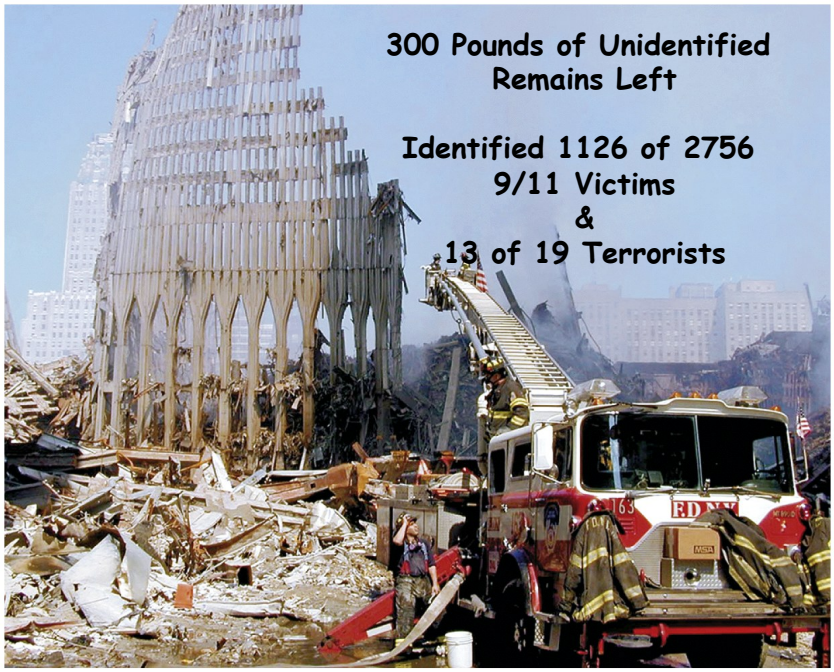
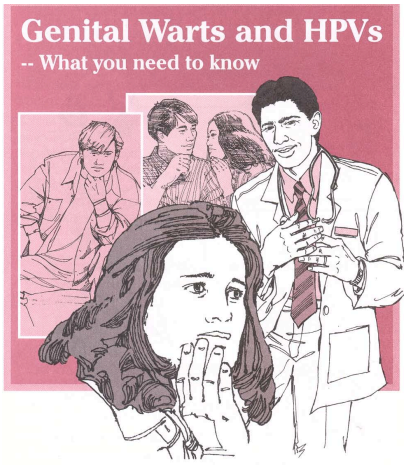


Figure 19-31
Genetics: A Conceptual Approach, Third Edition

Newsweek, January 12, 2009

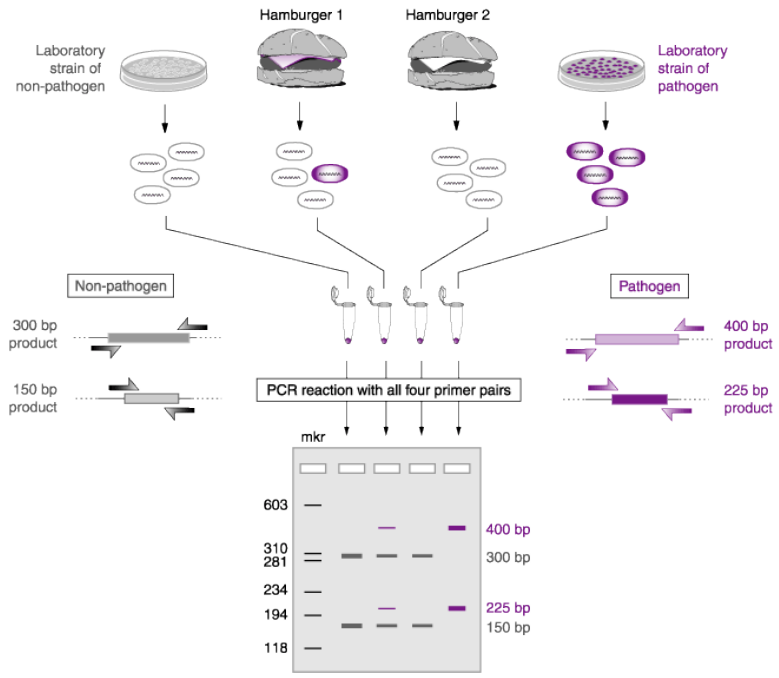
Using PCR To Detect Human Pathogens
(Viruses, Fungi, Bacteria)



ViroSeq™
HIV-1 Genotyping System

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

Using PCR To Detect Food Pathogens

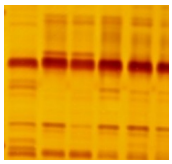


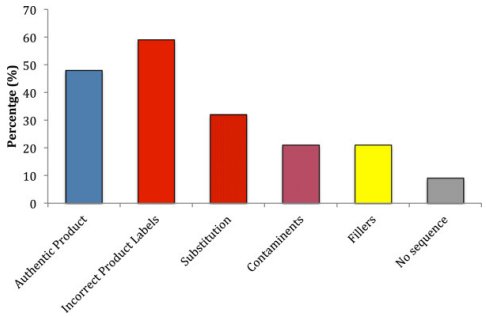
And Consumer Fraud in the Natural Food Industry

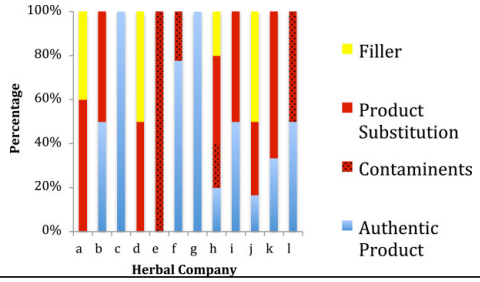
DNA barcoding detects contamination and substitution in North American herbal products

BMC Medicine, 11, 222, 2013

Barcoding = DNA Fingerprinting!





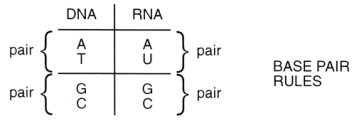


PCR Has Many Uses, Has Changed Many Fields, and Lead To New Ones That Have Had a Big Impact On Our Lives

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., Poaching 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

DNA Replication is Precise
But Mistakes or Mutations Can Occur!

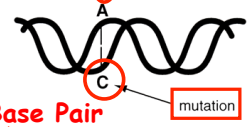


Think Tautomers!

Rare Base Mismatch

Gene A

Replication①



MUTATION DURING REPLICATION

mutation

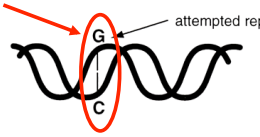
C mispairs with A

See Mutation As Change in Phenotype

New Base Pair

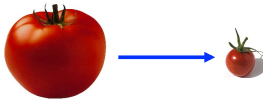
attempted repair

Replication②
Gene A'
Allelic Variant



Change DNA Sequence From A = T to G ≡ C

∴ Change Protein Amino Acid Sequence ⇨ Alter Function!



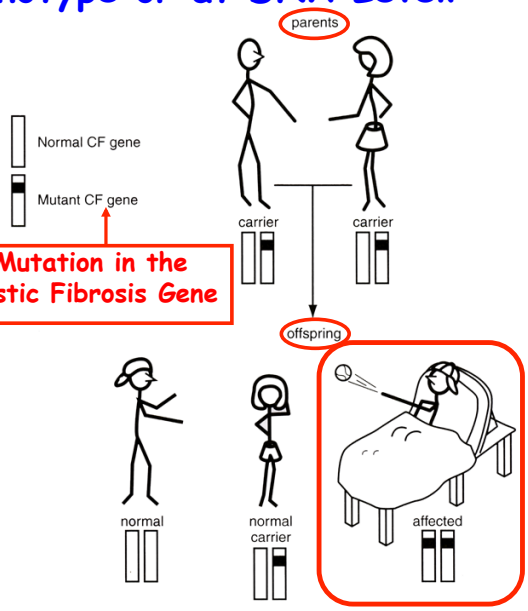
Big Tomato to Small Tomato

Mutation in Genes Are Rare
But Are Inherited & Can Be Followed in Families By Phenotype or at DNA Level!

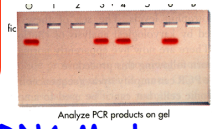
One Gene Per Gamete

♀ + ♂

Two Genes per Somatic Cells



Mutation in the Cystic Fibrosis Gene

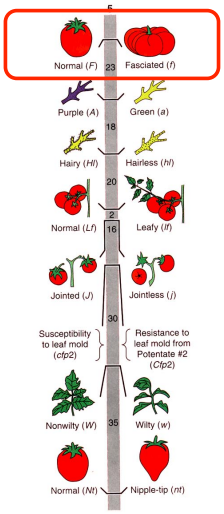


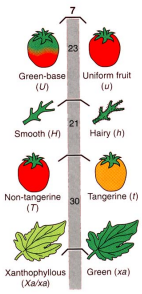
How Follow Inheritance?
What Allows Disease To Be Followed?

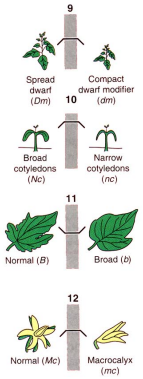
DNA Marker or Fingerprint!

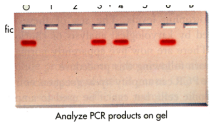
Alternative Forms of the Same Gene Lead to Genetic Diversity

Alleles









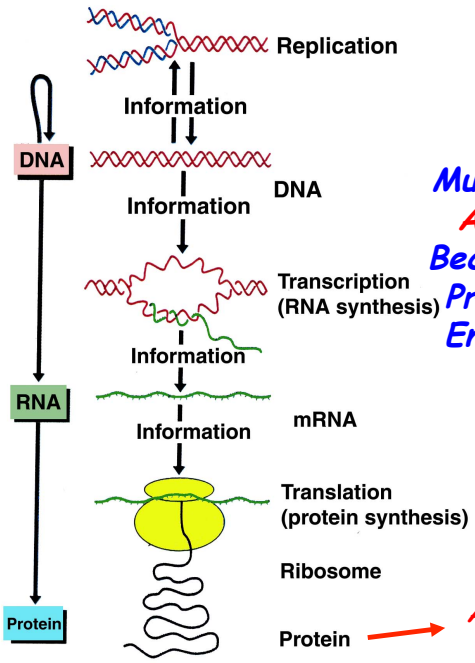
Can Follow These Traits With DNA Markers As Well

mutations result in genetic diversity!!!

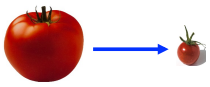
Spontaneous Mutations Give Rise To Alleles, or Different Forms of the Same Gene, And result in Small DNA Sequence Changes (e.g., SNPs or Single Nucleotide Polymorphisms)

Translating The Genetic Code Into Proteins is a Conserved Process

Mutations Are Inherited Because Altered Gene Replicates

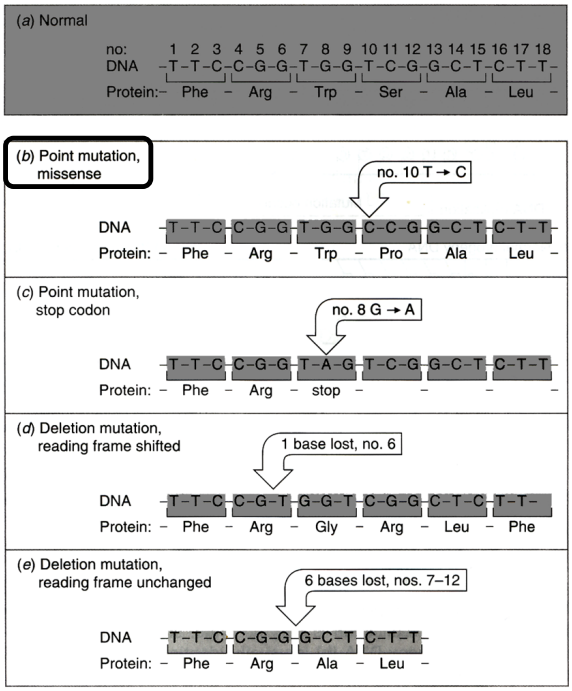


Mutations Lead To Altered Protein Because mRNA and Protein Sequence Encoded By Gene Changes



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

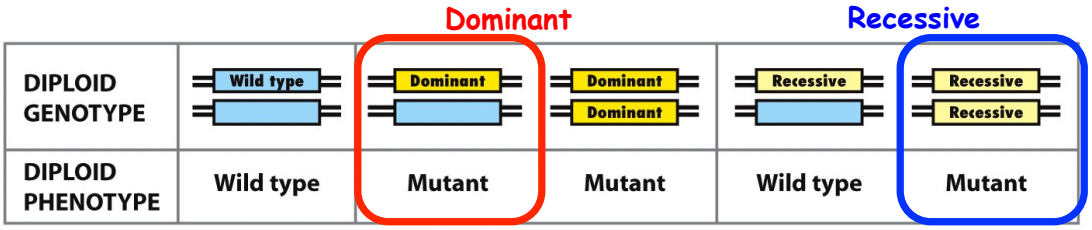
∴

Phenotype Changes

Human Genetic Disorders Occur As a Result of Mutations

TABLE 13.2 Some Important Genetic Disorders

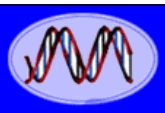
Disorder	Symptom	Defect	Dominant/ Recessive	Frequency Among Human Births
Hemophilia	Blood fails to clot	Defective blood-clotting factor VIII	X-linked recessive	1/10,000 (Caucasian males)
Huntington disease	Brain tissue gradually deteriorates in middle age	Production of an inhibitor of brain cell metabolism	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



Need One Allele

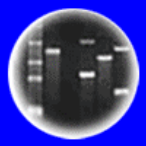
Need Two Alleles

Figure 5-2
Molecular Cell Biology, Sixth Edition



DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

ARTICLE

Nature, October 10, 2010

doi:10.1038/nature09534

A map of human genome variation from population-scale sequencing

The 1000 Genomes Project Consortium*

The 1000 Genomes Project aims to provide a deep characterization of human genome sequence variation as a foundation for investigating the relationship between genotype and phenotype. Here we present results of the pilot phase of the project, designed to develop and compare different strategies for genome-wide sequencing with high-throughput platforms. We undertook three projects: low-coverage whole-genome sequencing of 179 individuals from four populations; high-coverage sequencing of two mother-father-child trios; and exon-targeted sequencing of 697 individuals from seven populations. We describe the location, allele frequency and local haplotype structure of approximately 15 million single nucleotide polymorphisms, 1 million short insertions and deletions, and 20,000 structural variants, most of which were previously undescribed. We show that, because we have catalogued the vast majority of common variation, over 95% of the currently accessible variants found in any individual are present in this data set. On average, each person is found to carry approximately 250 to 300 loss-of-function variants in annotated genes and 50 to 100 variants previously implicated in inherited disorders. We demonstrate how these results can be used to inform association and functional studies. From the two trios, we directly estimate the rate of *de novo* germline base substitution mutations to be approximately 10^{-8} per base pair per generation. We explore the data with regard to signatures of natural selection, and identify a marked reduction of genetic variation in the neighbourhood of genes, due to selection at linked sites. These methods and public data will support the next phase of human genetic research.

- Sequenced Genomes of ~900 individuals
- From Seven Different Global Populations
- Found 250-300 Loss-Of-Function Mutations (KOs) Per Person
- Found 50-100 Mutations Implicated in Genetic Disorders Per Person
- 10^{-8} bp Mutations Per Generation (30 per Genome)

ARTICLE

doi:10.1038/nature11396

Rate of *de novo* mutations and the importance of father's age to disease risk

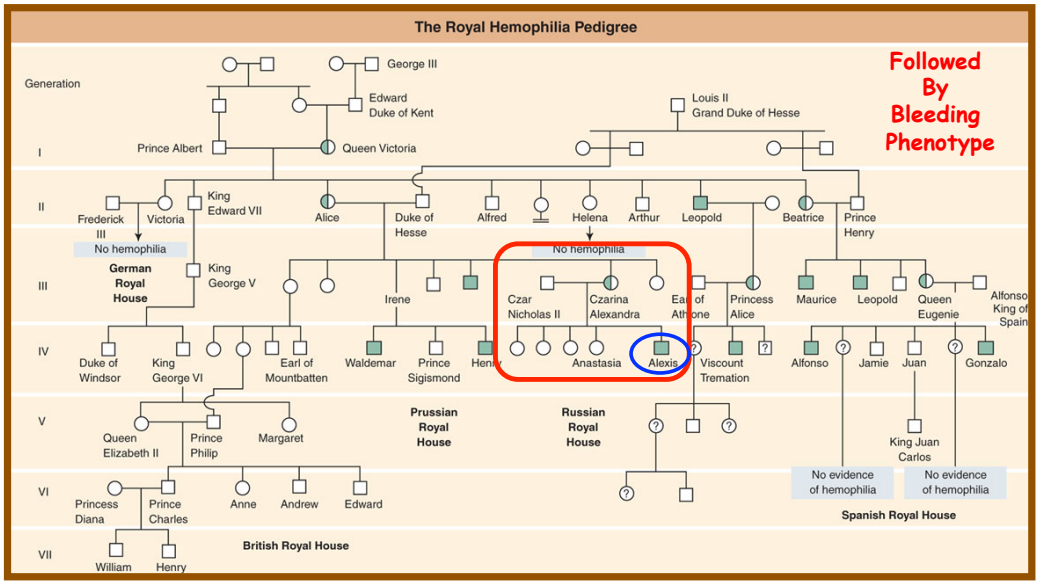
Augustine Kong[1], Michael L. Frigge[1], Gisli Masson[1], Soren Besenbacher[1,2], Patrick Sulem[1], Gisli Magnusson[1], Sigurjon A. Gudjonsson[1], Asgeir Sigurdsson[1], Aslaug Jonasdottir[1], Adalbjorg Jonasdottir[1], Wendy S. W. Wong[3], Gunnar Sigurdsson[1], G. Bragi Walters[1], Stacy Steinberg[1], Hannes Helgason[1], Gudmar Thorleifsson[1], Daniel F. Gudbjartsson[1], Agnar Helgason[1,4], Olafur Th. Magnusson[1], Unnur Thorsteinsdottir[1,5] & Kari Stefansson[1,5]

Mutations generate sequence diversity and provide a substrate for selection. The rate of *de novo* mutations is therefore of major importance to evolution. Here we conduct a study of genome-wide mutation rates by sequencing the entire genomes of 78 Icelandic parent-offspring trios at high coverage. We show that in our samples, with an average father's age of 29.7, the average *de novo* mutation rate is 1.20×10^{-8} per nucleotide per generation. Most notably, the diversity in mutation rate of single nucleotide polymorphisms is dominated by the age of the father at conception of the child. The effect is an increase of about two mutations per year. An exponential model estimates paternal mutations doubling every 16.5 years. After accounting for random Poisson variation, father's age is estimated to explain nearly all of the remaining variation in the *de novo* mutation counts. These observations shed light on the importance of the father's age on the risk of diseases such as schizophrenia and autism.

August 22, 2012

Father's Age Is Linked to Risk of Autism and Schizophrenia

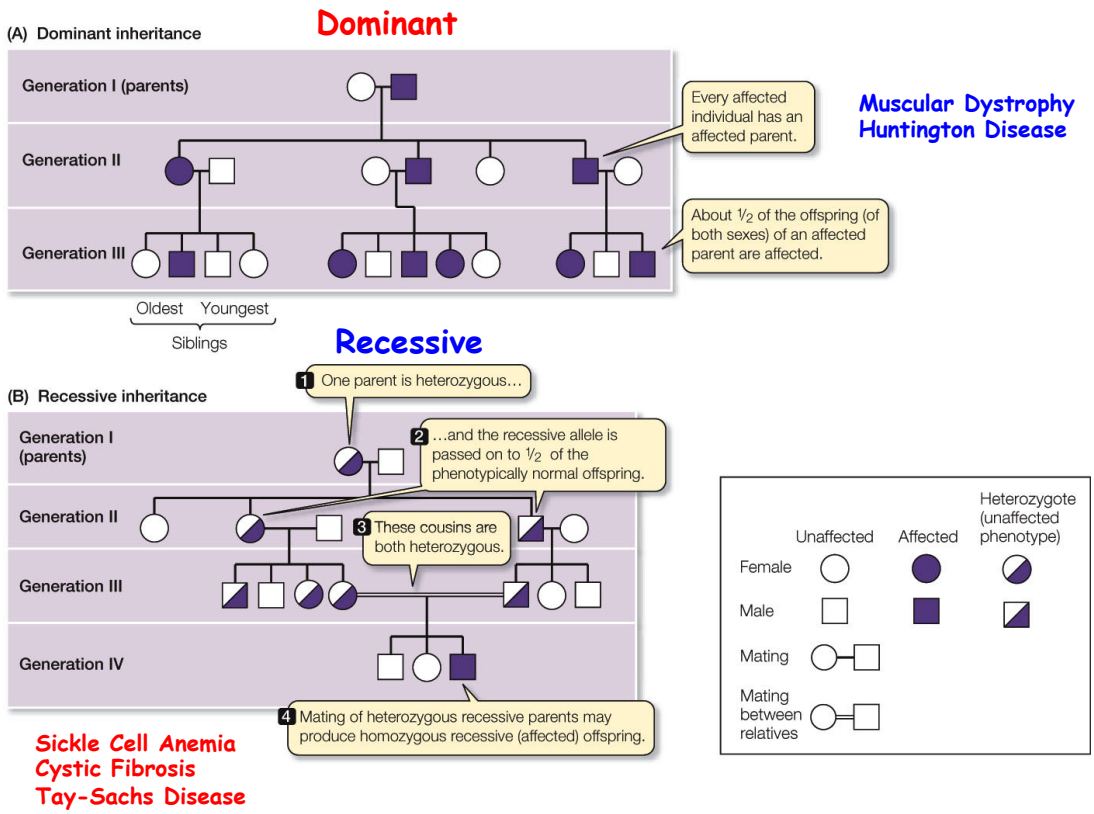
Pedigrees Can Be Used To Follow Disease Genes in Human Families



Recessive Sex Linked

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

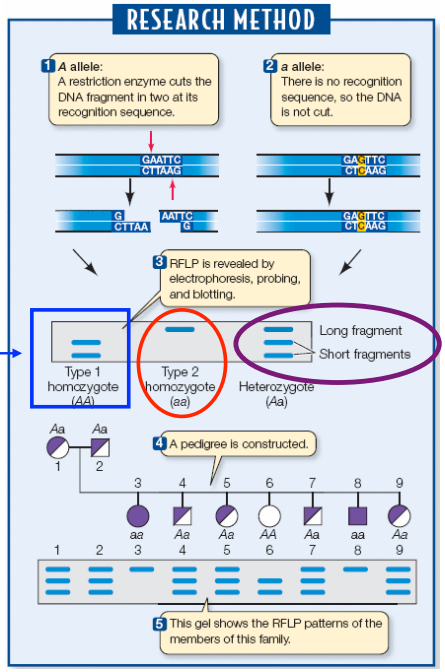
Each Type of Inheritance Predicts Specific Results in Each Generation



Muscular Dystrophy
Huntington Disease

Sickle Cell Anemia
Cystic Fibrosis
Tay-Sachs Disease

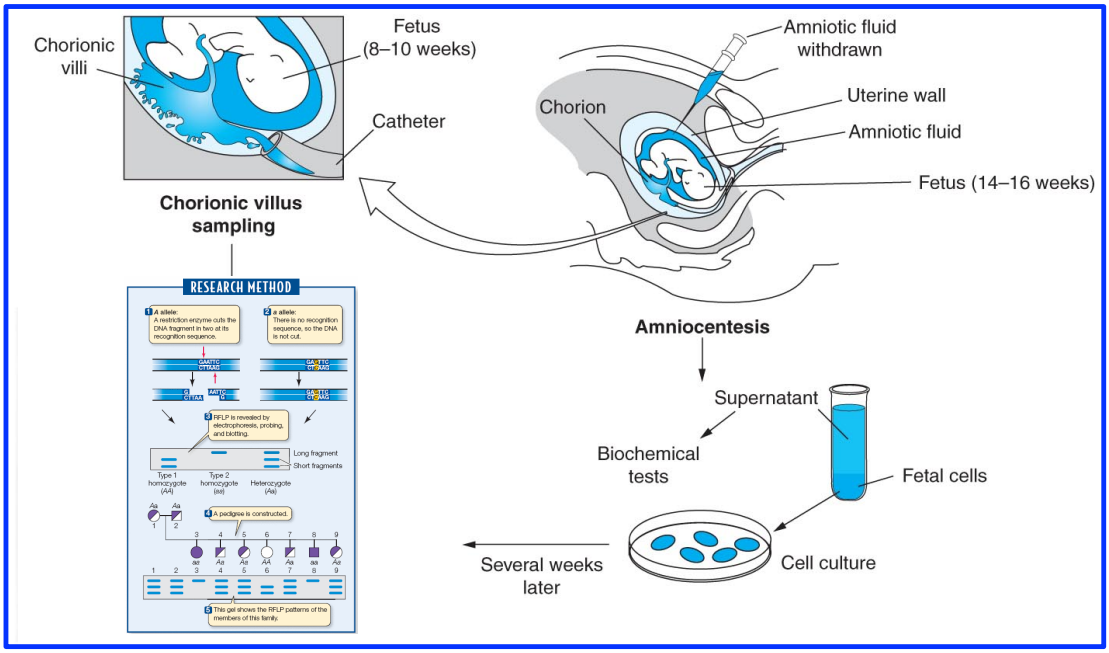
Genetic Diseases Can Be Followed in Families Using Molecular Methods (e.g., DNA Blots or PCR)



DNA Fingerprints

RFLP –Restriction Fragment Length Polymorphism

DNA Testing Can Be Carried Out Before Child Birth During Pregnancy



RESEARCH ARTICLE **New Non-Invasive DNA Tests Are Available Based on PCR**

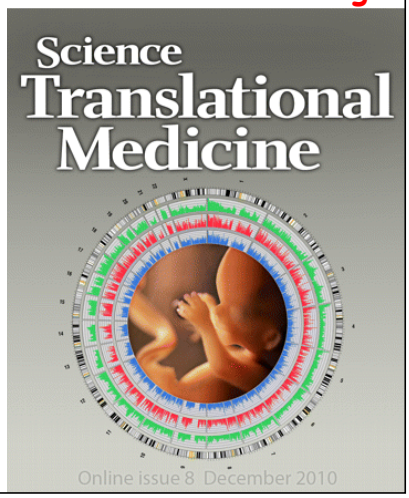
PRENATAL DIAGNOSIS

Maternal Plasma DNA Sequencing Reveals the Genome-Wide Genetic and Mutational Profile of the Fetus

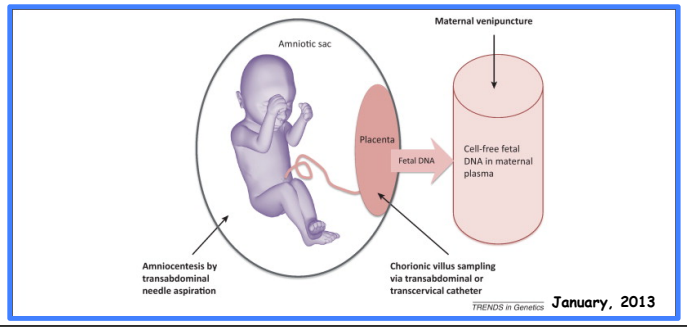
Science Translational Medicine, December 8, 2010 (61,1-12)

Sequencing DNA From the Blood of a Pregnant Woman Allows the Complete Genome Of the Fetus to Be Decoded!

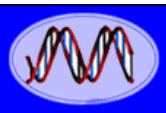
A New Era in DNA Testing!!



~10% of DNA in Maternal Plasma is From the Fetus

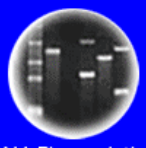


January, 2013



DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



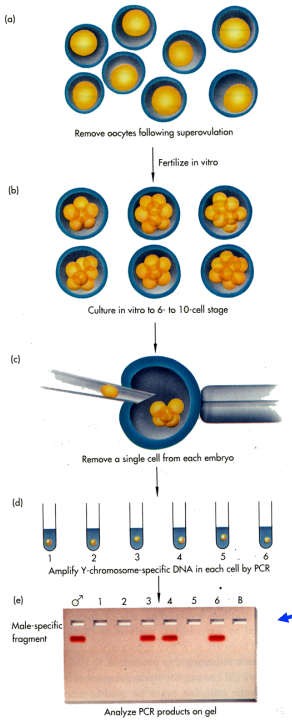
DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

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

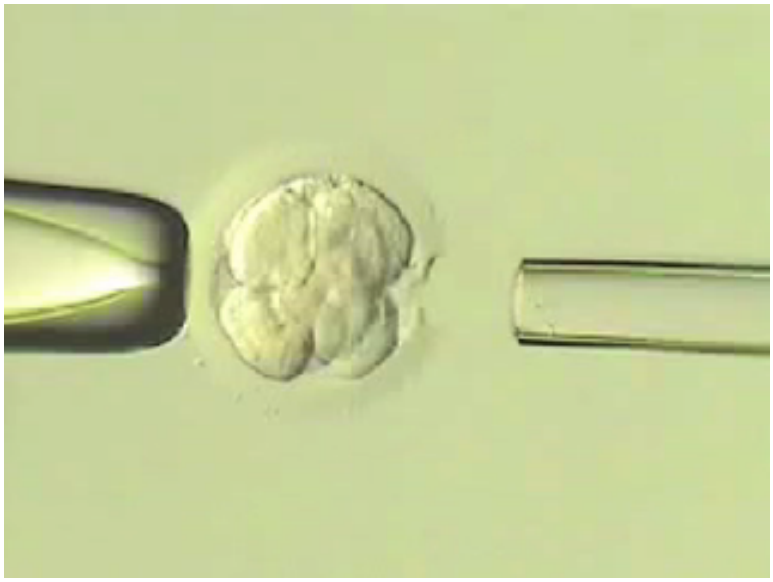
PGD
Pre-
Implantation
Genetic
Diagnosis



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

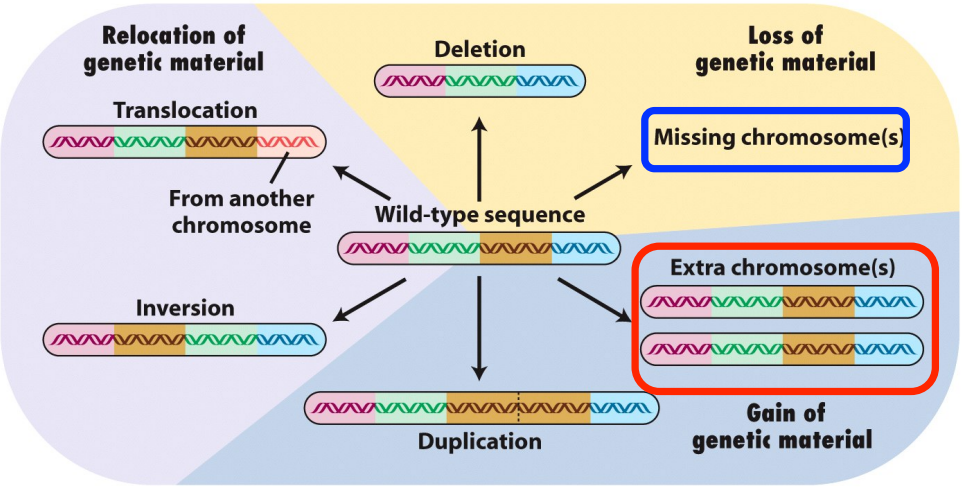
Sex Determination in 8-cell Embryo!

Determining the Genetic Identity of a Human Embryo Before Implantation!



Prenatal Genetic Diagnosis (PGD)

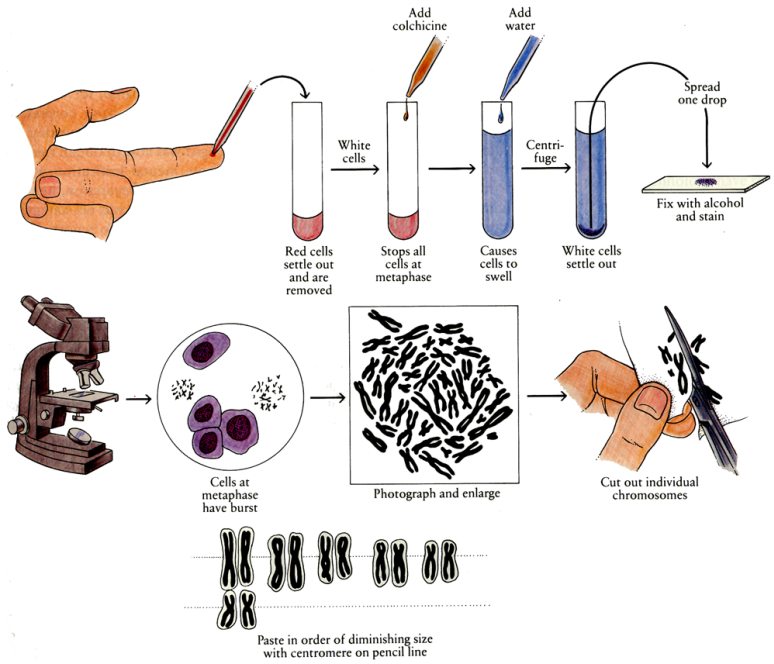
"Mutations" Can Also Occur By Large Chromosomal Changes



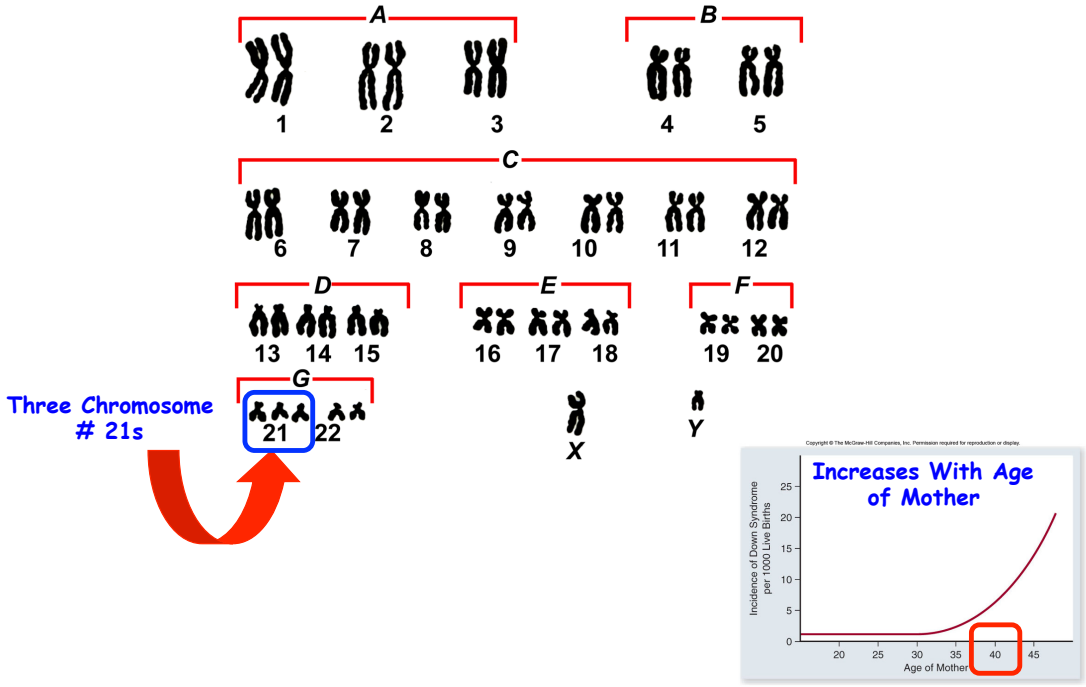
These changes affect many genes!

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

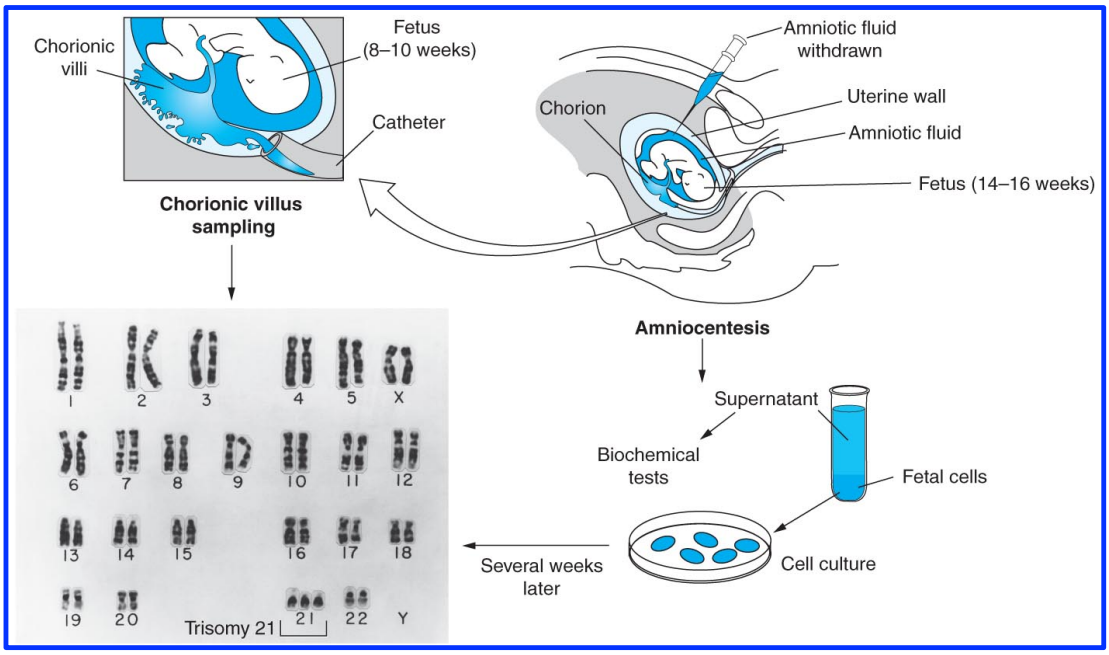
Karyotypes Can Be Used To Detect Changes in Chromosome Structure and Number



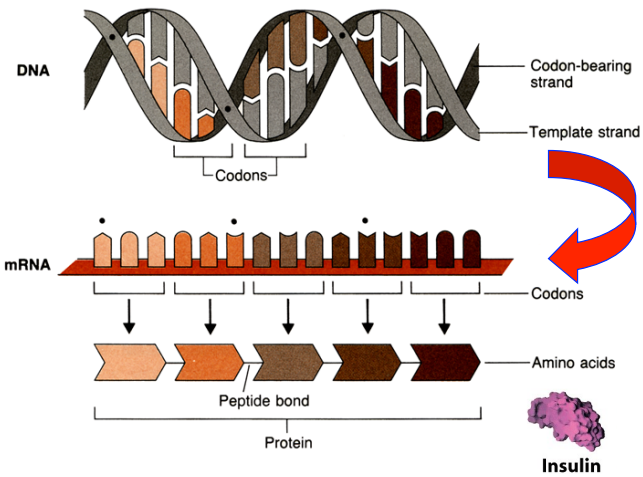
A Down's Syndrome Karyotype



Chromosome Testing Can Be Carried Out During Pregnancy or Before (New DNA Tests)



② 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

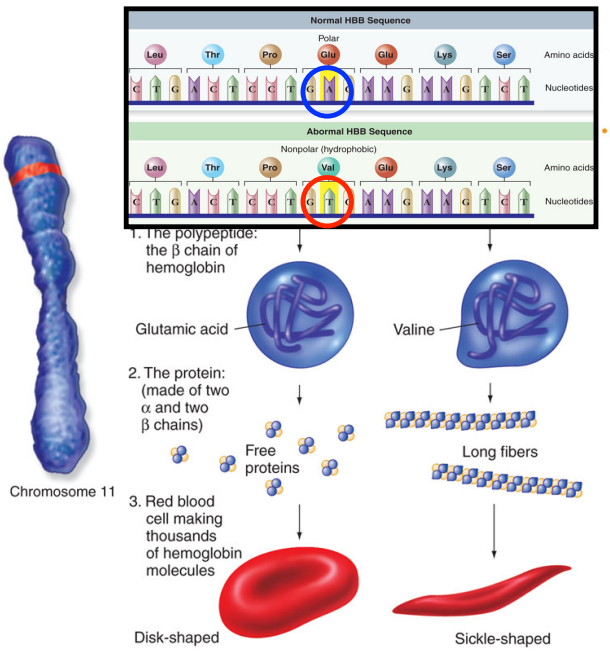
Genetic Code on mRNA Translated to Protein Sequence

∴ Sequence of Gene
Sequence of mRNA
Sequence of Protein

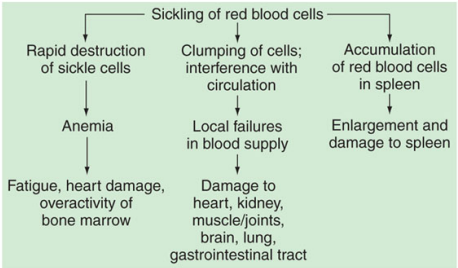
Colinearity of Sequences!

Know Sequence
Know Protein → Engineer New Protein

Human Genetic Disorders Occur As A Result of Mutations



(b) Sickle-cell anemia is pleiotrophic

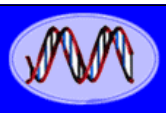


(c) β-chain substitutions/variants

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
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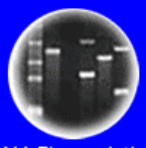
Entire Genetic Code of a Bacteria

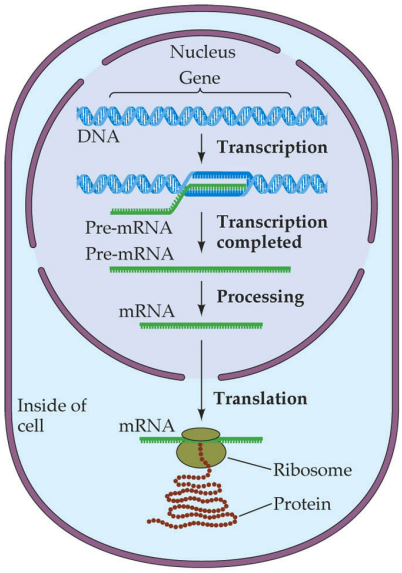


DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

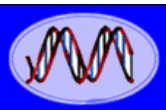
Plants of Tomorrow

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
© 2004 Sinauer Associates, Inc. and W. H. Freeman & Co.

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



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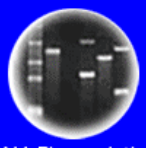

DNA Fingerprinting

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Plants of Tomorrow

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

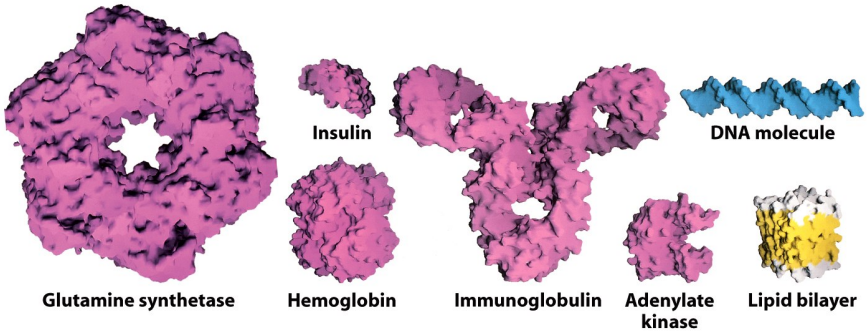
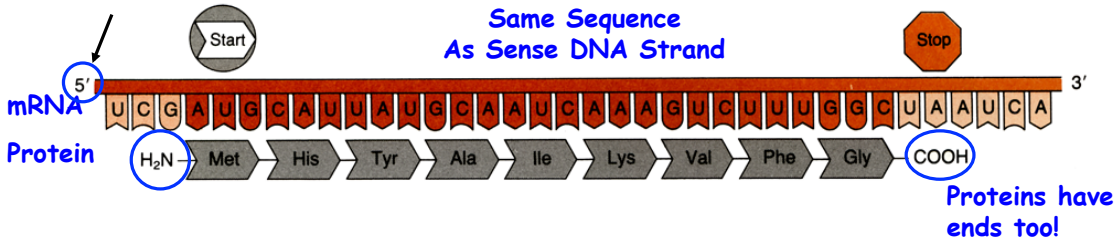


Figure 1-9
Molecular Cell Biology, Sixth Edition
© 2008 W. H. Freeman and Company

Novel Cell Functions & Phenotypes

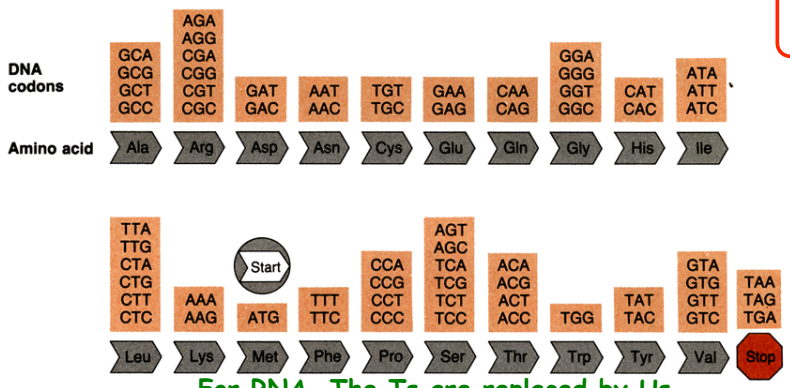
Genetic Code Allows The Sequence of Nucleotides in mRNA/ sense strand of Gene to be Translated into Sequence of Amino Acids in Proteins



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?



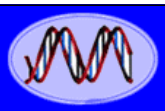
For RNA, The Ts are replaced by Us.

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!



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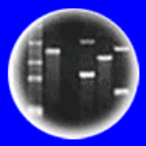
Genetic Code of Life

Entire Genetic Code of a Bacteria



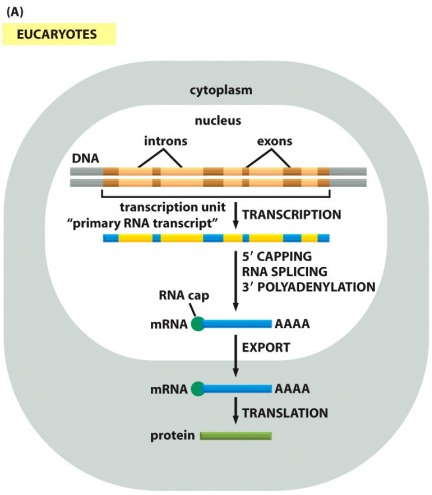
DNA Fingerprinting

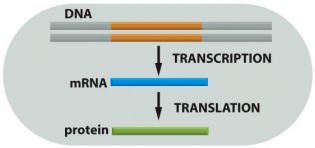
Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

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

Eukaryotic and Prokaryotic Gene Expression Processes Differ Slightly

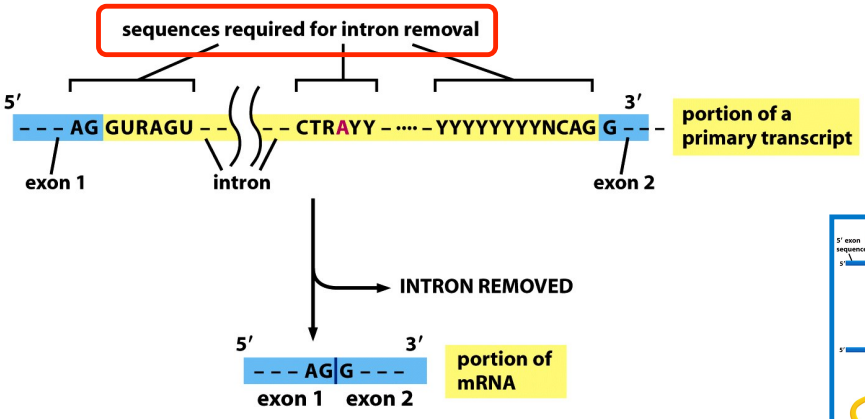


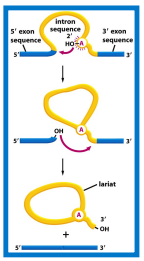


Genes Differ
Switches Differ
Genetic Code the Same
General Processes Same
Eukaryotic Gene Have Introns & Non-Coding Region in Gene!

Eukaryotic Cells Must Remove Non-Coding Region of RNA Before Genetic Code Can Be Translated Continuously!
What Are the Implications For Genetic Engineering?

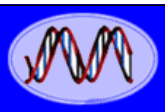
Yo! It's In The Sequences!





Specific Sequences Required For RNA Splicing!

What Happens If These Sequences Are Mutated in a Gene?



DNA
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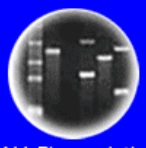

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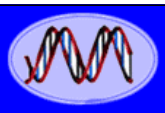
Implications For "Yo - Its in The DNA!!"

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!



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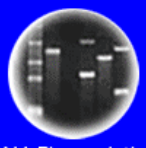

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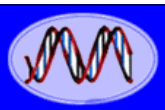
Summary: Engineering Genes Requires:

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!!*



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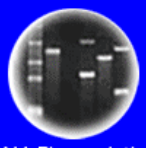

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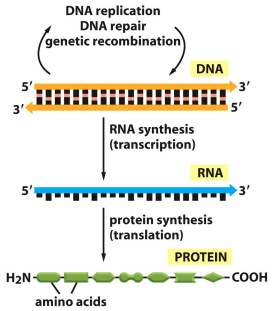
How Do Genes Work & What are Genes in Context of…

↓

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!

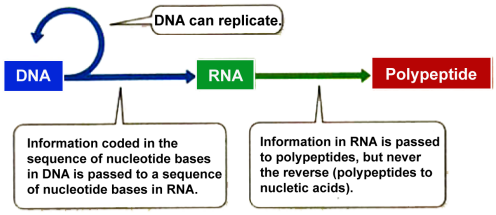
There's NO HOCUS POCUS
All Hypothesis Are Testable!!

"Behind" All Traits!

Same Processes!

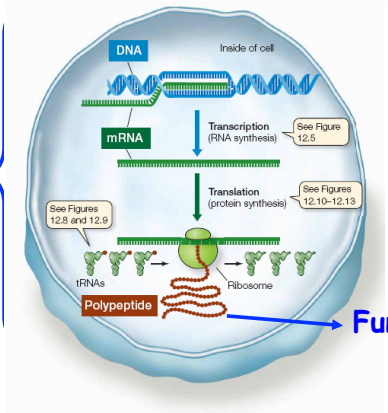
How Do Genes Work-Not As Simple As We Think!

① Replication



② Gene Activity to Function & Phenotype

Gene Activity
↓
Protein
↓
Function
↓
Phenotype (Trait)



Function →

But Precise Cellular Rules Are Followed That We Can Use For Genetic Engineering!