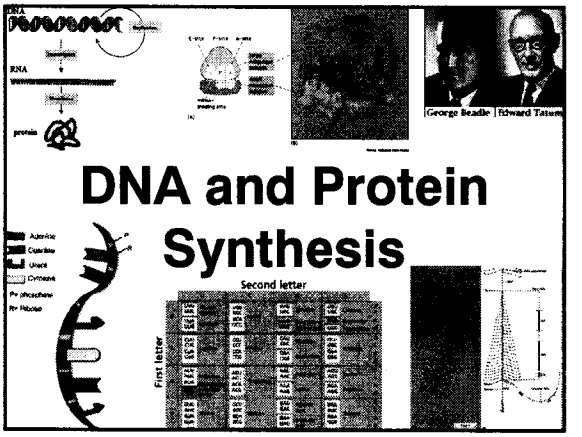
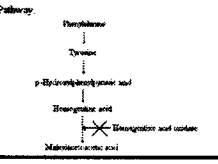
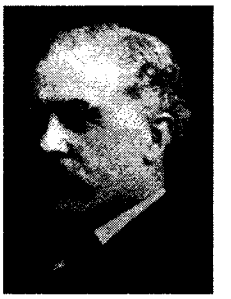


DNA and Protein Synthesis

I. What Genes Do

A. Sir Archibald **Garrod**
1. English Physician
2. Said inherited defects (alkaptonuria) could be caused by the lack of a particular enzyme.
3. Knowing that enzymes are proteins, Garrod suggested **link between genes and proteins.**

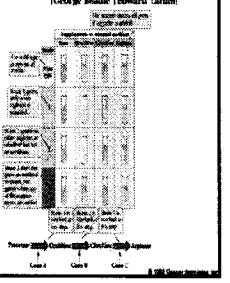




Sir Archibald Garrod, around 1910.

I. What Genes Do

B. George **Beadle** and Edward **Tatum**
1. X-rayed spores of red bread mold, *Neurospora crassa* (to mutate)
2. Some resulting cultures lacked a particular enzyme for growth on medium.
3. They found that a single gene was mutated, which resulted in the lack of a single enzyme.
4. They stated **one gene-one enzyme** hypothesis: one gene specifies synthesis of one enzyme.

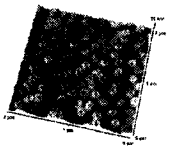


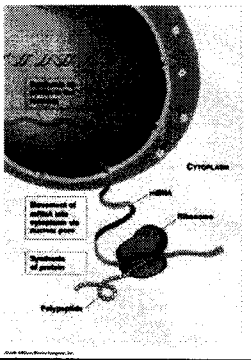
I. What Genes Do

C. Linus **Pauling** and Harvey **Itano**
1. Compared hemoglobin.
2. Found Sickle-cell hemoglobin differed from normal hemoglobin by using electrophoresis.
3. Formulated the **one gene-one polypeptide** hypothesis: each gene specifies one polypeptide of a protein.

II. How Genes Are Expressed

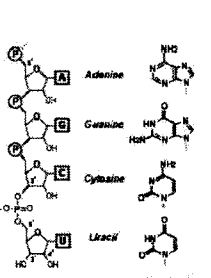
A. DNA nucleotides ultimately determine amino acid sequence in proteins.
B. DNA molecule cannot directly control the sequence of amino acids because DNA is restricted to nucleus.
C. Go-between is **ribonucleic acid** (RNA).





III. RNA

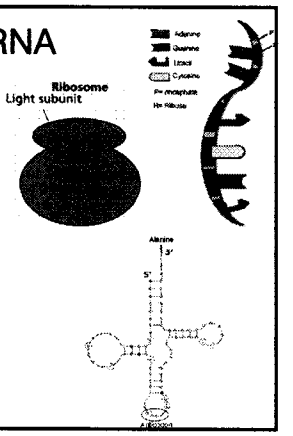
A. RNA is a polymer of nucleotides.
B. Unlike DNA, RNA is:
1. Single-stranded
2. Contains the sugar ribose
3. Contains the base **uracil** instead of thymine.



III. RNA

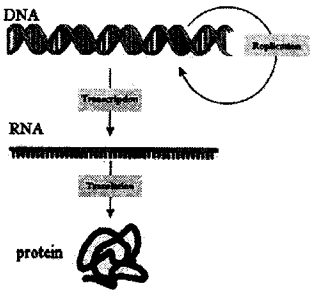
C. There are three major classes of RNA.
   1. Messenger RNA (**mRNA**) takes a message from DNA in nucleus to ribosomes in cytoplasm.
   2. Ribosomal RNA (**rRNA**) and proteins make up ribosomes where proteins are synthesized.
   3. Transfer RNA (**tRNA**) transfers a particular amino acid to a ribosome.

D. tRNA and rRNA are transcribed from DNA templates and are products themselves.



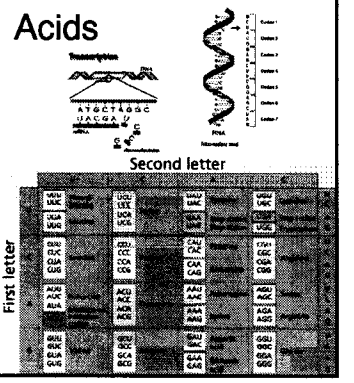
IV. Central Dogma of Molecular Biology

A. DNA undergoes **transcription** to mRNA
B. mRNA undergoes **translation** to a protein.



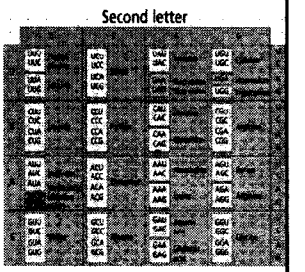
V. How Genes Code for Amino Acids

A. DNA serves as a template to build RNA
B. RNA contains the **genetic code**.
   1. Code is comprised of 64 three-base code words (codons).
   2. **Codon** consists of 3 nucleotide bases of mRNA. (4^3=64)
   3. Codes for amino acid or stops translation.



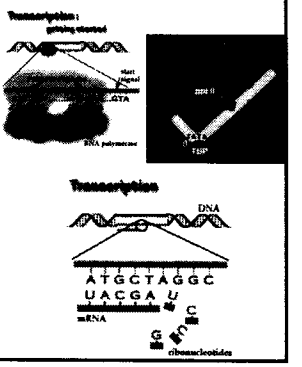
V. How Genes Code for Amino Acids

4. There are 64 triplets to code for 20 amino acids.
5. Each codon has only one meaning.
6. There is one start codon and three stop codons.
7. The Code Is Universal
   a) Suggests the code dates to very first organisms.
   b) Once established, changes would be very disruptive.



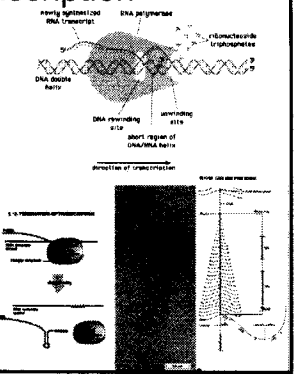
VI. Transcription

A. Messenger RNA is Formed
   1. Transcription begins when **RNA polymerase** attaches to a **promoter** on DNA.
   2. Promoter is DNA region that defines start of gene, direction of transcription, and strand copied. (**TATA Box** in Eukaryotes)
   3. **Transcription factor** is needed for polymerase to bind to DNA.
   4. Complementary RNA nucleotides pair with DNA nucleotides of the strand.



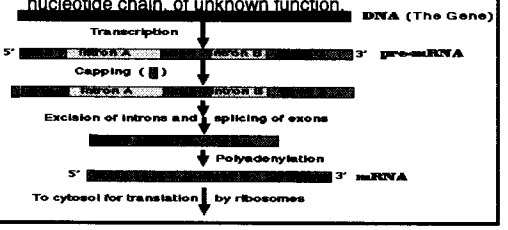
VI. Transcription

5. RNA polymerase joins RNA nucleotides.
6. **Terminator sequence** causes RNA polymerase to stop transcribing DNA, and to release mRNA
7. Many copies of mRNA are made from the DNA molecule at the same time.
8. Process produces many copies of a protein in a shorter period of time than if a single copy of DNA.



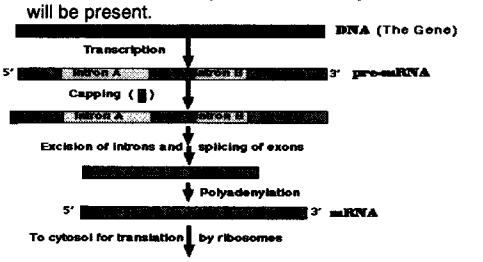
VI. Transcription

B. Messenger RNA is Processed (Eukaryotes)
   1. Ends of the mRNA molecule are altered: a cap is put on 5' end and a poly-A tail is put on 3' end.
      a) **"Cap"** is a modified guanine (G), tells a ribosome where to attach to begin translation.
      b) The **"poly-A tail"** consists of a 150-200 adenine (A) nucleotide chain, of unknown function.



VI. Transcription

2. **Introns**, are removed by **spliceosomes**.
   a) **Exon** is portion of mRNA transcript eventually expressed.
   b) The simpler the eukaryote, the less likely that introns will be present.

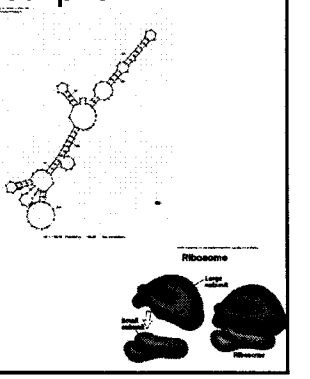


VI. Transcription

3. **Ribozymes**
   a) RNAs with an enzymatic function restricted to cleaving RNA at specific locations.
   b) RNA could have served as both genetic material and as first enzymes in early life forms.
   c) Therefore **RNA came first**.

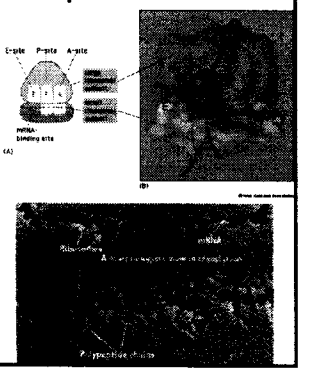
VI. Transcription

C. Ribosomal RNA (**rRNA**)
   1. Produced off DNA in the nucleolus.
   2. Packaged with a variety of proteins into 2 subunits.
   3. Can float free in cytosol or attach to endoplasmic reticulum.
   4. Prokaryotic cells contain about 10,000 ribosomes; eukaryotic cells contain many times more



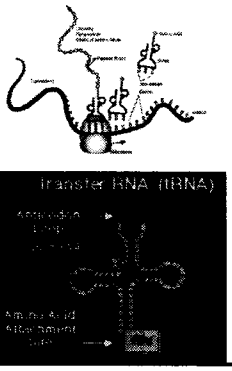
VI. Transcription

5. Ribosomes have a binding site for mRNA
6. Each ribosome contains the **P site** (for peptide) and the **A site** (for amino acid).
7. **Polyribosomes** are clusters of several ribosomes synthesizing the same protein



VII. Translation

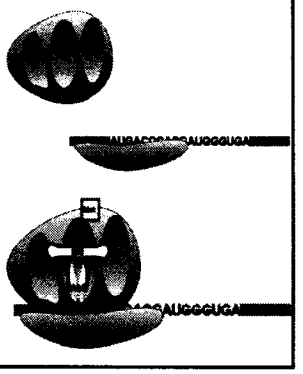
A. Takes place in cytoplasm
B. One language (nucleic acids) is translated into another language (protein)
C. Transfer RNA
   1. Transfers amino acids to the ribosomes.
   2. tRNA is a single-stranded ribonucleic acid that doubles back on itself to create a cloverleaf structure
   3. One end binds to amino acid; other end has an **anticodon** that binds to mRNA codon



VII. Translation

D. Chain Initiation

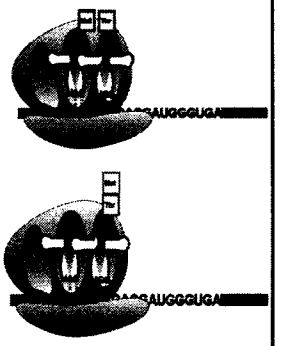
1. Small ribosomal subunit attaches to mRNA at the start codon (AUG).
2. First or initiator tRNA pairs with this codon; then large ribosomal subunit joins to small subunit
3. **Initiation factor proteins** are required to bring necessary components together



VII. Translation

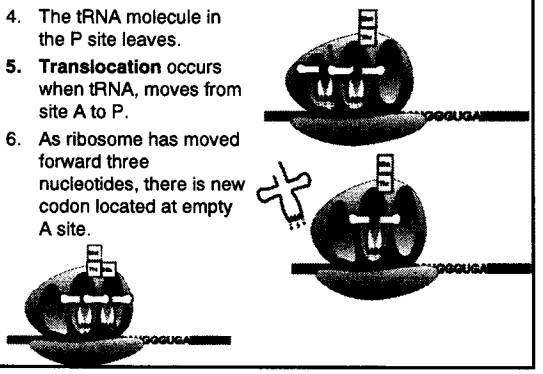
E. Chain Elongation

1. New tRNA arrives at A site
2. Amino acid at P site is attached by a peptide bond to the newly arrived amino acid.
3. Reaction is catalyzed by a **ribozyme** of the larger subunit.



VII. Translation

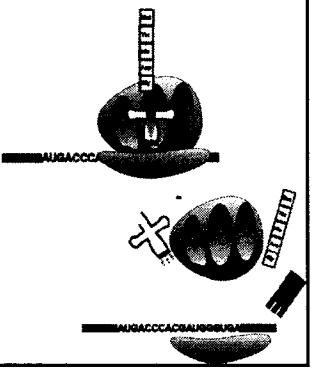
4. The tRNA molecule in the P site leaves.
5. **Translocation** occurs when tRNA, moves from site A to P.
6. As ribosome has moved forward three nucleotides, there is new codon located at empty A site.



VII. Translation

F. Chain Termination

1. Occurs at stop codon that does not code for amino acid.
2. **Release factor protein** binds to stop codon.
3. The polypeptide is enzymatically cleaved from the last tRNA.
4. tRNA and polypeptide leave the ribosome, which dissociates into its two subunits.

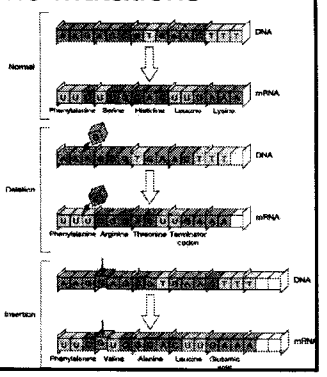


VIII. Gene Mutations

A. Changes in DNA nucleotides

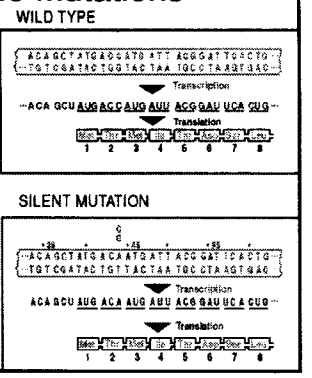
B. Point Mutations

1. **Frameshift Mutations**
   a) Base-pair insertion or deletion
   b) The result is frequently a nonfunctional protein.



VIII. Gene Mutations

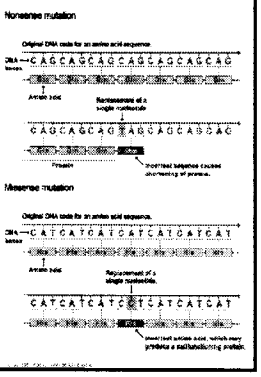
2. **Base-pair substitutions**
   a) **Silent mutations**
      1) Changes to codons that have same effect
      2) ACC to ACA both code threonine.



VIII. Gene Mutations

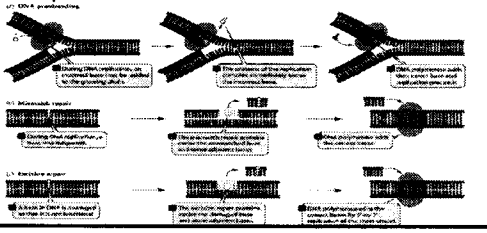
b) Nonsense mutation
1) A change that terminates the protein
2) CAG to TAG (a stop codon)

c) Missense mutation
1) A change that changes the amino acid
2) CAT to CCT incorporates proline instead of histidine



IX. Cause and Repair of Mutations

A. Mutations due to DNA replication errors are rare.
B. DNA polymerase proofreads new strand against old, and repairs any irregularities.
C. Reduces mistakes to one out of every one billion nucleotide pairs replicated.



IX. Cause and Repair of Mutations

A. Mutagens are environmental substances that cause mutations.
B. Common mutagens are radiation and organic carcinogens.
C. Mutation in gametes only affects offspring.
D. Mutation in the body cells may result in cancer.

IX. Cause and Repair of Mutations

E. UV radiation
1. Penetrates skin, breaks DNA of underlying tissues.
2. Where two thymine molecules are near each other, UV bonds them together as **thymine dimers**.
3. Usually dimers are removed from damaged DNA by special enzymes called **repair enzymes**.
4. Lack of repair enzymes produces xeroderma pigmentosum and higher incidence of skin cancer.