Molecular Biology of Gene & Inheritance

زیست شناسی ملکولی ژن و وراثت

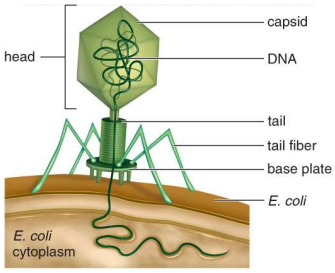
DISCOVERY OF DNA

- 1952—Hershey & Chase determine that DNA rather than protein carries genetic information
- 1953—Rosalind Franklin captures image of DNA with x-ray crystalography
- 1953—Watson & Crick describe the double-helix structure of DNA

DNA, NOT PROTEIN, IS THE GENETIC MATERIAL

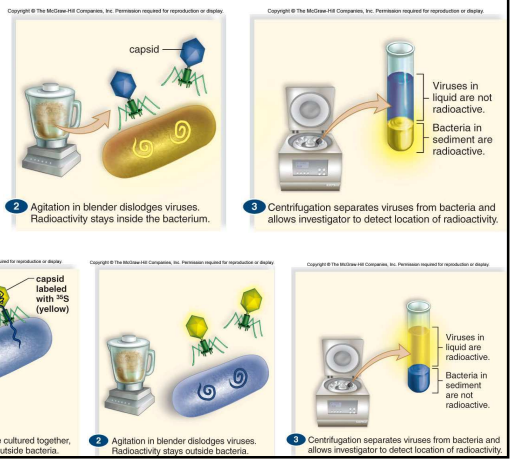
Hershey and Chase Experiment

- In their experiment, Hershey and Chase relied on a chemical difference between DNA and protein to solve whether DNA or protein was the genetic material



Structure of the virus (T2 bacteriophage) used by Hershey and Chase

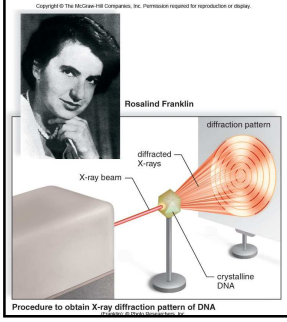
Hershey and Chase - Experiments

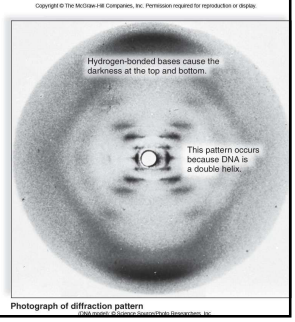


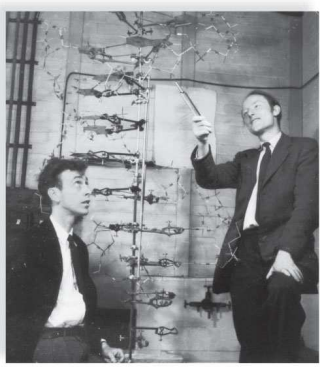
DNA IS A DOUBLE HELIX

The double helix suggests that the stability and variability of the molecule is in the sequence of bases

X-ray Diffraction of DNA



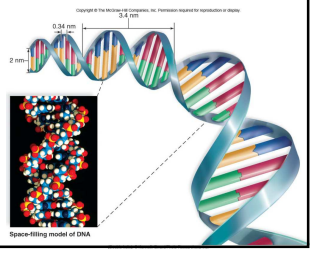




Watson and Crick with the DNA model they built.

(Watson, Crick): © A. Barrington Brown/Photo Researchers, Inc.

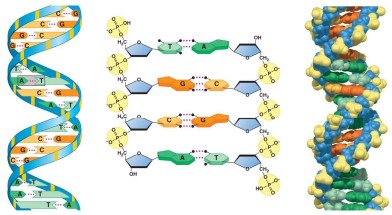
THE WATSON & CRICK MODEL OF DNA



Space-filling model of DNA

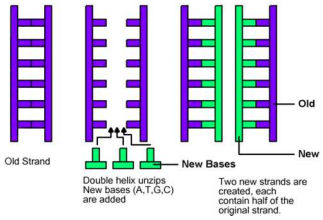
DNA STRUCTURE

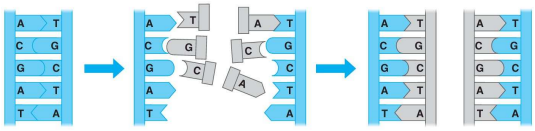
- Comprised of 4 nucleotides
  - Adenine
  - Thymine
  - Guanine
  - Cytosine
- Hydrogen bonds attach nucleotides
  - A-T, C-G



DNA REPLICATION

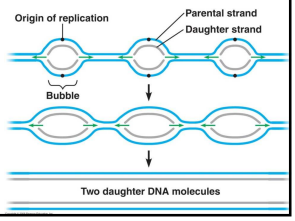
- Happens in S phase of Interphase
- Semiconservative replication
  - One parent strand ends up in each daughter DNA



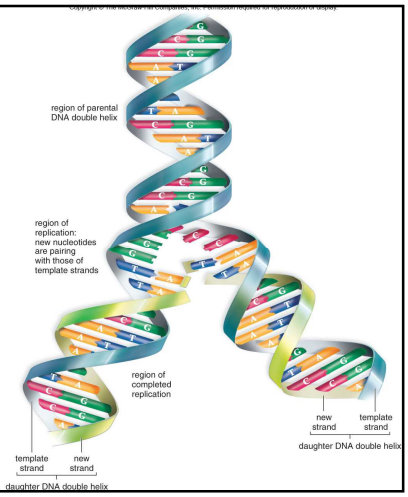


DNA REPLICATION

1. *Unwinding:* Old strands are "unzipped"; Helicase separates hydrogen bonds between base pairs.
2. Occurs in multiple locations on DNA at the same time
3. *Complementary base pairing:* New complementary nucleotides are positioned by the process of base pairing; DNA polymerase binds to each side of the "bubble".
4. *Joining:* Complementary nucleotides join to form new strands
   - Each daughter DNA molecule contains a template strand, or old strand, and a new strand

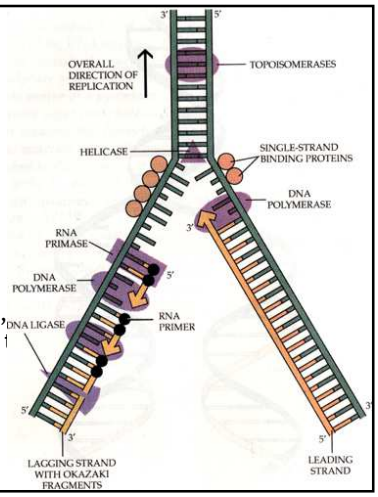


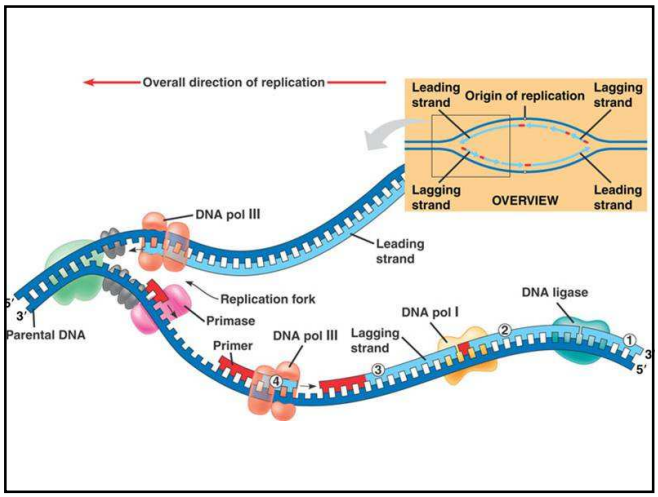
SEMICONSERVATIVE REPLICATION (SIMPLIFIED)



DNA REPLICATION

- DNA polymerase moves along the strand, attaching free nucleotides to complementary bases.
  - **ALWAYS** A-T and C-G!
- DNA ligase splices (links, ligates) sections of DNA t form one strand.

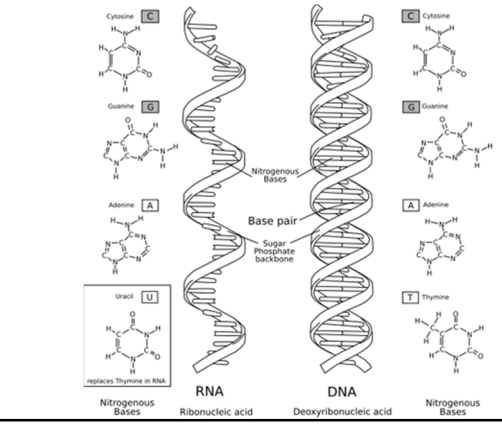




DNA VS. RNA

DNA	RNA
Double Helix	Single Strand
Thymine	Uracil
Inside Nucleus	Can Leave Nucleus
Entire genetic code	Only one gene

DNA VS. RNA



RNA

- Messenger RNA
  - mRNA
  - Direct copy from DNA
  - Has codons
- Transfer RNA
  - tRNA
  - Has anticodons
  - Binds to amino acids
    - Specific for each anticodon
- Ribosomal RNA
  - rRNA
  - Comprises part of ribosomes

THE MAKING OF A PROTEIN REQUIRES **TRANSCRIPTION** AND **TRANSLATION**

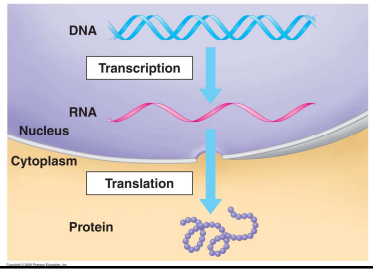
Gene - segment of DNA that specifies the amino acid sequence of a protein

Transcription: DNA serves as a template for RNA formation
- DNA is transcribed, monomer by monomer, into RNA

Translation : RNA transcript directs the sequence of amino acids in polypeptide biosynthesis

PROTEIN SYNTHESIS

- Copy of a gene made from the DNA
- Copy moves to ribosomes
- Protein is created from this “blueprint”

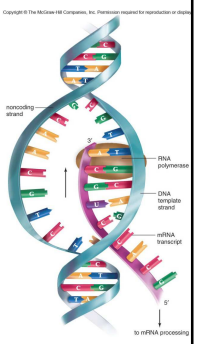


PROTEIN SYNTHESIS SUMMARY

- RNA Polymerase unravels part of the DNA strand
- The polymerase creates a template based on a section of DNA. This is the mRNA.
- mRNA leaves the nucleus
- mRNA binds to ribosome
- tRNA carries an amino acid (AA), matches to a section of the mRNA in the ribosome
- Another tRNA carries the next AA, the two AAs bond
- tRNA leaves
- Subsequent AAs continue to bond, forming a peptide chain
- At the end of the sequence, the peptide breaks off into the cytoplasm, the ribosome releases the mRNA, and the mRNA breaks apart to be recycled.

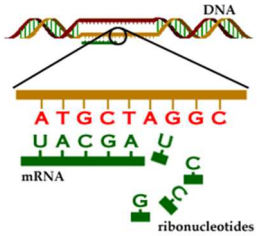
TRANSCRIPTION

- "The process by which an mRNA template, carrying the sequence of the protein, is produced for the translation step from the genome."
- Copying something to be read by someone else in another place.
- In this case…copying the gene to be used as an instruction manual to make protein in another part of the cell.

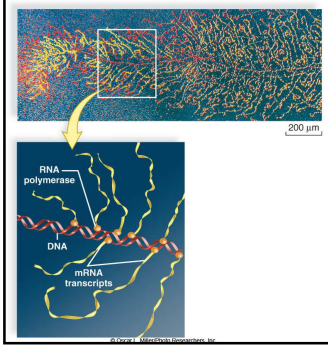


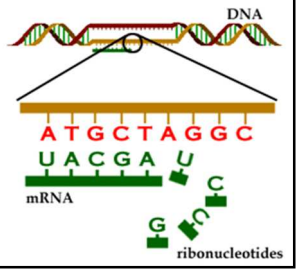
STEP BY STEP!

- Initiation
  - RNA polymerase binds to a specific part of the DNA strand. This is the gene.
  - Polymerase unravels this part of the strand, separating the base pairs.



- Elongation
  - Polymerase begins to slide along the DNA
  - Ribonucleotides match to opposite base, then bond
  - This creates a chain, which is the mRNA

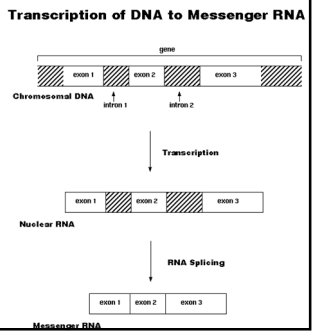




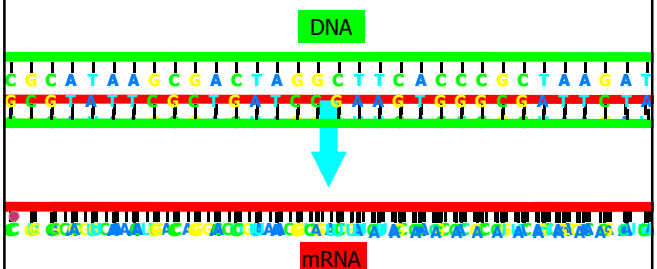
- Termination
  - Introns (unwanted parts) are "cut out" and removed
  - Exons (coding parts) are fused together
  - A "cap" is put on the end of the mRNA for protection

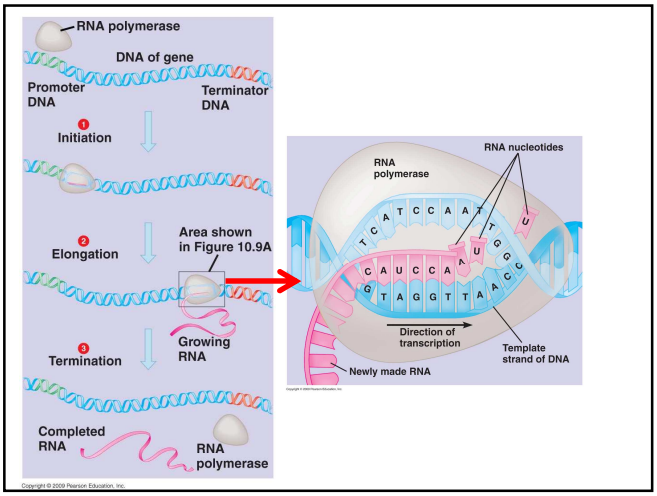
Function of Introns:

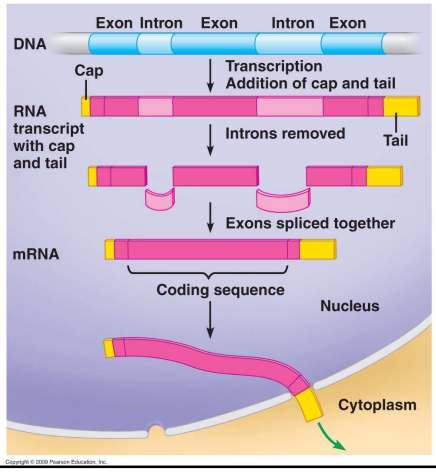
- Might allow exons to be put together in different sequences so that various mRNAs and proteins can result from a single gene
- Some introns might regulate gene expression by feeding back to determine which coding genes are to be expressed and how they should be spliced



TRANSCRIPTION







TRANSLATION

- "Protein translation involves the transfer of information from the mRNA into a peptide, composed of amino acids. This process is mediated by the ribosome, with the adaptation of the RNA sequence into amino acids mediated by transfer RNA."
- Taking something in a language you can't use, and making it into a language that you can use.
- In this case…taking the "language" of the DNA & mRNA, which the cell can't directly use, and converting it into the "language" of proteins, which the cell can use.

THE GENETIC CODE FOR AMINO ACIDS IS A TRIPLET CODE

Genetic code - sequence of nucleotides in DNA specifies the order of amino acids in a polypeptide

- **Codon** - three base sequence corresponding to a specific amino acid

Important properties of the genetic code:

- The genetic code is degenerate
- The genetic code has a precision
- The code has start and stop signals

First Base	Second Base U	Second Base C	Second Base A	Second Base G	Third Base
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U
	UUC phenylalanine	UCC serine	UAC tyrosine	UGC cysteine	C
	UUA leucine	UCA serine	UAA *stop*	UGA *stop*	A
	UUG leucine	UCG serine	UAG *stop*	UGG tryptophan	G
C	CUU leucine	CCU proline	CAU histidine	CGU arginine	U
	CUC leucine	CCC proline	CAC histidine	CGC arginine	C
	CUA leucine	CCA proline	CAA glutamine	CGA arginine	A
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	G
A	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	C
	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	A
	AUG *(start)* methionine	ACG threonine	AAG lysine	AGG arginine	G
G	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U
	GUC valine	GCC alanine	GAC aspartate	GGC glycine	C
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	A
	GUG valine	GCG alanine	GAG glutamate	GGG glycine	G

mRNA Codons

DNA A T G G C A A G T T T C
RNA U A C C G U U C A A A G

U A C C G U U C A A G

U A C C G U U C A A A G

Tyrosine Arginine Serine **Lysine**

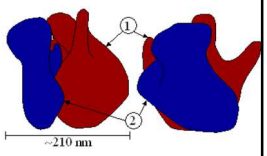
First Base	Second Base U	Second Base C	Second Base A	Second Base G	Third Base
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U
	UUC phenylalanine	UCC serine	UAC tyrosine	UGC cysteine	C
	UUA leucine	UCA serine	UAA *stop*	UGA *stop*	A
	UUG leucine	UCG serine	UAG *stop*	UGG tryptophan	G
C	CUU leucine	CCU proline	CAU histidine	CGU arginine	U
	CUC leucine	CCC proline	CAC histidine	CGC arginine	C
	CUA leucine	CCA proline	CAA glutamine	CGA arginine	A
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	G
A	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	C
	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	A
	AUG *(start)* methionine	ACG threonine	AAG lysine	AGG arginine	G
G	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U
	GUC valine	GCC alanine	GAC aspartate	GGC glycine	C
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	A
	GUG valine	GCG alanine	GAG glutamate	GGG glycine	G

mRNA Codons

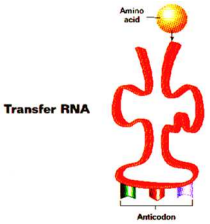
Start & Stop

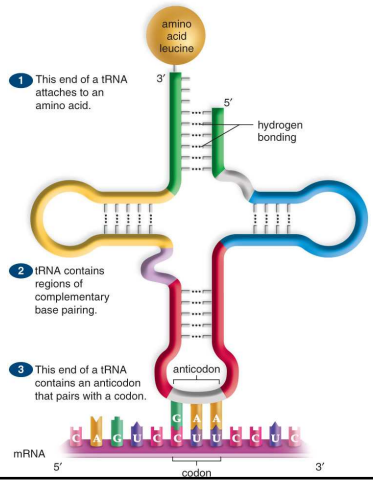
STEP BY STEP! (AGAIN)

- Ribosomes (two subunits) are in cytoplasm
- tRNA attaches to amino acids in cytoplasm
- Ribosome binds to the beginning of the mRNA chain



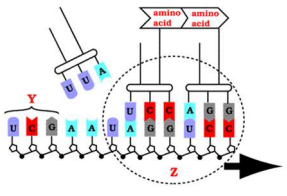
- **Anticodon** - a group of three bases that is complementary to a specific **codon** of mRNA at a ribosome

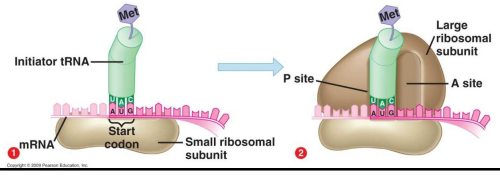




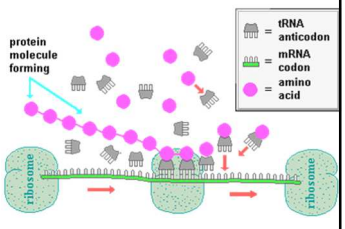
CLOVERLEAF MODEL OF TRNA

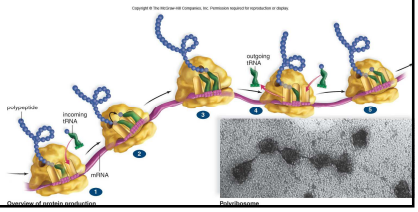
- Initiation
  - Starts with a 3-base section of the template, a "codon", specifically the "start codon"
  - tRNA with matching "anticodon" attaches
  - Another tRNA matches to the next codon
  - Amino acids bond



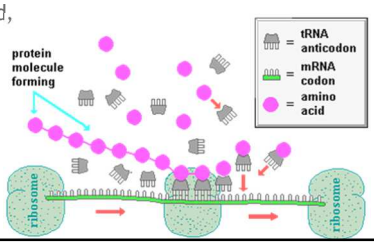


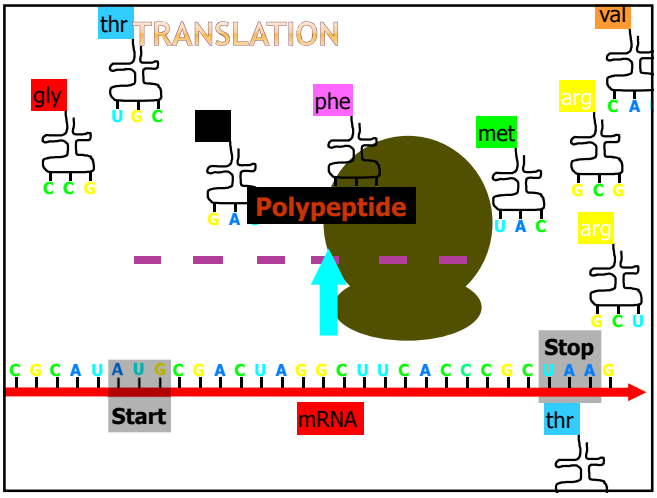
- Elongation
  - Ribosome moves down the mRNA one codon at a time
  - tRNA continues to match codon to anticodon, bringing more AAs
  - AAs bond, forming a lengthening chain

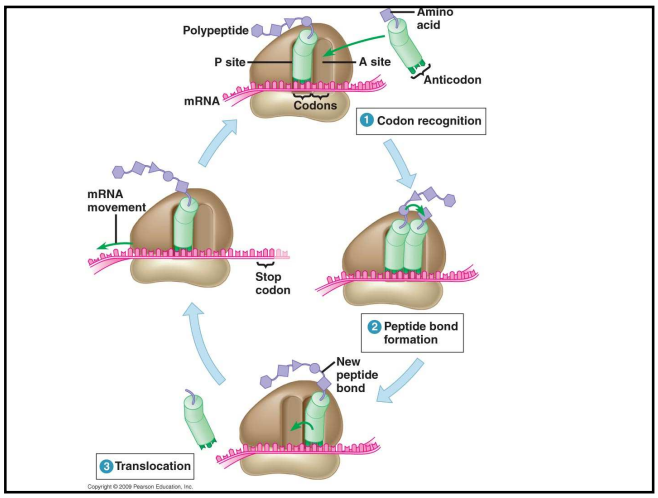




- Termination
  - Ribosome reaches "stop codon"
  - Creation stops, and a release factor binds to the stop codon
  - Ribosome releases, polypeptide can be modified and used, mRNA is recycled

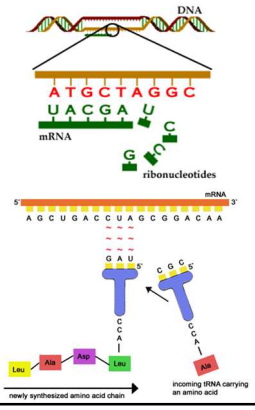






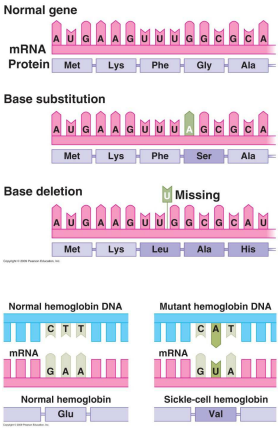
BRING IT ALL TOGETHER....

- Transcription
  - Initiation
  - Elongation
  - Termination
- Translation
  - Initiation
  - Elongation
  - Termination



MUTATIONS

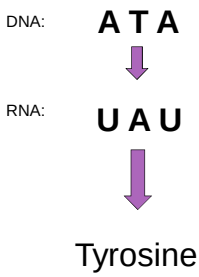
- Changes in the DNA sequence
  - Alterations in sequence of nucleotides
- Altering the DNA alters the mRNA
- Altering mRNA changes the codons
- Since amino acids are specific for a codon, the polypeptide chain can be different during translation



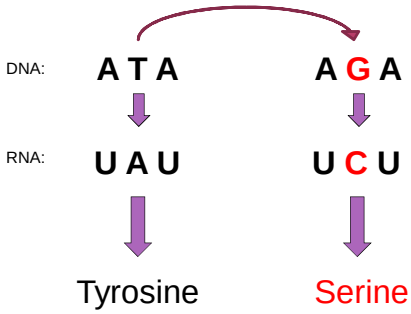
Types of Mutations

Point Mutations - a change in a single DNA nucleotide and, therefore, a change in a specific codon

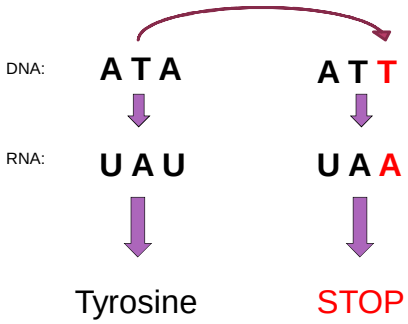
Wild-Type



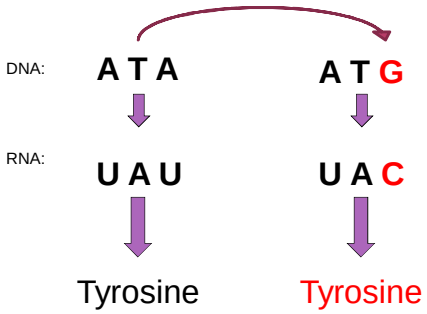
Missense



Nonsense



Silent



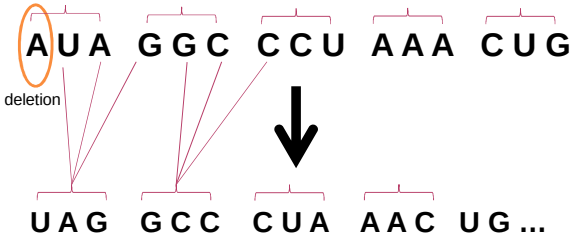
Types of Mutations

Deletion Mutations - the loss of one or more nucleotides in the DNA.

Addition Mutations – the addition of one or more nucleotides in the DNA.

Frame-Shift Mutations – ribosome reading-frame of the mRNA shifts, so ribosome is reading "out of frame."

Frame Shift
(due to a deletion mutation)



MANY AGENTS CAN CAUSE MUTATIONS

Some mutations are spontaneous while others are due to environmental mutagens

Environmental Mutagens

- **Mutagen -** an environmental agent that increases the chances of a mutation
- **Carcinogens -** cancer-causing agents
  - Tobacco smoke contains a number of organic chemicals that are known carcinogens