Translation
Genetic Code
&
Mutations

Translation

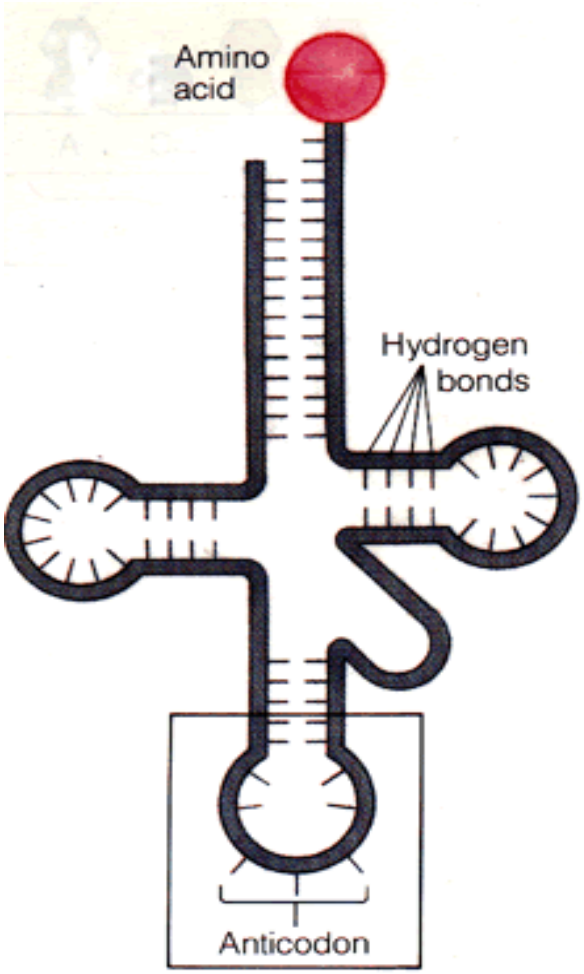
- Translation of mRNA into protein is accomplished by the ribosome.
- Ribosomes bind to the translation initiation sequence on the mRNA, then move down the RNA in a 5' to 3' direction.

  "N-terminal".

  "C-terminal".
- Each group of 3 nucleotides in the mRNA is a "codon", which codes for 1 amino acids. Transfer RNA is the adapter between the 3 bases of the codon and the corresponding amino acid.

Transfer RNA

- Transfer RNA molecules are short RNAs that fold into a characteristic cloverleaf pattern.
- Each tRNA has 3 bases that make up the anticodon. These bases pair with the 3 bases of the codon on mRNA during translation.
- Each tRNA has its corresponding amino acid attached to the 3' end. A set of enzymes, the "aminoacyl tRNA synthetases", are used to "charge" the tRNA with the proper amino acid.
- Some tRNAs can pair with more than one codon. The third base of the anticodon is called the "wobble position", and it can form base pairs with several different nucleotides.

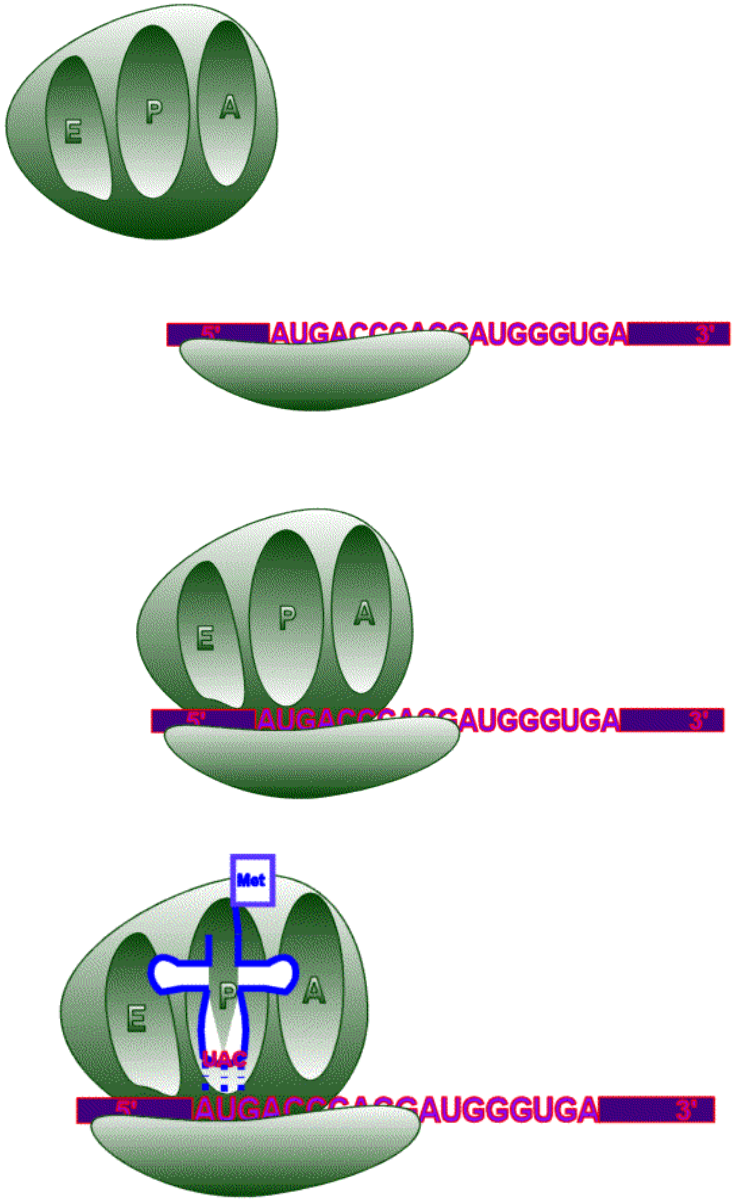


Initiation of Translation

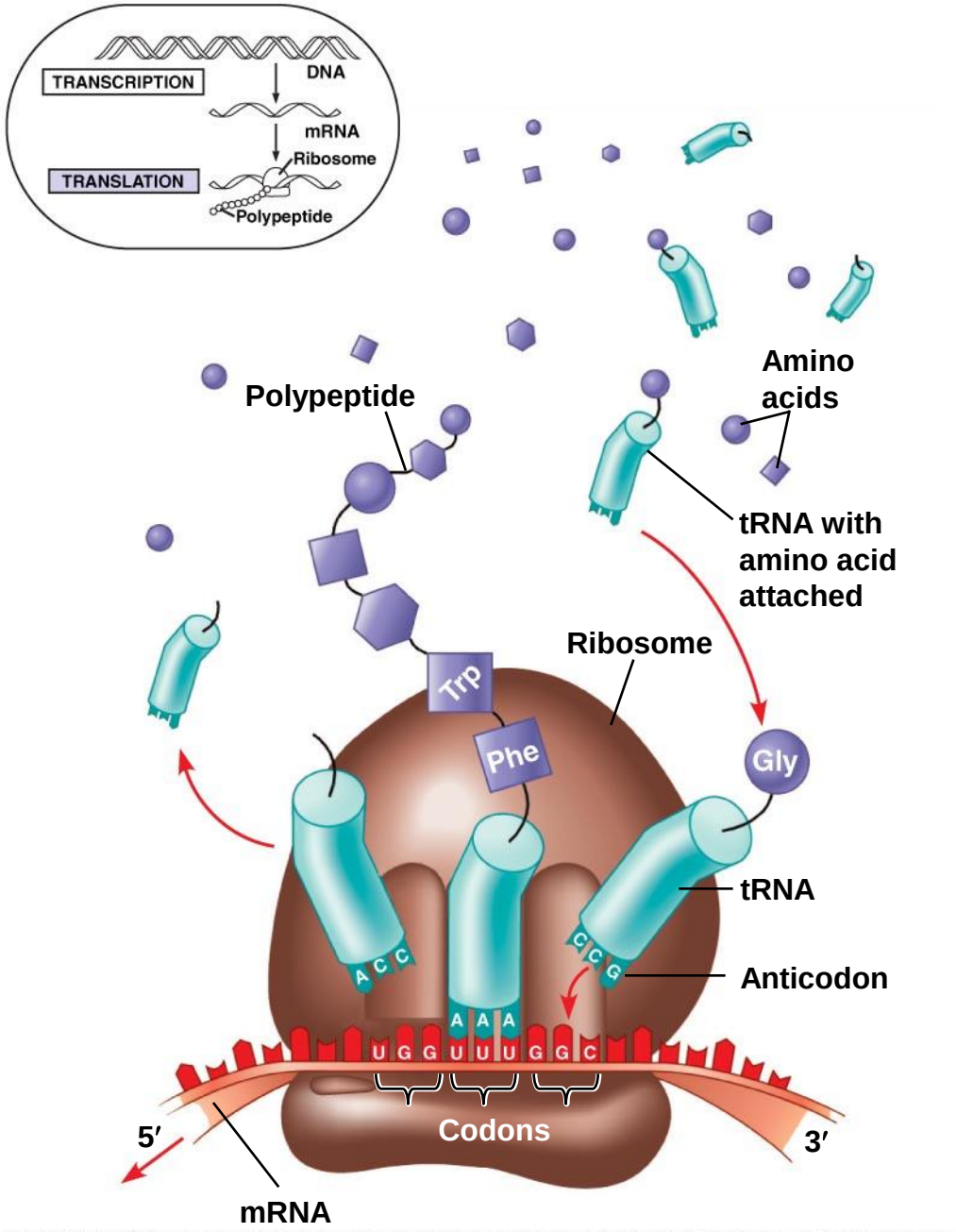
- In prokaryotes, ribosomes bind to specific translation initiation sites. There can be several different initiation sites on a messenger RNA: a prokaryotic mRNA can code for several different proteins. Translation begins at an AUG codon. The modified amino acid methionine is always the first amino acid of the new polypeptide.
- In eukaryotes, ribosomes bind to the 5' cap, then move down the mRNA until they reach the first AUG, the codon for methionine. Translation starts from this point. Eukaryotic mRNAs code for only a single gene.
- Note that translation does not start at the first base of the mRNA. There is an untranslated region at the beginning of the mRNA, the 5' untranslated region (5' UTR).

More Initiation

- The initiation process involves first joining the mRNA, the initiator methionine-tRNA, and the small ribosomal subunit. Several “initiation factors”--additional proteins--are also involved. The large ribosomal subunit then joins the complex.



LE 17-13



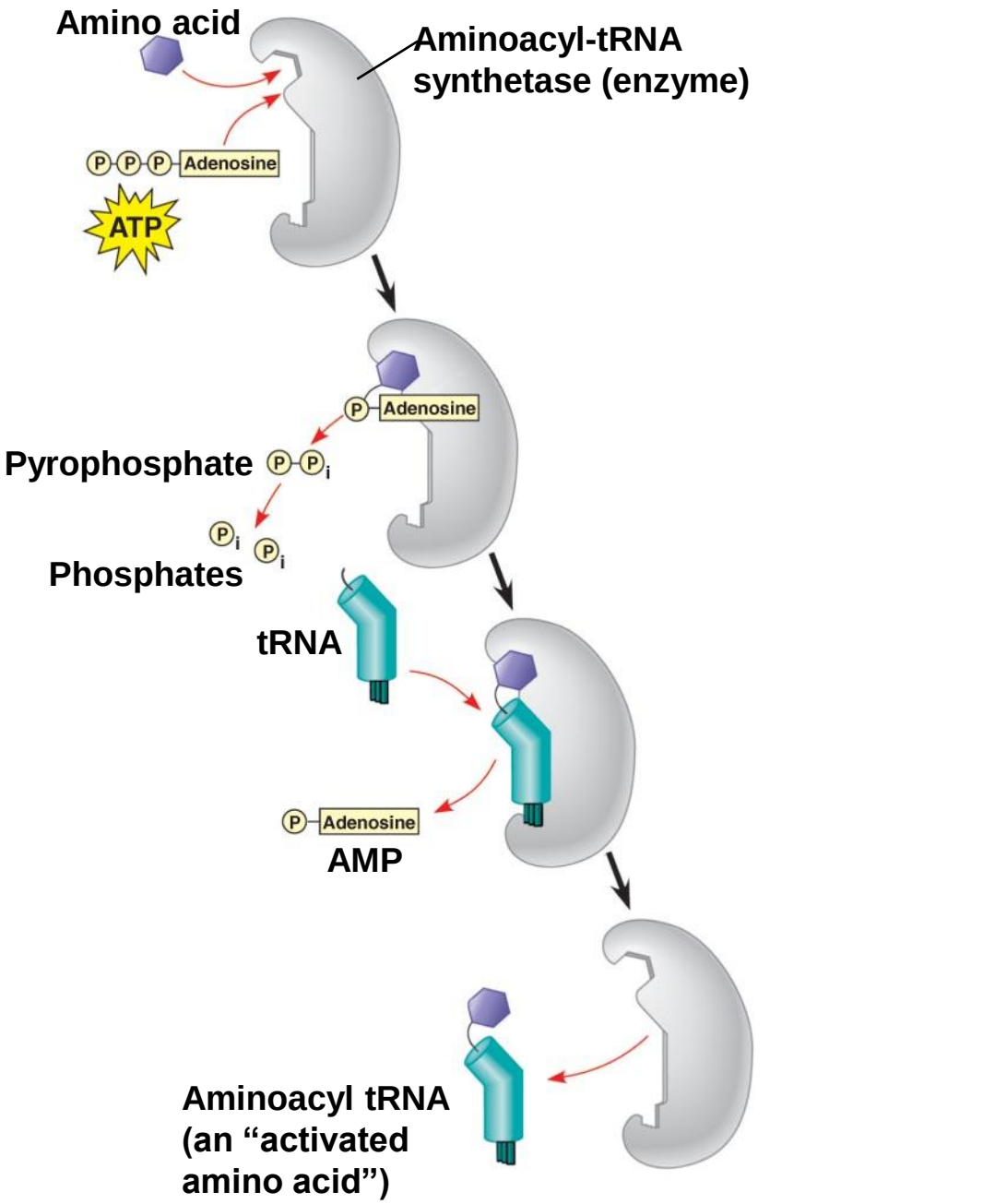
Accurate translation requires two steps

1. a correct match between tRNA and an amino acid
   - Catalyzed by aminoacyl-tRNA synthetase

2. a correct match between the tRNA anticodon and an mRNA codon

LE 17-15

1.



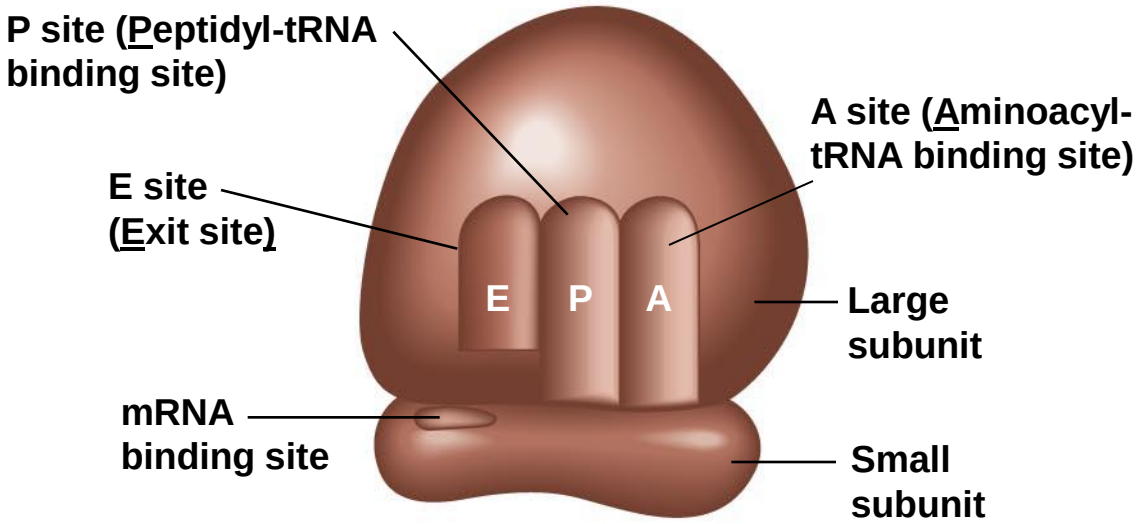
Elongation

- The ribosome has 2 sites for tRNAs, called P and A. The initial tRNA with attached amino acid is in the P site. A new tRNA, corresponding to the next codon on the mRNA, binds to the A site. The ribosome catalyzes a transfer of the amino acid from the P site onto the amino acid at the A site, forming a new peptide bond.
- The ribosome then moves down one codon. The now-empty tRNA at the P site is displaced off the ribosome, and the tRNA that has the growing peptide chain on it is moved from the A site to the P site.

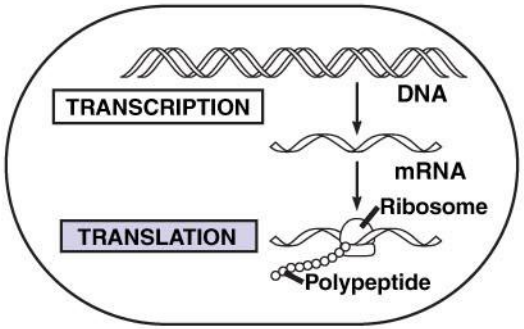
- The process is then repeated:
  - the tRNA at the P site holds the peptide chain, and a new tRNA binds to the A site.
  - the peptide chain is transferred onto the amino acid attached to the A site tRNA.
  - the ribosome moves down one codon, displacing the empty P site tRNA and moving the tRNA with the peptide chain from the A site to the P site.

LE 17-16b

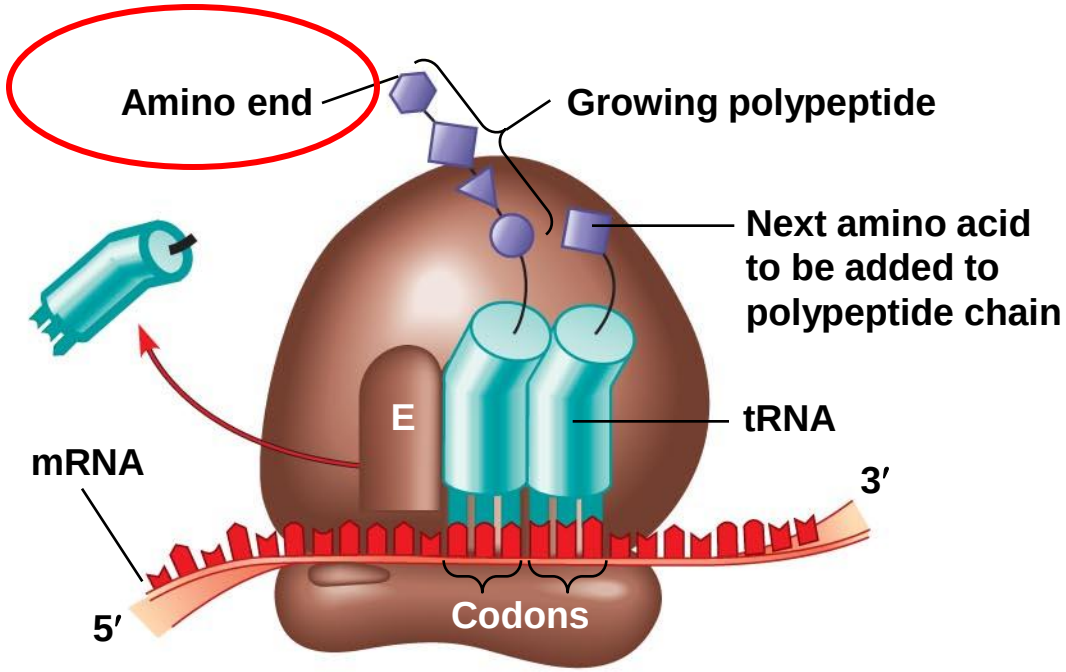
Schematic model showing binding sites on ribosome

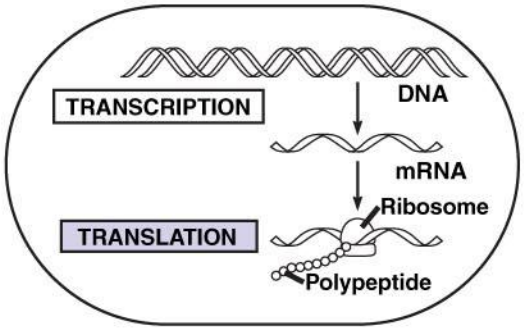


(b)



LE 17-16c



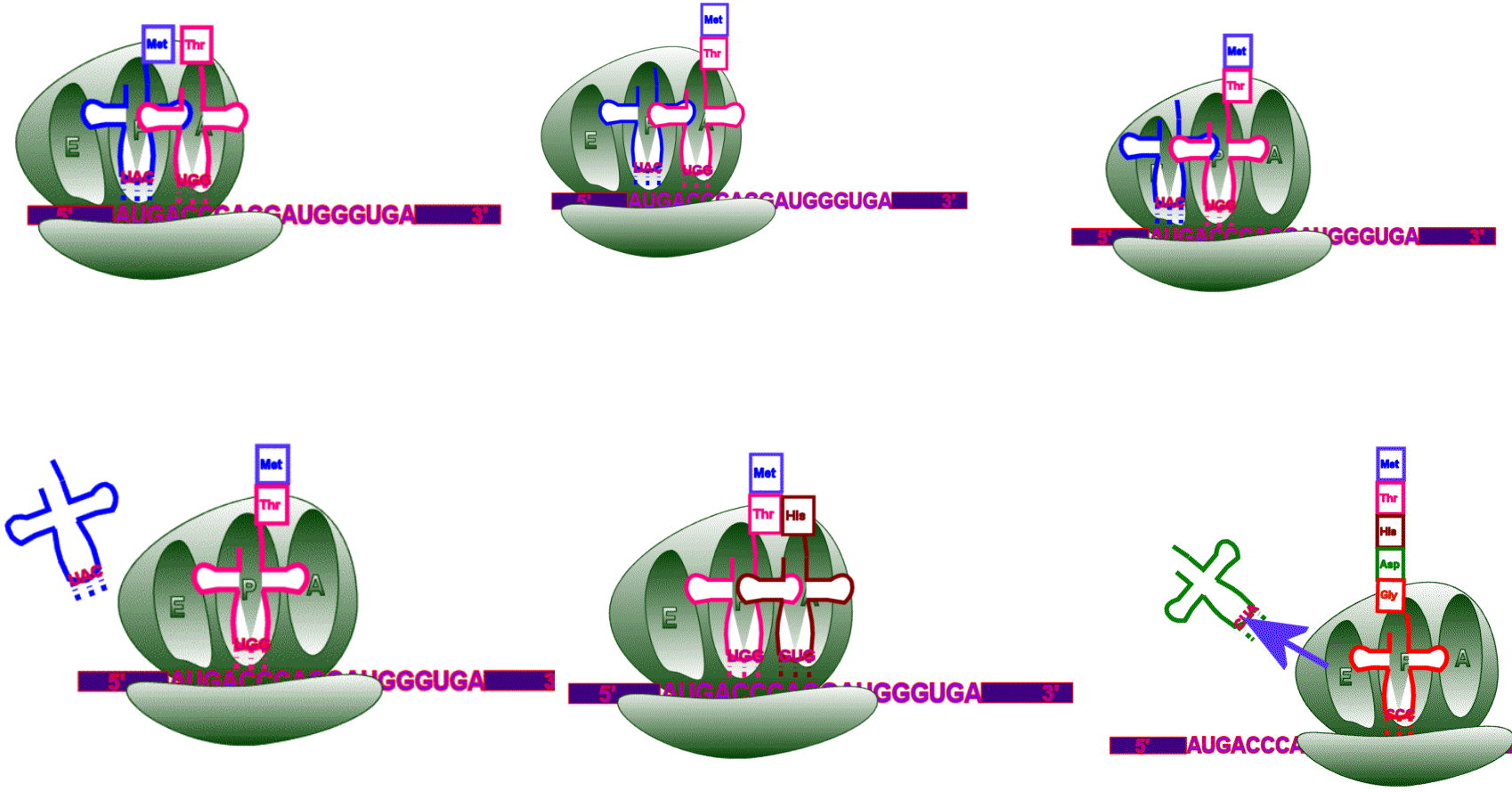


(c) Schematic model with mRNA and tRNA

Ribosome translates 5’ to 3’ on mRNA.

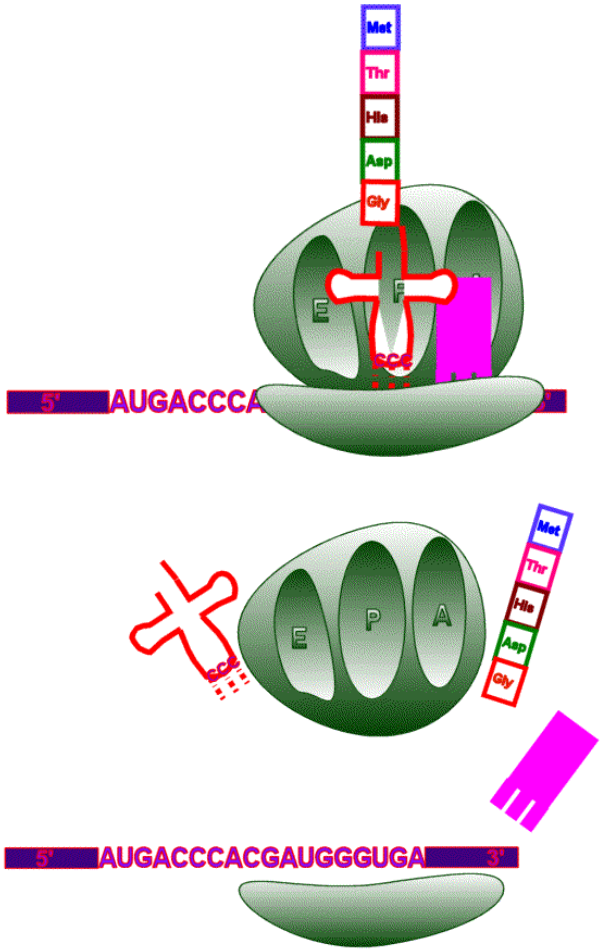
Polypeptide chain grows amino end first, carboxyl end last.

Elongation



Termination

- Three codons are called “stop codons”. They code for no amino acid, and all protein-coding regions end in a stop codon.
- When the ribosome reaches a stop codon, there is no tRNA that binds to it. Instead, proteins called “release factors” bind, and cause the ribosome, the mRNA, and the new polypeptide to separate. The new polypeptide is completed.
- Note that the mRNA continues on past the stop codon. The remaining portion is not translated: it is the 3’ untranslated region (3’ UTR).

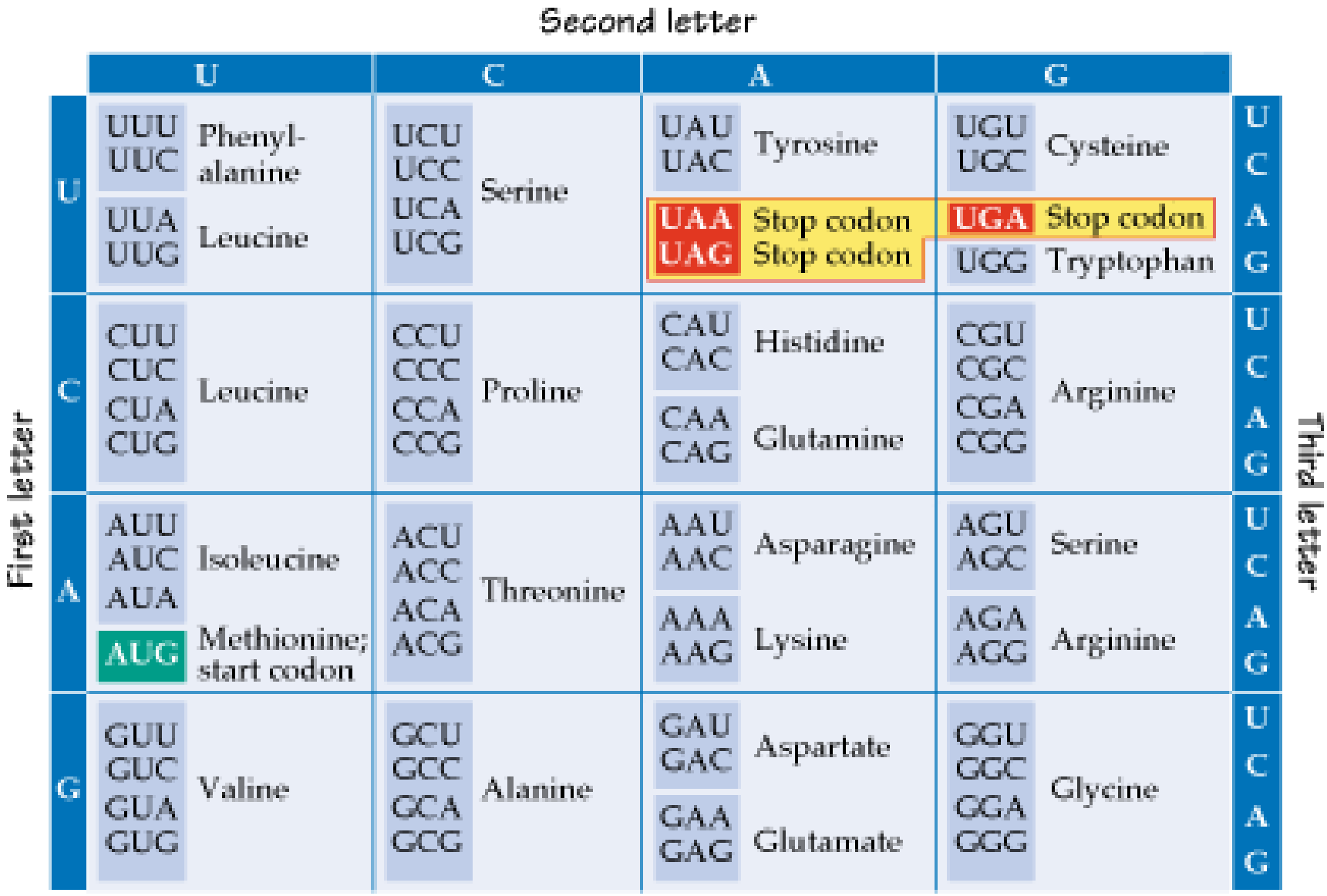


Post-Translational Modification

- New polypeptides usually fold themselves spontaneously into their active conformation. However, some proteins are helped and guided in the folding process by chaperone proteins
- Many proteins have sugars, phosphate groups, fatty acids, and other molecules covalently attached to certain amino acids. Most of this is done in the endoplasmic reticulum.
- Many proteins are targeted to specific organelles within the cell. Targeting is accomplished through “signal sequences” on the polypeptide. In the case of proteins that go into the endoplasmic reticulum, the signal sequence is a group of amino acids at the N terminal of the polypeptide, which are removed from the final protein after translation.

The Genetic Code

- Each group of 3 nucleotides on the mRNA is a codon. Since there are 4 bases, there are $4^3 = 64$ possible codons, which must code for 20 different amino acids.
- More than one codon is used for most amino acids: the genetic code is “degenerate”. This means that it is not possible to take a protein sequence and deduce exactly the base sequence of the gene it came from.
- In most cases, the third base of the codon (the wobble base) can be altered without changing the amino acid.
- AUG is used as the start codon. All proteins are initially translated with methionine in the first position, although it is often removed after translation. There are also internal methionines in most proteins, coded by the same AUG codon.
- There are 3 stop codons, also called “nonsense” codons. Proteins end in a stop codon, which codes for no amino acid.


Second letter
U
C
A
G
First letter
Third letter
U
UUU UUC Phenyl-alanine
UUA UUG Leucine
UCU UCC UCA UCG Serine
UAU UAC Tyrosine
UAA Stop codon
UAG Stop codon
UGU UGC Cysteine
UGA Stop codon
UGG Tryptophan
C
CUU CUC CUA CUG Leucine
CCU CCC CCA CCG Proline
CAU CAC Histidine
CAA CAG Glutamine
CGU CGC CGA CGG Arginine
A
AUU AUC AUA Isoleucine
AUG Methionine; start codon
ACU ACC ACA ACG Threonine
AAU AAC Asparagine
AAA AAG Lysine
AGU AGC Serine
AGA AGG Arginine
G
GUU GUC GUA GUG Valine
GCU GCC GCA GCG Alanine
GAU GAC Aspartate
GAA GAG Glutamate
GGU GGC GGA GGG Glycine

More Genetic Code

- The genetic code is universal. It is used in both prokaryotes and eukaryotes.
- However, some variants exist, mostly in mitochondria which have very few genes.
- For instance, CUA codes for leucine in the universal code, but in yeast mitochondria it codes for threonine. Similarly, AGA codes for arginine in the universal code, but in human and Drosophila mitochondria it is a stop codon.

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Types of Mutations

- Point Mutations
  - Base Pair Substitutions
    - Silent
    - Missense
    - Nonsense
    - Frameshift Mutations
- Variation in Chromosome Number
- Chromosome Abnormalities
  - Deletions
  - Translocations
  - Duplications
  - Inversions

Mutations: genetic material changes in a cell

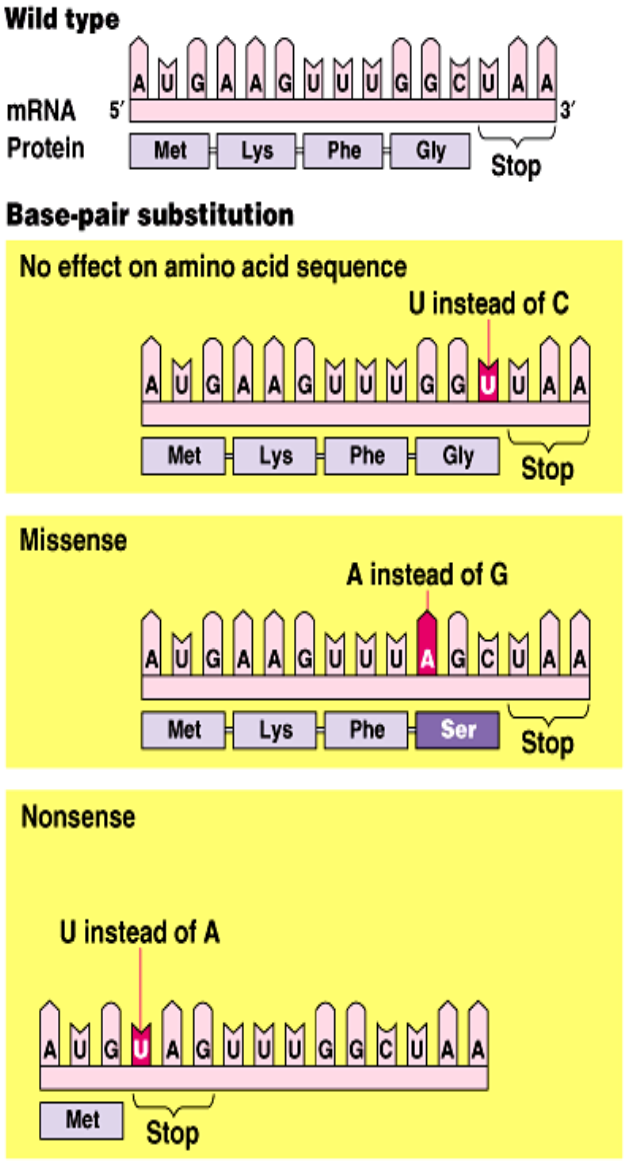
- **Point mutations**….

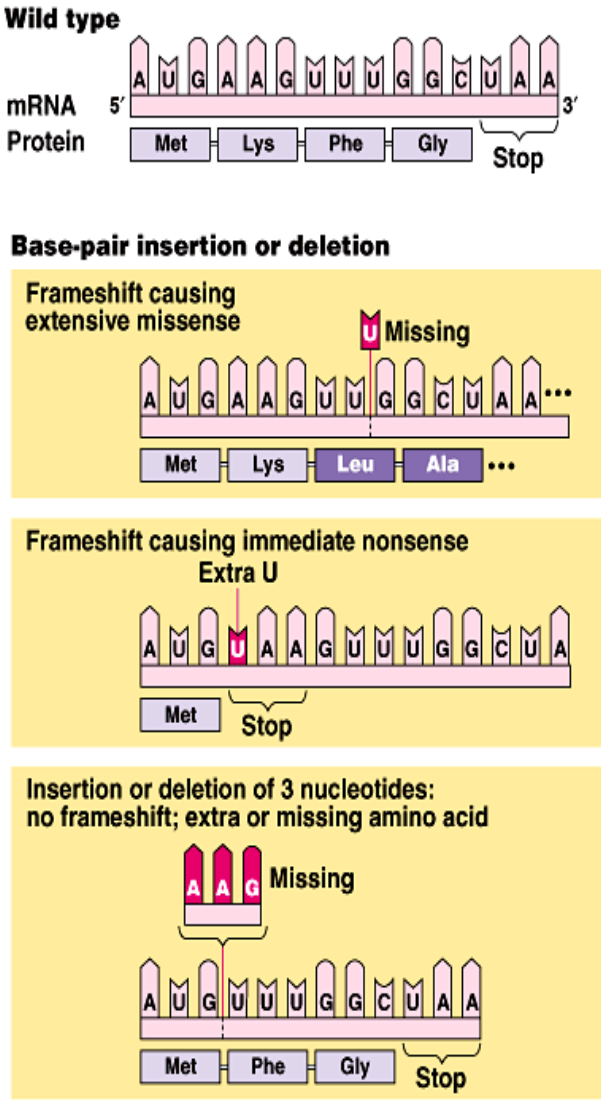
  Changes in 1 or a few base pairs in a single gene

  – **Base-pair substitutions**:
  - ***silent mutations***
    no effect on protein
  - ***missense***
    Δ to a different amino acid (different protein)
  - ***nonsense***
    Δ to a stop codon and a nonfunctional protein

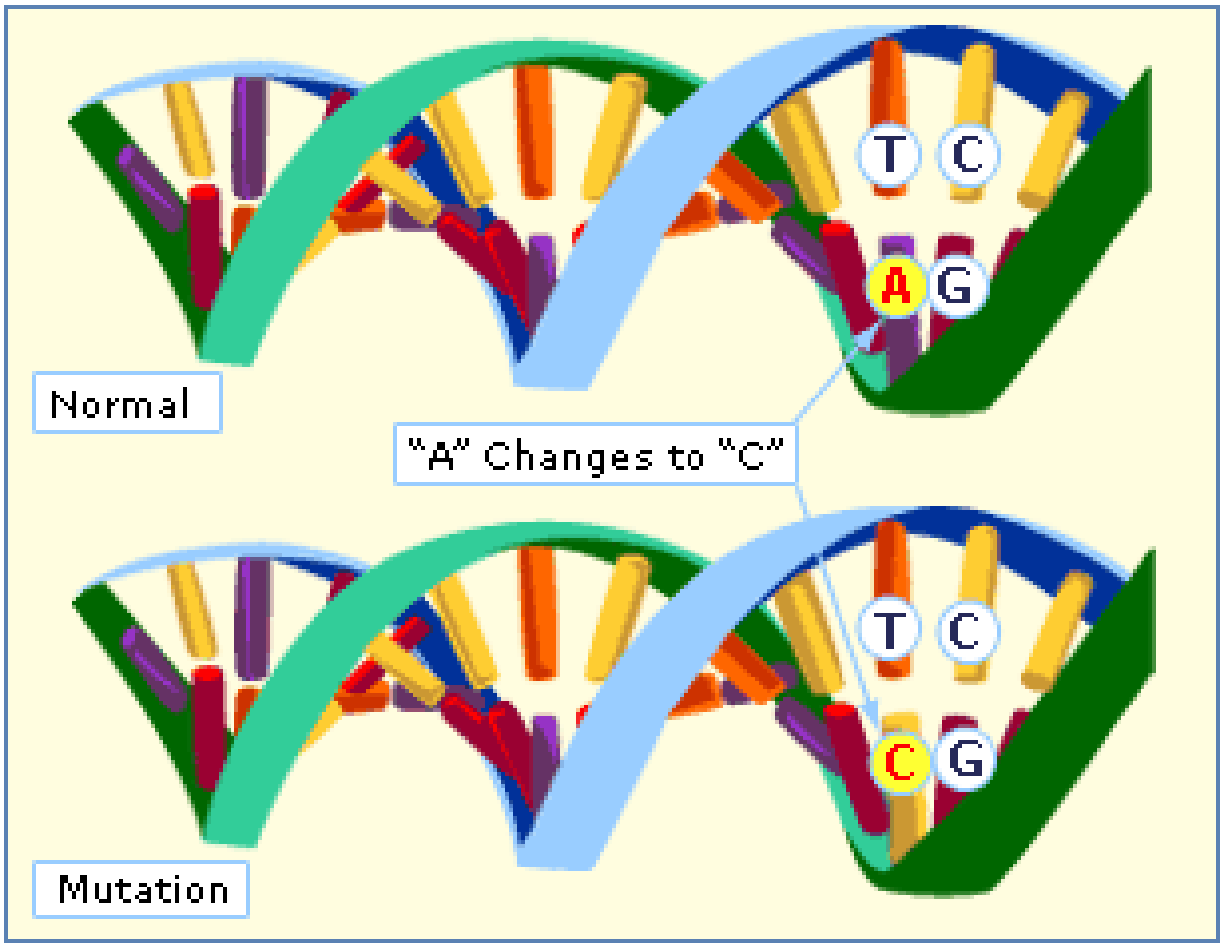
  – **Base-pair insertions or deletions:**
  additions or losses of nucleotide pairs in a gene; alters the 'reading frame' of triplets~*frameshift mutation*

- **Mutagens:** physical and chemical agents that change DNA





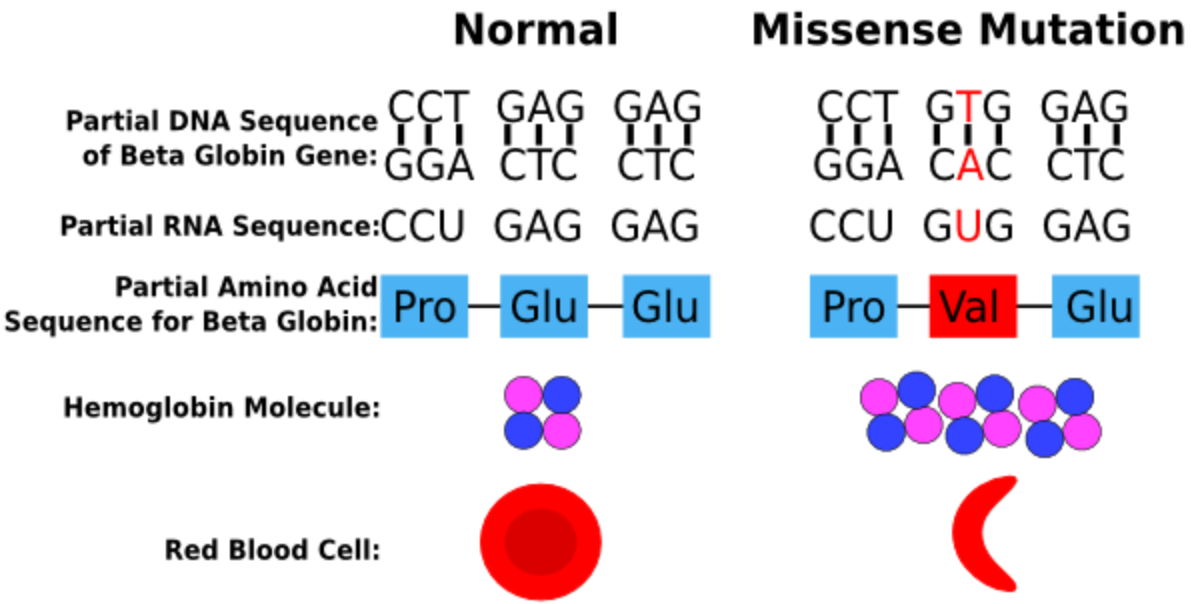
Point Mutations



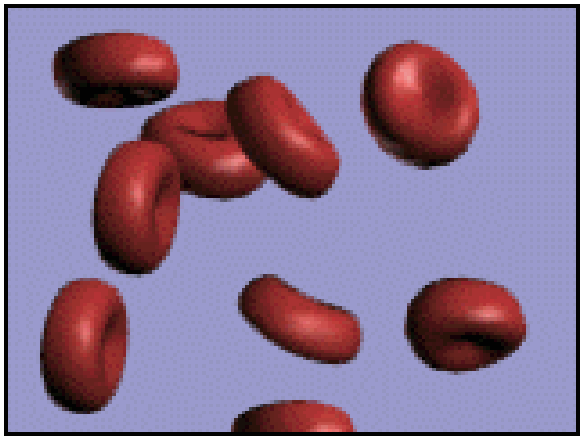
Base-Pair Substitution Mutation

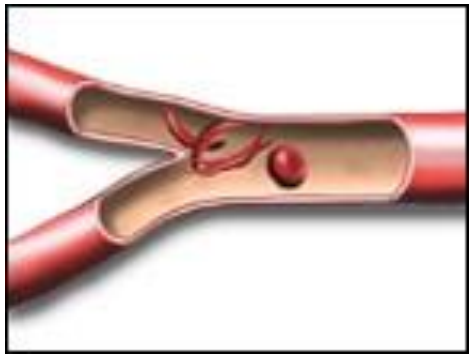
Ex) Missense

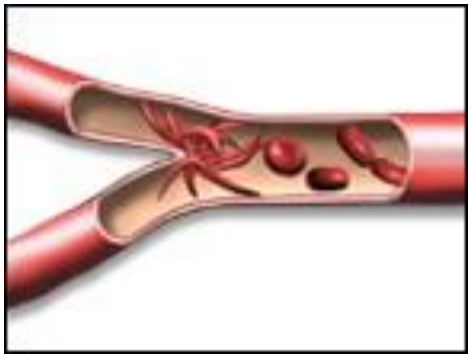
- One Amino Acid Substituted for Another
- Sickle Cell Anemia
  - Valine is replaced with Glutamic Acid

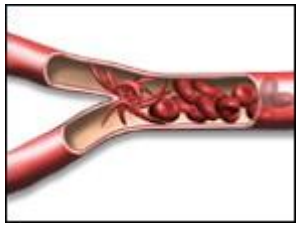


Sickle Cell Anemia



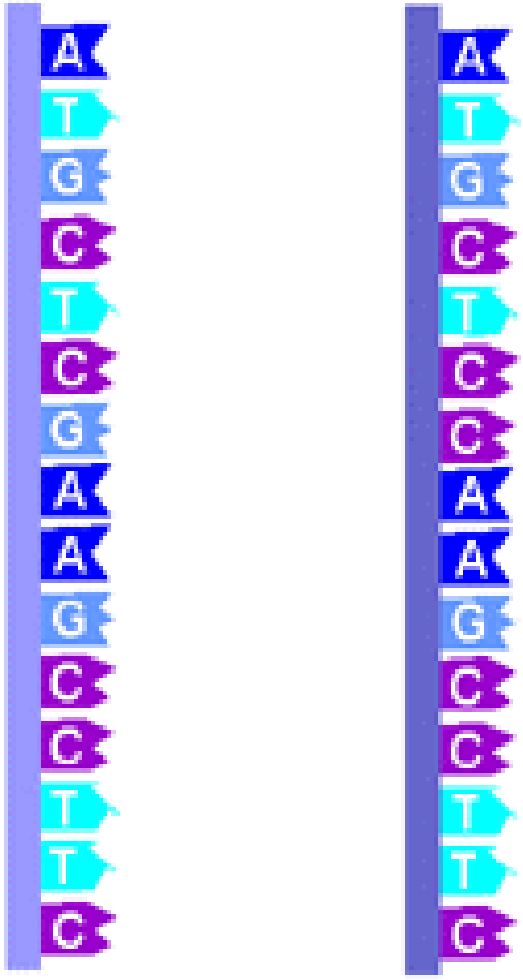




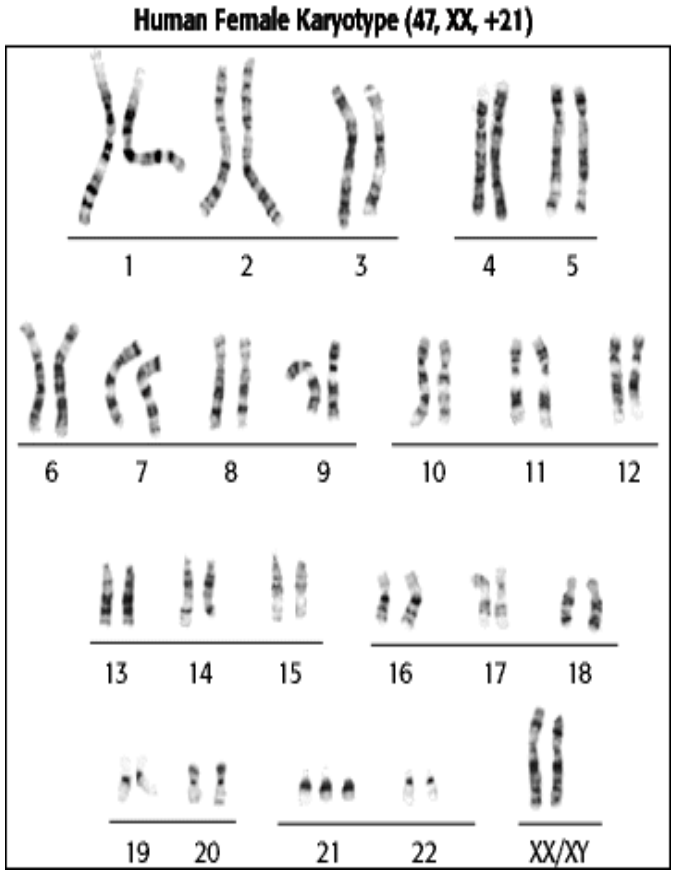


Deletion
Shifts Reading Frame

- A deletion of one or more bases on a section of the chromosome.



Variation in Chromosome Number



- Having any number of chromosomes that does not equal 23 pairs.
- Ex) Down Syndrome – 3 Chromosome 21's

Chromosome Abnormalities

Translocations

- When one piece of a chromosome breaks off and attaches to another chromosome

Animated Translocation

Duplications

- Occurs during crossing over and one chromosome ends up with more genes than it received.

Inversions

- A reversal in the order of a segment of a chromosome