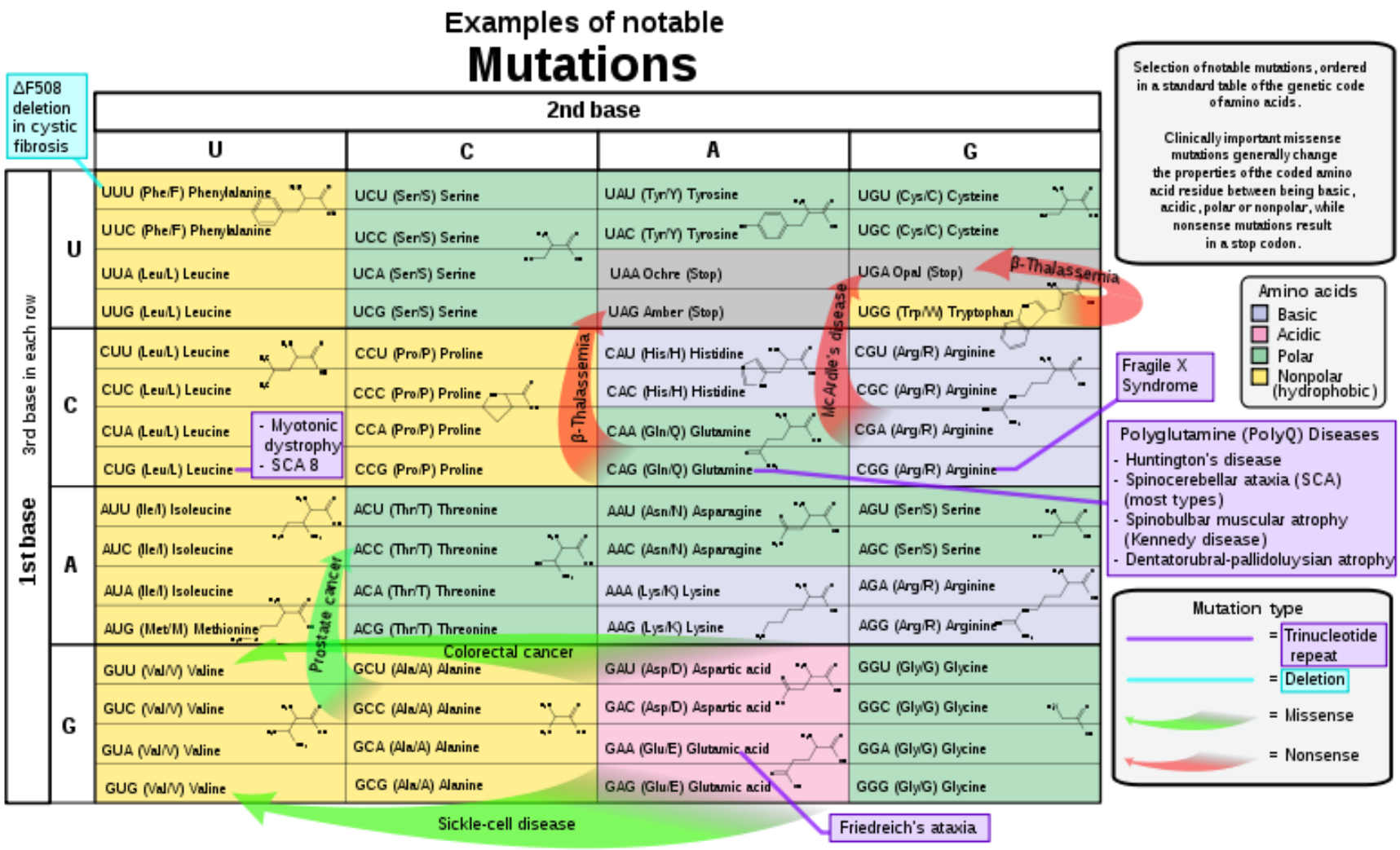
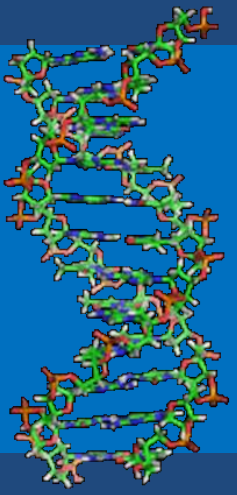
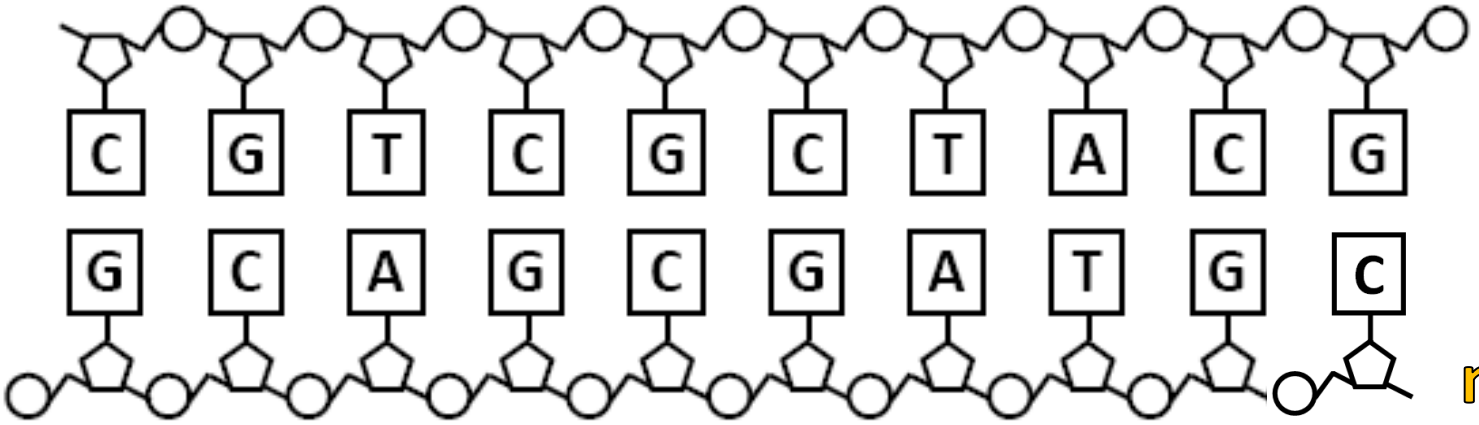
Mutations


Examples of notable
Mutations
ΔF508 deletion in cystic fibrosis
2nd base
1st base
3rd base in each row
U
C
A
G
UUU (Phe/F) Phenylalanine
UUC (Phe/F) Phenylalanine
UUA (Leu/L) Leucine
UUG (Leu/L) Leucine
UCU (Ser/S) Serine
UCC (Ser/S) Serine
UCA (Ser/S) Serine
UCG (Ser/S) Serine
UAU (Tyr/Y) Tyrosine
UAC (Tyr/Y) Tyrosine
UAA Ochre (Stop)
UAG Amber (Stop)
UGU (Cys/C) Cysteine
UGC (Cys/C) Cysteine
UGA Opal (Stop)
UGG (Trp/W) Tryptophan
CUU (Leu/L) Leucine
CUC (Leu/L) Leucine
CUA (Leu/L) Leucine
CUG (Leu/L) Leucine
CCU (Pro/P) Proline
CCC (Pro/P) Proline
CCA (Pro/P) Proline
CCG (Pro/P) Proline
CAU (His/H) Histidine
CAC (His/H) Histidine
CAA (Gln/Q) Glutamine
CAG (Gln/Q) Glutamine
CGU (Arg/R) Arginine
CGC (Arg/R) Arginine
CGA (Arg/R) Arginine
CGG (Arg/R) Arginine
AUU (Ile/I) Isoleucine
AUC (Ile/I) Isoleucine
AUA (Ile/I) Isoleucine
AUG (Met/M) Methionine
ACU (Thr/T) Threonine
ACC (Thr/T) Threonine
ACA (Thr/T) Threonine
ACG (Thr/T) Threonine
AAU (Asn/N) Asparagine
AAC (Asn/N) Asparagine
AAA (Lys/K) Lysine
AAG (Lys/K) Lysine
AGU (Ser/S) Serine
AGC (Ser/S) Serine
AGA (Arg/R) Arginine
AGG (Arg/R) Arginine
GUU (Val/V) Valine
GUC (Val/V) Valine
GUA (Val/V) Valine
GUG (Val/V) Valine
GCU (Ala/A) Alanine
GCC (Ala/A) Alanine
GCA (Ala/A) Alanine
GCG (Ala/A) Alanine
GAU (Asp/D) Aspartic acid
GAC (Asp/D) Aspartic acid
GAA (Glu/E) Glutamic acid
GAG (Glu/E) Glutamic acid
GGU (Gly/G) Glycine
GGC (Gly/G) Glycine
GGA (Gly/G) Glycine
GGG (Gly/G) Glycine
- Myotonic dystrophy
- SCA 8
β-Thalassemia
McArdle's disease
β-Thalassemia
Fragile X Syndrome
Prostate cancer
Colorectal cancer
Sickle-cell disease
Friedreich's ataxia
Selection of notable mutations, ordered in a standard table of the genetic code of amino acids.
Clinically important missense mutations generally change the properties of the coded amino acid residue between being basic, acidic, polar or nonpolar, while nonsense mutations result in a stop codon.
Amino acids
Basic
Acidic
Polar
Nonpolar (hydrophobic)
Polyglutamine (PolyQ) Diseases
- Huntington's disease
- Spinocerebellar ataxia (SCA) (most types)
- Spinobulbar muscular atrophy (Kennedy disease)
- Dentatorubral-pallidoluysian atrophy
Mutation type
= Trinucleotide repeat
= Deletion
= Missense
= Nonsense

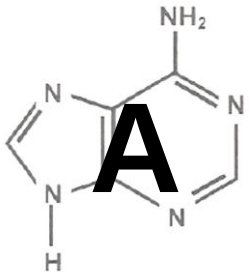
All living things contain ***genetic material*** in the form of **DNA**.

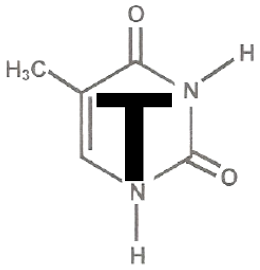


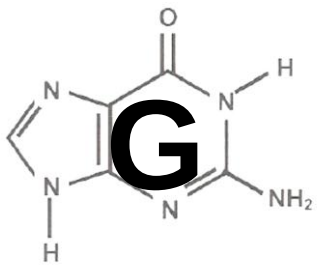


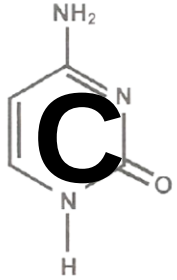
All living things make their DNA out of the same four **nucleotides**.

This means that *ALL living things* use the same 4 **nitrogen bases** to encode the **information** needed by the cell to make *proteins*.

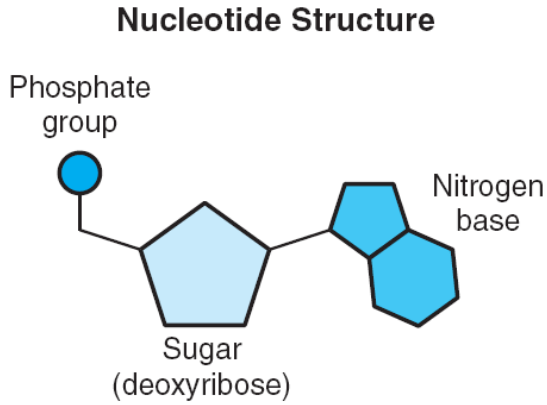








Adenine **Thymine** **Guanine** **Cytosine**

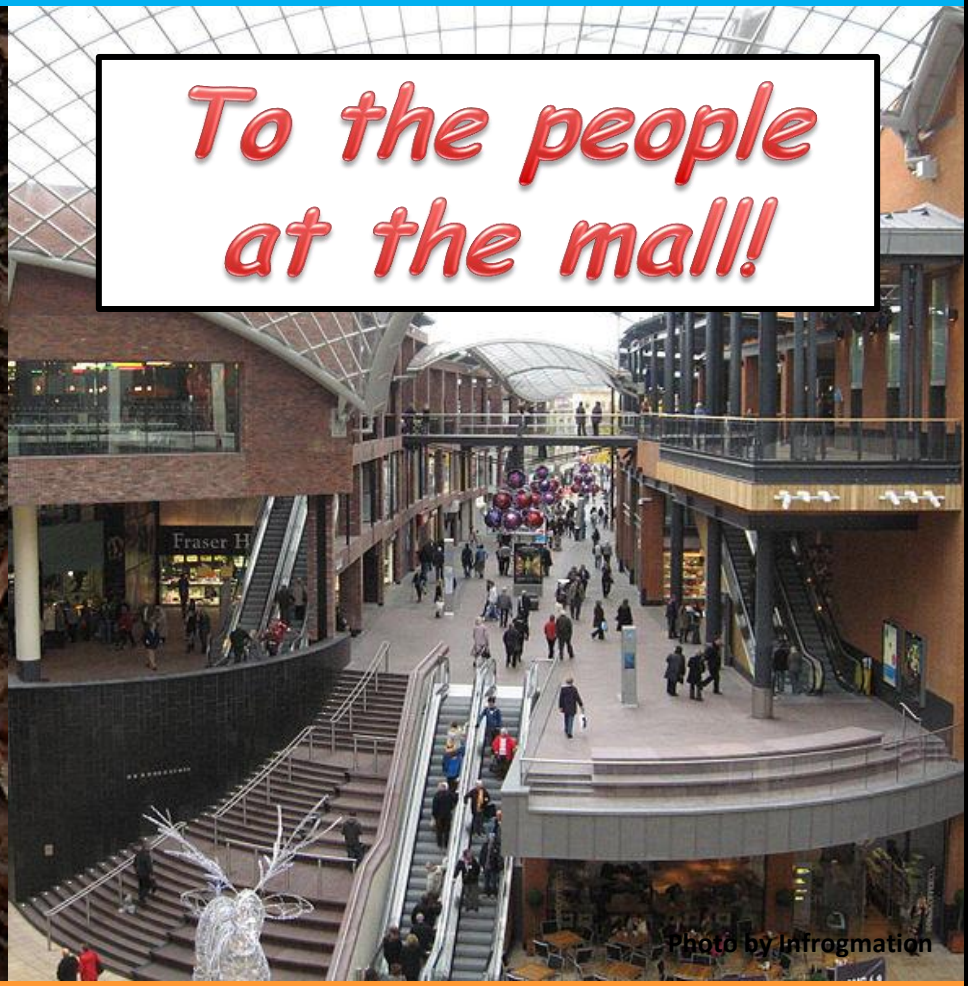


The genetic code is written using the nitrogen bases. The ***order of nitrogen bases*** in each gene determines the sequence of amino acids.

The Genetic Code is common to all...

From the fungus in the ground,

Photo by Archenzo



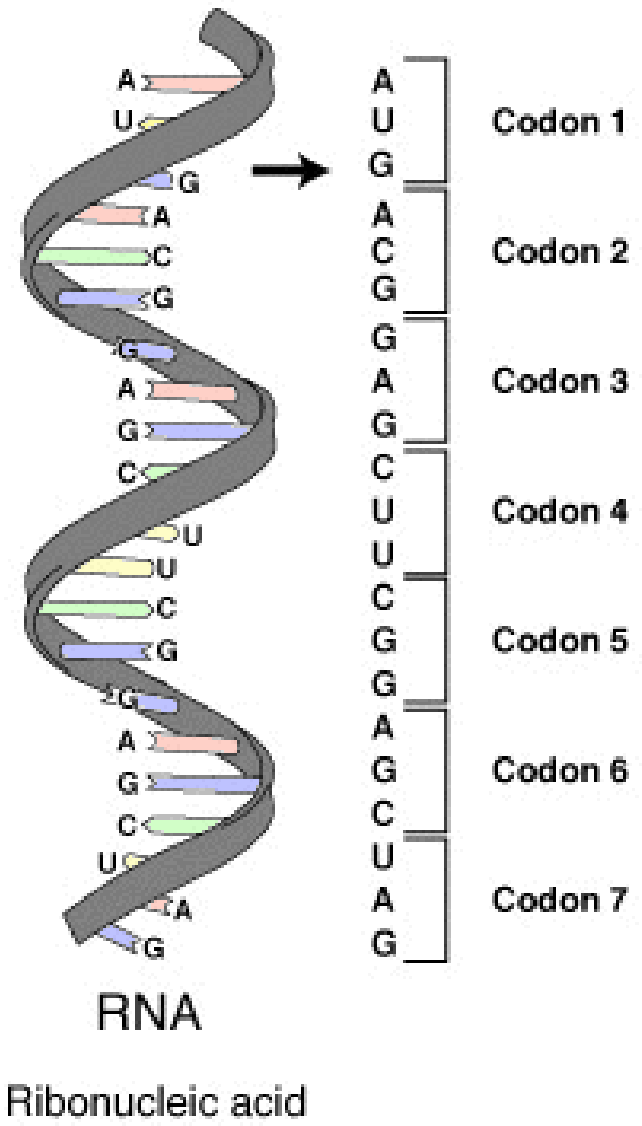
To the people at the mall!

Photo by Infrogmation

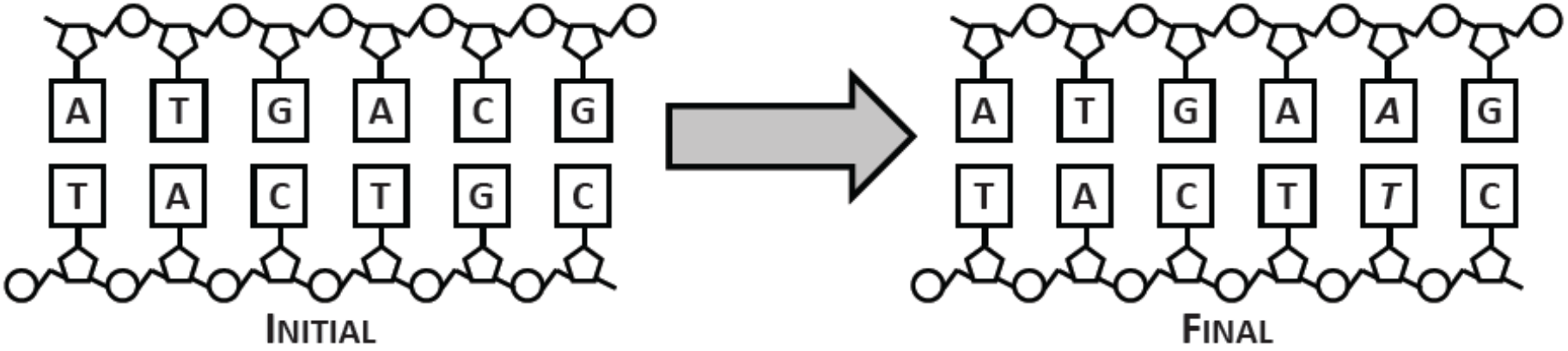
Genetic Code

Each set of 3 nucleotides is known as a *codon*. The sequence of bases in the codon determines the *amino acid* in the protein.

Because codons are three nucleotides long, they are also called nucleotide *triplets*.



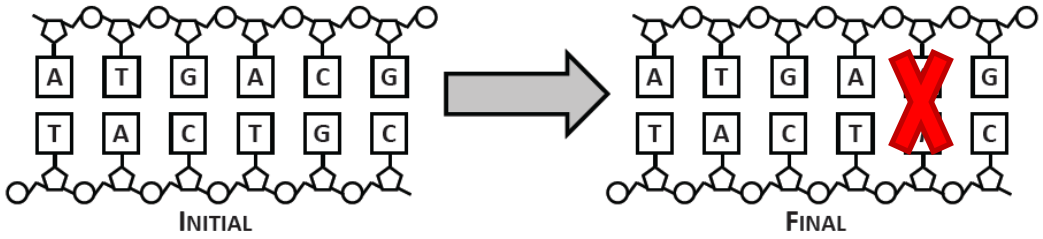
If there is a ***change*** to a nucleotide triplet, there could be a ***change*** to the sequence of amino acids!

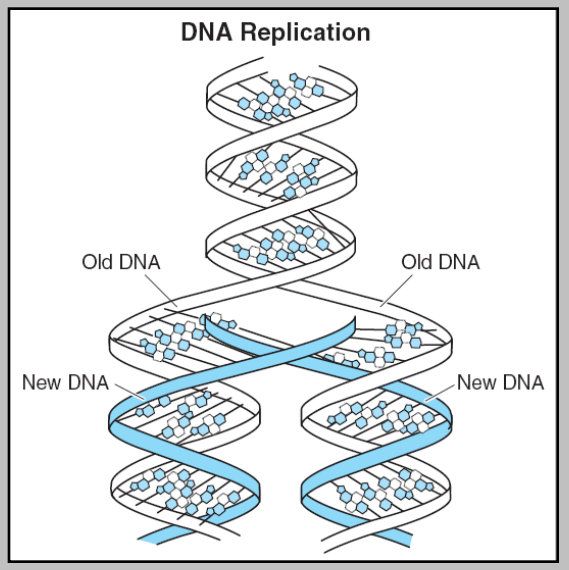


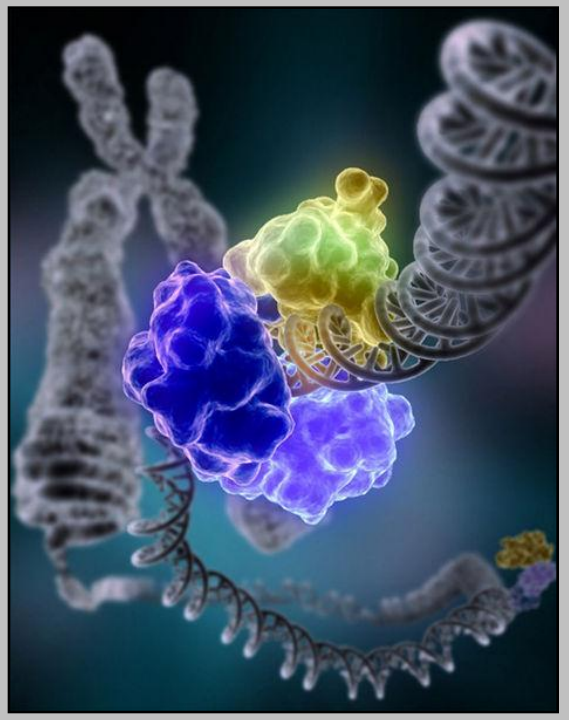
Whenever there is *any change* to the sequence of DNA, it is called a **mutation**.

Mutations

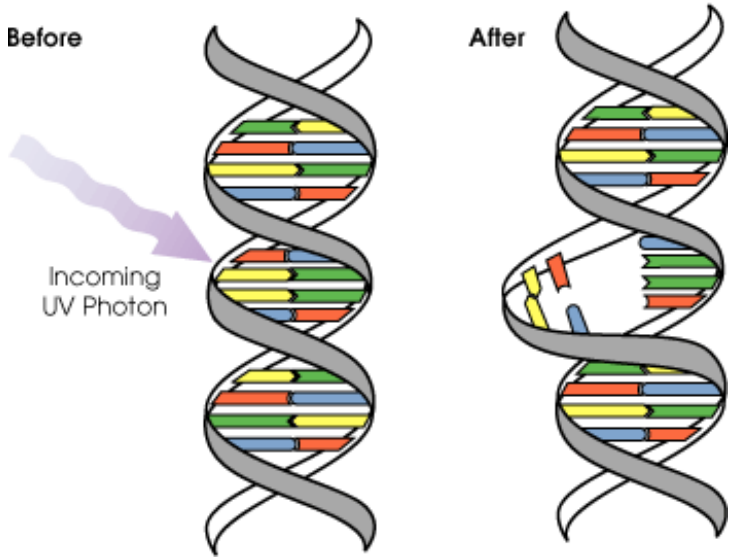
Mutations occur naturally when an organism copies or repairs its DNA incorrectly, but these occurrences are very rare.







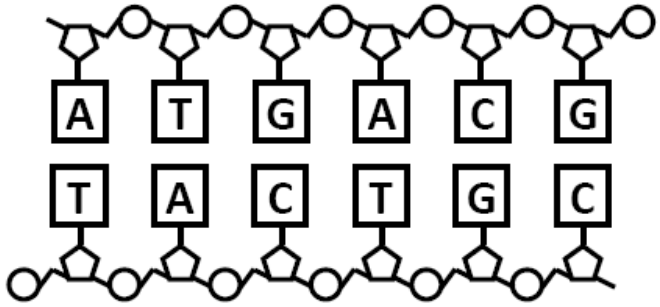
Mutations can be induced by ***chemicals*** or high energy ***radiation***. Anything that causes a mutation is called a **mutagen**.



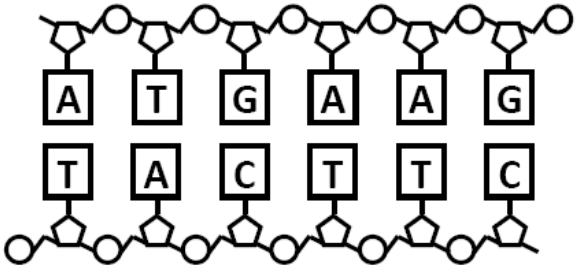
Thymine dimer induced by UV light.

Ultraviolet, x-rays and gamma radiation can all damage DNA.

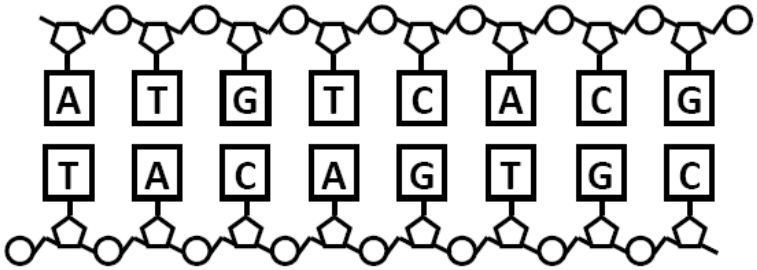
Today we will discuss three types of mutations and evaluate their significance. They are insertions, deletions and substitutions. Decide which strand to the right shows each mutation type based on the original strand shown below.



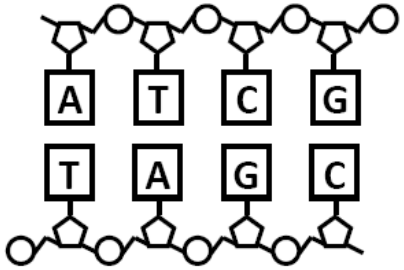
Original DNA Strand



Mutant 1: substitution



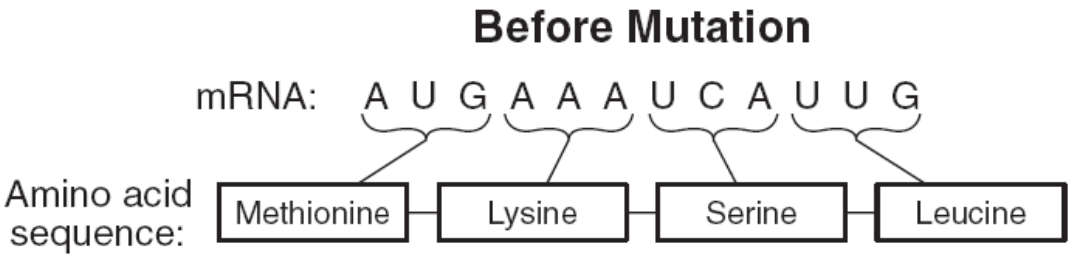
Mutant 2: insertion

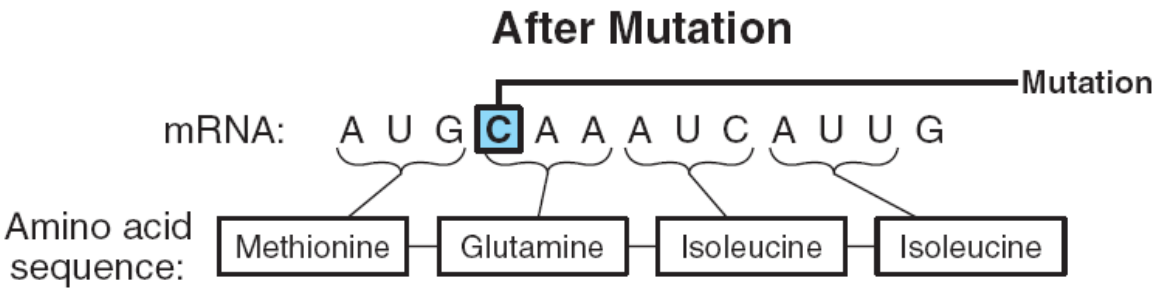


Mutant 3: deletion

Mutations

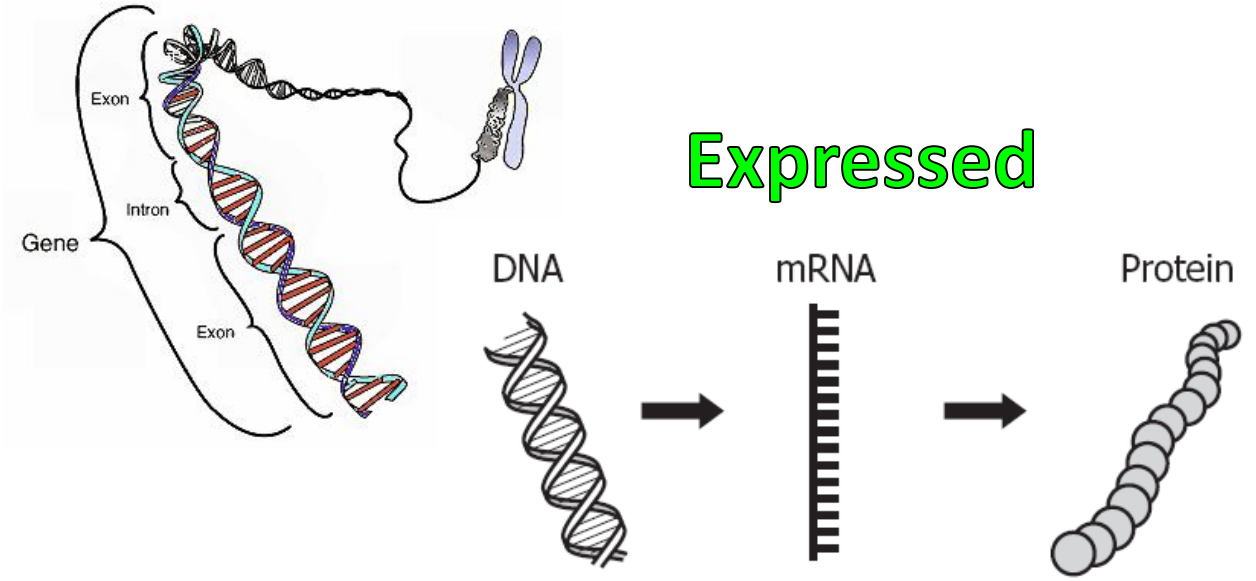
In order to evaluate how a mutation will affect a protein, you have to translate the amino acid sequence. Without doing this, you *cannot* evaluate the significance of a mutation.





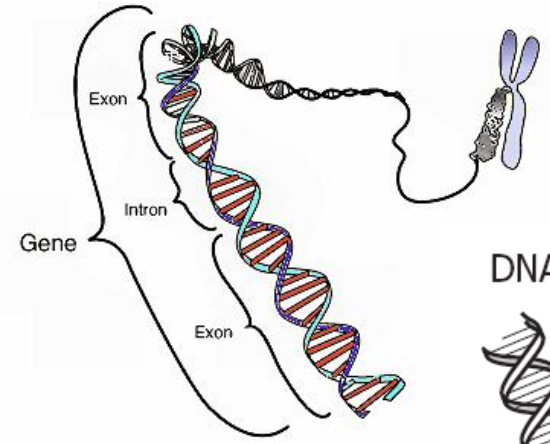
Mutations

Important Fact: Mutations are only significant if they affect genes that are being ***expressed***. Mutations to *unexpressed* genes are typically harmless since they do not affect the cell.



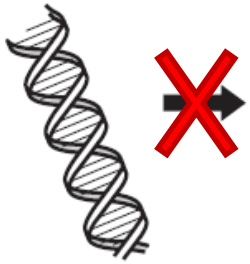
Mutations

Important Fact: Mutations are only significant if they affect genes that are being ***expressed***. Mutations to *unexpressed* genes are typically harmless since they do not affect the cell.



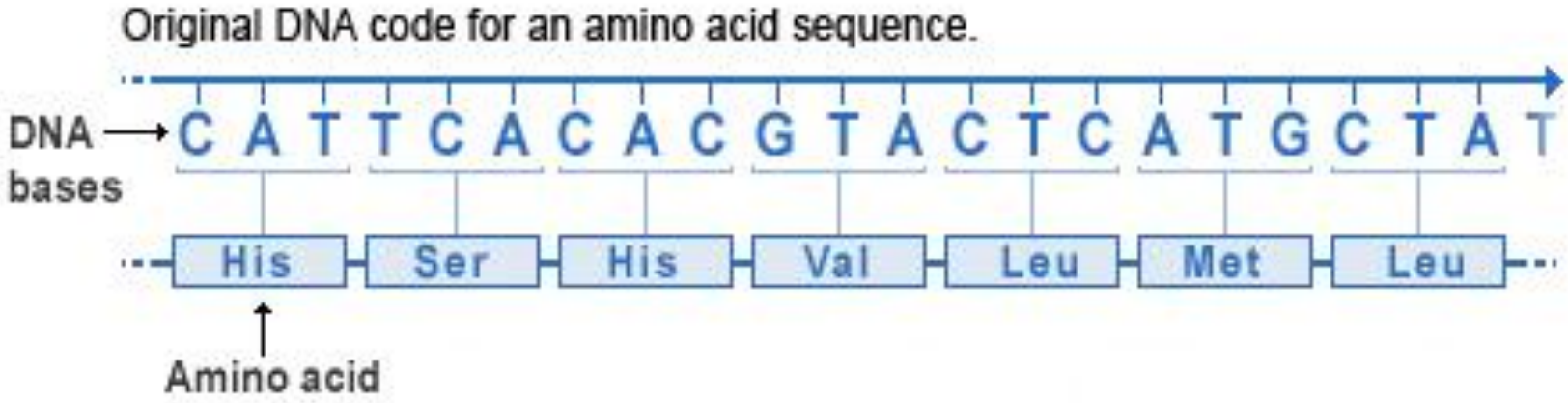
Unexpressed

DNA

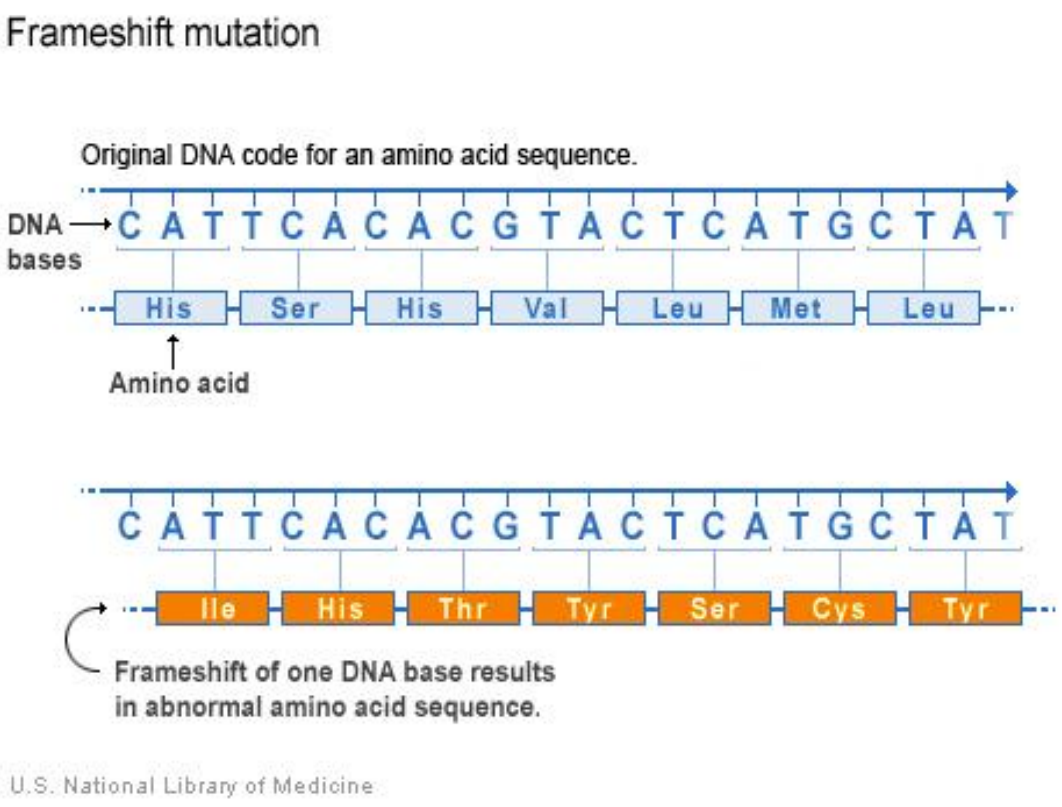


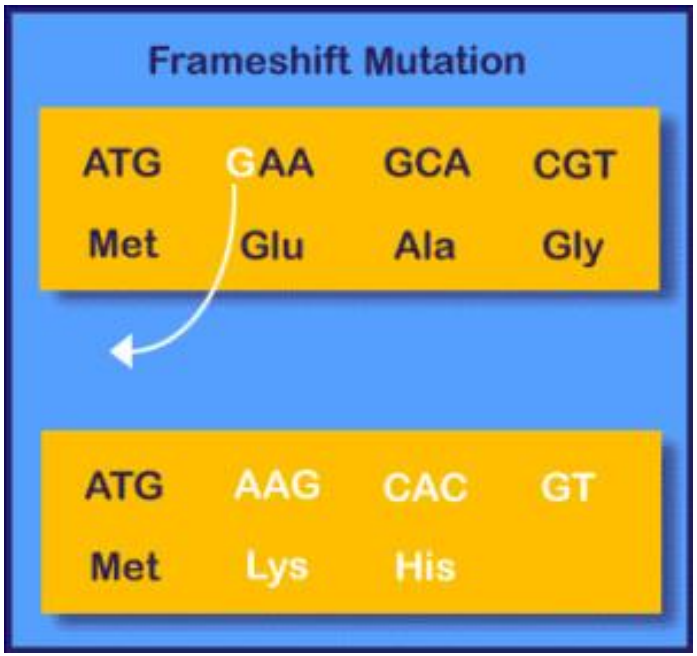
No Products!

Mutations

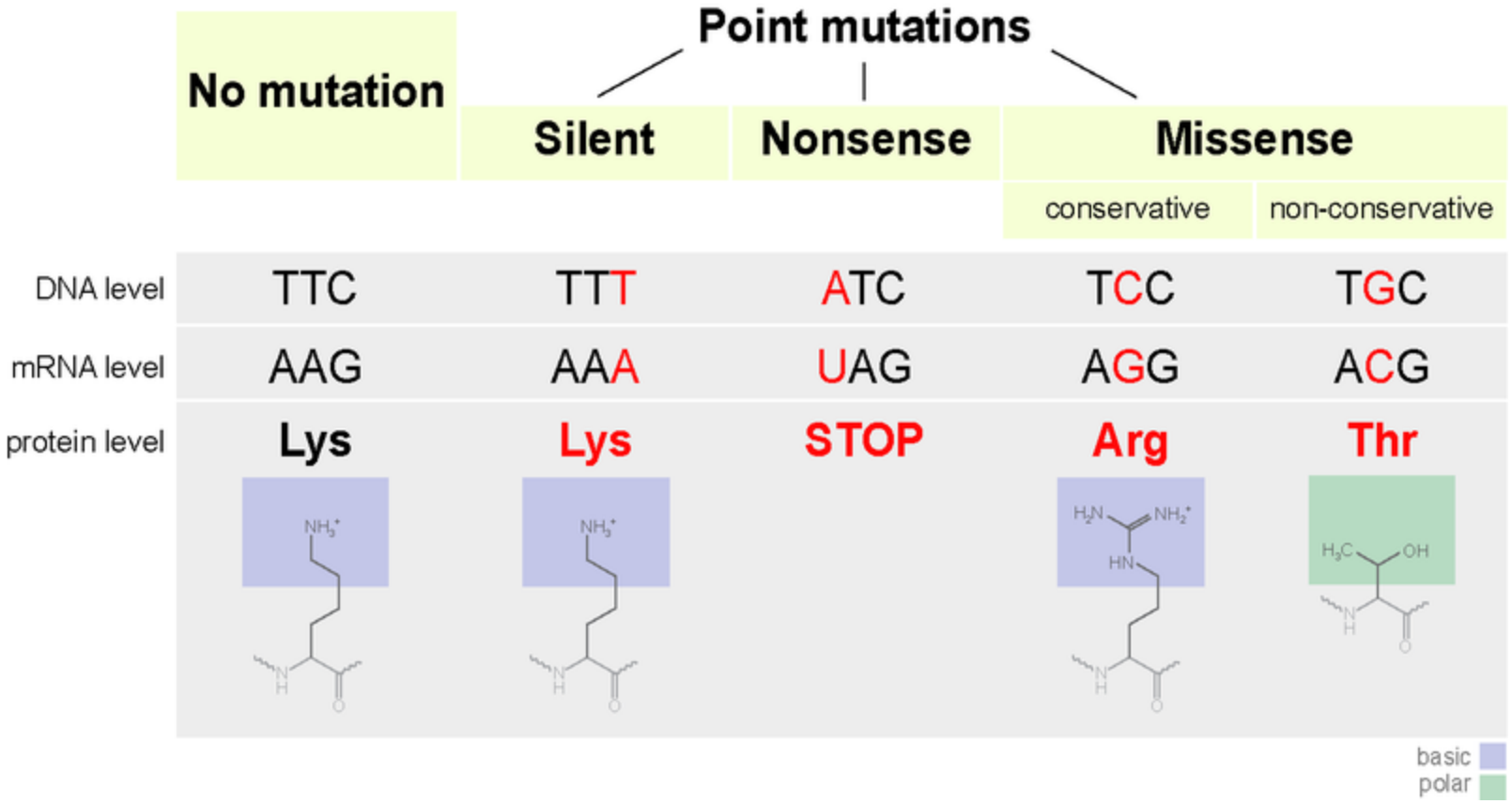


The section of a gene that codes for a protein is known as the *reading frame*. This frame contains all of the codons which are the nucleotide triplets.

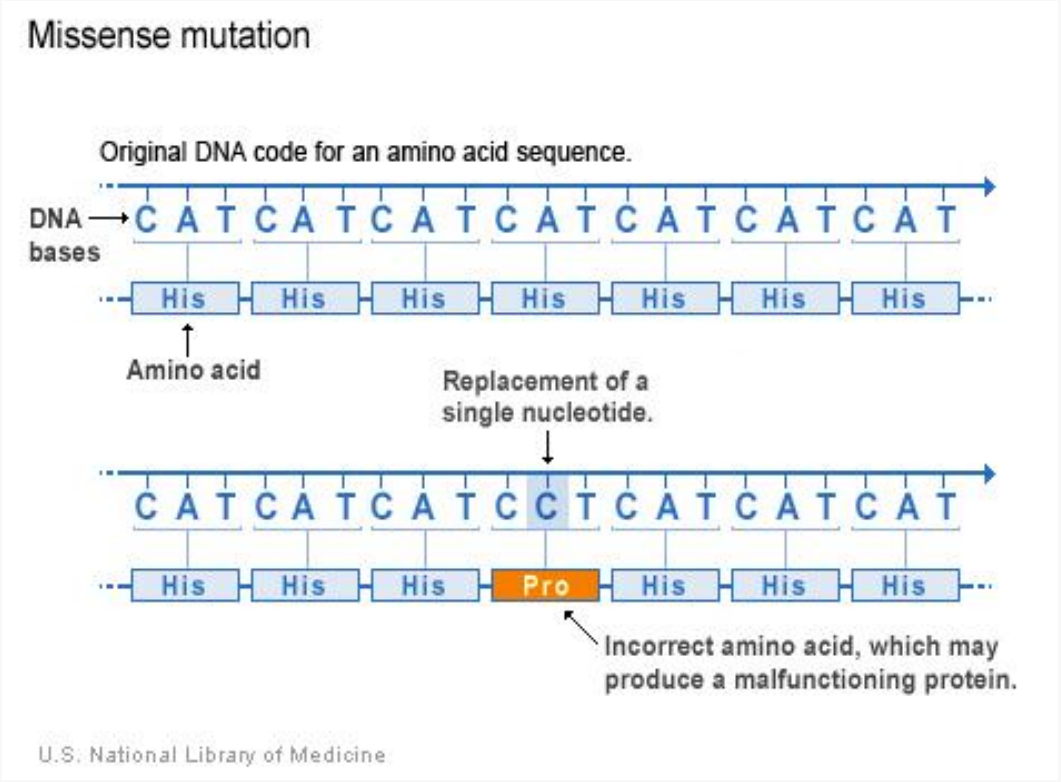


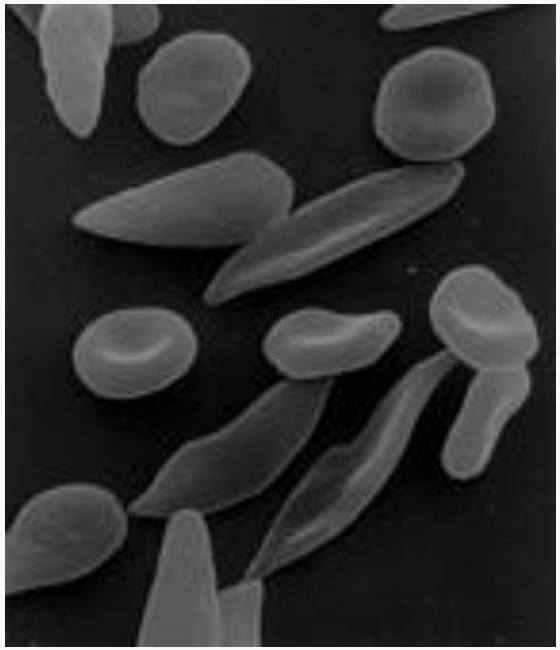


When an insertion or deletion of nucleotides occurs that is *not* divisible by 3, it causes a shift in the reading frame. This is known as a ***frame shift mutation*** and it can change ALL of the amino acids that follow the mutation.

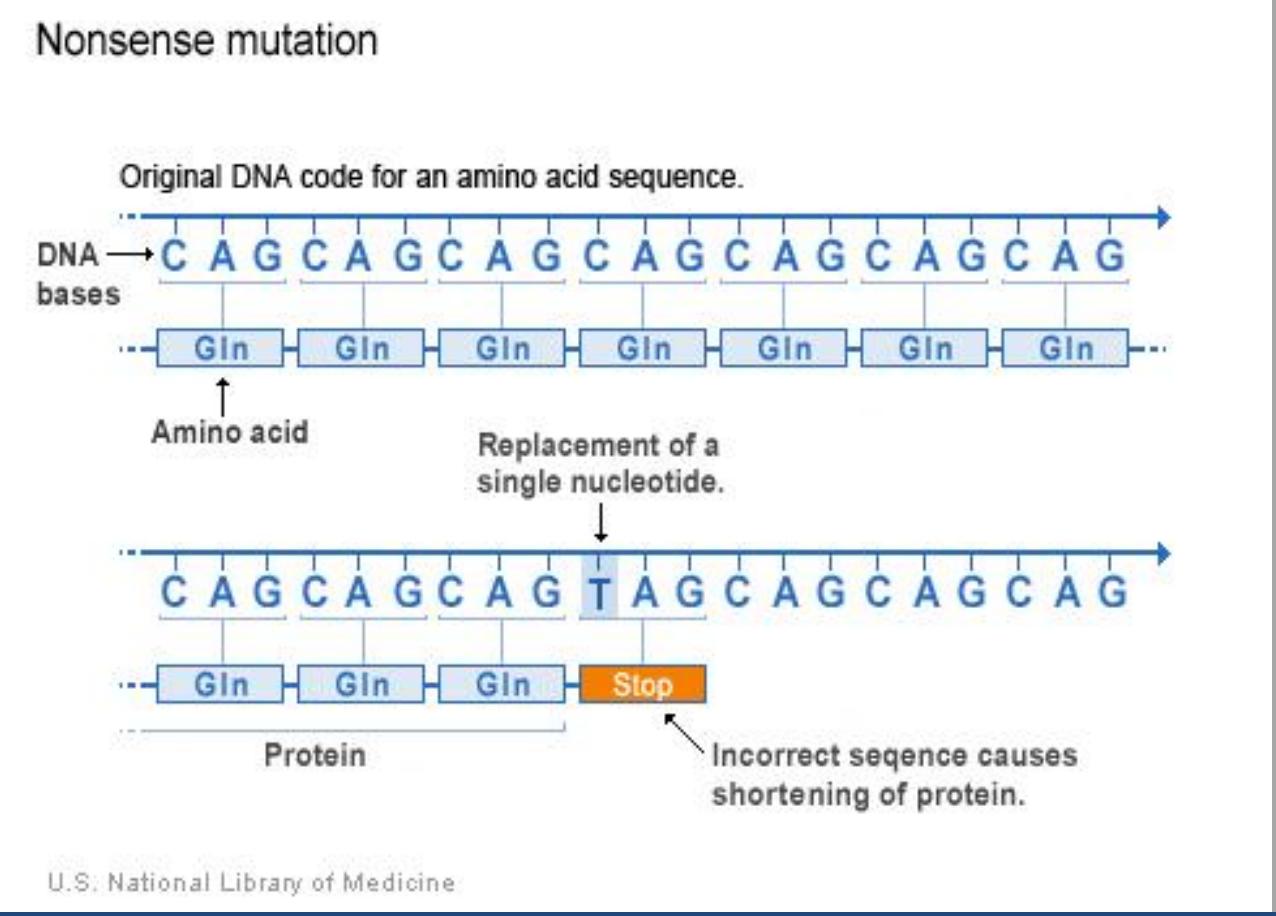


Substitutions are also called point mutations because they involve changing a single base pair, and there is a wide range of consequences that happen as the result of a base pair substitution.





If a point mutation simply *changes the identity of one amino acid*, it is a ***missense mutation***. These mutations may have little effect, or they might have serious consequences as in the case of *sickle-cell anemia*.



Remember:

"STOP the NONSENSE!"

A point mutation can result in the formation of a stop codon. This is known as a *nonsense mutation*. This makes the protein is shorter than normal and it typically does not function correctly.

Strand 1: 3′ C G C A A C A T A 5′
Strand 2: 5′ G C G T T G T A T 3′

Original DNA Segment

Transcription: G C G U U G U A U

Translation: Ala - Leu - Tyr

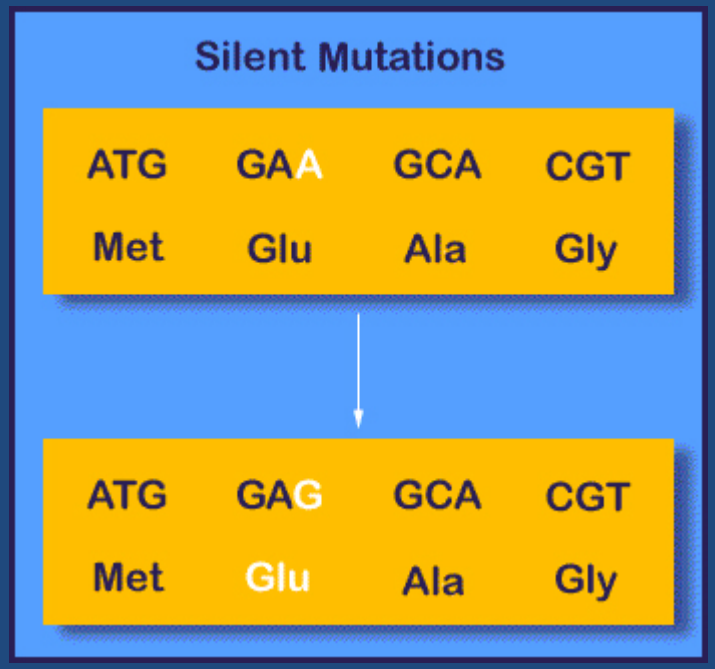
Strand 1: 3′ C G C A A ***T*** A T A 5′
Strand 2: 5′ G C G T T ***A*** T A T 3′

Mutation

Transcription: G C G U U A U A U

Translation: Ala - Leu - Tyr

If a point mutation does not cause a change to the amino acid sequence, it is called a ***silent mutation***. This is because the mutation does not cause an effect that can be observed in the protein.



proline – leucine – threonine proline – STOP

5’ CCG|UUG|ACC 3’ → 5’ CCG|U<u>A</u>G|ACC 3’

1. The chain above represents three codons. Which of the following changes would be expected in the amino acid chain if the mutation shown above occurred?

A The amino acid sequence would be shorter than expected.
B The identity of one amino acid would change.
C The amino acid sequence would remain unchanged.
D The identities of more than one amino acid would change.

2. What type of mutation is illustrated in question 1?

A frame shift mutation
B nonsense mutation
C silent mutation
D missense mutation

threonine – alanine - phenylalanine threonine – alanine - phenylalanine

$5'$ ACG|GCA|UUU $3'$ $\rightarrow$ $5'$ ACG|GC*G*|UUU $3'$

3. The chain above represents three codons. Which of the following changes would be expected in the amino acid chain if the mutation shown above occurred?

A The amino acid sequence would be shorter than expected.
B The identity of one amino acid would change.
C The amino acid sequence would remain unchanged.
D The identities of more than one amino acid would change.

4. What type of mutation is illustrated in question 3?

A frame shift mutation
B nonsense mutation
C silent mutation
D missense mutation