DNA mutation

By:

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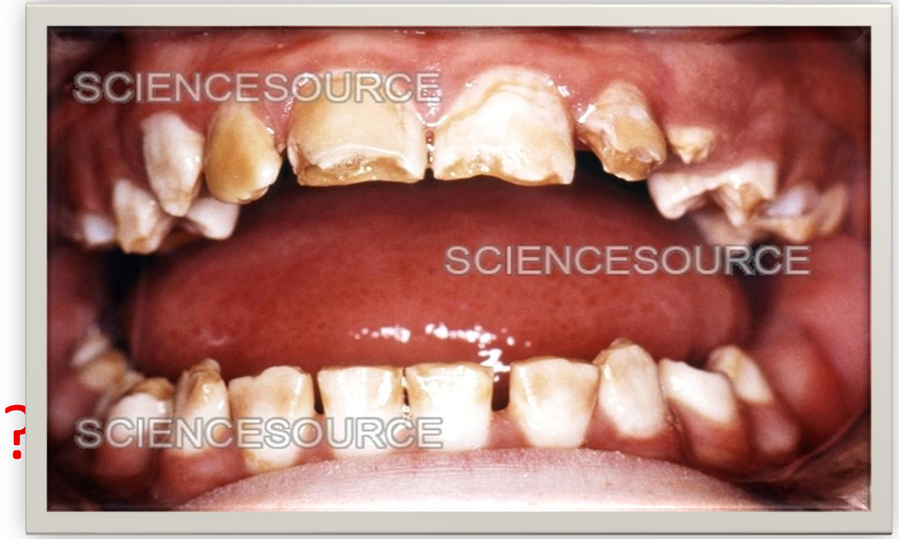
Learning outcomes

- Understand the concept of DNA mutations.
- Identify causes of DNA mutations and different types of mutagens.
- Determine different types of DNA mutations.
- Recognize effects of DNA mutations.
- Correlate DNA mutation with different diseases.

Case Study: Amelogenesis Imperfecta (AI)

A 10-year-old child is brought to the dental clinic by his parents complaining of: Yellowish-brown discoloration of teeth , Increased sensitivity to hot and cold & Teeth appear small and easily worn down. On examination: Enamel is thin and poorly mineralized ,Multiple teeth show chipping and attrition . Family history reveals that the father had similar dental problems

- What is the most likely diagnosis?
- What part of the tooth is affected?
- Could this condition be genetic? If yes, how?



DNA mutation

Definition:

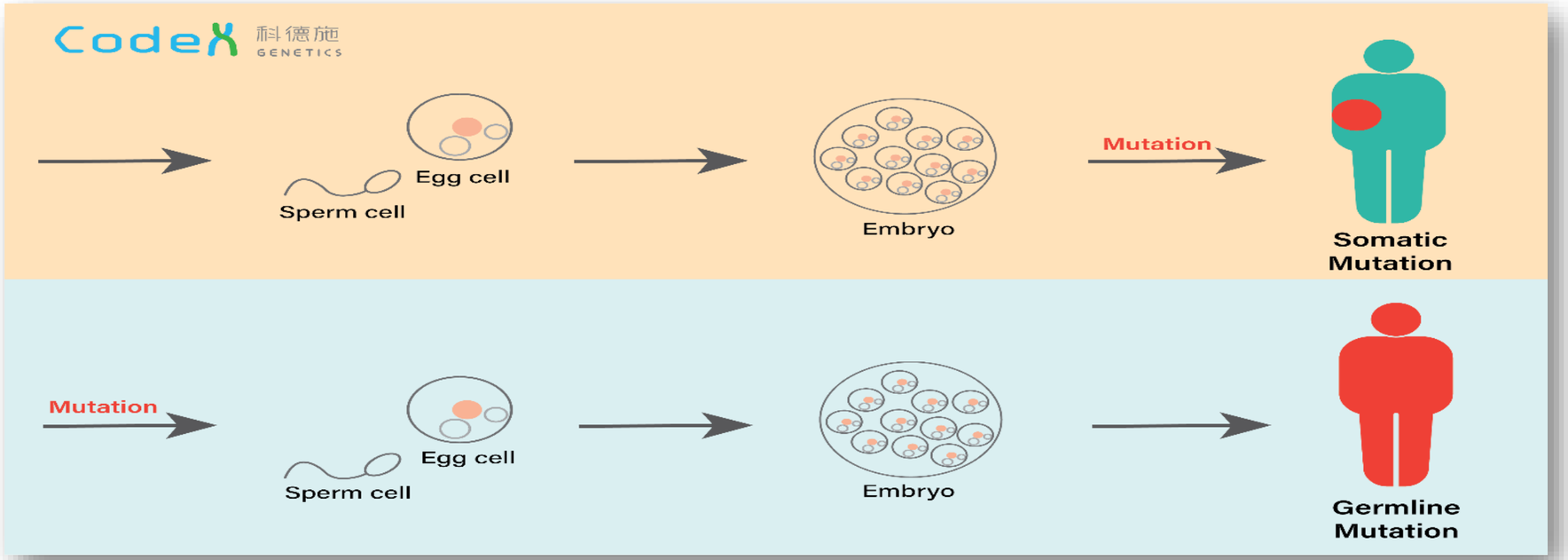
- It is a permanent change in the nucleotide sequence of a section of DNA due to replacement, deletion (removal) or insertion (addition) of one or more bases.
- This Permanent change in DNA sequence may alter the encoding polypeptide sequence resulting in an altered gene product and /or regulation)

DNA mutation

❑ According to the sites: It may be:

1- Germinal mutations occur in germ cells and can be passed on to offspring

2- Somatic mutations occur in somatic cells and cannot be transmitted to offspring, but may lead to diseases



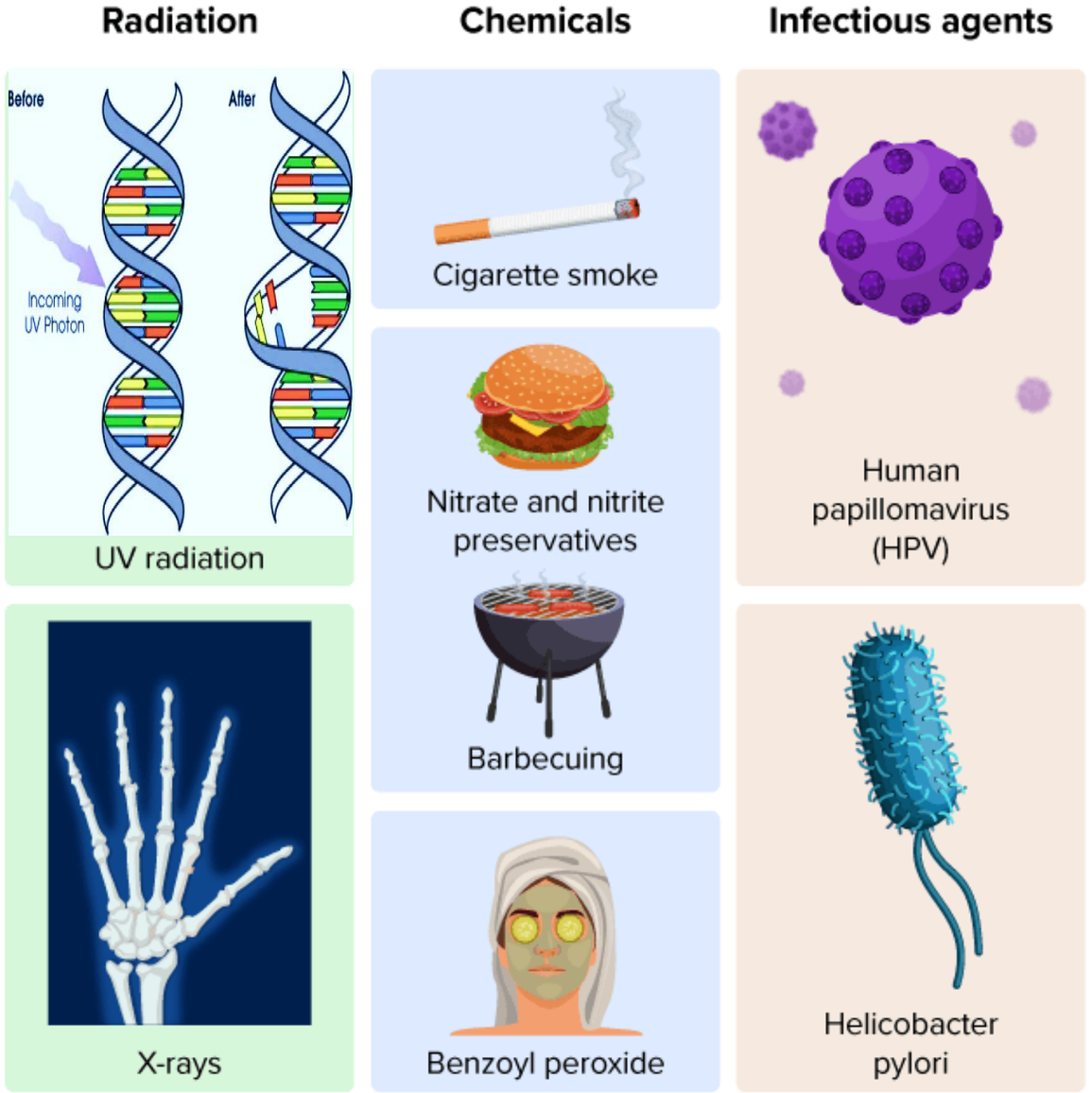
Causes of DNA mutation

1- Spontaneously:

- ❑ Without any outside influence.
- ❑ Uncorrected errors during DNA replication or DNA repair.

2- Induced:

- ❑ Environmental factors. anything in the environment that can cause a mutation is known as a **mutagen.**



Mutagen

- A mutagen is an agent that induces a permanent change to the genetic material of an organism.
- Mutagens may be physical, chemical or biological

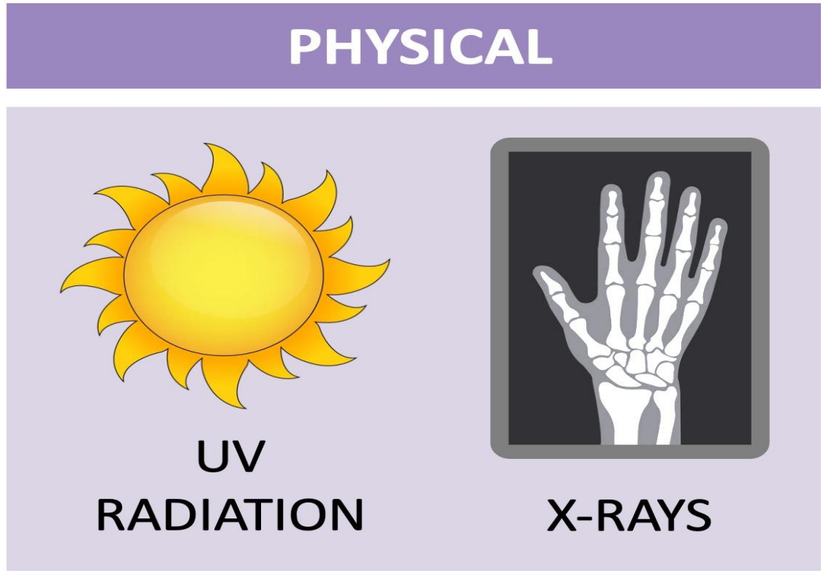
Types of Mutagens

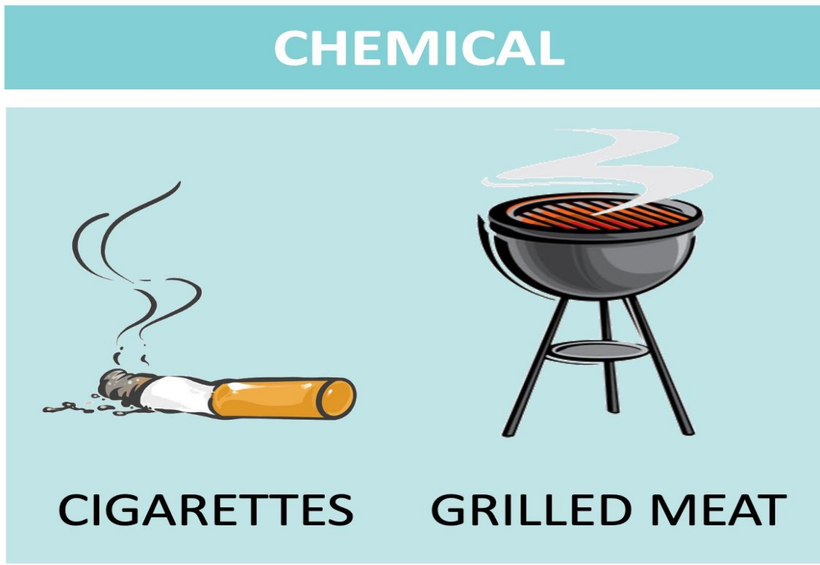
❑ Physical:

- Ionizing radiation (gamma rays and X-rays)
- Non-ionizing radiation (Ultraviolet radiation)

❑ Chemical: (Carcinogens)

1. Cigarette smoke (benzopyrene)
2. Anticancer base analogs and alkylating agent (formed by grilling meat)
1. Oxidative Free radicals.
2. Aflatoxin found in some food molds (leads to liver cancer)

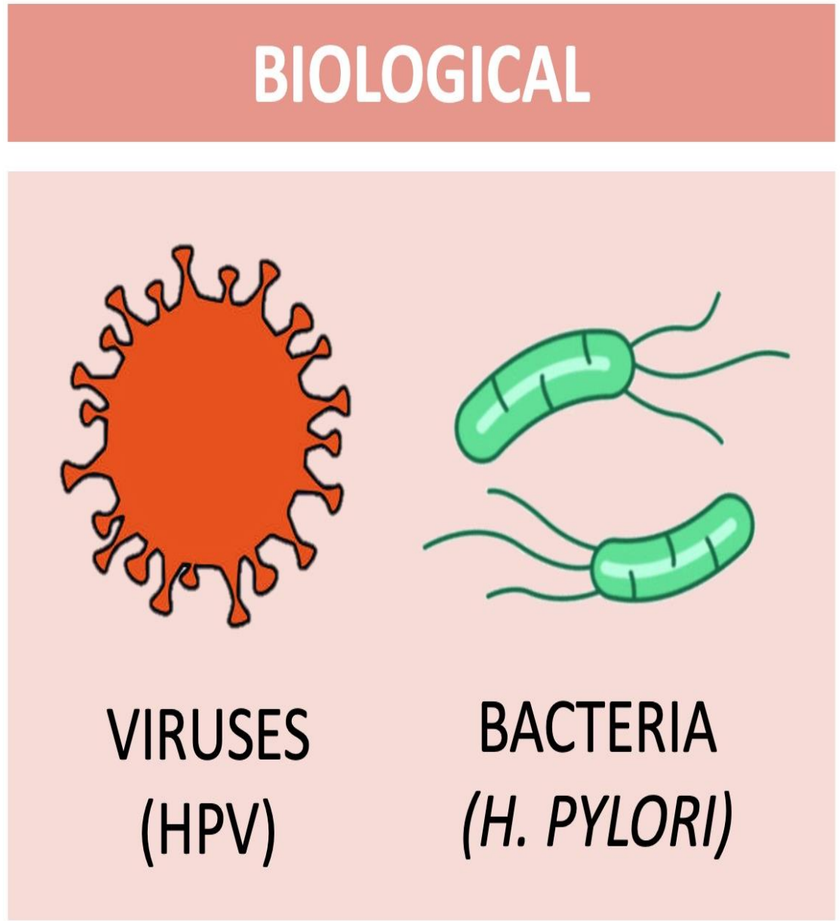




Types of Mutagens

❑ Biological:

- ➢ Some **viruses** are known to cause cancer e.g.
  - Hepatitis C virus (HCV): causes Heptocellular carcinoma
  - Human papiloma virus (HPV) causes cancer cervix
- ➢ Certain **Bacteria** are known to cause cancer
  - e.g. H. Pylori cause cancer stomach



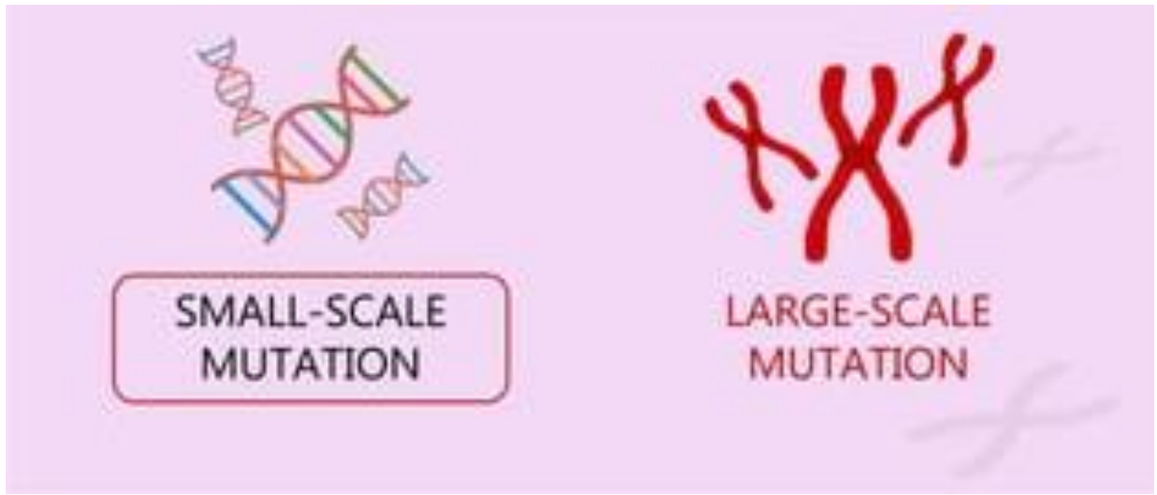
Types of Mutations

1- Small scale Mutation: (1-20 base mutation)

- Point Mutations (base substitution)
- Insertion, deletion mutation

2- Large scale Mutation (ranged from Exon to part of chromosome)

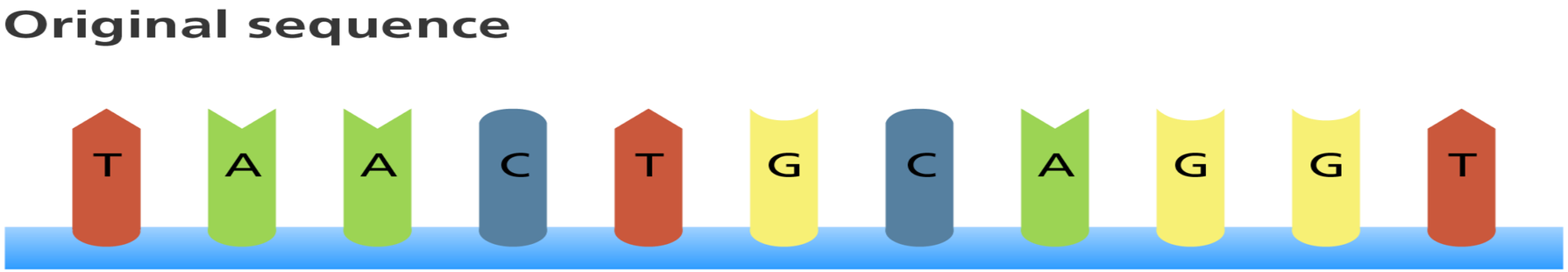
- Large deletion
- Inversion
- Duplication
- Translocation

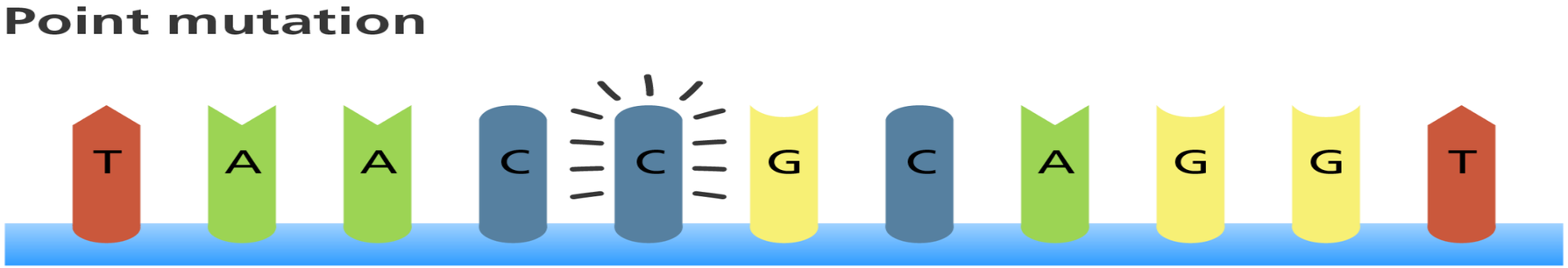


Types of Mutations

1- Point Mutations (base substitution):

occurs when one **base pair** is substituted for (replaced with) another.



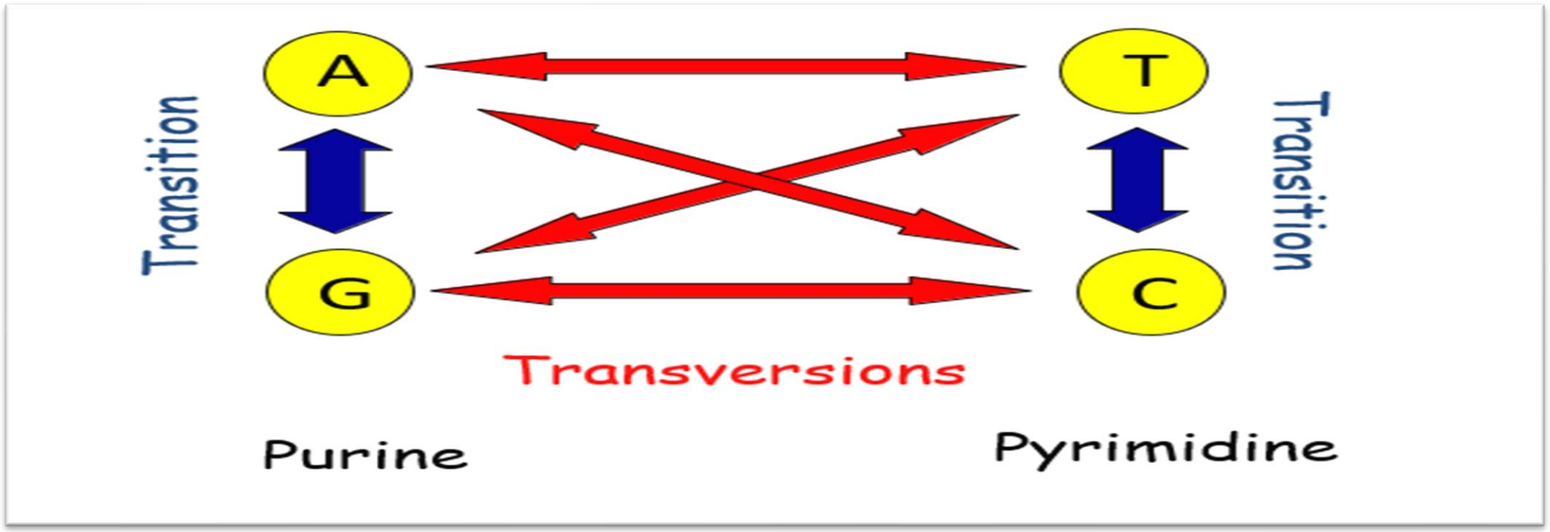


Types of Mutations

1- Point Mutations (base substitution):

❑It may be:

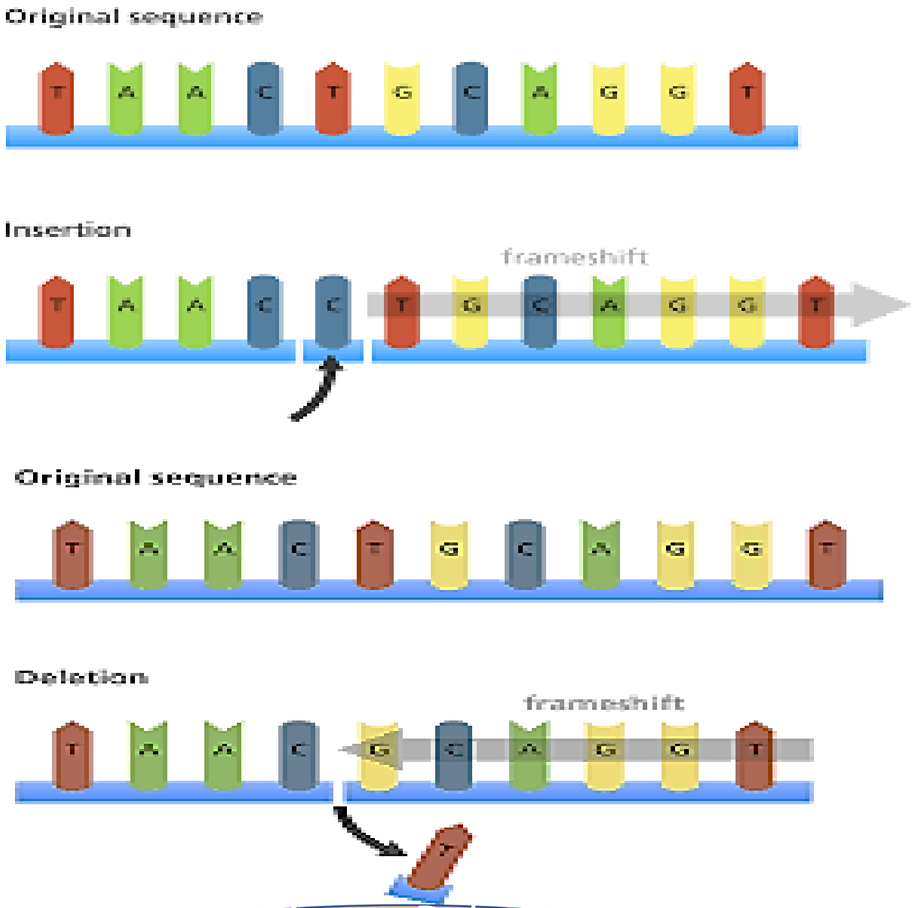
- **Transition:** if a purine is substituted with a different purine (A → G) or a pyrimidine, for a different pyrimidine (C → T).
- **Transversion:** purine is substituted with a pyrimidine or a pyrimidine with a purine.



Types of Mutations

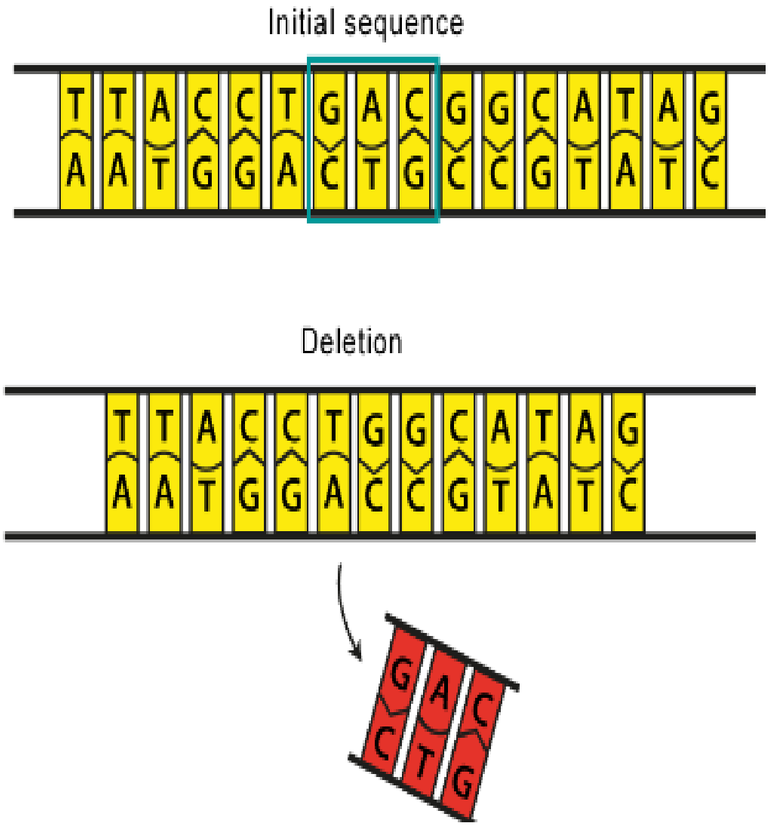
2- Insertion, deletion mutation:

Insertion or deletion of one or more bases



Insertion or Deletion of one or 2 bases

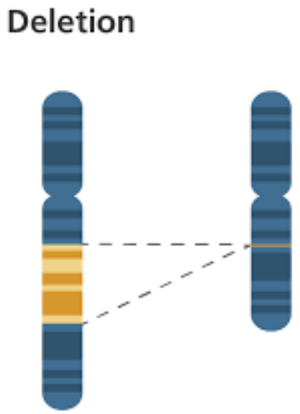
frameshift mutations



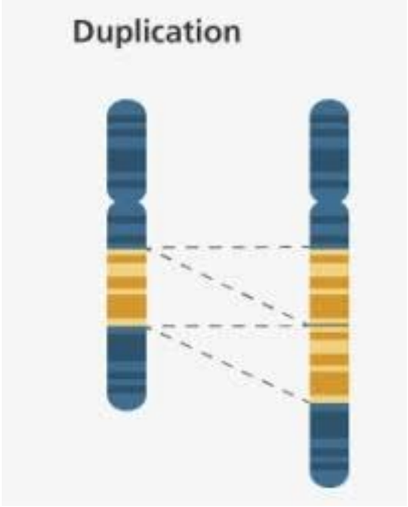
Insertion or Deletion of multiple of 3 bases

3- Chromosomal mutation: (from exon to whole chromosome)

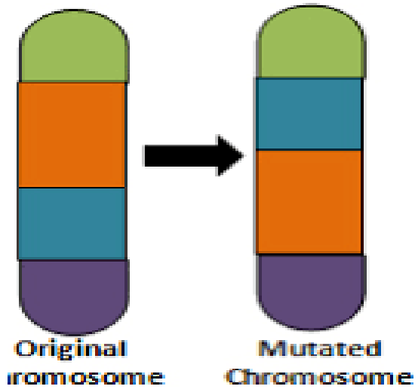
Large Deletion



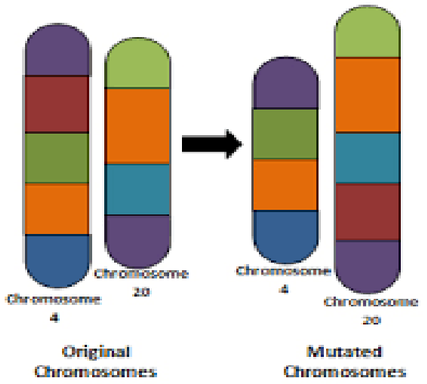
Duplication



Inversion



Translocation



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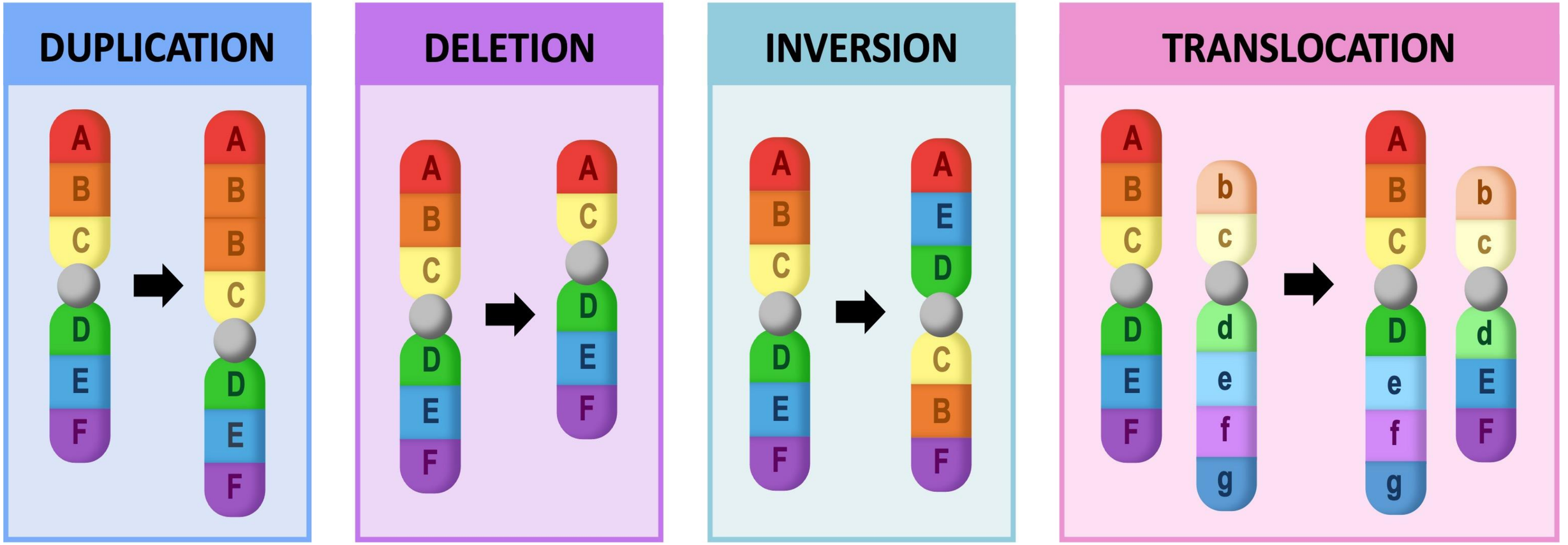
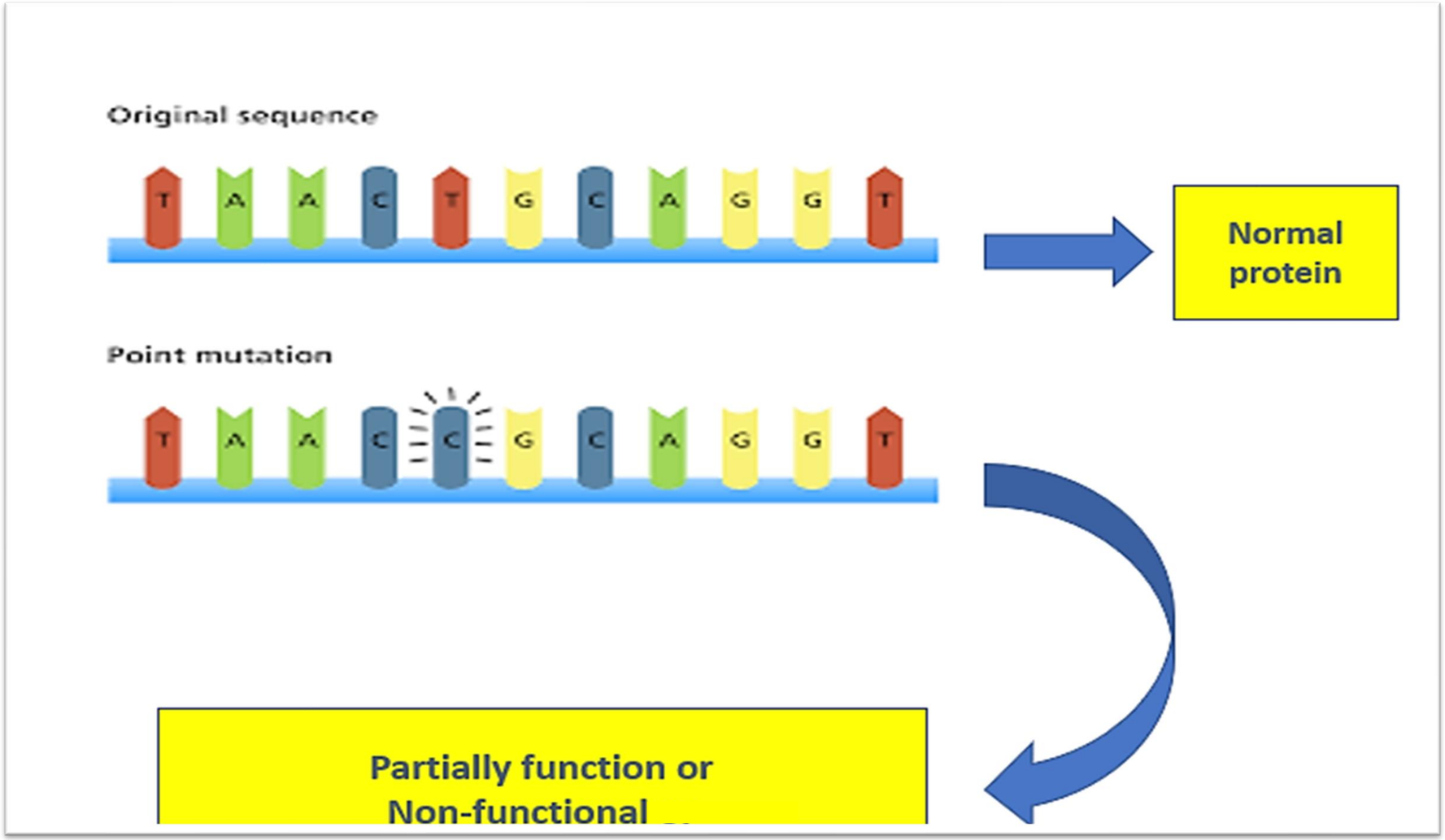


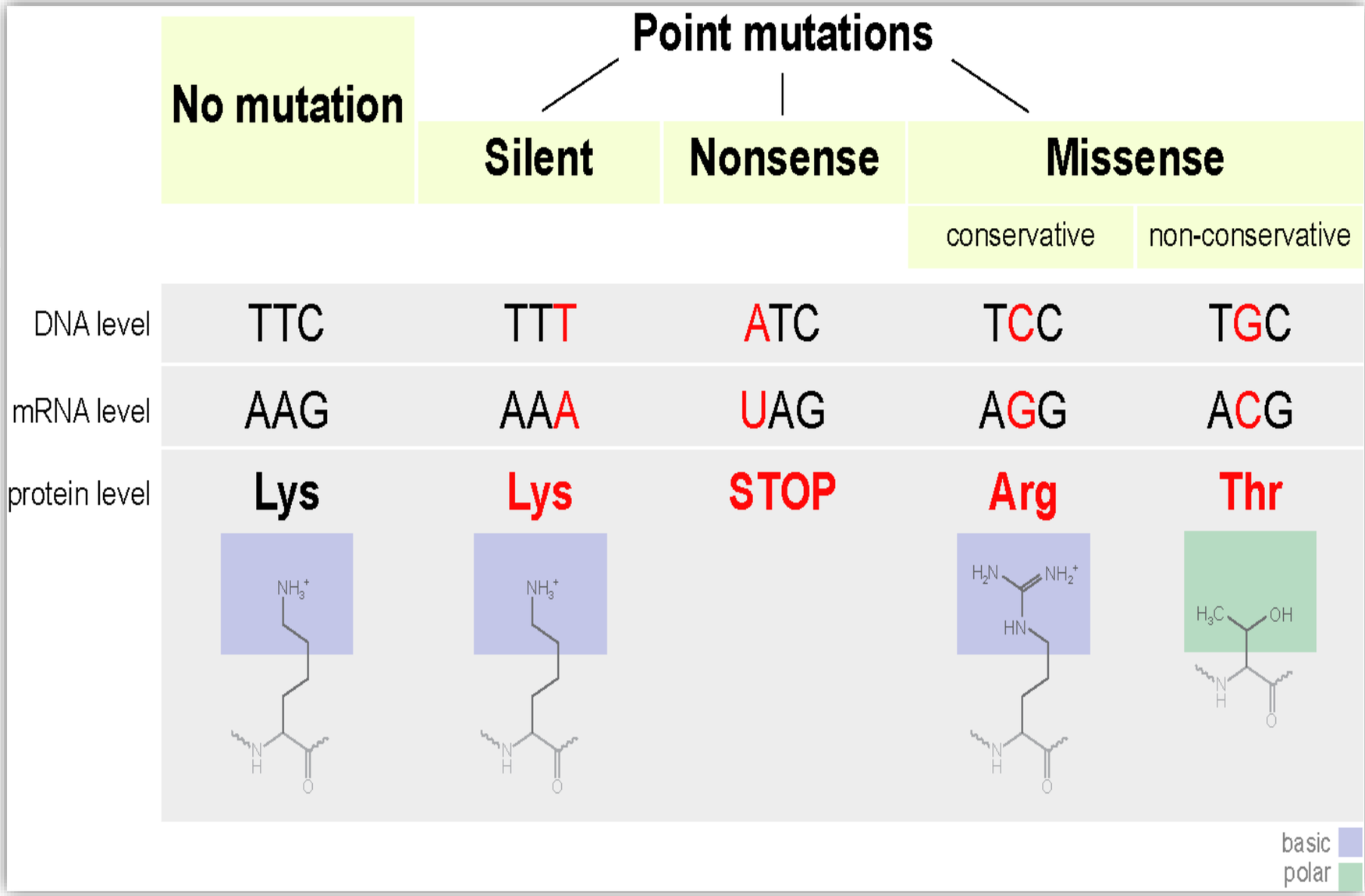
Effects of mutation



Effects of Mutations

2- Point mutation:

- ❑ Silent mutation
- ❑ Nonsense mutation
- ❑ Missense mutation
- ❑ Sense mutation



Effects of Mutations

1- Point Mutations (base substitution):

1. Silent mutation:

- a nucleotide is substituted but the same amino acid is produced.
- This can occur because multiple codons can code for the same amino acid (Degeneracy).

2. Missense mutation:

- Occurs when one nucleotide is substituted and a different codon is formed that produces a different amino acid in the sequence of amino acids.

Effects of Mutations

1- Point Mutations (base substitution):

3. Nonsense mutation:

- Occurs when one nucleotide is substituted leading to the formation of a stop codon (UAG, UAA, or UGA in RNA) instead of a codon that codes for an amino acid. This will stop the production of the amino acid chain.
- This leads to premature termination of the amino acid sequence and prevent the correct protein from being produced.

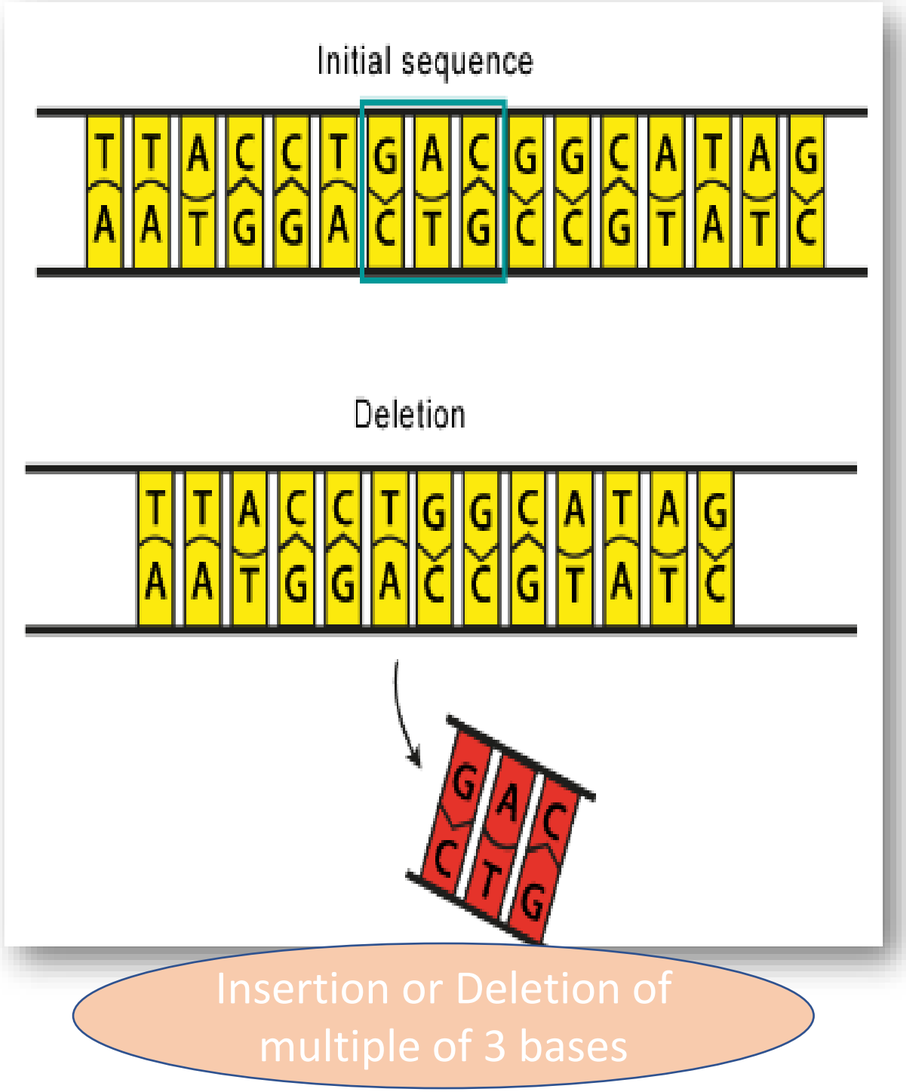
4. Sense mutation:

- Occurs when one nucleotide is substituted and this leads to change in a stop codon to a codon that codes for an amino acid.

Effects of Mutations

2- Insertion, deletion mutation:

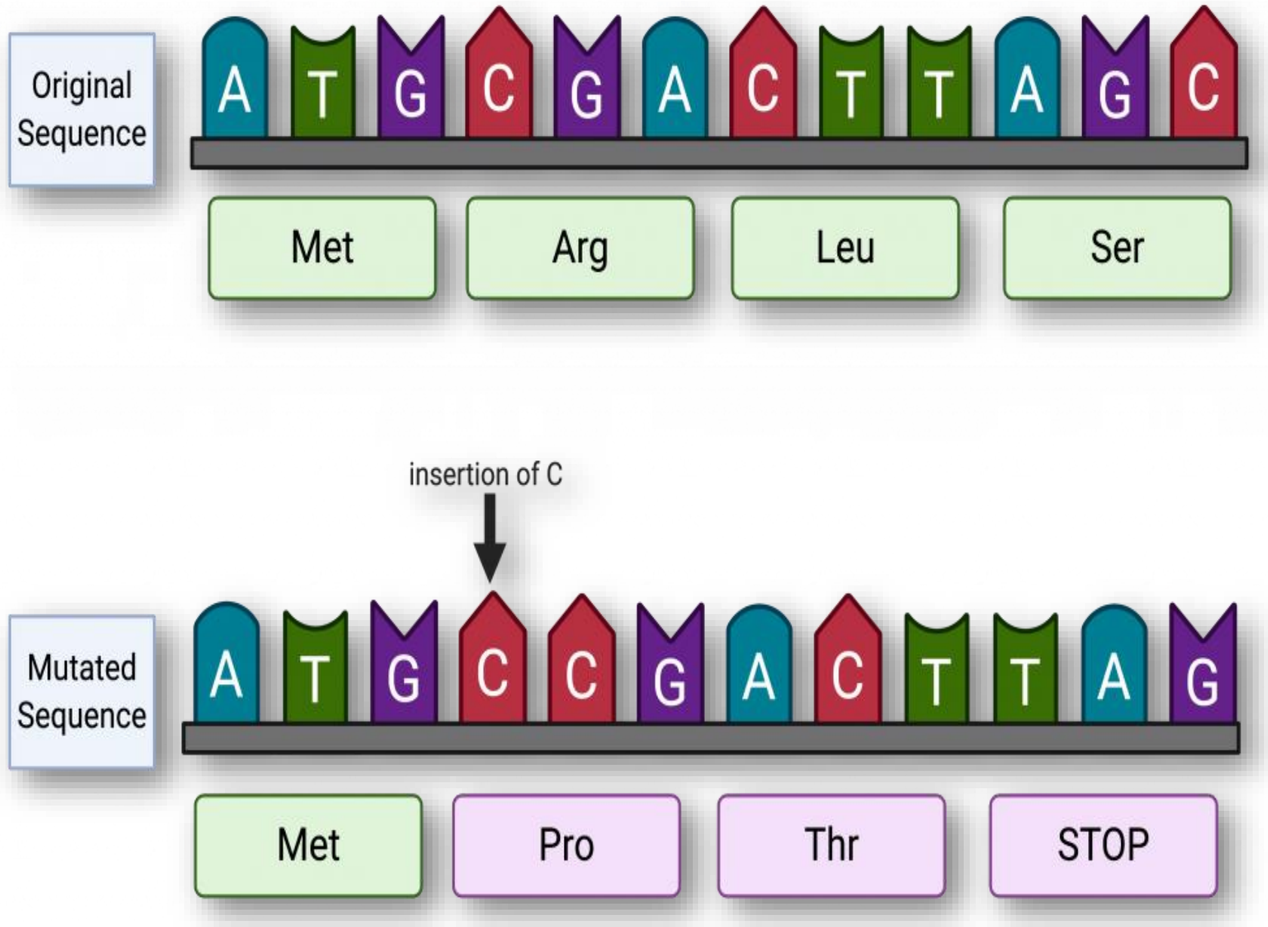
Insertion or deletion of three (or multiple of three) nucleotides will result in addition or removal of amino acid to the protein) during translation of an mRNA created from the mutated gene.



Effects of Mutations

2- Insertion, deletion (frame shift mutation):

- Insertion or deletion of one or two bases
- This lead to Garbled translation of mRNA distal to single nucleotide deletion/insertion (changing the reading frame)
- May lead to premature termination of polypeptide due to appearance of nonsense codon near the COOH terminus.




ACTIVITIES

Transcribe the following sequence of DNA into RNA then to protein sequence :

DNA: AAG CGT ACC ATT

mRNA:

Protein:

If the following changes occur in DNA sequence what do you notice?

DNA: AAG CGC ACC ATT

mRNA:

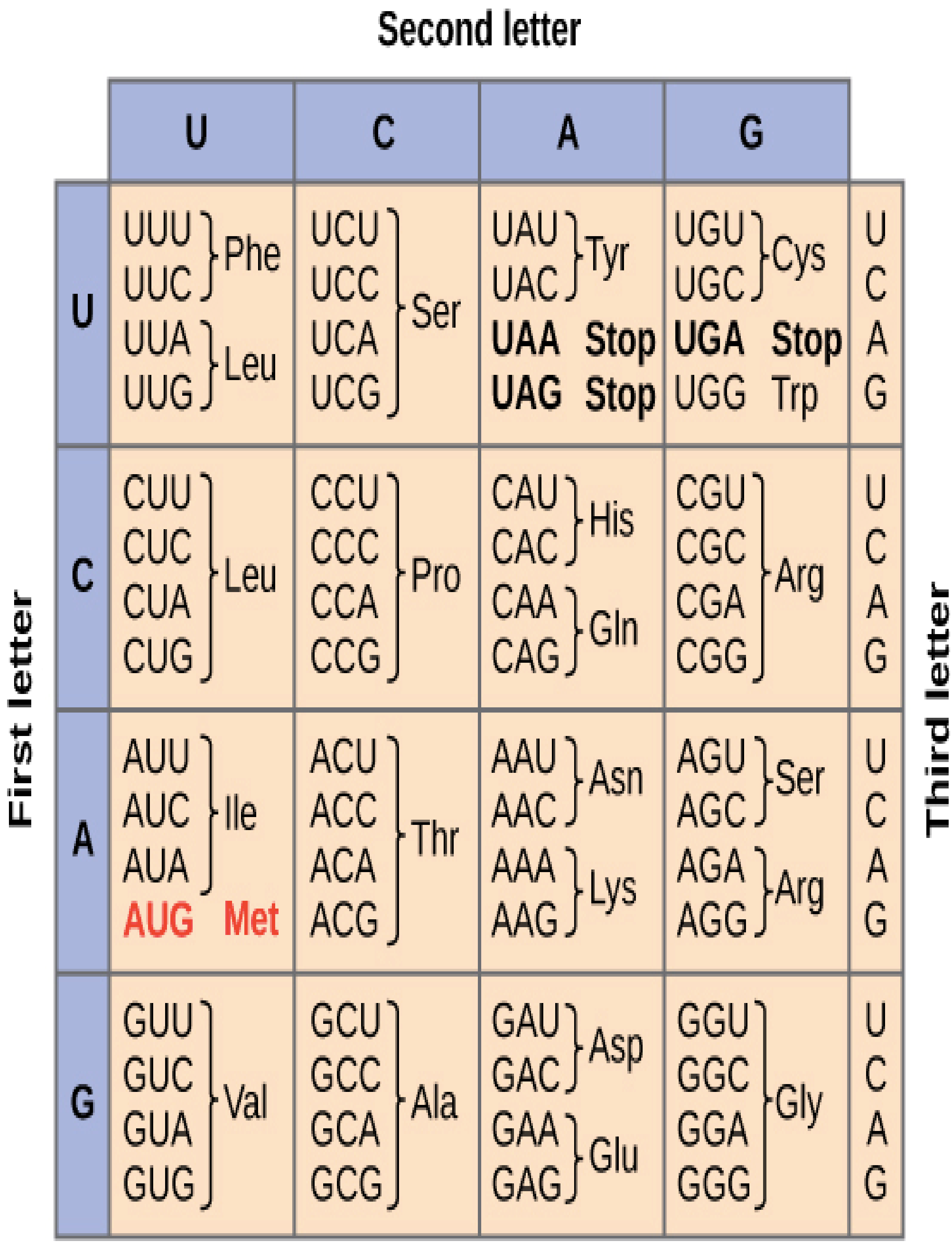
DNA: AAG GGT ACC ATT

mRNA:

DNA: AAG CGT ACT ATT

mRNA:

Mention the type & effect of mutation at each



Second letter

First letter	U	C	A	G	Third letter
U	UUU, UUC Phe UUA, UUG Leu	UCU, UCC, UCA, UCG Ser	UAU, UAC Tyr **UAA Stop** **UAG Stop**	UGU, UGC Cys **UGA Stop** UGG Trp	U C A G
C	CUU, CUC, CUA, CUG Leu	CCU, CCC, CCA, CCG Pro	CAU, CAC His CAA, CAG Gln	CGU, CGC, CGA, CGG Arg	U C A G
A	AUU, AUC, AUA Ile AUG Met	ACU, ACC, ACA, ACG Thr	AAU, AAC Asn AAA, AAG Lys	AGU, AGC Ser AGA, AGG Arg	U C A G
G	GUU, GUC, GUA, GUG Val	GCU, GCC, GCA, GCG Ala	GAU, GAC Asp GAA, GAG Glu	GGU, GGC, GGA, GGG Gly	U C A G

Transcribe the following sequence of DNA into RNA then to protein sequence :

DNA: AAG CGT ACC ATT

mRNA:

Protein:

If the following changes occur in DNA sequenc

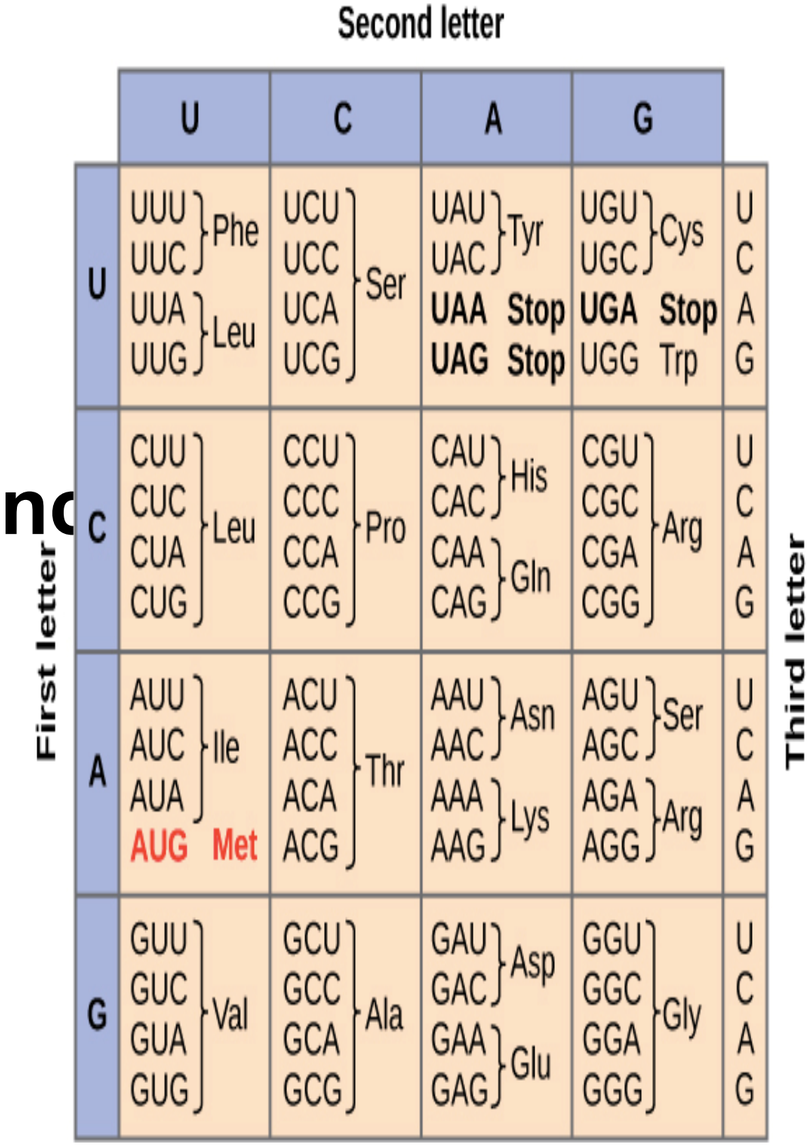
what do you notice?

DNA: AAG CGT ACA TT

mRNA:

DNA: AAG CAG TAC CAT T

mRNA:



Second letter

First letter	U		C		A		G		Third letter
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		**UAA**	**Stop**	**UGA**	**Stop**	A
	UUG		UCG		**UAG**	**Stop**	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G


Thank you