

Bioinformatics I

Wild-types and mutants

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What is a genotype?

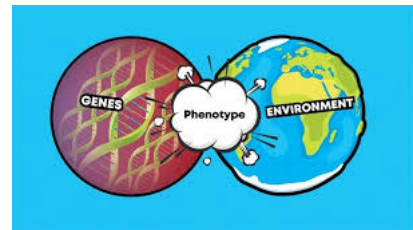
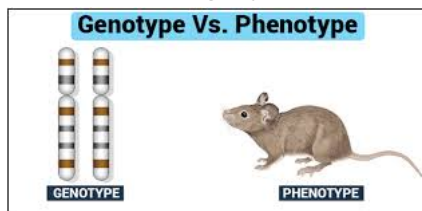


- The term "genotype" refers to the genetic makeup of an organism; in other words, it describes an organism's complete set of genes.
- It can be used to refer to the alleles.
- Humans are diploid organisms, which means that they have two alleles at each genetic position, or locus, with one allele inherited from each parent. Each pair of alleles represents the genotype of a specific gene.

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What is a phenotype?

- A **phenotype** is an individual's observable traits, such as height, eye color, and blood type.
- The genetic contribution to the **phenotype** is called the genotype.
Some traits are largely determined by the genotype, while other traits are largely determined by environmental factors.

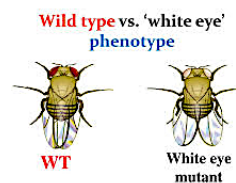


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Wild-Type WT and mutations



- **Wild-Type WT** (the natural **phenotype** was expressed form a genotype)
- **Wild type (WT)** refers to the phenotype of the typical form of a species as it occurs in nature.
- **Species** a group of living organisms consisting of similar individuals.
- Such as Human, rat, rabbits, pigs....
- A **mutation** is a replacement or substitution in any gene that can be expressed into a different amino acid which can change the function or the structure of the proteins. It is named as (**mutant**).
- It can be appeared **naturally**.
- The **mutagenesis** can be done in the lab.
- Note: not all the mutations are Harm !



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A mutated gene can cause disease !

- A **mutation** is a change that occurs in our DNA sequence, either due to mistakes when the DNA is copied or as the result of environmental factors such as UV light and cigarette smoke etc.

<i>Normal gene</i>	... ACT CCT	GAG	GAG	AAG ...
Protein	... Thr – Pro –	Glu	– Glu –	Lys ...
<i>Mutated gene</i>	... ACT CCT	GTG	GAG	AAG ...
Protein	... Thr – Pro –	Val	– Glu –	Lys ...

In the gene for that protein chain, the normal GAG codon has been **mutated** (altered) to GTG.

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How do you name the substituted mutation ?

- From the previous example:
- Substitution is the main cause of mutations.
- To give a name:
- Glutamic acid (site =3) Valine
- OR: **Glu3Val**, OR: **E3V** (very common name to a mutant).

		1	2	3	4	5	
Protein	...	Thr	– Pro	– Glu	– Glu	– Lys	...
Mutation	...	Thr	– Pro	– Val	– Glu	– Lys	...

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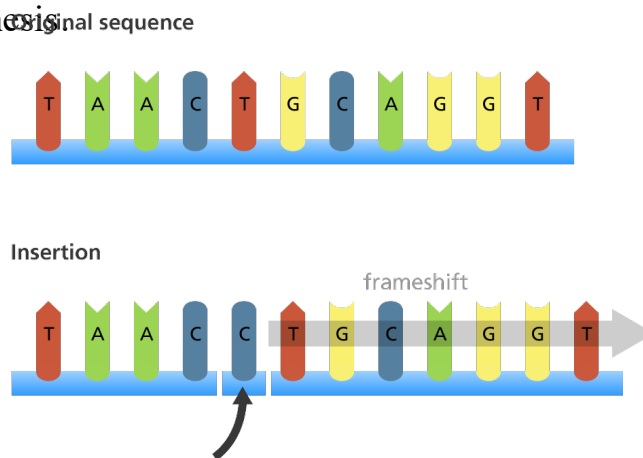
How do you check the mutation

WT	L	E	D	E	L	V	S	L	Q	K	K	L	K	G	T	E	D	E
	CTG	GAA	GAC	GAG	CTG	GTG	AGC	CTG	CAA	AAG	AAA	CTG	AAG	GGC	GGC	GGC	GGC	GGC
	GAC CTT CTG CTC GAC CAC TCG GAC GTT CTC TTT GAC TTC																	
Mutant	L	E	D	E	L	V	S	L	Q	E	K	L	K	G	T	E	D	E
	CTG	GAA	GAC	GAG	CTG	GTG	AGC	CTG	CAA	GAG	AAA	CTG	AAG	GGC	GGC	GGC	GGC	GGC
	AGC CTG CAA GAG AAA CTG AAG GGC GGC GGC GGC GGC																	

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Types of Mutations that could appear during the synthesis of proteins; such as insertion

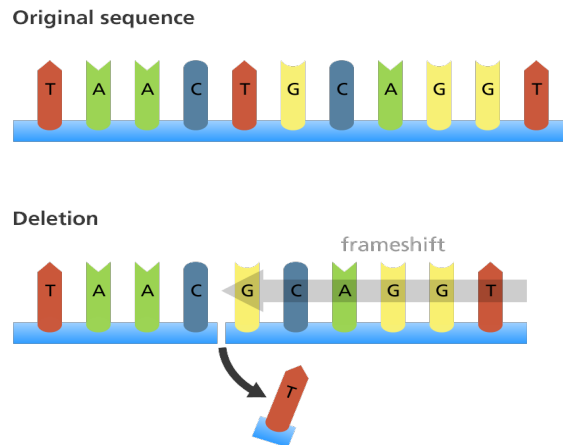
- **Insertion:** when a single nucleotide or more are inserted during the protein synthesis



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Other factors could lead to Mutations; such as deletion

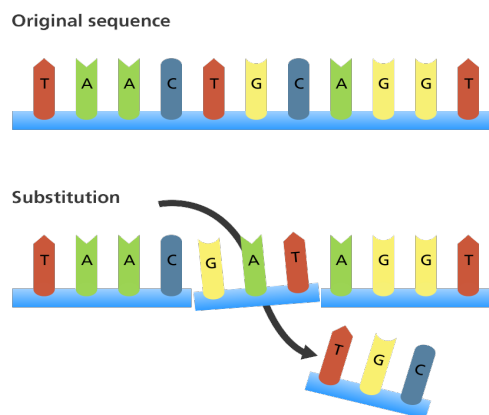
Deletion: when a single nucleotide or more are deleted during the protein synthesis.



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Other factors could lead to Mutations; such as deletion

Deletion: when a single nucleotide or more are substituted during the protein synthesis.



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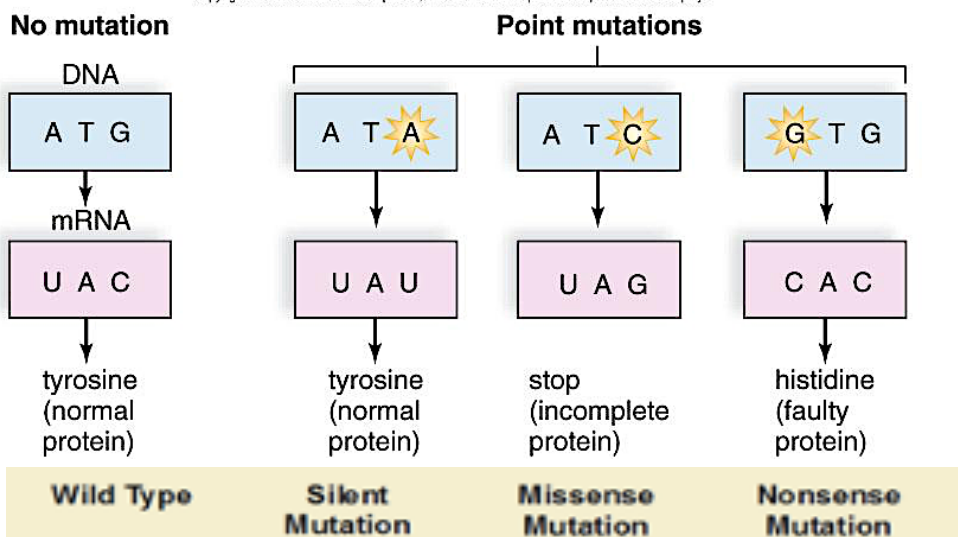
What is the difference between point mutation and frameshift mutation?

- Point mutation is an alteration of **a single nucleotide** in a gene whereas frameshift mutation involves **one or more nucleotide changes** of a particular gene.
- Point mutations are mainly nucleotide substitutions, which lead to silent, missense or nonsense mutations. Frameshift mutations occur by insertion or deletion of nucleotides.

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What are the types of Mutations?

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What other factors could cause mutation?

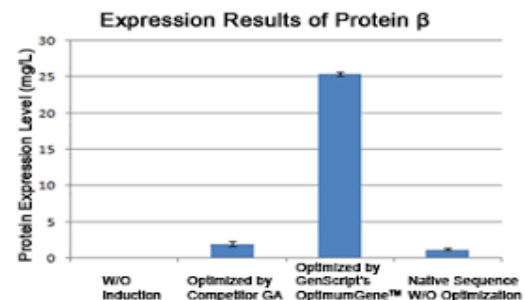
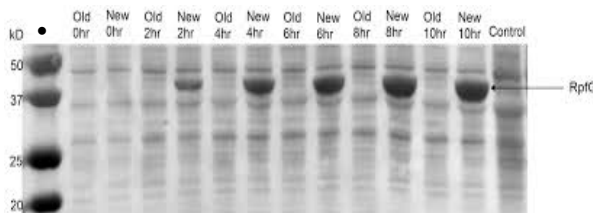
- There are also environmental causes for mutations:
- Substitution one or more bp (less problematic than others).
- Errors in DNA Replication.
- Errors in DNA Recombination.
- Chemical Damage to DNA.
- Radiation.

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What can silent mutation be used for? What is a codon optimization?

- It is a designing for a DNA sequence that could result in a same protein sequence by a chemical synthesis but with high protein expression. So, the propose of that:
- It is to increase the level of protein expression. For example:

- M D A I K
- ATG GAC GCG ATT AAG
- ATG GAC GCT ATC AAA



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Define?

- **Nonsense Mutations:** the alteration of a nucleotide in a particular codon may introduce a stop codon to the gene. This stops the translation of the protein at halfway of the complete protein.
- **Silent mutations,** a single base pair has changed in a particular **codon**, the same **amino acid** is coded by the altered codon as well.
- **Missense mutations,** once the alteration occurs in a particular codon by a nucleotide substitution, the codon is altered in such a way to code a different amino acid.