Subject: Biology

Grade: 12

Section: LS

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Unit: Reproduction and Genetics

Chapter 3: Genetic variation and polymorphism

Document 2: Mutations and multiple alleles. P:60

Definition of mutation

A change in the nucleotide sequence of DNA changes the corresponding sequence of messenger RNA and can ultimately change the amino acid sequence of the corresponding protein, according to the Genetic Codes Table.

Note :

Mutations that affect a single nucleotide are called point mutations and those that affect 2 or more nucleotides are called extended mutations.

Transcription and translation

Transcription: is the operation of copying (transcribing) information, encoded by DNA, into identical information, in the form of mRNA. It takes place in the nucleus. Transcription requires the separation of the two strands of the DNA molecule at the level of the concerned gene. Only one of the two strands of DNA carries the information that will be transcribed. It is called the transcribed strand

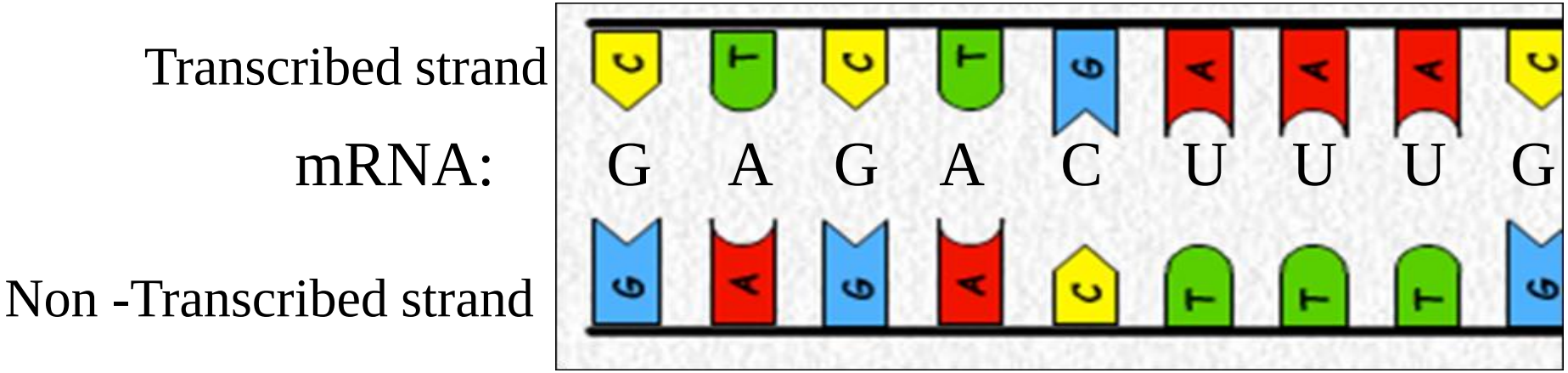
Translation: is the process of protein synthesis in which the genetic information encoded in mRNA is translated into a sequence of amino acids in a polypeptide chain, and occurs in the cytoplasm

Determine the sequence of messenger RNA

The method of determining the sequence of messenger RNA differs depending on whether the DNA strand given is the transcribed strand or the non-transcribed strand

1- If it is the transcribed strand of DNA, the sequence of the messenger RNA is **complementary** to that of the given DNA. C in DNA will correspond to a G in RNA (and vice versa), an A correspond to a U, a T to an A

2- If the strand of DNA is not transcribed, the sequence of the messenger RNA is the **same (identical) to** that of the given DNA; simply replace the thymine T nucleotides with uracil U nucleotides.



For many years, geneticists believed that a gene exists only under two allelic forms. Nowadays, we know that a gene can have many different allelic forms which result from multiple mutations.

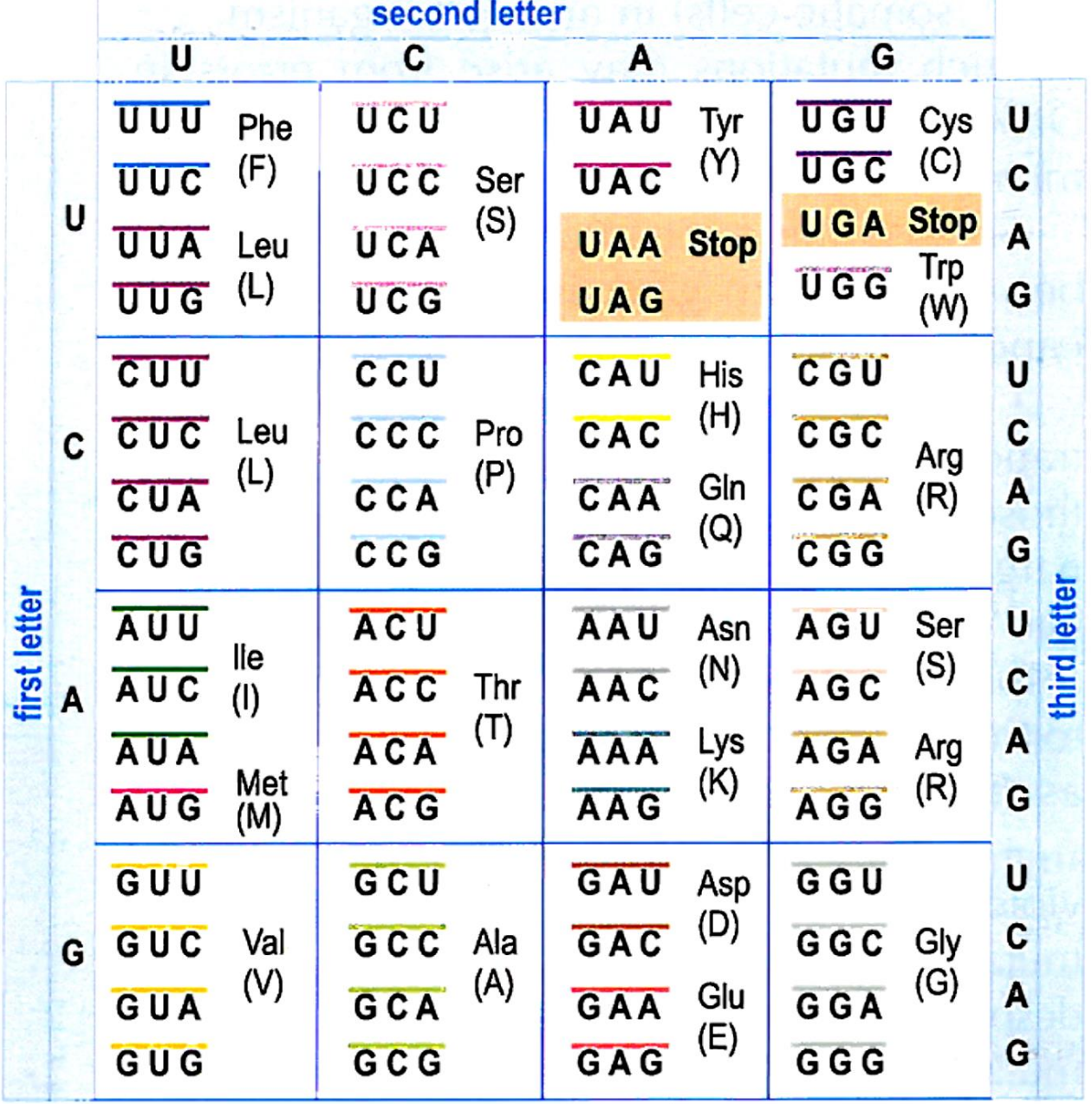
What are the different types of gene mutations?

What is the relationship between mutations and multiple alleles?

1 - Types of gene mutations

Gene mutations, which are due to accidents taking place at the level of the nucleotides of a gene, are different from chromosome mutations which affect the number and the structure of the chromosomes

A change in the nucleotide sequence of the DNA of a gene alters the corresponding sequence of the messenger RNA and may ultimately alter the amino acid sequence of the corresponding protein, according to the genetic code table (Doc. a).



first letter	second letter U	second letter C	second letter A	second letter G	third letter
U	UUU Phe (F)	UCU Ser (S)	UAU Tyr (Y)	UGU Cys (C)	U
	UUC Phe (F)	UCC Ser (S)	UAC Tyr (Y)	UGC Cys (C)	C
	UUA Leu (L)	UCA Ser (S)	UAA Stop	UGA Stop	A
	UUG Leu (L)	UCG Ser (S)	UAG Stop	UGG Trp (W)	G
C	CUU Leu (L)	CCU Pro (P)	CAU His (H)	CGU Arg (R)	U
	CUC Leu (L)	CCC Pro (P)	CAC His (H)	CGC Arg (R)	C
	CUA Leu (L)	CCA Pro (P)	CAA Gln (Q)	CGA Arg (R)	A
	CUG Leu (L)	CCG Pro (P)	CAG Gln (Q)	CGG Arg (R)	G
A	AUU Ile (I)	ACU Thr (T)	AAU Asn (N)	AGU Ser (S)	U
	AUC Ile (I)	ACC Thr (T)	AAC Asn (N)	AGC Ser (S)	C
	AUA Ile (I)	ACA Thr (T)	AAA Lys (K)	AGA Arg (R)	A
	AUG Met (M)	ACG Thr (T)	AAG Lys (K)	AGG Arg (R)	G
G	GUU Val (V)	GCU Ala (A)	GAU Asp (D)	GGU Gly (G)	U
	GUC Val (V)	GCC Ala (A)	GAC Asp (D)	GGC Gly (G)	C
	GUA Val (V)	GCA Ala (A)	GAA Glu (E)	GGA Gly (G)	A
	GUG Val (V)	GCG Ala (A)	GAG Glu (E)	GGG Gly (G)	G

Doc.a *Genetic code. Each amino acid is by convention designated by one or three letters.*

Mutations which affect a single nucleotide are called point mutations. More stretched mutations, which affect hundreds or thousands of nucleotides can also occur.

The main types of mutations of genes result either from a nucleotide substitution, or from a deletion (loss) or insertion" (gain) of a nucleotide (Doc. b).

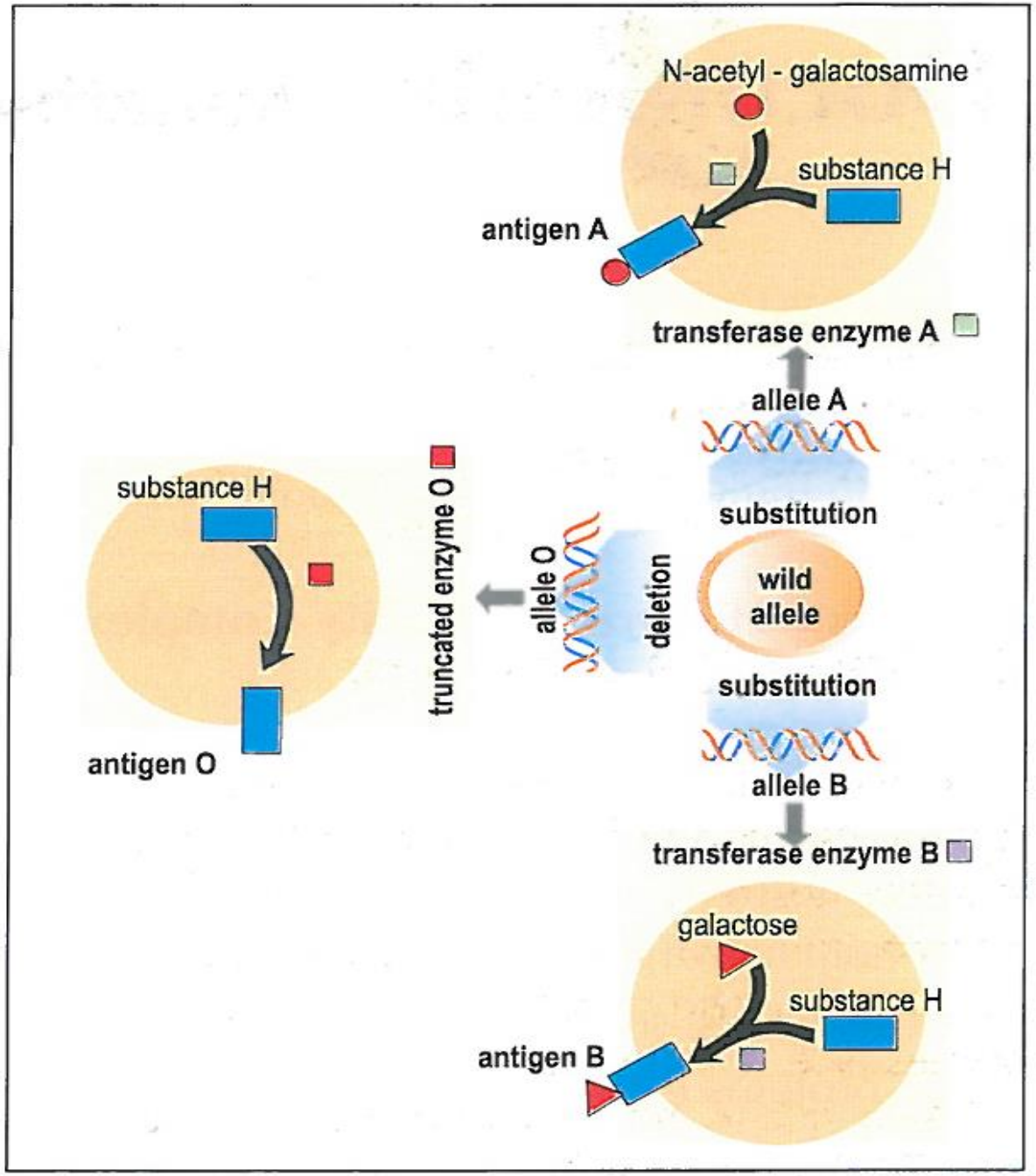
type of mutation	non-transcribed DNA strand of a normal gene and corresponding amino acids	non-transcribed DNA strand of the mutant gene and corresponding amino acids	effect of the mutation
substitution	...ICCA-GAG-ACTI... Pro - Glu - Thr	...ICCA-GTG-ACTI... Pro - Val - Thr	missense altered polypeptide
	...ICCA-GAG-ACTI... Pro - Glu - Thr	...ICCA-GAA-ACTI... Pro - Glu - Thr	silent no detectable change
	...ICCA-GAG-ACTI... Pro - Glu - Thr	...ICCA-TAG-ACTI... Pro - Stop -	nonsense incomplete polypeptide
deletion	...ITAC-ACC-ACG-AI... Tyr - Thr - Thr	...ITAC-CGA-CGAI... Tyr - Pro - Arg	frame-shift altered polypeptide
insertion	...ITAC-ACC-ACG-AI... Tyr - Thr - Thr	...ITAC-GAC-CAC-GAI... Tyr - Asp - His	frame-shift altered polypeptide

Doc. b *Main types of point mutations and their consequences. The non-transcribed DNA strand (coding strand) gives a quick and direct reading of the messenger RNA by just replacing thymine (T) with Uracil (U).*

2 – Genes and Multiple alleles

A classical example of multiple alleles in humans is the ABO blood group system (Doc.c). This system is defined by the presence of **O, A and B molecules** at the surface of red blood cells: These molecules have the same basic structure, **called substance H,** but they differ by the absence or presence of **a supplementary sugar**.

Sugar addition is controlled by an enzyme called **transferase** coded by three allelic genes, A, B and O that derive from different mutations of the same ancestral gene.



Doc.c Human ABO blood groups.

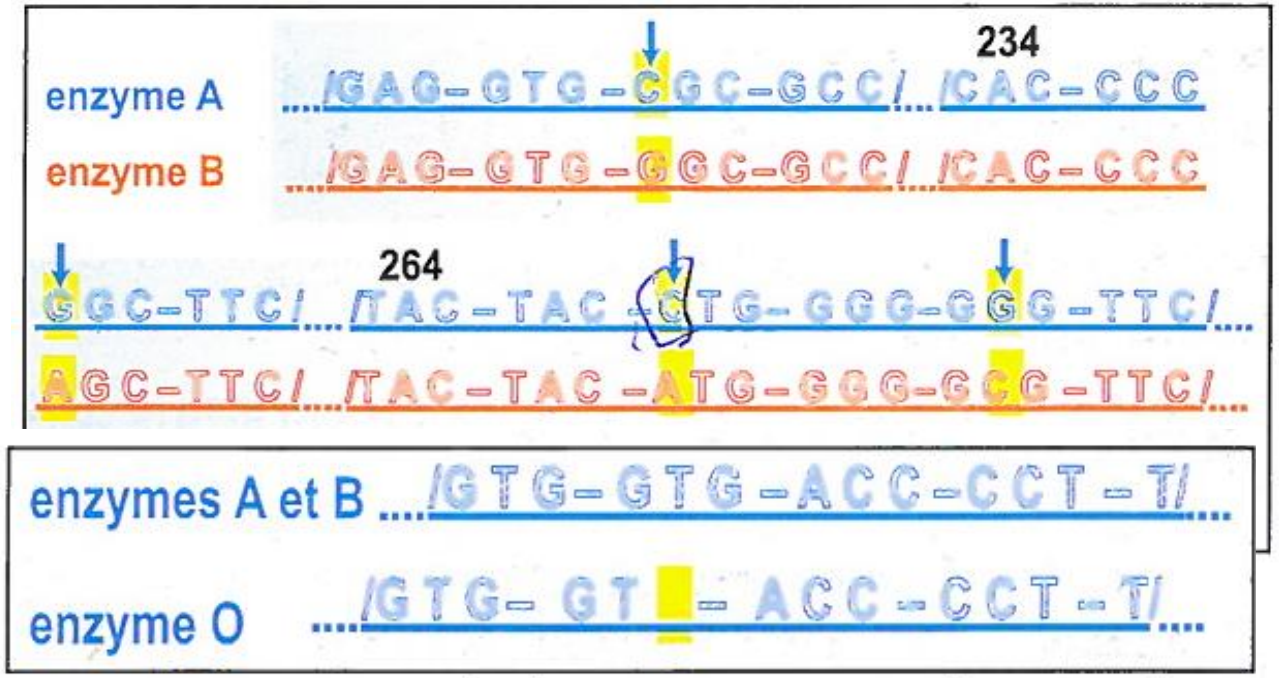
In fact, four mutations, due to substitution of four nucleic acid sequences of alleles A and B, lead to the modification of 4 amino acids in the enzyme. This is turn induces a change in the enzyme function (Doc. d).

The enzyme coded by allele A adds a sugar, the **N-acetyl galactosamine**, to substance H, and transforms it into **molecule A**.

The enzyme coded by allele B adds another sugar, **the galactose**, to substance H and transforms it into molecule B.

Allele o has undergone a small deletion and codes for a truncated, inactivated enzyme that does **not add any supplementary sugar** to substance H (Doc. e).

Such a situation, characterized by the presence of many functional alleles of the same gene, is termed genetic polymorphism



Doc.e *Non-transcribed DNA sequence of A,B, and O enzymes.*

Gene codes for the enzyme transferase has 3 alleles : A, B and o

Enzyme of the allele8 A dd N- acetyl galactosamine to the sub.h, enzyme of the allele B adds galactose to sub.H. and the ezyme of allele o which is inactive does not add any sugar to Sub. h

1. Explain, using the example of the missense mutation (Doc. b), how a change in the nucleotide sequence of a gene alters the corresponding proteins.

	Normal gene	Mutant gene
Non transcribed DNA strand	…CCA – GAG – ACT …	…CCA – GTG – ACT …
Transcribed DNA strand	… CGT – CTC – TGA …	… GGT – CAC – TGA …
Messenger RNA	… CCA – GAG – ACU …	… CCA – GUG – ACU ….
Amino acids	… Pro – Glu – Thr ….	… Pro – Val – Thr …

2. Does a mutation always alter the function of a protein? Justify the answer.

No, silent mutations that change the nucleotide sequence without changing the sequence or function of amino acids) and mutations in non-coding sequences may go unnoticed and not affect the function of the protein.

3. Indicate the type of mutations where the amino acid sequence situated after the mutation site changes?

Mutation by deletion or insertion change the reading frame of the translation and lead to a different amino acid sequence after the site of mutation.

4. a- Give precisely the structural difference between molecules O, A and B.

Molecule A has a supplementary sugar, the N-acetyl galactosamine.

Molecule B has a different supplementary sugar, the galactose.

Molecule o has substance H, without a supplementary sugar.

b- Determine the cause of this difference

Mutations cause diverse alleles of the same gene. Allele O is due to a deletion of an ancestral gene, which leads to a truncated enzyme, whereas alleles A and B are due to a mutation (by substitution), leading of 4 different amino acids.

5. Draw out the definition of genetic polymorphism and its possible cause.

Genetic polymorphism refers to the simultaneous occurrence, in a population of allelic variations. This is due to a mutation affecting the DNA sequence(gene)

Polymorphism is due to polallelelism because of mutations of the gene

	Normal gene	Mutant gene
Non transcribed DNA strand	…CCA – GAG – ACT …	…CCA – GTG – ACT …
Transcribed DNA strand	… CGT – CTC – TGA …	… GGT – CAC – TGA …
Messenger RNA	… CCA – GAG – ACU …	… CCA – GUG – ACU ….
Amino acids	… Pro – Glu – Thr ….	… Pro – Val – Thr …

2. No, silent mutations that change the nucleotide sequence without changing the sequence or function of amino acids) and mutations in non-coding sequences may go unnoticed and not affect the function of the protein.

3. Mutation by deletion or insertion change the reading frame of the translation and lead to a different amino acid sequence after the site of mutation.

4. a- Molecule A has a supplementary sugar, the N-acetyl galactosamine.

Molecule B has a different supplementary sugar, the galactose.

Molecule o has substance H, without a supplementary sugar.

b- Mutations cause diverse alleles of the same gene. Allele O is due to a deletion of an ancestral gene, which leads to a truncated enzyme, whereas alleles A and B are due to a mutation (by substitution), leading of 4 different amino acids.

5. Genetic polymorphism refers to the simultaneous occurrence, in a population of allelic variations. This is