Ch.3/Doc.2: Mutations & Multiple Alleles
Ch.3/Doc.3: Polymorphic Genes in a Population

- Define genetic polymorphism & multiple alleles.
- Explain, through examples, that a gene can have many different allelic forms.
- Specify the relation between mutation & multiple alleles.

Mutations

1) Based on acquired knowledge, construct a concept map which represents the different types of mutation.

2) Define the following terms: Point mutation – Mutation by substitution – Missense mutation – Nonesense mutation – Silent mutation (silent substitution)– Mutation by deletion – Mutation by addition (insertion).

3) Fill the following table with the missing information:

Type of mutation	Non-transcribed DNA strand of a normal gene & corresponding amino acids	Non-transcribed DNA strand of the mutant gene & corresponding amino acids	Effect of mutation
	…./CCA - GAG - ACT/….	…./CCA - GTG - ACT/….	
	…./TAC - ACC -ACG- A/…	…./TAC - GAC - CAC-GA/…	
	…./ CCA - GAG - ACT/ ….	…./CCA - TAG - ACT/….	
	…./TAC - ACC - ACG A/…	…./TAC -CCA - CGA/…	
	…./ CCA - GAG - ACT/….	…./CCA - GAA - ACT/….	

4) Pro.2 Indicate whether a mutation always alters the function of a protein. Justify the answer.

Genes & Multiple Alleles

First Example: ABO Blood Groups

5) Referring to Doc.e & f/ P.61 of your textbook, compare the non-transcribed DNA sequence of A with B enzymes. Draw a conclusion regarding the types of mutations involved.

6) Referring to Doc.e & f/ P.61 of your textbook, <u>compare</u> the DNA sequences of Enzyme O with that of Enzymes A & B. <u>Explain</u> the reason why Enzyme O is nonfunctional.

Second Example: HLA

7) <u>Schematize</u> the chromosomes carrying the MHC genes.

8) *Pro.2* <u>Define</u> the wild-type allele.

Third Example: Beta- Globin Gene

9) A hemoglobin molecule consists of 4 polypeptide chains: 2 α polypeptides (globins) coded for by an α-globin gene, & 2 β polypeptides coded for by a β-globin gene, & where each polypeptide is associated with a heme group. If a person is normal, then he is said to have hemoglobin which has 2 normal α polypeptides & 2 normal β polypeptides. (Refer to Doc.d/ P.63 of your textbook).

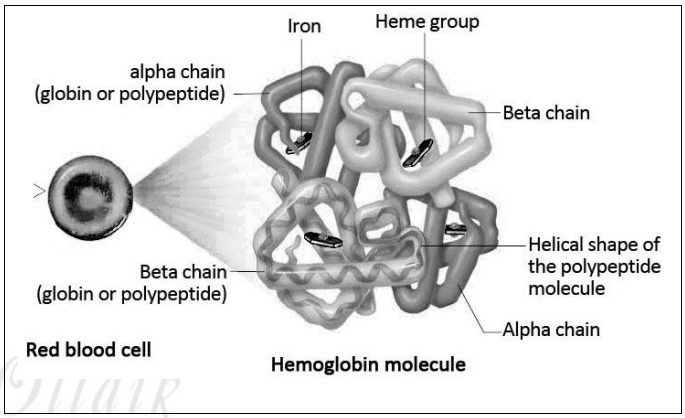
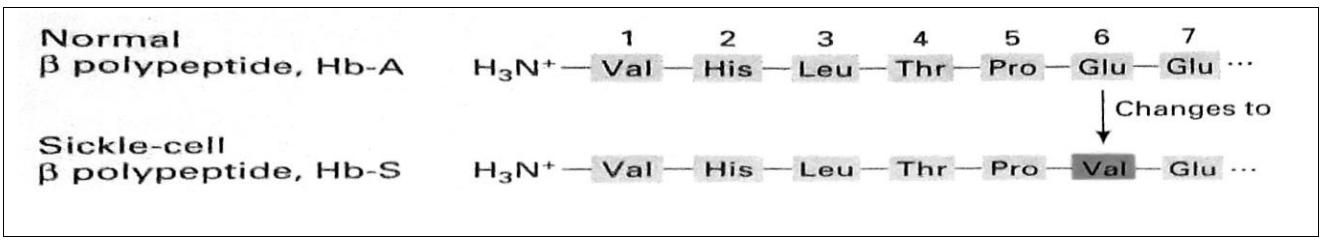


Figure 1 represents the first 7 amino acids in normal & sickled hemoglobin β polypeptides. <u>Compare</u> the 2 sequences.



10) Given the adjacent figure. Comment.

11) Pro.3 Indicate the cause of the genetic polymorphism in the β-globin.

12) Pro.4 Explain why thalassemia has different degrees of severity.

13)

Examples of amino acid substitutions found in (a) α and (b) β polypeptides of various human hemoglobin variants.

a) α-chain

	Amino acid position							
	1	2	16	30	57	58	68	141
Normal	Val	Leu	Lys	Glu	Gly	His	Asn	Arg
Hb variants:								
HbI	Val	Leu	Asp	Glu	Gly	His	Asn	Arg
Hb-G Honolulu	Val	Leu	Lys	Gln	Gly	His	Asn	Arg
Hb Norfolk	Val	Leu	Lys	Glu	Asp	His	Asn	Arg
Hb-M Boston	Val	Leu	Lys	Glu	Gly	Tyr	Asn	Arg
Hb-G Philadelphia	Val	Leu	Lys	Glu	Gly	His	Lys	Arg

b) β-chain

	Amino acid position									
	1	2	3	6	7	26	63	67	121	146
Normal	Val	His	Leu	Glu	Glu	Glu	His	Val	Glu	His
Hb variants:										
Hb-S	Val	His	Leu	Val	Glu	Glu	His	Val	Glu	His
Hb-C	Val	His	Leu	Lys	Glu	Glu	His	Val	Glu	His
Hb-G San Jose	Val	His	Leu	Glu	Gly	Glu	His	Val	Glu	His
Hb-E	Val	His	Leu	Glu	Glu	Lys	His	Val	Glu	His
Hb-M Saskatoon	Val	His	Leu	Glu	Glu	Glu	Tyr	Val	Glu	His
Hb Zurich	Val	His	Leu	Glu	Glu	Glu	Arg	Val	Glu	His
Hb-M Milwaukee-1	Val	His	Leu	Glu	Glu	Glu	His	Glu	Glu	His
Hb-D β Punjab	Val	His	Leu	Glu	Glu	Glu	His	Val	Gln	His

a. The sequence in Case 1 represents that for a part of the β-chain of normal hemoglobin HbA. Fill the related document with the missing information.

a. The document in Case 2 represents the mutated hemoglobin HbS responsible for sickle-cell anemia. Fill the related document with the missing information.

b. Compare the DNA sequence for HbA with that of HbS, & then derive a conclusion concerning the kind of mutation involved.

Case 1	Case 2
normal DNA transcribed strand ... TGA – GGT – CTC – CTC – TTC... 4 5 6 7 8	normal DNA transcribed strand ... TGA – GGT – CTC – CTC – TTC... 4 5 6 7 8
m RNA	mutated DNA strand ... TGA – GGT – CAC – CTC – TTC... 4 5 6 7 8
amino acids	m RNA
	amino acids

c. Compare the 2 DNA sequences in the following document where the mutated DNA strand is that for a patient suffering from Chinese β-Thalassemia, & then derive a conclusion concerning the kind of mutation involved.

d. Compare the 2 sequences in the adjacent document where the mutated DNA strand is that for a patient suffering from β–Thalassemia, & then derive a conclusion concerning the kind of mutation involved.

Related to part d

normal DNA transcribed strand
... TGA – GGT – CTC – CTC – TTC
4 5 6 7 8

mutated DNA strand
... TGA – GGT – CCC – TCT – TC
4 5 6 7 8

Related to part e

normal DNA transcribed strand
...CGG – TTT – TCA – CTA...
70 71 72 73

mutated DNA strand
...CGG – TTT – TTC- ACT...
70 71 72 73

14) Justify why each of the previously mentioned gene examples is an example of multiple alleles.