ثانوية الصويري الرسمية/1497	امتحان : السعي الثاني	التاريخ:9/1/2024
رقم الهاتف 08/565075	المادة: علوم الحياة	العلامة:/20
محافظة البقاع/قضاء البقاع الغربي	الصف:الثالث الثانوي علوم حياة	المدة:90 دقيقة
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Exercise 1 (10 points) **Pulmonary Emphysema**

Pulmonary emphysema is a fatal disease characterized by an increasingly severe respiratory failure. This disease is due to a progressive destruction of the lung tissue by the proteases of the white blood cells. In fact, in the normal case, there are substances in the blood plasma called alpha antitrypsin (aT) which protect the pulmonary cells from being destroyed by inhibiting the action of proteases.

Allele	Nucleotide sequence of the fragment of the non-transcribed strand
M_1	181 184 .... ATC AAC GAT TAC ...
M_2	181 184 .... ATC AAC GAT TAG ...

Document 1

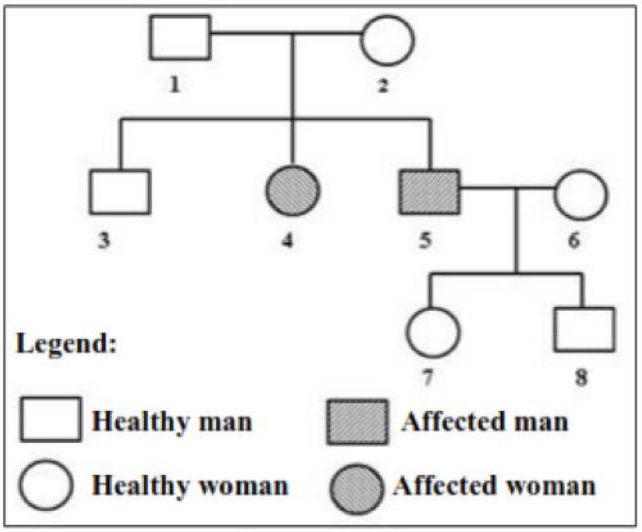
1- Pick out from the text the cause of pulmonary emphysema.

Alpha antitrypsin (aT) is a protein composed of 418 amino acids produced by liver cells. Document 1 shows the nucleotide sequence of a fragment of the normal allele (M1) and that of the allele of the disease (M2) of the gene responsible for the synthesis of "aT".

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

2- Determine:
2-1- The type and position of mutation.
2-2- The amino acid sequence of the portion of the alpha antitrypsin coded by the fragment of the allele M1 and that coded by the fragment of the allele M2.
3- Explain how the modification in the nucleotide sequence (document 1) lead to the appearance of pulmonary emphysema.

Document 3 represents the pedigree of a family of which some members are affected by pulmonary emphysema. This family comes from a population in which for each 120 individuals, one person is heterozygous.



Document 3

4- Specify whether the allele M2 which is responsible for this disease is dominant or recessive.
5- Determine the chromosomal localization of the gene responsible for pulmonary emphysema.
6- Write the genotype of individuals 3,4 and 8. Justify the answer.
7- Determine the risk to have an affected child:
7-1- For couple 5-6.
7-2- For individual three if he married a normal female.

Individual 8 is a heavy smoker and has manifested the same symptoms of pulmonary emphysema.

8- Show that there is a factor other than the genetic factor that could provoke this disease.

Exercise 2 (10pts) Hemochromatosis

Hemochromatosis is a genetic disease that is not manifested until adult age. It is caused by mutation of HFE gene situated on chromosome 6. Diagnostic molecular tests allow finding a treatment that increases the life of affected individuals. Two normal parents living in north Europe have an affected child. They wish to know the risk of developing this disease among their three other children.

1- Determine the mode of inheritance of this disease (dominant or recessive and localization).

The alleles of the HFE gene, of the three children of the family understudy, were isolated. A portion of 387 base pairs of these alleles are shown in document 1. The DNA analysis uses RsaI restriction enzyme. The fragments obtained are separated by electrophoresis.

The **restriction site** of enzyme RsaI is **GT │AC** (cuts between T and A).

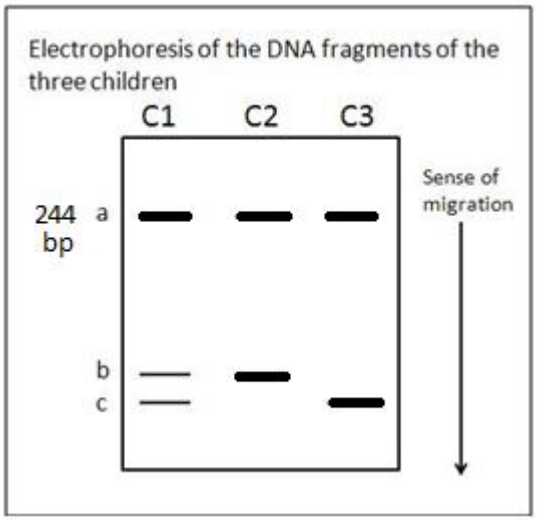
DNA sequence of the 387 nucleotides is used for molecular diagnosis. The rest of the sequence is identical for the two alleles and doesn't present any restriction sites for RsaI enzyme. The result is shown in document 1.

Nucleotide n^0 / Allele name	1 to 239	240					245					250		270				274				278	279 to 387
HFE normal	…	G	C	T	G	T	A	C	C	C	C	C	…	A	C	G	T	G	C	C	A	G	…
HFE abnormal	…	G	C	T	G	T	A	C	C	C	C	C	…	A	C	G	T	A	C	C	A	G	…

Document 1

The results of electrophoresis of the above DNA fragments formed different bands which are realized in document2. During electrophoresis only fragments above 50 nucleotides are visible.

C1, C2, and C3 correspond to the three children.



Document 2

2- Indicate the type and position of mutation that took place.

3- Specify the number and length of fragments obtained from each allele after enzymatic digestion.

4- Determine the length of fragments obtained after electrophoresis in document 2 (a,b and c).

5- Establish a diagnosis for each of the three children.

Answer key

Exercise 1 (10 points) **Pulmonary Emphysema**

1- A progressive destruction of the lung tissue by the proteases of the white blood cells.

2- 1- All nucleotides are the same between both alleles except for the third nucleotide in the 184th triplet where C in allele M1 was replaced by G in M1. Therefore, the type of this mutation is substitution mutation.

2- 2- mRNA resulting from the transcription of the allele M1:

… AUC AAC GAU UAC …

Sequence of the amino acids of the polypeptide coded by the allele M1:

… -Ile - Asn - Asp - Tyr - …

mRNA resulting from the transcription of the allele M2:

… AUC AAC GAU UAG…

Sequence of the amino acids of the polypeptide coded by the allele M2:

… -Ile - Asn – Asp

3- The mutation by substitution at the level of the 3rd nucleotide of triplet number 184 (C is replaced by G) is transcribed at the level of mRNA gives a truncated polypeptide having 183 amino acids instead of 418, leading to an non-functional protein alphaantitrypsin (aT). This explains why alpha-antitrypsin is not found in the blood of an individual affected by pulmonary emphysema and consequently the pulmonary tissue is not protected against protease degradation and the patient shows manifestation of pulmonary emphysema.

4- The allele of the disease is recessive. The parents 1 and 2 are normal but gave two affected children 4 and 5. These children have taken the mutant allele from at least one of the parents. This parent does not phenotypically express the disease, so the mutant allele is being masked by the normal one.
N: normal dominant allele. m: mutant recessive allele.

5- If the studied gene is carried on the non-homologous part of Y, in this case, any affected boy would necessarily have a sick father. For example, the affected boy 5 must have taken Y^m from his father who would have as genotype XY^m. Possessing such genotype, father 1 should be affected, which is not the case.
If the studied gene is carried on the non-homologous part of chromosome X: in this case, the affected daughter 4 would have X^m // X^m as genotype (purity is the criterion of recessivity). She should have taken one of her mutant alleles Xm from her father 1 who would have as genotype Xm // Y who phenotypically should be affected, which is not the case.
If the studied gene is carried on the homologous parts of X and Y: in this case, the affected boy 5 would have as genotype X^m // Y^m, and his sister 4 would have as genotype X^m // X^m They have taken respectively Y^m and X^m from their father 1. This latter should have as genotype X^m // Y^m and would be phenotypically affected. It's not the case.
Therefore, the studied gene is not gonosomal but it is autosomal.

6- 3: N//N or N//m since he is normal so he necessarily has the normal allele and since the normal allele is dominant so it can be expressed in both homozygous and heterozygous states.
4: m//m since she is affected by a recessive disease and recessivity is a character of purity.
8: N//m since he is normal so he necessarily has the normal allele and he must have inherited an allele m from his affected father.

7- 1- Risk= probability of father to be heterozygous × probability of father to transmit the allele of the disease if he was heterozygous × probability of mother to be heterozygous × probability of mother to transmit the allele of the disease if she was heterozygous

The mother is normal with no family history so she could be either N//N or N//m. if she was N//N then she will give all of her children the normal allele which is dominant and thus all of them will be normal so the risk will be zero.
Her probability to be N//m is 1/120. Her probability to transmit m if she was heterozygous is ½.
The father is affected m//m so his probability to transmit the allele of the disease is 1.
Risk= 1×1/120×1/2= 1/240.
7-2- Individual 3 is normal he could be N//N or N//m. if she was N//N then he will give all of his children the normal allele which is dominant and thus all of them will be normal so the risk will be zero.
Since he has affected siblings and normal parents who are heterozygous so his probability to be heterozygous is 2/3. His probability to transmit m if he was heterozygous is ½.
His wife is normal with no family history so her probability to be N//m is 1/120. Her probability to transmit m if she was heterozygous is ½.
Risk= 2/3×1/2×1/120×1/2=1/720.

8- Despite the presence of a normal allele in his genotype (heterozygous), individual 8 develops the same symptoms of pulmonary emphysema. Being a heavy smoker promotes the development of the disease. This shows that smoking is an environmental factor other than the genetic factor that could provoke this disease.

Exercise 2 (10pts) **Hemochromatosis**

1- Since two normal parents gave birth to an affected child, therefore the parents carry the allele of the disease but it is masked by the normal allele. So the allele of the disease is recessive.

2- The gene is autosomal since the gene which causes the disease is located on chromosome 6, an autosome. (1/2pt)
Let N be the normal allele and d be the allele of the disease.

3- Type of mutation: substitution mutation.
Position: the 274th nucleotide in the normal allele is G it was replaced by A in the abnormal allele. (1/2pt)

4- The normal allele contains only one restriction site thus it will be cut once between nucleotides 244 and 245 yielding two fragments of lengths: 1st fragment= 244bp and 2nd fragment= 387-244= 143bp.
The abnormal allele contains two restriction sites thus it will be cut twice between nucleotides 244 and 245 and between 273 and 274 yielding three fragments of lengths: 1st fragment= 244bp and 2nd fragment= 273-244= 29bp and 3rd fragment=387-273=114bp. (11/2 pts)

5- It is given that during electrophoresis only fragments above 50 nucleotides are visible, therefore, fragments of lengths 244bp, 143bp and 114bp will be visible but that of length 29bp will not appear on the gel. Moreover, since fragments migrate in a gel according to their size where the smallest is the fastest, so fragment a is 244bp, fragment b is 143bp and fragment c is 114bp. (1pt)

6- Child C1 shows one thick band corresponding to fragment a and one band corresponding to fragment b and one for c. since fragment b corresponds to normal allele and c corresponds to abnormal allele, so he possesses both alleles and he is heterozygous N//d. (1/2pt)
Child C2 shows 2 thick bands for fragments a and b which coth correspond to the normal allele so he is homozygous normal N//N. (1/2 pt)
Child C3 shows 2 thick bands for fragments a and c which coth correspond to the abnormal allele so he is homozygous affected d//d. (1/2pt)