This is a Class 1 exam

Lebanon Evangelical School for Boys and Girls

# Lebanon Evangelical School

for Boys and Girls — Loueizeh - Baabda

# Stage Exam 01

## 11NOV2022

| Do NOT write in this box. Your MARK will be placed here. |
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|---|---|---|
| Subject : | Biology | |
| Class : | 12E | |
| Teacher : | Christine Khalil | |
| Duration : | 1 hour | |
| Please write your answers on a separate sheet of paper. | | |
| Your name : | | *Time taken to complete exam* |
| Your Class : | | |
| Exam Room : | | |
| How many sheets, including cover sheet : | | |

- Do not open this paper until the teacher in charge instructs you to do so.
- The most important thing to remember in taking an exam is NEVER PANIC.
- If you are caught cheating in this exam, you will be awarded zero for ALL exams that are taken on this day.

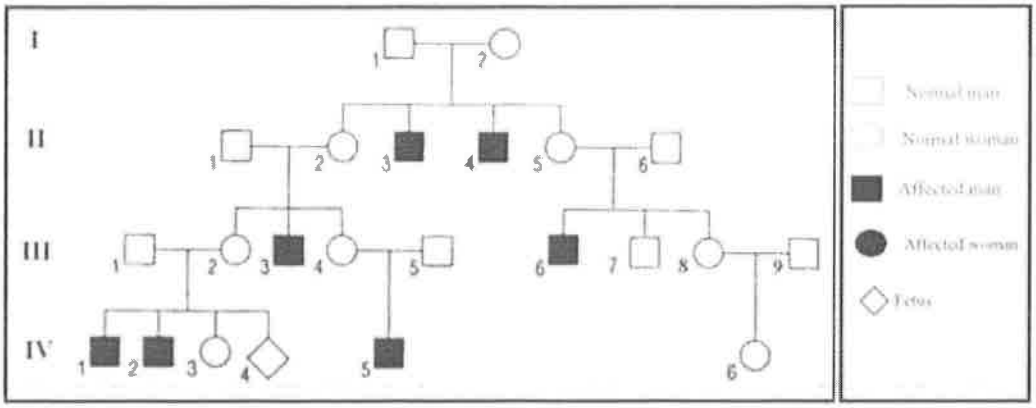
## Fabry Disease

Fabry disease is a type of lysosomal storage disease. Lysosomes are round structures found in the cells of the body that are full of enzymes. Lysosomal enzymes help breakdown proteins, carbohydrates, fats and other substances.

In Fabry disease, there is a deficiency in the enzyme alpha-galactosidase (α-GAL enzyme) which helps breakdown of a fatty substance called Gb3. Without enough α-GAL enzyme, Gb3 builds up in cells throughout the body and the progressive accumulation of this substance can affect the function of the skin, eyes, gastro-intestinal system, kidney, heart, brain and nervous system.

Fabry disease is the result of a mutation of the gene responsible for making α-GAL enzyme, which is located on the X chromosome. Fabry affects mostly males though rarely females may inherit the disease.

Document 1 represents the pedigree of a family, whose certain members are affected with Fabry disease.




**Document 1**

1. Specify whether the allele responsible for Fabry disease is dominant or recessive. (1)
2. Show that the gene responsible for the disease is localized on the non-homologous segment of chromosome X. (1.5)
3. Indicate the genotype (s) of each of the following individuals: III 1, III 2, IV 1 and IV 3. (2)
4. Determine the risk of the fetus IV 4 to be affected with the disease. (2)

Ultrasound scan was done to determine the sex of the fetus. It revealed that it is a girl. The doctor then prescribed DNA analysis by the method of Southern blotting. The used probe permits to

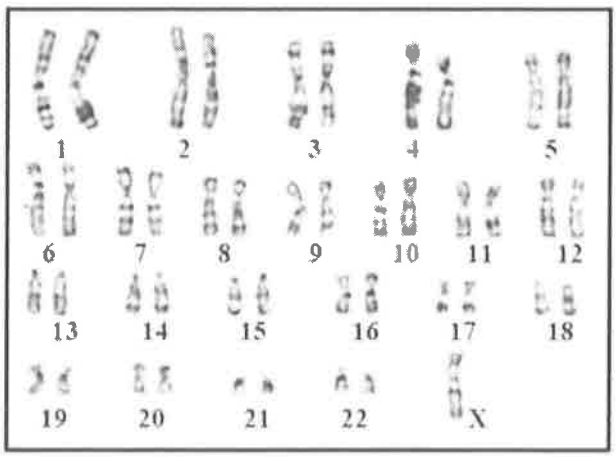
distinguish the mutant and the normal alleles of the GLA gene. The obtained results are shown in document 2.

| | $III_1$ | $III_2$ | $IV_1$ | IV3 | Fetus IV4 |
|---|---|---|---|---|---|
| Allele 1 | ——— | ——— | | ▬▬ | |
| Allele 2 | | ——— | ——— | | ——— |

**Document 2**

5. Indicate which of the two alleles, 1 or 2, is responsible for this disease. Justify your answer. (1)
6. Specify, based on document 2, the problem of the child that will be born. (1)

The doctor completed the diagnosis by establishing the karyotype of the fetus. The obtained result is shown in document 3.




**Document 3**

7. Indicate one method that allows us to obtain cells from the fetus in order to perform a karyotype. (1)
8. Specify, based on documents 2 and 3, the diagnosis of the fetus. (1.5)
9. Determine in this girl:
   9.1.The parental origin of Fabry disease. (1.5)
   9.2.The parental origin of the chromosomal abnormality. (1.5)

**Answer key for SE01 12E**

1. The allele of the disease is recessive. The parents I 1 and I 2 are normal but gave two affected children II 3 and II 4. 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 f is being masked by the normal one N which is dominant. (1)
2. Fabry affects mostly males though rarely females may inherit the disease. The pedigree shows that all affected individuals are males. This indicates that the gene responsible for the disease is sex linked, it is neither located on an autosome nor on the homologous segment of X and Y, then it is either located on the non-homologous segment of X or non-homologous segment of Y. If the gene is localized on the non-homologous segment of Y chromosome, sons should have the same phenotypes as their fathers, but the pedigree shows that all affected sons have healthy father. IV 1 is an affected male of genotype X $Y^I$, he should have inherited $Y^I$ from his father III 1 who should be affected of genotype X $Y^I$ but this is not the case and the gene is localized on the non-homologous segment of X. (1.5)
3. Genotype of III 1: $X^N$ Y, Normal male who expresses the only allele he has on X.
   Genotype of III 2: $X^N/X^I$ phenotypically normal so must have the normal allele and had affected children IV1 IV2 who should have received the affected allele from her.
   Genotype of IV 1: $X^I$ Y affected male who expresses the only allele he has on X
   Genotype of IV 3: $X^N$ $X^I$ or $X^N$ $X^N$ Normal allele is dominant and can be expressed in a homozygous or a heterozygous state. (2)
4. The fetus IV 4 has a heterozygous mother III 2 of genotype $X^N$ $X^I$ that produces 2 types of gametes of equal proportion: ½ $X^N$ and ½ $X^I$ and it has a healthy father III 1 of genotype $X^N$ Y that produces 2 types of gametes of equal proportion: ½ $X^N$ and ½Y.
   -If the fetus was a boy, he obligatory will receive chromosome Y from his father and the probability to receive the chromosome $X^I$ from his mother will be ½. Then, the risk of this fetus to be an affected boy is ½. (1)
   -If the fetus was a girl, the risk will be null since she will receive obligatory $X^N$ from her father. Therefore, the fetus will be necessarily healthy regardless of the gamete received from her mother. (1)

5. Allele 2 is responsible for the disease, because document 2 shows that boy IV 1 who is affected and of genotype $X^f$ Y possesses a single allele 2. (1)
6. The ultrasound scan revealed that the fetus is a girl, hence she has 2 X chromosomes, then she must have 2 alleles, but according to document 2 she presents only one allele. Therefore, she is a girl with one X. (1)
7. Amniocentesis or any relevant method (1),
8. The DNA analysis shows that the girl has only allele 2 which corresponds to the allele of the disease f. The karyotype shows the presence of only one sex chromosome instead of two. This sex chromosome is X. So her unique X carries the allele of the disease f, therefore the girl has Turner syndrome and affected by Fabry disease. (1.5)
9. 1. The girl has monosomy X and is affected by Fabry disease. Her unique X carries the allele f. Since, her father is healthy of genotype $X^N$ Y, then he doesn't have $X^f$. Consequently, this girl has certainly inherited $X^f$ from her heterozygote mother of genotype $X^N X^f$. Hence, the origin of Fabry disease in this girl is maternal. (1.5)
    2. Since the origin of the only X in this female is of maternal origin, this means that this female results from the fertilization of a female gamete having one X chromosome with a male gamete lacking any sex chromosome. Hence, the origin of the chromosomal abnormality (monosomy X) is paternal. (1.5)