This is a Class 1 exam

Lebanon Evangelical School for Boys and Girls

Loueizeh - Baabda

Mock Exams : Pt2

13, 14, 15 JUN2022

Do NOT write in this box. Your MARK will be placed here.

Subject :	Biology
Class :	12E
Teacher :	Christine Khalil
Duration :	2 hours 30 minutes

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 :		

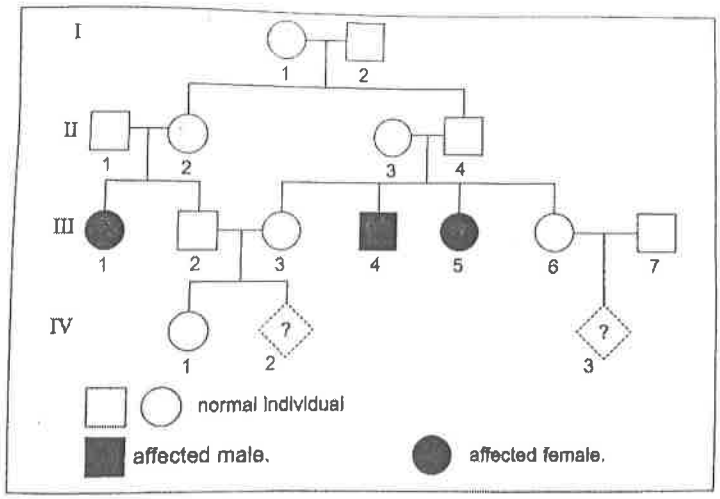
- Do not open this paper until the teacher in charge instructs you to do so.
- The most important thing to remember in taking an exam is NEVER PANIC.
- If you are caught cheating in this exam, you will be awarded zero for ALL exams that are taken on this day.

Exercise 1 (11 points)

Phenylketonuria is a metabolic disease of genetic origin that affects 1/10 000 children at birth. It is characterized by the accumulation, in the blood, of the phenylpyruvate (phenyl acetone). This product is harmful for neurons during the first 10 years of life. Normally, the phenylalanine (food amino acid), is metabolized by PAH enzyme into tyrosine in the presence of a co-factor DHBP. The most frequent reason of the disease is the absence of PAH activity; so the excess phenylalanine is transformed into phenylpyruvate. A systematic tracking of this disease starts at birth. A diet without phenylalanine during the first 10 years of life, permits to avoid the observed troubles.

Statistics done on an isolated community allows to identify 20 heterozygous out of 800 tested children due to PAH.

The following genealogical tree is that of a family of this community of which some of its members are affected by the disease.



1. Determine if the allele responsible for the disease is dominant or recessive. (1)

2. Indicate the chromosomal location of the studied gene. (1.5)

3. Calculate the birth rate (risk) of children having phenylketonuria in this community. (1)

4. Formulate a hypothesis which explains the difference between this rate and the world's rate. (1)

Two sisters (III - 3 and III - 6) consult a geneticist in order to evaluate the risk for their fetus IV2 and IV3 to be affected by this disease.

5. Evaluate the risks for the fetus of IV2 and IV3 to be affected by the disease, compare these risks and explain the differences. (2)

6. How can the last answer confirm the hypothesis issued in question 4? (1)

The daughter III1 gets married with a phenylketonuria man against the opinion of the genetic advice. Their first child is normal.

7. a. In what is this result surprising? (1)

b. Knowing that all tests enabled us to prove that the child is legitimate, give a hypothesis that can explain this result. (1)

The husband of III1 shows a normal value and activity of PAH.

8. Show that this result validates the previous hypothesis (7b). What do you suggest for origin of the father's disease? (1.5)

Exercise 2 (7 points)

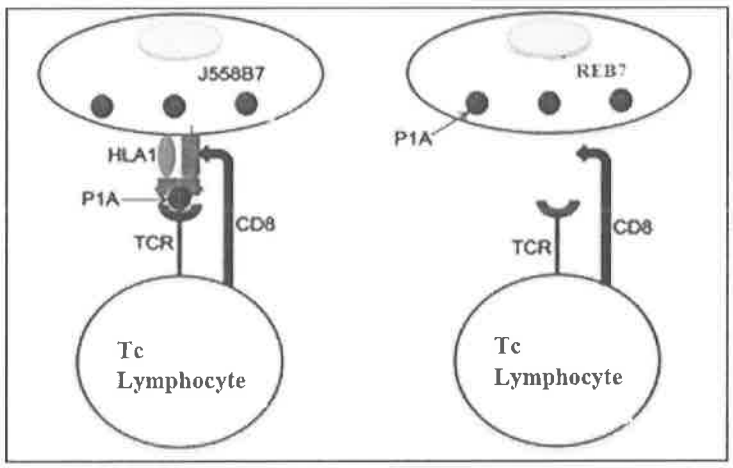
Cancer results from excessive production of cells in the body. In order to understand how the cancerous cells can escape the immune system, scientists used animal models similar to human cases.

Study 1: In a mouse S1, we graft modified cancerous tumor cells called J558B7, and we observe an abnormal cell proliferation. A strong immune response is then initiated and it succeeds in quickly eliminating the tumor by lysing the cancerous cells. However, some cancerous cells are capable of resisting to the action of the immune system and they keep growing. These cells are called REB7. The aim of the exercise is to determine how REB7 can escape the action of the immune system.

Study 2: Cancerous cells produce a peptide called P1A that distinguishes them for the other cells of the body. P1A is recognized by the T lymphocytes as a non-self-peptide. This peptide is found in both types of cancerous cells: J558B7 and REB7. Document 1 shows an activated T lymphocyte in presence of a J558B7 cell and another in presence of REB7 cell.

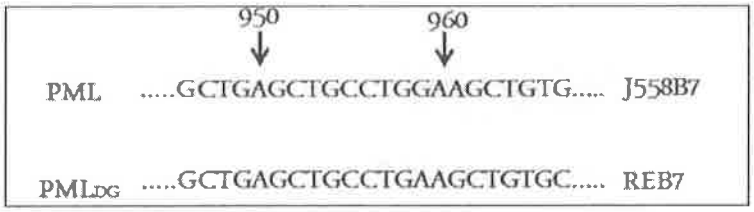
1. Based on document 1 and your acquired knowledge, explain how Tc lymphocytes recognize and lyse J558B7 cells. (2)

2. Explain why Tc lymphocytes do not attack REB7 cells. (1)



Document 1

The PML gene encodes for the PML protein that is necessary for the association and expression of HLA molecules on the surface of cells. Document 2 shows the sequence of nucleotides of the normal PML allele found in J558B7 cells and the sequence of the mutated PMLDG allele found in REB7 cells.



Document 2

3. Indicate the type and the position of the mutation in the PMLDG allele. (1)

Experiment: In a mouse S1, we graft cancerous tumor cells and we observe an abnormal cell proliferation. Few days later, Tc lymphocytes are taken from the S1 mouse and cultured in different culture media with tumor cancerous cells genetically modified in a way to add one of the 2 alleles of the PML gene. The conditions and the results are shown in document 3.

Culture Medium	**1**	**2**
Cells added to the medium	Tc lymphocytes from the S1 mouse + REB7 cells +PMLDG gene	Tc lymphocytes from the S1 mouse + REB7 cells +PML gene
Results	No lysis of REB7 cells	Lysis of REB7 cells

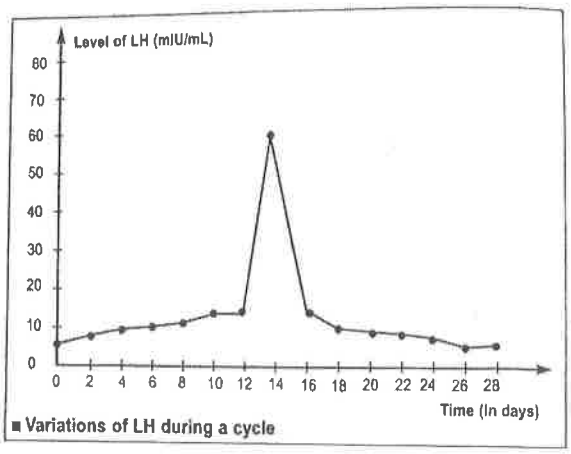
Document 3

4. Interpret the results shown in document 3. (1.5)

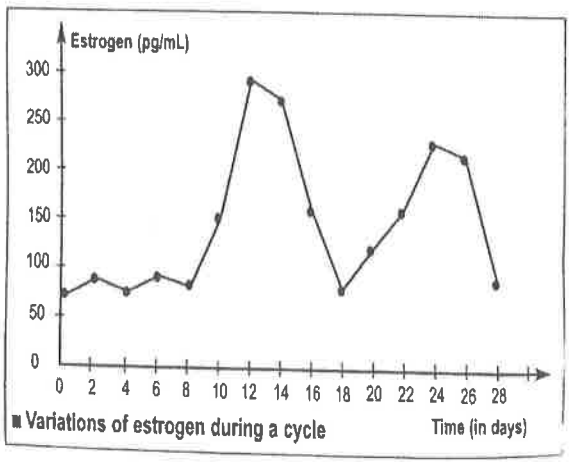
5. Explain, based on what precedes and your acquired knowledge, how REB7 cells escape from the lysis by Tc lymphocytes. (1.5)

Exercise 3 (7 points)

A 30-year-old woman (A) consults a doctor because she is sterile. Profound analysis showed the presence of normal follicles in her ovaries. To be able to identify the origin of sterility, the doctor ordered blood tests to check her LH and estrogen concentrations. The results are shown in documents 1 and 2.



Document 1



Document 2

1. Convert both graphs in documents 1 and 2 into the same table. (2)

The treating doctor affirms that these results suggest an absence of abnormality at the level of the hypothalamus, pituitary gland and the ovaries function.

2. Justify the doctor's affirmation. (1)

3. Formulate a hypothesis to explain the origin of sterility of woman (A). (1)

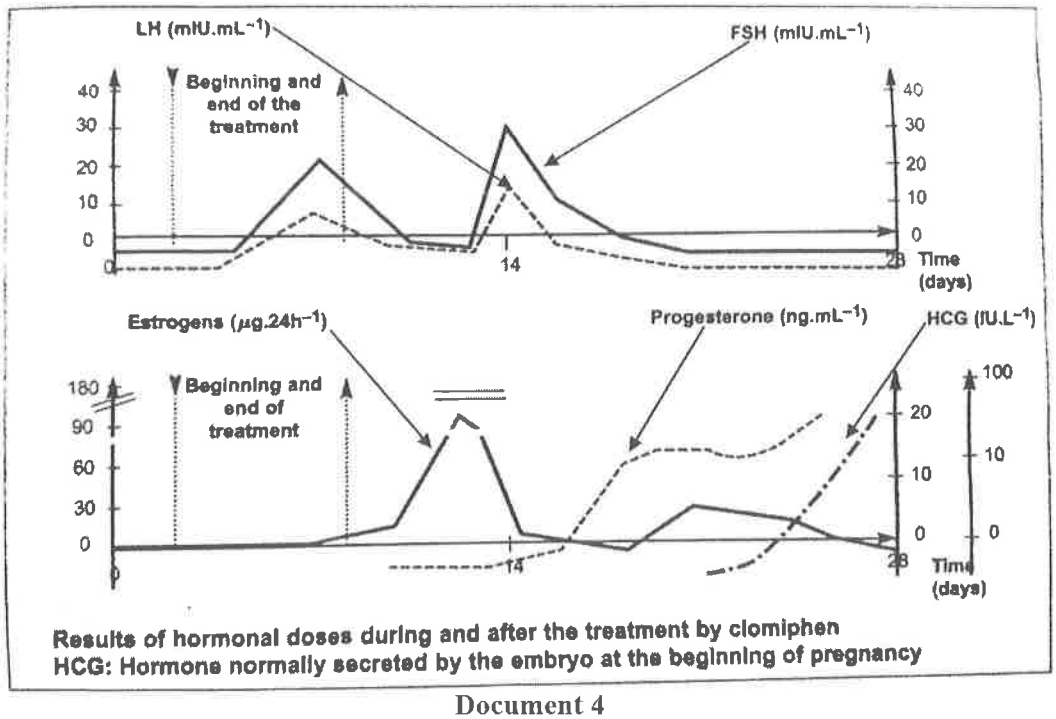
A second woman (B) also suffers from sterility. The following table (document 3) summarizes the concentrations of LH and estrogen of this woman.

Days after the period's beginning	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
LH concentration (mIU/mL)	5,3	5,9	6,8	8	6,5	6,3	7	6,2	6,8	6	6,5	7,3	7,3	6,8	6,5
Estrogen (pg/mL)	29,1	30,6	30	30,3	30,3	30,4	29,9	29,3	30	30,3	30,1	29,9	30	30,1	30,3

Document 3

4. Deduce the probable cause of sterility of woman (B). (1.5)

The treating doctor proposes a clomiphen treatment for woman (B). This is an analogous structure of estrogen which inhibits estrogen's action by binding on their receptors at the level of the hypothalamo-pituitary gland complex. The results of the hormone levels after the treatment are shown in document 4.



Document 4

5. Based on document 4 and your acquired knowledge, explain the consequences of this treatment on the sterility problem of woman (B). (1.5)

Answer key for Mock 2 12E

Exercise 1 (11 points)

1. The non-affected parents II 1, II 2 and II 3, II 4, have given respectively affected Children III 1, on one side, and III 4, III 5 on the other. In every couple at least one of the parents has the affected allele that doesn't appear in his phenotype. This allele is therefore recessive; the normal allele is dominant. Let "N" be the symbol of the allele responsible for the normal phenotype and "a" be symbol of the allele responsible for the affected phenotype. (1)

2. If the gene is carried by the non-homologous segment of Y, all the boys must have their father's phenotype. So III 4 affected of genotype $X\ Y^a$ should have received Y^a from his father II 4 whose genotype should be $X\ Y^a$ and should be affected but this is not the case.

If the gene is carried by the non-homologous segment of X, the affected girl III 5 of genotype $X^a\ X^a$ should have received X^a from her father II 4 whose genotype should be $X^a\ Y$ and should be affected but this is not the case.

If the gene is carried by the homologous segment of X and Y, the affected boy III 4 of genotype $X^a\ Y^a$ should have received Y^a from his father II 4, and his sister III 5 who is also affected of genotype $X^a\ X^a$ should have received X^a from her father II4 so the father II4 should have a genotype of $X^a\ Y^a$ and should be affected but this is not the case. Therefore, the gene is carried by an autosome. (1.5)

3. To have an affected child from two healthy parents, it would be necessary that the two parents are heterozygous of genotype Na. Probability for each parent to be heterozygous is 20/800 = 1/40.

For the two to be heterozygous is: 1/40 x1/40

Heterozygous parents have one risk over 4 to give a homozygous child of genotype aa (Results of F2 in a monohybrid case). The phenylketonuria children birth rate in this community is therefore: 1/40 x 1/40 x ¼ = 1/6400. (1)

4. (The obtained rate 1/6400 is higher than the world's rate 1/10000). Hypothesis: The inbreeding in this isolated community is the cause of the increase in the phenylketonuria children's birth rate. (1)

5. For IV 2: parents of fetus III 2 and III 3 have both, at least one affected brother or sister (III 1, III 4 and III 5). The grand-parents II 1, II 2, II 3 and II 4 are therefore heterozygous of genotype Na. 3 descendants over 4 of these grand-parents must have normal phenotype [N] of which 2/3 are heterozygous. The risk that the 2 parents are heterozygous is 2/3 x 2/3. If III 2 and III 3 are heterozygous, they have a risk of ¼ to have an affected child. The risk for IV 2 to be affected is 2/3 x 2/3 x ¼ = 1/9.

For IV 3: the mother III6 has the same risk as her sister III 3 to be heterozygous 2/3. The father is a part of the same community; he has a risk of 1/40 to be heterozygous. If III 6 and III 7 are heterozygous, they have a ¼ chance to have an affected child. Thus the risk for fetus IV 3 to be affected is: 2/3 x 1/40 x ¼ = 1/240.

Fetus IV2 has a higher risk 1/9 to be affected by the disease than fetus IV3 1/240. Parents III 2 and III 6 are 2 cousins descendants of the same family where the affected allele is present. For couple III 6 and III 7, only 1 of the 2 parents (III 6) has descended from such a family. This illustrates well the fact that inbreeding increases the risk of attack by rare recessive diseases. (2)

6. The fact that the studied community is genetically isolated suggests the presence of frequent inbreeding marriage. The previous answers prove that inbreeding increases the risk of attack by the disease. Hence, the hypothesis is confirmed. (1)

7.a. This result is surprising because the disease being recessive, the 2 parents should have the genotype aa. They should not have any normal children Na or NN. (1)

b. Hypothesis: this disease is controlled by 2 different genes. (1)

8. The rate and normal activity of PAH in the husband indicates a different origin of the disease. This validates the previous hypothesis. According to the given, phenylalanine is metabolized by PAH in the presence of DHBP (cofactor). This suggests that the origin of the father's disease is the absence of DHBP coded by a gene which is different from that of PAH. (1.5)

Exercise 2 (7 points)

1. The specific Tc lymphocyte activated against the tumor recognizes through their TCR the non-self-peptide P1A exposed on the surface of J558B7 cells inside HLA I molecules (double

recognition) and attaches to it through their CD8. The Tc lymphocyte will then release their perforin content. Perforin assembles into polymers that form a hollow channel through the target cell membrane (J558B7). The Tc also releases granzymes that penetrate into the target cell through the polyperforin channels. Granzymes trigger an enzymatic chain reaction within the cancerous cell leading to DNA degradation and cell death. (2)

2. REB7 cells don't present HLA I molecules on their surface, therefore P1A peptide remains in the cytoplasm and will not be exposed on the surface of these cells. Activated Tc lymphocytes specific against the tumor cannot recognize it (cannot perform double recognition) and therefore do not attack it. (1)

3. Both DNA sequences are identical except starting from the position 958/959. A deletion of the G nucleotide at position 958/959 has occurred in the PMLDG gene leading to a change in the reading frame (frameshift). (1)

4. The culture of Tc lymphocytes taken from a S1 mouse injected with cancerous cells in presence of REB7 cells and PMLDG gene does not lead to the lysis of REB7 cells. However, the culture of Tc lymphocytes taken from a S1 mouse injected with cancerous cells in presence of REB7 cells and PML gene leads to the lysis of REB7 cells. This indicates that PML is necessary for the action of Tc lymphocytes. (1.5)

5. The PML gene encodes for the PML protein which is necessary for the association and expression of HLA molecules on the surface of cells. In REB7 cells, this gene exists in a mutated form PMLDG that codes for an abnormal PML protein which is non-functional and will not express the HLA molecules on the surface of REB7 cells. These HLA molecules are indispensable for the double recognition of cancerous cells by Tc lymphocytes that should recognize the complex HLA I and the P1A peptide (protein synthesized inside cancerous cells including REB7). Due to the absence of HLA molecules, Tc lymphocytes will not recognize REB7 cells anymore and therefore escape from the lysis. (1.5)

Exercise 3 (7 points)

1. Table showing the variations of LH and estrogen concentrations during a cycle. (2)

Days after the beginning of period	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
LH concentration (mIU/mL)	6	8	9.5	10	11	13	13	60	13	10	9.5	9	7	6	6.5
Estrogens (pg/mL)	70	87	75	90	81	150	290	270	160	80	120	160	230	215	90

2. The obtained results show a normal evolution of LH with a peak in the middle of the cycle. This indicates the normal state of the hypothalamic stimulation and the pituitary secretion. Also, this evolution suggests the presence of positive feedback exerted by the estrogen on the pituitary gland. This is confirmed by the high level of estrogen on the 12th day, which indicates a normal development of the follicles which were also checked and found to be normal. The fall in level of estrogens during few days after the peak of LH indicates a follicle transformation into yellow body after ovulation. These results show a normal state of endocrinien control and of ovarian functioning. (1)

3. Hypothesis: Woman A might have a problem in her genital tract. (1)

4. Through the 28 days, the analysis of blood for LH and estrogen levels shows an estrogen's quasi constant level of 30 pg/ml and an LH level oscillating around 6.5 mIU/mL (a minimum of 5.3 and maximum of 8 mIU/mL). This shows an absence of cyclic variations especially a discharge of estradiol on the 12th day that starts the peak of LH at of the beginning of ovulation. We can deduce that the probable cause of sterility in woman B is the absence of ovulation. (1.5)

5. Clomiphen is an antagonist of estrogen that inhibits their action at the level of the hypothalamo-pituitary axis. Its action is translated during the treatment by a peak of LH and FSH. After the end of treatment, we successively observe:

- A peak of estradiol secreted by the follicles where the growth is stimulated by the high levels of FSH.

- A peak of LH and FSH due to the positive feedback exerted by the estrogen's peak.

- An increase in the level of progesterone secreted by the yellow body after ovulation. This is a proof that the treatment is successful.

- Following progesterone increase with the appearance of HCG. This shows the implantation of embryo in the uterus and the cyclic transformation of yellow body into pregnancy yellow body. The treatment has succeeded. (1.5)