Grade 12 LS	Biology Second term Exam	Date: 11-3-2022 Duration: 120 minutes

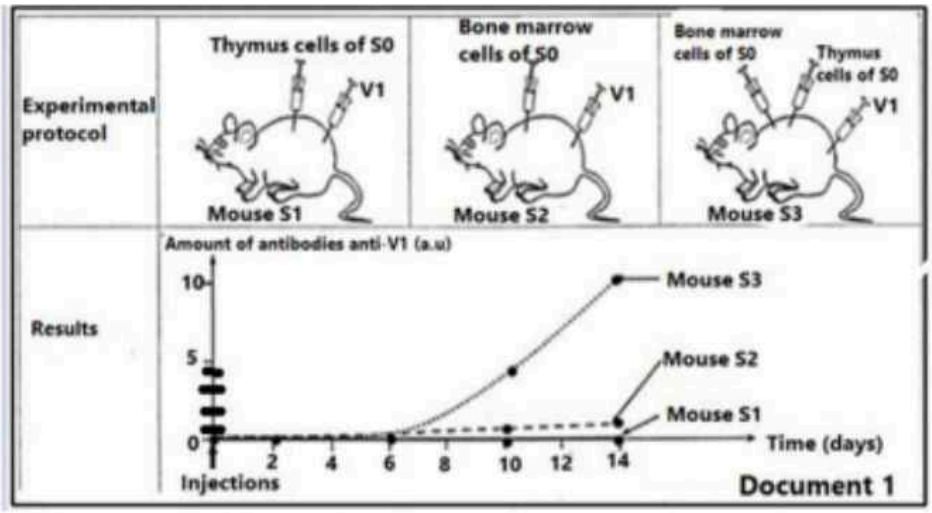
➢ Exercise 1: Immunity of the organism

In order to study the mechanism of the immune response developed against a V1 virus, we carry out the following experiments:

Experiment 1:

We realized in three irradiated and thymectomized mice S1, S2 and S3 injections of V1 and immune cells of thymus and/or bone marrow collected in another S0 mouse.

Then, we measured the rate of anti-V1 antibodies in each of the three mice S1, S2 and S3. All of these mice are histocompatible and not immune to V1. The experimental conditions and the results are given in document 1.



Document 1

1. Explain the interest in irradiation and thymus removal in experiment 1.
2. Draw in the same table the results of experiment 1 (document 1).
3. **3.1.** Analyze experiment 1 (doc 1)
   3.2. Derive the necessary condition for the production of a large quantity of anti-V1 antibodies.
4. Name the cells that secrete anti-V1 antibodies that are involved in the immune response triggered against V1.

Experiment 2:

Document 2 presents, at two different times T1 then T2, the observations of an electron microscope showed Tc lymphocytes (TLc) of S4 mouse that received an injection of V1 a few days ago and put in cultivation in the presence of infected S4 cells or not infected by V1, infected by V2 or with cells of S5 not compatible with S4 and infected with V1.

		1	2	3	4
Cultures		TLc of S4 + cells of S4 infected by V1	TLc of S4 + cells of S4 non-infected	TLc of S4 + cells of S4 infected by V2	TLc of S4 + cells of S5 infected by V1
Results	Time T1	TLc of S4 Cells of S4 infected by V1	TLc of S4 Cells of S4 non-infected	TLc of S4 Cells of S4 infected by V2	TLc of S4 Cells of S5 infected by V1
	Time T2	Lysis of cells of S4 infecetd by V1	No lysis of cells of S4 non-infecetd	No lysis of cells of S4 infecetd by V2	No lysis of cells of S5 infecetd by V1

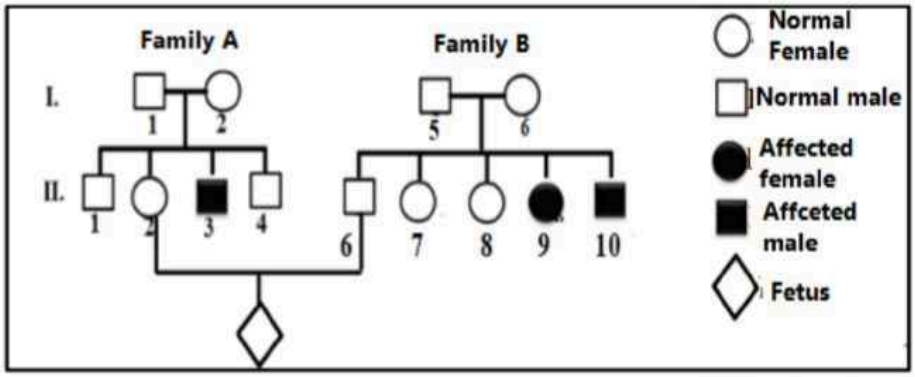
Document 2

5. Pick out from document 2 the name of a 2nd cell which intervenes in the immune response triggered against V1.
6. Interpret the results of experiment 2 (document 2).
7. Explain the results at times T1 and T2 of experiment 2 (document 2).

➢ Exercise 2 Albinism

Albinism is a hereditary disease characterized by the absence of pigmentation of skin and hair. The risk of the birth of a child with albinism in the world is equal to 1/20000. This disease is due to the absence of the melanin which is responsible for the pigment skin color and hair. The pedigrees of document 1 show the transmission of this disease in two families A and B.

1. Specify whether the albinism allele is dominant or recessive.
2. Discuss logically the location of the albinism allele.
3. Woman II2 and man II6 are married and expecting a baby.
   - **3.1.** Determine the couple's risk of having an affected child.
   - **3.2.** Compare this risk to the global risk.
   - **3.3.** Formulate a hypothesis to explain this difference.



Document 1

➢ Albinism is due to a gene, represented as three alleles:

- Two alleles TYRCOD (1) and TYRCOD (2) which encode the synthesis of an enzyme "tyrosinase", essential for the biosynthesis of colored melanin from colorless tyrosine in the skin cells.
- a TYRALBA 3 allele which codes for the non-functional form of the enzyme tyrosinase.

• It was possible to identify two alleles of this gene by the use of two restriction enzymes: Xho I and XhoII. The results obtained are represented in document 2 below:

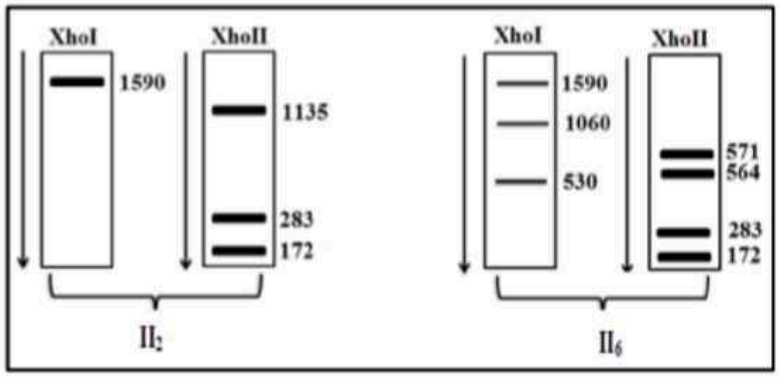
Alleles	Enzyme XhoII		Enzyme XhoI	
	Number of sites	Lengths of Fragments (bp)	Number of sites	Lengths of Fragments (bp)
TYRCOD (1)	2	172,283,1135	0	1590
TYRCOD (2)	3	172,283,564,571	0	1590
TYRALBA (3)	3	172,283,564,571	1	530,1060

Document 2

4. Explain the action of the enzymes XhoI and XhoII on each of the three alleles.

The couple's DNA (II2 ,II6) is analyzed using both enzymes XhoI and Xho II, then we separate the restriction fragments obtained by gel electrophoresis. The results are shown in document 3.

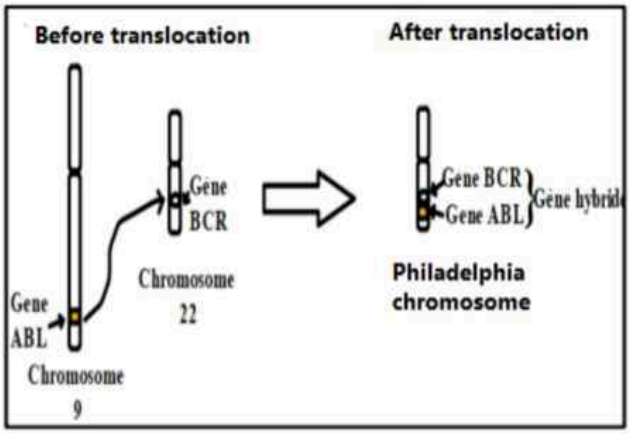
5. Write the genotypes of the individuals II2 and II6. Justify.
6. Specify whether the DNA analysis of the couple make it possible to know the exact phenotype of their fetus.



Document 3

➢ Exercise 3: A chromosomal translocation

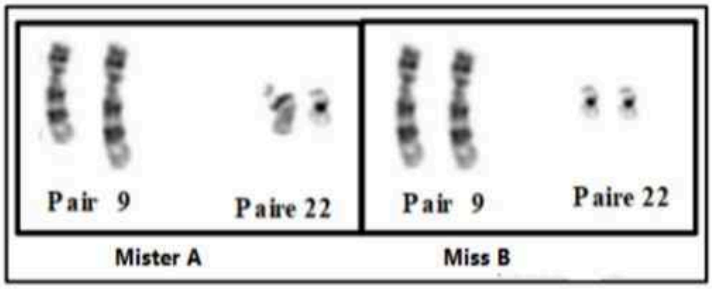
Chromosomal translocations have been linked to different types of human leukemia (blood cancer). By chromosomal translocation a segment of a chromosome is broken, then reattached to another chromosome. By result of this event two genes can be combined. In this case a new gene will be created resulting from the combination of different genes. This in return results in a cancer development. This is the case of Philadelphia chromosome found in 90% of patients with myeloid chronic leukemia (blood cancer). This translocation is well known (document 1) and leads to the fusion of a gene called ABL, which is located on chromosome 9, at a gene on chromosome 22 called BCR. The fusion of the BCR and ABL genes produces a new hybrid gene that encodes a mutant protein that disrupts proliferation cells and results in blood cancer.



Document 1

1. Explain how gene fusion BCR and ABL produces a new gene hybrid that codes for a protein mutant.

Document 2 shows the partial karyotypes of Mr. A, affected by myeloid leukemia (blood cancer) and his normal wife B with normal family members.



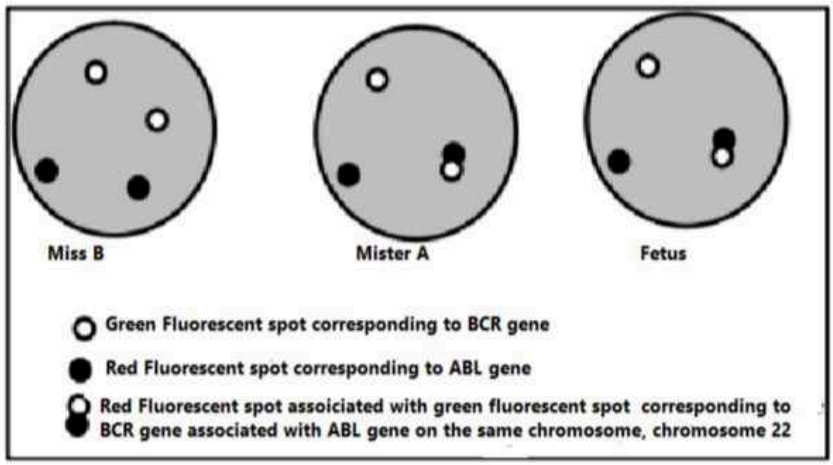
Document 2

2. Compare the pairs of chromosomes 9 and 22 of mister A with those of his wife B in document 2.

Mrs B is pregnant, she wonders about the risk of her fetus being affected by myeloid leukemia.

3. Make the necessary factorial analysis to know the risk of her fetus to be with myeloid leukemia.

In order to validate the risk that threatens the fetus of woman B to be affected by myeloid leukemia, her doctor decides to make the technique of hybridization in situ (FISH) on cells from the mother, father and fetus. This technique allows to identify specific genes within a cell. Its principle is to use a DNA probe associated with a fluorescent substance capable of hybridizing with a specific DNA sequence of a cell. In this experiment the doctor used two probes, one specific for the ABL gene (red fluorescence), the other for the BCR gene (green fluorescence). Document 3 shows an interpretation of the hybridization figures.



Document 3

4. "The doctor used two probes, one specific for the ABL gene, the other for the BCR gene". List the characteristics of each of the two probes.

5. Deduce, from the results of document 3, the exact diagnosis of the fetus concerning myeloid leukemia.

Key answer for Biology second term exam 2021-2022-Grade 12 LS

Exercise 1 (9 points)

1 (1)

Irradiation (prior destruction of bone marrow stem cells) and thymus removal from S1, S2 and S3 mice in this experiment make the mice devoid of primary lymphoid organs and hence of immune cells; this makes it possible to ensure that the immune reaction triggered by each of the 3 mice comes only from the injected cells.
In this case, the role of the injected immune cells can be demonstrated.
(To ensure that the immune response triggered by the mice is due only to the injected cell.)

2 (2)

Time in days		0 (injection of V1)	2	6	10	14
Amount of antibodies anti V1 (a.u) in	S1	0	0	0	0	0
	S2	0	0	0	1	1
	S3	0	0	0	4	10

Title: table showing the amount of antibodies anti V1 (a.u) is S1,S2 and S3 as function of time (days).

3.1 (1.5)

At t=0 days which is the time of injection, the amount of antibodies anti-V1 was the same 0 a.u in all mice S1, S2 and S3 which all was injected by V1 but injected with thymus cells, bone marrow cells, thymus and bone marrow cells for S1, S2,S3 respectively.
As the time increases from 0 to 6 days, the amount of anti-V1 remained the constant in all mice S1, S2 and S3.
But as the time increases from 6 to 14 a.u, the amount of antibodies anti-V1 remained constant only in S1 injected with thymus cells only, increased slightly to 1 a.u at t=14 days in S2 which was injected by bone marrow cells only, and increased more than that in S2 to reach 10 a.u at t=14 days in S3 which was injected by both bone marrow and thymus cells.

3.2 (0.5)

The necessary condition for the production of a large quantity of anti-V1 antibodies is the presence of both thymus and bone marrow cells that ensure cellular cooperation to produce antibodies.

4 (0.5)

BLs that differentiate into plasma cells.

5 (0.5)

Tc lymphocytes

6 (1)

There was lysis of cells of S4 **infected by V1** when they were put in culture 1 with TLc of S4 while there was no lysis of cells of **S4 non-infected** (culture 2) nor that of S4 infected **by another virus V2** (culture 3). Nor S5 cells infected by the same virus V1 of TLc **but not compatible** with the S4 strain (culture 4).
This means that the TLc of S4 acts only against infected cells with V1 and of the same strain.

7 (2)

- TLc cells taken from S4 infected by V1 are activated and have TCR receptors that recognize only **the self S4 HLA complex and the non-self peptide (the V1 peptide)** which is expressed only at the surface of S4 cells infected by the V1 where there is lysis of these cells.
- The S4 cells not infected by the V1 virus present on their surface **only the HLA molecules themselves and do not present the non-self peptide on their surface**, so they are not identified by the TLcs and are not lysed.
- The S4 cells infected with the V2 virus present on their surface **only the HLA molecules of S4 and the peptide of the V2 (non-self) virus which is different from V2** then they are not identified by the TLCs and are not lysed.
- The S5 cells infected with the V1 virus present **on their surface only the HLA molecules of S5 and the peptide of the V1 (non-self) virus** then they are not identified by the TLcs and are not lysed.

	Exercise 2 (8 points)	
1	The albinism allele is recessive with respect to the normal allele since two normal parents I1 and I2 gave birth to an affected albinism child II3 which has inherited the affected allele from at least of one of the two parents which indicates that the parents carry the albinism allele in the masked state in their genotypes. Let N be the symbol of the normal dominant allele Let a be the symbol of the recessive albinism allele. Or because the normal couple I5, I6 in family B …..	0.5
2	**If the disease is located on the part specific to Y (non-homologous part of Y):** then there should be no daughter affected but this is not the case since daughter II9 is affected. If the disease is located on the part specific to Y (non-homologous part of Y) all normal males (fathers) should gave birth to normal buys but in this pedigree I1 normal X//YN gave birth to an affected boy II3 X//Ya. So this is not the case. **If the disease is located on the part specific to X (non-homologous part of X):** The affected daughter [a] should have as genotype Xa//Xa. She will necessarily inherit one Xa from her mother II6 (carrier) and one Xa from her father I5. But I5 is normal male XN//Y which is not the case. **If the disease is located on the part specific to X and Y (Homologous part of X and Y):** II9 is affected [a] so she must have a genotype Xa//Xa then she must inherit Xa from father I5 and other Xa from mother I6. II10 is affected male who must have the genotype Xa//Ya inheriting the Xa from his mother I6 and Ya from his father I5. So, the genotype of the father I5 should be Xa//Ya but this is not the case since I5 is of normal phenotype. Then, the albinism allele is located on the autosome.	1
3.1	The risk for the normal couple (II2,II6) to have an affected child with albinism of genotype a//a = risk of the two parents II2 and II6 to be hybrid * risk of the couple to have a homozygous child with a//a genotype: • II2 is a normal female so she might be homozygous (a//a) or heterozygous (N//a). The risk to be heterozygous is 2/3 since II2 has an affected sibling II3. • II6 is a normal male so he might be homozygous (a//a) or heterozygous (N//a). The risk to be heterozygous is 2/3 since II6 has affected siblings II9 and II10. • Being heterozygous, II2and II6 produce 2 types of gametes: ½ N and ½ a The risk in general of a normal heterozygous couple to have a child with a recessive and homozygote genotype= ½ d * ½ d= ¼ • The risk of the fetus to be affected risk of the two parents II2 and II6 to be hybrid * risk of the couple to have a homozygous child with a//a genotype = 2/3×2/3×1/4= 1/9	1
3.2	The risk of this couple is 1/9 which is much greater than that is the world 1/20000	0.5
3.3	Hypothesis: The increased risk of the birth of a child with albinism is due to a consanguineous marriage.	1
4	-The Xho II enzyme cuts the TYRCOD 1 allele at 2 sites and yields 3 restriction fragments of size 172, 283, 1135 bp, but it cuts TYRCOD 2 and TYRALBA3 fragments identically in three sites and gives 4 restriction fragments for each, of size 172, 283, 564, 571 bp; this is due to the presence of 2 Xho II recognition sites at the level of the TYRCOD1 allele and the presence of 3 recognition sites of this same enzyme at the level of the TYRCOD2 alleles and TYRALBA 3 due to a mutation at a recognition site.	1 1

	-The XhoI enzyme does not present any restriction site at the level of the TYRCOD l alleles and TYRCOD 2; then it cuts neither the TYRCOD l allele nor the TYRCOD 2 allele and gives a single fragment of size 1590 bp, but this same enzyme cuts the TYRALBA 3 allele at 1 site giving 2 restriction fragments of size 530, 1060 bp this is due to the absence of a site of recognition of XHoI at the level of the TYRCOD2 and TYRALBA 3 alleles and the presence of a single recognition site of this same enzyme at the level of the TYRALBA 3 allele due to a mutation at the recognition site.	
5	II2: Homozygous of genotype N//N With XhoI the electrophoresis (DNA analysis) shows 1 thick fragment of size 1590 bp which corresponds to one of the alleles TYRCOD (1) OR TYRCOD (2) which are normal. With XhoII the electrophoresis shows 3 thick bands of size 172,283 and 1135 bp which corresponds to the allele TYRCOD (1) which is normal allele. → This shows that II6 has 2 normal alleles. II6: Heterozygous of genotype N//a With XhoI the electrophoresis shows 3 fragment 530,1060 and 530 bp which corresponds to one of the alleles TYRCOD (1) {1590} bp and another allele TYRALBA (3) that gives with XhoI 230,1060 bp. Then II6 has 2 alleles one normal and one affected. With XhoI the electrophoresis obtained 4 fragments 172,283,564,571 bp which corresponds to either TYRCOD 1 and TYRALBA 3. Then, II6 has the allele TYRCOD 1 (normal) and TYALBA 3 (abnormal).	1.5
6	We can know the exact phenotype of the fetus since the father II2 in homozygous normal and will gives 1 single type of gamete 1 N. The father I16 of genotype: N//a gives 2 types of ½ N and ½ a gamete. The fetus will necessarily inherit from his mother II2 one XN; then, the phenotype of the fetus will be normal regardless of the other allele inherited from the mother II6 II2 of genotype N//N.	0.5

Exercise 3 (8 points)

1	The translocation indicated in the text results in the fusion of two genes, one from the chromosome 22 called BCR and the other of chromosome 9 called ABL, this fusion leads to the formation of a hybrid gene of a longer nucleotide sequence resulting in the synthesis of a mutant protein with a longer amino acid sequence. This new protein formed has a new spatial configuration and a new function that disturbs the cell proliferation This explains the appearance of cancer.	1.5
2	Regarding Pair 9: Both have two 9 chromosomes. But, mister A have 1 normal 9 chromosome and one 9 chromosomes shorter than the other 1 and shorter than that of miss B who has 2 homologous 9 chromosomes of equal size. Regarding chromosome 21: Both have two 22 chromosomes. But, mister A have 1 normal 22 chromosome and one 22 chromosomes longer than the other 1 and longer than that of miss B who has 2 homologous 22 chromosomes of equal size.	1.5
3	Phenotype of parents: ♂ affected father * normal mother ♀ Genotype of parents: $9,9^{-}$; $22,22^{+}$ * 9,9;22,22 Gametes of parents: (9,22) ¼ (9^{-},22) ¼ (9,22^{+}) ¼ (9^{-},22^{+}) ¼ (9,22) 1 Table of cross:	2

	9,22 ¼	9^{-},22 ¼	9,22^{+} ¼	9^{-},22^{+} ¼
9,22 (1)	9//9 22//22 ¼	9//9^{-} 22/22 ¼	9//9 22//22^{+} ¼	9//9^{-} 22//22^{+} ¼

The couple's children will be: ¼ normal (9.9; 22.22);
¼ (9.9^{-}, 22.22) with structural abnormality

	¼ (9.9 , 22.22^{+}) with Myeloid leukemia ¼ (9.9^{-} , 22.22^{+}) with Myeloid leukemia So, the risk of this couple to have fetus with myeloid leukemia =1/2.	
4	The characteristics of the two probes: single-stranded, fluorescent, monolocus, sequences of known DNA where one is complementary to the ABL gene, the other complementary to the BCR gene	1.5
5	As the diagram for interpreting fetal hybridization figures shows, a green fluorescent spot corresponding to the BCR gene, a red fluorescent spot corresponding to the ABL gene and a red spot associated with a green spot corresponding to a BCR gene associated with an ABL gene on the same chromosome, chromosome 22 like his father, and as the father has chronic myeloid leukemia (cancer of the blood), so the fetus definitely has leukemia chronic myeloid (blood cancer).	1.5