Exercise 1 (5 pts) **Spermatogenesis**

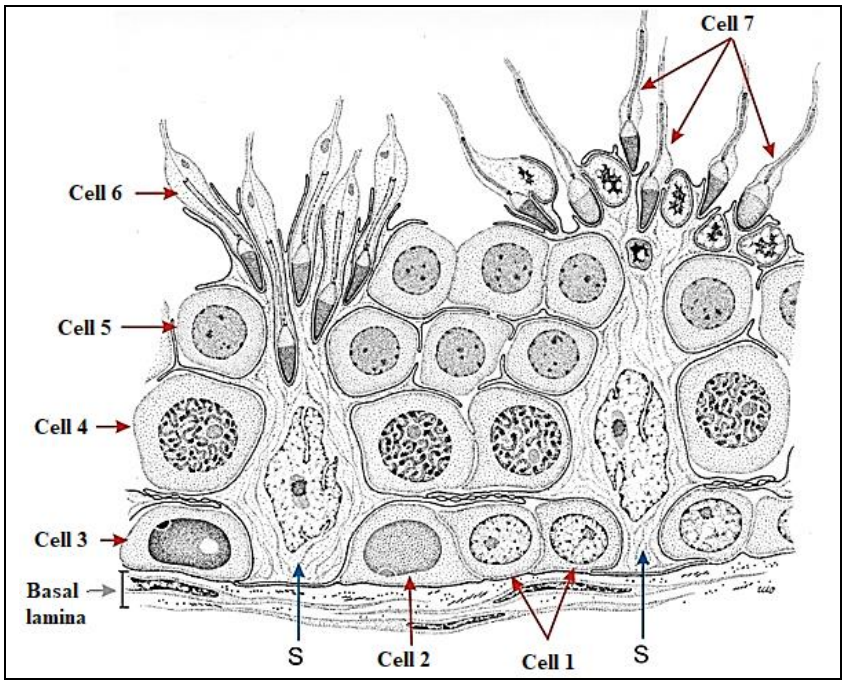
In humans, spermatogenic cells need to be maintained at around 2°C below the body temperature (37°C) to function. This is done by the regulation of blood flow and the positioning of the muscles, which keeps the scrotum away from the heat of the body.

Spermatogenesis can be defined as the process occurring in the male gonad of sexually reproducing organisms, wherein the undifferentiated male germ cells develop into spermatocytes, which then transform into spermatozoa. This process begins at puberty and ends generally at death.

The process of spermatogenesis is very sensitive, and can be affected by the slightest change in the levels of hormones such as testosterone produced due to the action of the hypothalamus, pituitary gland, and Leydig cells.

Deficiencies in diet, exposure to strong drugs, alcoholism, and presence of diseases can adversely affect the rate of sperm formation.

Document 1 shows a section at the level of a seminiferous tubule where spermatogenesis occurs.



Document 1

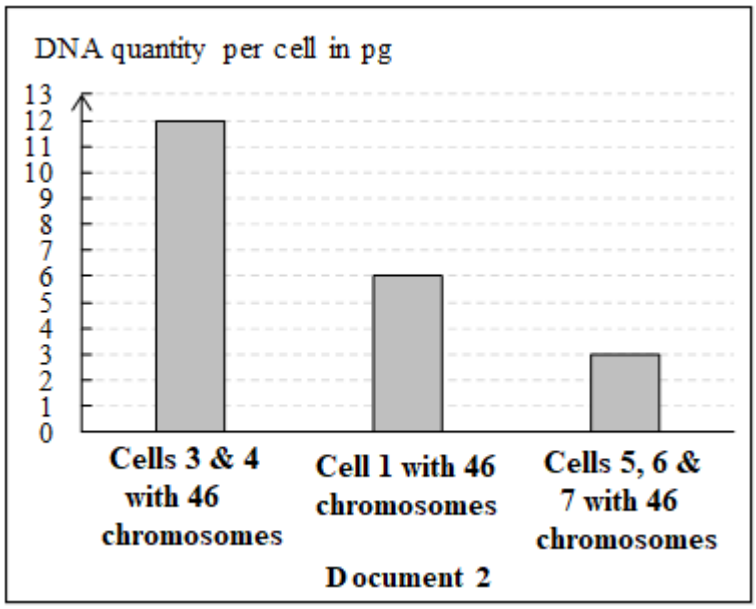
1. **Indicate**, by referring to the text:

1.1. The temperature at which spermtogenic cells are functional.

1.2. The names of the organs involved in the production of testosterone.

2. **Justify** that all the cells (1, 2, and 3) in document 1 are spermatogonia cells.
3. **Identify** the cells indicated by (S, 4 and 7) in document 1.

The DNA quantity is measured in some of the cells shown in document 1, the bar graph of document 2 shows the obtained results.



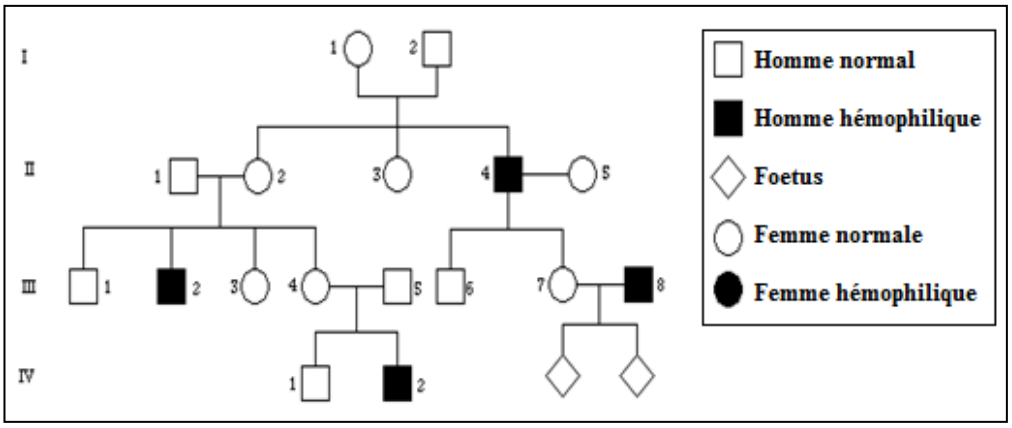
Document 2

4. **Explain** the difference in the DNA quantity between the spermatogonia 1 and the spermatogonia 3.

5. **Identify** the cell 5. **Justify**, referring to document 2 and your acquired knowledge, the answer.

Exercise 2: (5 pts) **Transmission of Hemophilia B**

Hemophilia B is a rare monogenic disease characterized by a deficiency of an enzymatic system involved in blood coagulation. Document 1 shows the pedigree of a family some members of which, colored in black, are affected.



Document 1

1. **Is** the hemophilia B allele dominant or recessive? **Justify** the answer.
2. Knowing that affected females die during fetal life, **discuss** logically the chromosomal location of the gene responsible for hemophilia B.

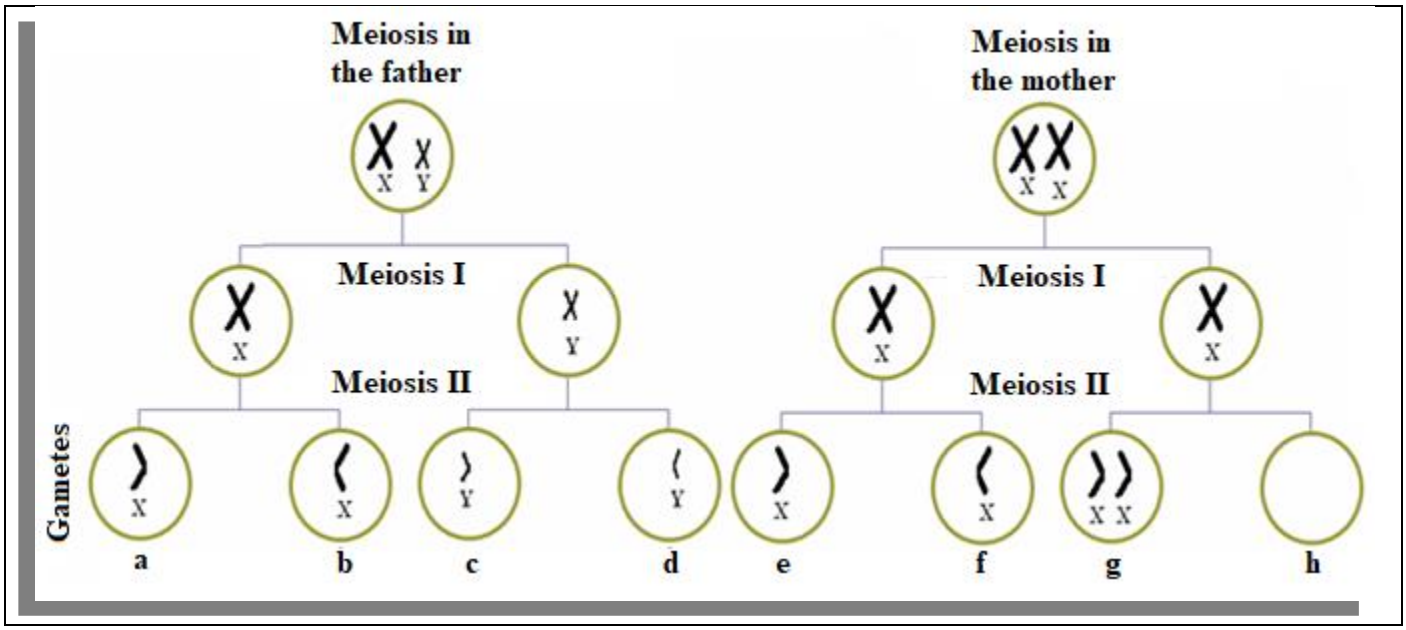
The couple (III_7-III_8) gives birth to two daughters:

• Natalie, who survives, but she shows several sexual abnormalities: atrophy of the ovaries, poorly developed breasts, in addition she is affected by hemophilia B.

• Raja, a normal, non-hemophilic girl.

3. **Are** Natalie and Raja identical twins? **Justify** the answer.
4. **Formulate** a hypothesis concerning the survival of Natalie which is hemophilic with sexual abnormalities.

Document 2 shows the gametes produced by the father III-8 and those produced by the mother III-7 (only the gonosomes are represented but the other chromosomes are normal).

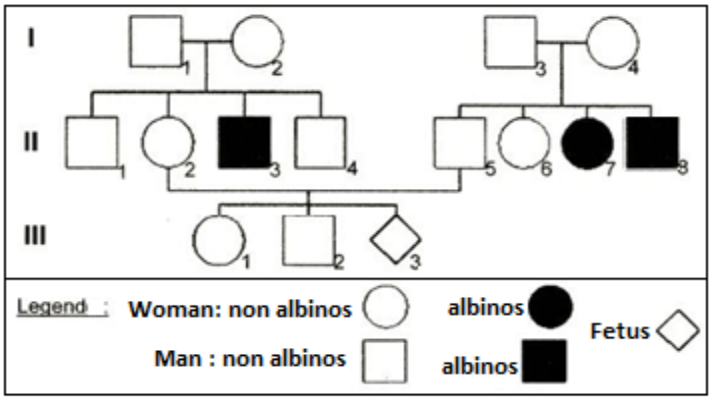


Document 2

5. **Does document 2 validate** your formulated hypothesis? **Justify** your answer by indicating the gametes that are at the origin of the zygote corresponding to Natalie.

Exercise 3: (4 pts) Transmission of albinism

In humans, albinism is a recessive genetic disease that affects 1/20000 individual among a given population. This disease is due to the absence of melanin, a pigment responsible for hair and skin coloration. The adjacent genealogical pedigree (doc1) shows the transmission of this disease in two families.



Document 1: pedigree of the a family affected by the albinism

1. **1.1. Compare** the frequency of albinism in these two families to that in population.
   1.2. What advice can you give to these families?
2. **Determine** the chromosomal localization of the gene responsible for albinism.
3. **Specify** the genotype of each of the individuals: II_4, & II_7.
4. **Determine** the risk for the fetus III_3 to be a child affected.by albinism

Exercise 4: (6 pts) An advantage of a Chromosomal Abnormality

Scientists have observed that individuals with certain chromosomal abnormalities have a lower risk of developing solid cancerous tumors. To verify this observation, several studies in addition to an experiment have been conducted.

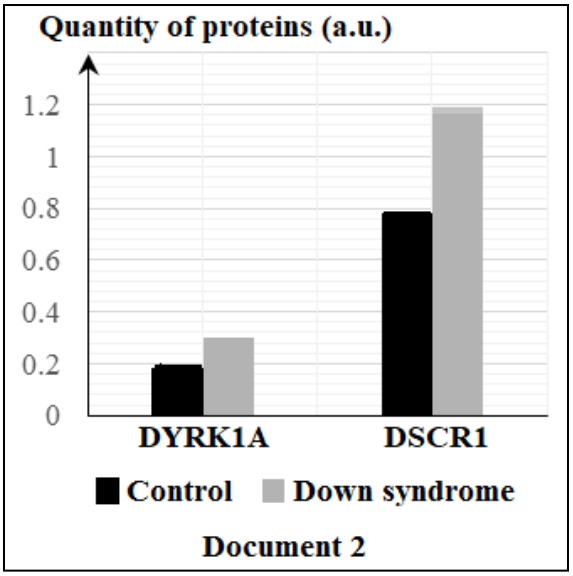
Karyotype	Chromosome 14	Chromosome 21
Normal Individual		
Affected individual A		
Affected individual B		

Document 1

Study 1: A partial karyotype is prepared in a normal individual as well as two affected individuals A and B. Both A and B show the same phenotype and the same symptoms: wide neck, specific facial shape, metabolic troubles and mental retardation of more or less importance. The results of this study, showing only the chromosomes concerning the anomaly, are illustrated in document 1.

1. **Identify** the chromosomal abnormality revealed by the partial karyotype of individual A.
2. **Justify** why individuals A and B have the same phenotype.

Study 2: Scientists measured the quantity of two proteins coded by the genes, DYRK1A and DSCR1, located on chromosome 21. Document 2 shows the results of the measurements in control individuals and those affected by Down syndrome.



Document 2

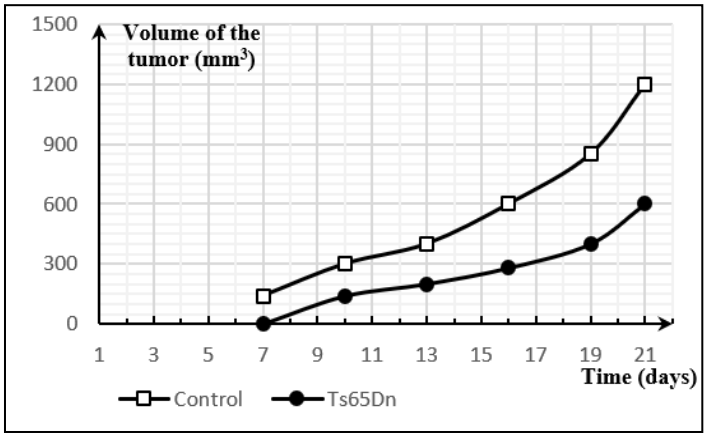
3. **Represent** the obtained results of document 2 in a table.

4.1.Compare the results shown in document 2.

4.2. What can you **conclude**?

Experiment: Artificial cancer is induced in control mice and Ts65Dn mice, which are mouse models used for Down syndrome having 3 copies of each of DYRK1A and DSCR1 genes. The volume (growth) of the cancerous tumor is then measured for 3 weeks and the results are represented in document 3.

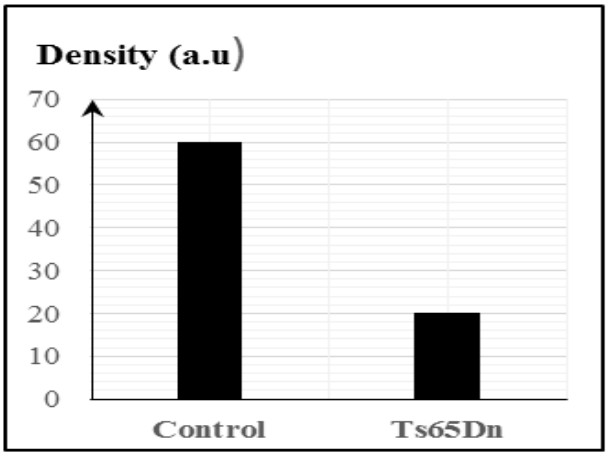
5. **Show**, using document 3, **that** Down syndrome can delay (slow down) the growth of cancerous tumor.



Document 3

Study 3: The density (development) of the blood vessels in artificially induced cancer tumor is measured in the Ts65Dn mice as well as in control mice. Note that the blood vessels provide the oxygen and necessary nutrients for the multiplication and survival of cancerous tumor cells. The obtained results of the study are represented in document 4.

6. **What** can you **draw out** from the results of document 4?
7. **Explain**, based on all what proceeds, why individuals with Down syndrome have a lower risk of developing solid cancerous tumor.



Document 4

Exercise	Expected answers	Note
1	1.1. 35°C or around 2°C below the body temperature (37˚C). 1.2. Hypothalamus, pituitary gland and testicles (because testosterone is produced by the testicles)	¼ ¾
	2. Because all the cells 1, 2 & 3 are located near to the basal lamina of seminiferous tubules where spermatogenesis starts to occur.	½
	3. Cell S: as it is located between the germ cells in the seminiferous tubules, then it is a Sertoli cell (that ensures the protection and nutrition of the germ cells) **Cell 4:** as the cell has a larger size than the other germ cells where it makes the growth phase, then it is a spermatocyte I. **Cell 7:** it is a cell having an elongated shape (has a flagellum) and located near to the lumen of seminiferous tubule, then it is a sperm cell.	½ ½ ½
	4. The chromosomes are made of DNA and the cell 1(spermatogonium) has a DNA quantity 6 pg which is half of that of spermatogonium 3 (12 pg). This is due to the number of chromatids in the chromosomes of each cell where in cell 1 each chromosome is made of 1 chrd because this cell is schematized just after mitosis (before interphase) while in cell 3 each chr is made of 2 chrds because it is schematized after replication during the S phase of interphase. So, the DNA quantity in cell 3 is double than that of cell 1/	1
	5. The cell 5 has an amount of DNA (3 pg) which is ¼ of the total amount in the mother spermatogonium cell (12 pg), then this cell has achieved meiosis and contain 23 chrs of 1 chrd, so it is a haploid cell and as it has a round shape (doc.1) then it is a spermatid (it is not a sperm cell).	1

2	1. Recessive, because normal parents (I1, 12) have an affected child (II4), so the allele of the disease is found at least in one parent but hidden or masked by the normal allele.	¾
	2. Affected individuals belong to the same sex (all are boys), this discrimination in the sex means that the gene may not be autosomal or gonosomal on the common part of X and Y but the most probable is that it is gonosomal on the proper part of X or Y: If it is located on the proper part of Y, each affected boy should have an affected father and each normal boy should have a normal father but it is not the case where the affected boy (II4) has a normal father and the normal boy (III6) has an affected father. In addition, as the affected girls die during fetal life, so this allele is lethal and then causes the death of individuals at homozygote state (only females can be homozygous X^dX^d but males having only one chr X remain alive with genotype X^dY if they are affected). This confirms the chromosomal localization of the gene on the proper part of the gonosome X.	1 ¼
	3. No they are different twins, because they are phenotypically different (Natalie is hemophilic but Raja is normal) so they are genotypically different but identical twins must have identical genetic information (same genotype).	¾
	4. **Hypothesis:** may be Natalie suffer from a gonosomal abnormality and have one chr X instead of two.	½
	5. Yes, Natalie is hemophilic. If she has a genotype X^dX^d, she will die during fetal life but it is not the case, she survived with several sexual abnormalities (atrophy of ovaries, poorly developed breasts) and these abnormalities generally characterize the girls with Turner syndrome that is due to a gonosomal monosomy X. As she is affected then she received a gonosome X with hemophilic allele from her affected father (III8: XdY) and not from her normal mother (III7) beacuse if she received XN from the mother, she will be normal because N is dominant allele and if she received Xd from the mother, she will die (**d** is a lethal allele), so the gamete of the mother must be lacking a gonosome X. Document 2 confirms this suggestion where the father's meiosis occurs normally and results in normal gametes (no chromosomal abnormalities are shown) contrarily with that of the mother (a non-disjunction of sister chromatids during meiosis II and results in abnormalities in her gametes). Then, the father's gamete must carry Xd (gamete **a** or **b**) and the mother's gamete must have no gonosome X (gamete **h**).	1 ¾
3	1.1. The frequency of albinism in a family is ¼ and in the other family (½) much more than that of the population (1/20000). 1.2. Should not have a marriage between individuals from these families among each other.	½ ¼
	2. If the gene is located on the proper part of Y, each affected boy should have an affected father but it is not the case where the affected boy (II3) has a normal father. If the gene is located on the proper part of X, then the affected girl II7 should have a genotype XdXd and must receive Xd from her father (I3) that becomes affected but he is normal, then it is not the case. If the gene is located on the common part of X and Y, then the affected girl II7 should have a genotype XdXd and must receive Xd from her father (I3) and the affected boy II8 should have a genotype XdYd and receive Yd from his father (I3) and becomes affected but he is normal, then it is not the case. So, the gene is not gonosomal but autosomal.	1
	3. II4: NN or Nd, because he is normal and the normal allele which is dominant can be expressed in both homozygote and heterozygote states. II7: dd, she is affected and the abnormal allele which is recessive cannot be expressed except in homozygote state.	1 ¼
	4. The parents of the mother II2 are obligatory hybrid (Nd) because they are normal and have an affected child (II3) so each one of the parents can give ½ a gamete with mutant allele d and ½ the normal allele N:	

	½ N	½ d
½ N	NN 1/3	Nd 1/3
½ d	Nd 1/3	dd

The probability of the mother to be hybrid (Nd)is then 2/3. 1

Same justification for the father II5 because he has normal parents and an affected sister, so his parents are obligatory hybrid and the father should have 2/3 as a probability to be hybrid.
Each hybrid individual can give ½ the mutant allele to his/her children
The risk for the fetus III3 to be affected becomes:

2/3 (hybrid father) × ½ (♂d) ×2/3 (hybrid mother) × ½ (♀) = 1/9

1. Individual A has two copies of chromosome 14 having the same number and size as those of a normal individual. However, individual A, has 3 copies of chromosome 21 having the same size which is more than that of the normal individual who has 2 copies of chromosome 21 of same size. Thus, the chromosomal abnormality in individual A is due to the free extra copy of chromosome 21/ Thus, individual A is affected by trisomy 21 having 3 free copies of chromosome 21. ¾

2. Individual B has trisomy 21 because he has three chromosomes 21: two free chromosomes 21 and one chromosome 21 translocated on one of the pairs of chromosome 14 which is longer than its homologue. On the other hand, individual A has trisomy 21 due to 3 free copies of chromosomes 21. Both individuals A and B have the same number of chromosome 21 and as such they have the same phenotype. ¾

3.

Individual / **Quantity of protein (au) coded by the gene**	Control	Affected by Down Syndrome
DYRK1A	0,18	0,3
DSCR1	0,78	1,17

Title: Table showing the variations in the quantity of two proteins coded by the DYRK1 and DSCR1 genes in control individuals and those affected by Down syndrome. 1

4

4.1. The quantity of proteins coded by the DYRK1A genes, in individuals with Down syndrome is 0.3 a.u, is greater than that in control individuals which is 0.18 a.u. Similarly, the quantity of protein coded by DSCR1 genes in individuals with Down syndrome is 1.17 a.u, is greater than that in control individuals which is 0.78 a.u ½

4.2. We conclude that individuals with Down Syndrome produce a higher quantity of both proteins. ¼

5. In Ts65Dn mice affected by Down syndrome and having 3 copies of each of the DYRK1A and DSCR1 genes, the volume of cancerous tumors is almost nil at day 7 after artificially inducing cancer. This volume is less than that in control mice which is 140 mm^3 at the same day. This volume increases over time in both mice but more significantly in the control mice to reach a maximum of 1200 mm^3 at the 21st day, which is about 2 times greater than that of the Ts65Dn mice which increases to 600 mm^3 at the same day. This means that in both types of mice there has been a development in cancerous tumors and this development is more important/significant in mice that have 2 chromosomes 21 (control mice) compared to mice that have 3 chromosomes 21 (Ts65Dn) and affected by trisomy 21.Therefore, Down syndrome can delay (slow down) the growth of cancerous tumors. 1

6. We draw out that Down syndrome reduces the density (development) of blood vessels in tumors and attenuates the supply of oxygen and nutrients necessary for the multiplication and survival of cancerous tumor cells. ½

7. In individuals affected by Down syndrome, the genes DYRK1A and DSCR1 carried by chromosome 21 and present in 3 copies instead of 2 have several consequences such as the production of the proteins coded by these genes in a larger quantity compared to the control.

	Moreover, it leads to the slowing down of the growth of cancerous tumors by reducing the development of the blood vessels which are essential for the supply of nutrients and oxygen required for multiplication and survival of cancer cells. As such, cancerous tumors grow less rapidly in individuals with Down syndrome than the control subjects. Hence individuals with Down syndrome have a lower risk of developing solid cancerous tumors.	1 ¼