TEMASEK JUNIOR COLLEGE

2022 JC2 PRELIMINARY EXAMINATION

Higher 2

CANDIDATE NAME									
CENTRE NUMBER	**S**					INDEX NUMBER				

BIOLOGY **9744/03**

Paper 3 Long Structured and Free Response Questions **13 SEPTEMBER 2022**

PART I **2 hours**

Candidates answer on the Question Paper.
No Additional Materials are required.

READ THESE INSTRUCTIONS FIRST

Write your Center number, index number and name in the spaces at the top of this page.
Write in dark blue or black pen.
You may use an HB pencil for any diagrams or graphs.
Do not use staples, paper clips, glue or correction fluid.
DO **NOT** WRITE IN ANY BARCODES.

Section A
Answer **all** questions in the spaces provided on the Question Paper.

Section B
Answer any **one** question in spaces provided on the Question Paper.

The use of an approved scientific calculator is expected, where appropriate.
You may lose marks if you do not show any working or if you do not use appropriate units.

The number of marks is given in the brackets [ ] at the end of each question or part question.

For Examiner's Use	
1	**/ 9**
2	**/ 17**
3	**/ 24**
4 / 5	**/ 25**

Section A

Answer **all** questions in this section.

1 To investigate other conditions affecting rate of photosynthesis, two sets of plants, **A** and **B**, were grown from seeds at different concentrations of carbon dioxide:

- **A** – normal atmospheric concentration of carbon dioxide (0.033%)
- **B** – twice the normal atmospheric concentration of carbon dioxide (0.066%)

The rates of photosynthesis at different light intensities for the two sets of plants were measured and shown in Fig. 1.1.

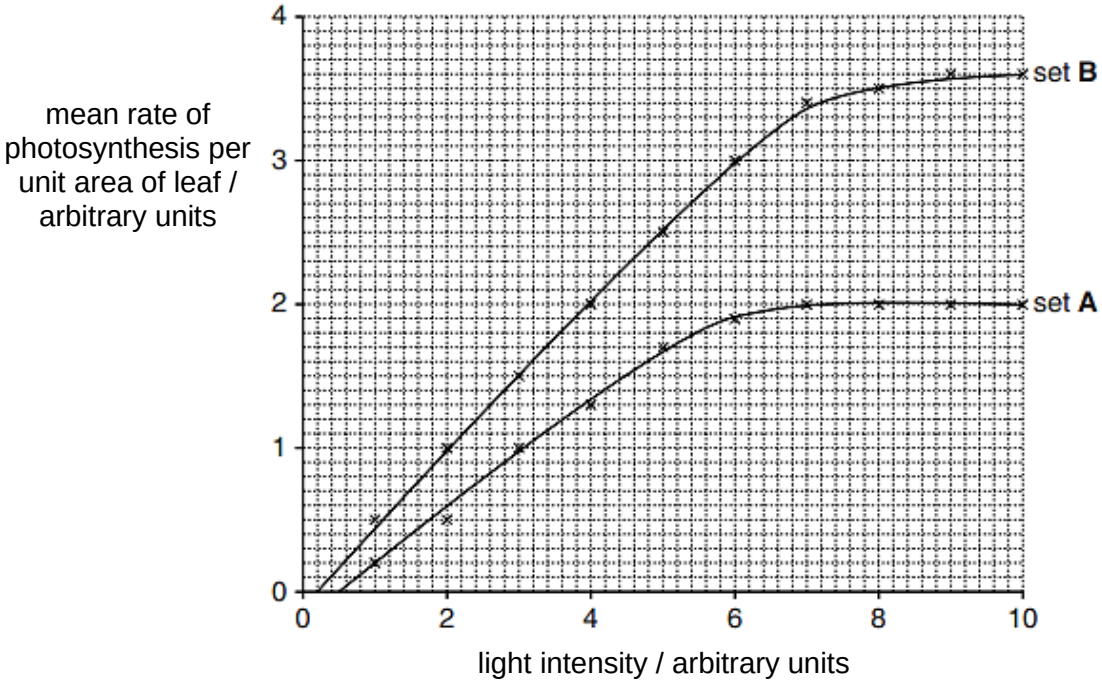


Fig. 1.1

(a) With reference to Fig. 1.1,

(i) describe and explain, in terms of limiting factors, the results from the plants in set **A**; [2]

1. **QF: As light intensity increases from 0.5 to 6 a.u., mean rate of photosynthesis increases from 0 a.u. to 1.9 a.u.**
   A: 5.4 – 7 a.u. for upper limit with correct y-axis values quoted
2. **light intensity is main limiting factor**
3. **QF: As light intensity increases from 6 a.u. to 10 a.u., mean rate of photosynthesis remains constant / levels off / reaches plateau at 2 a.u.**
   A: Continue from point 1 QF
4. **Light intensity is not limiting, CO_2 concentration is limiting**
   Note: many students missed out the word "concentration" – the phrase "carbon dioxide is limiting" is not accurate

- ½ if student used (a.u.) without abbreviating at the start of the answer since question did not abbreviate

Marker's comments:
Some students are still using phrases such as "increase at a fast rate / slow rate" – LAST REMINDER to avoid using the word RATE to describe a graph (unless it's the title of the axis)
Some students also gave unnecessary details such as WHY light intensity affects rate of photosynthesis – look at the number of marks to guide you in deciding how much details to include in your answer.

(ii) explain the difference between the results of set **A** and set **B** at high light intensities. [2]

1. **QF: Twice as much carbon dioxide in set B than set A**
2. **Higher rate of carbon fixation**
3. **During Calvin cycle**
4. **QF: CO_2 concentration is limiting in set A at high light intensities from 6 a.u. onwards while CO_2 concentration (A: temperature) will be limiting in set B at light intensity from 9.6 a.u. (A: 9.8, 10)**
   Idea: Another factor becomes limiting when the rate of photosynthesis plateaus with QF

(b) Fig. 1.2 is a graph showing the estimated area of trees that have been removed from tropical forests between 2001 and 2017.

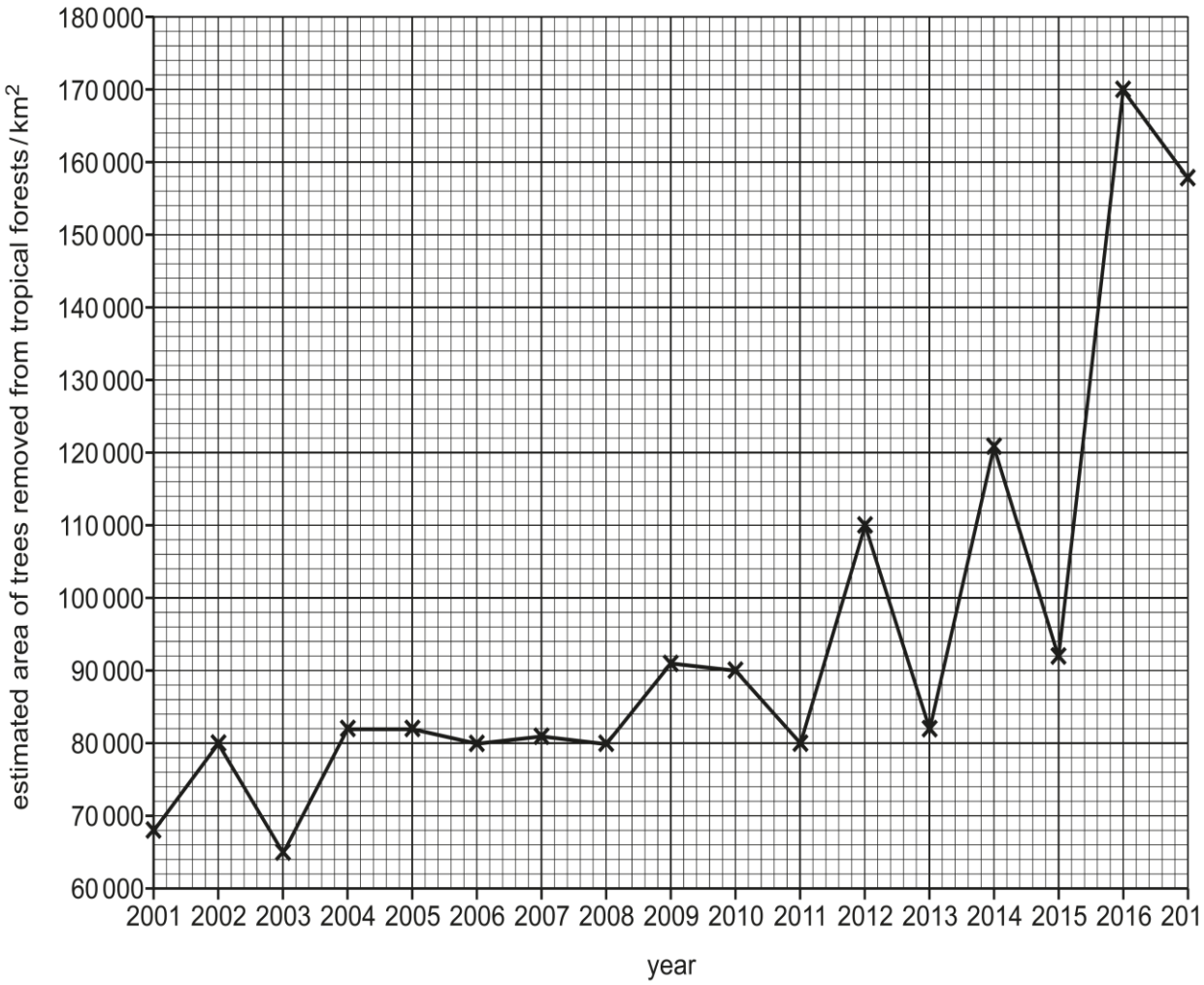


Fig. 1.2

(i) State the year which had the lowest estimated area of trees removed from tropical forests on Fig. 1.2. [1]

2003

(ii) State the area of trees removed in 2012 on Fig. 1.2. [1]

110 000 km^2 (Note: 0 marks if no units)

(iii) A student made three statements about the data in Fig. 1.2:

1 The number of trees cut down increases every year.
2 The number of trees cut down in 2014 was three times more than the number of trees cut down in 2003.
3 Fewer trees were cut down in 2017 than in 2016.

Complete Table 1.1 by using the data in Fig. 1.2 to decide if each statement is true or false and state the evidence that supports your decision.

Table 1.1

statement	true or false	evidence from Fig. 1.2
1	**false**	**Decreases in 2002 / 2005 / 2007 / 2010 / 2012 / 2014 / 2016** **or** **No increase in 2004** **or** **Although the general trend shows an increase, it does not increase every year / some years increase and some years decrease**
2	**false**	**65 000 km^2 were cut down in 2003 and 121 000 km^2 in 2014 which is less than three times** **or** **three times more would be 195 000 km^2 which is more than the number cut down in 2014** **or** **1.86 times (not 3 times) the number were cut down**
3	**true**	**more trees were cut down in 2016 than in 2017** **or** **170 000 km^2 trees were cut down in 2016 and 158 000 km^2 were cut down in 2016**

Max [1] – if no evidence stated for all 3 statements but T/F correct
Ecf [1/2] if T/F wrong but evidence supports
Ecf [1/2] if T/F correct but evidence not clear
-1/2 m if QF wrong

[3]

[Total: 9]

2 Hepatitis is the inflammation of the liver and can be caused by a number of different hepatitis viruses. Presently, the only effective vaccines available are for hepatitis A and B.

(a) Outline the immune response that leads to the production of antibodies after vaccination. [3]

1. **Vaccine contains hepatitis antigen / attenuated hepatitis virus**

2. **APC / macrophage phagocytose and present hepatitis antigen from vaccine to specific naive CD4 T cells and naive B cells**
   Note: it MUST be clear that the antigen is presented in this part of the answer. No marks awarded if it is mentioned that T/B cell receptor recognize and bind to antigen because it is not clear that the antigen was presented in this step.

3. **Naive CD4 T cells activated, which proliferate and differentiate to form helper T and memory T cells.**

4. **Helper T cells secrete cytokines**

5. **Completes activation of naïve B cells to proliferate and differentiate into plasma cells and memory B cells.**

6. **Plasma B cells produce antibodies specific to hepatitis antigen**

7. **Vaccination trigger active immunity / active immune response**

General comments:
Differentiate between use of 'pathogen' and 'antigen'.
Be specific – use the context to add specificity!
A handful of students misinterpreted the question and described secondary immune response instead.

(b) Briefly describe how plasma cells produce and release antibodies. [4]

1. **Transcription of light and heavy chain gene produces pre-mRNA**
2. **Pre-mRNA processing take place.**
3. **Ribosomes on rER translate mRNA**
4. **Heavy and light chains of antibodies move into rER lumen.**
   (A: if heavy and light chain mentioned later in answer)
   (R: polypeptide chain IF "light and heavy chain gene" mentioned in MP1)
   (ECF: polypeptide chain IF "light and heavy chain gene" not mentioned in MP1)

5. **These are enclosed in ER/ transport vesicle which pinch / bud off from ER**
6. **to cis face of Golgi apparatus (GA).**
7. **Heavy and light chains are joined by disulfide bonds and glycosylated / addition of carbohydrate side chain as they move through the GA**
   (R: chemical modification only)

8. **The secretory vesicle buds off from trans-face of GA, fuse with the plasma membrane. Thus, releasing the antibodies out of the cell via exocytosis.**

[1/2] – mention of light chain and heavy chain gene (if wrong focus)

(c) Scientists observed that liver cells damaged by hepatitis infection switch on a gene known as the *Fas* gene, which caused infected liver cells to self-destruct.

This finding led to the research which produced a successful treatment for hepatitis in mice whereby the *Fas* gene was silenced using the technique of RNA interference.

This involved injecting mice infected with hepatitis with RNA molecules of 21 to 23 nucleotides in length. The sequence of this small interfering RNA (siRNA) matched part of the *Fas* gene. Once in the liver cell the two strands of the siRNA are separated so that one strand binds to the mRNA transcript of the *Fas* gene.

This caused the mRNA to be degraded by enzymes, therefore preventing the gene product from being made. As a result, liver cell death is prevented and the mice with hepatitis survived.

(i) Describe **one** way in which the function of mRNA differs from that of DNA. [1]

1. mRNA is translated / used to synthesize protein while DNA is transcribed / used to synthesize mRNA;
mRNA is used to synthesize protein while DNA is for the storage of genetic information;
mRNA is used to carry genetic information out of nucleus while DNA is for the storage of genetic information
OR

2. mRNA contain short-term genetic information while DNA contain long term genetic information

Examiner's comments:

- **Many students would say that mRNA is used for transcription whereas DNA is not OR mRNA carries genetic information out of nucleus while DNA cannot leave the nucleus. This does not answer the question on how the function differs.**
- **Some students even compared the reactivity / stability of the molecule which is definitely the wrong focus.**

(ii) Suggest **one** way in which the structure of siRNA differs from that of mRNA. [1]

1. siRNA has fewer nucleotides than mRNA / only matches part of gene.
OR

2. siRNA double-stranded while mRNA is single-stranded

Examiner's comments:
A number of students mentioned how siRNA and mRNA are complementary to different sequences. It is quite a menial difference since at the end of the day, the siRNA is complementary to mRNA (which is complementary to the *Fas* gene).

(iii) State how one strand of the siRNA can bind to the mRNA of the *Fas* gene. [1]

1. Via complementary base-pairing between purines and pyrimidines;

2. Adenine with uracil with cytosine with guanine
Note: Missing from most answers

Examiner's comments:
A handful of students mentioned the complementarity of the sequences but missed out the focus of the question: how they bind.

(d) The technique of RNA interference has also been used to slow down replication of HIV (Human Immunodeficiency Virus) *in vitro*. This is an important breakthrough in the treatment of AIDS.

The siRNA is attached to a carrier molecule which binds to HIV glycoproteins embedded in the plasma membrane of infected cell. This allows the carrier molecule with siRNA to enter the infected cell.

siRNA sequences that which are complementary to HIV RNA will trigger the destruction of the HIV RNA, preventing the virus from multiplying.

The siRNA would only affect gene expression in cells infected with HIV. Suggest **one** reason why this is so. [1]

Note: The focus of the question is WHY siRNA only affects / enters cells infected with HIV. Not how siRNA works or why siRNA does not affect / enter normal, non-infected cells.

1. **Only infected cells have HIV glycoprotein on surface;**
2. **So carrier molecule can recognize and bind to these cells and siRNA can only enter these cells**
   OR
3. **Only infected cells contain HIV RNA**
4. **Base sequence of siRNA is only complementary to the HIV RNA so that enzymes can destroy it**

Examiner's comments:

- **Very badly done. Many students did not answer the question directly and went on about how normal cells are not infected because they do not have HIV glycoproteins or because they don't have HIV RNA.**
- **Students were also unable to accurately express that it is the carrier molecule that recognizes and binds to the glycoproteins (not the siRNA).**

(e) Another approach is to use RNA interference to silence genes that code for cell surface receptors, such as the CD4 and CCR5 molecules on white blood cells.

If these genes are not expressed, HIV cannot bind to and infect the white blood cells. Table 2.1 summarizes some information regarding the two cell surface receptors used by HIV to bind to and infect white blood cells.

Table 2.1

	cell surface receptor	
	CD4	**CCR5**
type of cell with this receptor	Memory T lymphocyte which divide by mitosis	Macrophage which are long-lived and do not undergo mitosis

Experiments have been carried out where,

- siRNAs matching the CD4 mRNA were introduced into test tube containing memory T lymphocytes;

- siRNAs matching the CCR5 mRNA were introduced into test tube containing macrophages.

In both cases HIV was present and the presence of the siRNAs reduced its replication.

Using Table 2.1, suggest with reasons which test tube would have a greater reduction in HIV replication. [2]

1. **Test tube containing macrophages with CCR5 receptors [1]**
   [1/2] – macrophage / CCR5 only
2. **only one treatment needed for macrophages with CCR5 because siRNAs has longer effects in long-lived cells; OWTTE [1/2]**
3. **In the other test-tube there are fewer siRNAs per cell when memory T lymphocytes divide; OWTTE [1/2]**
   OR
   it means that repeat treatments needed for lymphocytes / CD4; [1/2]

Marker's comments:

- **siRNA is a novel context which required a lot of reading and application. Based on context, it is clear that siRNA only targets mRNA and prevents them from being translated. Question: does this mean that the "silencing" can be passed down to daughter cells? What is passed down during mitosis? Are the genes still present? Can siRNA that entered the parent cell be passed down?**
- **Common misinterpretation of context and question – "memory T lymphocytes divide more so there are more viruses therefore greater reduction". This is very convoluted and overcomplicating the context.**
- **Some also failed to notice the change in context and harped on the previous context where siRNA can only enter cells that are already infected with HIV thus affect memory T lymphocytes more which results in greater reduction.**
- **Most students were unable to identify the right test tube.**
- **Reminder to make use of the full context. Some responses did not include any link or reference to siRNA at all.**
- **LEARN the skills needed and question analysis techniques to tackle such questions like this (as opposed to memorizing the answer).**

(f) Antibiotics are prescribed to people who have AIDS for the treatment of secondary infections such as bacterial infections.

(i) Describe the mode of action of antibiotics, such as penicillin, on bacteria. [2]

1. **Penicillin binds irreversibly / inhibits transpeptidase**
   (R: 'binds' ONLY)
   Note: many students are mixing up the enzymes transpeptidase and peptidyl transferase.

2. **thus inhibiting the cross-linking of two peptidoglycan chains.**
   (R: no 'inhibit' if students wrote 'binding irreversibly' in MP1 – binding irreversibly does not equate to inhibition).
   Note: students commonly stated the function of transpeptidase but did not state explicitly that the function cannot happen.

3. **Penicillin also stimulates the release of autolysins (R: granzyme / perforin) which make small pores in the existing cell wall (R: cell surface membrane)**

4. **The cell wall of dividing bacterium weakens and osmolysis occurs**
   (R: autolysis)
   Note: It is common for students to miss out 'cell wall weakens'.

Marker's comments:
There was a named example provided – penicillin. Students were expected to state the mode of action of penicillin not general modes.

(ii) Explain why antibiotics are prescribed to treat secondary infections, but not for HIV infection.[2]

1. **Antibiotics are only effective against bacteria**
2. **but not viruses**

3. **Viruses do not have cell walls, ribosomes or cell membranes or metabolic enzyme that antibiotic work on [1]**
   Note: must state at least 2 specific organelles
   Reject: vague mention of cell machinery or virus is non-cellular since thi question is about the effects of antibiotics.
   OR
4. **Viruses are within cells, idea that antibiotics cannot reach them.**

Marker's comments:
Many students indicated that viruses are not living therefore they cannot die or other words to that effect. This is very wrong.

[Total: 17]

3 A diagram of a chromosome from a dividing cell is shown in Fig. 3.1.

Fig. 3.1

(a) A dividing cell is at risk of losing genetic material each time DNA replication occurs due to the end replication problem.

(i) Explain why the end replication problem takes place. [2]

1. **removal of RNA primer located at the 5' end of daughter strand.**
   Reject: DNA primer
   Must state "daughter strand"
   Must state 5' end of daughter strand in your answer once

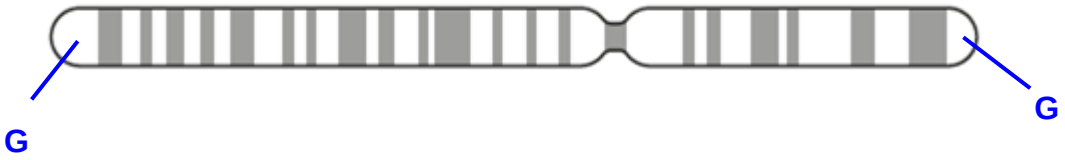
2. **RNA primer cannot be replaced with DNA nucleotides**
   Must state "replace"
   Reject: "primer replaced with DNA polymerase"

3. **because there is no existing 3'–OH group available for DNA polymerase to add deoxynucleotides.**
   Reject: "end of DNA has no 3' end"

4. **So a gap at the 5' end of the daughter strand**
   Reject: "5' gap"

(ii) On Fig. 3.1, add a label line and the letter **G** to show the location on the chromosome of an area that helps to prevent the loss of genes. [1]

- **Draw a label line [1/2]; must be pointing to correct region**
- **Label G [1/2]**



(iii) State **one** other function of this region of the chromosome. [1]

Importance reminders:

1. **Abbreviations**
   BP: Bind to Proteins

Any one:

1. **Telomeres bind to proteins (shelterin) that protect the chromosomal ends from joining to other chromosomes and from degradation / prevent apoptosis of cells**
   Note: Must write "bind proteins" to get the mark.

2. **Length of telomeres determines life span of cells – if telomere shortened to critical length, will lead to apoptosis.**

3. **In cells where telomerase enzyme is present - telomeres provides the recognition site for telomerase to recognise and bind to lengthen DNA**
   Reject: removes end-replication problem.

(iv) Compare the structures of telomeres and centromeres. [2]

Importance reminders:

1. **The focus is on structures NOT function**
2. **Many students did not apply what has been taught and left out similarity**
3. **Reject low level similarities such as both are made up of nucleotides / part of DNA since centromere and telomere is covered in your syllabus.**

Similarities [1]

S1. **Both are made up of repeating sequences/ repetitive DNA;**

S2. **Both are made up of non-coding sequences/ are non-coding;**

Differences [any 1]

D1. **Telomere is found at the ends of linear chromosomes while centromeres are found at a point along the chromosomes / not at the ends of chromosomes**
Reject: centromere is found between 2 sister chromatids
Reject: centromere found at constricted region because the constricted region is only visible when the DNA is condensed as chromosomes

D2. **Telomeres occur in two regions on a chromosome while centromere occurs at only one region on a chromosome**

D3. **Centromeres contain binding site for kinetochore proteins to bind while telomeres do not have such binding sites / binding sites for telomere proteins**

D4. **Telomeres has a recognition site for telomerase to bind while centromere does not have such a recognition site;**

(b) Telomere length is maintained in most eukaryotic cells by telomerase. The core components of this ribonucleoprotein enzyme include a protein catalytic subunit (TERT), and an RNA subunit that contains a short template sequence essential for the synthesis of telomeric repeats.

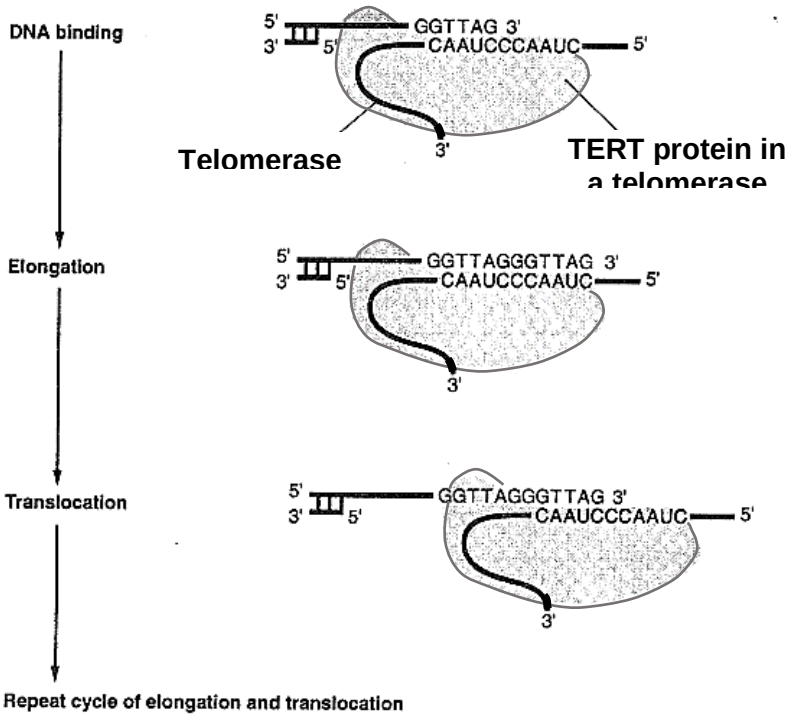


Fig. 3.2

With reference to Fig. 3.2, explain the role of the TERT protein and RNA subunit in telomerase involved in the lengthening of telomeres. [3]

Importance reminders:

1. **ONLY nucleic acid and nucleic acid can form complementary base pairing**
2. **Protein CANNOT form complementary base pair**
   - a protein which recognize and bind to nucleic acid (e.g. DNA) – it is shape of the protein DNA binding domain complementary in shape to the sequence of bases on the DNA
3. **Students MUST know the role of the RNA strand – it is the template**
4. **TERT protein – it is the enzyme with the active site**
5. **In the lengthening of telomeres – the DNA strand is NOT the template at the start of the process. Please revise!**
6. **Reject: if students explain the process as standard DNA replication process**
7. **Some students confused telomeres with telomerase**
8. **MUST write clearly "3", "5", "D" & "R".**

1. **Shape of TERT active site is complementary in shape to a telomeric DNA sequence**
   Telomerase enzyme contains a short strand of RNA in its active site.

2. **QF: RNA sequence CAAUC is complementary to telomeric DNA sequence GTTAG**
   Note: Must ensure the 2 sequences stated is the same number of bases

3. **Telomerase recognize and bind to telomere.**
4. **The RNA acts as a template to extend the 3' end of the telomere DNA**
5. **Free DNA nucleotides (GGTTAG) base pairs with RNA template,**
6. **telomerase catalyse formation of phosphodiester bond between nucleotides.**
   Reject: H-bonds
   Reason: formation of hydrogen bonds between complementary bases does not require any enzymes

7. **Telomerase moves to the right and synthesize another repeat, elongating the telomere**
   OR
   TERT & RNA subunit involved in synthesizing another repeat

(c) Telomerase activity is observed to be high in embryonic stem cells but not in adult stem cells. Cancer cells are also known to exhibit high levels of telomerase activity.

The high levels of telomerase activity in cancer cells could be due to mutations which involve the *TERT* locus where the *TERT* gene is located, as shown in Fig. 3.3 and Fig. 3.4.

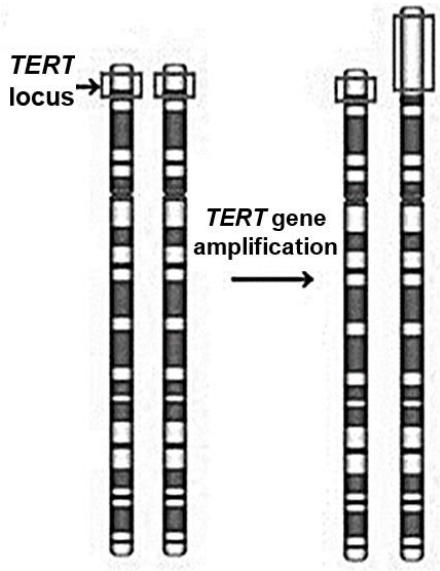


Fig. 3.3

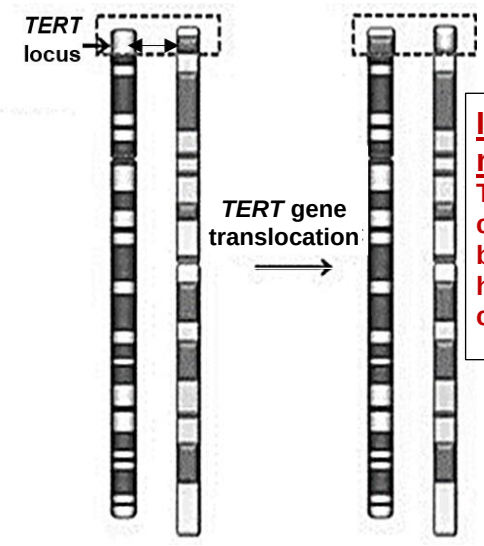


Fig. 3.4

Important note:
This is NOT crossing over between homologous chromosomes

Suggest how the mutations that involve the *TERT* locus shown in the Fig. 3.3 and Fig. 3.4 could result in the high levels of telomerase activity in cancer cells.

Important reminder:

1. **Students MUST make use of the information provided to answer this question since it is a novel context.**
2. **Although the TERT gene is NOT a proto-oncogene - the concept of gene amplication and translocation of the gene – students need to apply the knowledge from the Cancer topic.**
3. **This is found on p.15 of Cancer Lect notes.**
   Only the stronger students were able to the concept to answer this question

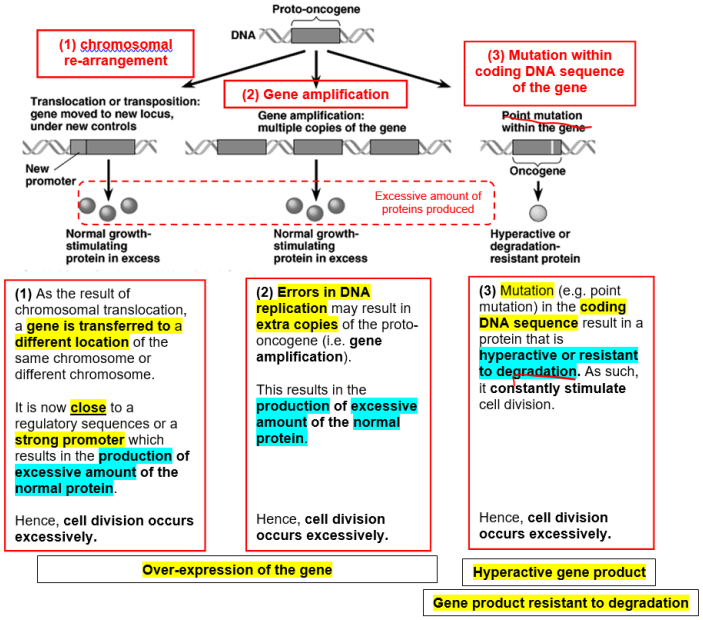


Fig. 3.3 **[1]**

1. **Gene amplification resulting in more copies of the *TERT* gene,**
2. **therefore the expression of more TERT proteins and increased telomerase activity.**

Reject: the gene become longer
Reason: an increase in nucleotide sequence would mean that the 3D conformation of protein will be changed → non-functional
Reject phrasing: "gene synthesize the protein"
Reason: gene can only code for protein

Fig. 3.4 **[1]**

1. **Translocation resulting in the *TERT* gene under the control of a strong active promotor and**
   Note: a strong promoter means high rate of transcription
   Reject: close to enhancer
   Reason: Enhancer (distal control element) does not need to be located near to promoter. Once the activator binds the DNA bends to bring activator near to promoter to increase rate of transcription
2. **increasing the expression of *TERT* gene / production of more TERT proteins and telomerase activity.**

(d) A cell dividing uncontrollably could be due to a dysregulation of the cell cycle.

Fig. 3.5 shows regulatory proteins involved in controlling two major checkpoints of the cell cycle. Two of these proteins are cyclin-dependent-kinases (Cdks) and cyclins. In each cell cycle, Cdk levels remain constant while cyclins undergo synthesis and degradation.

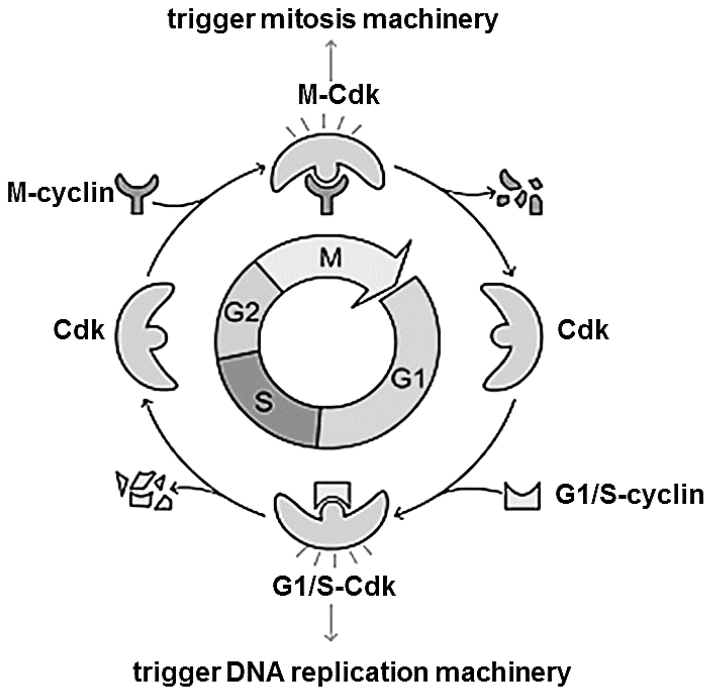


Fig. 3.5

With reference to Fig. 3.5,

(i) describe the effects of cyclins on cyclin-dependent-kinases; [1]

important Reminders:

1. **The focus is on cdk & 1 mark**
2. **No need to describe further effects**
3. **Since the effects is from the figure, MUST QF**

1. **G1/S-cyclin binds to Cdk (QF) to form G1/S-Cdk (QF) and activate it.**

2. **M-cyclin binds to Cdk (QF) to form M-Cdk (QF) and activate it.**

(ii) suggest why a mutated *M-cyclin* gene may be classified as an oncogene. [2]

Important note:
Abbreviation
C: Constant
UCD: Uncontrolled Cell Division
CFP: Code For Protein

1. **Oncogene codes for protein that stimulates uncontrolled / excessive cell division**
   Reject phrasing: "gene synthesize the protein"
   Reason: gene can only code for protein
   Reject phrasing: "abnormal cell division"
   Reject: excessive cell growth – it does not imply cell division

2. **The mutated M-cyclin gene can lead to a gain of function mutation**
3. **QF: producing excessive M-cyclin OR M-cyclin which are resistant to degradation.**
4. **M-cdk complex will be formed continuously OR M-cdk complex is continuously activated OR M-cyclin remains bound continuously**

5. **Mitosis machinery is triggered continuously as a result cell division takes place continuously.**

(e) In pancreatic cancer, the dysregulation of the cell cycle is due to a mutation of the *Ras* proto-oncogene. This results in faults in the signalling pathways. Fig. 3.6 shows the role of Ras protein in a cell signalling pathway.

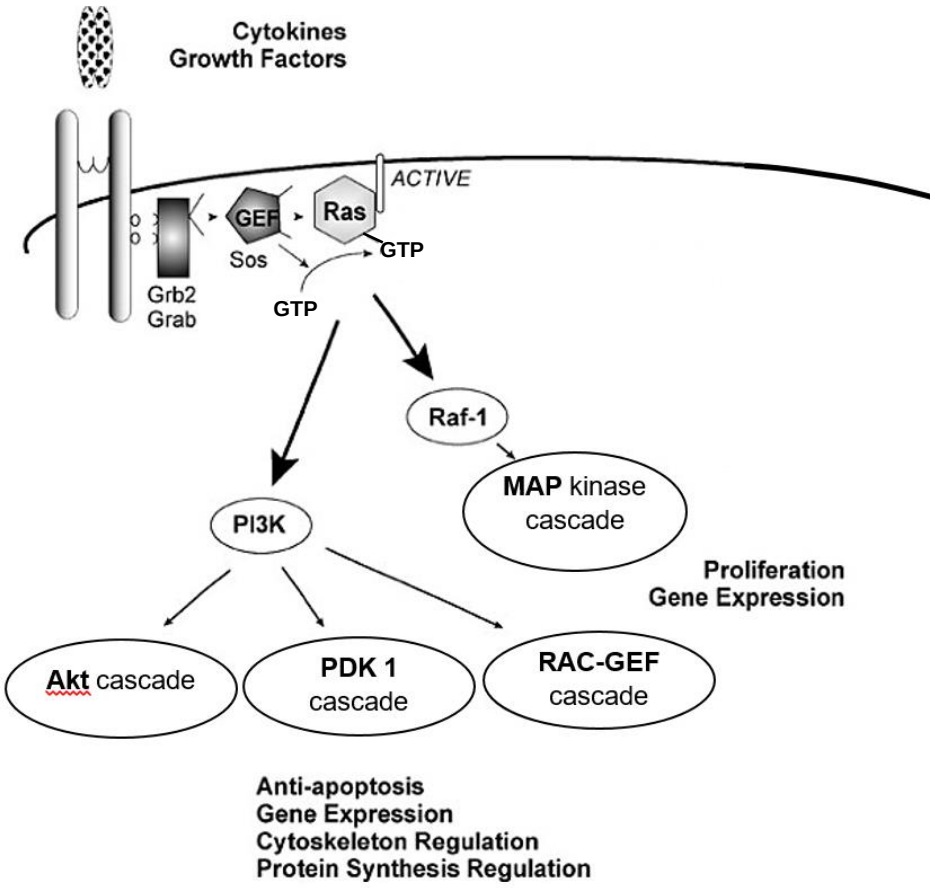


Fig. 3.6

With reference to Fig. 3.6,

(i) explain why a mutated *Ras* gene results in a Ras protein that is always in the active state; [1]

1. **Mutated Ras protein, means that GTPase unable to hydrolyse GTP to GDP**
2. **GTP remains bound to Ras protein**

(ii) describe how a mutated Ras protein will cause the cell to divide uncontrollably. [2]

Important note:

1. **For cell signaling question – student MUST QF from figure.**
2. **Usually the arrow implies "activate"**
   - it does NOT imply "synthesize" unless mentioned in the preamble
   - it does NOT imply "phosphorylate" unless mentioned in the preamble or in the fig
3. **Students MUST clearly state "constantly" in their answer since this is with reference to a mutated Ras protein which is constantly in the active form.**

1. **P13K is constantly activated**
2. **Akt cascase, PDK 1 cascade, RAC-GEF cascade is constantly activated to cause anti-apoptosis, gene expression, cytoskeleton regulation and protein synthesis regulation**
3. **Raf-1 is constantly activated**
4. **MAP kinase cascade are constantly activated to cause proliferation and gene expression**

(f) **(i)** Outline how a tumour forms. [2]

1. **Uncontrolled cell division**
2. **Due mutations that accumulated in a SINGLE / SAME cell**
   Any examples: **Proto-oncogene mutated to become oncogene / gain in function mutation of proto-oncogene / loss of function mutation of tumor suppressor genes**
3. **Loss of contact inhibition / cells continue to grow when they contact other cells / loss of density-dependent inhibition**
   Reject: anchorage-dependent inhibition for this situation because there is no need to address metastasis
4. **Angiogenesis occurs**
5. **Cells do not undergo apoptosis**

(ii) Malignant tumour cells do not undergo apoptosis. If a malignant tumour cell divides every 8 hours, starting with one of these cells, how many tumour cells will be present after 4 weeks?

1. There are 3 cycles in 1 day – because 1 cycle takes 8 hours
2. 4 weeks = 28 days
3. Total number of cycles = 28 X 3 = 84 cycles
4. 2^{84} **[1/2]**

Number of tumour cells **1.93×10^{25} [1/2]**

(g) In a different cancer known as chronic lymphocytic leukaemia (CLL), some maturing B cells of a person's immune system are affected. The disease results in B lymphocytes which are cancerous.

Rituximab is a drug used to treat CLL. It binds to a protein called CD20 on the surface of B cells. If sufficient Rituximab binds to a B cell, it will cause natural killer cells to bind to the bound Rituximab and trigger apoptosis of the B cell.

Rituximab kills **both** healthy and cancerous B cells. The body then produces new B cells.

The amount of CD20 on the surface of B cells varies from one person to another. Doctors investigated the relationship between the amount of CD20 on the B cells of a patient and the percentage of B cells destroyed by Rituximab.

Fig. 3.7 shows the doctors' results. Each cross is the result for one patient.

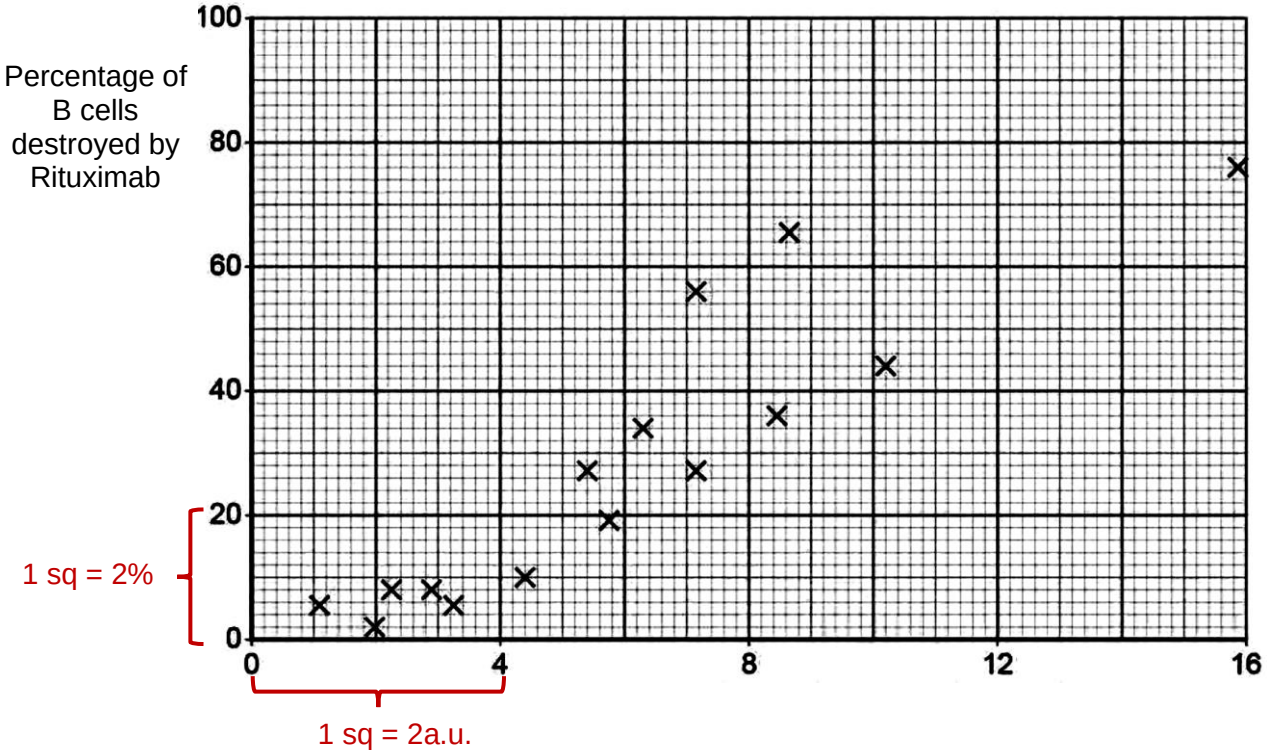


Fig. 3.7

(i) Based on the data in Fig. 3.7, discuss the effectiveness of Rituximab in treating patients with CLL. [2]

Important note:

1. **MUST QF accurately**
2. **MUST state INDEPENDENT VARIABLE 1st**
3. **"Discuss" – refers opposite viewpoints**

Idea that it is effective: [1 mark]

1. **Effective only if there are more CD20 on B cells which leads to higher the percentage of B cells destroyed**
   QF: 8.6 a.u. CD20 resulted in 66% B cells destroyed which was higher than 5.4 a.u. CD20 with only 27% B cells destroyed (Any other examples accepted)
   Just QF one point.

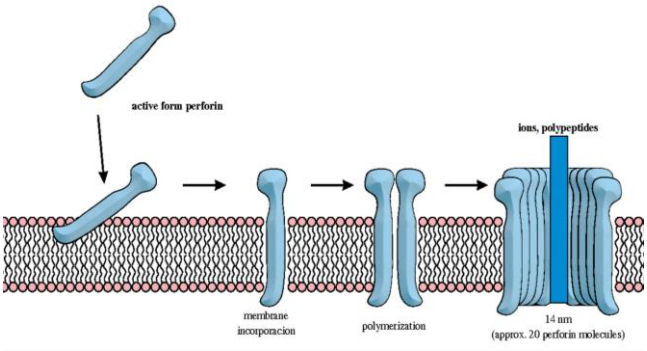
Idea that it is not that effective: Any one [1 mark]

Impt note:
Focus of the question: effectiveness in treating CLL rather than whether the patient will survive or not.
Therefore reject reference to the destruction of immune system by the drug
Also the drug does not target lymphoid stem cells, therefore it is possible to replace B cells – look at the preamble

2. **Not effective below 5 a.u. CD 20 which resulted in less than 10% B cells destroyed**
   QF: 2 a.u. CD20 only 2% B cells destroyed
3. **Not all patients with same amount of CD20 show same effectiveness**
   E.g. QF two patients at 7.1 a.u. CD20, one with 36% B cells destroyed which is lower 56% B cells destroyed.
4. **Not all patients with high amount of CD20 show high effectiveness**
   E.g. QF 10.2 a.u. CD20 resulted in 44% B cells destroyed which is lower than another patient with 8.6 a.u. CD20 with 66% B cells destroyed.
5. **Data shows at most only 76% of B cells so it will not cure CLL / only slows it but doesn't stop CLL**
6. **All data does not indicate if healthy B cells or only cancerous cells were killed**

(ii) Explain how natural killer cells kill cancer cells. [2]

1. **Natural killer cells recognize and bind to Rituxima on cancer B cells.**
   Note: All students missed out this point which is based on the context of the question
2. **Natural killer cells also recognize and bind to abnormal proteins on cancer B cells.**
   Reject: "detect" or "recognize" – these 2 words on their own do not imply binding
3. **Release perforin which binds to surface of cell and form pores in cell surface membrane.**
   Reminder: do NOT write cell wall – humans are not plants!
   Reject: "form holes" – perforins actually form perforin pores
   Reject: "perforate" – which refers to holes being formed



Side view of perforin pore

4. **Release granzymes penetrate cell to induce apoptosis.**

[Total: 24]

H

TEMASEK JUNIOR COLLEGE

2022 JC2 PRELIMINARY EXAMINATION

Higher 2

TEMASEK JUNIOR COLLEGE

CANDIDATE NAME									
CENTRE NUMBER	**S**					INDEX NUMBER				

BIOLOGY **9744/03**

Paper 3 Long Structured and Free Response Questions **13 SEPTEMBER 2022**

PART II **2 hours**

Candidates answer on the Question Paper.
No Additional Materials are required.

Section B

Answer **one** question in this section.

4 **(a)** Explain how somatic recombination, hyper-mutation and class switching result in millions of different antibody molecules [13]

(b) Biological specificity is one of the most widespread and characteristic properties of living organisms.

Biological specificity is most pronounced and best understood at the cellular and molecular levels of organization. Using examples, explain the importance of shapes fitting together in cells and organisms. [12]

[Total: 25]

5 **(a)** Describe the events that occur during the mitotic cell cycle and explain the normal functions of blood stem cells in a living organism. [13]

(b) Describe and explain the effects of different types of mutations on the proteins of eukaryotes. [12]

[Total: 25]

4 (a)

Important Reminders:

1. **Students must memorize these 3 processes and use the correct terms and phrases**
2. **Student CANNOT use the word "gene" to replace "gene segment"**

QWC:

- **Address all 3 processes**
- **Paragraphing**

Somatic recombination [max 6 marks] - SR

1. **During maturation of B cell**
2. **in the bone marrow**
3. **It refers to different ways of selecting and joining**
4. **different V and J gene segments in each light chain gene variable region**
5. **different V, D and J gene segments in each heavy chain gene variable region**
   Note: for marking point 4 & 5, must use "gene segment" is required to get the marks.

6. **There can only be one specific VJ gene segment in the light chain gene and**
7. **only one VDJ segment in the heavy chain gene in each mature naïve B cell.**
8. **Segments not selected are permanently deleted.**
9. **Each combination of V and J in the light chain gene codes for a variable region with a**
10. **different amino acid sequence in the light chain of the antibody**
11. **Each combination of V, D and J in the heavy chain gene codes for a variable region**
    Note: "codes for" must be written at least once for marking points 9 & 11.

12. **with a different amino acid sequence in the heavy chain of the antibody.**
13. **This leads to different antigen-binding specificity in the variable region.**
14. **As result, different antibody with antigen-binding site of different 3-D conformation form the many different combinations of the variable region of the antigen-binding site.**

Somatic hypermutation [max 2 marks] - ***HM***

1. **during proliferation after activation by antigen**
   Note: hypermutation takes place during proliferation stage when DNA replication take place

2. **and cytokines released by helper T cells, to produce memory cells and plasma cells.**
3. **high rates of point mutations in both heavy chain and light chain variable region coding sequences (after somatic recombination has taken place) in mature naïve B cells.**
4. **This results in antibodies which binds to the specific antigen with greater affinity,**
5. **with no changes in antigen-binding specificity.**
6. **This is affinity maturation of the antibody OR such that the antibody binds to antigen most effectively.**
7. **Only B cells that produce antibodies which binds more strongly to the specific antigen (greater affinity) will be selected to continue to proliferate.**

Class switching [MAX 4 marks] - CS

1. mature naïve B cells or memory B cells switching from production of one class of antibody to another OR IgM to IgG

Important note:

1. Plasma B cells do NOT undergo class switching. Once plasma cells produce IgM, the same cell will continue to produce and secrete IgM.
2. It is also incorrect to describe antibody undergo class switching.

2. after activation by antigen binding
3. and cytokines from a helper T cell
4. Only the HEAVY CHAIN CONSTANT, C_H regions are changed by
5. the selection of different heavy chain C_H gene segments.
6. Class switching does not change specificity to antigen,
7. only change its effector function / Fc region
8. One heavy chain C_μ, C_δ, C_γ, C_ε, C_α gene segment selected.
9. C_γ gene segment selected to form IgG
10. The rest of the heavy chain gene segments which are not selected are permanently deleted.
11. The selected C_H gene segment is joined to the same variable region of heavy chain (VDJ).
12. More heavy chain class switching takes place in memory B cells during secondary immune response, leading to most plasma cells releasing IgG.

4 (b)

Important Reminders:

1. Focus is on importance of shapes fitting together – therefore students must clearly describe how the biological molecules fit together
2. Students should not just describe different processes without addressing the question
3. Many students did not mention "shape of active site" for all the enzymes mentioned in their answer
4. It is not necessary to describe the details of each process that the enzyme is involved in – just the immediate effects of the enzyme

QWC:

- Address at least 3 aspects of fitting and its importance
- Paragraphing
- MUST state what are binding and the importance of binding

[Define biological specificity] [Max 1]

1. [Definition] Shapes of molecules is complementary to shape of other molecules, so can they recognize and bind to each other.

[General Principles on Enzymes: Enzymes bind to substrate] [Max 3]

2. [Lock and Key] Shape of enzyme active site is complementary to shape of substrate [1/2]
3. to form ES complex → form products [1/2]
   OR
   [Induced Fit] → Shape of active site is complementary to shape of substrate,
   but slight conformational change after substrate binding to fit more snugly
   [NOTE: Phrase the above statement very carefully! The substrate and enzyme are complementary in shape.]

4. [Product] Product formed → Different shape → leaves active site

5. [Competitive inhibitor] Shape of competitive inhibitor complementary to shape of active site
6. → Compete with substrate to bind at active site → Decrease rate of enzyme activity

7. [Non-competitive inhibitor] Shape of non-competitive inhibitor complementary to shape of site away from active site
8. → binds → Changes conformation of enzyme active site → Decrease rate of enzymatic reaction

9. [Allosteric site] Shape of allosteric activator / allosteric inhibitor is complementary to shape of allosteric site
10. → Change conformation of enzyme active site → Increase / Decrease rate of enzymatic reaction; Regulate enzyme activity

[Photosynthesis / Respiration: Enzyme binds to substrate] [Max 2]

11. [CO2 fixation] Shape of carbon dioxide complementary to shape of rubisco active site
12. → Synthesize 3-phosphoglycerate → leads to synthesis of sugars

13. [Photosynthesis / Respiration] Shape of ATP synthase active site is complementary to shape of ADP and P_i
14. → Synthesize ATP → Drive metabolic reaction

15. [Photosynthesis] Shape of NADP reductase active site is complementary to shape of $NADP^+$ and H^+
16. → Synthesize NADPH → Carbon reduction in Calvin cycle
[Accept: Other enzymes with substrates and functions stated]

[Transport: Protein binds to other chemical molecules] [Max 1]

17. [Transport protein] channel protein or carrier protein

a. Shape of binding site of hydrophilic channel of protein is complementary to shape of molecule
b. → Facilitated diffusion

OR

a. Shape of binding site of carrier protein is complementary to shape of molecule
b. → Facilitated diffusion / Active transport

18. [Receptor-mediated endocytosis] Shape of receptor is complementary to shape of molecule / pathogen
19. → Receptor mediated endocytosis

[Cell Cycle: Protein binds to protein] [Max 1]

20. [Spindle fibre] Shape of spindle fibre complementary to shape of kinetochore / centromere
21. → spindle fibre attach to kinetochore / centromere on chromosome → Arrange chromosome at equator in metaphase / Separation of chromosome or chromatids in anaphase

22. [CDK] Shape of CDK is complementary to shape of cyclin
23. → activation of cdk → Stimulate cell cycle activity

[Nucleic acid: shape of complementary nitrogenous bases fitting together] [Max 2]

24. Shape of complementary bases fitting together in complementary base pairing in nucleic acids

25. [DNA Structure] Complementary base pairing between DNA strands
26. → Formation of double-stranded DNA helix → Stability of structure of DNA molecule

27. [tRNA Structure] Complementary base pairing within tRNA
28. → maintain structure of tRNA
[Accept: rRNA, telomerase RNA]

29. [DNA Replication] Complementary base pairing between DNA template and free deoxyribonucleotides
30. → DNA replication

31. [Transcription] Complementary base pairing between DNA template and free ribonucleotides
32. → mRNA synthesis / transcription

33. [Post-transcriptional modification] Complementary base pairing between snRNA of spliceosome and splice site
34. → RNA splicing

35. [Translation] Complementary base pairing between codon of mRNA and anti-codon of tRNA
36. → Translation / Synthesis of proteins

37. [Lengthening Telomere] Complementary base pairing between free DNA nucleotides and telomerase RNA template
38. → lengthening of telomeres
[Accept: Telomere (DNA) and telomeric RNA]

[Protein binds to nucleic acid: Shape complementary in shape] [Max 4]
39. [Replication] Shape of helicase active site is complementary to shape of DNA sequence at Ori
40. → to separate two parental strands
OR
[Replication]
41. Shape of DNA polymerase active site is complementary to shape of 5' phosphate group of in-coming nucleotide and 3'-OH of the last nucleotide of growing daughter strand.
42. → catalyse formation of phosphodiester bond between nucleotides → DNA replication
Note: this is the immediate effect of DNA polymerase
OR
43. Shape of ligase active site is complementary to shape of 5' phosphate group of free (DNA) nucleotide and 3' OH group of adjacent nucleotide
44. → Seals nick between DNA fragments during DNA replication
[Accept: Proofreading ability of DNA polymerase]

45. [Transcription Factors] Shape of DNA binding domain of general transcription factor / activator / repressor is complementary to shape of DNA sequence at promoter / enhancer / silencer
46. → forms transcription initiation complex / Increase / Decrease rate of transcription

47. [Transcription] Shape of DNA polymerase active site is complementary to shape of 5' phosphate group of in-coming nucleotide and 3'-OH of the last nucleotide of growing mRNA strand.
48. → Formation of phosphodiester bond between nucleotides of mRNA during transcription
Note: this is the immediate effect of RNA polymerase

49. [Amino acid activation] Shape of amino acid + shape of anticodon of tRNA is complementary to shape of aminoacyl-tRNA synthetase active site →
50. Synthesis of amino acyl tRNA complex / Amino acid activation

51. [Translation Initiation Factors / Repressors] Shape of eIF / translational repressor is complementary to shape of mRNA sequence at 5' UTR / 3' UTR
52. → Increase / Decrease rate of translation

53. [Peptidyl transferase] Shape of peptidyl transferase is complementary to shape of aminoacyl-tRNA
54. → Formation of peptide bond between amino acids to form polypeptide during translation

55. [Release factor] Shape of release factor is complementary to shape of mRNA sequence at stop codon
56. → Termination of translation

[Bacteria] [Max 2]

57. [Restriction enzyme] Shape of restriction site of restriction enzyme is complementary to shape of sequence at restriction site
58. → Cut DNA at restriction site / Hydrolyse phosphodiester bonds

59. [Operon] Shape of inducer / corepressor is complementary to shape of repressor → Switch on / off operon → Rapid response to changes in environment
60. [Repressor] Shape of DNA binding domain of repressor is complementary to shape of DNA sequence at operator → Binding of active repressor at operator → Prevent transcription
61. [CAP binding site] Shape of CAP is complementary to shape of CAP-binding site → Switch on operon
[Accept: cAMP and CAP are complementary in shape]

[Cell Signalling] [Max 2]

62. [Receptor] Shape of ligand is complementary to shape of ligand-binding site of receptor (e.g. insulin or glucagon receptor)
63. → Signal reception → Cell signalling pathway
64. [Signal transduction] Shape of second messenger is complementary to shape of effector protein
65. → Cellular response
[Accept: Any relay proteins, effector proteins, Ras]

[Pathogens and antibiotics] [Max 2]

66. [Phage] Shape of tail fibre in phage is complementary to shape of receptors on surface of *E coli* → Binding of phage / Entry of phage DNA into host cell [Reject: Entry of phage]

67. [Influenza] Shape of haemagglutinin in influenza virus is complementary to shape of sialic acid receptors on respiratory epithelial cells → Endocytosis / Entry of influenza virus into host cell
OR
[HIV] Shape of gp120 / gp41 in HIV is complementary to shape of CD_4 receptors on immune cells / T-helper cells → Fusion of HIV viral envelope with plasma membrane of $CD4^+$ immune cells
[Accept: Protease, Integrase, Reverse transcriptase]

68. [Bacteria] Shape of antigen in pathogen (e.g. Pathogen Associated Molecular Pattern) is complementary to shape of antigen-binding site on receptor on macrophage → Elicit immune response / phagocytosis / inflammatory response

69. [Antibiotics] Shape of penicillin is complementary to shape of transpeptidase in bacteria → Inhibit formation of peptide cross-links between peptidoglycan → Kill bacteria

[Immunology] [Max 2]

70. [B-cell receptor] Shape of antigen-binding site of B cell receptor is complementary to shape of antigen → Elicit immune response / Activation of B cell
[Accept: Epitope of antigen]

71. [T-cell receptor] Shape of antigen-binding site of T cell receptor is complementary to shape of antigen on MHC of antigen presenting cell (including B cell) → Activation of T and B cell OR Proliferation and activation → Adaptive immune response OR Formation of memory T and B cells
[Accept: NK cells]

72. [Antibodies] Shape of antigen-binding site of antibodies is complementary to shape of antigen → antibody recognize and binds to antigen → leads to Opsonization / Agglutination / Neutralisation of toxins / Complement activation / Antibody-dependent cytotoxicity

73. [Vaccine] Shape of antigen in vaccine is complementary to shape antigen-binding site of receptors on B cells cells → Elicit immune response

74. Shape of viral glycoprotein spike is complementary to shape of receptor on host cell surface membrane.

[Others] [Max 1]

75. [Cell-cell adhesion / Cell-cell recognition] Shape of glycoprotein / glycolipid / protein of one cell is complementary to the receptors of another cell → Cell-cell adhesion / Cell-cell recognition

5 (a)

Mitosis [max 9]

Note: "mitotic cell cycle" implies the need to focus on mitosis not interphase.

1. Prophase [1/2]
2. Chromosomes become visible due to condensation of chromatin. [1/2]
3. Each chromosome consists of two sister chromatids, which are joined at the centromere. [1/2]
   R: joined by the centromere
   R: joined to a centromere
   (expression error which makes the whole point inaccurate)
4. The nucleolus disappears. [1/2]
   Many students mixed up nucleolus with nucleus.
5. In animal cells, the centrosomes migrate to opposite poles of the cell. [1/2]
   Many students wrote centrioles instead of centrosomes.
6. Spindle fibres extend from each pole towards the equator of the cell. [1/2]
7. Nuclear envelope breaks down. [1/2]
   R: Nuclear membrane
   R: disappears
   MAX 3

   If students did not write point 7,
8. Nuclear lamina and nuclear pore complexes dissociate.
9. Nuclear envelope fragments into vesicles.
   Both 8 and 9 must be written to be awarded ½ marks.

10. Metaphase [1/2]
11. Spindle fibres attach to the kinetochore at the centromere of the chromosome. [1/2]
12. Chromosomes arrange themselves 90° to the spindle axis, in a single row, [1/2]
    R: straight line
13. at the metaphase plate / equator of the cell. [1/2]

14. Anaphase [1/2]
15. The centromere of each chromosome divides, [1/2]
16. causing the sister chromatids of each chromosome to separate. [1/2]
17. The sister chromatids move to opposite poles of the cell, centromeres first. [1/2]
    If students did not write sister chromatids, deduct once only (i.e. will not get point 16, get point 17)
18. This is due to the shortening of the spindle fibres. [1/2]
19. The cell elongates as non- kinetochore spindle fibres lengthen. [1/2]
    MAX 2

20. Telophase [1/2]
21. The sister chromatids reach the respective poles of the cell [1/2]
22. and become the chromosomes of the daughter cells. [1/2]
23. The chromosomes uncoil (R: unwind) and become chromatin. [1/2]
24. Nucleolus in each nucleus reappears. [1/2]
    Many students mixed up nucleolus and nucleus.
25. Nuclear envelope reforms around the chromosomes at each pole. [1/2]
    R: reappears
    R: nuclear membrane
26. The spindle fibres break down.
    MAX 3

    If students did not write point 25,
27. Nuclear lamina and nuclear pore complexes reassemble.

28. Nuclear membrane vesicles fuse.
    Both 27 and 28 must be written to be awarded ½ marks.

Stem Cells [max 3]

29. Myeloid and lymphoid stem cells
30. Multipotent
31. Blood cells have limited life spans
32. Continually replaced by the division and differentiation of blood stem cells / constant renewal of blood cells (R: constant renewal of blood)
33. Replace dead and worn out cells
34. Lymphoid stem cells differentiate (R: give rise to / form) to form white blood cells (e.g. T lymphocytes, B lymphocytes)
35. Myeloid stem cells differentiate (R: give rise to / form) to form red blood cells and other types of white blood cells

Marker's comments:
Many students elaborate on the different functions of the different lymphocytes and WBCs which is not the focus of the question. The question is asking for function of stem cells NOT function of cells found in immune system.

QWC:
P – paragraphing
Q – Address both parts of question

5(b)

Note the requirements of the question:
(1) Describe different types of mutation
(2) Explain the effects on proteins of eukaryotes

Many students went off focus – if mutations were harmful or not, genetic variation, cell cycle checkpoints, listed too many named examples despite question not stating it as a requirement. This resulted in them scoring 0.5 – 2 marks despite writing many factually correct statements.

1 mark EACH:
[Gene Mutation] **[Max 8]**

General comments:
- **Avoid writing generic phrases such as "protein is affected" – be specific, how is it affected? Functional? Non-functional?**
- **Be mindful of terms used and learn to be specific by naming the types of mutation / type of effect (e.g. silent, missense, nonsense) rather than give a generic answer such as "substitution mutation can result in change in amino acid or not".**

1. Gene mutation is the change in nucleotide sequence / codon, and subsequently amino acid sequence

2. Substitution: Replacement of one or more nucleotides

3. Silent mutation → Same amino acid → Protein structure and function not affected
4. Mutation in non-coding region → Same amino acid → Protein structure and function not affected
5. Mutation in splice site → Spliceosome unable to bind → Unable to splice → Non-functional protein

6. Missense mutation → Different codon that codes for different amino acid → Change in primary, secondary and tertiary structure → Protein structure and function may be affected / Non-functional protein / Solubility affected

7. If mutation occurs at crucial site / catalytic site / active site → Protein / Enzyme structure and function affected
   [Accept: Mutation in control elements, centromere]
8. If mutation occurs at non-crucial site → Protein / Enzyme structure and function not greatly affected

9. Nonsense mutation → Stop codon → Premature termination of translation → Truncated / Shorter non-functional protein

10. Insertion/ Deletion: Addition / Removal of nucleotide
11. (Non-multiples of 3) Frameshift mutations → Affects reading of codons / reading frame downstream of mutation → Sequence of amino acids downstream of mutation being completely altered → Non-functional protein / Shorter protein
12. (Multiples of 3) Removal of (one) amino acid → No effect / Non-functional protein / Shorter protein

13. [Example of gene mutation]
    - Substitution T changes to A in template strand of beta-globin gene → Hydrophilic glutamine changes to hydrophobic valine in haemoglobin → Hydrophobic region → Polymerization of HbS / Crystallization of HbS into rod-like fibres → Sickle cell anaemia
    - ras → unable to hydrolyse ATP → constant activation of cell signaling → uncontrolled cell division
    - Somatic hypermutation → Greater diversity / repertoire of B cell receptor / antibodies → Increased possibility of greater binding affinity of antibody to antigen
    - mutated *p53* tumour suppressor genes / DNA repair gene → Unable to detect or repair DNA damage / Initiate apoptosis → Uncontrolled cell division

[Chromosomal Aberration] [Max 4]

General comments:
Most students faced difficulties in describing chromosomal structure mutations clearly and did not know what the possible effects on proteins are, commonly mixing up "no proteins synthesized" and "non-functional proteins synthesized".

14. Chromosome aberration is the change in structure or number of chromosome

[Changes in chromosomal structure]
15. Duplication → Set of genes repeated / Extra copy of genes → More protein products synthesized

16. Deletion → Loss of a region of chromosome → Shorter chromosome missing certain genes → Proteins not synthesized / Loss-of-function

17. Inversion → Breaking and reattachment of chromosome in reverse orientation → Non-functional protein synthesized

18. Translocation → Breaking and joining of chromosome to another non-homologous chromosome
    WITH If chromosome is translocated to strong promoter → Overexpression of proteins (e.g. proto-oncogene → oncogene)
    OR
    If chromosome is translocated to a region which is transcriptionally not active / heavily methylated → Proteins not synthesised (e.g. mutated tumour suppressor genes)

[Changes in chromosomal numbers]

19. Aneuploidy → Gain / Loss of one or more chromosomes
    WITH
    Loss of certain genes → Proteins in deleted regions not synthesized
    OR
    Extra copy of certain genes → More protein products synthesized

20. Polyploidy → Gain / Loss of one or more SETS of chromosomes
    WITH
    Mostly lethal in animals
    OR
    Not lethal in plants

21. [Example of chromosomal aberration]
    - e.g. Trisomy 21 → Down syndrome

[Gain-of-function / Loss-of-function]

22. e.g. Chromosome is translocated to strong promoter → Overexpression of proteins

23. e.g. Chromosome is translocated to a region which is transcriptionally not active / heavily methylated → Proteins not synthesized

QWC:
P – Paragraphing
G – Gene mutation + effect
C – Chromosomal mutation + effect