YISHUN INNOVA JUNIOR COLLEGE
JC2 PRELIMINARY EXAM
Higher 2

NAME **ANSWERS**

INDEX NO | CG

BIOLOGY **9744/03**

Paper 3 Long Structured and Free-Response Questions **15 Sep 2025**

2 hours

Candidates answer on the Question Paper.

No Additional Materials are required.

READ THESE INSTRUCTIONS FIRST

Write your name and class in the spaces at the top of this page.
Write in dark blue or black pen on both sides of the paper.
You may use an HB pencil for any diagrams or graphs.
Do not use staples, paper clips, highlighters, glue or correction fluid/tape.

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

Section B
Answer any **one** question in the spaces provided on the Question Paper.
Indicate the question you have attempted at the top of page **18**.

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

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

For Examiner's Use	
Section A	
1	**/ 32**
2	**/ 10**
3	**/ 8**
Section B	
4 or 5	**/ 25**
Total	**/ 75**

This document consists of **25** printed pages and **1** blank page.

Section A

Answer **all** questions in this section.

1 Glioblastoma multiforme (GBM) is the most common and most aggressive form of brain cancer, often resulting in low survival rates.

It is characterised by uncontrolled growth, abnormal chromosomal structures, altered gene expression, and increased glycolysis. The exact genetic cause of GBM is unknown, prompting research into possible mechanisms such as chromosomal aberrations and gene mutations.

One focus is the epidermal growth factor receptor (EGFR) gene on chromosome 7, which encodes a receptor tyrosine kinase specific to certain growth factors. Patients with GBM often show overexpression of the EGFR gene. Aberrations in chromosome 7 and a significant increase in metabolic activity have also been detected.

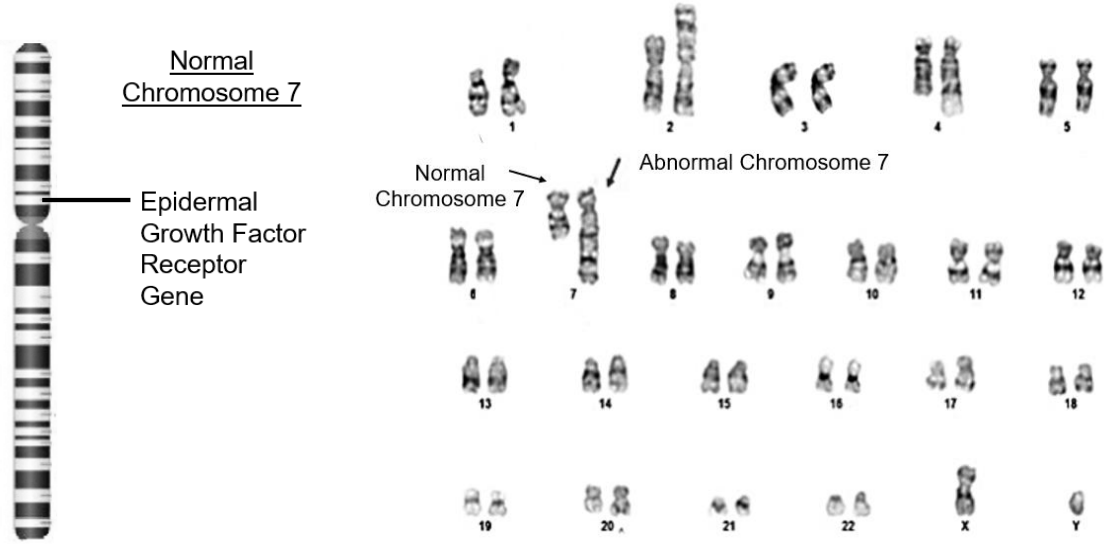

Fig. 1.1

(a) **(i)** Describe how accurate chromosomal segregation during nuclear division prevents cancer.

1 **Accurate chromosome segregation ensures daughter cells receive the correct number of chromosomes/ same amount of DNA.**

2 **Errors (e.g. aneuploidy) can lead to loss/gain of genes, disrupting cell cycle regulation and contributing to cancer.**

Or prevent loss /gain of genes which may disrupt mitotic regulation and accumulation of such errors may contribute to cancer. [2]

Examiner feedback: Most students did not give precise answer which included unnecessary elaboration of mitosis, meiosis, separation of the homologous chromosomes, and sister chromatids

(ii) With reference to Fig. 1.1, explain how chromosomal aberrations can lead to GBM.

1 **EGFR gene is a proto-oncogene**

2 **Gene amplification/ Addition/ Hyperactivity of EGFR gene on chromosome 7 leads to increased expression, hence GBM.**

[R] Loss of gene, normal chromosome is shorter than abnormal

Examiner feedback: Most students were unable to identify EGFR as an proto-oncogene [2]

Capsaicin is a lipophilic compound. It is abundant in *Capsicum* species (pepper) fruit and it is the main bioactive constituent responsible for tissue irritation and burning sensation.

Capsaicin has shown significant potential as an effective chemopreventive agent. Chemoprevention refers to the use of agents that inhibit or delay the development of tumour and before the onset of tumour cell invasion.

There is increasing interest in using capsaicin as an alternative cancer therapy.

Fig. 1.3 shows some of the many effects of capsaicin in chemoprevention.

↑ shows that the activity of the named molecule that is enhanced by capsaicin.
↓ shows that the activity of the named molecule that is decreased by capsaicin.

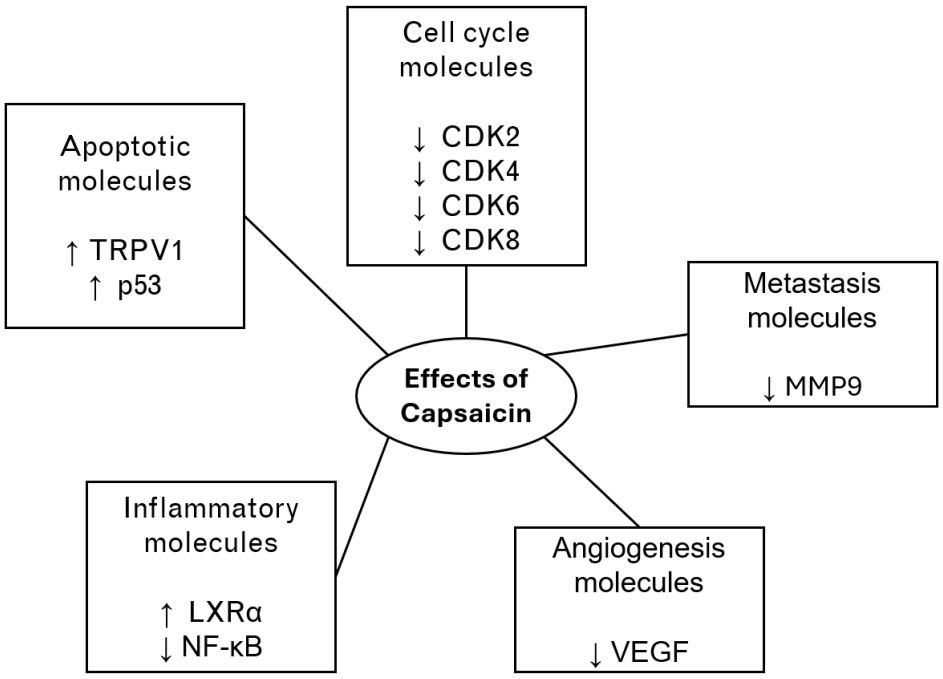

Fig. 1.2

(b) (i) Tumours are known to secrete VEGF and MMP-9.

With reference to Fig. 1.3, explain why capsaicin is an effective chemopreventive agent.

1	**Capsaicin lowers the activity of VEGF and MMP-9,**
	thereby inhibiting tumour growth/ angiogenesis and metastasis
2	**Tumours secrete VEGF to stimulate the blood vessels formation**
	that supply nutrients for tumour growth (idea of angiogenesis)
	OR AW prevent formation of blood vessels
	and supply of nutrients to tumours;
3	**They also secrete MMP-9 to allow cancer cells to invade**
	and spread (idea of metastasis)
	OR AW prevent the cancer cells from invading and spreading
	to establish secondary tumours ; [3]

Examiner feedback: This part was generally well answered. Most candidates demonstrated a good understanding of the experimental context and were able to relate the role of capsaicin to the regulation of VEGF and MMP9 in cancer progression. Many candidates correctly identified that capsaicin reduced the expression of VEGF and MMP9, and were able to explain how reduced VEGF leads to decreased angiogenesis while reduced MMP9 results in lower rates of metastasis. In addition, most were able to define angiogenesis as the formation of new blood vessels and metastasis as the spread of cancer cells to secondary sites.

A small number of candidates, however, **misinterpreted the context by describing the effects of other molecules shown in Figure 1.2 rather than focusing on VEGF and MMP9 as required.** This suggests the need to read the question carefully and ensure that responses remain focused on the molecules specified. Another group of candidates only stated that capsaicin reduced VEGF and MMP9 levels, without extending their answers to explain the consequences of this reduction, such as reduced blood vessel formation and reduced spread of cancerous cells to other tissues.

When tackling data-based questions involving experimental figures, candidates **should pay close attention to the molecules specified in the question and avoid diverting into unrelated aspects of the figure.** It is also important to remember that examiners look for both identification of what is observed in the data and explanation of why this observation is biologically significant. For full credit, molecular changes must be linked clearly to their biological consequences in the context of the disease or process studied. Candidates are encouraged to use precise biological terms such as “angiogenesis” and “metastasis”, but these should be accompanied by clear explanations of what they mean in context.

(ii) Cyclins interact with one of the classes of molecules that capsaicin affects.

Identify this class of molecules in Fig. 1.2 that cyclins interact with and explain how capsaicin's effect on it could help to treat or prevent cancer.

1 **Cyclin-dependent kinases (CDKs)/ Cell Cycle Molecules/ CDK**

2 **Capsaicin reduces the activity of CDKs**

and cause cell cycle arrest at the checkpoints ;

3 **This slows or stops cell cycle progression,**

which can prevent uncontrolled cell division and reduce growth of cancerous cells; [3]

Examiner's feedback:

This part of the question revealed greater variation in performance compared to the previous one. About half of the cohort were unable to correctly identify the class of molecules that cyclins interact with in the cell cycle from Figure 1.2. The intended answer was **cyclin-dependent kinases (CDKs), and students were expected to provide the full name**. Those who answered correctly often relied on the header provided in the figure, writing "cell cycle molecules" instead. While this was not the original answer in the mark scheme, credit was awarded for this phrasing as it reflected an appropriate interpretation of the figure.

A noticeable number of candidates incorrectly identified apoptotic molecules, suggesting that they had not carefully read the figure or confused different categories of molecules. Among those who did correctly identify cell cycle molecules, several were unable to extend their answer by explaining how reduced CDK activity would help to reduce cancer development. This second step was crucial, as the question required both identification and explanation.

Candidates are reminded that when questions involve interpreting figures, precision in terminology is important, and answers should go beyond simply naming the molecules. It is necessary to explain the biological significance of these interactions in the context provided. In this case, candidates needed to make the link that reduced CDK activity slows or halts the progression of the cell cycle, thereby preventing uncontrolled cell division which is characteristic of cancer. In future, students should take care to not only identify the correct molecules but also articulate clearly the consequences of their altered activity for the development of disease.

One of the mechanisms involved in capsaicin's chemopreventive action is its anti-inflammatory effect. Fig. 1.4 illustrates how capsaicin blocks the NF-κB-mediated inflammatory response.

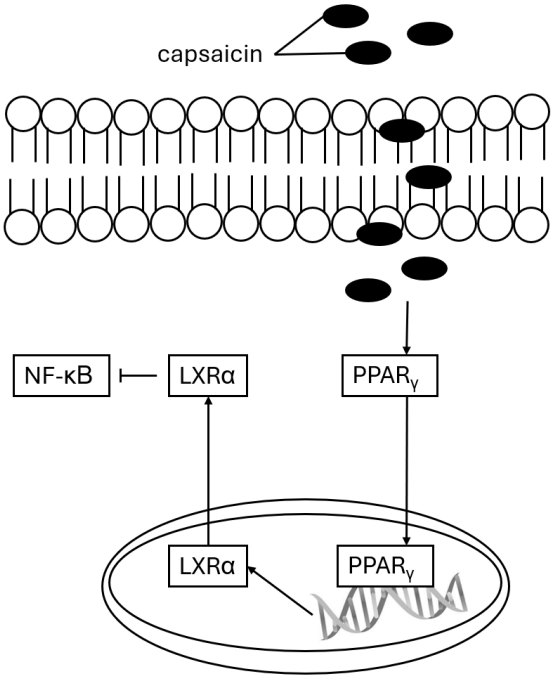

Fig. 1.4

(c) **(i)** With reference to the information provided, suggest the role of $PPAR_{\gamma}$ in the anti-inflammation response.

Transcription factor / General Transcription factor / Specific Transcription factor / Activator ;

Idea increase transcription [1]

[R] Repressor/ Secondary Messager

Examiner's Feedback:

Only a minority of candidates answered this part correctly. The question was intended to test whether students could state the role of PPAR-gamma as a transcription factor. However, some candidates, likely unable to recall or identify that PPAR-gamma belongs to this class of molecules, instead elaborated on how PPAR-gamma performs its function. While this was not the direct intention of the question, credit was awarded to these responses as they demonstrated sufficient understanding of the role of PPAR-gamma.

A common misconception observed was that many candidates mistakenly identified **PPAR-gamma as a second messenger.** This error suggests a gap in understanding of the nature of second messengers. Students need to **remember that second messengers are not proteins but are usually small, inorganic molecules or ions such as calcium ions or cyclic AMP**. Transcription factors, in contrast, are proteins that regulate gene expression by binding to specific DNA sequences.

Moving forward, students should revise the **classification of key molecules in signaling pathways and be able to distinguish clearly between transcription factors, receptors, kinases** and second messengers. Precision in terminology is essential, and careful attention must be paid to the biochemical nature of the molecules involved, as this determines their role in cellular processes.

(ii) Tumour proliferation, in GBM, is often associated with significant inflammation in its microenvironment.

Using the information provided, explain how capsaicin is useful in the treatment to reduce the inflammation in the tumour microenvironment.

1 **Fig. 1.3 shows that capsaicin activates $PPAR_{\gamma}$,**

$PPAR_{\gamma}$ increases LXRα expression / activity ;

2 **LXRα blocks NF-κB in the tumour microenvironment;**

so reducing inflammation; [2]

Examiner's feedback:
Most candidates were able to answer this part correctly. They explained that PPAR-gamma increases the expression of LXR-alpha, which in turn blocks NF-kappa B, thereby reducing inflammation. These responses showed that many students were able to follow the signalling cascade described and connect it to the biological outcome of reduced inflammation.

It was noted, however, that a small handful of candidates left this question unattempted. This may indicate uncertainty or lack of confidence when interpreting molecular pathways that involve several steps. Students are reminded that questions of this type typically require them to trace the sequence of molecular events and explain the functional consequence at the cellular level. Careful reading of the figure, combined with knowledge of the roles of each molecule, will allow the pathway to be reconstructed logically.

Future improvement can be achieved by practicing the interpretation of signaling cascades, with an emphasis on linking molecular interactions to their physiological outcomes. This will ensure that students feel more confident and are able to attempt such questions even when the pathways appear complex.

Patients with another form of glioblastoma have been found to carry mutations in the TP53 gene. Fig. 1.2 shows part of the sequencing data for a normal TP53 allele and a mutant TP53 allele.

Normal	A	A	A	C	A	C	A	C	A	C	C	T
Mutant	A	A	A	C	A	T	G	C	A	C	C	T

Fig. 1.2

(d) **(i)** With reference to Fig. 1.1 and 1.2, explain the differences between point mutations and chromosomal aberrations.

1 **Point mutation: change in a single nucleotide base (e.g., substitution, insertion, deletion)**

2 **Example: Single nucleotide base substitution in Fig 1.2, where Cytosine is replaced with Thymine.**

3 **Chromosomal aberration: change in chromosomes structure/ chromosome number (e.g., gene duplicate, chromosome become longer) / changes in chromosome no.**

4 **Example: Gene duplication/addition in Chromosome 7 in Fig 1.1**
[R] Gene deletion

Examiner feedback: Some students did not provide definitions for point mutations and chromosomal aberrations. Examples must be referenced without generalisation. Examples that were piecemealed from the preamble were rejected.

[4]

(ii) With reference to Fig. 1.2, explain how mutation results in brain tumours.

1 **Missense mutation may lead to change in amino acid sequence, changes in R group interactions, hence a misfolded/ non-functional TP53 protein.**

2 **TP53 loses ability to bind DNA / DNA binding site no longer complementary to DNA sequence, hence unable to bind**

3 **Failure to arrest the cell cycle or induce apoptosis or repair DNA → uncontrolled cell proliferation.**

Examiner feedback: Unnecessary elaboration on how missense mutation resulted in the transcription and translation of the non-functioning protein were seen in many scripts.

[3]

Capsaicin can induce apoptosis in cancer cells such as GBM. One of the major pro-apoptotic mechanisms of capsaicin is via the vanilloid receptors, TRPV1, a non-selective calcium channel that is functionally involved in cell death in a wide variety of cancer cells. Fig. 1.5 shows the TRPV1 dependent apoptosis pathway.

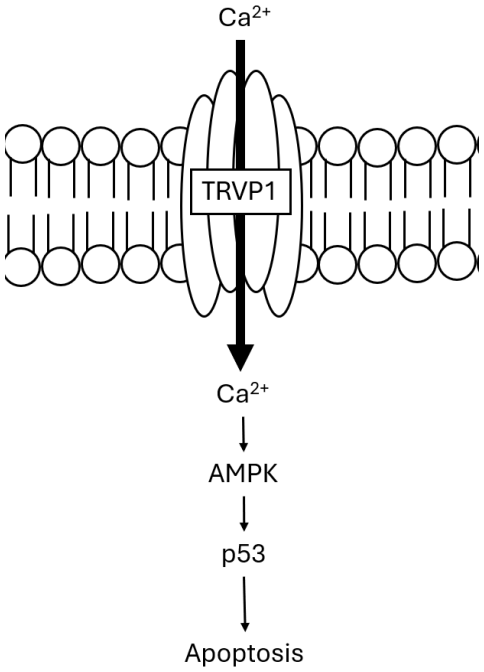

Fig. 1.5

(e) **(i)** TP53 gene codes for p53 proteins.

Using the information provided thus far, explain how the mutation in the TP53 gene reduces the effect of capsaicin on tumour size.

1. **A mutation in the TP53 gene means p53 is non-functional/ unable to bind to AMPK**

2. **Even if capsaicin increases TRVP1 and p53 protein levels, apoptosis is not induced**

[2]

Examiner's feedback:
Most candidates were able to answer this part correctly. They explained that a mutation in TP53 results in

- Less production of p53 proteins
- Non-functional p53 proteins

Which ultimately does not induce apoptosis.

Some candidates made reference to the pathway in Fig 1.5, stating that AMPK is no longer able to bind to the mutated p53, and hence unable to trigger the apoptosis pathway, which is accepted and encouraged.

(ii) In a study, mice with functional TP53 showed an average tumour size reduction from 180 mm³ to 117 mm³ after capsaicin treatment.

Calculate the percentage decrease in tumour size. Show your working.

1 **(180−117) / 180 × 100**

2 **= 35%** [2]

Examiner's feedback:
Most candidates were able to answer this part correctly

A new therapeutic cancer treatment was developed, using capsaicin. A clinical trial of this therapy was conducted with 10 patients. The five years overall survival rate for patients with recurrent GBM treated with capsaicin was compared to traditional chemotherapy conducted with 17 patients.

Table 1.1

	probability						
df	0.25	0.20	0.15	0.10	0.05	0.025	0.01
25	0.684	0.856	1.058	1.316	1.708	2.060	2.485
26	0.684	0.856	1.058	1.315	1.706	2.056	2.479
27	0.684	0.855	1.057	1.314	1.703	2.052	2.473

(f) **(i)** State the degree of freedom in this t-test.

25 [1]

Examiner's feedback:

Most candidates could not answer this part correctly.

This question required candidates to state the correct degree of freedom (df) in the t-test, calculated as $(n_1 + n_2 - 2)$. With sample sizes of 10 and 17, the correct df is 25.

Common errors included:
- **27:** Candidates forgot the formula requires subtracting 2.
- **26:** Candidates confused the t-test with the chi-square test, which uses (n – 1).
- **0.05:** This indicates confusion between the concept of p values and degrees of freedom

Moving Forward, students should:
- Apply the correct formula for t-test degrees of freedom $(n_1 + n_2 - 2)$.
- Practise comparing it with the chi-square df formula $(n - 1)$ to avoid confusion.
- Carefully read statistical tables to distinguish between **degrees of freedom** and **probability values**.
- Reinforce learning by attempting past paper questions involving different sample sizes.

(ii) The lead physician hypothesised that capsaicin treatment improves overall survival rate compared to traditional chemotherapy. A t-test was performed, yielding a value of t = 0.66.

Explain the significance of the t-test value in relation to the lead physician's hypothesis.

1 **At df = 25 for p = 0.05,**

calculated t-value of 0.66 is much lower than the critical t-value at 1.708

2 **This means the difference in survival rates between the capsaicin therapy and traditional chemotherapy**

is not statistically significant and is due to chance alone;

3 **Therefore, there is insufficient evidence/ incorrect**

to support the lead physician's hypothesis that capsaicin improves overall survival; [3]

Examiner's feedback:
Most candidates could not answer this part correctly.

Common errors included:

1. **Not identifying the correct critical t-value** at df = 25, p = 0.05 (1.708).

2. **Failing to compare calculated T value (0.66) with the critical T value (1.708)**, and hence not establishing significance.

3. **Misinterpreting the T values**
   - *calculated t > critical t = statistically significant*
   - *calculated t < critical t = not statistically significant*.

4. **Incorrect interpretation of non-significance**
   - if there is **no significant difference**
     → Not much difference between new therapy and traditional therapy
     → Insufficient evidence to support that new therapy works
     → Reject physician hypothesis

   - If there is a significant difference
     → Some meaningful difference between new therapy and traditional therapy
     → Sufficient evidence to support that new therapy works
     → Accept physician hypothesis

Candidates need more practice applying the logic of statistical tests to real biological contexts (what means are being compared?), rather than memorising steps in isolation.

GBM cells exhibit the Warburg effect, also known as 'aerobic glycolysis', a phenomenon in which cells preferentially undergo glycolysis followed by fermentation when oxygen is available. This leads to the increased generation of additional metabolites that benefits proliferating cells.

In an experiment, GBM cells and healthy cells were cultured under laboratory conditions with a fixed supply of glucose for 10 hours. The ATP production per glucose molecule was measured in arbitrary units and recorded over time.

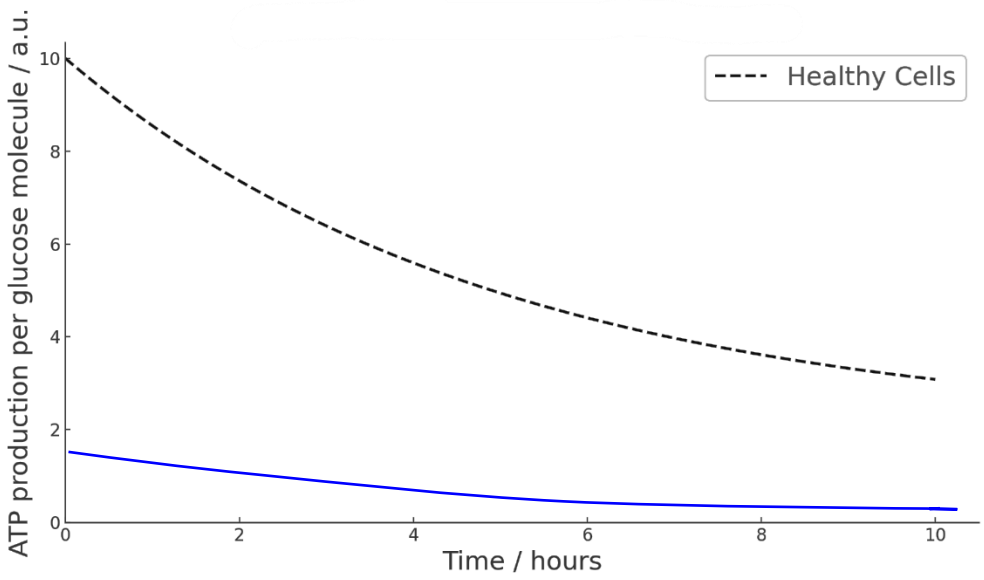

Fig 1.6

(g) (i) Sketch a graph in Fig 1.6 showing the ATP production for GBM cancer cells. [1]

Drawing must show a lower rate of ATP production, starting below 10 as opposed to healthy cells (since rate of ATP production is much lower without oxidative phosphorylation in cancer cells)

Idea that student know the difference between

- **substrate level phosphorylation vs oxidative phosphorylation**
- **Fixed supply of glucose**

Examiner feedback: From the preamble, a fix supply of glucose denote that the supply of glucose is finite, a curve is to be expected. Horizontal line graph can only happen if there is a constant supply of glucose (infinite amount). From theory, anaerobic respiration produces significantly less ATP than aerobic respiration, y-axis should not start from 10 a.u.. Marking scheme has been relaxed to award mark as long as the starting point on the y-axis is less than 10 a.u. but a better answer will start from about 2 a.u..

(ii) Name a final product due to the Warburg effect.

Lactate / Lactic acid

Examiner feedback: Students fail to realise that the context is mammalian cancer cells, ethanol is produced in (yeast/plant) anaerobic respiration.

[1]

Asides from capsaicin, scientists are also looking into drugs which target the glycolytic pathway in cancer cells. Fig. 1.7 shows the glycolytic pathway in cancer cells.

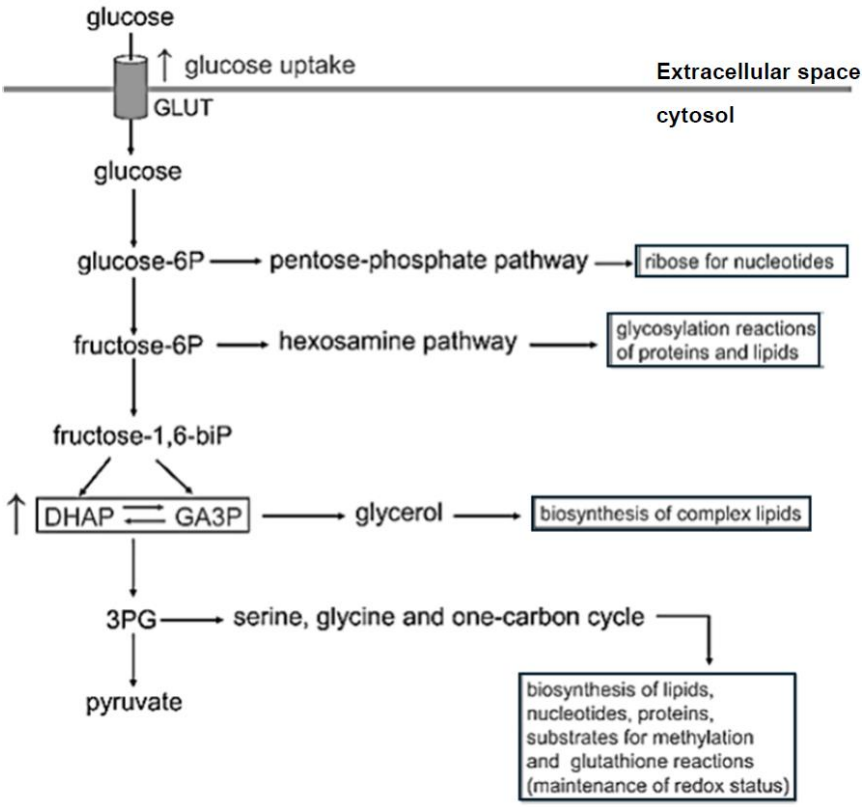

Fig 1.7

(iii) Suggest the mechanism of action of such drugs and one possible limitation.

1 **Targeting glycolytic enzymes (e.g., hexokinase, PFK) reduces ATP / biosynthetic precursor supply, slowing proliferation in cancer cells.**

2 **Challenge: Normal cells which also undergo glycolysis can be affected by the drug, leading to off-target effects**

Examiner feedback: Many students adapted the given glycolytic pathway to synthesis an appropriate answer. **Limitation should be made in reference to the suggested mechanism.** Generalised limitation such as expensive drug, repeat dosage and delay oral drug reactions are not accepted as the latter are normal occurrence in any oral medication.

[2]

[Total: 32]

2 Recent advancements in gene therapy explore the use of viral vectors to deliver therapeutic genes into the immune cells of HIV-infected patients.

Understanding viral structure is key to designing effective vectors. Viruses are classified as naked or enveloped, affecting entry into host cells, environmental stability, and response to disinfectants.

Fig. 2.1 shows the structure of HIV, a prevalent global disease that is a key focus in gene therapy research.

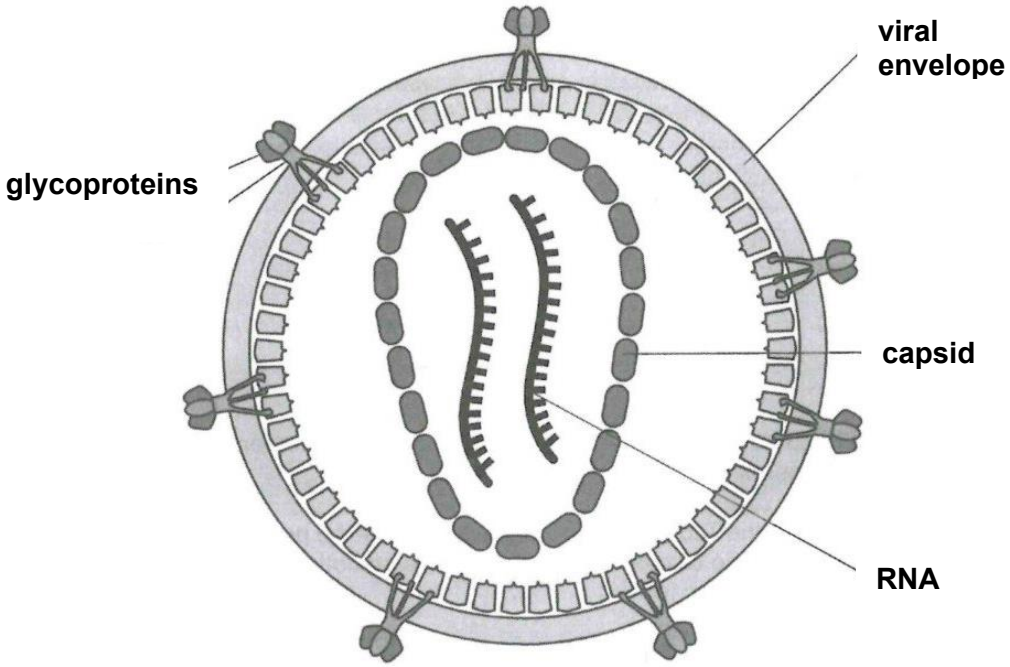

Fig 2.1

(a) **(i)** With reference to Fig. 2.1, compare the structure of HIV with T4 bacteriophage.

1. **Similarities: Both HIV and T4 bacteriophage genetic material enclosed by a protein capsid**

2. **Difference: HIV contains positive sense single-stranded RNA while T4 bacteriophage contains double-stranded DNA**
[R] Negative Sense RNA / Double stranded RNA / Segmented RNA

3. **Difference: HIV is an enveloped virus with a viral envelope while T4 bacteriophage is a naked virus with no envelope.**
[R] Envelope vs Capsid

4 **Difference: HIV has 2 surface glycoproteins (e.g. gp120 and gp41) for host recognition and entry, while T4 does not (uses tail fibres for attachment)**
[R] Hemagglutinin/ Neuraminidase

5 **Difference: HIV carries the enzyme reverse transcriptase/integrase/ HIV Protease while T4 bacteriophage has lysozyme.**

6 **Difference: HIV has a conical/ cone-shaped capsid while T4 bacteriophage has an icosahedral capsid head**

Any 1 similarity + 1 difference [2]

Examiner feedback: Many students did not give one similarity and one difference. For precision, do note that the HIV's capsid is conical and bacteriophage is icosahedral in shape.

(ii) "T4 Bacteriophages are possible viral vectors to deliver correct genes to human immune cells."

Discuss whether this statement is true and explain your reasoning.

1. **Bacteriophages are viruses that infect bacteria, so they lack the necessary proteins and mechanisms to enter human cells.**
Hence, they cannot directly deliver genes into human immune cells.

[1]

Examiner feedback: A significant number of students missed the point that viruses have specific hosts. Having a lytic or lysogenic cycle has no impact in such instance.

(b) Gene therapy for HIV works by modifying a patient's cells to resist or eliminate the virus. One mechanism involves introducing therapeutic genes into the genome of target cells, enabling them to express proteins that either block HIV entry or inhibit HIV enzymes.

Lentiviral vectors are often used to deliver these genes into cells. They work by entering target cells and inserting the therapeutic genes into the cell's DNA, allowing the cell to produce helpful proteins over time. Fig. 2.2 shows the structure of a lentiviral vector.

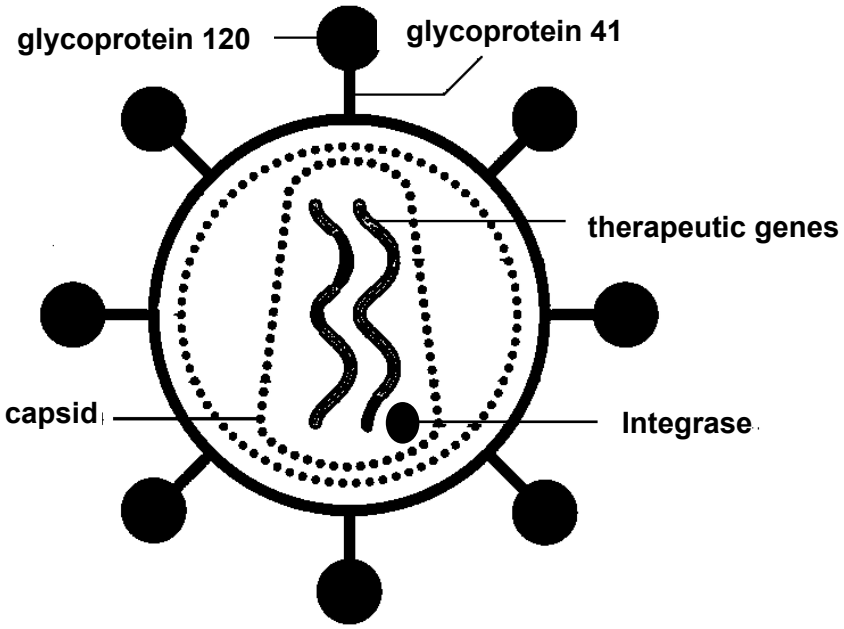

Fig 2.2

(i) With reference to Figures 2.1 and 2.2, explain why lentiviruses are suitable viral vectors for the treatment of HIV.

1. **Lentiviral vectors possess same/ glycoproteins to HIV (gp120 and gp41), which enable them to bind to CD4 receptors on T-helper cells.**
2. **The presence of integrase allows the therapeutic gene to be stably integrated into the host genome.**

[2]

(ii) Suggest three different products encoded by therapeutic genes and explain how each product helps in the treatment of HIV.

1. **Non-functional (CCR5/ T-cell) receptor, which prevents HIV from binding to the co-receptor on the host T cell surface, thereby blocking viral entry.**
2. **Inhibitor of the HIV envelope glycoproteins gp120 or gp41, which blocks the virus from attaching to or fusing with the host cell membrane, thus preventing entry into $CD4^+$ T cells.**
3. **Inhibitor of reverse transcriptase, which prevents the conversion of viral RNA into DNA, thus halting early stages of HIV replication.**
4. **Inhibitor of integrase, which blocks the integration of viral DNA into the host genome, disrupting provirus formation.**
5. **Inhibitor of HIV protease, which prevents the cleavage of viral polyproteins, disrupting viral assembly.**
6. **Nuclease targeting HIV genome, which degrades viral RNA or DNA, preventing replication inside host cells.** [3]

Any 3 of the 6 marking points
R: non-functional HIV protease/ reverse transcriptase"
→ ✗ Incorrect. These viral enzymes are made by HIV, not the host cell. Gene therapy modifies host cell behaviour, not the virus directly

Examiner feedback: Students should identify the specific type of proteins or enzymes when answering this question.

(c) Viruses such as influenza can undergo antigenic shift or antigenic drift to evade host immune responses.

(i) Explain why antigenic drift occurs more frequently in HIV.

Due to its high mutation rate/ lack of proofreading from reverse transcriptase to gradual changes in surface glycoproteins like gp120

Key idea: Susceptible to mutation leading the lack of proofreading mechanism [1]

(ii) Explain why antigenic shift occurs less frequently in HIV.

HIV does not undergo antigenic shift because it has a non-segmented RNA genome (unlike influenza which has 8 segmented genome), so genome segment reassortment is not possible.

Key Idea: Segmented genome [1]

Examiner feedback: Poor attempt for this question. Students should brush up on their content with reference to the definitions of antigenic drift and antigenic shift.

[Total: 10]

3 Fossil and genetic evidence suggests that *Homo sapiens* and *Homo neanderthalensis* shared a common ancestor approximately 600,000 years ago.

Fig. 3.1 illustrates the proposed relationships between various hominin species based on fossil skull morphology.

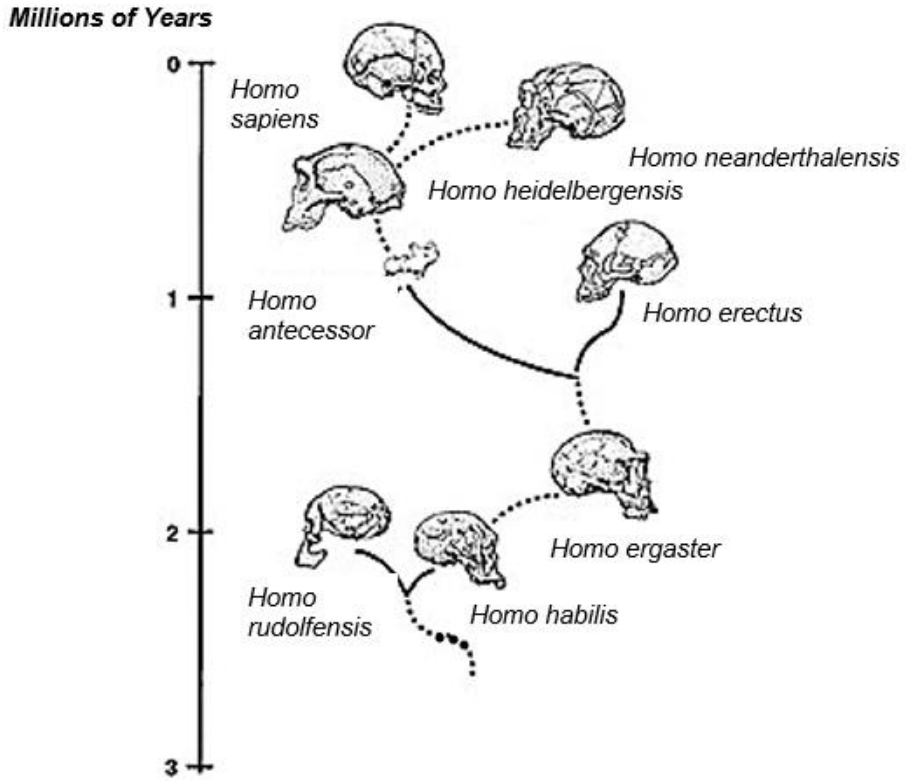

Fig 3.1

(a) With reference to Fig. 3.1 and the theory of natural selection, explain how fossil evidence supports the classification of *Homo sapiens* and *Homo neanderthalensis* as different species.

1. Common Ancestor: Fig. 3.1 shows that H. sapiens and H. neanderthalensis diverged from a common ancestor (Homo heidelbergensis),

2. Microevolution: Different populations of the common ancestor were exposed to different selection pressures due to different environments,

3 favourable traits within each population were selected for, leading to a change in allelic frequency over time

[R] Passing on traits (skull shape)/ genes

4 Macroevolution: Over time, the isolated populations accumulated different mutations, causing genetic divergence.

5 Morphological Species Concept: This eventually led to significant differences in morphology as shown in Fig 3.1, and hence considered different species.

Penalty for binomial nomenclature – no attempt to underline species name. Underline must be separated e.g. Homo Sapiens not Homo Sapiens

Examiner feedback: There is no need to explain natural selection from the earliest hominoids. Micro evolution should always happen before macro evolution.

[3]

Cladograms and phylogenetic trees are both branching diagrams used to represent evolutionary relationships among organisms. Cladograms specifically show the order of branching based on shared derived characteristics.

(b) Explain whether cladograms are a form of biological classification or phylogeny.

1. Classification organises species according to shared characteristics only while, phylogeny is the organises species according to both shared characteristics and evolutionary relationships.

2. Since cladograms illustrates evolutionary relationships, they are based on phylogeny.

Key Idea: Cladogram is not classification + Cladogram is phylogeny

Examiner feedback: Many students fail to explain that cladogram consists of both evolutionary relationship and shared characteristics while biological classification is simply shared characteristics.

[2]

Scientists have proposed two main hypotheses to explain the origin and global spread of modern humans, as shown in Fig 3.2.

- **The Out of Africa hypothesis** suggests that *Homo sapiens* evolved in Africa around 200,000 years ago and later migrated to other parts of the world, replacing local populations such as *Homo neanderthalensis*.

- **The Multiregional hypothesis** proposes that modern humans evolved simultaneously in different regions from earlier hominins such as *Homo erectus*, with continuous gene flow between populations across Africa, Europe, and Asia maintaining the species.

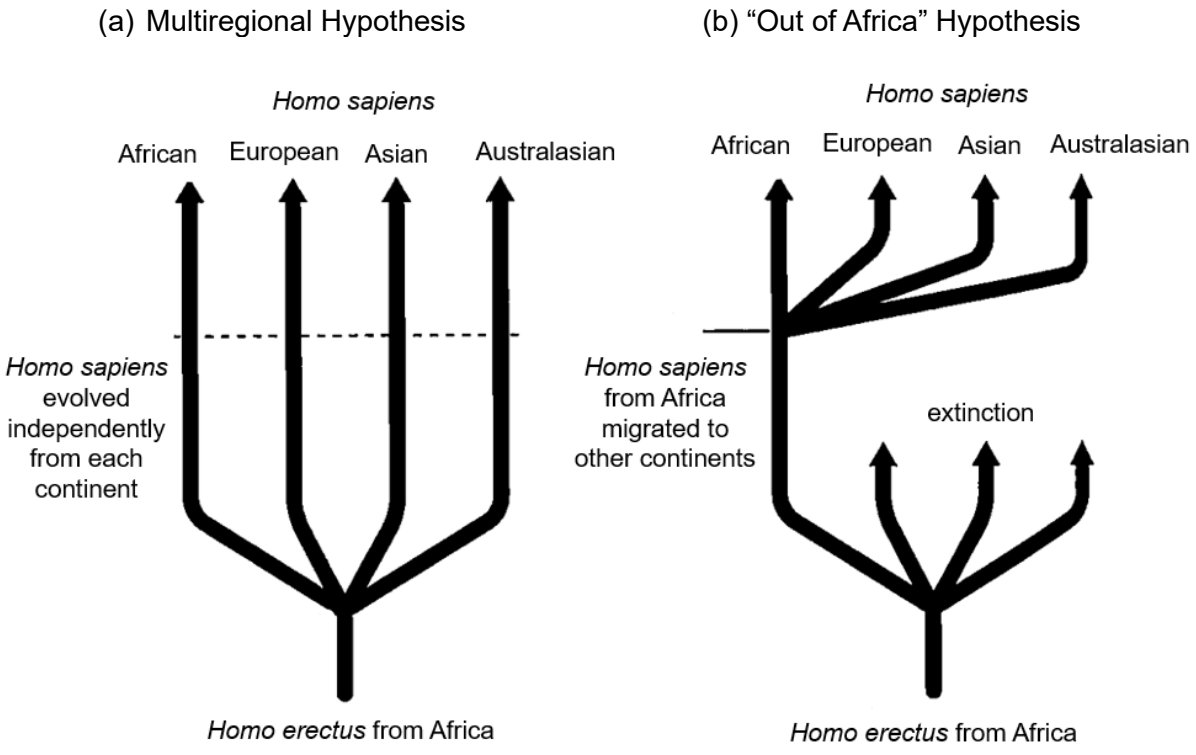

Fig 3.2

(c) With reference to Fig. 3.2, suggest one type of scientific evidence that could help determine whether the Multiregional hypothesis or the Out of Africa hypothesis is more likely to be correct.

Explain how this evidence supports one of the hypotheses.

Molecular Homology

1.1 **Molecular data, such as mitochondrial DNA (mtDNA) or Y-chromosome sequences, can be compared between modern human populations.**

1.2 **If African populations show the highest genetic diversity, this suggests they have had the longest time to accumulate mutations.**

1.3 **This supports the Out of Africa hypothesis, as it implies Homo sapiens originated in Africa, and other populations descended from this ancestral gene pool.**

Anatomical Homology/ Fossil Evidence

2.1 **Fossil evidence, such as skull and bone structures, can be used to compare the anatomical features of ancient human species across different regions.**

2.2 **If the oldest fossils of anatomically modern humans are consistently found in Africa, this suggests that Homo sapiens first evolved there.**

2.3 **Supports the Out of Africa hypothesis, as it implies Homo sapiens originated in Africa and migrated outward, replacing other hominins in Europe and Asia.**

Examiner feedback: Many students misread the question and attempted to explain natural selection or argued for and against each of the hypothesis.

[3]

[Total: 8]

Section B

Answer **ONE** question in this section.

Write your answers on the lined paper provided at the end of this Question Paper.
Your answers should be illustrated by large, clearly labelled diagrams, were appropriate.
Your answers must be in continuous prose, where appropriate.
You answers must be set out in parts **(a)**, **(b)**, etc., as indicated in the question.

4 **(a)** DNA replication is necessary for cell division. In cancer, cells divide rapidly and uncontrollably, making the DNA replication process an important target for treatment. Some chemotherapeutic drugs interfere with DNA replication by inhibiting enzymes or adding chemical groups such as alkyl groups to DNA bases, which disrupt the DNA structure.

Suggest how chemotherapeutic drugs can interfere with DNA replication to slow cancer progression. Include possible side effects of such treatments. [13]

Some mechanisms of Chemotherapy drugs targeting DNA replication:

- **Inhibition of enzymes involved in DNA replication**
- **Mimicking DNA building blocks, causing replication errors**
- **Disrupting structure of DNA**

Inhibition of enzymes during Initiation Stage

1. **Inhibition of helicase** prevents unwinding of the DNA double helix, halting formation of replication forks.
2. **Inhibition of single-stranded binding proteins** (SSBs) allows reannealing of DNA strands, blocking replication.
3. **Inhibition of topoisomerase** prevents relaxation of supercoiling ahead of the fork, stalling progression.

Inhibition of enzymes during Elongation stage

4. **Inhibition of primase** prevents synthesis of RNA primers, so DNA polymerase cannot initiate synthesis.
5. **Inhibition of DNA polymerase III** blocks elongation of new strands, preventing replication.
6. **Use of nucleotide analogues** (e.g. 5-fluorouracil, gemcitabine) disrupts base pairing or causes premature chain termination. [AVP: Idea of mimicking DNA building blocks]
7. **Alkylating agents** add alkyl groups to DNA bases, disrupting DNA structure and interfering with DNA replication [AVP: Idea of adding components which disrupts structure of DNA]

Inhibition of enzymes during Termination

8. **Inhibition of DNA polymerase I** prevents replacement of RNA primers with deoxyribonucleotides
9. **Inhibition of DNA polymerase I** affects proofreading, leading to accumulation of mutations and potentially non-functional proteins.
10. **Inhibition of DNA ligase** prevents joining of Okazaki fragments, leaving the lagging strand incomplete.

Inhibition of enzymes that help with end replication problem

11. **Inhibition of telomerase** exacerbates the end replication problem, leading to telomere shortening and senescence.

Inhibition of enzymes involved in chromatin remodelling

12. **Inhibition of histone acetyltransferase** prevents the addition of acetyl groups to histone, keeping DNA condensed
13. **Inhibition of DNA demethylase** prevents the removal of methyl groups on DNA, keeping DNA condensed

Consequences to Cell Cycle (during S phase)

14. Inhibiting DNA replication increases DNA damage
15. Fails G2 checkpoint, unable to proceed to mitosis
16. Leading to cell cycle arrest, apoptosis, or senescence.
17. Uncontrolled cell division disrupted, cancer progression is slowed

Possible side effects

18. These drugs may also target DNA replication in non-cancerous, rapidly dividing cells, such as those in the gut lining, hair follicles, and bone marrow, leading to side effects like nausea, hair loss, and immunosuppression.

QWC – Quality of Written Communication

Criteria	Descriptors (specific to DNA Replication)	Mark
Scientific Language	Uses correct biological terms such as **helicase**, **DNA polymerase III**, **Okazaki fragments**, **telomerase**, **nucleotide analogues**, and **alkylating agents** accurately throughout the explanation.	✓ / ✗
Logical Structure and Flow	Information is logically grouped by **stages of DNA replication** (initiation, elongation, termination, end-replication), followed by **cell cycle consequences** and **side effects**. Clear progression of ideas.	✓ / ✗
Clarity and Precision	Sentences clearly explain **the mechanisms of inhibition** and **effects on replication** with no ambiguity. Side effects are precisely linked to **non-cancerous dividing cells**.	✓ / ✗

Award 1 bonus mark for QWC if all 3 criteria are met.
Award **0** if **any one** criterion is not fully met.

Examiner's feedback:

Most candidates manage to highlight some targets of chemotherapeutic drugs in DNA replication. Some **common issues identified include**:

1. Time Management:
Many candidates wrote overly long answers (often not relevant to the question) for this question, leaving insufficient time for the next question.

2. Understanding Question Requirements:

- Many did not annotate or plan before writing, leading to unfocused and excessively long essays (double penalisation: lack of structure + wasted time).
- Several misinterpreted the scope, focusing ***on transcription, translation, or gene expression*** instead of DNA replication.
- Others treated the question as a depth essay, writing detailed accounts of general mechanisms (e.g., competitive vs non-competitive inhibition, histone acetylation & DNA methylation) rather than demonstrating breadth across DNA replication mechanisms.

- Some ignored the fact that the question had **three components**:
  (i) chemotherapeutic drugs on DNA replication,
  (ii) impact on cancer progression
  (iii) possible side effects.

3. DNA Replication Component

- Some answers only listed enzymes (helicase, ligase, etc.) with no elaboration, while others wrote excessively detailed accounts instead of concise mechanisms.
- Single-stranded binding proteins (SSBs) were frequently omitted.
- Primase was confused with RNA polymerase, showing weak understanding of DNA replication, confusion with Transcription
- Many did not recognise the two distinct functions of DNA polymerase I (primer replacement and proofreading).
- Telomerase was often missed, showing weak connection of concepts DNA replication and end replication problem.
- Candidates failed to use the preamble clue alkylating *agents*, which was creditworthy.
- DNA alkylation ≠ DNA methylation, which are different processes.
  - ***DNA alkylation*** is the addition of any alkyl group to a DNA base, causing DNA damage and potential mutations,
  - ***DNA methylation*** is a specific type of alkylation involving the addition of a methyl group, which functions as a key epigenetic regulator controlling gene expression rather than causing damage.
- Some students manage to introduce nucleotide analogues, which is a good extrapolation from their knowledge, showing good understanding.

4. Cancer Progression Component

- Many failed to link inhibition of DNA replication to **cell cycle checkpoints**, especially the **G2 checkpoint**.
- Instead of explaining how cells undergo arrest, apoptosis, or senescence, some gave vague statements like “cancer progression is slowed”

5. Side Effects Component

- Many did not recognise that **healthy, rapidly dividing cells** (gut lining, hair follicles, bone marrow) are also affected. Instead, answers focused only on outcomes such as “hair loss” or “immunosuppression” without linking these to affected cell types.
- Some candidates wrote at length about **mutations** in cancer cells, which was not the focus of this part of the question.
- A few incorrectly described **drug limitations** such as cost as “side effects,” which was not creditworthy.

Moving Forward

Candidates should:

- **Manage time carefully** and plan/annotate essays before writing.
- Identify the **exact scope** of the question and structure responses around the three required components.
- Identify if it is a **breadth or depth essays**, covering a range of mechanisms rather than excessive depth in one.
- **Identify all biological concepts** involved in the question, then explicitly link them to form a proper narrative.
  - E.g. Inhibition of DNA replication → cell cycle checkpoints (G2) → apoptosis or senescence → cancer.

(b) Cells synthesise a variety of macromolecules essential for life, including carbohydrates, lipids, and proteins. Many of these macromolecules are polymers formed by the repeated linking of monomers.

Describe how the structure of different biomolecules and formation of polymers enables the storage of glycogen in liver cells. [12]

Revised Mark Scheme

Lipids – Phospholipids (max 4 marks)

1. [Structure] Phospholipids consist of a [glycerol] backbone, [two fatty acid tails], and a [phosphate group];
2. [Formation] These components are joined by [ester bonds] formed through [condensation reactions];
3. [Structure] Their [amphipathic nature] (hydrophilic phosphate head and hydrophobic fatty acid tails) allows them to form [phospholipid bilayers];
4. [Function] These bilayers form [cell surface membranes] and [organelle membranes], compartmentalising liver cells and supporting glycogen-related signalling and transport;

Proteins – Membrane Proteins, Enzymes, and Regulatory Proteins (Max 8 marks)

5. [Formation] Proteins are polymers of [amino acids] joined by [peptide bonds] through [condensation reactions];
6. [Structure] Polypeptides fold into [tertiary or quaternary structures] stabilised by [hydrogen bonds, ionic bonds, disulfide bridges], and [hydrophobic interactions];

Receptors:

7. [Structure] The [insulin receptor] is a [receptor tyrosine kinase] with an extracellular ligand-binding domain and an intracellular kinase domain;
8. [Function] Upon insulin binding, the receptor activates a signalling cascade that promotes [glucose uptake] and [glycogen synthesis] by activating [glycogen synthase];

Transport Proteins:

9. [Function] [GLUT2] is a glucose transporter that enables [facilitated diffusion] of glucose into hepatocytes, providing the substrate for glycogen synthesis;

Enzymes:

10. [Structure] [Glycogen synthase] has an active site that binds [UDP-glucose] and facilitates glycogen elongation;
13. [Function] It catalyses the formation of [α-1,4 glycosidic bonds] to elongate glycogen chains;
11. [Function] [Branching enzyme] introduces [α-1,6 linkages], creating branches that increase glycogen's solubility and accessibility;

Regulation:

12. [Function] [Protein kinases and phosphatases] regulate the activation/inactivation of enzymes by [phosphorylation] and [dephosphorylation], toggling between glycogen synthesis and breakdown;

Carbohydrates – Glycogen (max 4 marks)

16. [Structure] Glycogen is a [branched polysaccharide] made of repeating [α-glucose] monomers;
17. [Formation] Glucose monomers are joined by [α-1,4 glycosidic bonds] with [α-1,6 bonds] at branch points, all formed via [condensation reactions];
18. [Structure] The molecule is [compact], [highly branched], and [insoluble];
19. [Function] Its insolubility prevents glycogen from disrupting the [osmotic potential] of the liver cell;
20. [Function] Its branched structure provides multiple [terminal glucose residues] for rapid mobilisation or synthesis of glucose;

Nucleic Acids – DNA and mRNA (max 4 marks)

21. [Formation] DNA and RNA are polymers of [nucleotides] joined by [phosphodiester bonds] through [condensation reactions];
22. [Function] DNA stores genes coding for [glycogen synthase, receptors, and transporters] essential for glycogen metabolism;
23. [Function] Transcription produces [mRNA] that carries the genetic instructions to [ribosomes] for protein synthesis;
24. [Function] Translation of mRNA allows production of enzymes and receptors needed to regulate [glycogen synthesis and breakdown];

QWC – Quality of Written Communication

Criteria	Descriptors (specific to Biomolecules)	Ma
Scientific Language	Correct terminology is used throughout (e.g. *glycerol*, *fatty acids*, *phosphate group*, *peptide bonds*, *glycosidic bonds*, *nucleotide*, *phosphodiester bonds*).	✓ /
Logical Structure and Flow	Biomolecules are clearly grouped by type (lipid, protein, carbohydrate, nucleic acid), and each follows a logical pattern: **monomer/component → formation → structure → function**.	✓ /
Clarity and Precision	Each biomolecule is described precisely, linking structure to function relevant to glycogen storage and metabolism (e.g. **"7 alpha-helices"**, **"branching improves storage"**).	✓ /

Award 1 bonus mark for QWC if all 3 criteria are met.
Award **0** if **any one** criterion is not fully met.

Examiner's feedback:
This question exposed several weaknesses in candidates' exam technique and understanding of the scope of the content. The most significant issue was poor time management. A considerable number of candidates produced overly short responses for a 12-mark question, often written hastily in messy handwriting and without clear organisation. Some left the question largely unattempted. This suggests that candidates may not have allocated sufficient time to plan and structure their answers, leading to responses that were incomplete or lacking in coherence.

Another issue was misinterpretation of the question requirements. The scope was clearly directed at polymers involved in glycogen storage, yet some candidates included irrelevant polymers such as cellulose, haemoglobin, triglycerides or starch. This reflected a failure to read the context carefully and to identify what the question was asking.

Even among those who recognised glycogen as relevant, many went into unnecessary depth describing its structure and properties. The question, however, required breadth rather than depth. Candidates were expected to identify one example of a polymer from each class of biomolecules associated with glycogen storage. For instance, in the carbohydrate class, glycogen itself should have been mentioned; in the lipid class, the phospholipids of liver cell membranes could be highlighted; in the protein class, glycogen synthase should have been recognised; and in the nucleic acid class, the gene coding for glycogen synthase could have been included. Those who failed to demonstrate this breadth lost out on significant credit.

A further common error was the confusion between glycogen and starch. Several candidates wrongly described glycogen as being made up of amylose and amylopectin, which are structural components of starch. This revealed gaps in knowledge of the distinctions between different storage polysaccharides.

For improvement, students should ensure that they allocate time proportionate to the marks available and present their answers in a clear, organised manner. They should carefully read the question to determine its scope, paying attention to whether breadth or depth is required. Finally, they must review and consolidate their understanding of key storage polymers to avoid fundamental misconceptions such as conflating starch with glycogen.

[Total: 25]

5 (a) Explain how the structure of nucleic acids enables accurate transmission and regulation of genetic information from one cell generation to the next.

[13]

I. DNA – Deoxyribonucleic Acid (15 marks)

1. **[Structure]** DNA is composed of [two antiparallel strands] forming a [double helix];
2. **[Structure]** The strands are held together by [hydrogen bonds] between complementary bases: A-T and G-C;
3. **[Structure]** The [sugar-phosphate backbone], linked by strong [phosphodiester bonds], provides chemical stability and resists degradation, protecting the integrity of genetic information;
4. **[Structure]** [Hydrophobic base stacking interactions] between nitrogenous bases in the core of the helix enhance structural stability;
5. **[Transmission]** The [complementary base pairing] enables [each strand to act as a template] during replication, ensuring base accuracy;
6. **[Transmission]** The [double-stranded nature] allows [semi-conservative replication], where each new molecule retains one original strand;
7. **[Transmission]** DNA polymerases recognise the structure of the [3' hydroxyl end] to synthesise in the 5' to 3' direction, controlling strand elongation;
8. **[Transmission]** The [template (non-coding) strand of DNA] provides the sequence used by RNA polymerase during transcription to synthesise a complementary mRNA strand;
9. **[Regulation]** DNA is wrapped around [histone proteins], and chromatin remodelling controls gene access;
10. **[Regulation]** The [methylation of cytosine bases] alters chromatin structure, allowing [long-term silencing of genes];
11. **[Regulation]** Specific [promoter sequences] within the DNA serve as structured binding sites for transcription factors;
12. **[Transmission]** The [supercoiled chromatin structure], further compacted into [chromosomes], enables efficient DNA packing and ensures even segregation during mitosis and meiosis;
13. **[Transmission]** The [repetitive telomeric sequences] at chromosome ends prevent degradation and preserve coding regions, supporting genomic integrity across divisions;
14. **[Transmission]** The [centromeric DNA region] recruits [kinetochore proteins], ensuring correct attachment to spindle fibres and equal segregation of sister chromatids;
15. **[Transmission]** The [hydrophobic interactions and base stacking] between nitrogenous bases contribute to helical stability, helping preserve DNA structure for accurate replication and transcription;

II. mRNA – Messenger RNA (6 marks)

16. **[Structure]** mRNA is a [single-stranded polymer] with a linear sequence of codons complementary to the DNA template;
17. **[Structure]** mRNA includes [untranslated regions (UTRs)] that influence translation efficiency and stability;

18. **[Transmission]** This structure allows mRNA to be [threaded through ribosomes], translating genetic information into amino acid sequences;
19. **[Transmission]** The presence of [start (AUG) and stop codons] in mRNA defines the correct reading frame and termination point, ensuring accurate translation of genetic information into polypeptides;
20. **[Regulation]** Post-transcriptional modifications — [5' cap and 3' poly-A tail] — protect the mRNA from degradation and facilitate ribosome binding;
21. **[Regulation]** The exon-intron structure of pre-mRNA allows for [alternative splicing], generating different proteins from the same gene;

III. tRNA – Transfer RNA (3 marks)

22. **[Structure]** tRNA has a [cloverleaf shape] with an [anticodon loop] and a [3' amino acid attachment site];
23. **[Transmission]** The anticodon loop allows specific [base pairing with mRNA codons], ensuring that the correct amino acid is delivered during translation;
24. **[Regulation]** Structural base modifications in tRNA (e.g., inosine in the anticodon) allow [wobble pairing], influencing codon flexibility and translation rate;

IV. rRNA – Ribosomal RNA (3 marks)

25. **[Structure]** rRNA folds into [complex secondary structures] and combines with proteins to form the ribosome;
26. **[Transmission]** The ribosome's structure allows [accurate alignment of mRNA and tRNA], ensuring correct translation of the genetic message;
27. **[Regulation]** The [rRNA active site] catalyses peptide bond formation and regulates the [rate of elongation] during translation;

QWC – Quality of Written Communication

Criteria	Descriptors (specific to nucleic acid topic)	Mark
Scientific Language	Accurate and consistent use of key molecular biology terms	✓ / ✗
Logical Structure and Flow	Clear sequence. Ideas flow smoothly with logical transitions between sections.	✓ / ✗
Clarity and Precision	Sentences are concise and precise. Ideas are clearly expressed with no ambiguity. Technical details are well-integrated into explanations.	✓ / ✗

Award 1 bonus mark for QWC if all 3 criteria are met.
Award **0** if **any one** criterion is not fully met.

Examiner's feedback:
A major weakness in this question was once again poor time management. Many candidates produced responses that were far too short for a 13-mark question, often written in messy handwriting and without clear organisation. Some responses were left incomplete or not attempted at all, indicating that insufficient time was allocated for this question. Candidates are reminded that the length, structure and level of detail in their answers should be proportionate to the marks available, and that clear organisation is essential for examiners to follow their reasoning.

The question required students to draw on learning outcomes related to the structure of nucleic acids and to explain how structural features enable the accurate transmission of genetic information through replication, transcription and translation, as well as how they enable regulation at the transcriptional and translational levels. However, many responses focused too narrowly on DNA. Instead of demonstrating breadth across all relevant nucleic acids, students went into unnecessary depth about DNA structure alone. The stronger answers were those that included relevant points from each nucleic acid: DNA, mRNA, tRNA and rRNA.

Another common problem was the inclusion of irrelevant details. For example, some candidates described amino acid activation in protein synthesis or elaborated at length on the full process of DNA replication. These digressions were not creditworthy because they did not address the structural features of nucleic acids or their role in information transmission and regulation, which was the focus of the question.

To improve, candidates should pay careful attention to the scope of the question and avoid writing everything they know about a familiar topic. Instead, they should identify the key structural features of each nucleic acid and link these features directly to their roles in replication, transcription, translation and regulation. A concise but broad approach that spans DNA, mRNA, tRNA and rRNA will yield more marks than an overly detailed account of one molecule. Effective planning before writing will also help ensure that responses are well structured, comprehensive and proportionate to the marks available.

(b) With reference to blood stem cells, explain how ligand-receptor interactions and downstream signaling regulate stem cell activity in the body.

[12]

Marking Points (Max: 12 marks)

Note: Award 1 mark per correct point. Points must be biologically valid, relevant, and not repeated.

A. Stem Cell Fundamentals (CI1.5)

1. Blood stem cells are multipotent stem cells that give rise to lymphoid and myeloid lineages.
2. These stem cells function to replenish blood cell types (e.g. red blood cells, neutrophils, lymphocytes).
3. Stem cells maintain balance between self-renewal and differentiation to sustain blood cell production. (asymmetrical differentiation)

B. Ligand-Receptor Interaction (CI3.3)

4. Stem cell activity is regulated by **extracellular signaling molecules** (ligands) in the stem cell niche.
5. Ligands (e.g. growth factors or cytokines) bind to specific **cell surface receptors** on stem cells.
6. Ligand binding induces a **conformational change** in the receptor.
7. In receptors such as tyrosine kinase receptors, this triggers **autophosphorylation** of intracellular domains.
8. In G-protein coupled receptors (if applicable), ligand binding activates the **G-protein subunits**.

C. Signal Transduction & Amplification (CI3.3)

9. Signal is relayed through a **phosphorylation cascade** involving intracellular kinases.
10. **Second messengers** such as cyclic AMP (cAMP) may amplify the signal inside the cell.
11. Signal amplification ensures a small ligand quantity results in a large cellular response.

D. Cellular Response (CI3.3, CI1.5 Integration) – Max 3 marks

12. Chromatin remodelling – Histone Acetyltransferase
13. Chromatin remodelling – DNA methylation
14. Final cellular response may involve **activation of transcription factors (activators/ repressors)**.
15. Gene expression changes can promote either **stem cell self-renewal** or **differentiation**.
16. The nature of the response depends on **ligand identity, receptor type, and cellular context**.
17. This tight regulation ensures stem cells respond appropriately to physiological needs, such as increased red blood cell production during blood loss.

QWC – Quality of Written Communication

Criteria	Descriptors (specific to stem cells and signalling)	Mark
Scientific Language	Consistently uses accurate terminology related to stem cells and signalling (e.g. *multipotent*, *ligand-receptor interaction*, *phosphorylation cascade*, *gene expression*, *differentiation*).	✓ / ✗
Logical Structure and Flow	Ideas are presented in a clear sequence: stem cell context → receptor-ligand interaction → signal transduction → resulting cellular outcome. Transitions between concepts are smooth.	✓ / ✗

Clarity and Precision	Sentences are well-constructed, with precise phrasing. No ambiguity or confusion in explaining cause-effect relationships in signalling and stem cell regulation.	✓ / ✗

Award 1 bonus mark for QWC if all 3 criteria are met.
Award **0** if **any one** criterion is not fully met.

Examiner's feedback:
Most candidates showed some awareness of stem cells as multipotent and their role in producing different blood cell lineages. However, many struggled to connect this with the molecular details of receptor-ligand interactions and downstream signalling
Common Issues include:

Time Management & Planning
- A noticeable number of candidates did not attempt this question due to poor time allocation on earlier questions.
- Among those who attempted, weak planning led to answers that were either overly descriptive of stem cells alone, or signalling alone, without integration.

Scope Misinterpretation
- Many focused exclusively on stem cell types (multipotent, pluripotent, totipotent), rather than addressing regulation by signalling.
- Others regurgitated generic signalling pathways (insulin/glucagon and blood glucose regulation), with responses unrelated to stem cell differentiation.
- Very few candidates explicitly linked **extracellular signals** to **self-renewal/differentiation** in blood stem cells.

Cell Signalling Pathways
- **Strengths**: Ligand-receptor interactions were generally well described, and candidates demonstrated knowledge of second messengers, phosphorylation cascades, and signal amplification.
- **Weaknesses**:
  - Many failed to state clearly that the ligand must be complementary to its receptor, an important conceptual point.
  - Cellular responses were poorly described: candidates rarely went beyond "gene expression" to describe the role of transcription factors, chromatin remodelling, or how such regulation directs stem cell fate decisions.
  - Answers often lacked contextualisation — e.g. connecting signalling outcomes to **differentiation into blood cell lineages**.

Moving Forward, students should:
- Allocate time effectively and plan essays with annotations
- Stay focused on the **specific context** (blood stem cells) rather than drifting to unrelated pathways.
- Strengthen knowledge of **cellular responses**, especially transcription factor activation and chromatin-level regulation, and always link these back to **self-renewal or differentiation** of stem cells.
- Practise writing with logical sequencing: *Stem cell context → Ligand-receptor binding → Signal transduction → Gene expression & regulation → Differentiation outcome* (contextualised to question)

[Total: 25]