HWA CHONG INSTITUTION
JC2 Preliminary Examinations
Higher 2

CANDIDATE NAME		**CT GROUP**	23S7__

CENTRE NUMBER		**INDEX NUMBER**	

BIOLOGY

9744/03

Paper 3 Long Structured and Free-response Questions

10 September 2024

Candidates answer on the Question Paper.

2 hours

No Additional Materials are required.

INSTRUCTIONS TO CANDIDATES

There are **four** question booklets (**I - IV**) to this paper. Write your **name, CT group, Centre number** and **index number** in the spaces provided at the top of this cover page and on the lines provided at the top of the cover pages of Booklets **II, III** and **IV**.

Write in dark blue or black pen.

You may use an HB pencil for any diagrams or graphs

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.

INFORMATION FOR CANDIDATES

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.

You are reminded of the need for good English and clear presentation in your answer.

For Examiners' Use	
Section A	
1	/ 30
2	/ 10
3	/ 10
Section B	
4 or 5	/ 25
Final Mark	

This document consists of **20** printed pages.

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SECTION A

Answer **all** the questions in this section.

QUESTION 1

Multistep signalling pathways control cellular functions through complex protein interactions. When some these pathways are dysregulated, it can lead to uncontrolled cell growth and cancer.

(a) Outline the advantages of having such multistep pathways.

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..... [2]

Chronic inflammation is known to contribute to cancer development. Researchers are examining how signalling molecules like interleukin-6 (IL6), a cytokine, is important for the body's response to infection and inflammation.

Fig. 1.1 shows the IL6 signalling pathway. IL6 binds to its receptor, IL6R. The complex binds with gp130, which functions similarly to a receptor tyrosine kinase (RTK). The tyrosine kinase on gp130, JAK, activates downstream pathways that drive inflammation.

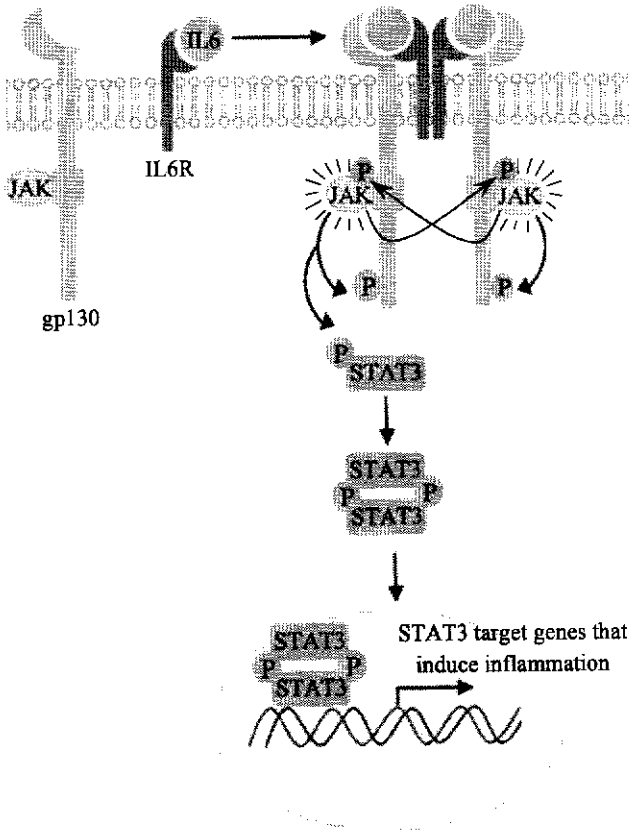

Fig. 1.1

(b)(i) Explain why IL6 cannot act directly on the DNA in the nucleus.

[2]

(ii) Based on your knowledge on RTKs and with reference to Fig. 1.1, explain how IL6 leads to a cellular response.

[5]

(iii) STAT3 activation is regulated by negative feedback. When STAT3 activation is excessive, more SOCS3 protein is synthesised, leading to ubiquitination of gp130.

Suggest how regulation of STAT3 activation is an example of negative feedback.

[3]

To understand the role of gp130 and IL6R on the IL6 signalling pathway, further studies were conducted on cell lines *in vitro*.

The extracellular domain of gp130 is predicted to have six individual regions (R1-R6) as shown in Fig. 1.2. To investigate the region(s) required for activation of the IL6 signalling pathway, researchers created 3 deletion mutants. The sites of deletions of individual regions in the mutants Δ4, Δ5, Δ6 are marked by arrowheads. For example, Δ4 mutant has a missing R4 region.

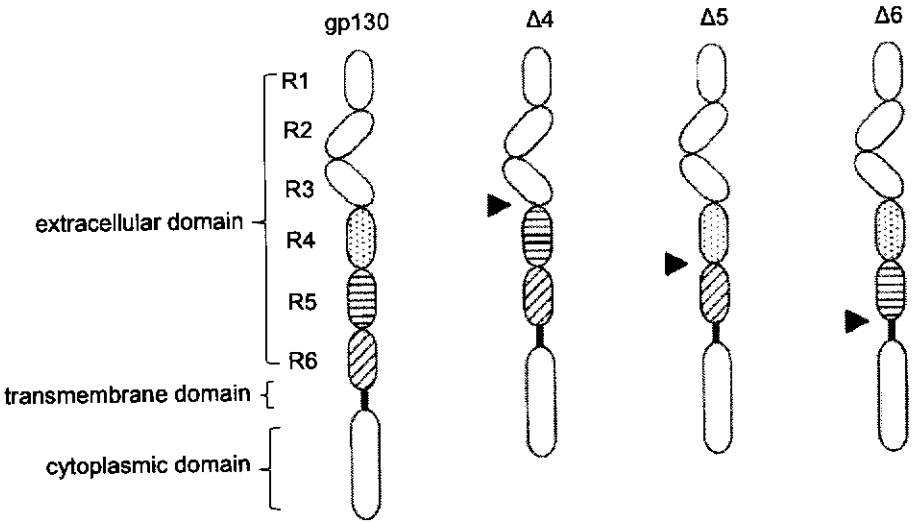

Fig. 1.2

Table 1.1 shows detection of STAT3 activation in gp130-expressing cells (wild type) and Δ4, Δ5, Δ6 mutants in the presence of IL6 and IL6R.

Table 1.1

	wild type	mutants		
		Δ4	Δ5	Δ6
detection of STAT3 activation	yes	no	no	no

(c)(I) With reference to Fig. 1.2 and Table 1.1, identify and explain which region(s) of gp130 are required for IL6 signalling pathway.

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..... [3]

(ii) Explain how the structure of the transmembrane domain of gp130 contributes to its function.

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..... [2]

Different forms of IL6R also allow variation in IL6 signalling pathway. Fig. 1.3 shows how process **Q** at the RNA level can lead to two forms of IL6R, membrane-bound (M) and soluble form (S). Both forms can bind to the ligand IL6 and the receptor gp130.

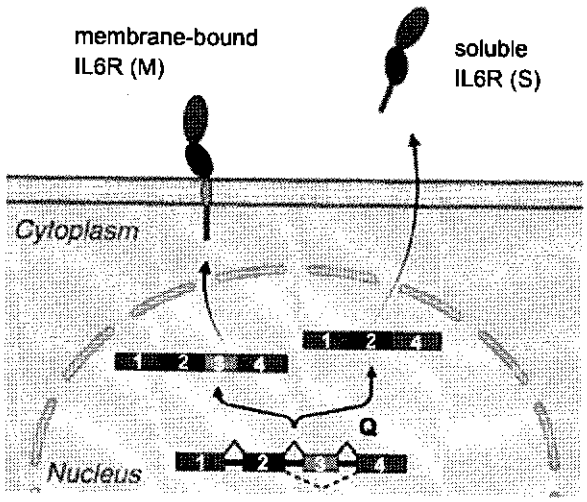

Fig. 1.3

(d) With reference to Fig. 1.3, explain the significance of process **Q** in the formation of membrane-bound and soluble forms of IL6R.

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..... [3]

The IL6 signalling pathway is associated with prolonged chronic inflammation, which promotes cancer progression, such as pancreatic ductal adenocarcinoma (PDAC).

PDAC starts in the pancreas, an organ that aids digestion and blood sugar regulation. Symptoms can include digestive issues, loss of appetite, fatigue, stomach pain and weight loss. By the time PDAC is diagnosed, it has often already spread, making early detection challenging.

(e) Suggest why early detection of PDAC is challenging.

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..... [1]

Several genes are implicated in the development of PDAC, including those in the IL6 signalling pathway, such as *gp130, STAT3, and JAK*.

Table 1.2

gene mutations	detected among PDAC patients / %
gp130	60
STAT3	5
JAK	1

(f)(i) Table 1.2 shows mutations in genes of the IL6 pathway found in the pancreas of PDAC patients. Knowledge of these mutations is crucial for developing more effective treatments to treat PDAC by targeting the chronic inflammation due to excessive IL6 signalling.

Using the information in Fig. 1.1 and Table 1.2, identify which gene is the best target for effective treatments and explain your choice.

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..... [3]

(ii) Table 1.3 shows a few genes that are often found to be mutated in PDAC patients.

With your knowledge and the relevant data provided, complete Table 1.3 to predict:

- the level of gene expression, using "↑" or "↓"
- if the gene is a proto-oncogene (POG) or tumour suppressor gene (TSG).

Table 1.3

gene	level of expression	POG or TSG
p53	↓	TSG
STAT3		
SOCS3		

[2]

Question 1 continues on page 8

(g) To investigate the effects of gp130 mutations on pancreatic cells, researchers used two groups of mice:

- group A, a control group (gp130)
- group B, with a specific gp130 deletion (gp130Δ).

Both groups were treated with diethylnitrosamine (DEN), a chemical that damages the pancreas and can induce cancer, through injections at a dose of 25 mg/kg body weight. These injections started at 14 days old and were administered at various intervals until 40 weeks of age where the pancreas were harvested.

Fig. 1.4 and 1.5 show:

- cumulative tumour diameter measured at 24 weeks of age – this reflects tumour initiation
- number of tumours counted at 40 weeks of age – this reflects tumour progression.

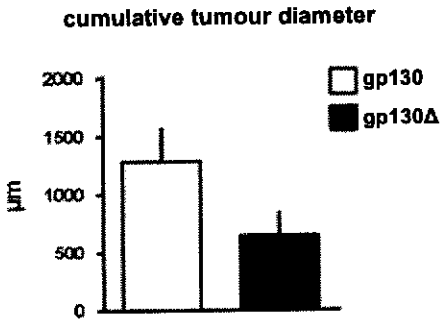

Fig. 1.4

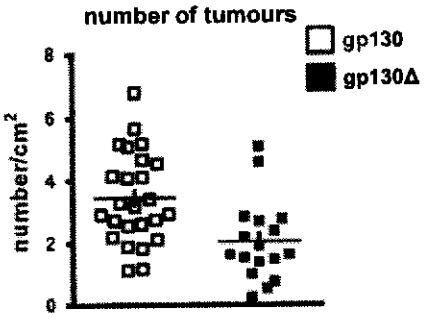

Fig. 1.5

(i) Calculate the amount of DEN to be injected into a 14-day old mouse that weighs 10 g. You should show your working.

amount of DEN injected = ... μg [1]

(ii) Discuss the effect of gp130 on tumour initiation and tumour progression.

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..... [3]

[Total: 30]

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QUESTION 2

Interferon-alpha (IFN-α) can be produced as a recombinant human protein to treat some types of cancer. The gene *IFNA2* codes for IFN-α.

One method of producing recombinant IFN-α uses genetically engineered *Escherichia coli* bacteria that contain recombinant plasmids. Each recombinant plasmid contains:

- the gene *IFNA2*
- three regulatory sequences of the *lac* operon (promoter, operator and *lacI*)
- a gene for antibiotic resistance, AMP^R.

Each of the sequences for the *lacI* gene and AMP^R gene contains its own promoter. As a result, these genes are always expressed in *E. coli* bacteria that contain this recombinant plasmid.

Fig. 2.1 is a diagram of the recombinant plasmid. The promoter regions of the *lacI* gene and AMP^R gene are **not** shown.

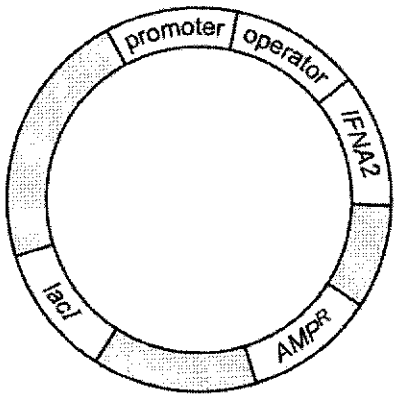

Fig. 2.1

(a) The gene *IFNA2* is obtained via reverse transcription of the mature mRNA extracted from B lymphocytes, which produce IFN-α, and ligated into the recombinant plasmid carrying the promoter and operator of the *lac* operon as shown in Fig. 2.1.

Explain why the gene *IFNA2* must be obtained via reverse transcription of the mature mRNA instead of directly from the genome of B lymphocytes.

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..... [2]

(b) The start of transcription of the gene *IFNA2* by *E. coli* with the recombinant plasmid shown in Fig. 2.1 needs to be controlled to obtain an optimum yield of IFN-α.

Scientists investigated the effect of two inducers of transcription on the production of recombinant IFN-α:

- lactose, which is converted to allolactose in *E. coli*
- IPTG, which is a synthetic molecule with a very similar structure to allolactose. IPTG **cannot** be broken down by *E. coli*.

The scientists grew three cultures of *E. coli* containing the recombinant plasmid in the same growth medium. The growth medium contained glucose, amino acids, essential vitamins, minerals and antibiotic ampicillin. The growth medium did **not** contain lactose.

After four hours, either lactose or IPTG at the same concentration was added to two of the cultures of *E. coli*. As a control, the third culture of *E. coli* was grown without adding lactose or IPTG.

The concentration of recombinant IFN-α in the cultures was measured at different time over a period of 28 hours. The results are shown in Fig. 2.2.

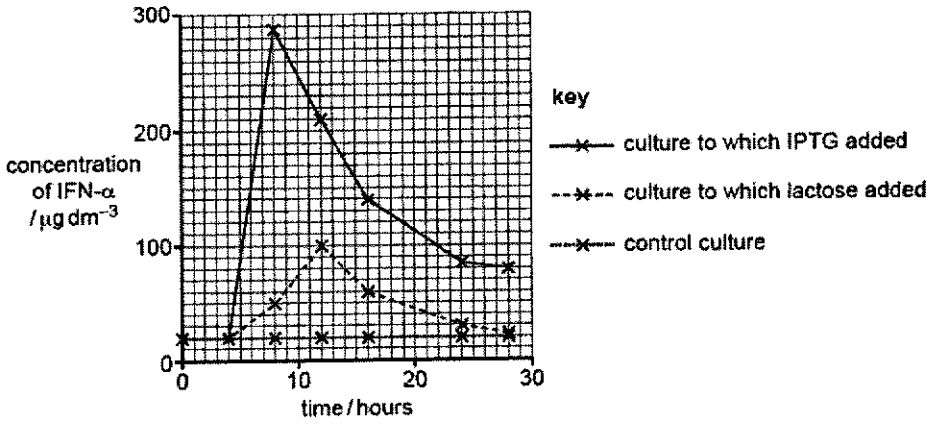

Fig. 2.2

(i) The regulatory sequences of the *lac* operon contained in the recombinant plasmid are involved in the control of transcription of the gene *IFNA2*.

Explain the role of the gene *lacI* in the control of transcription of the *IFNA2* gene between **0 hours** and **4 hours**.

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..... [2]

(ii) With reference to Fig. 2.2, describe the changes in the concentration of recombinant IFN-α in the culture containing IPTG from when IPTG was added at **4 hours** to the end of the experiment at **28 hours**.

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..... [3]

(iii) Suggest **two** reasons for the difference between the concentration of recombinant IFN-α in the culture at **8 hours** in the presence of lactose and the concentration of recombinant IFN-α in the culture at **8 hours** in the presence of IPTG.

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..... [2]

(c) The gene *AMP*^{R} in the plasmid shown in Fig. 2.1 codes for a protein that provides resistance to the antibiotic ampicillin.

Suggest how *AMP*^{R} allows genetically engineered *E. coli* containing the recombinant plasmid to be identified.

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..... [1]

[Total: 10]

QUESTION 3

Many species of plants in the genus *Ipomoea* are grown for their attractive flowers.

(a) The common morning glory, *Ipomoea purpurea*, has a gene that determines flower colour.

The gene has two alleles:

- a dominant allele that results in purple flowers
- a recessive allele that results in red flowers.

A student recorded the flower colour of all the *I. purpurea* plants in a field. There were 660 plants with purple flowers and 440 plants with red flowers.

Assuming that the Hardy-Weinberg principle applies to this population, calculate the number of plants in the field that are heterozygous.

Use the equations: $p + q = 1$

$p^2 + 2pq + q^2 = 1$

Show your working and give your answer to the nearest whole number.

number of heterozygous plants = ... [3]

(b) The Japanese morning glory, *I. nil*, has over 20 different flower colour phenotypes, including shades of blue, purple, red and pink.

The flower colour of *I. nil* is controlled by at least four genes. The flower colour can change gradually after the flowers open each morning and can change with fluctuations in the carbon dioxide concentration of the surrounding air.

A student concluded that flower colour in *I. nil* shows continuous variation.

Explain why the student made this conclusion.

1 .....

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2 .....

..... [2]

(c) Scientists investigated the response of stomata to changing carbon dioxide (CO_2) concentrations in the beach morning glory, *I. pes-caprae*.

The scientists placed *I. pes-caprae* plants in chambers. They measured the width of open stomata (stomatal apertures) after the plants had been exposed to different CO_2 concentrations for 40 minutes. Light intensity and temperature were kept constant.

The relationship between CO_2 concentration and the mean width of stomatal apertures is shown in Fig. 3.1.

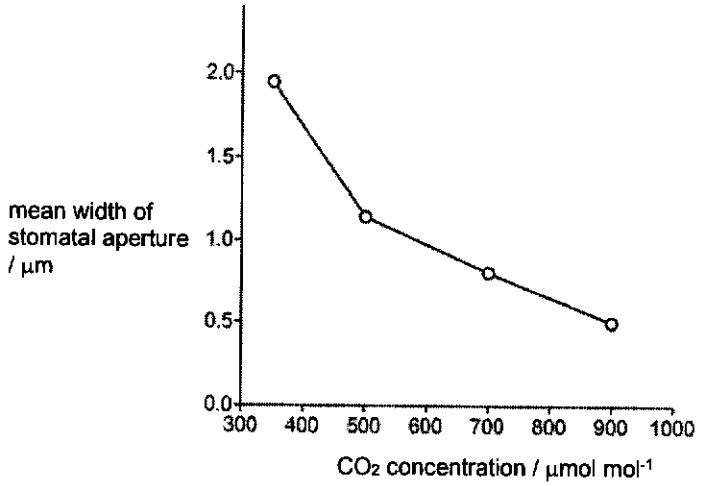

Fig. 3.1

(i) The current atmospheric CO_2 concentration is 400 μmol mol^{-1}.

In the future, climate change may reduce water availability and increase atmospheric CO_2 concentrations in some habitats.

Explain how the stomatal response shown in Fig. 3.1 would allow *I. pes-caprae* to survive the effects of climate change.

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..... [3]

(ii) It has been hypothesised that an increase in atmospheric CO_2 concentrations might result in an increase in the rate of photosynthesis and consequently, an increase in growth of plants.

Suggest why there might not be significant increase in growth of *I. pes-caprae* plants despite increase in atmospheric CO_2 concentrations.

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..... [2]

[Total: 10]

--- END OF SECTION A ---

SECTION B

Answer **one** question in this section.

Write your answers on the lined paper provided at the end of this Question Paper.

Your answer should be illustrated by large, clearly labelled diagrams, where appropriate.

Your answers must be in continuous prose, where appropriate.

Your answers must be set out in parts **(a)** and **(b)**, as indicated in the question.

QUESTION 4

(a) Describe the features of DNA structure that allow DNA to stably store and accurately replicate large amount of genetic information. [15]

(b) Discuss how the processes of cell division allow DNA to be stably inherited and yet, capable of genetic variation in eukaryotes. [10]

[Total: 25]

QUESTION 5

(a) Describe the features of the processes of aerobic respiration that allow energy from a glucose molecule to be harnessed. [15]

(b) Discuss the significance of membranes in aerobic respiration. [10]

[Total: 25]

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--- END OF SECTION B ---

--- END OF PAPER---

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2024 JC2 9744 H2 BIOLOGY
PRELIMINARY EXAMINATIONS PAPER 3 MARK SCHEME

QUESTION 1

(a) Outline the advantages of having such multistep pathways. [2]

1. ref. to signal amplification
2. ref. to coordination / regulation
3. ref. to specificity of response

(b)(i) Explain why IL6 cannot act directly on the DNA in the nucleus. [2]

1. IL-6 is hydrophilic
2. cannot pass through cell membrane

(ii) Based on your knowledge on RTKs and with reference to Fig. 1.1, explain how IL6 leads to a cellular response. [5]

1. IL6-IL6R complex binds to gp130
2. gp130 dimerises
3. ref. to cross-phosphorylation
4. JAK phosphorylates STAT3
5. dimerised STAT3 activate expression of gene

(iii) Suggest how regulation of STAT3 activation is an example of negative feedback. [3]

1. ref to. relevant stimulus
2. ref. to gp130 degraded
3. ref. to idea of negative feedback in this context

(c)(i) With reference to Fig. 1.2 and Table 1.1, identify and explain which region(s) of gp130 are required for IL6 signalling pathway. [3]

1. ref. to R4, R5, R6 required
2. ref. to relevant supporting data from Fig. 1.2
3. ref. to relevant supporting data from Table 1.1

(ii) Explain how the structure of the transmembrane domain of gp130 contributes to its function. [2]

1. ref. to hydrophobic nature
2. ref. to embedding of gp130 within membrane

(d) With reference to Fig. 1.3, explain the significance of process **Q** in the formation of membrane-bound and soluble forms of IL6R. [3]

1. ref. to alternative splicing
2. ref. to relevant supporting data from Fig. 1.3
3. ref. to relevant supporting data from Fig. 1.3

(e) Suggest why early detection of PDAC is challenging. [1]

ref. to any valid reason

(f)(i) Using the information in Fig. 1.1 and Table 1.2, identify which gene is the best target for effective treatments and explain your choice. [3]

1. gp130 gene
2. ref. to relevant supporting data from Fig. 1.1
3. ref. to relevant supporting data from Table 1.2

(ii) Table 1.3 shows a few genes that are often found to be mutated in PDAC patients.
With your knowledge and the relevant data provided, complete Table 1.3 to predict:

- the level of gene expression, using "↑" or "↓"
- if the gene is a proto-oncogene (POG) or tumour suppressor gene (TSG).

Table 1.3

gene	level of expression	POG or TSG
p53	↓	TSG
STAT3	↑	POG
SOCS3	↓	TSG

[2]

(g)(i) Calculate the amount of DEN to be injected into a 14-day old mouse that weighs 10 g. You should show your working. [1]

250 µg

(ii) Discuss the effect of gp130 on tumour initiation and tumour progression. [3]

1. gp130 promotes tumour initiation and progression
2. ref. to relevant supporting data from Fig. 1.4
3. ref. to relevant supporting data from Fig. 1.5

[Total: 30]

QUESTION 2

(a) Explain why the gene *IFNA2* must be obtained via reverse transcription of the mature mRNA instead of directly from the genome of B lymphocytes. [2]

1 mature mRNA only contains exons

2 mature mRNA is reversed transcribed to give continuous coding DNA sequence

3 *E. coli* does not have spliceosomes

(b)(i) Explain the role of the gene *lacI* in the control of transcription of the *IFNA2* gene between **0 hours** and **4 hours**. [2]

1 *lacI* is regulatory gene

2 repressor binds to operator and prevents transcription

(ii) With reference to Fig. 2.2, describe the changes in the concentration of recombinant IFN-α in the culture containing IPTG from when IPTG was added at **4 hours** to the end of the experiment at **28 hours**. [3]

1 concentration of IFN-α produced increases steeply after addition of IPTG

2 peak is at 8 hours / 4 hours after addition of IPTG

3 decrease is less steep

4 correct data quoted with units

(iii) Suggest **two** reasons for the difference between the concentration of recombinant IFN-α in the culture at **8 hours** in the presence of lactose and the concentration of recombinant IFN-α in the culture at **8 hours** in the presence of IPTG. [2]

1 lactose has to be converted to allolactose

2 lactose is broken down, hence less lactose / allolactose bind to repressor

3 IPTG will be at higher concentration than allolactose

4 IPTG has higher affinity for repressor protein than allolactose

5 more IPTG enters

(c) Suggest how AMP^R allows genetically engineered *E. coli* containing the recombinant plasmid to be identified. [1]

only *E. coli* that have taken up the plasmid will grow in the presence of ampicillin

[Total: 10]

QUESTION 3

(a) Assuming that the Hardy-Weinberg principle applies to this population, calculate the number of plants in the field that are heterozygous. [3]

Show your working and give your answer to the nearest whole number.

1 use formula $p^2 + 2pq + q^2 = 1$ and total number of plants to calculate genotypic frequency

2 calculate allelic frequency of dominant and recessive alleles

3 use allelic frequencies to calculate number of heterozygous plants in the field

(b) A student concluded that flower colour in *I. nil* shows continuous variation.

Explain why the student made this conclusion. [2]

1 colours not discrete / range / include intermediates

2 more than one genes

3 environment affects colour

(c)(i) Explain how the stomatal response shown in Fig. 3.1 would allow *I. pes-caprae* to survive the effects of climate change. [3]

1 increase in CO_2 concentration causes mean width of stomatal aperture to decrease

2 less water lost through stomata

3 compensates for low water availability

(ii) It has been hypothesised that an increase in atmospheric CO_2 concentrations might result in an increase in the rate of photosynthesis and consequently, an increase in growth of plants.

Suggest why there might not be significant increase in growth of *I. pes-caprae* plants despite increase in atmospheric CO_2 concentrations. [2]

1 increased in earth surface temperature leads to an increase in the rate of enzyme-catalysed reactions

2 increase in rate of respiration, leading to loss of carbon as CO_2

[Total: 10]

QUESTION 4

(a) Describe the features of DNA structure that allow DNA to stably store and accurately replicate large amount of genetic information. [15]

S1 DNA being less susceptible to degradation
S2 2' carbon of deoxyribose having an attached hydrogen atom
S3 DNA coiling into a tight helix
S4 sugar-phosphate backbone of a DNA chain
S5 phosphodiester bonds formed between 5' phosphate and 3' hydroxyl groups
S6 phosphodiester bonds being covalent bonds
S7 double helix structure
S8 phosphate groups that project outside the double-helix
S9 exposure to outside influences of only the sugar-phosphate backbone
S10 nitrogenous bases that orientate inwards toward the central axis
S11 nitrogenous bases being safely tucked inside the double-helix
S12 extensive hydrogen bonds between base pairs
S13 hydrophobic interactions between the stacked base pairs
S14 DNA double-helix being wound around histones to form nucleosomes
S15 nucleosomes being folded into higher order structures such as solenoid / chromosome

A1 to complementary base-pairing
A2 between A and T and between C and G
A3 base sequence of one strand could determine the base sequence of its complementary strand
A4 both strands acting as <u>templates</u> for semi-conservative DNA replication
A5 genetic information being redundant / present more than once in DNA molecule
A6 use of intact strand as a template for repair
A7 base sequence along each DNA strand can be varied in countless ways
A8 each gene having a unique base sequence

(b) Discuss how the processes of cell division allow DNA to be stably inherited and yet, capable of genetic variation in eukaryotes. [10]

S1 each DNA molecule undergoing semi-conservative DNA replication
S2 production of two genetically identical (daughter) DNA molecules
S3 coiling of chromatin into discrete chromosomes
S4 preventing entanglement of chromatin and DNA breakage during the separation of genetic material
S5 chromosomes aligning singly at the metaphase plate / equatorial plate
S6 separation of sister chromatids towards opposite poles of the cell
S7 daughter chromosomes reaching the opposite poles of the cell
S8 cytokinesis as the division of the cytoplasm to produce two daughter cells
S9 each daughter cell having the complete diploid set of DNA / daughter chromosomes being distributed equally to the daughter cells

V1 pairing of homologous chromosomes
V2 crossing over between the non-sister chromatids of homologous chromosomes
V3 new combinations of paternal and maternal alleles
V4 independent assortment of homologous chromosomes
V5 random distribution of paternal and maternal chromosomes

[Total: 25]

QUESTION 5

(a) Describe the features of the processes of aerobic respiration that allow energy from a glucose molecule to be harnessed. [15]

A1 enzyme-catalysed reactions e.g. glucose / pyruvate / citrate being the substrates
A2 redox reactions
A3 substrate-level phosphorylation during glycolysis / Krebs cycle
A4 oxidative phosphorylation
A5 reduced coenzymes transfer electrons down the electron transport chain
A6 across the inner mitochondrial membrane
A7 final electron acceptor oxygen being reduced to water
A8 energy released from the electrons flowing through the ETC
A9 power the pumping of H^+ ions across the inner mitochondrial membrane
A10 to establish an proton gradient
A11 diffusion of hydrogen ions through the ATP synthase complex
A12 phosphorylation of ADP
A13 3 ATP per NADH and 2 ATP per $FADH_2$
A14 glycolysis occurring in cytosol / cytoplasm
A15 link reaction / Krebs cycle occurring in mitochondrial matrix in the presence of oxygen

(b) Discuss the significance of membranes in aerobic respiration. [10]

M1 hydrophobic core of cell surface membrane
M2 formation of an effective barrier to the movement of polar / charged molecules
M3 phosphorylated glucose being retained in cytoplasm
M4 transporter proteins allowing for facilitated diffusion such as glucose transporters (GLUT) on cell surface membrane
M5 inner mitochondrial membrane being highly folded
M6 increasing surface area for embedding electron transport chain / ATP synthase
M7 electron transport chain allowing for movement of electrons down energy levels
M8 ATP synthase catalysing phosphorylation of ADP with P_i to ATP
M9 inner mitochondrial membrane, being selectively permeable
M10 formation of proton gradient
M11 compartmentalisation
M12 intermembrane space being more acidic than the cytosol
M13 providing the optimum conditions for cytosolic enzymes to function

[Total: 25]