## 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 templates 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]