UNIVERSITY OF BOLTON

SCHOOL OF CLINICAL & BIOMEDICAL SCIENCES

BSC (HONS) MEDICAL BIOLOGY
BSC (HONS) BIOMEDICAL SCIENCE

SEMESTER ONE EXAMINATION 2024/25

MOLECULAR GENETICS

MODULE NO: BIO5008

Date: Friday 10 January 2025 **Time: 14:00 – 16:30**

INSTRUCTIONS TO CANDIDATES:

Candidates are advised that the examiners attach importance to legibility of writing and clarity of expression. YOU ARE STRONGLY ADVISED TO PLAN YOUR ANSWERS

This examination paper carries a total of 150 marks.

This examination is 2 hours and 30 minutes long.

There are TWO sections on this paper.

Section A: Answer ALL questions.

Section B: Answer TWO questions.

INSTRUCTIONS TO INVIGILATORS:

Please ensure all candidates are provided with a copy of the supplementary document

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Answer **ALL** questions in Section A and **TWO** questions from Section B.

Make use of labelled diagrams where appropriate.

Section A – answer ALL questions. Total of 50 marks available for Section A

A 20-year-old female patient, Precious, presents to A&E with severe pain in her chest, back, and joints. She has a known history of sickle cell anaemia and has had multiple hospitalizations for crises. On physical examination she appears to be in significant distress, with a heart rate of 118 beats per minute (typical adult resting heart rate is 60-100 bpm), a respiratory rate of 26 breaths per minute (normal rate 12-20 bpm), and a blood pressure of 130/85 mmHg (normal range is <120/<80 mmHg). Her oxygen saturation is 92% on room air (normal level is 95%-100%). Bloods are drawn and sent to the laboratory. The results are shown below.

Analyte	**Result**	**Reference range**
Sodium	140 mmol/L	135 – 145 mmol/L
Potassium	5.0 mmol/L	3.5 - 5.3 mmol/L
Urea	7.4 mmol/L	2.5 - 7.8 mmol/L
WBC	8 x 10^9 cells/L	4 – 11 x 10^9 cells/L
Hb	6.5 g/dL	12 – 16 g/dL
RCC (Red Cell Count)	2.9 x 10^{12} cells/L	3.8 - 5.5 x 10^{12} cells/L
Hct (Haematocrit)	0.25 L/L	0.37 - 0.47 L/L
Reticulocyte %	3.2	0.5 - 1.5
CRP	4.0 mg/L	0.6 - 5 mg/L

Table 1: Results from blood test.

1. **From the results in Table 1, identify which of these physical examination and laboratory results can be attributed to the disease and relate them to the physiological processes occurring in sickle cell crisis. [8 marks]**

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2. **Outline the genetic basis of sickle cell anaemia. What mutation causes this condition, and how does it affect the haemoglobin protein? Relate the molecular changes caused by this mutation to the symptoms of the disease.** **[8 marks]**

The A&E doctor starts Precious on supplementary oxygen and decides that she requires an urgent blood transfusion to stabilize her condition. Her previous blood grouping results are shown below:

Table 2: Blood grouping results:

Blood Group System	**Result**
ABO	A
Rh D	Positive
Rh CE	ce

3. **Using Table 2 for guidance, outline the genes involved in the production of these blood group antigens. Include the proteins produced by these genes and their roles in the production of these blood group antigens in your answer.** **[8 marks]**

4. **Elucidate the possible genotypes of this patient at the 4 genetic loci given in your answer above?** **[4 marks]**

5. **The transfusion lab issues a unit of blood with the phenotype O, Rh D negative, CE. Is this blood suitable for transfusion into this patient? Justify your answer.** **[4 marks]**

Precious feels better after her transfusion and is discharged. A week later she has a follow up appointment with her consultant haematologist. Her haematologist suggests to her that she would be a good candidate for CRISPR based gene therapy.

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6. **Explain how CRISPR gene therapy can be used to correct the genetic defect that is causing Precious's symptoms.**

[8 marks]

Precious agrees that she would like to go ahead with the CRISPR based gene-therapy. Her haemopoietic stem cells are harvested and sent to the processing laboratory. Once the gene edited cells have been created qPCR (Quantitative Polymerase Chain Reaction) is used to confirm that the desired gene is now in place before the transformed cells are transfused back into Precious. qPCR uses a combination of PCR and fluorescent probes that bind to the SNP of interest. As the DNA from Precious's CRISPR modified cells is amplified by PCR, the fluorescent probes will bind the SNP and the fluorescent signal will increase if it is present.
The sequence of the wild type haemoglobin beta gene (HBB) is given in Figure 1.

5'
ATG**GTG**CATCTGACTCCTGAGGAGAAGTCTGCCGTTACTGCCCTGTGGGGCAA
GGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGCTGCTGGTGGTC
TACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGAT
GCTGTTATGGGCAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGTGC
CTTTAGTGATGGCCTGGCTCACCTGGACAACCTCAAGGGCACCTTTGCCACAC
TGAGTGAGCTGCACTGTGACAAGCTGCACGTGGATCCTGAGAACTTCAGGCTC
CTGGGCAACGTGCTGGTCTGTGTGCTGGCCCATCACTTTGGCAAAGAATTCAC
CCCACCAGTGCAGGCTGCCTATCAGAAAGTGGTGGCTGGTGTGGCTAATGCCC
TGGCCCACAAGT**ATC**AGGGACCGGGTGTTCATAGCTAA 3'

Figure 1: DNA sequence of the WT HBB gene.

7. **Design a primer pair to be used in the qPCR reaction. Use the underlined sequence as the starting point for your primers. Calculate the C/G content and Tm to ensure that the sequences you have designed are suitable.**

[10 marks]

[Total 50 marks]

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Section B – answer TWO questions

1. Discuss in depth the process of transcription, highlighting the roles of key proteins and outlining how cells regulate this process to control gene expression.

[50 marks]

2. Over the years, the advancement of molecular genetics has been due to the development of many of the components of the "molecular toolkit". In as much detail as possible describe the following and outline how they can be used in molecular genetics:
    - DNA ligase
    - Reverse transcriptase
    - CRISPR/Cas9
    - Plasmid vector
    - DNA polymerase

[10 marks each: 50 marks total]

3. Consider the role of silent, missense and nonsense mutations in DNA and explain how, if at all, they lead to genetic disease. Give two specific examples of diseases where any of the three are the cause.

[50 marks]

4. Give two examples of gene editing tools and explain how they each could be used to cure a well-known genetic disorder of your choice. **Different disorders should be used to support each example.**

[50 marks]

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5. Alzheimer's disease is often thought of as an age-related disorder (ARD). Describe how Alzheimer's leads to neurodegeneration and outline how our growing understanding of genetics, suggests that genes may contribute more than we thought to ARDs. Other examples of ARDs may be used to support your answer.

[50 marks]

[Total 100 marks]

END OF QUESTIONS