UNIVERSITY OF GREATER MANCHESTER

SCHOOL OF HEALTH, SCIENCE AND SOCIETY

BSc (HONS) MEDICAL BIOLOGY
BSc (HONS) BIOMEDICAL SCIENCE

SEMESTER ONE EXAMINATION 2025/2026

MOLECULAR GENETICS

MODULE NO: BIO5008/BIO5028

Date: Monday 12 January 2026 **Time: 10.00 am – 12.30 pm**

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.

There are TWO sections on this paper.

Section A: Answer ALL questions.

Section B: Answer TWO questions.

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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 66-year-old female, Margaret was bought to the GP due to increasing concern by her family. She was increasingly forgetful and confused. Her daughter stated that she was often frustrated by her mental state – leading to outbursts of anger. Her daughter stated that this had been ongoing for approximately 6 months, and getting increasingly worse, to the point where Margaret was now unable to live independently, often forgetting to eat and drink for the day unless reminded.
In accordance with NICE guidance NG97 the GP ordered some blood tests for Margaret to try and determine if the cause of the change in her mental state is due to a reversible cause of cognitive decline. The results are shown in table 1 below.

Table 1: Blood test results for Margaret

Analyte	Result	Reference range
Sodium	148 mmol/L	135 – 145 mmol/L
Potassium	4.2 mmol/L	3.5 - 5.3 mmol/L
Urea	8.1 mmol/L	2.5 - 7.8 mmol/L
WBC	8 x 10^9 cells/L	4 – 11 x 10^9 cells/L
Hb	11.6 g/dL	12 – 15 g/dL
CRP	2.2 mg/L	0.6 - 5 mg/L

1. **Which of these analytes are out of range?**

3 marks

The GP suspects that the changes in Margaret's blood test results are due to her poor diet and mild dehydration. He prescribes Margaret oral iron and the tests are repeated a week later. On repeat her Hb has increased and her other analytes are within normal limits.

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The GP makes a referral for Margaret to a specialist memory clinic in secondary care. A Mini-Mental State Examination (MMSE) scored 23/30, indicating mild cognitive impairment. An MRI revealed mild hippocampal atrophy. Margaret was enrolled on a clinical trial through the memory clinic. As part of this trial a PET scan was performed, using Tau-specific radiotracers, which demonstrated neurofibrillary tangles. A diagnosis of Alzheimer's disease was made and home-based care was provided for Margaret.

2. a) What other structural change in the brain, that can be seen on a PET scan, is associated with Alzheimer's disease?

(2 marks)

b) Why is genetic testing not routinely used to make a diagnosis of Alzheimer's disease?

(2 marks)

Total 4 marks

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As part of the clinical trial that Margaret is enrolled in, she undergoes genetic testing for genes associated with Alzheimer's disease. She undergoes genotyping for specific risk variants associated with Alzheimer's disease, as well as having a polygenic risk score calculated.

Polygenic Risk Scores can be calculated by looking at various genes associated with a protective or deleterious effect for a specific disease. The data to allow us to calculate Polygenic Risk Scores comes from Genome Wide Association Studies.

3. Explain briefly how data from Genome Wide Association Studies can be used to calculate Polygenic Risk scores.

5 marks

The results of Margaret's genetic testing are shown in table 2 below

Table 2: Genetic test results for Margaret

Test	Result
APOE genotyping	ε3/ε4
Whole exome sequencing	Wild type APP, PSEN1 and PSEN2
Polygenic Risk Score	Elevated Risk Score based on multiple SNPs associated with Alzheimer's risk in Genome Wide Association Studies

4. a) Which of these genetic tests demonstrates a result that could be associated with Margaret developing Alzheimer's?

(2 marks)

b) Explain the proposed biological mechanism that accounts for variants in APP, PSEN1 and PSEN2 being associated with Alzheimer's disease.

(8 marks)

Total 10 marks

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The majority of Alzheimer's associated APP, PSEN1 and PSEN2 variants are inherited in an autosomal dominant manner

5. a) Explain the meaning of autosomal dominant inheritance?

(2 marks)

b) Why do pathogenic genes with an autosomal recessive inheritance pattern require two copies for the effects to be seen?

(2 marks)

Total 4 marks

Margaret's daughter, Alex, decides she would like to know her personal genetic status in regards to her likelihood of developing Alzheimer's disease. She pays for private testing. Her results are shown in table 3 below.

Table 3: Genetic test results for Alex (Margaret's daughter)

Test	Result
APOE genotyping	ε3/ε3
Whole exome sequencing	Wild type APP, PSEN1 and PSEN2
Polygenic Risk Score	Non-elevated Risk Score based on multiple SNPs associated with Alzheimer's risk in Genome Wide Association Studies

6. a) Is there any evidence from the test results given above that Margaret's daughter is at greater risk of developing Alzheimer's disease?

(1 mark)

b) Explain the association between APOE variants and risk of developing Alzheimer's disease.

(9 marks)

c) How might genetic counselling differ for someone with a known PSEN1 mutation versus someone with an APOE ε4 allele?

(4 marks)

Total 14 marks

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The clinicians working on the clinical trial that Margaret is enrolled in think they may have discovered a new gene variant associated with Alzheimer's disease. The sequence for the gene is given below.

5' TTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGATGCT

AGCTGGTT**ATG**GAGAAGTCTGCCGTTACGCCCTGTGGGGCAAGGGCACTGTG

TGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGCAGGCTGCTGGTGGTCTA

TTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGATGCTGT

ATGGGCAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGTGCCTTTAG

ATGGCCTGGCTCACCTGGACAACCTCAAGGGCACCTTTGCCACACTGAGTGAG

CTGGTCTGTGTGCTGGCCCATCACTTTGGCAAAGAATTCACCCCACCAGTGCG

AAAGTGGTGGCTGGTGTGGCTAATGGCACTGTGACAAGCTGCAC**TAA**CCTATC

GCACTGTGACAAGCTGCACGTGGATCCTGAGAACTTCAGGCTCCTGGGCAC 3'

The clinicians want to sequence the gene from their study participant samples, they propose to do this by first amplifying the sequence in their samples by using PCR and then using Sanger sequencing

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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 from the following five choices. You should spend approximately 45 minutes on each question.

8. The Central Dogma of Molecular Biology describes the flow of genetic information from DNA to RNA to protein. In this process DNA is the molecule responsible for the storage and safekeeping of the genetic code. In as much detail as possible, describe **THREE** experiments that proved this was the case.

50 marks

9. In detail, discuss the role of the promoter sequence in gene expression. Using bacterial promoters as examples, explain how expression can be controlled either positively or negatively using inducers or repressors.

50 marks

10. The central dogma theory explains how we can convert a four-letter DNA code into a 20-letter amino acid code. Explain how mutations in the genetic code result in the incorrect folding of proteins and how this can produce non-functioning protein variants. Within your answer provide two examples of misfolded proteins that are responsible for genetic disease.

50 marks

11. In as much detail as possible, outline the process of translation in prokaryotes and explain any differences that occur in eukaryotic protein synthesis.

50 marks

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12. The use of molecular genetics in medicine is a novel concept in healthcare but is becoming more commonplace in the treatment of disease. Using examples to support your answer, explain fully how specific techniques are currently used to both identify disease and design treatments, which help to improve modern medicine.

50 marks

Total 100 marks

END OF QUESTIONS