Module Code: BIO00016H

Examination Candidate Number: _________

Desk Number: _________

BSc Degree Examinations 2018-9

Department:
BIOLOGY

Title of Exam:
Glycobiology

Time Allowed:
2 hours

Marking Scheme:
Total marks available for this paper: 100
Section A: Short Answer / Problem / Experimental Design questions (50 marks)
Section B: Essay question (marked out of 100, weighted 50 marks)

Instructions:
Section A: Answer all questions in the spaces provided on the examination paper
Section B: Answer either question A or B. Write your answer in the green answer booklet provided and attach it to the back of the question paper using the cable tie provided.

Materials Supplied:
Green Answer Booklet

For marker use only
Office use only:

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DO NOT WRITE ON THIS BOOKLET BEFORE THE EXAM BEGINS
DO NOT TURN OVER THIS PAGE UNTIL INSTRUCTED TO DO SO BY AN INVIGILATOR
Most serum proteins are glycoproteins, and their attached glycans are often functionally important. The following study has investigated the glycans of serum proteins over time.

**Figure 1**: Serum proteins were biotinylated upon production, and then isolated from the serum 0 h, 24 h, 48 h and 72 h after biotinylation. Binding of lectins to the total isolated serum protein sample was measured and is shown on the graph. Lectin specificities are:

- SNA – terminal sialic acid
- RCA – terminal GlcNAc-Gal
- WGA – terminal GlcNAc
- ConA – mannose

Statistically significant differences between the different days are shown with asterisks (* p<0.05, ** p<0.01, *** p<0.005)
b) Provide three conclusions that can be drawn from the data in figure 1 about the changes that glycans undergo upon 3 days of incubation in serum.

(2 marks each, total of 6 marks)

i)

ii)

iii)

c) Briefly explain how the half-life of the serum proteins will be affected by the changes in their glycosylation.

(4 marks)

d) Describe two methods that manufacturers can use to increase the serum half-life of drugs by using the knowledge about glycans’ effects on turnover in serum.

(2 marks)

i)

ii)
Question 2

a) Complex N-glycans are often associated with cancer progression. Based on your knowledge of complex N-glycan biosynthesis what type of enzyme inhibitor would be useful for treating cancer. (3 marks)

b) Describe an analytical experiment that can verify the alterations in glycan structures caused by the inhibitor. (4 marks)

c) Describe the advantages and limitations of using model organisms such as S. cerevisiae to verify the identity of pathogenic mutations in CDG patients. (5 marks)
d) In the context of glycobiology, briefly describe the cause of a “lysosomal storage disease” and a pharmaceutical approach for its treatment. (5 marks)

e) The glycan moieties that are responsible for the targeting of lysosomal hydrolases and those responsible for the binding of the dystrophin/dystroglycan complex to the lamina are very different. Yet, they do contain a similar chemical feature, what is this? (2 marks)
Question 3

You identify a protein-linked glycan that is highly elevated in a diseased tissue. The following observations are made:
   i) it can be cleaved from the protein by PNGaseF
   ii) mass spectrometry tells you it contains:
       5 N-acetyl-hexosamines
       6 hexoses
       1 fucose
       2 sialic acids
   iii) endo-beta-galactosidase and exo-N-acetyl glucosaminidase cleavage leaves a glycan containing:
       2 N-acetyl-hexosamines
       3 hexoses
       1 fucose

Draw a schematic structure of a glycan that is consistent with all this information, based on your knowledge of glycan biosynthesis and enzyme specificities, and explain your reasoning. (6 marks)
Question 4
Mucus forms a thick layer in the human gut. Outline what mucus is primarily composed of and how different bacteria could make use of this material during colonisation of the gut. (6 marks)

Question 5
The bacterium *Haemophilus influenzae* is able to scavenge sialic acid from its environment to glycosylate its own cell surface for immune evasion. Describe evidence that was used to support the idea that a specific sialic acid transporter was essential for this process. (4 marks)
SECTION B: Essay question

Answer one question in the green answer booklet provided.

Remember to write your candidate number on the front of the answer booklet and indicate whether you have answered question A or B at the top of the page.

Mark total for this section: 50

EITHER

A) Explain the current limitations and challenges of producing glycoprotein drugs with designed N-glycans in prokaryotic and eukaryotic expression systems.

OR

B) Compare and contrast glycoside hydrolases (GHs) and glycosyltransferases (GTs) and the methods used to classify them. Include in your answer discussion of

- Amino-acid sequences
- 3-D structures
- Reaction mechanisms
- Strategies for inhibition
- Why GH inhibitors are more commonly available than GT inhibitors?
- What could be the advantage of GT inhibitors over GH inhibitors for disease treatments?