Module Code: BIO00041H

Examination Candidate Number: __________

Desk Number: __________

BSc Degree Examinations 2018-9

Department:
BIOLOGY

Title of Exam:
Principles of Molecular Virology

Time Allowed:
2 hours

Marking Scheme:
Total marks available for this paper: 100
The marks available for each question are indicated on the paper

Instructions:
Section A: Answer all questions in the spaces provided on the examination paper

Section B: Answer either question A or question B. Write your answer on the separate paper provided and attach it to the back of the question paper using the cable tie provided.

Materials Supplied:
CALCULATOR
GREEN ANSWER BOOKLET

For marker use only:
Office use only:

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</tbody>
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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

Page 1 of 9
SECTION A: Short Answer / Problem / Experimental Design questions

Answer all questions in the spaces provided

Mark total for this section: 50

1. How do phages T4 and Phi 6 differ in their mode of entry into bacteria? Briefly describe the mechanisms involved.  

   (5 marks)

2. What are virus factories? Use two specific examples to illustrate their diversity.  

   (5 marks)
3. State five factors that favour tissue damage during viral infection. Provide an example for each of the factors you discuss. \[10 \text{ marks}\]
4. Hepatitis B virus assembles into polymorphic, icosahedral capsids, which can have two sizes. Type A and B capsids have approximately 180 and 240 subunits of capsid protein per genetic strand, respectively.

   a) What are the T-numbers of the two capsid sizes? (2 marks)

   b) Using the formula for allowed T-numbers, describe the two capsids in terms of h and k. (2 marks)

   c) How many pentamers and hexamers are in each capsid? (2 marks)

   d) Which (if any) of the capsids have chiral tilings? (1 mark)

   e) What experimental techniques would commonly be used to determine the details of the virus structure? What are their limitations? (3 marks)
5. A scientist is working on a new therapeutic strategy to stop HIV transmission. The aim is to generate a lentivirus-based gene delivery system that can be used in clinic to knock-down CCR5 with an interfering RNA (iRNA).

a) Describe the principle of lentivirus-based gene delivery and how to design a lentiviral vector.                             (5 marks)

b) How do you explain the choice of a CCR5-specific iRNA?                                                        (3 marks)

The space above the line should be sufficient for your answer.
The scientist has now produced four 15ml stocks of lentiviruses (samples 1 to 4) and is using a p24 ELISA kit to determine the viral titer of each stock. The assay is performed on 100 µl of serial dilutions from each sample and the optical density (OD) values read for this ELISA are presented in the table below.

<table>
<thead>
<tr>
<th>Dilutions</th>
<th>Sample 1</th>
<th>Sample 2</th>
<th>Sample 3</th>
<th>Sample 4</th>
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<tbody>
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<td>0.05</td>
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</table>

c) Briefly explain what the p24 ELISA measures and how this assay allows for the determination of a viral titer. What is the titer for each stock (samples 1 to 4)? *(4 marks)*
d) The scientist wants to test the ability of these stocks to infect target cells. This experiment is set up so that $10^5$ cells are incubated with viruses at a MOI=10. What volume of each lentiviral stock is needed to carry out this experiment? Is it feasible for all samples and why? (2 marks)

e) After 48h of incubation, infectivity is assessed using immunofluorescence detection of viral p24 in infected cells. The proportion of cells positively stained for p24 is analysed by flow cytometry, and the results are as follows:
- 90% for cells incubated with Sample 1
- 12% of cells incubated with Sample 4
Based on this information and the results from the p24 ELISA, briefly provide an explanation for the difference between the two lentiviral stocks, sample 1 and 4. (4 marks)
f) Using sample 1, the scientist was able to show full knock-down of CCR5 in cultured cells, an encouraging step towards a therapeutic application. However, can you provide an experimental limitation in using a lentivirus-based system in patients? (2 marks)

The space above the line should be sufficient for your answer.
SECTION B: Essay question

Answer one question on the separate paper provided

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

Mark total for this section: 50

EITHER

A. Compare and contrast immune evasion mechanisms between herpesviruses and HIV.

OR

B. Discuss the complications a virus faces when assembling in vivo and provide examples of how viruses from different Baltimore classes overcome these issues.