BSc Stage 3 Degree Examinations 2018-19

Department:
Biology

Title of Exam:
Human Molecular Parasitology

Submission deadline:
Monday 13th May 2019, 12 noon

- This Paper has 3 parts: Answer all questions in Section A (25 marks) and Section B (25 marks). Answer one question from Section C (50 marks)
- Total marks available for this paper: 100
- Work should be submitted via the Yorkshare VLE.

Instructions for Candidates:
Your assignment will be put through turnitin on submission.
All questions should be answered on this question paper.
All questions should be answered using Arial font size 11 or larger.

Materials Supplied:
Data for Section A, Paper for Section B: Rojas et al., Cell, 2018.
Section A: Short answer problem solving (25 marks).

Your experiments have revealed that infection of laboratory mice with schistosome parasites results in the strong induction of an immune cell called “regulatory B cells”. These cells develop at 6 weeks post-infection and remain at high levels thereafter.

Question 1

What parasite lifecycle stage(s) are likely responsible for inducing the regulatory B cells? Justify your answer and provide an appropriate reference.

(100 word limit; 2 marks)

Question 2

You collect secreted material from the parasite and show this is able to induce regulatory B cells in vitro. Next, you perform biochemical fractionation and proteomic analysis of the secretions and identify a single candidate protein. You express this as a recombinant protein in both bacteria and in a mammalian cell line. You next separate the proteins by SDS-PAGE, stain with Coomassie reagent and see the banding pattern below. Only the mammalian-expressed recombinant displays biological activity i.e. induction of regulatory B cells. In the figure below, “bac” = recombinant protein produced in bacteria; “mam” = recombinant protein produced in mammalian cells; Molecular weight protein markers indicated.

Suggest a reason for the difference in SDS-PAGE banding patterns, describe an experimental approach to assess if this is the case, and provide an explanation for how this difference might alter bioactivity between these recombinant proteins.

(200 word limit; 5 marks)
**Question 3**

The amino acid sequence of the bioactive candidate molecule is below. Identify conserved protein domains, and an ortholog in a non-schistosome trematode and a cestode. What sequence feature would lead you to predict the molecule is secreted?

MLSQITVLLLHAAVYRLTSADGHRAPFCDRYRFHGEKRLLLWQRAATRDSTALHTAQDWAELHSE
DGWKNSPLISRAEUVGESISVRTSTGHEDDMACHMECNTWHSVDAEPVYYENGLGQAHNFQLLHDS
DREVFGKHICILGVCSCVAMWRDPGNAPGDYYEHVFRPCEFSSKVWCPQIPIFNYRFNLCTPKLVGTE
SLTESWGEQEQVRKEICDLCDDSGPTKKIYLVGPGKVMYNSCCCHGVRTKRCRKEVFJKLMNOPQKH
HKASISSTDGHTEYYKPLYETIHTVVQLHQQYRWQHGSKPVLDQNLIDLFAQQCATHILQQSELSHENY
DYRDOKCDESFFSLWQNGPVMCMLQEHSYQEGYQYKFISEYDSVQGIHMFLQHVWTEFRR
NGVGISHQSSKSWEPALPRDKSMIEVELYHQPDCVISQFQNLWKADL

(100 word limit, 4 marks)

**Question 4**

You measure serum antibodies titers against the candidate molecule in a group of individuals from Kenya in an area endemic for schistosomiasis (see attached excel file). You also measure antibody levels in a non-endemic cohort in the UK.

a) Why does this data suggest that antibody responses to this molecule may protect against infection?  
(50 word limit; 1 mark)

b) Why would vaccination with this molecule be potentially problematic?  
(50 word limit; 1 mark)

c) Explain the outlier in the non-endemic cohort  
(50 word limit; 1 mark)

**Question 5**

Discuss the relative merits of Heligmosomoides polygyrus and Nippostrongylus brasiliensis as models of human hookworm infection.  
(300 word limit; 6 marks)

**Question 6**
Section B: Paper Analysis (25 marks).

The following questions refer to Rojas et al., Cell 2018. Cite figures and/or papers where appropriate. (doi:10.1016/j.cell.2018.10.041); pdf supplied on the VLE.

Question 1
What significant advances does the research of Rojas et al make to the T.brucei research field, given the context of Mony et al (doi:10.1038/nature12864)?

(200 word limit; 5 marks)

Question 2
Figure 1C demonstrates GPR89 is specifically expressed in slender stage (SL) T. brucei parasites. Describe how this impacts T.brucei infection dynamics.

(150 word limit; 4 marks)

Question 3
Why is the bacterial GPR89 homolog (YjdL) able to be ectopically expressed for up to 72 hours (Fig 4B), whereas TbGPR89 ectopic expression is reduced after 24hrs (Fig 1E)? How good is the molecular evidence to support the authors' explanation?

(150 word limit; 4 marks)

Question 4
Assuming both ectopic proteins are under control of the same 3’UTR, provide an explanation for the difference in TbGPR89 versus YjdL ectopic stability in T.brucei.

(150 word limit; 4 marks)

Question 5
Describe the in silico, in vitro and in vivo evidence that demonstrates that TbGPR89 functions as a POT and not a GPCR?

(8 marks total)
In silico  (50 word limit; 1 mark)

In vitro  (150 word limit; 3 marks)

In vivo  (200 word limit; 4 marks)

Section C: Short essays. Answer only one from the following (1,000 word limit; 50 marks).

A) Surface molecules are essential for survival of *Trypanosoma brucei* in the blood and for *Plasmodium* entry into host cells. How and why are the molecules structurally and functionally different?

OR

B) Parasite genome editing is a new approach to assess the function of putative immunomodulatory molecules from parasitic helminths. What has gene knockout revealed so far about parasitic helminths and what are the current limitations to this approach?

OR

C) The closely related *T.cruzi* and *Leishmania* spp. parasites both have amastigote lifecycle stages which are morphologically similar, yet display key evolutionary distinctions. Compare and contrast the role each of these play in each parasite’s lifecycle progression, infectivity, disease progression and targeted eradication.