

Answer question 1 from section A and one question from section B. Both section A and section B carry equal marks.

SECTION A (Answer question 1)

1. Write short notes on EACH of the following:

- a. Give two examples of how next generation nucleic acid sequencing is being used to understand parasite biology.
- b. Using a diagram, illustrate how trypanosomes produce mature mRNA.
- c. What diagnostic tests are used for the different clinical stages of African trypanosomiasis?
- d. What drugs are currently used to treat leishmaniasis? Describe the major problems associated with the use of these therapeutics.

SECTION B (Chose one question from questions 2 - 6)

2. Discuss how the mechanisms of host cell invasion of *Toxoplasma gondii* and *Leishmania spp.* differ and how this impacts disease transmission.
3. What are the mechanisms that African trypanosomes use to avoid the innate host immune response?
4. Write an essay on the mechanisms of cytoadherence and the role of antigenic variation in malaria pathogenesis.
5. Drug-resistance threatens to undermine many treatments used against parasitic protozoan disease. Using African trypanosomiasis as an example, describe our understanding of mechanisms of resistance to currently used drugs. How might this knowledge be exploited to combat disease and aid development of new chemotherapeutic agents?
6. A combination therapy is used for the treatment of Human African Trypanosomiasis. Describe the advantages of this approach over current monotherapies and give details of the proposed mechanisms of action.

End of paper

**Answer question 1 from section A and one question from section B.
Both section A and section B carry equal marks.**

SECTION A (Answer question 1)

1. Write short notes on EACH of the following:
 - a. Explain the concept of a drug discovery screening cascade.
 - b. Using a clearly labelled diagram, illustrate the role of epigenetics in *Trypanosoma brucei* gene expression.
 - c. There are several mechanisms by which parasites can become resistant to drugs. Give two specific examples of drug resistance mechanisms employed by protozoan parasites.
 - d. Describe, with the aid of a diagram, how affinity chromatography and quantitative proteomics are used to identify diagnostic antigens.

SECTION B (Chose one question from questions 2 - 4)

2. What is the evidence that the surface of African trypanosomes participates in immune evasion and drug sensitivity?
3. Describe the haemozoin degradation pathway in *Plasmodium* parasites. Give two examples of anti-malarial drugs that target this pathway.
4. What gene expression features in particular present challenges in terms of developing anti-parasite vaccines? Use at least two parasites as examples.

End of paper

Answer question 1 from section A and one question from section B. Both section A and section B carry equal marks.

SECTION A (Answer question 1)

1. Write short notes on EACH of the following:

A. The salient features of a trypanosomatid genome.

B. Three criteria that are used to select appropriate targets for drug discovery and why.

C. How are affinity chromatography and proteomics used for the design of diagnostics?

D. How do Plasmodium and Cryptosporidium resemble and differ from each other with regards to ALL of the following characteristics: Life cycle, population affected and organelles (at least 2 examples)? Provide descriptive examples as evidence of your comparisons.

SECTION B (Answer one question)

2. Discuss how target-based drug discovery is performed and the role of structural biology in this process.

3. Compare the mechanisms by which a named Apicomplexan and Kinetoplastid parasite evade the host immune response.

4. Describe the major components of the most advanced malaria vaccine. Evaluate the advantages and disadvantages of this strategy.

End of paper

BS42012 2019

Part A and Part B carry equal marks.

Part A Answer all three parts

1. Write short notes on the following;

- A. How can the crystal structure of a protein drug target aid in drug discover?
- B. In what ways are CRISPR/Cas9-based approaches impacting research on parasites?
- C. How could you use mass spectrometry/proteomics to design a diagnostic tool?

Part B Answer one question

- 2. What is the rationale for screening cascades and the relevance of mode of actions studies to phenotypic screen drug discovery?
- 3. Describe genome organisation and gene expression control in trypanosomatids, including a description of variant surface glycoprotein coat expression and switching.
- 4. Describe the sexual life cycle of Plasmodium, and explain one mechanism concerning how asexual Plasmodium parasites "commit" to sexual stages.