BSc / MSc Degree Examinations 2018-9

Department:
Biology

Title of Exam:
Mechanism to Therapies

Submission deadline:
Monday 13th May 2019, 12pm

Allocation of Marks:
Marks per questions will be allocated as shown below.

Instructions for Candidates:
Before answering the questions read the following paper (supplied):

In your responses to questions do not exceed the suggested word limits and use appropriate references to support your statements. References do not count towards the word count. Please use The New England Journal of Medicine referencing style. Your essay should be submitted as a Word document (.doc or .docx) via the VLE. Please refer to Departmental WEB pages for late submission penalties.
Question 1

In van Vollenhoven et al., pulmonary tuberculosis was a severe adverse effect observed in patients receiving Tofacitinib (Table 3). Explain the mechanistic basis underpinning this presentation. Your explanation should be supported by evidence from pre-clinical models and human genetics studies.

(10 marks; maximum 150-200 words)

Question 2

Development of other autoimmune conditions could be a severe adverse effect of the use of anti-inflammatory biologics for the treatment of Rheumatoid Arthritis or Ulcerative Colitis/Crohn’s Disease. Give relevant examples and discuss whether this can also be the case for JAK inhibition with Tofacitinib through the same or different mechanisms.

(20 marks; 300 – 400 words)

Question 3

There are currently four FDA-approved JAK inhibitors and more than 10 in clinical trials. These inhibitors exhibit varying levels of specificity toward the subtypes of JAK proteins.

a) Why is subtype specificity so important in the development of these drugs?

(10 marks; 150-200 words)

b) You have designed a small molecule inhibitor in silico that you hope will be highly specific to JAK1. Design a series of experiments to test the specificity and efficacy of this small molecule using in vitro (cell lines) and in vivo (animal) methods.

(20 marks; 300-400 words)

Question 4

What physiological parameters might influence the pharmacokinetics of tofacitinib. Explain your answers and give at least 2 examples of how a parameter you have named influenced a drug’s PK.

(10 marks; 100-150 words)
Question 5

What imaging techniques could be used to track the pharmacokinetics (PK) and pharmacodynamics (PD) of i) small molecules and ii) biologics to treat rheumatoid arthritis. Briefly describe the techniques and the requirements and design of the imaging experiments. Provide evidence for your statements.

(30 marks, 400-500 words)