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**POSTGRADUATE INSTITUTE OF MEDICINE**
**UNIVERSITY OF COLOMBO**

**POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE**
**EXAMINATION – JULY 2019**

**Date :-** 11th July 2019 **Time:-** 9.30 a.m. -12.30 p.m.

**SEQ PAPER -MODULE 5**
**(Laboratory Management, Molecular Diagnosis and Therapeutics)**

Answer **all six (06)** questions.
Answer each question in a **separate** book.

1.

**Part - A**

1.1. Briefly outline the design aspects you would incorporate in a molecular diagnostic laboratory in order to minimize Polymerase Chain Reaction (PCR) contamination. (30 marks)

1.2. Briefly explain how you would safely dispose electrophoresis buffer solution containing ethidium bromide after use. (20 marks)

**Part - B**

1.3. State four (04) common pre-analytical errors that may occur during sample collection for molecular diagnosis. (20 marks)

1.4. State one (01) method that you would recommend to eliminate each pre-analytical error stated in 1.3. (30 marks)

Contd…../2-

2.

**Part - A**

2.1. A 74-year-old male patient presented to the hospital with high-grade fever and scrotal pain for 4 days duration. On examination, he was found to have a Fournier gangrene. A heavy growth of *Staphylococcus aureus* was isolated from the pus culture of the lesion which was suspected to be resistant to methicillin.

2.1.1. State how you would confirm methicillin resistance in a conventional bacteriology laboratory. (20 marks)

2.1.2. Outline how you would confirm the isolate as methicillin-resistant *Staphylococcus aureus* (MRSA) using a molecular diagnostic method . (30 marks)

**Part - B**

2.2. Briefly outline the role of molecular based diagnostic assays for virology in the management of post renal transplant patients. (30 marks)

2.3. Briefly state how you should collect and transport clinical specimens from a patient with severe lower respiratory tract infection for molecular diagnosis of respiratory viral infections. (20 marks)

3.

**Part - A**

A 2 ml heparinised blood sample is sent to a cytogenetics laboratory requesting karyotyping. The clinical information provided indicates that the suspected diagnosis is a microdeletion of chromosome 22q11.

3.1. Give reasons and comment on the appropriateness of karyotyping in this case. (20 marks)

3.2. State two (02) investigations for confirmation of the diagnosis, indicating the benefits and disadvantages of each test. (30 marks)

Contd..../3-

**Part - B**

3.3. State three (03) steps in the preparation of biopsy tissue for application of molecular diagnostics. (15 marks)

3.4. State the steps involved in the use of fluorescent *in situ* hybridization test on tissue samples. (15 marks)

3.5. Describe how the fluorescent *in situ* hybridization test is useful as an adjunct to immunohistochemistry test in determining the Her 2 receptor status of breast cancer. (20 marks)

4.

**Part - A**

4.1. List two (02) Polymerase Chain Reaction (PCR) based molecular techniques that can be used to detect single nucleotide mutations in blood disorders. (20 marks)

4.2. State which one of the techniques listed in 4.1 above that you would recommend to be used as a routine diagnostic assay for the detection of JAK2 V617F mutation. Indicate reasons. (30 marks)

**Part - B**

4.3. State what is meant by the term "personalized medicine". (10 marks)

4.4. Briefly explain how the concepts of personalized medicine is applied in the management of chronic myeloid leukaemia. (40 marks)

5.

5.1. Define following two (02) terms (20 marks)

5.1.1. Myeloma cells

5.1.2. Hybridoma

5.2. Briefly explain the role of Polyethylene Glycol (PEG) in the production of monoclonal antibody using hybridoma technology. (20 marks)

5.3. Briefly explain three (03) general uses of monoclonal antibodies (Mabs) that are specific for wide range of epitopes. (60 marks)

Contd..../4-

6.

**Part - A**

6.1. Define the term "targeted therapy". (10 marks)

6.2. State three classes of therapeutic agents used in targeted therapy. (10 marks)

6.3. State three malignant solid tumours and name one targeted therapy agent used to treat each of these tumours. (30 marks)

**Part - B**

6.4. Indicate the herapeutic applications of the following recombinant products and state the genetic/structural modifications done to the recombinant molecule to increase the therapeutic efficacy. (50 marks)

6.4.1. Glargine

6.4.2. Somatotropin

6.4.3. Filgrastim

6.4.4. Lepirudin

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**POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE - E3**
**EXAMINATION – JULY 2019**

**Date :-** 12th July 2019 **Time:-** 9.30 a.m. -12.30 p.m.

**SEQ PAPER -MODULE 6**
**(Special Topics)**

Answer **all six (06)** questions.
Answer each question in a **separate** book.

1.

1.1. Draw a box and whisker plot naming all components. (25 marks)

1.2. Describe how a box and whisker plot can be used to present data. (15 marks)

1.3. State two (02) differences between a histogram and a bar diagram. (10 marks)

1.4. The following table presents the relationship between the employment status and those having diabetes mellitus in a given population.

| Employment status | Diabetes present | Diabetes absent | Total |
|---|---|---|---|
| Employed | 93(83.0%) | 19(17.0%) | 112 |
| Not employed | 150(52.6%) | 97(47.4%) | 247 |
| Total | 243 | 116 | 359 |

Pearson chi square value =17.5
Degrees of freedom =1
p value =0.0001

1.4.1. Define the 'p' value. (20 marks)

1.4.2. Interpret the findings. (30 marks)

Contd…./2-

2. Write notes on:

2.1. The eugenics movement (25 marks)

2.2. Biobanking (25 marks)

2.3. Responsible conduct of research (RCR) (50 marks)

3.

3.1. A researcher was trying to identify a suitable molecule to bind to the active site of a certain enzyme. He has prepared three possible drug analogs by adding different functional groups to a naturally binding ligand and conducted a molecular docking study. The docking results are summarized in the following table.

| Ligand | Naturally binding ligand | Analog01 | Analog02 | Analog03 |
|---|---|---|---|---|
| Docking score ($kJ\ mol^{-1}$) | -322.05 | -492.55 | -319.32 | -52.01 |
| Distance from COM of the ligand to the center of active site (nm) | 0.52 | 1.55 | 0.57 | 0.51 |

3.1.1 Identify the best alternative molecule to the naturally binding ligand to bind into the active site of the enzyme, giving reasons. (Note: COM – center of mass) (10 marks)

3.1.2 List the four classes of molecular descriptors (structural properties) used in Quantitative Structure Activity Relationship (QSAR) analysis. (15 marks)

3.2.

3.2.1. What are the different methods available for computer-based modeling of 3-Dimensional structure of proteins? (10 marks)

3.2.2. State the method that would generate reliable 3-Dimensional structure of proteins and list the assumption made in the method mentioned. (15 marks)

3.2.3. Briefly discuss the following, giving examples.

(a) OMIM database (20 marks)

(b) Secondary databases (15 marks)

(c) UniprotKB (15 marks)

Contd…../3-

4.

4.1.

4.1.1. What is the underlying principle of distance-based methods in phylogenetic analysis? (25 marks)

4.1.2. Distance based methods vary in the way they construct the tree. Name two distance based phylogenetic analysis methods that use the clustering algorithm. (25 marks)

4.1.3. Name two distance based phylogenetic analysis methods that use optimality criteria. (25 marks)

4.1.4. 'Bootstrap analysis' is the most commonly used method to determine the support of the relationships in a tree. Briefly explain the methodology and the main objectives of performing bootstrap analysis. (25 marks)

5.

5.1. What is meant by "genetically modified crop plant"? (20 marks)

5.2. Discuss the environmental biosafety issues and the risk assessments you would consider when growing a genetically modified crop that expresses an insecticidal protein. (40 marks)

5.3. What do you understand by "food safety" issues of food derived from genetically modified crops? (40 marks)

6.

6.1. Briefly outline the requirements that need to be fulfilled in order to obtain intellectual property protection. (40 marks)

6.2. What is meant by commercialization of research? (30 marks)

6.3. If you want to establish a Biotechnology company in Sri Lanka, outline three (03) problems you would face and state how you would overcome these problems. (30 marks)