POSTGRADUATE INSTITUTE OF MEDICINE
UNIVERSITY OF COLOMBO

POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE
E3 EXAMINATION - MAY 2014

Date : 5th May 2014 **Time :** 9.00 a.m. – 12.00 noon

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

1.

1.1. Your institute is planning to set up a molecular biology diagnostic laboratory. Describe the basic structural requirements that need to be conveyed to the engineering department. (40 marks)

1.2. Compare and contrast between biosafety level class two and class three safety cabinets with regard to structural features relevant to safety. (30 marks)

1.3. Describe in a stepwise manner the actions that would be taken in the event of a spill of a sample of blood on a tiled floor. (30 marks)

2.

2.1. A patient with a positive diagnosis for chronic hepatitis B (HBV) infection completed a treatment schedule with the drug "Lamuvidine" for 6 months. At the end of treatment, the patient yielded a hepatitis B viral load of $1x10^2$ copies/mL, and subsequently, 24 weeks after stopping treatment, a viral load of 1.5×10^5 copies/mL.

2.1.1. State your conclusions and explain the reasons for the observations above. (30 marks)

2.1.2. In addition to "base line viral load testing", name one (01) other DNA based test that would have helped the clinician to determine the initial treatment plan. (10 marks)

Contd..../2-

2.2. Briefly outline the "Reverse Hybridization" method that can be used to detect the genotype of an infectious agent. (25 marks)

2.3. State three (03) situations where polymerase chain reaction (PCR) based diagnosis is important in detecting Human Immunodeficiency Virus (HIV) in humans. (15 marks)

2.4. State the objective of applying nucleic acid based technology (NAT) to screen blood donors for human immunodeficiency (HIV), hepatitis B, and hepatitis C viruses . (20 marks)

3.

3.1. A patient is suspected of being infected with the Dengue virus

3.1.1. Name the molecular based assay/test you would order. (05 marks)

3.1.2. State the main factor you would consider when ordering the above mentioned assay/test. (15 marks)

3.2. Explain briefly the importance of identifying the circulating genotype/s of the Dengue virus. (25 marks)

3.3. Polymerase chain reaction (PCR) inhibition resulting in false negative results is a major problem encountered frequently in PCR based detection of *M. tuberculosis*.

Describe two (02) measures you would employ to monitor the problem with regard to the above false negative results. (30 marks)

3.4.

3.4.1. List two (02) techniques that can be used to detect the JAK2 mutation.

3.4.2. Explain briefly giving reasons which method stated above is the better technique for routine diagnostic testing. (25 marks)

Contd..../3-

4.

4.1.

4.1.1. List the basic steps involved in preparation of monoclonal antibodies using hybridoma technology. (30 marks)

4.1.2. List four (04) problems associated in production of monoclonal antibodies using hybridoma technology. (20 marks)

4.2.

4.2.1. State the advantages and disadvantages of two protein expression systems. (30 marks)

4.2.2. State two (02) factors affecting the expression of heterologous proteins. (05 marks)

4.2.3. Explain how one of the above mentioned factors affect the expression of heterologous proteins. (15 marks)

5.

5.1. Cationic-lipid–pDNA complexes (cationic lipoplexes) are one of the most versatile tools for delivering therapeutic genes.

5.1.1. What is the basic structure of a cationic lipoplex? (10 marks)

5.1.2. State the cellular barriers that must be overcome by cationic-lipid–pDNA complexes before the gene can be expressed in the nucleus of the target cell. (20 marks)

5.1.3. Using a diagram explain the endosomal escape mechanism of lipoplexes in releasing DNA into the cell. (20 marks)

5.2.

5.2.1. List the categories of recombinant DNA (rDNA) products developed using rDNA technology for human use and give three examples for each category. (25 marks)

5.2.2. State the different analogues of recombinant insulin. (10 marks)

5.2.3. Indicate how these have significantly improved the long-term control of blood glucose in diabetic patients. (15 marks)

Contd..../4-

6.

6.1.

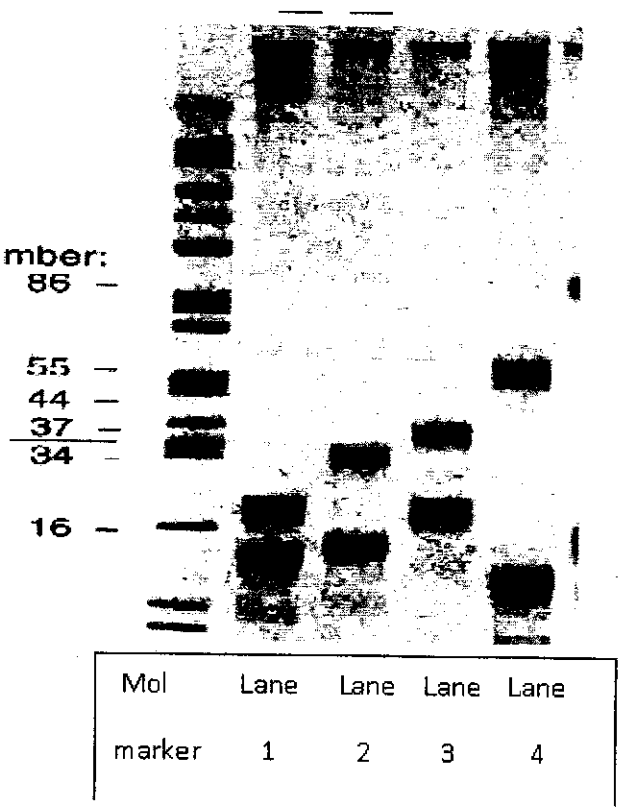
6.1.1. What is a "Dominant Negative Mutation" ? (10 marks)

6.1.2. Name the mutation repair mechanism that can be used to correct a dominant negative mutation. (10 marks)

6.1.3. Name two (02) DNA based methods that could potentially be used to prevent the expression of a mutated gene by blocking translation process in protein synthesis. (10 marks)

6.1.4. Briefly explain the term "suicide gene therapy". (20 marks)

6.2.



Lane 1 and 2 - normal controls

Lane 3 – AP's father

Lane 4 - AP

The above is result of genetic testing for identification of **Huntington disease**. This is a late onset, autosomal dominant neurological condition associated with an expansion of a CAG repeats. Normally there are less than 35 CAG repeats. AP is 25 years old and wants to find out if he is going to develop Huntington disease which affects his father.

Contd.../5-

6.2.1. State the name given to the type of genetic test being performed on AP. (10 marks)

5.2.2. State the sizes of the CAG alleles in

(a) AP's father
(b) AP (20 marks)

6.2.2. State giving your reasons whether AP is likley to develop Huntington disease. (20 marks)

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POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE
E3 EXAMINATION - MAY 2014

Date : 6th May 2014 **Time :** 9.00 a.m. – 12.00 noon

SEQ PAPER – MODULE 6
(Special Topics)

(I) one book

1.

1.1. The following table presents the pattern of observation of eye lesions due to onchocerciasis infection in 1302 people by their area of residency.

Area of residence	Eye lesions		Total
	Present	Absent	
Forest area	134 (66.67%)	620 (56.31%)	754 (57.91%)
Savannah Area	67(33.33%)	481 (43.69 %)	548 (42.09%)
Total	201 (100.0%)	1101 (100.0%)	1302 (100.0%)

Pearson chi2 (1) = 7.4761 Pr = 0.006

1.1.1. Describe the pattern based on the data shown in the table. (10 marks)

1.1.2. Write a null hypothesis for a statistical test relevant to these findings. (10 marks)

1.1.3. Name the statistical test that was used to determine the association between the area of residence and presence of eye lesions. (10 marks)

1.1.4. Interpret the results. (20 marks)

1.2. What is p value? (25 marks)

1.3. Describe the criteria based on which an appropriate statistical test is chosen? (25 marks)

Contd.../2-

2.

2.1. Discuss the ethical issues which arise in conducting a research project involving the situations given below.

2.1.1. Collection of 2 mL of venous blood from children. (20 marks)

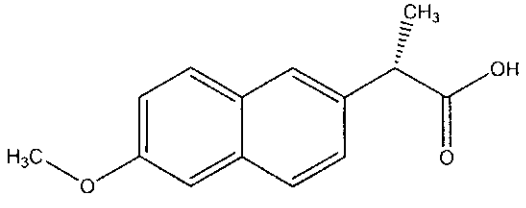
2.1.2. Sending stored DNA samples of patients to a foreign country for laboratory testing. (30 marks)

2.2. What is knowledge based protein modeling? (10 marks)

2.3. What are the assumptions made in comparative modeling of proteins? (15 marks)

2.4. Name the three (03) molecular docking models and give a reason to use one model predominantly over the other two docking models. (10 marks)

2.5. List the steps to be followed in Computer Aided Drug Designing of the molecule given below using HyperChem software.



(15 marks)

3.

3.1. Briefly explain the importance of using substitution matrices in sequence alignment. (20 marks)

3.2. What are the two (02) major approaches used in phylogenetic analysis? Briefly explain the underlying principle of each approach. (30 marks)

3.3. Discuss briefly three (03) of the following giving examples where ever possible. (50 marks)

(a) Sequence-structure deficit
(b) Primer design using bioinformatics tools
(c) Gap penalty
(d) Primary protein sequence database
(e) Search of a GenBank entry using keywords

Contd..../3-

4.

4.1. "In recent years, many biotech companies have failed to perform as a business entity and were forced to close their facilities."

Explain this statement giving suitable examples. (60 marks)

4.2. Explain how biotech industries attempt to gain market share. (40 marks)

5.

5.1. Discuss the strengths, weaknesses, opportunities, and threats in setting up a biotech industry in Sri Lanka. (50 marks)

5.2. It is believed that transgenic/genetically modified crop plants could provide solutions to some of the challenges that present day agriculture face due to climate change and population increase.

5.2.1. What is a transgenic/genetically modified (GM) crop plant? (15 marks)

5.2.2. What are the environmental biosafety issues and risk assessments you would consider in growing a GM crop that expresses insecticidal Cry protein of *Bacillus thuringiensis* (Bt) against a lepidopteron pest? (35 marks)

6. Application of DNA typing (DNA testing) is highly advantageous over "classical blood and tissue typing methods" for human identity testing in forensics.

6.1. What are "classical blood and tissue typing methods" for human identity testing in forensics? (20 marks)

6.2 Discuss the drawbacks of using "classical blood and tissue typing methods" for human identification. (30 marks)

6.3 Contrasting to your answer above why DNA typing is highly advantageous for human identification in forensics? (50 marks)