POSTGRADUATE INSTITUTE OF MEDICINE
UNIVERSITY OF COLOMBO

POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE
SEMESTER II (REPEAT) EXAMINATION – NOVEMBER 2010

Date :- 8th November 2010 **Time :-** 1.00 p.m. – 4.00 p.m.

SEQ PAPER I
(GENETICS AND HUMAN DISEASES MODULE)

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

1.

1.1. Explain briefly why somatic genetic disorders are not inherited. (20 marks)

1.2.

1.2.1 Giving examples, list the types of chromosomal aberrations in relation to human chromosomal disorders. (20 marks)

1.2.2. State the mechanism/s that cause aneuploidy. (20 marks)

1.2.3 Explain how triploidy occurs. (20 marks)

1.3. Outline the genetic consequences of reciprocal translocations. (20 marks)

2.

2.1 Regarding X-linked inheritance:

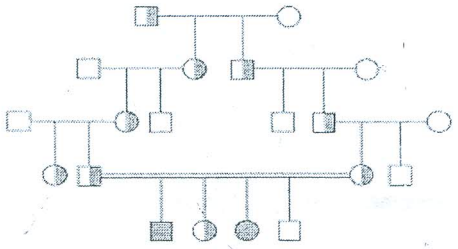
2.1.1. State a disorder that causes the death of affected males in childhood. (15marks)

2.1.2. State the mechanism causing mosaic pigmentation in the fundus of female carriers of X linked ocular albinism. (15 marks)

2.1.3. Outline risk(s) of a man with haemophilia having affected children (his wife is not a carrier). (30 marks)

Contd..../2-

2.2. Regarding the pedigree chart given below:



2.2.1 State the most likely pattern of inheritance in this family. (15 marks)

2.2.2 Explain your answer in 2.2.1 giving evidence from the pedigree chart. (25 marks)

3.

3.1. Outline Briefly the need for biological systems to have DNA repair mechanisms. (25 marks)

3.2. Explain the following;

3.2.1. Failure to repair deaminated bases leads to point mutations in DNA. (15 marks)

3.2.2. Benzopyrene can cause mutations in DNA. (15 marks)

3.2.3. Suppressor mutations have the ability to correct mutations elsewhere in the genome. (15 marks)

3.3 What are intercalating agents? Explain how they could cause mutations in DNA. (20 marks)

4.

4.1. List three (3) well established risk factors for developing breast cancer. (15 marks)

4.2. List three (3) less well established risk factors for developing breast cancer. (15 marks)

4.3. List two (2) syndromes in which the risk of breast cancer is higher than normal. (10 marks)

4.4.1. Name one gene responsible for inherited breast cancer. (10 marks)

4.4.2. Describe the actions of the gene mentioned in 4.4.1. (20 marks)

4.5. List three (3) tests useful in guiding treatment of breast cancer. (30 marks)

Contd..../3

5. Sitha is a teacher. Her husband Ranil is a businessman. Their 4 month old baby boy Samitha has a congenital (present at birth) heart defect and a cleft palate. Baby Samitha is suspected of having a syndrome and is referred for a genetic opinion.

The family history is as follows

Sitha Samaranayake born in 1985

Parents — Father Ranjan born in 1955; died 2008 heart attack
Mother Ramani born in 1959 healthy.
Had one miscarriage at 8 weeks pregnancy
Parents are first cousins

Sitha's siblings — Brothers → Jayantha born in 1980 congenital heart defect surgically repaired at 3 years
Jayantha's son (aged 1 year) has a cleft palate

Anura born in 1986 healthy
No children

Ranil de Silva born in 1977 History of asthma

Parents — Father Lakshman born in 1950. Died of lung cancer in 2000
Mother Sumana born in 1955 reasonably healthy apart from high blood pressure

Ranil's siblings — Brother Anil born in 1980 Well
Twin sister (identical) Lalani and Jalani born in 1982
Lalani has a daughter aged 5 years -well

5.1. Define the term "syndrome" (10 marks)

5.2. State two (2) possible underlying causes of a syndrome and give an example for each. (20 marks)

5.3. Draw the family pedigree. (30 marks)

5.4. List two (2) possible genetic mechanisms for the abnormalities in baby Samitha (20 marks)

5.5. State the recurrence risk of the problems stated in your answer to question 5.4 (20 marks)

Contd.../4-

6. A child with short stature is found to have the karyotype 45,X

6.1. State the clinical diagnosis for this condition. (10 marks)

6.2. Describe how this abnormality was caused. (10 marks)

6.3. Describe two (2) other chromosome anomalies that could give rise to the condition mentioned in 6.1. (20 marks)

6.4. List five (5) mechanisms that modify the expression of autosomal dominant traits. (20 marks)

6.5. Describe briefly two (2) of the mechanisms you listed in 6.3 above. (40 marks)

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POSTGRADUATE DIPLOMA IN MOLECULAR MEDICINE
SEMESTER II (REPEAT) EXAMINATION – NOVEMBER 2010

Date :- 9th November 2010 **Time :-** 9.00 a.m. – 12.00 noon

SEQ PAPER II
(BIOINFORMATICS AND MOLECULAR THERAPEUTICS MODULE)

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

Note: For all the questions given below, web addresses are NOT required

1. Your molecular laboratory has been involved in **DNA sequencing** of a gene, coding for a surface protein of *Plasmodium falciparum* parasite strain found in Sri Lanka. At the end of this exercise, you find that you have a pBluescriptII clone with a 1100 bp DNA fragment.

1.1. Mention briefly the most appropriate approach to determine whether this DNA sequence has been previously reported in malaria parasites. (20 marks)

1.2 You want to deduce the amino acid sequence encoded by the above gene. Indicate how you would obtain the corresponding amino acid sequence using the available bioinformatics tools. (20 marks)

1.3 You have used the NCBI Blast server to look for a match for the above deduced amino acid sequence and the best alignment contained in the following section. What do the "+" signify in the alignment? (20 marks)

```
Query:     1 MDYTTGQILTAGNEHQQRNPASLTKLMTGYVVDRAIDSHRITPDDIVTVGRDAWAKDNPV 60
             MDY +G++L  GN  ++ +PASLTK+MT YVV +A+ + +I   D+VTVG+DAWA  NP
Sbjct:    45 MDYASGKVLAEGNADEKLDPASLTKIMTSYVVGQALKADKIKLTDMVTVGKDAWATGNPA 104
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Contd.../2-

1.4 To determine whether a protein homologous to the *Plasmodium falciparum* surface protein is present in *Plasmodium vivax* parasites, which BLAST strategy is best suited ?
Note: You will use the deduced amino acid sequence of the *Plasmodium falciparum* surface protein as the query for this BLAST search. (20 marks)

1.5 If you need to extend your BLAST search to include distantly related protein sequences, which BLAST strategy is best suited? (20 marks)

2.

2.1 Name three (3) sequence alignment methods that can be used for a "pair-wise" sequence comparison. (20 marks)

2.2 What is the best alignment method suitable to analyze single nucleotide polymorphisms (SNPs) between closely related species? (15 marks)

2.3 Write short descriptions on the following, giving information about the type of sequence data they contain:

2.3.1. Database of Expressed Sequence Tags (dbEST) (20 marks)

2.3.2. High-throughput genomic sequences (HTGS) (20 marks)

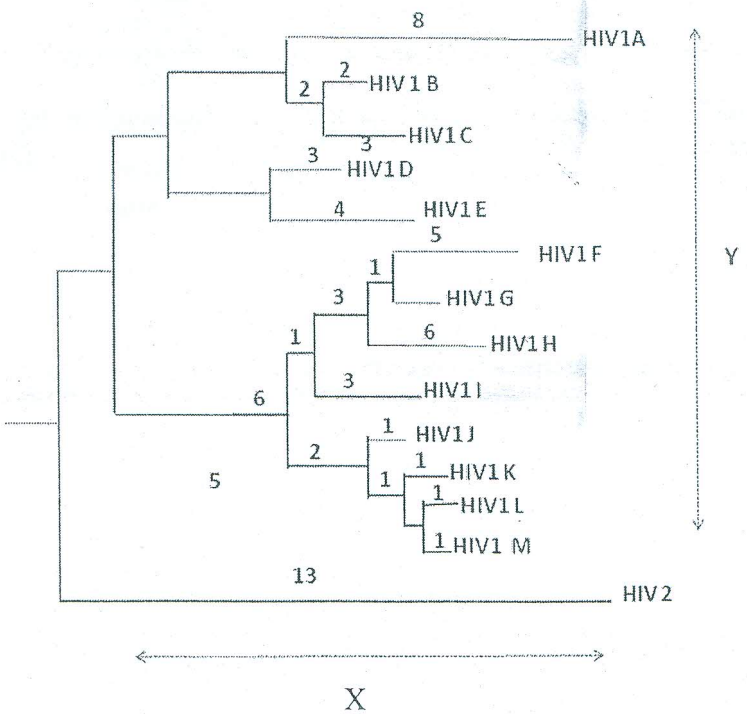
2.4 GenBank entries for human Retinol Binding Protein consist of one entry in the UniGene division and 200 entries in the corresponding Expressed Sequence Tag (EST) division. What does this signify?
(25 marks)

Contd..../3-

3.

3.1 Evolutionary relationships among different taxa could be depicted using different phylogenetic trees. Showing appropriate figures explain what cladograms and phylograms mean. (30 marks)

3. 2 Given below is the Neighbour joining phylogenetic tree constructed using Envelope gp160 sequences of HIV 1 (isolates A to M) and HIV 2 isolates derived from the same geographical locale. Comment on the phylogenetic relationships and evolutionary aspects of HIV1 isolates. (40 marks)



3.3 State what is meant by knowledge-based protein modeling (30 marks)

Contd.../4-

4.

4.1 Explain briefly, what is meant by "*in vivo*" gene therapy. (25 marks)

4.2 List three (3) modes of non-viral gene delivery approaches used in "ex-vivo" gene therapy. (15 marks)

4.3 State two (2) limitations of retroviral vectors for gene transfer. (20 marks)

4.4 Outline briefly, using a schematic diagram, how you would engineer an adeno-associated viral vector suitable for a therapeutic gene transfer. (40 marks)

5.

5.1 Briefly mention two (2) potential applications of anti-sense oligonucleotides as therapeutic agents. (20 marks)

5.2

5.2.1 What do you understand by the term "RNA interference"?
(Note: mechanism of action is not required in your answer) (25 marks)

5.2.2. State two (2) human diseases where RNA interference has potential therapeutic Benefits. (15 marks)

5.3 State two (2) drawbacks of adult stem cells when compared to embryonic stem cells, as therapeutic agents. (20 marks)

5.4.List two (2) DNA based approaches that can be used in therapeutic management of cancers. (20 marks)

Contd.../5-

6.

6.1. Explain briefly the important factor/s you would consider in selecting an expression system for producing recombinant therapeutic proteins. (10 marks)

6.2

6.2.1. Different constructs of recombinant human insulin with specific modes of action have been produced to treat diabetes mellitus. Discuss the above statement giving examples. (30 marks)

6.2.2. List three (03) recombinant proteins, other than recombinant insulin, used as therapeutics. (15 marks)

6.3.

6.3.1. List the three (03) main types of recombinant monoclonal antibodies used for therapeutic purposes. (15 marks)

6.3.2. Discuss briefly the therapeutic applications of one of the above recombinant monoclonal antibodies, giving an example. (20 marks)

6.4 Discuss the problems associated with producing an effective DNA vaccine against the Dengue viral infection. (10 marks)

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SEMESTER II (REPEAT) EXAMINATION – NOVEMBER 2010

Date :- 11th November 2010 **Time :-** 1.00 p..m. – 4.00 p.m.

ESSAY PAPER

Write essay on our (04) topics selecting at least ONE TOPIC from each part. **(100 marks each).**
Answer each essay in a separate answer book.

PART A

1. Extracellular matrix disorders
2. Apoptosis and cancer
3. Ethics of genetic testing
4. Chromosome abnormalities and their clinical implications

PART B

1. *In situ* hybridization
2. PCR in infectious disease diagnosis
3. Genetically modified organisms
4. Applications of DNA fingerprinting