Ref. No. Ex/SC/BT/PG/Core/TH/333/2023

M. Sc. (Biotechnology) Examination, 2023

(2nd Year, 1st Smester)

Subject : GENOMICS AND PROTEOMICS

Paper : MSBT 333

Time : Two hours Full Marks : 40

Group -A

Answer Question No. 1 and 8 and any three questions from Q. 2 to Q.7

1. Answer any five questions 5X2=10

(a) State the law of "Independent Assortment" as proposed by Mendel? What is the condition with respect to the relative chromosomal locations of the two alleles that must be satisfied for independent assortment to happen?

(b) Present a logical argument that suggests that the mechanism of determination of sex in human is different from that in *Drosophila*?

(c) What do you mean by "molecular marker"? Mention one technique by which you will be able to differentiate between the different allelic forms of molecular markers.

(d) State "One gene-One Enzyme" hypothesis. Also, state whether this hypothesis is still valid today. If not, how would you modify it?

(e) What do you mean by Tiled Microarray technique? What is the benefit of this technique over the conventional microarray?

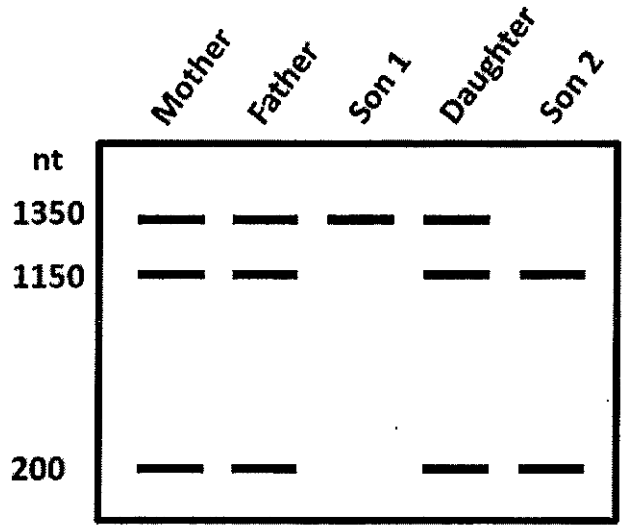
(f) Explain how the use of "barcode" helps in multiplexing during the library preparation for RNA sequencing?

(g) Differentiate between biological replicates and technical replicates.

(h) What is the function of "TOPHAT" Pipeline? Exactly how does this pipeline work?

2. (a) FISH analysis with a probe of unknown sequence (the label of the sample on the tube fell off) reveals a fluorescent spot at one end of every chromosome. Could this be
(i) a unique gene probe?
(ii) a centromere probe?
(iii) a telomere probe? 2

(b) Sickle cell anemia is a recessive genetic disease caused due to a point mutation in the 6th codon abolishing one of the MspII endonuclease digestion site present in β-globin gene. MspII digested DNA from a normal person gives two bands, 1150 bp and 200 bp in β-globin gene. The MspII digestion pattern of β-globin gene from the blood samples from the members of a family is given below:



Explain the MspII digestion data and provide the genotype (with respect to Sickle cell anemia) of each of the family member. 3

3. (a) In *Drosophila*, the gene for bobbed bristles (recessive allele bb, bobbed bristles; wild type alleles bb^+ normal bristles) is located on the X chromosome and on a homologous segment on the Y chromosome. Give the genotypes and phenotypes of the offspring from the following crosses:

(i) $X^{bb} X^{bb} \times X^{bb} Y^{bb+}$,
(ii) $X^{bb} X^{bb} \times X^{bb+} Y^{bb}$,
(iii) $X^{bb+} X^{bb} \times X^{bb+} Y^{bb}$
(iv) $X^{bb+} X^{bb} \times X^{bb} Y^{bb+}$.

3

(b) In *Drosophila,* The allele for white eyes is sex-linked and recessive to the wild-type allele, red eyes. When white-eyed males were crossed with red-eyed females, the F1 progeny consisted of 433 red-eyed females and 420 red-eyed males. The F2 progeny showed the following results:

Red-eyed males 105
Red-eyed females 204
White-eyed males 96
White-eyed females 0

Do these data fit the appropriate genetic hypothesis? 2

4. (a) In an *in situ* hybridization experiment, a certain clone bound to only the X chromosome in a boy with no disease symptoms. However, in a boy with Duchenne muscular dystrophy (X-linked recessive disease), it bound to the X chromosome and to an autosome. Explain. Could this clone be useful in isolating the DMD gene? 2

(b) With 10% recombination between genes a and h, 15% recombination between genes h and c, the order being a h c, and a coefficient of coincidence value of 1.0, calculate the expected gametic frequencies in an individual with the genotype Aa Hh Cc in coupling to aahhcc. 3

5. You identified a new protein in *Saccharomyces cerevisiae*. A preliminary bioinformatic analysis is indicating that this protein could be a transcription factor, because it has a putative leucin zipper domain (which can potentially bind DNA) and a stretch of polyglutamine (PolyQ) towards the c-terminal end of the primary sequence. Suggest an experimental approach to identify (i) the comprehensive list of the target genes in the genome (at the genome-wide scale) of this newly identified protein factor, and (ii) if the protein truly binds DNA, 3+2 = 5

6. (a) Mention the size of oligonucleotides which are typically used for Oligonucleotide-based Microarray. Mention one advantage for using oligo-based microarray over DNA or cDNA microarray. How the oligonucleotide probes are spotted onto the solid matrix? 2

(b) You want to determine the total pool of "antisense" transcripts that become stabilized (increased) in yeast *Saccharomyces cerevisiae*, when it is grown in presence of a metal ion in the medium with respect to the absence of that metal ion. Which technique will be appropriate to find out the answer of this question? Since, you are looking to determine the anti-sense transcripts, what specific step you must carry out when designing your experiment. 3

7. (a) What do you mean by "probe set" in a microarray experiment? Briefly explain why a combination of perfectly matched and a mismatched oligonucleotide is used to design such a probe set. 1

(b) Briefly outline the pipeline involved in RNA Sequencing technology. You may present a workflow diagram of RNA sequencing technique with a brief description of individual steps within small boxes without long description. 4

8. What is a short-read NGS? Describe the steps used in short-read NGS chemistry with examples of any specific NGS platform. 1+4

Or,

Write a note on two primary long-read NGS technologies used in human genome sequencing 2.5 + 2.5

Group B (Answer any *two* questions, each containing 5 marks), Total 10

9. (A) What are the advantages of using IPG (immobilized pH gradient) strips to separate proteins on the basis of isoelectric point? (2)
   (B) Briefly describe the elctrospray and chemical ionization methods in mass spectrometry. (1.5x2 =3)

10. (A) What are the basic components required for a mass spectrometry? (3)
    (B) What is the function of electron multiplier in mass spectrometry? (2)

11. (A) Tryptic digestion of a heptapeptide consists of three Lysin, two alanine, one tyrosine and one phenylalanine results in two fragments with one tripeptide and one tetrapeptide. Find out the sequence of amino acids of the heptapeptide. (Note: One Lysine is terminally located) (2)

    (B) Write three advantages and three disadvantages of cell labelling by SILAC for quantitative proteomic analysis. (1.5 x 2=3)

12. (A) What are the important features of tryptic digestion in proteomics? (2)

    (B) Following is the amino acid sequence, subjected to tryptic digestion for mass spectrometric analysis. Write down the different peptide fragments that you would get after tryptic digestion. (1)

    RLVEVALGKIGGGANTRGYEVALVNTKFWMCSMVALPGMSWFRH

    (C) How does quadrupole analyze the mass of a peptide in a mass spectrometry? (2)

13. (A) What are molecular ions, fragment ions and base peak in mass spectrometric analysis? (2)

    (B) What does MALDI-TOF stand for? Explain briefly the basis of this technique for the analysis of proteins? (1+2)=3