

M. SC. BIO-TECHNOLOGY PART II EXAMINATION, 2017**MOLECULAR GENETICS, GENOMICS AND PROTEOMICS****PAPER - 2/2**

Time : Four hours

Full Marks : 100

GROUP A

Answer **Question No. 1** and **any five** Questions from following
taking at least **two** from each Part

Part - IAnswer **all** questions.

8x1=8

1. (a) How the term “incomplete-dominance” differs from “co-dominance” at the molecular level? Explain with an example.
- (b) Present an evidence that crossing-over occurs at four-strand stage of the chromatids.
- (c) What is SRY locus? What is its functional role?
- (d) How “phenylketonuria” (PKU) is resulted? Suggest a secondary cure for this disorder.
- (e) Briefly mention the working principles involved in Ion Torrent next generation sequencing platform.
- (f) What do you mean by “Genome Sequencing by ordered clone approach”?
- (g) What is “ChIP-on Chip”? State one of its applications in modern biology.
- (h) How the distance between the genes is expressed in chromosome mapping by recombination?
- (i) Why the yeast *cdc* mutants are relevant to human cancer?
- (j) Explain the technique of “dye-swapping” for validating the microarray data.

Part – II

2. (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) $X^{bb+} X^{bb} \times X^{bb} Y^{bb+}$.

4

- (b) What do you mean by the term “Synthetic lethality”? Explain how the phenomenon of synthetic lethality can be explained at the molecular level.

3

- (c) If an individual with genotype A/A.B/B is crossed to the one with genotype a/a.b/b, and the F1 is test-crossed, what percent of the testcross progeny will be a/a.b/b if the two genes are (a) unlinked, (b) completely linked (assume crossing over is zero), and (c) 10 map units apart.

3

[Turn over

3. (a) Explain what do you mean by “complementation group”? In an attempt to identify the genes involved in leucine biosynthesis in *Neurospora* you have initially mutagenized a wild type strain by methyl methane sulphonate. Initially you have obtained 745 strains who failed to grow on minimal media lacking leucine, but all of them have grown fine on rich YPD medium. Outline an approach how you would ascertain if all 745 leucine-auxotrophic mutant strains belong to one class. If not, how you would classify them experimentally using systematic genetic analysis? 4

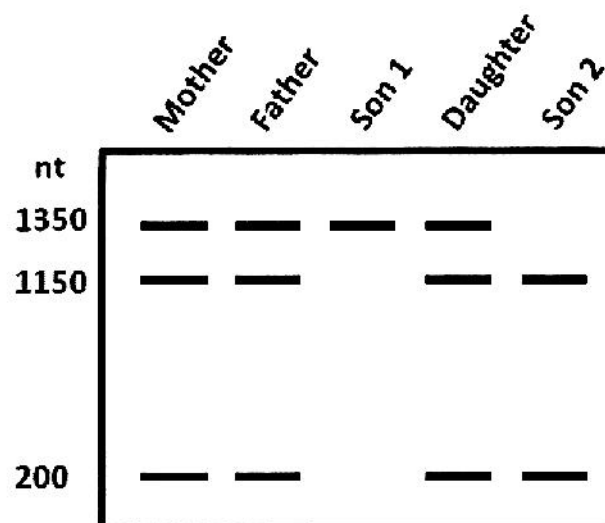
(b) If both partners were known to be carriers (Cc) for albinism, what is the chance of the following combinations in the family of four:

- (i) All four normal
- (ii) Three normal and one albino
- (iii) Two normal and two albino
- (v) One normal and three albino

4

(c) What do you mean by “penetrance” and “suppression”? Provide examples. 2

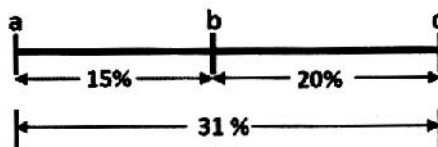
4. (a) Sickle cell anemia is a recessive genetic disease caused due to a point mutation in the 6th codon abolishing one of the MspII endonuclease digestion site present in β -globin gene. MspII digested DNA from a normal person gives two bands, 1150 bp and 200 bp in β -globin gene. The MspII digestion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

(b) What is “Criss-cross” inheritance pattern? In what kind of inheritance this pattern is observed. Explain with diagrams why this kind of pattern is followed in such inheritance? 4

5. (a) The accompanying diagram summarizes the recombination frequencies observed in a large experiment to study three linked genes a, b, and c.



What was the observed frequency of double crossing-over in this experiment? Calculate the interference

4

- (b) Write short notes (*any three*):

2×3=6

- (i) Epistasis
- (ii) LOD Score
- (iii) Linkage Group
- (iv) Tetrad
- (v) FOA

6. (a) The following offspring phenotypes were obtained from a cross between *Drosophila* females heterozygous for three alleles, approximated vein, curled wing, and stripped thorax (+app, +cu, +sr) and male homozygous for those alleles:

Phenotypes	Number
+ + +	337
app cu sr	348
+ cu sr	58
app + +	49
+ + sr	55
app cu +	48
+ cu +	3
app + sr	2
Total	900

Construct a linkage map and calculate the coefficient of coincidence

7

- (b) Normal Chromosome of a certain organism has the following configuration of genes:

A B C D E F G H

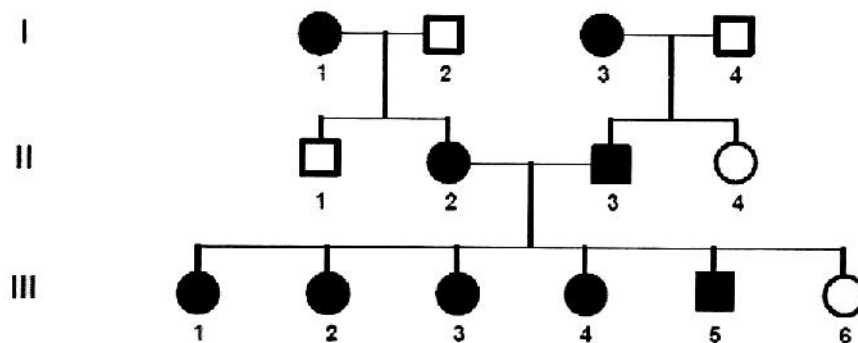
A horizontal line representing a chromosome with a small circle in the middle. Above the line, the letters A, B, C, D, E, F, G, and H are arranged in a row, corresponding to the positions of the genes on the chromosome.

One member of this organism was irradiated with UV-radiation and crossed with the opposite mating type having recessive alleles for all these genes. In the progeny of the cross, organism with following types of genotypic configuration were obtained in addition to individuals with normal configuration. Account for the observed results:

- (i) $\frac{A \ B \ C \ F \ E \ D \ G \ H}{\circ}$
- (ii) $\frac{A \ B \ E \ F \ G \ H}{\circ}$
- (iii) $\frac{A \ B \ C \ D \ E \ F \ E \ F \ G \ H}{\circ}$

3

7. (a) Assume the pedigree presented below to be straight forward, with no complication. Trait W, found in the individuals represented by the standard symbols, is rare in the population at large



State which of the following pattern of transmission for W are consistent with or excluded by this pedigree.

(i) Autosomal recessive, (ii) Autosomal dominant, (iii) X-linked recessive, (iv) X-linked dominant and (v) Y-linked.

Define the genotype of each of the individuals

6

(b) Provide two evidences which indicate that helped to establish that Chromosomes are the seats of heredity?

2

(c) If a man of blood group AB marries a woman of blood group A whose father was of blood group O, to what different blood groups can this man and woman expect their children to belong?

2

Part – III

8. (a) Mention two basic strategies which are typically used in massive sequencing projects to construct the sequence of the whole genome? What do you mean by the term “contig”? 3+1
- (b) Mention briefly the basic principle involved in Pyro-sequencing technique. 4
- (c) Two particular contigs are suspected to be adjacent, possibly separated by repetitive DNA. How would you bridge these two gaped contigs? Would you expect this approach to work in every occasion? 2
9. (a) What is the meaning of “base-calling” in next-generation sequencing platforms? Explain the principle of reversible terminator technology of DNA sequencing used by Illumina Genome Analyzer. 2+4
- (b) How the next-generation technology can be utilized to analyze the transcriptome of cell under two different environmental cues ? 4
10. 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) if the protein truly binds DNA (ii) truly a transcription factor and (iii) the sequence of the putative target binding sites and (iv) the comprehensive list of the target genes in the genome (at the genome-wide scale) of this newly identified protein factor. 2+2+3+3
11. (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? 3
- (b) 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. 3
- (c) Why is it necessary to validate the expression dataset obtained from microarray analysis performed at the “transcriptomic” scale. Mention two methods which are routinely used to validate the expression datasets. 2+2

GROUP B

[Q. No. 12 is compulsory and answer **any one** from Q. No. 13 & 14]

12. a) Why is proteomics considered more complicated than genomics? (1)
- b) What is the function of SDS and beta-mercaptoethanol in SDS-PAGE? (1)
13. i) What is the basic principles of separation of proteins in 2D-GEL electrophoresis? Describe how would you perform isoelectric focusing gel electrophoresis in order to separate proteins? (1+3=4)
- ii) What is the important feature of tryptic digestion in proteomics? (2)
- iii) Briefly describe the electrospray and chemical ionization methods in mass spectrometry. (2+2=4)
14. i) What are the basic components required for a mass spectrometry? (2)
- ii) What does MALDI-TOF stand for? Explain briefly the basis of this technique for the analysis of proteins? (1+5=6)
- iii) What is the function of electron multiplier in mass spectrometry? (2)

GROUP C

[Answer any three questions (3x10 = 30)]

15. a) It is known that one strand of the donor DNA enters the recipient chromosome in case of conjugation. Can you design an experiment to prove this point?
- b) In conjugation, we often use antibiotic sensitive Hfr donor to kill it when required. Where in the chromosome, with respect to the origin of transfer, should your gene for selection reside in such a case?
16. a) What kind of mutations are generated by nitrous acid and proflavine?
- b) A mutation in phage lambda does not allow it to lysogenize wild type E.coli cells. Also a mutation in E.coli does not allow wild type lambda to integrate in it. But when you infect the mutant lambda to the mutant E.coli, you get some lysogens. Give such an example.
17. a) What makes Bacteriophage P1 useful for transduction of DNA from E.coli to a wide range of bacterial species.
- b) Give reasons for your choice of the genetic tools to map genes in E.coli and S. typhi located 100000 nucleotides apart and 5000 nucleotides apart?
18. a) Describe an experiment to show that the transposable elements are mobile genetic elements.
- b) What is the molecular explanation for a P male x P female being viable, but a P male x P female, dysgenic in the fruit fly D. melanogaster.