Test Code: RHG-I (Short answer type) & RHG-II (Descriptive type) 2007

Junior Research fellowship in Human Genetics

Syllabus

1. Cell growth, Division, Differentiation, Senescence

2. Metabolism of protein, carbohydrate and lipids in relation to diseases.

3. Replication, Transcription, Translation, Genetic code & protein synthesis, Enzymes, Co-enzymes, Receptor mediated cell functions, regulation of gene expression

4. Cancer genetics, etiological factors for different types of cancers

5. Population genetics, genetics of single and multi loci diseases

6. Modern methodologies in cell/tissue culture, Chromosome techniques, PCR ELISA, Immunocyto/histochemical techniques, Hybridization techniques and other molecular biology techniques

7. Gene therapy and modification of gene expression (anti-sense RNA, RNAi/miRNA, chromatin remodeling) transgenic and knockout mouse, tissue specific knock-out of gene

8. Cancer biology, Abnormal cell growth, Oncogenes & Tumour suppressor genes, Programmed cell death, Cell signaling, Immunomodifiers

9. Basic Statistics: Mean, Median, Mode, Standard deviation, Correlation and Regression, Simple probability calculations

10. Biostatistics: Chi- square and ‘t’ test, Hardy-Weinberg equilibrium law, Linkage Disequilibrium

Sample Questions RHG-I (Short answer types)

1. Consider an autosomal locus with three alleles A1, A2 and A3. Suppose the frequencies of the alleles in a random mating population are 0.6, 0.3 and 0.1, respectively. What is the total frequency of heterozygotes at this locus in this population?
2. If, on an average, there were one nucleotide change per 1kb of DNA per one million years, how many nucleotide changes would you expect if you compared 10kb of two DNA sequences that diverged from each other 10 million years ago?
3. A mutation in an essential human gene changes the 5' splice site of a large intron from GT to CC. Predict the phenotype of an individual homozygous for this mutation.
4. What is the genetic map of a locus containing the genes x, y, and z, if the frequencies of recombination are 0.5% between x and z, 0.2% between x and y, and 0.7% between y and z? (You may assume that there is no interference.)
5. Let Y denote the total length (number of nucleotides) of all introns of a gene and X denote the total length (number of nucleotides) of all exons of a gene. Suppose for a set of genes it is found that $Y=X^2$, what is the correlation between the total intron length and the total exon length of these genes?
6. How many copies of a specific gene sequence can be obtained after 10 and 30 cycles of PCR amplification from a haploid and a diploid cell, respectively? Justify your answer.

7. Digestion of a 4kb DNA molecule with KpnI yields two fragments of sizes 1kb and 3kb. Hind III digestion of the same DNA yields fragments of sizes 1.5 kb and 2.5 kb. Finally digestion with KpnI and HindIII in combination yields fragments of sizes 0.5kb, 1kb and 2.5 kb. Draw a restriction map indicating the positions of the KpnI and HindIII cleavage sites.
8. Both embryonic and cancer cells divide quickly -: how can these two types of cells be distinguished?
9. How can RNase protection assay be used to quantitate the level of a particular mRNA species under different conditions?
10. What are the structural requirements for steroid hormone regulation? Discuss mechanism of involvement.

Sample Questions: RHG-II (Descriptive type)

1. In crosses of the fruit-fly *Drosophila*, Thomas Hunt Morgan collected data on 2839 flies pertaining to two autosomal loci. The first locus has two alleles denoted as *A* and *a*, while the second locus has two alleles denoted as *B* and *b*. The 2839 flies were all progeny of the following mating: *AaBb* x *aabb*. The observed frequencies of genotypes of the flies were: *AaBb*=1339, *Aabb*=151, *aaBb*=154 and *aabb*=1195. Provide a genetic model for these data (the relative locations of the two loci on chromosomes and an explanation for the observed genotype frequencies).
2. Explain Lambert- Beers Law. Why does the absorbance of equimolar amounts of tryptophan and tyrosine differ, at 280 nm? Explain why mutation of a protein can lead to change in absorbance at 280nm?
3. Phenylketonuria (PKU) is a rare autosomal recessive disease. A couple who are both normal decide to have children. The man has a brother with PKU and the woman has a sister with PKU. There are no other known cases in the family.
   a) Deduce the genotypes of the man's brother and woman's sister.
   b) What are the genotypes of the man and woman's parents?
   c) What is the probability that the couple's first child will have PKU?
4. What are the processes involved in X-chromosome inactivation in mammals?

5. a) Many cancers seem to involve environmental factors. Why, then, is cancer called a genetic disease?

   b) Discuss how programmed cell death / apoptosis participates in maintaining cellular homeostatis. Explain why DNA from apoptotic cells show up as 200bp ladder in agarose gels.

6. Describe how mRNA translation is initiated and terminated. Why is the genetic code a triplet instead of doublet or singlet code, considering the fact we have 20 different amino acids? How many different amino acid sequences are possible in a polypeptide 146 amino acids long?

7. Describe characteristic features of mismatch, base-excision and nucleotide excision repairs with examples.