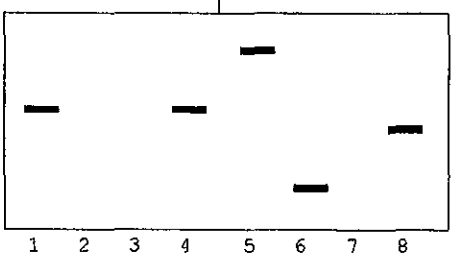
1. Many genes are essential during embryonic development and in the adult stage. Gene targeting is a powerful method to study the function of a gene by modifying the physical structure of the gene such that its function is knocked out. How can the function of an essential gene required for embryonic development be studied in an adult knockout mouse? (5%)

2. What experimental evidence supports the fluid mosaic model of biomembranes? Certain integral membrane proteins are significantly less mobile than others. What accounts for this reduced mobility? (5%)

3. Translation of proteins across the membrane of the endoplasmic reticulum (ER) is usually studied using microsomes, which are vesicles derived from the ER membrane during isolation. Microsomes from the rough ER carry ribosomes attached to their outer surface. Translation of proteins across microsomal membrane can be assessed by several experimental criteria: (1) protection of the newly synthesized protein from exogenously added proteases, and lack of protection from proteases when detergents are present to solubilize the protecting lipid bilayer; (2) glycosylation of newly synthesized proteins by oligosaccharide transferases, which are localized exclusively to the lumen of the ER; (3) cleavage of signal peptides by signal peptidase, which is also active only on the luminal side of the ER membrane. You have performed protein synthesis by translation of a purified mRNA with microsomes. You then treated the translation reactions in four different ways: (1) no treatment, (2) add a protease, (3) add a protease and detergent, and, (4) disrupt microsomes and add endoglycosidase H (endo H), which removes N-linked sugars that are added in the ER. An electrophoretic analysis of these samples is shown below.

Treatment	Microsomes Absent				Microsomes Present			
protease	-	+	+	-	-	+	+	-
detergent	-	-	+	-	-	-	+	-
endo H	-	-	-	+	-	-	-	+



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Is the protein of interest a glycoprotein? Why? Explain the migration of the proteins in lanes 5, 6, and 8. Is the protein of interest a transmembrane protein? Why? (10%)

4. Explain embryonic and adult stem cells, respectively. What are the advantages and disadvantages of working with embryonic and adult stem cells with respect to stem-cell therapies in humans? (5%)

5. Answer the questions about eukaryotic mRNA (10%)
   a. Name the three general posttranscriptional processing reactions that are observed in eukaryotic mRNA.
   b. What protein domain is essential to couple these processes with transcription?
   c. Describe the function of the structure present on the 5' and 3' ends of mature eukaryotic mRNA in translation initiation.
   d. In addition to the coding region, the mature mRNA contains 5' and 3' untranslated regions. What is their function?

6. A transcription factor named TF was investigated. Please explain the underlined terms. (15%)
   a. TF contains leucine zipper and basic amino acid domains.
   b. Its activation domain was mapped.
   c. The GFP-TF fusion protein was expressed in eukaryotic cells to demonstrate its subcellular localization.
   d. The expression of TF in cells was knocked down by a specific siRNA.
   e. The cells were transfected with the plasmid encoding FLAG-tagged TF and the *in vivo* DNA-binding activity of TF was analyzed by chromatin--immunoprecipitation assay.

7 Recent researches have implicated Z-DNA and quadruplex DNA in life processes. Briefly describe (a) how these variant forms of DNA can form in the middle of a section of B-DNA, and (b) the physiological roles they may play (8%).

8 Briefly describe the physiological roles of (a) DNA gyrase in prokaryotic cells, (b) proliferating cell nuclear antigen (PCNA), (c) replication factor C and (d) telomerase in eukaryotic cells (10%).

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9 How can breakdown in DNA repair play a role in the development of human cancers (3%)?

10 Each of the following pairs of primers has a problem if used in the polymerase chain reaction. Tell why the primers would not work well. (a) Forward primer 5' GCCCTCCGGAGACCCCATTGG 3', Reverse primer 5' TTCTAAGAAAAACTGTTAAGG 3' (b) Forward primer 5' TCGAATTGCCAATGAAGGTCCG 3', Reverse primer 5' CCTTCATTGGCAATTCGAGCCA 3' (4%).

11 Autophagy is a process in which cytoplasmic components are broken down by the cell from inside. Please discuss the possible roles of this phenomenon. (5%)

12. In the plasma membrane of mammalian cells, phospholipids are not uniformly distributed between the two monolayers. Please describe the patterns of different phospholipids found in each monolayer. (5%)

13. An asymmetric cell division produces two daughter cells with different properties. Please give an example of this event and discuss the consequence of this event. (5%)

14. What are hydropathy curve and its application? (5%)

15. Which organelle has its own DNA? How does this relate to maternal genetics? (5%)

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