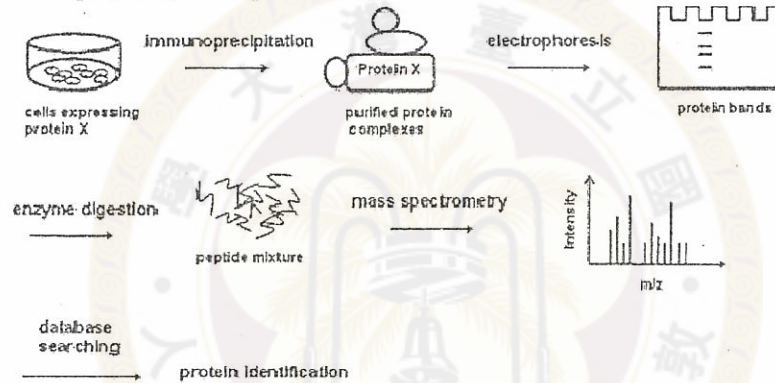


1. (A) The compound, 3'-azido-2'-deoxythymidine (AZT), has been widely used in the treatment of AIDS (acquired immune deficiency syndrome) disease. Please propose an explanation for the effectiveness of this compound. (B) 5'-aza-2'-deoxycytidine (an inhibitor of DNA methyltransferases) and trichostatins A (an inhibitor of histone deacetylases) are used as anti-cancer drugs. Please describe their mechanisms. (8%)
2. Human TNF-alpha has 233 amino acid residues.  
(A) What is the minimum number of nucleotide pairs required to code for this protein?  
(B) The length of TNF-alpha complete mRNA found in Entrez database is 1669 bases. How can you account for the discrepancy between the size you calculated and the actual length of the mRNA?  
(C) The expression of TNF-alpha mRNA is induced and degraded rapidly in response to the inflammatory signals. Please explain the possible regulation in both processes of transcription and RNA stability. (12%)
3. Explain the different ways in which eukaryotic transcription elongation is controlled. (5%)
4. Protein cysteine residues are prone to oxidation reaction in the presence of cytosolic oxidants such as nitric oxide and hydrogen peroxide. Please give the structures of cysteine side chain (2%) and its oxidized products by nitric oxide (2%) and hydrogen peroxide (2%).
5. Hypoxia inducible factor 1(HIF1) consists of a heterodimer of two basic helix-loop-helix proteins, HIF1-alpha, and HIF1-beta. HIF1-alpha accumulates under hypoxic conditions whereas HIF1-Beta is constitutively expressed. HIF1-Alpha is an important mediator of the hypoxic response of normal and tumor cells. Please explain why hypoxia leads to accumulation of HIF1-alpha in cells. (6%)
6. Please define an integral protein (3%) and demonstrate by experiments that a given protein is an integral membrane protein? (4%)
7. Cell compartmentation means a partitioning within cells due to the semi-permeable membranes which enclose each of the separate parts, e.g., mitochondria, lysosomes, endoplasmic reticulum, Golgi apparatus, etc. Please

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discuss the possible function of cell compartmentation. (6%)

8. A scientist is studying protein X and trying to identify cellular proteins that interact with protein X. He/She has prepared a monoclonal antibody against protein X and performed a series of experiments as shown in the following cartoon. Note that each protein band is cut for digestion with a protease into a mixture of peptides, which is then analyzed by mass spectrometry. Explain how to prepare a monoclonal antibody and the purposes of immunoprecipitation, electrophoresis, mass spectrometry, and data searching. (10%)



9. Describe how cells undergo apoptosis after ionizing irradiation. (5%)
10. The human olfactory system detects a wide range of odorant molecules by odorant receptors in mucosal epithelia. We usually lose the sense by which odors are perceived after a longer exposure to the odorant molecules. Explain the molecular mechanism underlying this phenomenon. (5%)
11. Heparin is a glycosaminoglycan with an anticoagulant effect that prevents blood clotting. What is glycosaminoglycan? Explain how heparin works as an anticoagulant. (5%)
12. A new antibiotic was recently discovered that inhibits prokaryotic protein synthesis. In the presence of the antibiotic, protein synthesis can be initiated, but only dipeptides that remain bound to the ribosome are formed. What specific step of protein synthesis is likely to be blocked by this antibiotic? (2%)
13. If perfect Watson-Crick base pairing was demanded between codons and anticodons, cells would need 61 different tRNAs. If there are only 20 amino

acids used in protein synthesis, how would you explain this excess number of tRNAs compared to amino acids? (4%) Conversely, how would you explain the fact that some cells contain fewer than 61 tRNAs? (4%)

14. What is the difference between a nucleoside and a nucleotide? (3%)
15. Why is there a need for a specialized structure at the ends of eukaryotic chromosomes and for the enzyme telomerase? (8%)
16. Describe how modification of histone tails can control chromatin condensation. (4%)

