

1. Please explain the iPSC (induced pluripotent stem cells) technique developed by Yamanaka and Takahashi and how this can be possible? (7%)
2. As proteins traverse the secretory pathway, they encounter compartments with increasingly acidic pH, from the endoplasmic reticulum whose pH is close to that of cytoplasm (7.2-7.4), to the Golgi (~ 6.2), to mature secretory granules (~ 5.5). The presence of H<sup>+</sup>-ATPase that pumps protons into the lumen and chloride channel that allows the flow of chloride ions into the lumen is needed for the efficient acidification of these organelles. Please discuss the roles of the chloride channel in this phenomenon. (5%)
3. Please describe the roles of endoplasmic reticulum in protein secretion. (6%)
4. The widespread nature of protein phosphorylation/dephosphorylation underscores its key role in cell metabolism, growth and differentiation. Please discuss all possible effects of phosphorylation on proteins. (7%)
5. You have isolated a fragment of viral DNA that totally encodes at least two proteins, 120 and 80 amino acids long. The DNA fragment is 400 base pairs long. (a) Why might you consider this unusual (4%)? (b) You sequence the two proteins and find no sequence homology. Propose a model to account for these findings (6%).
6. Describe (a) the possible outcomes that could occur because of a single base change in an mRNA (5%), (b) the composition and structure of a nucleosome (4%).
7. What is an Okazaki fragment (2%)? What enzyme(s) is (are) required for its formation in *E. coli* (4%)?
8. Detection of protein-protein interactions would help to define cellular and molecular function. Two techniques are used to identify associated proteins: (a) Immunoprecipitation and (b) Yeast two-hybrid analysis. Please describe these two methods briefly. (10 %)
9. If you are studying a liver-specific protein which contains 240 amino acids translated from a 1600 base mRNA. (10 %)
  - (a) Please explain the information about the length of its protein and mRNA.
  - (b) How do you clone this gene for protein expression by PCR method?

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- (C) The cloned gene will be expressed in bacteria and mammalian cells. What is the major difference on protein expressed in these two hosts?
- (d) There are *lac I* gene, bacteria promoter (P) and operator (O) on the *E.coli* expression vector. How to control protein expression by using this vector?
10. Although genomic information is uniform among the different cells of a complex organism, the epigenome varies from tissue to tissue, controlling the differential expression of genes and providing specific identity to each cell type. Write down the principle epigenetic control factors. (5 %)
11. Explain the principles and applications of confocal microscopy and cryoelectron microscopy. (10%)
12. Vesicular trafficking delivers newly synthesized proteins to their specific target sites in eukaryotic cells. A key step in vesicular trafficking is membrane fusion between vesicle and the target membrane, which is mediated by fusion proteins. What are the fusion proteins and how do the fusion proteins mediate membrane fusion? (5%)
13. Cell migration is stimulated by growth factors such as epidermal growth factor and platelet-derived growth factor. Small GTPases including Rho, Cdc42, and Rac are the downstream factors in regulation of cell migration. Describe the roles of these small GTPases in the signaling pathway that stimulates cell migration (5%).
14. Explain telomere and telomerase. Explain why telomerase activity is detected in human tumor cells, but not in normal cells (5%).

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