1. The Nobel Prize in Chemistry 2004 was awarded to three pioneers in studying the regulated protein degradation. Through their studies and others, we now know excessive formation followed by aggregation of improperly folded proteins could be detrimental to a living cell even an organism. Please describe three cellular mechanisms to monitor protein quality after protein synthesis and list the protein complex(es) involved in each mechanism. (10 points)
2. **(1)** Please define a transcription unit and list the difference(s) in the units, respectively, derived from prokaryotes and eukaryotes. (5 points)

   (2) Please provide an experimental approach and its principles used to study if any DNA-binding protein binds to the region which drives the expression of this transcription unit. (5 points)
3. **(A)** Short-answer questions: (1 point, each)

   (1) Restriction enzymes generate three types of termini. What are they?

   (2) Analysis of a DNA sample from a bacterium indicates that 16% of the bases are A. What fraction is C?

   (3) Can DNA be directly labeled with ^{32}P using labeled ATP and polynucleoidtide kinase? Please give your rationale.

   (4) Why is the activity of most polymerases inhibited by the addition of chelating agents such as EDTA?

   (5) A protein has a molecular weight of 7000 Da. Can you estimate how many amino acids residues the protein has? A double-stranded DNA has a molecular weight of 132000 Da. How long is the DNA molecule in base pairs?

   (B) Please briefly define the following terms (1 point, each).

   A protein has a molecular weight of 7,000 Da. Can you estimate how many amino acids residues the protein has? A double-stranded DNA has a molecular weight of 132,000 Da. How long is the DNA molecule in base pairs?

   (1) Provirus

   (2) Missense mutations

   (3) Open Reading Frame

   (4) CpG island

   (5) CpG motif
4. Please briefly answer the following questions. (10 points)

   (1) List two membrane interaction mechanisms for viruses to enter cells.

   (2) What is the major difference (or factor) that distinguishes the entry between HIV and influenza viruses?

   (3) What is the major difference that distinguishes the entry between polioviruses and adenoviruses?

   (4) Are these viruses enveloped or non-enveloped viruses?

   (5) Are they DNA viruses or RNA viruses?
5. If you are going to clone a conserved eukaryote gene from a mouse brain cDNA library by polymerase chain reaction (PCR), and the conserved sequences given to you are two peptide sequences encoded by this gene. One is Met(1)-Leu-Ile-Trp-Cys-Pro-Met, and the other is

(背面仍有題目，請繼續作答)

Ser(100)-Met-Ala-Leu-Trp-Pro-Cys. The (1) or (100) represents the position of the amino acid in the complete open reading frame. (10 points)

(1) Describe how you will apply the "wobble hypothesis' to design the primers (21mer) based on the conserved sequences.

(2) How many primers can you design from each conserved sequence based on the wobble hypothesis? Note that each amino acid has its own degenerate codes, and the number for each of them is listed in the following. Met:1, Leu:6, Ile:3, Trp:1, Cys:2, Pro:4, Ala:4, Ser:6.

(3) How will you use the primers to clone the rest of the sequence of this gene after you obtain an expected PCR product?

6. **(1)** Describe the major molecules involved in promoting the cell cycle progression (5 points).

(2) In cell cycle regulation, some gene's mutation results in loss of function and such mutation causes abnormal cell cycle regulation and even tumor formation. Give an example for such phenotype and explain the molecular mechanism. (5 points)

7. Both lymphocytes and monocytes can recognize invading bacteria with their cell surface receptors. (10 points)

(1) What are the differences between these receptors?

(2) Please describe the molecular structure of a B cell antigen receptor.

8. Most cell surface proteins are decorated with carbohydrates (glycosylated). (10 points)

(1) Please describe the sites on a peptide where the carbohydrates can be attached.

(2) In which intracellular compartments does the addition of carbohydrate happen?

(3) Why do these proteins need to be glycosylated?

9. Pop Biotechnology Institute cloned a gene named ABBA. Its gene product was found to be a cytoskeleton-associated protein that binds intermediate filaments and microtubules. Truncation study revealed that the c-terminus of ABBA is important for the binding of microtubules. A c-terminally truncated ABBA protein, unable to bind microtubules by itself, was found to completely eliminate the microtubule binding ability of the wild-type ABBA (ABBA-WT). Such a truncation mutant was named ABBA-DN (dominant negative). Transfection experiments showed that cells expressing ABBA-DN had decreased proliferation rates. When injected to nude mice, three independent stable lines bearing ABBA-DN demonstrated decreased tumorigenesis as compared to ABBA-WT. The expressions of ABBA-DN or ABBA-WT in the tumors were confirmed by Northern and Western analyses. It was concluded that ABBA is important for tumorigenesis. Disrupting its microtubule binding ability will decrease its effect in tumorigenesis. (10 points)

(1) Is there any problem with the conclusion? Please summarize it (or them).

(2) If you think there was a problem, what other experiments will you perform to solve the issue?

10. **(1)** What are the differences between benign and malignant tumors? (5 points)

(2) What is the key difference between neoplasia and hyperplasia? (5 points)