

單選題（請按照題目順序作答，每題 2 分）

- (1) 維持蛋白質二級結構主要穩定力量為何 (A) Hydrophobic interaction (B) Hydrogen bond (C) Electrostatic interaction (D) Disulfide bond
- (2) 下列何者不是蛋白質的 Post-translational modification (A) Proteolytic cleavage (B) Glycosylation (C) Ubiquitination (D) Sumoylation
- (3) 下列何者不影響 Membrane fluidity (A) Unsaturation of phospholipid (B) Cholesterol (C) Temperature (D) H<sub>2</sub>O
- (4) 下列何種方法無法選殖到蛋白質 cDNA (A) cDNA library screening (B) Reverse transcriptase PCR (C) Northern blotting (D) Yeast-two hybrid system
- (5) 利用下列何種方法無法瞭解蛋白質在細胞內之功能 (A) RNAi (B) Antisense oligomer (C) Ribozyme (D) cDNA microarray
- (6) 李君以 2 dimensional-electrophoresis 及質譜儀進行某一 Cancer cell 之蛋白質體分析，上網以 Bioinformatics 分析結果得到一 Novel protein，為進一步確認此蛋白質種類，可進行何種分析(A)Amino acid composition (B) Edman degradation (C) X-ray crystallography (D) Northern blotting
- (7) 下列技術何者不可分析蛋白質分子量 (A) Gel filtration (B) Mass spectrometry (C) SDS-polyacrylamide gel electrophoresis (D) Isoelectro-focusing
- (8) 進行 DNA 分離純化不可使用下列何種方式 (A) Agarose gel electrophoresis (B) Polyacrylamide gel electrophoresis (C) CsCl gradient centrifugation (D) Sucrose gradient centrifugation
- (9) 下列何者不影響蛋白質的 Cellular localization (A) Signal peptide (B) Nuclear export sequence (C) GPI anchor sequence (D) His-Tag
- (10) Purine 代謝的終產物為 (A) Urea (B) Urea acid (C) Xanthine (D) Hypoxanthine
- (11) 下列何種方式不可分析 Protein-protein interaction (A) Biocalorimetry (B) UV spectrophotometry (C) Gel filtration (D) Phage display
- (12) 下列何種 Modification 不會出現於 RNA (A) Methylation (B) Polyadenylation (C) Pseudouridylation (D) Acetylation
- (13) Histone proteins 與 DNA 的 interaction 受何種作用調控 (A) Phosphorylation (B) Adenosylribosylation (C) Acetylation (D) Oxidation
- (14) 下列何者不會幫助 Protein folding (A) Chaperon (b) Protein disulfide isomerase (C) Proline peptidyl isomerase (D) Proteosome
- (15) 下列何種 Amino acid residues 的側鏈不可作為酵素 Covalent catalysis 之主要參與者 (A) Ser (B) Cys (C) Glu (D) Lys
- (16) 下列何種方法不可分析 Protein-DNA interaction (A)Electrophoretic mobility shift (B) Chromatin immunoprecipitation (C) Biocalorimetry (D) Run-off transcription

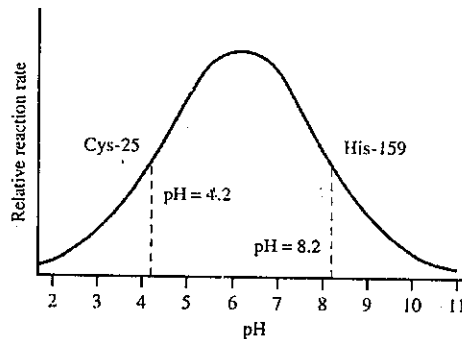
- (17) 下列者不是 Cell membrane 之特質 (A) Phospholipid asymmetry distribution (B) Flip-flap (C) Lipid oxidation (D) Phase transition
- (18) 下列何者不是 TCA cycle 的 intermediate (A) Citrate (B) Succinyl Co-A (C) Pyruvate (D) Oxaloacetate
- (19) 下列何者為 Transamination 的 Coenzyme (A) FAD (B) Coenzyme A (C) Pyridoxal-5'-phosphate (D) Thiamine phosphate
- (20) RNA-DNA hybrid 結構近似下列何者結構 (A) A-DNA (B) B-DNA (C) Z-DNA (D) G-Quarter
- (21) 下列何種 motif 具有 Coil-coil 結構 (A) Zinc finger (B) Helix-turn-helix (C) Leucine zipper (D) Greek key
- (22) Allosteric enzyme 如果具有 Negative cooperation 的酵素機制，以 Hill plot 作圖，Hill coefficient (n) 為何 (A)  $n > 1$  (B)  $n < 1$  (C)  $n = 1$  (D)  $n = K_m$  (Michaelis-Menten constant)
- (23) 下列何者為 Serine protease (A) Trypsin (B) Chymotrypsin (C) Subtilisin (D) HIV protease
- (24) 一具有四級結構的蛋白質，蛋白質如果為 Heterooligomer，請問可以下列何種試劑處理配合 Gel filtration 區分其分子之間是以 Noncovalent bonding 鍵結 (A) Reduction with Dithiothreitol (B) Digestion with trypsin (C) Dissolving in 8 M Urea (D) Modification with isothiocyanate
- (25) Topoisomerase 的生理功能為何 (A) Function in DNA transcription (B) Function in gene regulation (C) Function in replication termination (D) Function in splicing
- (26)  $Zn^{2+}$  在 Zinc finger 所扮演之角色為何 (A) Stabilize the interaction between DNA and Zinc finger (B) Stabilize the conformation of Zinc finger (C) Directly involve in the binding with DNA (D) Recruit other transcriptional factors
- (27) GPI anchor protein 分佈在 (A) Outside of cell membrane (B) Inside of cell membrane (C) Cellular cytoplasm (D) Cellular nuclear
- (28) DNA binding proteins 中，何者以  $\beta$ -sheet 結構和 DNA 結合 (A)  $\lambda$  repressor (B) TATA-box binding protein (C) Glucocorticoid receptor (D) GAL4
- (29) 下列何種試劑可與 DNA double strand 結合 (A) Ninhydrin (B) Ethidium bromide (C) Cyanogen bromide (D) Dabsyl chloride
- (30) Cholesterol 在 Cell membrane 中，對 Cell membrane 之特性影響為何 (A) Decrease the fluidity of cell membrane (B) Increase transition temperature (C) Increase the rate of flip-flap (D) Redistribution of lipid
- (31) 下列何者不是 Lipid 對 Protein 的 Modification (A) Myristoylation (B) Palmitoylation (C) Prenylation (D) Esteration
- (32) 對蛋白質進行 Glycosylation，下列 Amino acid 的側鏈會接上 Oligosaccharides (A) Ser, Gln (B) Ser, Asn (C) Thr, Asn (D) Thr, Gln

- (33) 一個酵素其作用機制遵循 Michaelis-Menten equation，如果  $[S] = 1 \text{ mM}$  其反應速度達到  $V_{\text{max}}$ ， $[S] = 0.1 K_m$  時，其  $v =$  (A)  $0.1 V_{\text{max}}$  (B)  $0.09 V_{\text{max}}$  (C)  $0.11 V_{\text{max}}$  (D)  $0.2 V_{\text{max}}$
- (34) 酵素作用機制遵循 Michaelis-Menten equation，如果 A 酵素之  $K_{\text{cat}}$  為 B 酵素之 5 倍，則 (A)  $V_{\text{max}(A)} = V_{\text{max}(B)}$  (B)  $V_{\text{max}(A)} = 5 V_{\text{max}(B)}$  (C)  $5 V_{\text{max}(A)} = V_{\text{max}(B)}$  (D) 無法計算
- (35) 以 NMR 分析蛋白質結構時，無法得知 (A) Dynamics of protein (B) Folding mechanism (C) Three-dimensional structure (D) Assembly of virus particle

複選題（請按照題目順序作答，全對才給分，每題 3 分）

- (1) 李君分析一酵素 pH 對 Activity 的 Profile 得知圖形如下，Cys-25 及 His-159 在此酵素中所扮演之角色為何

- (A) Cys-25 function as a general acid  
 (B) His-159 function as a general base  
 (C) His-159 function as general acid  
 (D) Both Cys-25 and His-159 function as general acid  
 (E)  $\text{H}_2\text{O}$  is essential for the catalytic activity

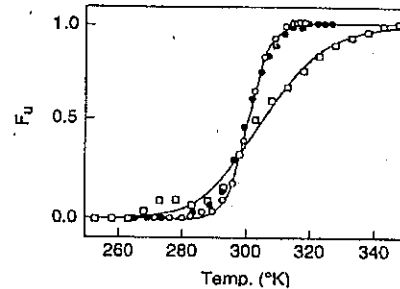


- (2) 承上題，進行 Site-directed mutagenesis 將 Cys-25 突變成之後 Ser-25，得到下列何種結果  
 (A) The same pH-activity profile (B) The enzymatic activity is no more observed  
 (C) The Ser-25 shifts its pKa value to 4.2 (D) The optimum pH for activity shifts to higher pH value (E) Although the pH-activity profile differs, the  $V_{\text{max}}$  remains unchanged
- (3) 下列對 Abzyme 描述何者為真 (A) The compound induced the production of abzyme is a transition analog (B) The interaction between abzyme and its substrate follows the mechanism of enzymatic catalysis (C) Abzyme only has three-dimensional structure (D) The enzymatic activity of abzyme has a Gibbs free energy  $>0$  (E) The  $\Delta H - T\Delta S$  value for the activity of abzyme is  $<0$
- (4) 對 Ribozyme 下列描述何者為真 (A) Ribozyme is a RNA molecule (B) Ribozyme can behave as a self-splicing enzyme (C) Ribozyme catalyzed the cleavage and ligation of DNA (D) Ribozyme can potentially apply in gene therapy (E) Ribozyme may have a peptidyl transferase activity

- (5) 何種機制可能促使 Protein evolution (A) Tautomerization of nucleotide (B) Ionization of nucleotide (C) Exon shuffling (D) Alternative splicing (E) Homologous recombination
- (6) 下列對 Membrane protein 描述何者為真 (A) The detergent should be included in the extraction buffer in order to purify integral membrane proteins (B) Ion channels are membrane proteins (C) The transmembrane domain of membrane proteins could be  $\alpha$ -helix or  $\beta$ -sheet (D) Bacteriorhodopsin is not a membrane protein (E) Membrane proteins interacts with phospholipid via hydrophobic forces

- (7) 右下圖為 Protein unfolding 實驗結果，分別使用 UV-VIS spectrophotometry, Fluorescence spectrophotometry 及 Circular dichroism 分析 RNase 的 Thermal stability，

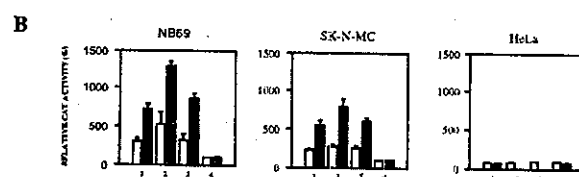
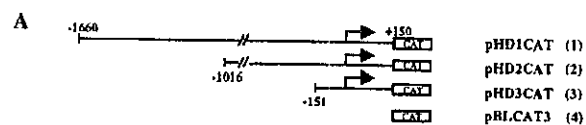
- 下列何者描述為真 (A) Increasing temperature results in unfolding of RNase (B) The temperature transition represent the breakage of noncovalent bonds (C) The results showed a two state transition (D) The ellipticity at 222 nm represent the change in the  $\beta$ -sheet structure of RNase (F) Unfolding experiments could not elucidate the structural stability of RNase



- , monitored by the absorbance at 286 nm  
 ●, monitored by fluorescence emission at 311.5 nm  
 □, monitored by circular dichroism (the ellipticity at 222 nm)

- (8) 有關 Allosteric enzyme 作用特點下列描述何者為真 (A) Allosteric enzyme could be described by KNF model or MWC model (B) Allosteric site is distal from catalytic site (C) Allosteric enzyme is composed of catalytic subunit and regulatory subunit (D) Allosteric factor is not a substrate (E) Allosteric enzyme could be regulated by feed-back regulation
- (9) 某一蛋白質和 DNA binding site 結合時以 Tetramer 結合，如果不和 DNA binding 則以 Monomer 結構存在，對此蛋白質進行 Mutagenesis 後，此蛋白質不再與 DNA binding，可以下列何種技術分析此一蛋白質分子結構變化 (A) SDS polyacrylamide gel electrophoresis (B) Gel filtration (C) Light scattering (D) Analytical ultracentrifugation (E) Circular dichroism

- (10) 以 CAT assay 分析 Promoter activity 得到下圖，何者敘述為真 (A) The results show that different cell lines should has different transcriptional factors (B) The -1660~-1016 region may contain repressor-binding sites (C) The -1016- +150 region contain transcriptional factor-binding sites (D) Deleting -1600~-1016 region does not affect the binding of transcriptional factors (E) Intracellular cAMP concentration does not affect the binding of transcription factors with promoter region



The open bars represent control experiments, and the solid bars represent that intracellular adenylyl cyclase has been activated.

Answer the following questions:

1. Describe the classification of histones in mammalian cells and explain how histone acetylation modulates gene transcription (10 points).
2. Describe the signal transduction pathway of G protein-coupled receptors (10 points).
3. Explain the methodology and application of yeast two hybrid technique (10 points).
4. Describe the functional role of mitochondria in the induction of apoptosis (10 points).
5. Mention the detailed mechanism of ubiquitin/proteasome-mediated protein degradation (15 points).
6. Mention protein components of a typical adherens junction and sketch a figure to describe its structure (15 points).
7. Describe the biochemical and structural changes of the stages of mitosis in eukaryotic cells (15 points).
8. Compare the advantage and weakness of antisense oligodeoxynucleotide, ribozyme and RNA interference in gene silencing (15 points).