※ 注意：請於試卷內之「非選擇題作答區」作答，並應註明作答之題號。

1. Growth hormone can activate which of the following kinases directly? (2%)
   (A) Janus Kinase
   (B) Protein Kinase A
   (C) Protein Kinase C
   (D) Protein Kinase G
   (E) Glycogen synthase kinase (GSK)

2. Which of the following assays can be used to determine hormone concentration in the blood? (2%)
   (A) isoelectric focusing
   (B) radioimmunoassays
   (C) polymerase chain reaction
   (D) agarose gel electrophoresis
   (E) polyacrylamide gel electrophoresis

3. Photons bind to rodopsins and cause the changes in second messenger concentration in the cells. Which of following is correct? (2%)
   (A) increase cAMP in the cells
   (B) increase cGMP in the cells
   (C) decrease cAMP in the cells
   (D) decrease cGMP in the cells
   (E) increase calcium release from endoplasmic reticulum in the cells

4. Kinase **could not** catalyze which of the following compounds? (2%)
   (A) Glucagon
   (B) Phosphorylase
   (C) Phosphatidylinositol
   (D) Deoxyribonucleotide
   (E) Phosphorylase kinase

5. In most cells, water moves in and out by osmosis through the lipid component of cell membranes. It was long suspected that some additional mechanism for water transport across membranes must exist. But it was not until 1992 that the first water channel (aquaporin-1) was reported by Professor Peter Agre at Johns Hopkins University. The pioneering discoveries and research on water channels by Agre and his colleagues resulted in the presentation of a Nobel Prize in Chemistry to Agre in 2003. Now, there are thirteen known types of aquaporins in mammals. Which of the following organ has the majority types of aquaporins? (2%)
   (A) skin
   (B) lung
   (C) liver
   (D) heart
   (E) kidney

見背面

6. NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex that controls transcription of DNA. NF-κB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet irradiation, oxidized LDL, and bacterial or viral antigens. In unstimulated cells, the NF-κB dimers are sequestered in the cytoplasm by a family of inhibitors, called I-κBs (Inhibitor of κB). After receptor activation on the cell membrane, which of the following event on I-κB is important for NF-κB translocation into nucleus? (2%)
   (A) Acetylation
   (B) Glycosylation
   (C) Demethylation
   (D) Phosphorylation
   (E) ADP-ribosylation

7. Human immunodeficiency virus type 1 (HIV-1) envelope (gp120) binding to DC-SIGN (dendritic cell-specific ICAM-3-grabbing nonintegrin), a C-type lectin that can facilitate HIV infection in cis and in trans, is largely dependent on high-mannose-content moieties. The investigator delineate the N-linked glycosylation (N-glycan) sites in gp120 that contribute to optimal DC-SIGN binding. 2G12 is a monoclonal antibody whose carbohydrate-dependent epitope involves distinct N-glycan sites on the silent face of gp120. Soluble DC-SIGN was able to block 2G12 binding to gp120, but not vice versa, suggesting that DC-SIGN binds to a more flexible combination of N-glycans than 2G12. Consistent with this observation, HIV strain JRCSF gp120 prebound to 2G12 was 10-fold more sensitive to mannan competition than gp120 that was not prebound in a DC-SIGN cell surface binding assay. The analysis of multiple mutant forms of the 2G12 epitope revealed one triple glycosylation mutant form, termed 134mut (carrying N293Q, N382Q, and N388Q mutations), that exhibited a significant increase in sensitivity to both mannan competition and endoglycosidase H digestion compared to that of the 124mut form (carrying N293Q, N328Q, and N388Q mutations) and wild-type gp120 in a DC-SIGN binding assay. Importantly, no such differences were observed when binding to Galanthus nivalis was assessed. The 134mut form of gp120 also exhibited decreased binding to DC-SIGN in the context of native envelope spikes on a virion, and virus bearing 134mut exhibited less efficient DC-SIGN-mediated infection in trans. Significantly, 124mut and 134mut differed by only one glycosylation site mutation in each construct, and both 124mut and 134mut viruses exhibited wild-type levels of infectivity when used in a direct infection assay. In summary, while DC-SIGN can bind to a flexible combination of N-glycans on gp120, its optimal binding site overlaps with specific N-glycans within the 2G12 epitope. Conformationally intact envelopes that are DC-SIGN binding deficient can be used to probe the in vivo biological functions of DC-SIGN. Which of the following description **is not** correct? (2%)
   (A) DC-SIGN is a HIV receptor.
   (B) DC-SIGN is located on immune cells.
   (C) DC-SIGN is a type I membrane protein.
   (D) Mutations are often found in HIV envelope proteins.
   (E) Virus binding to cell is mediated by a specific carbohydrate recognition.

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8. "Cystic fibrosis (CF) is inherited in an autosomal recessive manner. It is caused by the presence of mutations in both copies of the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Those with a single working copy are carriers and otherwise mostly normal. CF is most common among people of Northern European ancestry and affects about one out of every 3000 newborns. Screening of infants at birth takes place in some areas of the world." From the description, choose one best answer from the column that is involved in the symptoms of cystic fibrosis. (2%)
   (A) ATPase
   (B) Antiporter
   (C) Symporter
   (D) Water channel
   (E) Sodium channel
   (F) Calcium channel
   (G) Potassium channel
   (H) Chloride transporter

9. Choose one best answer from the column that is involved in the glucose transport. (2%)
   (A) ATPase
   (B) Antiporter
   (C) Symporter
   (D) Water channel
   (E) Sodium channel
   (F) Calcium channel
   (G) Potassium channel
   (H) Chloride transporter

10. "The existence of a hormone regulating hunger and energy expenditure was hypothesized based on studies of mutant obese mice that arose at random within a mouse colony at the Jackson Laboratory in 1950. Mice homozygous for the *ob* mutation (*ob/ob*) ate voraciously and were massively obese. In the 1960s, a second mutation causing obesity and a similar phenotype was identified by Douglas Coleman, also at the Jackson Laboratory, and was named diabetes (*db*), as both *ob/ob* and *db/db* were obese. Rudolph Leibel and Jeffrey M. Friedman reported the mapping of the *ob* gene in 1990. Consistent with Coleman's and Leibel's hypothesis, several subsequent studies from Leibel's and Friedman's labs and other groups confirmed that the *ob* gene encoded a novel hormone that circulated in blood and that could suppress food intake and body weight in *ob* and wild type mice, but not in *db* mice. In 1994, with the *ob* gene isolated, Friedman reported the discovery of the gene. In 1995, Caro's laboratory provided evidence that the mutations present in the mouse *ob* gene did not occur in humans. Furthermore the *ob* gene expression was increased in human obesity, which led to postulate the concept of specific hormone resistance. At the suggestion of Roger Guillemin, Friedman named this new hormone. It was the first fat cell-derived hormone to be discovered. Subsequent studies confirmed that the *db* gene encodes the cognate receptor and that it is expressed in the hypothalamus, a region of the brain known to regulate the sensation of hunger and body weight. In 2010, Douglas Coleman and Jeffrey M. Friedman received the Albert Lasker Award for Basic Medical Research. The awards are sometimes referred to as "America's Nobels". Almost 50% of the winners have won Nobel Prize later on." According to the description, what hormone is secreted by adipose tissue? (2%)

11. Describe similarities and differences of the transcriptional regulation between lactose and tryptophan operons in prokaryotes (8%).

12. Describe the transcriptional and post-transcriptional regulations of DNA-dependent RNA polymerase II in eukaryotes (8%).

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13. Three polypeptides, the sequences of which are represented below using the one-letter code for their amino acids, are present in a mixture: (6 %)

1. ATKNRASCLVPKHGALMFWRHKQLVSDPILQKRQHILVCRNAAG
2. GPYFGDEPLDVHDEPEEG
3. PHLLSAWKGMEGVGKSQSFAALIVILA

Of the three, which one would migrate most slowly during chromatography through:
(a) an ion-exchange resin; beads coated with positively charged groups?
(b) an ion-exchange resin; beads coated with negatively charged groups?
(c) a size-exclusion (gel-filtration) column designed to separate small peptides such as these?

14. Under appropriate conditions, hemoglobin dissociates into its four subunits. The isolated α subunit binds oxygen, but the O_2-saturation curve is hyperbolic rather than sigmoid. In addition, the binding of oxygen to the isolated α subunit is not affected by the presence of H^+, CO_2, or BPG. What do these observations indicate about the source of cooperativity in hemoglobin? (2 %)

15. Our growing understanding of how proteins fold allows researchers to make predictions about protein structure based on primary amino acid sequence data. Consider the following amino acid sequence.(6 %)

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Ile-	Ala-	His-	Thr-	Tyr-	Gly-	Pro-	Phe-	Glu-	Ala-	Ala-	Met-	Cys-	Lys-	Trp-	Glu-	Ala-	Gln-	Pro-	Asp-	Gly-	Met-	Glu-	Cys-	Ala-	Phe-	His-	Arg

(a) Where might bends or β turns occur?
(b) Where might intrachain disulfide cross-linkages be formed?
(c) Assuming that this sequence is part of a larger globular protein, indicate the probable location (the external surface or interior of the protein) of the following amino acid residues: Asp, Ile, Thr, Ala, Gln, Lys. Explain your reasoning.

16. Please determine the pI of the following peptides

Asp-His-Trp-Ser-Gly-Leu-Lys-Pro-Gly (2 %)

Amino acid	pK_1	pK_2	pK_R
Asp	1.88	9.60	3.65
His	1.82	9.17	6.00
Trp	2.38	9.39	
Ser	2.21	9.15	
Gly	2.34	9.60	
Leu	2.36	9.60	
Lys	2.18	8.95	10.53
Pro	1.99	10.96	

17. What is the function of glucose 6-phosphate in metabolism? (4 %)

18. How NADH and $FADH_2$ play roles in the generation of ATP when a cell undergoes oxidative phosphorylation? (4 %)

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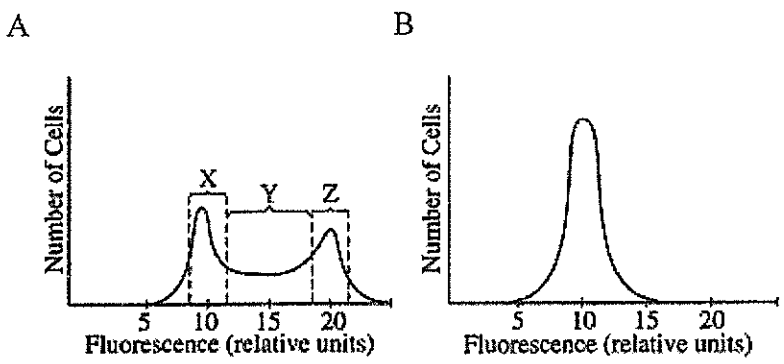
19. How glucagon and insulin regulate the glucose metabolism in human body? (4 %)

20. What is the important role of the Cori cycle for the metabolic cooperation between skeletal muscle and the liver? (4 %)

Questions 21-24

TW1 cells, a human fibroblast cell line, divide with an average generation time of 22 hours (G1=10 hr, S=6 hr, G2=5 hr, M=1 hr) when they are cultured in medium containing 10% fetal calf serum. To determine the effects of serum deprivation on cell cycle, cells were incubated in medium with or without serum for 48 hours, followed by being harvested and stained with propidium iodide (PI), which is a fluorescent molecule that binds DNA. DNA content (fluorescence) of the stained cells was then analyzed by flow cytometry, and the results are shown in the following figure.



21. Which of the panels (A or B) does indicate that the cells were cultured in medium without serum? (2 %)

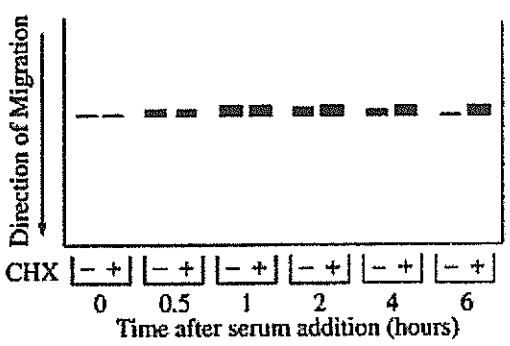
22. In panel A, the cells in the Y region are in what stage of the cell cycle? (2 %)

23. If the cells were cultured in the presence of ^{3}H-thymidine for 3 hours and then analyzed by flow cytometry, which of the regions (X, Y, Z) in panel A will **NOT** contain radioactive cells? (2 %)

24. In this experiment, what is the effect of serum deprivation on cell cycle? (2 %)

Questions 25-27

Continuing the experiment, the cells were incubated without serum for 48 hours and then treated with serum along or plus cycloheximide (CHX). At various times after treatment, total cellular RNA from each sample was isolated and then analyzed by gel electrophoresis, followed by Northern blotting to detect the mRNA level of *SV1* gene, which encodes a protein involved in regulating cell proliferation. The results are shown in the following figure.



SV1 mRNA

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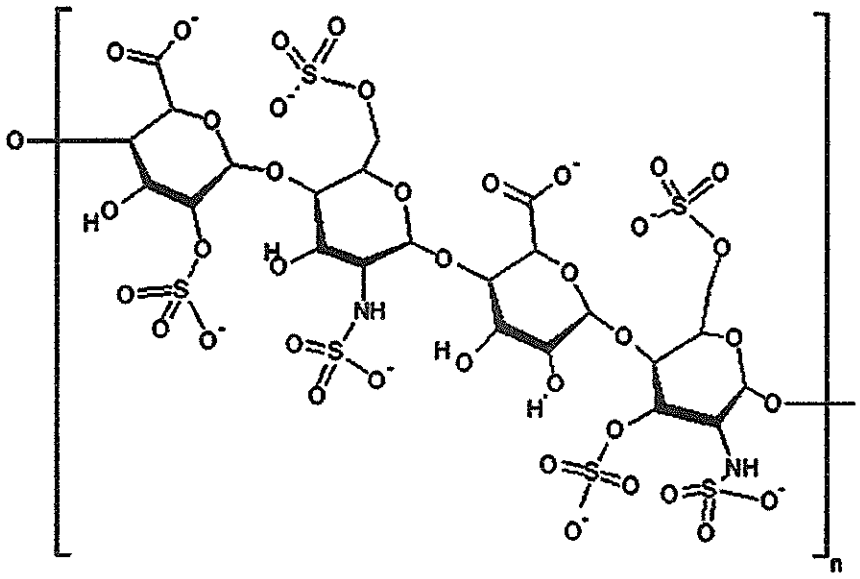
25. In addition to Northern blotting, please list one other method for RNA detection. (2 %)

26. CHX is an inhibitor of protein synthesis. What is the purpose for CHX treatment in this experiment? (3 %)

27. Based on the results shown in the figure above, what is the reason to explain the differences in the amounts of *SV1* mRNA from samples with *versus* without CHX treatment at 2, 4, and 6 hours? (3 %)

Multiple and single choice mixed questions 28-35

Use the diagram below and your knowledge of biochemistry to answer questions 28-31 (8 %).



28. which descriptions about the compound above are correct:
   (A) Component in proteoglycan
   (B) "N" can be up to 50,000 disacchrides per chain
   (C) the consensus attach site in the protein core is GxG.Ser
   (D) can bind to protein by ionic interaction
   (E) no protein core attached

29. which descriptions about the compound above are correct:
   (A) sensitive to heparinase treatment
   (B) serve as leukocytes homing molecules
   (C) can be degraded by hyalurondase
   (D) existing in mast cell granules
   (E) a type of glycosaminoglycan

30. The enzymes are involved in synthesis for the compounds above are
   (A) oligo-peptide transferase
   (B) Polymerase
   (C) Hyaluronic acid synthesase (HAS)
   (D) epimerse
   (E) sulfotrasferase

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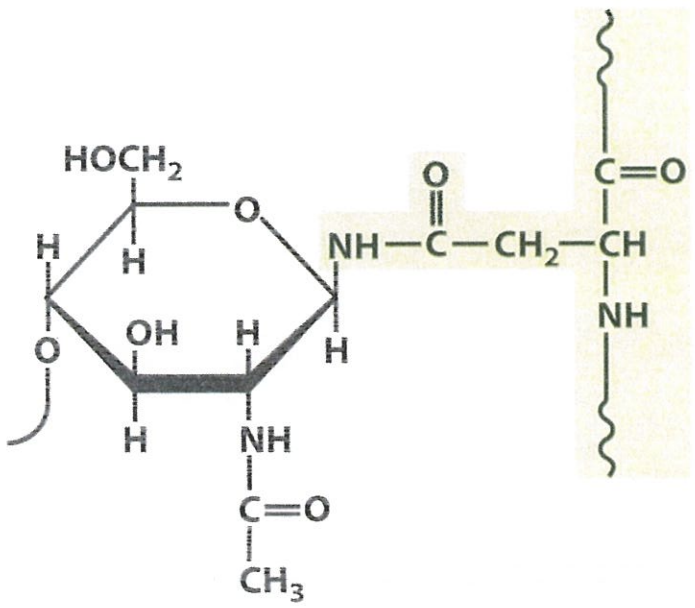
31. The biological functions of the above compound regulating a wide variety of biological activities, including
   (A) change protein conformation
   (B) angiogenesis
   (C) blood coagulation
   (D) tumor metastasis
   (E) protein sorting

Use the diagram below and your knowledge of biochemistry to answer questions 32-33 (4 %).



32. which descriptions about the compound above are correct:
   (A) O-link glycosylation
   (B) N-link glycosylation
   (C) Glycosaminoglycan modification
   (D) GalNAc
   (E) GlcNAc

33. which descriptions about the compound above are correct:
   (A) Refer to amino acid Ser
   (B) Refer to amino acid Thr
   (C) Refer to amino acid Asn
   (D) Involved in ER-Golgi protein sorting
   (E) Maintain correct protein conformation

34. which descriptions about the basal Membrane(BM) above are not correct: (2 %)
   (A) Lamin is a component of BM
   (B) Type II collagen is a component of BM
   (C) Perlecan is a proteoglycan in BM
   (D) Type 4 collagen existing in BM
   (E) Is required for maintain the polarity of epithelial cells

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35. Which peptide sequences can facilitate cells spread in Integrin-dependent manner? (2 %)

(A) sehradlsal
(B) sehrgelsal
(C) sehraelsal
(D) sehkgdlsal
(E) sehrgdlsal

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