國立彰化師範大學100學年度碩士班招生考試試題

系所：生物技術研究所　　科目：生物化學

☆☆請在答案紙上作答☆☆　　共6頁，第1頁

I. Multiple choices. Please choose the best answer for each question. (2% each)

1. Of the 20 standard amino acids, only _____ is not optically active. The reason is that its side chain _____.
   (A) alanine; is a simple methyl group (B) glycine; is a hydrogen atom
   (C) glycine; is unbranched (D) lysine; contains only nitrogen
   (E) proline; forms a covalent bond with the amino group

2. Which of the following statements about *cystine* is correct?
   (A) Cystine forms when the —CH_2—SH R group is oxidized to form a —CH_2—S—S—CH_2— disulfide bridge between two cysteines.
   (B) Cystine is an example of a nonstandard amino acid, derived by linking two standard amino acids.
   (C) Cystine is formed by the oxidation of the carboxylic acid group on cysteine.
   (D) Cystine is formed through a peptide linkage between two cysteines.
   (E) Two cystines are released when a —CH_2—S—S—CH_2— disulfide bridge is reduced to —CH_2—SH.

3. The peptide alanylglutamylglycylalanylleucine has:
   (A) a disulfide bridge. (B) five peptide bonds.
   (C) four peptide bonds. (D) no free carboxyl group.
   (E) two free amino groups.

4. A prosthetic group of a protein is a non-protein structure that is:
   (A) a ligand of the protein. (B) a part of the secondary structure of the protein.
   (C) a substrate of the protein. (D) permanently associated with the protein.
   (E) transiently bound to the protein.

5. One of the enzymes involved in glycolysis, aldolase, requires Zn^{2+} for catalysis. Under conditions of zinc deficiency, when the enzyme may lack zinc, it would be referred to as the:
   (A) apoenzyme. (B) coenzyme.
   (C) holoenzyme. (D) prosthetic group.
   (E) substrate.

6. The number of substrate molecules converted to product molecules in a given unit of time by a single enzyme molecule at saturation is referred to as the:
   (A) dissociation constant. (B) half-saturation constant.
   (C) maximum velocity. (D) Michaelis-Menten number.
   (E) turnover number.

7. Allosteric enzymes:
   (A) are regulated primarily by covalent modification.
   (B) usually catalyze several different reactions within a metabolic pathway.
   (C) usually have more than one polypeptide chain.

(D) usually have only one active site.

(E) usually show strict Michaelis-Menten kinetics.

8. Which of the following is a heteropolysaccharide?

(A) Cellulose　　(B) Chitin

(C) Glycogen　　(D) Hyaluronate

(E) Starch

9. Which of the following molecules or substances contains, or is derived from, fatty acids?

(A) Beeswax　　(B) Prostaglandins

(C) Sphingolipids　　(D) Triacylglycerols

(E) All of the above contain or are derived from fatty acids.

10. Non-steroidal anti-inflammatory drugs (NSAIDS) like aspirin and ibuprofen act by blocking production of:

(A) biological waxes.　　(B) prostaglandins.

(C) sphingolipids.　　(D) vitamin D.

(E) none of the above.

11. In one catalytic cycle, the Na^+/K^+ ATPase transporter transports:

(A) 2 Na^+ out, 3 K^+ in, and converts 1 ATP to ADP + P_i.

(B) 3 Na^+ out, 2 K^+ in, and converts 1 ATP to ADP + P_i.

(C) 3 Na^+ in, 2 K^+ out, and converts 1 ATP to ADP + P_i.

(D) 1 Na^+ out, 1 K^+ in, and converts 1 ATP to ADP + P_i.

(E) 2 Na^+ out, 3 K^+ in, and converts 1 ADP + P_i to ATP.

12. An enzyme used in both glycolysis and gluconeogenesis is:

(A) 3-phosphoglycerate kinase.　　(B) glucose 6-phosphatase.

(C) hexokinase.　　(D) phosphofructokinase-1.

(E) pyruvate kinase.

13. Which one of the following statements about gluconeogenesis is *false*?

(A) For starting materials, it can use carbon skeletons derived from certain amino acids.

(B) It consists entirely of the reactions of glycolysis, operating in the reverse direction.

(C) It employs the enzyme glucose 6-phosphatase.

(D) It is one of the ways that mammals maintain normal blood glucose levels between meals.

(E) It requires metabolic energy (ATP or GTP).

14. Which of the following statements is true of muscle glycogen phosphorylase?

(A) It catalyzes phosphorolysis of the ($\alpha 1 \rightarrow 6$) bonds at the branch points of glycogen.

(B) It catalyzes the degradation of glycogen by hydrolysis of glycosidic bonds.

(C) It degrades glycogen to form glucose 6-phosphate.

(D) It exists in an active *(a)* form and an inactive *(b)* form that is allosterically regulated by AMP.

(E) It removes glucose residues from the reducing ends of the glycogen chains.

15. The oxidative decarboxylation of α-ketoglutarate proceeds by means of multistep reactions in which all but one of the following cofactors are required. Which one is *not* required?
    (A) ATP　(B) Coenzyme A
    (C) Lipoic acid　(D) NAD+
    (E) Thiamine pyrophosphate

16. The conversion of 1 mol of pyruvate to 3 mol of CO_2 via pyruvate dehydrogenase and the citric acid cycle also yields _____ mol of NADH, _____ mol of $FADH_2$, and _____ mol of ATP (or GTP).
    (A) 2; 2; 2　(B) 3; 1; 1
    (C) 3; 2; 0　(D) 4; 1; 1
    (E) 4; 2; 1

17. The conversion of palmitoyl-CoA (16:0) to myristoyl-CoA (14:0) and 1 mol of acetyl-CoA by the β-oxidation pathway results in the net formation of:
    (A) 1 $FADH_2$ and 1 NADH.　(B) 1 $FADH_2$ and 1 NADPH.
    (C) 1 $FADH_2$, 1 NADH, and 1 ATP.　(D) 2 $FADH_2$ and 2 NADH.
    (E) 2 $FADH_2$, 2 NADH, and 1 ATP.

18. Which of these amino acids can be directly converted into a citric acid cycle intermediate by transamination?
    (A) glutamic acid　(B) serine
    (C) threonine　(D) tyrosine
    (E) proline

II. (每題3%)

閱讀下列短文後回答第1-5題 (每題3%)

引用：Aguilar and Mendoza (2006), Molecular Microbiology 62, p.p. 1507-1514

cis-Unsaturated fatty acids (UFAs) have crucial roles in membrane biology and signalling processes in organisms ranging from bacteria to humans. The relative UFA content of cellular phospholipids exerts a major influence on the physical properties of most biological membranes. UFAs have a much lower transition temperature than saturated fatty acids because the steric hindrance imparted by the rigid kink of the *cis*-double bond results in much poorer packing of the acyl chains. Thus, UFAs are key molecules in the regulation of cellular membrane fluidity. In addition to their structural role, UFAs have recently been recognized as signalling molecules involved in several essential cellular processes, such as cell differentiation and DNA replication. Alterations in UFA biosynthesis have been implicated in various disease states, including cardiovascular disease, obesity, non-insulin dependent diabetes mellitus, hypertension, neurological diseases and cancer. There are two major mechanisms by which living organisms synthesize UFAs: mostly of them use an oxygen-dependent fatty acid desaturation pathway, whereas many prokaryotes, including *Escherichia coli*, synthesize UFAs anaerobically. The fatty acyl desaturases, which introduce double bonds into fatty acyl chains, encompass a family of enzymes,

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representatives of which are found in all eukaryotes, as well as some prokaryotes such as cyanobacteria, bacilli, mycobacteria and pseudomonads. The reaction catalysed by these enzymes is an oxygen-dependent desaturation of the full-length fatty acid chain, either as an acyl-thioester or as a phospholipid fatty acid moiety, and requires a specific electron transport chain.

When poikilothermic organisms such as bacteria, plants and fish are exposed to suboptimal growth temperatures, their membrane lipids become more rigid, leading to subnormal functioning of cellular activities. Adaptation to such new conditions involves an increase in the proportion of UFAs in their membrane. The resulting increase in UFA content causes membrane lipid fluidity to return to its original state, or close to it, with concurrent restoration of normal cellular activity at the lower temperature.

Bacillus subtilis has only one desaturase, Δ5 desaturase (Δ5D), encoded by the *des* gene. The *B. subtilis* desaturase catalyses the introduction of a *cis*-double bond at the Δ5 position of existing saturated fatty acids in membrane phospholipids. *B. subtilis des* gene transcription increases in response to decreased temperature. A canonical two-component regulatory system comprising the histidine kinase DesK and the response regulator DesR regulates *des* expression. The sensor kinase DesK contains five transmembrane (TM) helices and a long cytoplasmic C-terminal tail, which harbours the kinase domain, DesKC. In vitro experiments show that DesKC undergoes autophosphorylation on the conserved His188. The phosphorylated kinase then transfers the phosphate to the Asp54 of the dimeric effector DesR, leading to the stabilization of a DesR-P tetramer. This tetramer binds two adjacent, non-identical DesR-P binding sites within the *des* promoter, leading to recruitment of RNA polymerase and activation of *des* transcription. Genetic and biochemical evidence suggests that the balance of two antagonistic DesK activities determines the DesR phosphorylation state: a phosphate donor for DesR and a phosphatase activity for DesR-P. As the activity of DesR as a transcriptional activator is modulated by its phosphorylation state, the output of the DesK–DesR signal transduction pathway is determined by switches between kinase-biased and phosphatase-biased DesK activities. The balance between these activities would be regulated by changes in growth temperature that, in turn, dictates the fluidity of membrane lipids.

1. 下列哪一種胞器含有大量 UFA？(A)染色體 (B)細菌的細胞壁 (C)細胞膜 (D)細菌的鞭毛 (E)核醣體
2. Fatty acid desaturase 可以造成 UFA 分子的何種改變？(A)環化 (B)碳鏈縮短 (C)碳鏈變長 (D)增加氫原子數 (E)彎折
3. Fatty acid desaturase 的作用需要下列哪一種成分？(A)電子傳遞鏈 (B) ATP (C)鎂離子 (D)鈣離子 (E)游離脂肪酸
4. 由文中敘述可確定 *Bacillus subtilis* 細胞內有兩種不同的 (A) Fatty acid desaturase 酵素 (B) DesK 活性 (C) DesR 蛋白質 (D) *des* 基因 (E) UFA 分子
5. Poikilothermic 一字的意義為(A)指數生長期的 (B)耐熱的 (C)厭氧的 (D)多型的 (E)變溫的

閱讀下列短文後回答第6-10題(每題3%)

引用：Levine and Puzio-kuter (2010) Science.330, p.p.1340-1344

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Normal cells and cancer cells use both glucose and glutamine as substrates to generate energy for the cell (ATP); to produce substrates to synthesize amino acids, nucleosides, and fatty acids; and to regulate the redox potential (number of oxidized molecules in a compartment divided by number of reduced molecules) so as to minimize the effects of reactive oxygen species (ROS) that damage membranes and proteins and cause mutations in a cell. Glucose contributes carbon, oxygen, and hydrogen for both anabolic processes and energy, whereas glutamine contributes nitrogen for synthesis of purines, pyrimidines, and nonessential amino acids. Metabolism of glutamine also produces the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) for the synthesis of fatty acids and the modulation of the redox potential in a cell. Glucose passing through the pentose phosphate pathway (PPP) also generates NADPH and ribose-5-phosphate for the synthesis of nucleotides. Normal adult differentiated cells have a low cell division rate (low turnover) and predominantly metabolize glucose to CO_2 and H_2O through glycolysis and the TCA cycle. This satisfies the needs of these cells for free energy supplied by efficient ATP generation during oxidative phosphorylation (complexes 1 to 4 in the oxidative phosphorylation chain) linked to the TCA cycle in mitochondria. There are several times, however, when regulated rapid cell division is required, such as during embryonic development, in wound healing (liver regeneration), or in the immune responses to specific antigens, where clonal selection provides increased cell numbers with increased immune specificity. Cancer cells share many of these same requirements for energy, substrates to grow and divide, and control of the redox potential and ROS in the cell.

What these processes have in common is a need to synthesize substrates for membranes, nucleic acids, and proteins (increase mass), which means not metabolizing all of the glucose to CO_2 and H_2O but instead providing the proper intermediates for cell growth. This is accomplished, in part, by slowing the entry of pyruvate into mitochondria, decreasing the conversion to acetyl-CoA, and slowing the rate of the TCA cycle. The pyruvate that builds up in aerobic glycolysis is, in part, converted into lactate that is secreted, eliminating it from the pool and keeping glycolysis active. The secreted lactate lowers the pH of the cellular environment and the extracellular matrix. This may influence remodeling of the matrix, permitting blood vessel invasion in response to angiogenic factors produced by the tumor. Furthermore, as a consequence of glycolysis, tumor lesions can become acidotic, which allows for the selection of motile cells that can break through the basement membrane and metastasize. The last step in glycolysis is catalyzed by pyruvate kinase, which receives input about both anabolic precursors and the energy status of the cell. Cancer cells make the fetal isoform of pyruvate kinase (the M2 isoform), which is a spliced variant of the gene that adds several amino acids, one of which is a tyrosine. This tyrosine is phosphorylated in cells with activated tyrosine kinase signaling, a hallmark of actively growing cells. Pyruvate kinase M2 is stimulated in a feedforward loop by fructose 1,6-bisphosphate, but the phosphotyrosine inhibits this positive regulation. Thus, in cancer cells the last step of glycolysis is slowed, resulting in a buildup of phosphorylated intermediates that can be used in anabolic synthesis and cell growth.

Rapidly dividing cells require favorable energetics [that is, higher ATP/adenosine diphosphate (ADP) and ATP/adenosinemonophosphate (AMP) ratios]. Many cancer cells satisfy this problem by taking up much larger

amounts of glucose than do normal cells. This results from facilitated glucose transport by one or more of several isozymes of membrane glucose transporters (GLUT 1 to 9). Once inside the cell, glucose is phosphorylated by one of several hexokinase enzymes (the first step in glycolysis) to keep it in the cell because of the charge added to glucose. The high concentrations of glucose in the cells of a cancer may be observed by positron emission tomography (PET) scans of radioactive F-19-2-deoxyglucose (FDG is not metabolized but is located in the cell), which is indicative of enhanced glucose uptake by cells. Many, but not all, cancers have this property of increasing glucose uptake.

6. 與正常細胞相比，癌細胞 (A)糖解作用較旺盛、TCA cycle 減緩 (B) TCA cycle 較旺盛、糖解作用減緩 (C)糖解作用與 TCA cycle 均較旺盛 (D)糖解作用與 TCA cycle 均減緩 (E)不使用 TCA cycle，只進行糖解作用
7. 癌細胞因上題中的代謝變化而排出較多 (A)CO_2 (B)ATP (C)乳酸 (D)葡萄糖 (E)丙酮酸
8. 癌細胞與正常細胞 pyruvate kinase 的差異在於(A)癌細胞的 pyruvate kinase 較短 (B)癌細胞的 pyruvate kinase 較常發生磷酸化 (C)癌細胞的 pyruvate kinase 由較多個次單元組成 (D)癌細胞的 pyruvate kinase 較穩定 (E)癌細胞的 pyruvate kinase 活性較強
9. 在本文中，FDG 的作用在於 (A)抑制癌細胞生長 (B)測量癌細胞內 ATP 對 AMP 的比值 (C)測量癌細胞糖解作用的速度 (D)測量癌細胞吸收葡萄糖的速度 (E)測量癌細胞葡萄糖磷酸化的速度
10. 下列哪一種細胞在代謝需求上與癌細胞最接近(A)老化的皮膚細胞 (B)因中毒而凋亡的肝細胞 (C)缺氧的腎臟細胞 (D)受到抗原刺激的 B 細胞 (E)激烈運動中的肌細胞

III. (34%) (from Lehninger)

1. Please describe the two general mechanisms of hormone action. (6%)
2. Please describe the regulation of fatty acid synthesis. (10%)
3. Please describe the defective oxidative phosphorylation in pancreatic belta cells blocks insulin secretion. (10%)
4. What are the functions of pentose phosphate pathway? (8%)