國立成功大學 104 學年度碩士班招生考試試題

系所組別：醫學檢驗生物技術學系

考試科目：生化與分生

考試日期：0212，節次：3

※ 考生請注意：本試題不可使用計算機。 請於答案卷(卡)作答，於本試題紙上作答者，不予計分。

1. Cellular signaling is enabled by specific protein-protein interactions that are frequently regulated by post-translational modifications (PTMs) of signaling molecules. Please describe three types of PTMs and their regulation of the physiological or pathological state of a cell. (9%)

2. Please read the abstract and answer the following questions: (16%)

   "Chromosomal rearrangements have a central role in the pathogenesis of human cancers and often result in the expression of therapeutically actionable gene fusions. A recently discovered example is a fusion between the genes echinoderm microtubule-associated protein like 4 (*EML4*) and anaplastic lymphoma kinase (*ALK*), generated by an inversion on the short arm of chromosome 2: inv(2)(p21p23). The *EML4–ALK* oncogene is detected in a subset of human non-small cell lung cancers (NSCLC) and is clinically relevant because it confers sensitivity to ALK inhibitors. Despite their importance, modelling such genetic events in mice has proven challenging and requires complex manipulation of the germ line. Here we describe an efficient method to induce specific chromosomal rearrangements *in vivo* using viral-mediated delivery of the CRISPR/Cas9 system to somatic cells of adult animals. We apply it to generate a mouse model of Eml4–Alk-driven lung cancer. The resulting tumors invariably harbour the *Eml4–Alk* inversion, express the *Eml4–Alk* fusion gene, display histopathological and molecular features typical of ALK^+ human NSCLCs, and respond to treatment with ALK inhibitors. The general strategy described here substantially expands our ability to model human cancers in mice and potentially in other organisms" (Nature **516**:423-427, 2014)

   (A) Explain how chromosomal rearrangements contribute to human cancers. (2%)
   (B) Describe the experiments the authors might have performed to complete this work. (8%)
   (C) Describe the impact of this study on the current knowledge. (3%)
   (D) Give a title to this abstract (in English). (3%)

3. Please describe the strategy for finding the gene(s) for a known product: zebrafish hemoglobin. (10%)

4. The persistent infection of Hepatitis C virus (HCV) is a major cause of liver cirrhosis and hepatocellular carcinoma. Through phylogenetic analysis of the 9,400-nucleotide whole genome or the subgenomic regions, such as the core, E1, or nonstructural (NS) 5B regions, HCV has been classified into seven genotypes and 67 subtypes. HCV genotype is one of the strongest baseline predictors of the sustained virological response to antiviral treatment with pegylated-interferon- alpha (PEG-IFN alpha) in combination with ribavirin (RBV) in patients with chronic hepatitis C (R. Y. Yang et al, Journal of Clinical Microbiology 52: 3685, 2014).

   Please describe principles and methods of three tests for genotyping of HCV. (15%)

5. Glucose degradation can be accomplished by a combination of the glycolytic and citric acid pathways. The enzymes for glycolysis are located in the cytosol, while the enzymes for the citric acid cycle are located in the mitochondria. What are two advantages in separating the enzymes for these major carbohydrate degradation pathways in different cellular compartments? (10 %)

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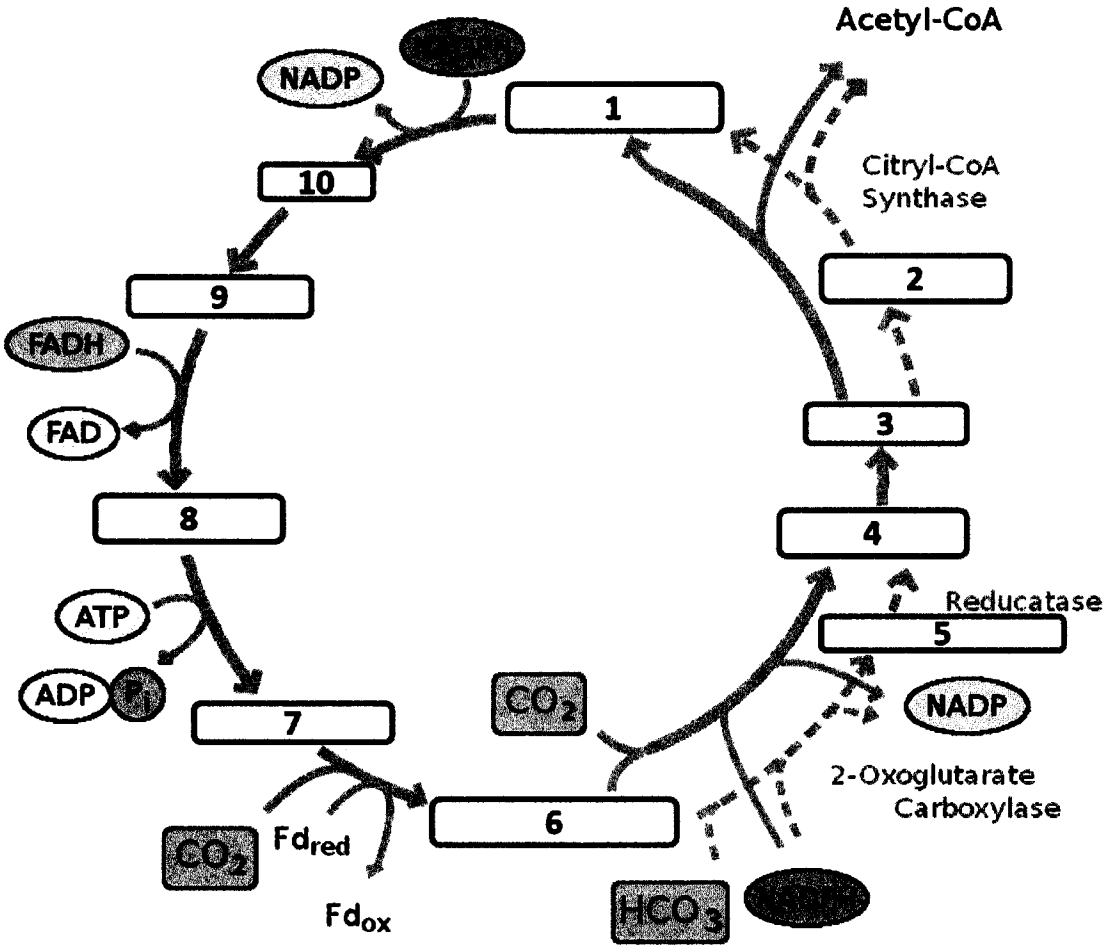
6. Fish oils are rich sources of omega-3 and polyunsaturated fatty acids and omega-6 fatty acids are relatively abundant in corn and sunflower oils. Classify the following fatty acids as omega-3, omega-6, or neither:
(a) linolenate, (b) linoleate, (c) arachidonate, (d) oleate (10 %)

7. For testing blood glucose, a drop of blood is placed on a paper strip impregnated with enzyme glucose oxidase and all the reagents necessary for the reaction

β-D-Glucose + O_2 → D-Gluconolactone + H_2O_2

The H_2O_2 produced causes a color change on the paper that indicates how much glucose is present. Since glucose oxidase is specific for the β anomer of glucose, why can the total blood glucose be measured? (5 %)

8. Please write the names of the substrates in TCA cycle (from number 1 to 10) (10%).



9. Protein K is a metalloprotease which participates in cell migration and remodeling. Compound A and B are competition and non-competition inhibitors for protein K, respectively. (1) Please describe how to calculate K_m and V_{max} for protein K (5 %). (2) Please draw the double reciprocal plots (Lineweaver-Burk plot) of the two mechanisms which must include four concentration levels of inhibitors (0, low, medium, and high) (10 %)