

※ 考生請注意：本試題不可使用計算機

1. Baby Lin, 3 month-old infant girl, was sent to the National Cheng Kung University Hospital. She had a severe seizure last night. When doctors examined her, they smelled "musty (moldy, bad) odor" from the baby. They did a screening test for Phenylketonuria on her and the results were positive. Further genetic analysis found that she has a mutation in the DNA sequences of an enzyme called phenylalanine hydroxylase. Please answer the following questions.

- (A) To treat this disease, what amino acid should Baby Lin avoid in the diets? (5%)
- (B) To treat this disease, what amino acid should Baby Lin take in the diets? (5%)
- (C) The doctors did not detect any phenylalanine hydroxylase protein expression in Baby Lin's blood samples. What kind of DNA mutation in the phenylalanine hydroxylase gene might Baby Lin have? (5%)
- (D) To continue with the above question (C), explain why your answer in (C) may be correct? (10%)
- (E) The doctors noticed that Baby Lin had lighter (less dark) hair, eyes and skin color than her 5 year-old normal healthy sister. They already know that production of melanin is important for the pigmentation of hair, eyes and skin. What hypothesis can they formulate to study the causal relationship between melanin and Phenylketonuria? (10%)
- (F) To continue with the above question (E), how do they test whether their hypothesis is right or wrong? (15%)

2. Dr. Robert Lefkowitz and Dr. Brian Kobilka won the 2012 Nobel Prize in chemistry for their work on G-protein-coupled receptors (GPCRs). Importantly, GPCRs are the target of about 40% of all modern medicinal drugs used for a variety of human diseases. Please answer the following questions.

- (A) GPCRs contain seven long hydrophobic helices. Where are GPCRs located in the cells? (5%)
- (B) G-protein was first discovered by the 1994 Nobel Medicine/Physiology Prize laureates Drs. Alfred Gilman and Martin Rodbell. Briefly explain what is G-protein and what is its major function? (10%)
- (C) To prove the existence of GPCRs, in 1968, Dr. Lefkowitz decided to develop a biologically relevant direct ligand-binding assay. To do so, he needed to label adrenocorticotrophic hormone (ACTH), a ligand for GPCRs. What did he use to label the ligand? (5%) (Hint: the ligand-binding assay needs to be very sensitive as the levels of ACTH receptor are low in the cells.)
- (D) To understand the actions of GPCRs, in the 1970s and 1980s, the Lefkowitz laboratory decided to purify the protein of β -adrenergic receptor, a GPCR. Please suggest a series of experiments to accomplish this goal. (15%)
- (E) Based on the short 19 amino acid peptide sequence of β -adrenergic receptor, in the 1980s, Dr. Kobilka decided to clone the gene of β -adrenergic receptor. Please suggest a series of experiments to accomplish this goal. (15%)