國立嘉義大學九十四學年度

生物科技研究所碩士班招生考試試題

科目：專業英文

1. After reading the following abstract, please describe briefly how OSBP controls ERK1/2 activation. (25%)

Oxysterol-binding protein (OSBP) is the founding member of a family of sterol-binding proteins implicated in vesicle transport, lipid metabolism, and signal transduction. Here, OSBP was found to function as a cholesterol-binding scaffolding protein coordinating the activity of two phosphatases to control the extracellular signal–regulated kinase (ERK) signaling pathway. Cytosolic OSBP formed a ~440-kilodalton oligomer with a member of the PTPPBS family of tyrosine phosphatases, the serine/threonine phosphatase PP2A, and cholesterol. This oligomer had dual specific phosphatase activity for phosphorylated ERK (pERK). When cell cholesterol was lowered, the oligomer disassembled and the level of pERK rose. The oligomer also disassembled when exposed to oxysterols. Increasing the amount of OSBP oligomer rendered cells resistant to the effects of cholesterol depletion and decreased the basal level of pERK. Thus, cholesterol functions through its interaction with OSBP outside of membranes to regulate the assembly of an oligomeric phosphatase that controls a key signaling pathway in the cell. *(Wang PY et al., Science, 307: 1472-1476, 2005).*

2. Please translate the paragraph in Chinese and write your impression. (25%)

A hard day's night

What is it that makes me get up early in the morning after too little sleep? When the previous day was spent wrestling with another failed experiment, and cutting short phone calls home for another bunch of articles that needed to be read? It's strange, but I can't answer straight away.

Making science work — even at a basic level like in my graduate research projects — is attractive to much more than my intellect. The lab is the place where I spend most of the day and part of the night as well. My colleagues are the first people I share my thoughts with. It's hard to explain this level of engagement and involvement to others outside my little research universe. But sometimes it's pivotal to face the truth: doing research converts me into an egoist who chases ideas and results, and thereby forgets about time and society.

Despite the intensity of my lab life, it is a relief to have some people outside who I can't talk to about the stuff that occupies me the whole day. They wouldn't understand a word about what I spend most of my time doing. So in the end it's this ignorance that saves me and makes my day. It's this small preserve outside science that gives me time to recharge and get up in the morning to start off to the lab for another long day. *(Langenhan, T, Naturejobs, 434: 120, 2005.)*

3. Read the following paragraphs and answer the questions. (32%)

Several human neurological diseases are associated with repeated trinucleotides in certain genes. These trinucleotide repeats exhibit an unusual genetic instability: Above a threshold of about 35 to 50 copies (100-150 bp), the repeats tend to expand, by an unknown mechanism, with successive generations. Because the overall length of the repeat typically correlates with the age of onset of the disease, descendants of an individual with a trinucleotide repeat disease tend to be more severely affected and at an earlier age. The disease is therefore said to exhibit genetic anticipation.

Some types of trinucleotide repeat diseases are caused by massive expansion (usually to hundreds of copies) of a trinucleotide in the noncoding region of a gene, for example, in a region upstream of the transcription start site, in a 5’ or 3’ untranslated region (UTR), or in an intron. These expansions generally affect gene expression. For example, myotonic dystrophy results from aberrant expression of a protein kinase. The severity of symptoms, progressive muscle weakness and wasting, correlate with the number of CTG repeats (>2000 in some cases).

In fragile X syndrome, the most common cause of mental retardation after Down’s syndrome, trinucleotide expansion ranging from hundreds to thousands of copies promotes the breakage of the tip of the X chromosome’s long arm. Like many trinucleotide repeat diseases, fragile X syndrome exhibits non-Medelian inheritance: Between 20% and 50% of males bearing the fragile X mutation are asymptomatic. Their daughters are likewise asymptomatic, but these daughters’ children have the symptom. Evidently, the fragile x defect is somehow activated by passage through a female.

Other trinucleotide repeat diseases result from the moderate expansion of a CAG triplet, which codes for glutamine, in the protein coding region of a gene. Presumably, these expansions yield nonfunctional proteins that kill cells, particularly in nervous system. Such a loss of neurons occurs in Huntington’s disease, a devastating condition characterized by progressively disordered movements (chorea) and emotional disturbances. This genetically dominant and invariably fatal disease has an age of onset of ~ 40 years and may follow a 10- to 20-year course. The repeated CAG sequences in the relevant gene, which codes for a 3145-residue polypeptide called Huntingtin, are normally present in 11 to 34 copies but increase to between 37 and 876 copies in affected individuals.

Questions:

a. Why trinucleotide repeat diseases are said to exhibit genetic anticipation? (8%)

b. Although both fragile X syndrome and Huntington’s disease are trinucleotide repeat diseases, what are the major differences between these diseases in terms of trinucleotide type, repeat number, location of trinucleotide repeat, and the mechanism that leads to the disease? (16%)

c. “Fragile X syndrome exhibits non-Medelian inheritance.” What does this mean? (8%)

4. Read the following paragraphs and answer the questions. (18%)

The extreme acidic conditions of the stomach are a necessary part of the digestive process: the low pH kills ingested microbes, denatures proteins, and activates the protease pepsin, which performs optimally at pH ~ 2.0. Pepsin has broad specificity for peptide bonds and is especially efficient at hydrolyzing the polypeptide chains of collagen.

The stomach itself is protected from its content by a thick layer of mucus, which is viscous mixture of water and heavily O-glycosylated proteins called mucins. Peptic ulcers may develop if stomach acid reaches the underlying gastric mucosa.

The (H^+-K^+)-ATPase of the gastric mucosa is activated by histamine stimulation of a cell-surface receptor. Compounds that block the process by competing with histamine for binding to the receptor can reduce HCl production. For example, cimetidine and its analogs, which resemble histamine, bind to the histamine receptor but do not activate the (H^+-K^+)-ATPase. Such drugs are widely prescribed to alleviate the painful and otherwise often fatal symptoms of peptic ulcers.

Many ulcers are ultimately caused by infection with the recently discovered bacterium *Helicobacter pylori*, which thrives in the nutrient-rich gastric mucus. Because the bacterium is thus somewhat sequestered from the host’s antimicrobial weaponry, it tends to induce a state of chronic inflammation of the stomach tissue, which then becomes susceptible to additional acid-induced damage. In such cases, antibiotics that eliminate the infection are therefore a better treatment for peptic ulcers than drugs such as cimetidine that merely relieve the symptoms.

Questions:

a. Why extreme acidic conditions of the stomach are necessary for the digestive process? (6%)

b. What are the two major causes that lead to peptic ulcers? (6%)

c. What are the ways (including rational mechanisms) that may be applied to treat peptic ulcers? (6%)