

THE UNIVERSITY OF MELBOURNE

DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

SEMESTER 2 ASSESSMENT, 2004

521-304 HORMONE & NEUROTRANSMITTER BIOCHEMISTRY

EXAM DURATION: **THREE (3) Hours**

READING TIME: **Fifteen (15) Minutes**

THIS PAPER HAS 4 PAGES

Instructions to Students:

This exam paper accounts for 80% of the total marks for the subject.

Marks are allocated in proportion to the time advised for each question or section.

This paper consists of **TWO (2)** sections, A and B.

SECTION A

You should attempt **THREE (3)** questions in Section A.

Suggested time – 40 minutes for each question.

All questions in this Section are of equal value.

SECTION B

You should attempt **FOUR (4)** questions in Section B.

Suggested time – 15 minutes for each question.

All questions in this Section are of equal value.

Use a **SEPARATE** examination book for **EACH** question.

Authorized Materials:

No specific materials are authorized.

Instructions to Invigilators:

Students need **SEVEN (7)** 6-page examination script books.

This paper may be reproduced and lodged with the Baillieu Library

SECTION A (Attempt **THREE (3)** of the following four (4) questions
(suggested time 40 minutes per question)
Use a **SEPARATE** script book for each question

Question 1

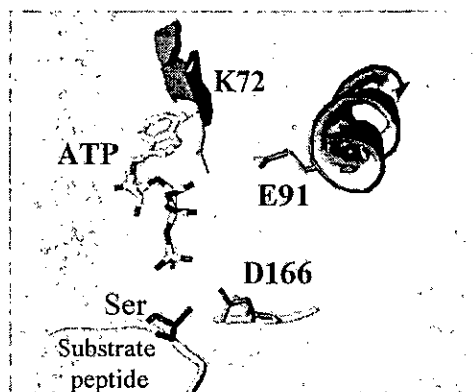
The functions of the protein phosphatase PP1 inhibitor DARPP-32 are modulated by phosphorylation of Thr-34 and Thr-75.

- A. Describe how phosphorylation of each site regulates the functions of DARPP-32 in neurons.
- B. With the help of a schematic diagram, describe how **CHRONIC** cocaine exposure alters the phosphorylation status of DARPP-32 in neurons of nucleus accumbens. Your answer should include the signaling pathways in neurons that are stimulated upon chronic cocaine exposure.

Question 2

The following diagram shows the catalytically critical residues, Lys-72, Glu-91, Asp-166, ATP and the substrate peptide, in the active site of cAMP-dependent protein kinase (PKA).

- A. Draw a schematic annotated diagram that depicts the catalytic mechanism of the PKA-catalysed phosphorylation reaction.
- B. Discuss the roles played by, Lys-72, Glu-91 and Asp-166 in the phosphorylation reaction catalysed by PKA. Your answer should include a model of the catalytic mechanism of the phosphorylation reaction.



SECTION A (continued)

Use a **SEPARATE** script book for each question

Question 3 (answer (1) one of the following 2 parts)

EITHER

This year's Nobel Prize in Physiology and Medicine was awarded to Richard Axel and Linda Buck "for their discoveries of odorant receptors and the organization of the olfactory system". To what broad class of membrane-bound receptors do the odorant receptors belong? Describe the different processes of signal transduction employed by members of this broad receptor class and the *intracellular* mechanisms responsible for signal transduction (amplification) and signal termination. Give examples of neurotransmitters and hormones that operate via this broad class of receptors?

OR

The glycine and GABA_A receptors belong to a family of ligand-gated ion channels. Describe the organization and properties of this receptor family and indicate with examples how individual members of this receptor family select between cations and anions.

Question 4

A great diversity of peptide neurotransmitters and peptide hormones are responsible for chemical communication between cells, tissues and organs in the body. Describe, with examples, the principal biochemical mechanisms responsible for generating this diversity.

SECTION B (Attempt FOUR (4) of the following seven (7) questions)
(suggested time 15 minutes per question)
Use a SEPARATE script book for each question

Question 5

With the help of an annotated diagram, describe how ACUTE cocaine exposure regulates the phosphorylation status of the NMDA receptor in neurons of the nucleus accumbens.

Question 6

Explain how adrenaline stimulation of skeletal muscle modulates the activity of sarcoplasmic reticulum Ca^{++} -ATPase (also called the Ca^{++} -pump).

Question 7

Describe the molecular basis of inactivation of glycogen synthase in skeletal muscle upon adrenaline stimulation.

Question 8

The nuclear receptor superfamily provides target tissues with an essential mechanism for hormonal control of gene expression. Describe the main structural features of this family of receptors giving examples of their ligands, mechanism(s) of signal transduction, and different effects on expression of target genes. Include in your answers any features that distinguish individual members this family. Use diagrams as appropriate.

Question 9

Axonal transport is responsible for maintenance of axonal integrity and for sensing changes in target tissue environment. Describe the cellular components and biochemical mechanisms responsible for anterograde and retrograde axonal transport and their role(s) following a nerve injury.

Question 10

The myelin sheath is responsible for fast saltatory conduction in nerve fibres. Describe the organization of proteins in the myelin sheath and their roles in recognition and compaction of peripheral and central myelin. How are these processes affected in demyelinating diseases.

Question 11

Parkinsons disease was the first disease of the nervous system to be identified as a molecular disease. Explain the proposed roles for alpha-synuclein and reactive oxygen species (ROS) in the pathogenesis of this disorder.

END OF EXAM