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THE UNIVERSITY OF MELBOURNE

DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

SEMESTER 2 ASSESSMENT, 2005

## 521-302 FUNCTIONAL GENOMICS

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

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

**THIS PAPER HAS 4 PAGES**

### **Instructions to Students:**

This paper consists of 8 Questions.

Use a **SEPARATE** script booklet for EACH QUESTION.

Question 1 is **compulsory** and is worth 10 marks.

Answer 5 of the remaining 7 questions, Questions 2-8.

Questions 2-8 are each worth 18 marks.

**Total marks for the paper:** 100

### **Authorized Materials:**

No specific materials are authorized.

### **Instructions to Invigilators:**

Students need **SIX** (6) 7-page script booklets.

**This paper is worth 80% of the total mark for the subject**

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## **This question is compulsory**

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### **Question 1 (10 marks, 18 minutes)**

A group of researchers are working on a gene called *Drielin* that is expressed in the liver and heart of mice. Their major goal is to discover the function of *Drielin* in the liver. They attempt to make gene-targeted mice where the *Drielin* gene is mutated so that a protein is not produced (gene knockout mice). However, all the *Drielin* mutant mice die in the uterus and none were born. They determine that this is because the heart does not develop properly in the early embryo due to the absence of the *Drielin* protein in the heart. Hence, they were unable to examine the function of the *Drielin* gene in the liver by this approach. Describe how the researchers could make genetically manipulated mice in which the *Drielin* gene is targeted so that the function of *Drielin* in the liver could be analysed. In other words, the new mice must not die due to the absence of *Drielin* protein in the heart. Your answer must include the steps involved in producing the genetically manipulated mice. Use diagrams if appropriate.

## **Answer 5 of the remaining 7 questions**

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### **Question 2 (18 marks, 32 minutes)**

**(start a new script booklet)**

A gene mapping approach using samples from a large number of patients has been used to localise a gene responsible for a particular disease of the liver to a 2 Mbp genomic segment that contains only two genes. For technical reasons it is not possible to localise the gene to a region smaller than the 2 Mbp segment containing these two genes.

- A. Describe one approach to determine which of these two genes is the one responsible for causing the disease. **(6 marks)**
- B. The molecular basis for the liver dysfunction is unclear. Describe three approaches that may help to determine the biochemical function of the gene once its identity is determined. **(12 marks)**

### **Question 3 (18 marks, 32 minutes)**

**(start a new script booklet)**

Describe events in the nucleus involving gene activator proteins and other proteins and protein complexes that could lead to the activation of transcription of a typical eukaryotic gene.

**Question 4 (18 marks, 32 minutes)**

**(start a new script booklet)**

- A. Describe the three-dimensional structure of a nucleosome. Your answer must include at least one diagram. (6 marks)
- B. i. Describe the modifications that occur on histone tails. (2 marks)
- ii. a. Which histone tail modification has an important and direct role in regulating gene transcription? (1 marks)
- b. Briefly describe how this modification is responsible for regulating gene transcription. (3 marks)
- C. Newly synthesised chromatin has roughly equivalent amounts of nucleosomes to the parental chromatin from which it is copied. Describe the origin(s) of the nucleosomes found on the newly synthesised chromatin. (6 marks)

**Question 5 (18 marks, 32 minutes)**

**(start a new script booklet)**

Answer **BOTH** parts A and B.

- A. Mass spectrometry is a key tool to identify proteins in complex biological systems. Describe the steps involved in two approaches that involve the use of mass spectrometry (described as “workflows” in the 521302 lecture) to identify proteins in complex mixtures.
- B. You are required to set up a research program to introduce a novel enzymatic activity into the plastids (chloroplasts) of rice grain using stable modification of the nuclear genome of the rice plants. Describe briefly the steps you would take to achieve this including in your answer key features of both the vector and the gene construct that you would use.

**Question 6 (18 marks, 32 minutes)**

**(start a new script booklet)**

RNA interference and antisense RNA are two techniques used for the specific knockdown of target gene expression.

- A. Describe, using diagrams where appropriate, the RNAi pathway. (6 marks)
- B. What are the key differences between RNAi and antisense RNA? (6 marks)
- C. Outline the approaches used for rational design of siRNA sequences? (6 marks)

**Question 7**

*(start a new script booklet)*

For each of the following molecules/pathways GIVE **ONE** example of an oncogene/tumour suppressor gene and briefly discuss why it promotes the development of cancer.

- A. Growth factor receptors.
- B. Signal transducing proteins.
- C. Transcription factors.
- D. DNA repair.
- E. Apoptosis.

**(5 x 3.6 marks = 18 marks)**

**Question 8**

*(start a new script booklet)*

- A. Describe two pieces of evidence demonstrating that cancer development requires multiple independent genetic changes.

**(6 marks)**

- B. Discuss the relationship between the control of G1 to S phase transition in the cell cycle, DNA repair and the development of tumours.

**(12 marks)**

**(Total = 18 marks)**

**END OF EXAM**