BSc Degree Examinations 2018-9

Department: BIOLOGY

Title of Exam: Epigenetics in Development and Disease

Time Allowed:
2 hours

Marking Scheme:
Total marks available for this paper: 100
Section A: Short Answer / Problem / Experimental Design questions (50 marks)
Section B: Essay question (marked out of 100, weighted 50 marks)

Instructions:
Section A: Answer all questions in the spaces provided on the examination paper
Section B: Answer either question A or B. Write your answer in the green answer booklet provided and attach it to the back of the question paper using the cable tie provided.

Materials Supplied:
Green Answer Booklet

For marker use only

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DO NOT WRITE ON THIS BOOKLET BEFORE THE EXAM BEGINS
DO NOT TURN OVER THIS PAGE UNTIL INSTRUCTED TO DO SO BY AN INVIGILATOR
SECTION A: Short Answer / Problem / Experimental Design questions
Answer all questions in the spaces provided
Mark total for this section: 50

Question 1
Briefly compare and contrast the mechanisms of action of HOTAIR and HOTTIP. (6 marks)

Question 2
a) Provide two lines of experimental evidence that indicate that the chromatin structure of embryonic stem cells is in an open and permissive state compared to that of differentiated cells. (4 marks)

b) Provide one line of experimental evidence that demonstrates the importance of Trithorax activity in maintaining stem cell identity. (3 marks)
Question 3

The involvement of Tet1 in controlling NANOG expression in embryonic stem (ES) cells was investigated. The left-hand graph of Fig. 1 shows results of ChIP experiments looking at the association of Tet1 with four regions of the Nanog promoter (1-4) in either control ES cells (Ctrl KD) or ES cells in which Tet1 levels were suppressed (Tet1 KD1). The right-hand graph shows levels of 5-methylcytosine in the same cells and at the same regions as used for the left-hand graph.

Fig. 1.

Fig.2 shows gene expression levels of Tet1 and Nanog in either normal ES cells (J1) or ES cells that are defective for three DNA methyltransferases (DNMT1, DNMT3a and DNMT3b: DNMT TKO). J1 and DNMT TKO cells were either functioning for Tet1 (Ctrl KD) or had Tet1 suppressed (Tet1 KD1).

Fig. 2.
a) Using the data from both Figures 1 and 2, suggest a model to explain the role of Tet1 in controlling Nanog expression in ES cells. Identify experimental evidence that supports your model. (6 marks)

b) Suggest an experiment that you could perform to test your model proposed in (a). Include the expected results in your answer. (3 marks)

Question 4
Female mice that are obese as a result of being fed a high fat diet (HFD) are known to produce higher numbers of defective embryos compared to females that are fed a normal diet (ND). Levels of Stella (PGC7) protein present in oocytes derived from ND and HFD females were evaluated by western blotting with Actin protein levels used as a control. (Fig. 3)
Oocytes obtained from ND and HFD females were fertilized and levels of 5mC (upper graph) and 5hmC (lower graph) measured in maternal and paternal pronuclei (PN) in the zygotes. Results are presented in Figure 4 as signal intensity in the paternal (pat.) and maternal (mat.) PN (left axis) or as a ratio of the signal for the paternal and maternal PN (right axis). Each data point represents one zygote (n=12).
Using your knowledge of Stella (PGC7) and the data shown in Fig. 3, provide an explanation for the data shown in Fig. 4. (6 marks)

Question 5

a) The DNA methylation profile of an Arabidopsis mutant defective for the RNA-directed methylation pathway was analyzed. Suggest how the profile will differ from that of a wild-type plant and why. (4 marks)
b) Four lines of *Arabidopsis* were grown in either control or salt stress conditions, and their progeny tested for salt tolerance by measuring percentage germination in 100 mM NaCl. The four lines were wild type (WT) and mutants defective in one of the three major DNA methyltransferases (*met1*, *cmt3* or *drm2*). What conclusions can you draw from the results of this experiment? (4 marks)
Question 6
Experiments have shown that foraging in ants is caste dependant, where minors always forage more than majors. Treatment of ants with the HDAC inhibitors VPA and TSA resulted in the data below.

a) Suggest a mechanistic explanation for these results. (3 marks)

b) Describe an experiment that would test your hypothesis. (4 marks)
Question 7

a) Design a strategy for epigenetic treatment of cancer. Explain your logic. (5 marks)

b) What is the effect of DNA methylation on the agouti epiallele? (2 marks)
SECTION B: Essay question

Answer one question in the green answer booklet provided.

Remember to write your candidate number on the front of the answer booklet and indicate whether you have answered question A or B at the top of the page.

Mark total for this section: 50

EITHER

A) Compare and contrast the molecular mechanisms and biological implications of X-inactivation and genomic imprinting.

OR

B) Discuss the epigenetic changes that are associated with cancer and speculate how, throughout the life of an individual, environmental factors may influence these changes.