

※ 考生請注意：本試題 可 不可 使用計算機

1. Robert Edwards is awarded the 2010 Nobel Prize in Physiology or Medicine for the development of *in vitro* fertilization (IVF). His achievements have made it possible to treat infertility, a medical condition afflicting a large proportion of humanity including more than 10% of all couples worldwide. Except for the “test tube baby”, what are the applications of IVF to the contemporary biomedical sciences (please provide at least 2 “different “ applications for the answer)? (10 points)
2. Please define the term ‘Epigenome’ and provide at least three possible mechanisms governing the epigenome. (10 points)
3. Let’s say you find the transcription levels of the four genes, including A, B, C, and D, are up-regulated by the mutation (presumably a lost-of-function mutation) of gene Y in the cancer cells from a genome-wide transcriptomic analysis. You therefore hypothesize that the transcription regulation of these four genes could be gene Y-dependent (through a Y direct or indirect manner). What’s your plan to study the relationship between gene Y and gene A, B, C, and D. Please design at least three “independent” experiments to prove this hypothesis. (30 points)
4. Describe the similarity and difference between eukaryotic and prokaryotic DNA replication. (10%)
5. Describe the DNA repair system in fixing double-stranded break in eucaryotic cells. (10%)
6. Describe the packing of DNA in interphase of eucaryotic cell. (10%)
7. Propose several possible mechanisms to explain why a transcription factor can activate transcription by binding to a DNA element located at 1000 bp upstream from the initiation site? (10%)

Question 8 reading the following abstract of a research paper.

Histone modifications are regarded as the carrier of epigenetic memory through cell divisions. How the marks facilitate cell cycle-dependent gene expression is poorly understood. The evolutionarily conserved AAA ATPase ANCCA (AAA nuclear coregulator cancer-associated protein)/ATAD2 was identified as a direct target of oncogene AIB1/ACTR/SRC-3 and a transcriptional coregulator for estrogen and androgen receptors and is strongly implicated in tumorigenesis. We report here that ANCCA directly interacts with E2F1 to E2F3 and that its N terminus interacts with both the N and C termini of E2F1. ANCCA preferentially associates via its bromodomain with H3 acetylated at lysine 14 (H3K14ac) and is required for key cell cycle gene expression and cancer cell proliferation. ANCCA associates with chromosomes at late mitosis, and its occupancy at E2F targets peaks at the G1-to-S transition. Strikingly, ANCCA is required for recruitment of specific E2Fs to their targets and chromatin assembly of the host cell factor 1 (HCF-1)-MLL histone methyltransferase complex. ANCCA depletion results in a marked decrease of the gene activation-linked H3K4me3 mark. Bromodomain mutations disable ANCCA function as an E2F coactivator and its ability to promote cancer cell proliferation,

(背面仍有題目,請繼續作答)

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while ANCCA overexpression in tumors correlates with tumor growth. Together, these results suggest that ANCCA acts as a pioneer factor in E2F-dependent gene activation and that a novel mechanism involving ANCCA bromodomain may contribute to cancer cell proliferation.

8. (a) please give a Title for this research paper, (b) what is the relationship between H3K14ac and H3K4me3 in this article? (10%)