



KENYATTA UNIVERSITY

UNIVERSITY EXAMINATIONS 2011/2012

SECOND SEMESTER EXAMINATION FOR THE DEGREE OF BACHELOR
OF SCIENCE IN MOLECULAR CELL BIOLOGY

SBC 218: GENOME ORGANIZATION I

DATE: Wednesday, 28th March, 2012

TIME: 8.00 a.m. – 10.00 a.m.

SECTION A: Instruction: Answer All questions in this section. (20 marks)

Part I: MCQs

1. In the history of DNA structure discovery,
 - A. Maurice Wilkins showed a diffraction pattern of DNA at a scientific meeting in Naples in 1952.
 - B. In october 1952, Rosalind Franklin succeeded in taking very good diffractograms of 'wet' DNA fibres.
 - C. Chargaff visited Cambridge in 1951 and he talked with Watson and Crick about complementarity of DNA bases.
 - D. In 1952, Watson conceived the idea that bases might hydrogen bond with one another
 - E. All of the above

2. Which of the following is untrue about nucleosome phasing?
 - A. Translational positioning describes the location of a histone octamer at successive turns of the double helix, which determines which sequences are located in core DNA regions.
 - B. Rotational positioning describes the location of the histone octamer relative to turns of the double helix, which determines which face of DNA is exposed on the nucleosome surface
 - C. The most common cause of nucleosome positioning is when proteins binding to DNA establish a boundary.

- D. Non of the above
3. Which of the following is true about nucleosome assembly and disassembly during replication?
- A. The "new" tetramers and dimers enter a pool that also includes "old" tetramers and dimers, assembled from newly synthesized histones.
 - B. Nucleosomes assemble ~800 bp behind the replication fork.
 - C. Assembly is initiated when H2A·H2B dimers bind to each of the daughter duplexes, assisted by CAF-1.
 - D. The replication fork displaces histone octamers, which then dissociate into H3₂·H4₂ tetramers and H2A·H2B dimers
 - E. All of the above
4. The following are true about ancillary factor, CAF-1. Which one is not?
- A. It consist of more than 5 subunits with a total mass of 283kD.
 - B. It is recruited to the replication fork by PCNA
 - C. it provides the link between replication and nucleosome assembly, ensuring that nucleosomes are assembled as soon as DNA has been replicated.
 - D. It functions by binding to newly synthesized H3 and H4.
 - E. None of the above
5. With regard to modification of histone proteins,
- A. Ser10 position of H3 is phosphorylated when chromosomes condense at mitosis.
 - B. Acetylation and methylation occur on the free (Σ) amino group of histidine.
 - C. Methylation also occurs on arginine and lysine.
 - D. Phosphorylation occurs on the hydroxyl group of serine and also on lysine.
 - E. All of the above
6. Which of the following is untrue about the drug, 5-azacytidine?
- A. produce indirect evidence that demethylation can result in gene expression.
 - B. The drug is incorporated into DNA in place of cytidine, and can be methylated, because the 5' position is blocked.
 - C. induces changes in the state of cellular differentiation
 - D. The drug activates genes on a silent X chromosome,
 - E. None of the above
7. The following is/are true about 10nm chromatin fibre, which one is not
- A. folded from 30 nm fibers and consist of a string of nucleosomes.
 - B. essentially a continuous string of nucleosomes.
 - C. is obtained under conditions of low ionic strength and does not require the presence of histone H1.

- D. B and C
- E. None of the above

8. The replication-independent pathway,
 - A. Exists for assembling nucleosomes during other phases of cell cycle,
 - B. it uses different variants of some of the histones from those used during replication.
 - C. The assembly process discriminates between H3 and H3.3 on the basis of their sequences, specifically excluding H3 from being utilized
 - D. CAF-1 is probably involved in replication-independent assembly
 - E. All of the above
9. Which of the following statement/s is or are untrue about nucleosome periodicity?
 - A. The pitch of the superhelix varies, with a discontinuity in the middle.
 - B. Regions of high curvature are arranged asymmetrically, and occur at positions ± 1 and ± 4 . These correspond to S6 and S8, and to S3 and S11, which are the sites least sensitive to DNAase I .
 - C. Most of the supercoiling occurs in the central 129 bp, which are coiled into 1.59 left-handed superhelical turns with a diameter of 80
 - D. The terminal sequences on either end make only a very small contribution to the overall curvature.
 - E. A and B
10. Which of the following statements is incorrect?
 - A. The micrococcal ladder is generated when only ~2% of the DNA in the nucleus is rendered acid-soluble (degraded to small fragments) by the enzyme.
 - B. >95% of the DNA is recovered in nucleosomes or multimers when micrococcal nuclease cleaves DNA of chromatin.
 - C. The length of DNA per nucleosome varies for individual tissues in a range from 264-360 bp.
 - D. When chromatin is digested with the enzyme micrococcal nuclease, the DNA is cleaved into integral multiples of a unit length.
 - E. All of the above

Part 2: Fill in the empty spaces (each is 1 mark).

11. Methylation of cytosine at CpG doublets is associated with.....
12. The basic nuclear DNA unit is the nucleosome, in which is wrapped around an octamer of histone (H) proteins
13. The average periodicity over the nucleosome is

14. When chromatin is visualized in conditions of greater ionic strength the is obtained
15. Each histone also has a flexible N-terminal tail, which has that may be important in chromatin function.
16. The phosphorylation of H1 is catalyzed by the that provides an essential trigger for mitosis.
17.(a)..... is predominantly responsible for maintaining methylation patterns during replication, whereas(b)..... are required for *de novo* methylation.
18. The ultimate effect of negative supercoiling is to generate a region of DNA in which
19. In periodicity, the refers to the number of base pairs per turn of the double helix.
20.describes the position of DNA with regard to the boundaries of the nucleosome

SECTION B: Answer All questions, each is 5 marks

21. Describe an experiment to prove that Nucleosomes have a common structure (5 marks)
22. A). outline the activities that lead to changes in DNA topology (3 marks)
 - b). Explain the meaning of the following terms (2 marks)
 - i). Packing ratio of DNA
 - ii). Superhelical density
 - iii). Topological isomers
 - iv). Cutting periodicity
23. Describe the organization of a histone octamer (5 marks)
24. The change in linking number is often given by the equation $\Delta L = \Delta W + \Delta T$.
Explain the implication of this equation with regard to various DNA topologies (5 marks)

25. A). what are isoschizomers? (1/2 mark)
- b). Using examples where possible, describe the use of isoschizomers in DNA structure analysis (3 marks)
- c) state the target sites of DNA methylation (1.5 marks)
26. a). Explain the mechanisms of action of various DNA Topoisomerases (2.5 marks)
- b). Outline the various features of histone proteins (2.5 marks)

Section C: Answer any two questions. Each is 10 marks

27. A). The double helix of DNA has been shown to exist in several different forms, depending upon sequence content and ionic conditions of crystal preparation. Discuss (5 marks)
- b). Discuss how the DNA structure was discovered (5 marks)
28. Describe how the DNA structure varies on the nucleosomal surface (10 marks)
29. A). Give a detailed description of Histone Modifications and explain how they affect gene activity (5 marks)
- b). Describe nucleosome phasing (5 marks)