Course Name : Epigenetics	Course Code : LS4108
Date of Exam: 29-11-2018	Duration: 2 hours
Instructor: Sanjeev Galande	Total Score: 35 marks

Instructions:

i. This question paper has 2 pages.
ii. Use illustrations and/or examples whenever appropriate.
iii. Be as concise as possible.

Q.1 How does the cross talk between transcription factor and DNA methylation take place? **(4 marks)**

Q.2 Is there a need for more than one type of DNA methyltransferase? Justify your answer. **(4 marks)**

Q.3 A group of chromatin biologists wanted to study the spatial organization of chromosomes within the nucleus in human cells. They observed that even though chromosomes 2 and 11 have great difference in terms of the amount of genetic material they carry (chromosome 2: 243 million base pairs; chromosome 11: 135 million base pairs), still they occupy similar volumes in the nucleus.

a. Can you give reasons for this observation?

b. What type of histone modifications would be predominant on these chromosomes? **(4 marks)**

Q.4 A researcher identified a novel protein, which has similar domain structure as some of the known proteins involved in chromatin organization. However, it is not possible to comment about the exact function of the protein based on sequence or structural homology. If you were the researcher, what series of experiments you would perform to establish function of novel protein as (rationale of the experiment is must) -

1. Methylation sensitive transcription factor

2. Regulator of gene expression by modulating DNA methylation levels.

3. Regulator of gene expression by altering chromatin organization.

4. Interactor of cis regulatory elements such as insulators and boundary elements. **(8 marks)**

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Q.5 As a researcher you are interested in studying transgenerational epigenetics and starting your own lab. Which paradigm would you choose for studying transgenerational epigenetic flow of information? Clearly state your hypothesis, justify choice of experimental system and design experiments to validate your hypothesis (epigenetics based only). **(5 marks)**

Q.6 What are different mechanisms of recruitment of PRC2 on the chromatin to regulate gene expression? RYBP proteins are known to recruit PRC1 complex to the target site. Explain the mechanism by which the recruitment would result in transcriptional repression of target loci. **(5 marks)**

Q.7 The long non-coding RNA Xist physically coats the X chromosome and manifests inactivation of X chromosome in mammalian females. In order to decipher the functionality of this molecule, a researcher has generated different mutations in Xist RNA. Upon performing RNA FISH for Xist along with immunostaining for repressive histone modification H3K27me3, following was observed with 3 different Xist mutants.

(i) Mutant 1 shows diffused Xist RNA localization and reduced H3K27me3 mark on the X chromosome

(ii) Mutant 2 shows proper Xist RNA coating and very less H3K27me3 mark on the X chromosome.

(iii) Mutant 3 shows very low Xist RNA expression (pin-point) and no H3K27me3 mark on the X chromosome

(iv) Mutant 4 shows proper Xist RNA coating as well as H3K27me3 colocalization on the X chromosome.

Determine which of these mutations affect (a) transcription of Xist, (b) tethering of Xist and (c) gene silencing established by Xist. **(5 marks)**