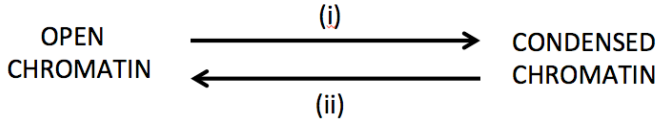
Genetics and Genomics in Medicine Chapter 6 Questions

Multiple Choice Questions

Question 6.1

With respect to the interconversion between open and condensed chromatin shown below:



Which of the directions (i) or (ii) would you anticipate would be the consequence of the following types of chromatin modification?

a) Histone acetylation.
b) DNA methylation.
c) Histone methylation.
d) Histone deacetylation.
e) DNA demethylation.

Question 6.2

With respect to microRNAs, which, if any, of the following statements, is false?

a) MicroRNA is a generic term that covers all tiny RNAs, ones that are less than 35 nucleotides long when mature.
b) MicroRNAs usually work as transcription factors.
c) MicroRNAs regulate target genes by binding to complementary sequences on one DNA strand of the target gene.
d) MicroRNAs normally regulate the expression of just a single target gene.

Question 6.3

With respect to microRNAs, which, if any, of the following statements, is true?

a) MicroRNA genes often occur in gene clusters within introns of protein-coding genes and are usually transcribed by RNA polymerase II.
b) Like an mRNA a miRNA is initially produced as a larger precursor RNA that, like the great majority of mRNAs, usually has a 5' cap and a poly(A) tail.
c) MicroRNAs are produced by germ-line cells only.
d) An miRNA is initially produced as a duplex RNA but in order to work it needs to be converted into a single-strand RNA.

Question 6.4

With respect to microRNAs, which, if any, of the following statements, is false?

a) A microRNA normally works by binding to perfectly complementary sequences within an RNA transcript, usually an mRNA.
b) Like the great majority of mRNAs an miRNA is usually produced as a larger precursor RNA that is capped and has a 3' poly(A) tail.
c) The precursor miRNA undergoes different types of post-transcriptional cleavage by endoribonucleases that are specific for double-stranded target sequences.
d) A nuclear endoribonuclease called dicer cleaves the miRNA precursor so that it forms a stem-loop RNA.

Question 6.5

With respect to how miRNAs work, which, if any, of the following statements, is false?

a) An miRNA is initially composed of two RNA strands, a passenger strand that will be destroyed and a complementary RNA, the guide strand, that is required for it to work.
b) an active miRNA regulates target protein-coding genes by binding to complementary sequences in the mRNA
c) A single miRNA normally binds to transcripts from just one target gene
d) A single type of mRNA can be regulated by multiple different miRNAs.

Question 6.6

MicroRNAs are important gene regulators, but the miRNAs are also regulated in turn by other RNAs. Which, if any, of the following classes of RNA are known to contain RNAs that regulate miRNAs?

a) Pseudogene RNA
b) Ribosomal RNA
c) Long noncoding RNA
d) Circular RNA

Question 6.7

Which, if any, of the following is not regularly an epigenetic phenomenon that depends on DNA methylation or chromatin modification?

a) X-chromosome inactivation.
b) A position effect in which a gene is silenced by an inversion where both breakpoints occur within a euchromatic environment.
c) Establishment of heterochromatin at a centromere.
d) Imprinting

Question 6.8

With respect to histone modifications, which, if any, of the following statements, is true?

a) histone acetylation always means adding an acetyl group to the side chain of a lysine residue.
b) in histone acetylation each lysine of the histone is acetylated.
c) in histone phosphorylation a phosphate group is transferred to the side chain of a serine .
d) in histone methylation it is the DNA that coils around a nucleosome that is methylated, not the histone itself.

Question 6.9

Some DNA sequences in our cells have high frequencies of methylated cytosines (hypermethylation); some others have a low frequency of methylated cytosines (hypomethylation). Which of the two methylation states best describes the kind of sequences listed in a) to d)?

a) satellite DNA in pericentromeric heterochromatin.
b) promoters.
c) dispersed transposon repeats.
d) CpG islands
e) enhancers.

Question 6.10

With respect to the DNA methylation mechanism in mammalian cells, which of the following statements, if any, is true?

a) The principal role of the DNMT1 DNA methyltransferase is in *de novo* methylation.
b) The DNMT3A and DNMT3B DNA methyltransferases require hemi-methylated DNA as a substrate and are responsible for methylating nascent DNA strands that are complementary to methylated parental DNA strands
c) Active DNA demethylation means removal of methyl groups from a hemi-methylated DNA double helix.
d) DNA methylation is not essential in mammalian development.

Question 6.11

With respect to CpG islands in our genomic DNA, which, if any, of the following descriptions do not apply?

a) frequently occurring (there are about 30,000 in the human genome).
b) long DNA sequences (typically from 10 kb to 100 kb in length).
c) low CG dinucleotide frequency.

d) frequently associated with transcriptional start sites.

Question 6.12

With respect to X-chromosome inactivation, which, if any, of the following statements are not correct ?

a) X-chromosome inactivation in mammals begins in the pre-implantation embryo
b) In humans all diploid cells that carry two normal X-chromosomes are subject to a random pattern of X-inactivation.
c) Once a decision has been made to inactivate an X chromosome (either the paternal or maternal X), all descendant cells show the same pattern of X-inactivation.
d) The inactivated X chromosome becomes a highly condensed Barr body in which genes are silenced across the length of the chromosome.

Question 6.13

With respect to noncoding RNA (ncRNA) , which, if any, of the following statements, is false?

a) Many long noncoding RNAs work in epigenetic regulation of gene expression.
b) Most regulatory long ncRNAs work as *trans*-acting regulators.
c) HOTAIR RNA is produced by a gene in the *HOXC* homeobox gene cluster at 12q13 but can regulate multiple genes within the HOXD gene cluster on chromosome 2.
d) HOTAIR RNA works as a scaffold that binds specific protein regulators at its two ends.

Question 6.14

With respect to epimutations, which, if any, of the following statements, is false, from a practical viewpoint?

a) The term *epimutation* means an unexpected change in chromatin conformation, causing a gene to be expressed in an abnormal way that is not related to its base sequence.
b) A primary epimutation is a change in chromatin confirmation that is not related directly to any change in the base sequence.
c) A secondary epimutation arises from a standard mutation that results in a profound change of expression in a gene that regulates chromatin conformation.
d) A “chromatin disease” is a disorder that is consistently caused by a primary epimutation.

Question 6.15

Which, if any, of the following descriptions is false?
Uniparental disomy

a) means that in a diploid cell two copies of the same chromosome are inherited from one parent.
b) is very rare.
c) can be the outcome of a trisomic zygote that is unstable and ejects a chromosome from one parent, but keeps two copies of the same chromosome from the other parent.
d) can occur when a sperm fertilizes an egg that lacks one chromosome, and the resulting unstable zygote is able to recover by duplicating the single chromosome.

Question 6.16

Which, if any, of the following descriptions is false?

a) Genomic imprinting in mammals really means that a very few genes are expressed from one allele only, according to the sex of the parent.
b) Imprinted genes are often found in clusters of genes, many of which are imprinted.
c) means that in a diploid cell two copies of the same chromosome are inherited from one parent
d) Within an imprinted gene cluster, all genes on one of the two parental chromosomes are silenced, but the equivalent genes on the other parental chromosome are not subject to silencing.

Question 6.17

Which, if any, of the following statements is incorrect?

a) In X-chromosome inactivation the inactivated X chromosome is epigenetically silenced by a transcript, the XIST RNA, that is produced from the active X chromosome.
b) The XIST RNA works by coating most of the X chromosome that is to be inactivated and then recruiting Polycomb proteins to condense the chromosome.
c) The inactivated X chromosome carries the kinds of histone modification that are typical of heterochromatin.
d) The pattern of X-chromosome inactivation is made randomly but once it has been established the same pattern of X-inactivation is propagated through all mitotic and meiotic cell divisions.

Question 6.18

With reference to imprinting disorders, which, if any, of the following statements is false?

a) About one quarter of individuals with Angelman syndrome lack a paternal chromosome 15.

b) With the exception of abnormal chromosome segregation, imprinting disorders always result from a deletion or inactivating mutation within, or spanning the imprinted gene cluster.
c) In some imprinting disorders, disease results from inappropriate biallelic expression of a gene.
d) Angelman and Prader-Willi syndrome are very different disorders but can be caused by precisely the same large deletion at 15q11-q13.

Question 6.19

a) With respect to imprinting control regions, which if any, of the following statements is true.
b) An imprinting control region is differentially methylated on paternal and maternal chromosomes
c) In some individuals with a disorder of imprinting, the disease occurs because an imprinted control region is inappropriately demethylated, and as a result a neighboring gene that it directly regulates is inappropriately inactivated.
d) In some individuals with a disorder of imprinting, the disease occurs because an imprinted control region is inappropriately demethylated, and as a result a neighboring gene is inappropriately activated.
e) In some individuals with a disorder of imprinting, the disease occurs because an imprinted control region is inappropriately methylated, and as a result a neighboring gene is inappropriately activated.

Question 6.20

With regard to the molecular pathogenesis of facioscapulohumeral dystrophy, which, if any, of the following can be implicated in the pathogenesis?

a) a variable number of tandem DNA repeats.
b) increased heterochromatin.
c) activation of a retrogene.
d) a regulator of methylation.

Question 6.21

Which, if any, of the following descriptions is inaccurate?
The epigenome

a) means the totality of epigenetic settings in a cell.
b) is variable between tissues.
c) does not vary between cells of the same type

d) can change in response to changes in the environment.

Essay and List Questions

Question 6.22
Circular RNAs are very common in human cells. A human fibroblast, for example, has about 25,000 different circular RNAs. What is the role of these RNAs?

Question 6.23
The nuclear genome in our cells makes four types of RNA polymerase, a simple RNA polymerase that is imported into mitochondria and is dedicated to transcribing mitochondrial DNA plus three types of multi-subunit RNA polymerase that transcribe nuclear DNA sequences. What types of DNA sequence are transcribed by the different nuclear RNA polymerases.

Question 6.24
List two examples of DNA-binding motifs commonly found in protein transcription factors. How do they bind to DNA?

Question 6.25
Splice junction sequences show a certain degree of sequence conservation. Give consensus sequences for the splice donor and splice acceptor sequences.

Question 6.26
How common is RNA editing in human cells and what types of RNA editing are seen?

Question 6.27
The pseudogene *PTENP1* is an example of a functional pseudogene that has an important role in gene regulation. Explain what its role is.

Question 6.28
List four types of epigenetic phenomena that involve DNA or chromatin modification

Question 6.29

Match individual variant histones i) to iv) to one or more of the possible functions listed in a) to g).

Varient histones

i) CENP-A
ii) H2AX
iii) H2A.Z
iv) H3.3

Functions

a) DNA replication
b) As a barrier to stop heterochromatin spreading
c) DNA repair
d) Transcriptional activation
e) Kinetochore assembly
f) Recombination
g) Genome maintenance

Question 6.30

DNA methylation is one epigenetic mechanism where it is easy to appreciate how the pattern of epigenetic settings is stably inherited from one cell generation to the next. What are the features of the DNA methylation mechanism that suggest this?

Question 6.31

How does uniparental diploidy occur in humans, and what are the consequences?

Question 6.32

According to the manner in which they work, three main classes of proteins that modify chromatin are recognized. What are these three classes and explain, with examples, what distinguishes the individual classes.

Question 6.33

What are the principal functions of DNA methylation in mammalian cells?

Question 6.34

Give four examples of different ways in which the active allele at an imprinted locus is known to be inactivated or not inherited in an imprinting disorder.

Question 6.35

Outline the major global changes in DNA methylation that occur during mammalian gametogenesis and early embryonic development.

Question 6.36

Angelman and Prader-Willi syndromes are very different disorders that can be caused by the precisely the same deletion on chromosome 15. How is that possible?

Question 6.37

Rett syndrome is a classic chromatin disease. What is meant by a chromatin disease and what are the characteristics of Rett disease?

Question 6.38

In some imprinting disorders the normal allele of an imprinted gene locus is inactivated (so that both alleles are silenced). Illustrate how this happens in Angelman and Prader-Willi syndromes.

Question 6.39

In Beckwith-Wiedemann syndrome an allele that is normally epigenetically silenced is somehow expressed, resulting in biallelic expression. Illustrate how the expression of relevant genes is altered to cause the disease.

Question 6.40

A classical position effect means that a gene can be partly or fully silenced simply if it is moved to a different chromosomal location. Explain how this happens.