Genetics and Genomics Chapter 4 Questions

Multiple Choice Questions

Question 4.1

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

a) Most of the inherited changes in our DNA arise because of exposure to extracellular mutagens, including radiation sources and chemical mutagens.
b) Most of the inherited changes in our DNA arise because of unavoidable endogenous errors in cellular mechanisms and harmful effects of certain natural molecules and atoms within our cells.
c) Errors in DNA replication and DNA repair are a major source of mutations in our cells.
d) Significant chemical damage is sustained by DNA because of its proximity to water molecules in our cells.

Question 4.2

With reference to base cross-linking, which, if any, of the following statements, is false?

a) Base cross-linking means that covalent bonds form between two bases.
b) The cross-linked bases are on opposing DNA strands.
c) The anti-cancer agent cisplatin causes a type of cross-linking between two guanine residues.
d) Pyrimidine dimers are a type of base cross-linking that is commonly induced by excess exposure to sunlight.

Question 4.3

Match individual environmental factors a) to e) to associated types of chemical damage to DNA i) to iv)

Environmental factors	**Chemical change to DNA**
a) ionizing radiation	i) intrastrand base cross-linking
b) cigarette smoke	ii) interstrand base cross-linking
c) ultraviolet radiation	iii) aromatic hydrocarbon DNA adducts
d) electrophilic alkylating agents	iv) increased reactive oxygen species (ROS)-mediated damage
e) automobile fumes	

Question 4.4

With reference to DNA repair, which of the following statements, if any, is false?

a) In the great majority of cases, DNA repair is some kind of mechanism that does not directly reverse the molecular steps that cause DNA damage.
b) Most of the time DNA repair involves a mechanism that makes a repair to both DNA strands.
c) When DNA repair involves repairing both DNA strands, the accuracy of the repair is higher in cells where the DNA has replicated than in cells before DNA replication.
d) DNA repair mechanisms are not evolutionarily well-conserved; human repair mechanisms differ significantly from those in the cells of other vertebrates.

Question 4.5

With reference to DNA repair, which of the following statements, if any, is false?

a) Crosslinking of bases on opposing DNA strands is especially problematic for cells because it presents an obstacle to DNA replication (the replication fork stalls).
b) Crosslinking of bases on opposing DNA strands can be problematic for cells because it may present an obstacle to transcription (the RNA polymerase stalls).
c) Double strand DNA breaks are a challenge for cells because if repair is not affected immediately the ends can drift apart quickly making correct repair impossible.
d) Repair of double stranded DNA breaks is easier in cells prior to DNA replication than after DNA replication has occurred.

Question 4.6

With reference to hydrolytic damage to DNA which of the following statements, if any, is false?

a) Hydrolytic attack commonly causes cleavage of the *N*-glycosidic bond, resulting in loss of bases.
b) Loss of pyrimidines is particularly common.
c) Hydrolytic attack also commonly causes amino groups to be stripped from bases (deamination).
d) Cytosines are often deaminated to give thymines.

Question 4.7

With reference to reactive oxygen species (ROS), which of the following statements, if any, is false?

a) ROS are an inevitable consequence of the chemical reactions that occur in cells and are formed by the incomplete one-electron reduction of oxygen.

b) Common examples of ROS include hydrogen peroxide (H_2O_2), superoxide anions (O_2^-) and hydroxyl radicals ($OH^·$).
c) ROS are generated in different intracellular compartments, but notably in mitochondria.
d) ROS are functionally valuable: they play important roles in both intercellular and intracellular signalling.

Question 4.8

With reference to aberrant methylation of bases which of the following statements, if any, is false?

a) *S*-adenosylmethionine donates methyl groups to a range of different molecules in cells and frequently inappropriately methylates bases in DNA.
b) Guanine is occasionally methylated to give *O*-6-methylguanine which base pairs with adenine rather than with cytidine.
c) In each nucleated cell, about 300-600 adenines are converted to 3-methyladenine per day.
d) 3-methyladenine can be a cytotoxic base: it distorts the double helix and that can disrupt crucial DNA-protein interactions.

Question 4.9

Match the types of DNA damage a) to g) to the most appropriate of the DNA repair mechanisms i) to v) that can be expected to repair the damage.

Type of DNA damage

a) disintegration of a sugar residue due to oxidative damage.
b) a simple base modification, such as 8-oxoguanine
c) a double-stranded DNA break occurring in G_1 phase.
d) a pyrimidine dimer
e) an abasic site due to depurination
f) a double-stranded DNA break occurring in G_2 phase.
g) a bulky aromatic hydrocarbon adduct that distorts the double helix.

DNA repair mechanisms

i) nonhomologous end joining
ii) base excision repair
iii) nucleotide excision repair
iv) homologous recombination-mediated DNA repair

Question 4.10

List three ways in which an unrepaired double-stranded DNA break can be highly dangerous to the cell in which it occurs.

Question 4.11

What, approximately, is the fraction of genetic variation in the nuclear genome is that is expected to have a harmful effect on gene function?

a) 50%.
b) 25%.
c) 10%.
d) 1%.

Question 4.12

Which, if any, of the following observations are *consistent* with the effect of purifying selection, and which, if any, are *consistent* with the effect of positive selection?

a) Human populations that are accustomed to high-starch diets have comparatively higher copy numbers of the α-amylase gene.
b) Telomere DNA sequences in vertebrates have tandem TTAGGG repeats
c) Humans show very high levels of heterozygosity at the classical HLA loci.
d) Human populations that live in more northerly latitudes have a high frequency of pale skin color.
e) Human calmodulin and an ortholog in *Drosophila* each have 149 amino acid differences and differ at just four amino acid positions.

Question 4.13

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

a) Each person makes many millions of different HLA proteins so as to be able to recognize and bind foreign antigens.
b) Classical HLA proteins are highly polymorphic; non-classical HLA proteins show very limited polymorphism.
c) Classical class I HLA proteins are displayed on the surface of very few cell types, notably immune system cells.
d) HLA proteins are the most polymorphic human proteins.

Question 4.14

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

a) As a result of many post-zygotic changes in the DNA of our cells, each of us is a genetic mosaic.
b) The vast majority of the post-zygotic DNA changes are random mutations.
c) The vast majority of the post-zygotic DNA changes do not affect gene expression.
d) Some post-zygotic DNA changes are programmed to occur in a very limited number of cell types.

Question 4.15

Classical class I and class II HLA proteins are both highly polymorphic heterodimers polymorphic heterodimers that help lymphocytes to recognize peptide antigens but they differ in many ways. Which, if any of the following statements, is true?

a) The two chains of any class I HLA protein are made by genes that are located on different chromosomes.
b) Each of the two protein chains of a classical class I HLA protein are highly polymorphic, unlike for classical class II HLA proteins where only one of the protein chains is polymorphic.
c) Class I HLA proteins assist helper T lymphocytes to recognize peptide antigens, whereas class II HLA proteins assist cytotoxic T lymphocytes to recognize peptide antigens.
d) Class II HLA proteins are expressed on the surfaces of almost all nucleated cells, but the expression of class I HLA proteins is confined to just a few types of cell, notably certain immune system cells.

Fill in the Blanks Questions

Question 4.16

Fill in the blanks below.

In the nuclear genome, a ___1____ means a unique location for A DNA sequence. At each diploid ___1____ a person has inherited two ___2____ , one that is paternally inherited and one that is maternally inherited. If the maternal and paternal ___2____ are identical, the person is said to be ____3____ at that ____1____, but if the maternal and paternal _____2_____ differ by even a single nucleotide, the person is said to be ____4_____ at that locus. Whereas women have 23 pairs of homologous chromosomes, men have 22 pairs of autosomal homologs but very different sex chromosomes. As a result, most of the DNA sequences on the X and on the Y chromosomes do not have a counterpart on the other sex chromosome. A ___1____on the X chromosome in men often, therefore, has just a maternal ____2____ , and most loci on the Y have just a paternal ____2____ allele. At loci like these, a man would be said to be _____5_____.

Question 4.17

Fill in the blanks below.

The DNA in our cells is susceptible to damage as a result of exposure to harmful radiation or to ____1____ mutagens. Excess exposure to ___2____ radiation within sunlight, for example, or to tobacco carcinogens induces harmful changes in our DNA. However, the most frequent changes in the base sequence of our DNA arise from _____3____ sources, arising from proximity to harmful chemicals within our cells, notably ____4____ ____5____ ____6____ , and as a consequence of occasional errors in various ____3____ mechanisms, such as DNA ____7____, DNA ____8____ , and chromosome ____9_____.

Essay, Lists & Diagram Questions

Question 4.18

Some of our DNA polymerases have a proofreading function. What is meant by this and how common is it.

Question 4.19

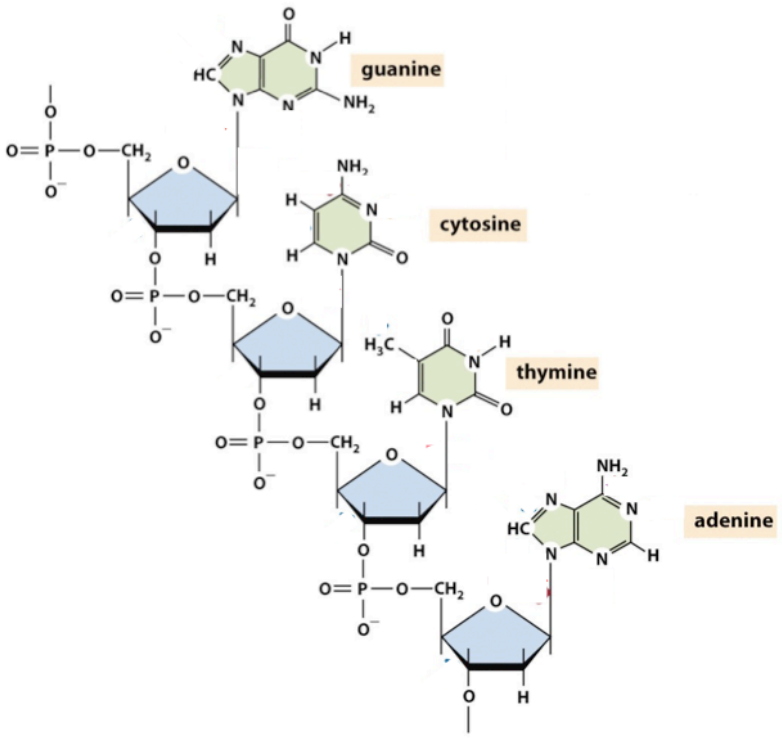
Outline the four broad classes of chemical damage to DNA.

Question 4.20

List three types of chemical reaction that cause damage to DNA, and illustrate your answer with examples.

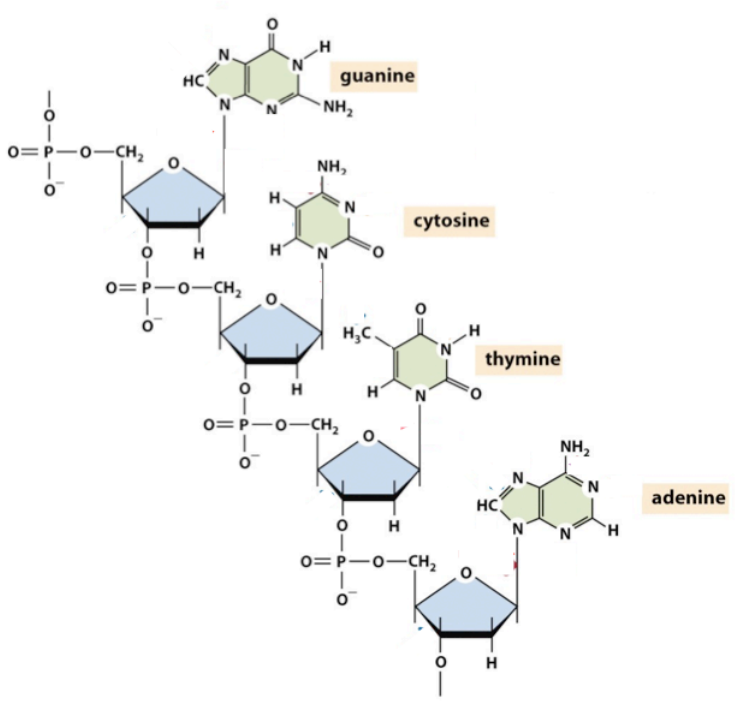
Question 4.21

On the diagram below, identify the covalent bonds that break when hydrolytic attack results in deamination.



Question 4.22

On the diagram below, identify the covalent bonds that break when hydrolytic attack results in depurination.

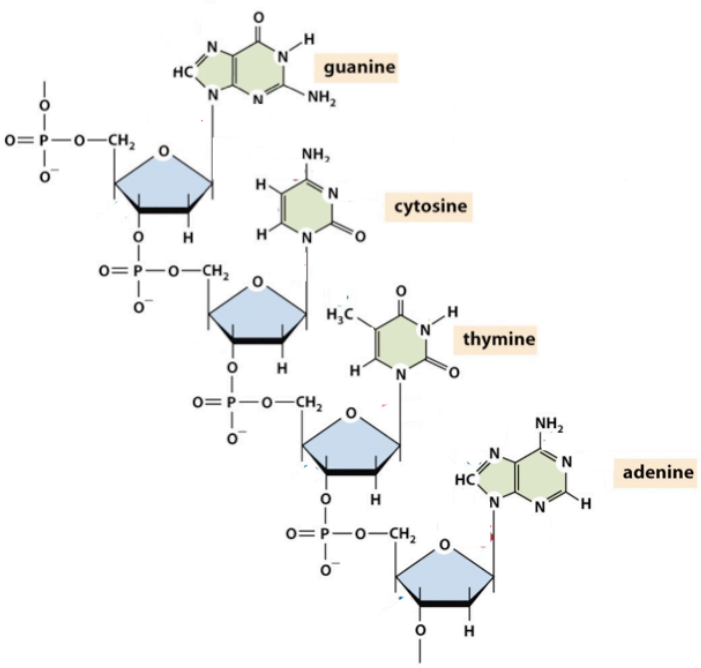


Question 4.23

List the major health consequences that arise as our DNA damage response and DNA repair systems become defective.

Question 4.24

On the diagram below, identify the covalent bonds that are susceptible to breakage as a result of oxidative damage.



Question 4.25

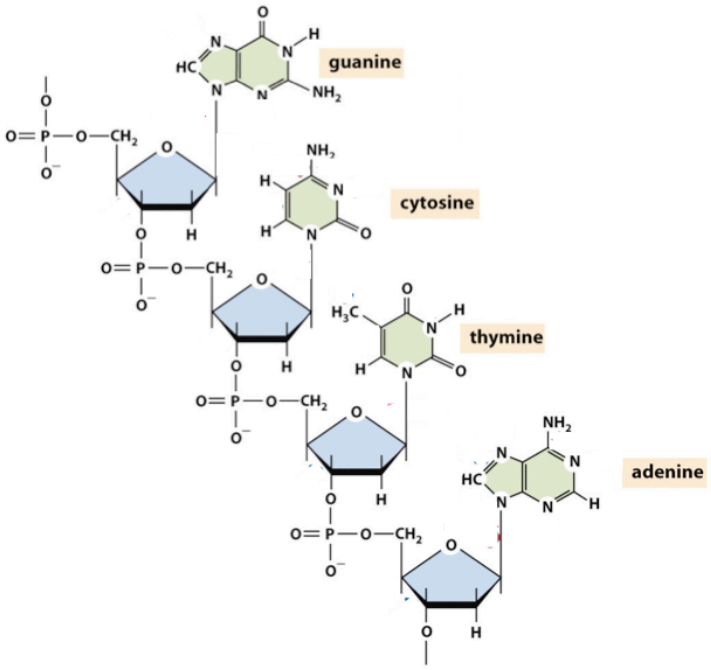
Most types of DNA damage are repaired by mechanisms that typically involves excising bases or nucleotides and then resynthesizing DNA. But certain types of DNA damage are directly reversible. Give two examples.

Question 4.26

What are the essential differences between base excision repair and nucleotide excision repair and what types of DNA damage are they dedicated to repairing?

Question 4.27

On the diagram below, identify the covalent bonds that are susceptible to breakage as a result of hydrolytic damage causing depyrimidination.



Question 4.28

The C→T transition is, by some distance, the most common base substitution in human (and vertebrate) DNA. What makes it so common?

Question 4.29

What is meant by non-classical DNA-dependent DNA polymerases? What roles do they play in our cells?

Question 4.30

What are single nucleotide polymorphisms and why do they occur at only certain nucleotides in our genome?

Question 4.31

Longer microsatellites are very prone to being polymorphic. What are microsatellites, why should long microsatellites be so prone to being polymorphic, and what is the mechanism that is responsible for the polymorphism?

Question 4.32
What is meant by balanced and unbalanced structural variation?

Question 4.33
With reference to positive selection, what is meant by a *selective sweep*?

Question 4.34
A human zygote has three immunoglobulin loci, one that specifies the heavy chain and two that specify the light chain. Taking into account differences between maternal and paternal alleles a B cell might be expected to have the potential of making a total of two different heavy chains and four different light chains, and therefore eight different immunoglobulins. Instead, each mature B cell makes just a single type of immunoglobulin. How does that happen?

Question 4.35
Our immunoglobulins, T-cell receptors and HLA proteins are thought to belong to one large superfamily of proteins based on their structures as well as their functions. In what ways do the structures of these three sets of proteins resemble each other?

Question 4.36
The HLA system is important in medicine for two major reasons. What are they?

Question 4.37
The programmed rearrangements at immunoglobulin loci in B cells and in T-cell receptor loci in T cells that are required for antibody and T-cell receptor diversity are cell-specific. What precisely does that mean?

Question 4.38
"The huge variation in immunoglobulins and T cell receptors is manifest at the level of the individual, but the huge variation in HLA proteins is expressed at the level of the population". What is meant by this statement?

Question 4.39

The human *HLA-DRB1* and the chimpanzee Patr-*DRB1* gene are orthologs. At the protein level, the human HLA-DRB1*0701 and HLA-DRB1*0302 alleles show 31 amino acid differences out of 270 amino acid positions. But human HLA-DRB1*0702 and the chimpanzee Patr-DRB1*0702 proteins are so closely related that they differ at only 2 positions out of the 270. What does the difference between these two pairwise comparisons tell us about the origins of HLA polymorphism?