Genetics and Genomics in Medicine Chapter 7 Questions

Multiple Choice Questions

Question 7.1

Depending on the base position within as codon, the percentage of base changes that alter the interpretation of the codon vary remarkably. Which of the following statements, if any, is true?

a) 100% of all possible base changes to the first base cause an altered interpretation for the codon.
b) 100% of all possible changes to the second base cause an altered interpretation for the codon.
c) About 30% of all possible changes to the third base cause an altered interpretation for the codon.
d) Less than 10% of all possible changes to the third base cause an altered interpretation for the codon.

Question 7.2

Which of the following changes is i) a synonymous mutation, ii) a conservative substitution, iii) a nonconservative substitution, iv) a stop-loss mutation, v) a stop-gain mutation.

a) UGA → UCA
b) UAC → UAA
c) AGA → AAA
d) AGA → CGA
e) UGU → CGU

Question 7.3

Concerning disorders resulting from unstable expansion of tandem oligonucleotide repeats, which, if any of the following statements is false.

a) The expansions can occur in coding DNA in some cases, and in noncoding DNA in other cases.
b) The repeats are of a variable number of nucleotides (from three to six) in both coding DNA and noncoding DNA.
c) The expansions in noncoding DNA are generally much larger in size than those in coding DNA.
d) The expanded arrays in noncoding DNA always result in loss of function of the host gene or of a neighboring gene.

Question 7.4

Match the descriptions of a type of mutation given in a) to d) with one of the possible mutations listed in i) to iv).

Description

a) A mutation that does not case a disease but that is unstable at mitosis and meiosis and can change into a pathogenic mutation.
b) A pathogenic mutation that is unstable at mitosis and meiosis and can result in progressively severe phenotypes.
c) A type of mutation that results in genetic mosaicism.
d) A class of mutation that is quite frequently associated with a gain of function.

Mutation

i) a post-zygotic (somatic) mutation
ii) a missense mutation
iii) a dynamic mutation
iv) a premutation

Question 7.5

Regarding mutations, which of the following statements, if any, is false?

a) A *de novo* mutation is one that has occurred post-zygotically.
b) Each of us has multiple genes where both the maternal and paternal alleles have inactivating mutations.
c) The vast majority of mutations in our DNA do not adversely affect gene expression.
d) The mitochondrial genome has a very high gene density and accordingly the mutation frequency in mtDNA is low.

Question 7.6

Regarding chromosome abnormalities, which of the following statements, if any, is false?

a) A Robertsonian translocation is a common example of an aneuploidy.
b) Nondisjunction is a common cause of aneuploidy
c) Triploidy is most commonly caused by fertilization of an egg by a diploid sperm.
d) Tetraploidy is usually due to replication of the zygote's DNA without cell division.

Question 7.7

Interpret the following examples of chromosome karyotypes.

a) 47,XX,+mar.
b) 45,XY,der(13;14)(q10:q10) .

c) 46,XX,del(15)(q11q13).
d) 46,XY,t(3;17)(q26q23)

Question 7.8

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

a) A person is said to be a chimera if he or she has two or more genetically different cells.
b) The diversity of immunoglobulins made by a person is due to genetic mosaicism.
c) Having cells that inactivate the paternal X and cells that inactivate the maternal X is an example of genetic mosaicism in female mammals.
d) A person with cell populations that are genetically different because they originated from two different zygotes is described as a genetic mosaic.

Question 7.9

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

a) A null allele is one where the gene has been deleted or received an inactivating mutation causing complete loss of gene function.
b) Inactivating point mutations are a common cause of pathogenesis in recessively inherited disorders.
c) Inactivating point mutations are a common cause of pathogenesis in dominantly inherited disorders.
d) When a gain-of-function allele is known to be pathogenic in a single gene disorder, a heterozygote will always show disease symptoms.

Question 7.10

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

a) Gain-of-function mutations are often missense mutations.
b) A missense mutation that has a dominant-negative effect can often produce a greater loss of protein function than a null mutation.
c) Pathogenic gain-of-function and loss-of-function mutations in the same gene produce different phenotypes .
d) A mutant protein that antagonizes the wild type protein produced from the normal allele is known as a hypomorph.

Fill in the Blanks Questions

Question 7.11

Fill in the blanks using numbers.

Depending on our ethnic background, each of us carries about ___1___or so mutations that would be expected to result in loss of gene function (with an average of ___2____ genes that are homozygously inactivated), plus about ____3____ missense variants that severely damage protein structure. When you factor in additional mutations in noncoding DNA, a normal person might be expected to have a total of over ____4____ damaging DNA variants.

Question 7.12

Fill in the blanks using single words or with one or two letters.

The most commonly used method in human chromosome banding is known as ___1___-banding, when the chromosomes are treated with trypsin and then stained with the ____2____ dye. The ____2____ dye binds preferentially to ___3____-rich regions in DNA and the staining produces a series of alternating ____4____ bands that are ____2___-positive and ___3____-rich and ____5____ bands that are ____2___-negative and ___6____-rich. The ____4____ bands have a generally ____7____ content of genes, whereas the ____5____ bands have a ____8____ content of genes.

Question 7.13

Fill in the blanks using single words.

A person with two or more genetically different cell lines is described as a genetic ___1____. Because we have so many cells in our bodies everyone will have cells that are genetically different as a result of ___2____ mutation; each of us is a genetic ___1___. People who have cells that originated from different zygotes are described as ___3____. That can happen when a person is a recipient of organ or cell _____4____. It can also happen during pregnancy at the earliest stages of development when non-identical ____5____ ___6___ fuse, and, more commonly at later stages of development, when there can be an exchange of cells between the ____7____ and the ___8___.

Question 7.14

Fill in the blanks using single words.

Human mitochondrial DNA is transmitted exclusively by ____1_____. As well as transmitting chromosomes to the oocyte, sperm also transmit _____2____ but they are selectively ___3____ in the early embryo. Because mtDNA replication is independent of the cell cycle and there are many mtDNA molecules per cell, a population of mutant mtDNA molecules can co-exist in a cell with a population of normal mtDNA molecules, a state known as _____4_____. Because mtDNA replication is ____5____ and because ____6____ expansion of mutant DNAs is variable, the proportion of mutant to normal mtDNAs in a cell can ___7____ significantly between cells in the same individual.

Essay and List Questions

Question 7.15
Genetic variation can cause disease by causing a gene product to have an altered sequence of amino acids or ribonucleotides, or by altering the amount of gene product that is made. Describe the different ways in which genetic variation leads to a change in the amount of gene product.

Question 7.16
The genetic code that is used in our mitochondrial differs from the "universal" genetic code in the case of four codons. What are these codons and how does their interpretation differ between nuclear DNA and mitochondrial DNA?

Question 7.17
Regarding chromosome nomenclature, explain the following terms:

a) distal
b) proximal
c) acentric chromosome
d) derivative chromosome

Question 7.18
Nonsynonymous mutations can be grouped into three classes. What are they?

Question 7.19
What is a synonymous substitution and when does it not mean a silent mutation?

Question 7.20
Why should our mitochondrial genetic code be different from our nuclear genetic code?

Question 7.21
Amino acids can be divided into non-polar amino acids and polar amino acids. List the five different classes of polar amino acids.

Answer 7.21

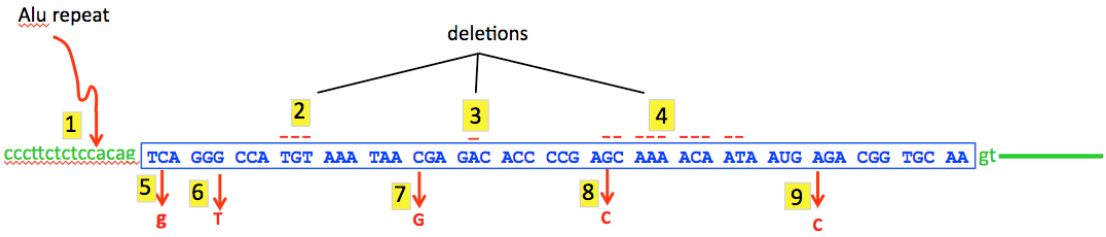
1) Basic (possess a positively charged side chain): arginine, lysine, histidine
2) Acidic (possess a negatively charged side chain): aspartate; glutamate
3) Amide group-containing: asparagine, glutamine
4) Hydroxyl group-containing: serine, threonine, tyrosine
5) Sulfhydryl group-containing: cysteine (but not methionine which is a non-polar amino acid)

Question 7.22

Why should cysteine be the least mutable amino acid?

Question 7.23

In the sequence below, the blue sequence represents an exon containing coding DNA near the beginning of a large gene and green lines and letters are flanking intron sequence. Nine mutations are shown: an insertion of an Alu repeat insertion plus three deletions at top and five single nucleotide substitutions below. Comment on the mutation class in each case and on its likely effect.



Question 7.24

What is the major natural role of the nonsense-mediated decay mechanism in our cells?

Question 7.25

What is a cryptic splice site? What are expected consequences of activation of i) a cryptic splice donor site located within an exon ii) a cryptic splice acceptor site within an intron?

Question 7.26

Certain sequence classes in our genome are particularly prone to mutations. List three examples and explain why they are so prone to mutations.

Question 7.27

The number of cell divisions needed to make human gametes differs extensively between men and women and also between different men. Explain these differences.

Question 7.28

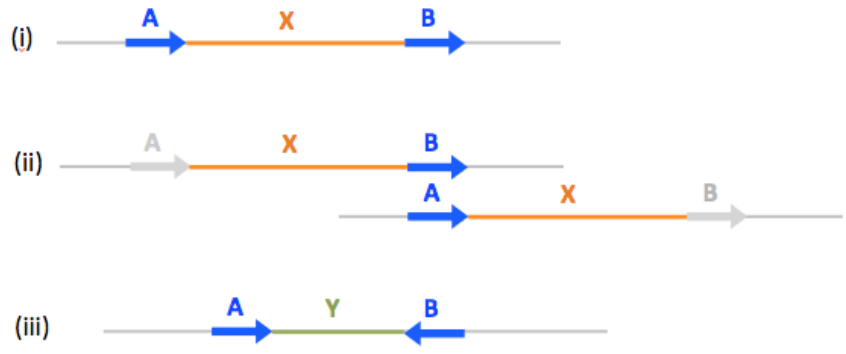
Two groups of human disorders involve expansion of tandem trinucleotide repeats in coding DNA to give gene products with abnormally long polyglutamine or polyalanine repeats. The pathogenic mechanisms have rather different characteristics, however in the way that the trinucleotide repeats expand. In what ways do they differ?

Question 7.29

Deletions, duplications and inversions in our DNA often result in interaction between tandem repeats, direct repeats, or inverted repeats. What are the essential differences between these repeat classes.

Question 7.30

Sequence exchange between two non-allelic copies of the same long sequence on chromosomal DNA molecules can have different consequences, depending on the positioning of the repeats that participate in sequence exchange. In (i) to (iii) imagine that there is sequence exchange between non-allelic sequence copies A and B shown by the blue arrows – the sequence exchange is between different chromatids of the same chromosome in the case of (ii). What types of sequence exchange might occur and what would be the likely outcome?



Question 7.31

List three examples of single gene disorders that show an extremely limited range of point mutations and explain why there should be such mutational homogeneity.

Question 7.32

Match each of the genetic mechanisms a) to d) with one or more of the possible outcomes i) to iv).

Genetic mechanisms

a) sequence exchange between inverted repeats on a single chromatid.
b) sequence exchange between non-allelic genes of a duplicated gene family on sister chromatids
c) sequence exchange between two identical direct repeats on a mtDNA molecule
d) sequence exchange between non-allelic genes of a duplicated gene family on nonsister chromatids

Possible outcomes

i) Gene conversion
ii) DNA deletion
iii) DNA duplication
iv) An inversion

Question 7.33

What is meant by aneuploidy, and how does it occur?

Question 7.34

Constitutional aneuploidy is occasionally viable in humans. Why should having fewer or extra copies of certain chromosomes be compatible with life, but not so in the case of other chromosomes?

Question 7.35

A chromosome has received two double-stranded breaks. What kinds of chromosome abnormalities can result?

Question 7.36

What are the characteristics of a Robertsonian translocation?

Question 7.37

How does just a single loss-of-function allele cause a dominantly inherited disorder?

Question 7.38

How can a missense mutation with a dominant-negative effect result in greater loss of protein function and more severe disease than a full length gene deletion at the same gene locus?

Question 7.39

Give two examples of genes where loss-of-function and gain-of-function mutations result in different disease phenotypes.

Question 7.40

Give three examples of disorders where the pathogenesis can result from recurring large deletions and one where the pathogenesis can result from a recurring large duplication.

Question 7.41

In terms of its contribution to pathogenesis which of the following mutant proteins is the odd one out, and why is it the exception?

a) β-globin carrying the p.Glu6Val substitution .
b) PI*Z and PI*E mutant α_1-antitrypsins
c) mutant CFTR protein with the common p.Phe508del deletion.
d) mutant prion proteins.

Question 7.42

Match each of the characteristics in a) to e) with the mutant alleles listed in (i) to (v).

Characteristic

a) impaired protein processing and secretion.
b) aberrant protein aggregation.
c) alteration of substrate specificity.
d) Paternal transmission and paternal age-effect.
e) Aberrant protein folding.

Mutant allele

i) the fibroblast growth factor receptor 3 p.Gly380Arg allele
ii) the Pittsburgh variant of α_1-antitrypsin
iii) the CFTR p.Phe508del mutant
iv) the PI*Z α_1-antitrypsin allele
v) the β^S-globin allele

Question 7.43

The pathogenesis of α_1-antitrypsin deficiency due to the common missense mutants PI*S and PI*Z is due to a failure in protein processing and secretion, and to aberrant protein aggregation. Explain how.

Question 7.44

“The pathogenesis of sickle cell anemia is due to aberrant protein aggregation. Explain how.

Question 7.45

The disease mechanism in prion protein diseases has sometimes been considered a type of epigenetic mechanism. On what basis?

Question 7.46

What are amyloid diseases? In what respects do neurodegenerative amyloid diseases resemble prion diseases?

Question 7.47

Studies of single gene disorders have sought to draw correlations between the genotypes at a disease locus and the phenotype of the single gene but the genotype-phenotype correlations are often poor. Even within families there may be significant variability in the phenotype of affected members (who are expected or known to have the same genotypes at the disease locus). List three factors that can explain why that should be so.