Genetics and Genomics in Medicine Chapter 11 Questions

Multiple Choice Questions

Question 11.1

Interpret the following DNA and amino acid variants:

a) g.410_411insC
b) p.Gly418*
c) c.*62A>T
d) c.142+4C>T

Question 11.2

Interpret the following DNA and amino acid variants:

a) c.*15A>G
b) p.Asp522del
c) c.-22T>G
d) c.121-6C>A

Question 11.3

Concerning prenatal diagnosis, which, if any, of the following statements is false?

a) It relies on surgical procedures to recover fetal tissues from a pregnant woman.
b) Chorion villus biopsies are typically taken around 16 weeks of gestation.
c) Amniotic fluid samples allow culturing of fetal cells for cytogenetic analyses as well as allowing DNA analyses.
d) There is always a small excess risk of miscarriage.

Question 11.4

Concerning preimplantation genetic diagnosis, which, if any, of the following statements is incorrect?

a) It is carried out within the context of assisted reproduction.
b) The analyses always involve genotyping just a single cell and so are technically difficult.
c) Sometime a single blastomere is analysed from the embryo.
d) Sometimes a polar body is analysed to infer the genotype of the embryo.

Question 11.5

Concerning genetic screening, which, if any, of the following statements is false?

a) Genetic screening is carried out primarily in communities and populations
b) In carrier screening the motivation is to identify carriers of a mutant allele for a severe autosomal recessive disorder that has a high prevalence in the community or population.
c) In most cases of pregnancy screening the motivation is to identify whether a fetus carries a genetic variant associated with a harmful single gene disorder.
d) In newborn screening the motivation is often to target early treatment for serious disorders for which early intervention can make a significant difference.

Question 11.6

Match the disorder a) to h) with the likelihood that it would be a focus for a genetic procedure listed in i) to vi)

Disorder

a) Huntington disease
b) Trisomy 21
c) phenylketonuria
d) β-thalassemia
e) familial hypercholesterolemia
f) polycystic kidney disease
g) breast cancer due to *BRCA1*
h) Tay-Sachs disease.

Genetic procedure

i) carrier screening
ii) prenatal diagnosis
iii) pre-symptomatic testing
iv) predictive testing
v) pregnancy screening
vi) neonatal screening

Fill in the Blanks Questions

Question 11.7

Fill in the blanks below with single words.

Traditional _____1_____ diagnosis has involved _____2_____ surgical procedures in which a sample of fetal cells is recovered and analysed. There have been two major approaches. In one case a sample is taken from the _____3____ (the outermost extra-embryonic ____4_____). Typically this sample is taken in the ____5_____ trimester of pregnancy. In the other case, a sample of _____6_____ fluid is taken that will contain cells from the _____7_____ , an inner extra-embryonic ____4_____. This procedure, called ____8_____ is taken at, or close to, 16 weeks of gestation; it provides fetal cells that can be processed to allow ____9_____ analyses as well as DNA analyses. Because of the surgical procedures involved there is a small excess risk of ____10_____. As a result, there has been a trend to develop non-_____2_____ _____1_____ diagnosis. That has been fuelled by _____11_____ _____12_____ sequencing of DNA from maternal ____13____.

Question 11.8

Fill in the blanks below with single words.

_____1_____ genetic diagnosis is carried out in the contact of assisted reproduction. It can be technically challenging because quite often analysis is carried out on a ____2_____ cell, that may be from the early stage _____3____ (the stage at which the embryo consists of just a very few cells that are individually called ____4_____). Another alternative, that can be used when the mother is at risk of transmitting a harmful genetic variant, is to infer the genotype of the _____5_____ by analysing a ____6____ ____7_____ (a cell that is created by one of the asymmetric cell divisions in female ____8_____). Because of technical difficulties in analysing a _____2_____ cell, some centers prefer to analyse _____9_____ cells from a late-stage _____3____.

Essay, Listing, and Matching Questions

Question 11.9
What is the basis of the ACCE framework for genetic testing?

Question 11.10
A genetic test for a marker M was carried out in 500 people affected by disease X and showed that 480 of the affected individuals typed positive for the marker. In a suitably matched set of 1000 healthy controls, just 80 people typed positive for marker.

i) Establish the sensitivity and specificity of the test.
ii) Work out the false positive rate and the positive predictive value
iii) Work out the false negative rate and the negative predictive value.

Question 11.11
Mutation scanning and mutation testing can be used to identify pathogenic mutations. What is the essential difference between these two approaches?

Question 11.12
Give an outline of the different laboratory approaches to testing for aneuploidies and discuss their relative merits.

Question 11.13
Describe the principles of arrayCGH and its applications in a diagnostic DNA laboratory.

Question 11.14
Why is there still a need for conventional karyotyping using chromosome banding techniques?

Question 11.15
What is involved in chromosome fluorescence in situ hybridization?

Question 11.16
What are the main uses of chromosome fluorescence in situ hybridization in a genetic service laboratory?

Question 11.17
What is involved in Southern blot hybridization?

Question 11.18
What are the main applications of Southern blot-hydridization as an assay in a genetics service laboratory?

Question 11.19
The triplet repeat-primed PCR assay is commonly used in analysing samples from individuals with unstable trinucleotide repeat expansions. What is involved in this method?

Question 11.20
Multiplex ligation-dependent probe amplifaction (MLPA) is an important technology used in genetics research and genetic testing. What uses is it put to in a genetics service laboratory and what is the basis of the method.

Question 11.21
Explain the principles underlying target-sequence enrichment from a complex nucleic acid population.

Question 11.22
List four different ways in which a known, specific single nucleotide mutation can be detected within a defined exon.

Question 11.23
What is meant by cascade testing?

Question 11.24

Prenatal diagnosis involves analysing samples originating from fetal cells (either recovered directly from fetal tissue, or from maternal blood samples). What are the aims of these procedures?

Question 11.25

Traditional prenatal diagnosis has typically meant analysing samples that have been recovered from the developing fetus by some type of invasive procedure. What is involved in these procedures?

Question 11.26

What is involved in preimplantation genetic diagnosis, and why is it carried out?

Question 11.27

With reference to genetic screening, what is the primary motivation for a) pregnancy screening, b) newborn screening, and c) carrier screening, and what types of disorders are involved?

Question 11.28

In cancer testing biomarkers based on DNA variants or gene expression profiles are increasingly important. List four types of role that biomarkers can have in cancer testing and illustrate your answer with examples.

Question 11.29

Give a summary of the principal anticipated benefits and challenges that might be expected from widespread clinical genome sequencing.

Question 11.30

What are the main ethical arguments against genetic manipulation of the germ line?

Question 11.31

Two important ethical principles that relate to genetic testing in children are the principle of beneficence and the “right to an open future”. Explain what is meant by these principles.

Question 11.32

Two ethical controversies relating to preimplantation genetic diagnosis involve sex selection and HLA selection. What are the issues involved?