Genetics and Genomics in Medicine Chapter 10 Questions

Multiple Choice Questions

Question 10.1

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

a) The p53 tumor suppressor regulates the G_2-M transition in the cell cycle by inhibiting the CDK2-cyclin E complex.
b) p53 regulates the CDK2-cyclin E complex by stimulating the p21 tumor suppressor.
c) The CDK2-cyclin E complex relies on stimulation by the E2F transcription factor.
d) The RB1 protein normally binds the E2F transcription factor to prevent it working and so acts as a brake on the cell cycle

Question 10.2

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

a) p53 acts as a brake on the cell cycle.
b) p53 and RB1 are mutually antagonistic.
c) p53 is normally inhibited by being bound to the MDM2 protein, but when phosphorylated, it changes conformation and is released from MDM2.
d) At high concentrations p53 stimulates the transcription of various genes that inhibit apoptosis.

Question 10.3

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

a) p53 acts as a brake on cell growth but stimulates apoptotic pathways.
b) apoptosis occurs only after a death signal is received by one cell from another cell.
c) the death signal starts a pathway that culminates in the activation of a class of proteolytic enzymes called caspases.
d) caspases attack cellular proteins and release an endonuclease that cleaves the cellular NA into small fragments.

Question 10.4

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

a) Chromothripsis is an extraordinary event in which multiple chromosomes within a cell are shattered into many pieces.

b) Chromothripsis is much more like to occur in cells where the *TP53* gene has received loss-of-function mutations.
c) Kataegis is a type of somatic hypermutation.
d) The mutations involved in a kataegis event are clustered in one subchromosomal region.

Question 10.5

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

a) Conventional chromosome banding analyses are often very difficult to carry out in the case of solid tumor samples.
b) Spectral karyotyping simply means standard chromosome FISH that is applied to tumor cells.
c) Genomewide analyses can be carried out by microarray hybridization to look for evidence of many types of chromosome abnormalities in solid tumors.
d) Genomewide analyses cannot be carried out by chromosome FISH analyses on cancer cells.

Question 10.6

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

a) Mismatch repair is dedicated to repairing errors made during DNA replication.
b) MutSα is responsible for recognizing single base mismatches during DNA replication.
c) MutSβ is responsible for recognizing all short insertion and deletion errors made during DNA replication.
d) MutLα contributes an endonuclease activity that is required to nick the DNA during DNA repair.

Question 10.7

Which, if any, of the following statements is incorrect or very likely to be incorrect?

a) Epigenetic dysregulation is essentially a universal feature of tumors.
b) Epigenetic dysregulation in cancer cells always arises as a result of mutation at a chromatin modifier locus.
c) There is an overall increase in DNA methylation across the genome of cancer cells but with local DNA hypomethylation at the promoters of a few hundred genes.
d) Epigenetic dysregulation may sometimes initiate tumorigenesis.

Fill in the Blanks Question

Question 10.8

Fill in the blanks below with single words.

_____1_____ is an important natural process that is devoted to eliminating diseased or potentially harmful deviant cells. There are two classes of pathways. In one of these neighboring cells deliver signals that are received by ____2____ on the surface of those cells selected to undergo ____1____. Other pathways, such as the mitochondrial ____1____ pathway, respond to certain types of ____ 3____damage (such as that caused by harmful ____4_____ ____5_____ species or exposure to dangerous levels of _____6_____ radiation). In most cases the _____1_____ pathway ends by inducing the cell to produce a class of proteolytic enzymes known as _____7_____. ____7_____ are the cell's executioners: they inactivate all kinds of important proteins in the cell, and they release an _____8_____ that cleaves DNA into small fragments. Because each of our cells has the potential to commit suicide, the pathways of _____1_____ need to be tightly regulated.

Essay, Listing, and Matching Questions

Question 10.9
With reference to cancer spreading what is involved in intravasation and extravasation?

Question 10.10
Cancers develop as a result of natural selection operating at the cellular level. What is meant by this, and if there is strong selection pressure on cells to evolve into cancer cells, why do we not all succumb to cancer?

Question 10.11
As cancer cells evolve they acquire distinguishing biological characteristics. Describe five of them and for each give examples of how the biological capability can be acquired.

Question 10.12
Distinguish between driver mutations and passenger mutations in cancer. How many driver mutations might be expected in cancers?

Question 10.13
As a cancer develops the mutation rate accelerates. How does that happen?

Question 10.14
Tumors gradually acquire mutations to evolve from benign to malignant lesions. Because that takes some time, cancer is primarily a disease of aging. So, how can childhood cancers be explained?

Question 10.15
List three classes of stromal cell that support the tumor microenvironment.

Question 10.16
There are two fundamental classes of cancer gene in our cells. What are they and what distinguishes them?

Question 10.17
The progression of normal colonic epithelium to colon cancer has been viewed as a multi-stage progression. What is known about how the cancer develops and which are the genes that are most frequently involved?

Question 10.18
Describe three classes of activation mechanism whereby normal cellular oncogenes are activated to become oncogenes.

Question 10.19
Cancer is sometimes viewed as a disease of stem cells. What is the evidence?

Question 10.20
What are double minute chromosomes and homogeneously staining regions, and why do they occur in some cancer cells?

Question 10.21
What is the Philadelphia chromosome and why is it a cause of cancer?

Question 10.22
The range of different point mutation classes and their locations within coding DNA are major features that differentiate oncogenes from tumor suppressor genes. Explain.

Question 10.23
Loci for previously unknown tumor suppressor genes have been mapped to specific chromosomes and specific chromosome regions by screening for loss of heterozygosity. Explain what is involved.

Question 10.24

Tumor suppressor genes have been classified into caretaker, gatekeeper and landscaper categories. What is meant by these categories? Illustrate your answer with examples for the first two categories.

Question 10.25

Not all cancer-susceptibility genes make proteins – some make noncoding RNAs. Give three examples of cancer-susceptibility genes that make long noncoding RNAs and explain how they are involved in cancer.

Question 10.26

Not all cancer-susceptibility genes make proteins – some make noncoding RNAs. Give two examples of miRNA genes that act as cancer-susceptibility genes and explain how they are involved in cancer.

Question 10.27

Illustrate how some tumor suppressor genes are non-classical in the sense that they can make a significant contribution to tumorigenesis after losing just one allele.

Question 10.28

Illustrate how some tumor suppressor genes are non-classical in the sense that they preferentially acquire missense mutations.

Question 10.29

How are MSI-positive tumors recognized and what does the MSI-positive property signify?

Question 10.30

Defective mismatch repair can occasionally occur in some other types of tumor, but it is particularly common in colorectal cancer. Why should that be?

Question 10.31

Match cancers a) to d) with one of the descriptions i) to iv)

Cancer	Description
a) adenocarcinoma	i) a benign tumor of epithelial tissue
b) papilloma	ii) a malignant tumor of multilayer epithelial tissue
c) squamous cell carcinoma	iii) a malignant tumor of epithelial origin
d) adenoma	iv) a benign tumor of multilayer epithelial tissue

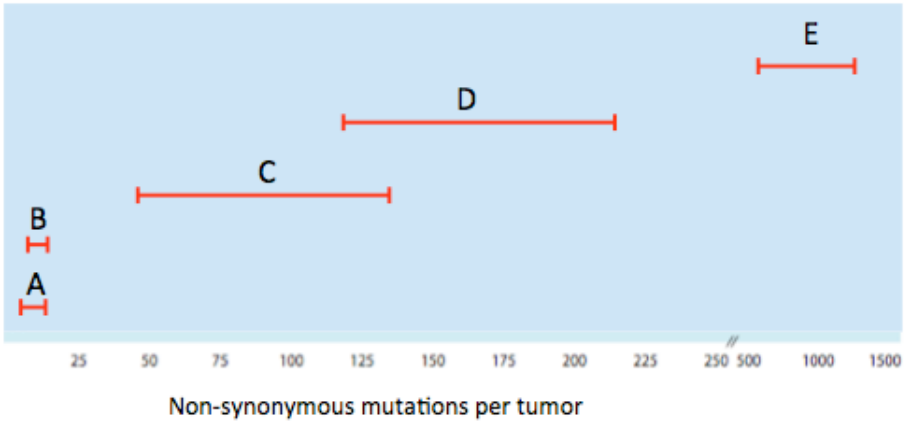
Question 10.32

The number of mutations in a cancer cell can vary. Match the different types of tumors listed in a) to e) with one of the three ranges for numbers of somatic substitutions per tumor given in i) to iii).

Type of tumor	Somatic substitution range
a) lung cancer	i) usually less than 1000
b) most adult cancers	ii) 1000-10,000
c) pediatric tumors	iii) significantly greater than 10,000
d) melanoma	
e) liquid tumors	

Question 10.33

In the figure below, which of the following are A to E likely to represent?
chronic lymphocyte leukemia; melanoma; medulloblastoma; microsatellite instability (MSI)-positive colorectal cancer; MSI-negative colorectal cancer.



Question 10.34

Recent studies have shown that non-classical cancer genes link metabolism to the epigenome. Explain the connection.

Question 10.35

The biological hallmarks of cancer are regulated by partially redundant signalling pathways and that can pose very significant challenges to therapeutic approaches that seek to inhibit a specific biological hallmark of cancer. Explain the challenges posed when using inhibitors of telomerase and of angiogenesis.

Question 10.36

What is meant by targeted cancer therapy? Illustrate your answer with reference to treatment for chronic myeloid leukemia.

Question 10.37

Tumor recurrence is a major problem in cancer gene therapy. Why should tumors recur so readily?

Question 10.38

Give three examples of mechanisms that explain the evolution of drug resistance in tumors.