Chapter 18: Regulation of Gene Expression

18.1 Explain how the trp and lac operons function.

18.2 Describe the stages of eukaryotic gene expression and the regulation that can occur at each stage.

18.3 Define "noncoding RNAs" and explain how they participate in regulating gene expression, including their effects on chromatin.

18.4 Explain how differential gene expression leads to the different cell types in a multicellular organism.

18.5 Describe how cancer can result from genetic changes that affect cell cycle control.

The overview for Chapter 18 introduces the idea that although an organism's cells have all genes in the genome, not all genes are expressed in every cell. What regulates gene expression? Gene expression in prokaryotic cells differs from that in eukaryotic cells. How do disruptions in gene regulation lead to cancer? This chapter gives you a look at how genes are expressed and modulated. Understanding gene expression will be a foundation for many other topics in biology and makes this a very important chapter for your careful study.

Study Tip: The concept that each gene requires a specific set of transcription factors and that this specificity can control the expression of genes is the central idea of this chapter. Use Figure 18.1 in your text to visualize how a gene can be turned on (expressed) or not turned on.

What is differential gene expression?

Concept 18.1 Bacteria often respond to environmental change by regulating transcription

LO 18.1: Explain how the trp and lac operons function.

1. All genes are not "on" all the time. Using the metabolic needs of *E. coli*, explain how this conserves energy resources.

2. What are the two main ways of controlling metabolism in bacterial cells? Which is a short-term response, and which is a long-term response?

3. *Feedback inhibition* is a recurring mechanism throughout biological systems. Is the regulation of tryptophan synthesis by *E. coli* achieved by *positive* or *negative feedback*? Explain your choice.

4. Enzymatic pathways involve a series of different enzymes that catalyze reactions in sequence, as is shown in Figure 18.2 in your text. For this to occur in bacteria, the genes that code for these enzymes are *coordinately controlled* by being clustered in units known as *operons.* To better understand how an operon functions, begin by explaining the role of each of the following:

   a. *promoter*

   b. *operator*

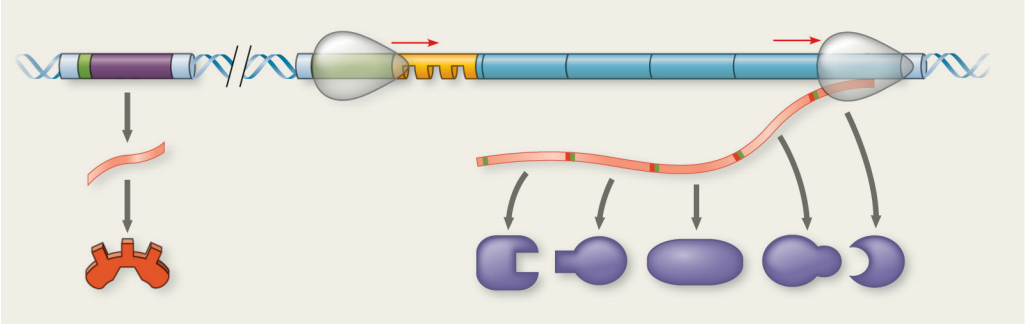
   c. *operon*

   d. *repressor*

   e. *regulatory genes*

   f. *corepressor*

5. Using Figure 18.3 in your text as your guide, label every part of the *trp* operon including the regulatory gene. As you label the following diagram, mentally review the function of each structure.



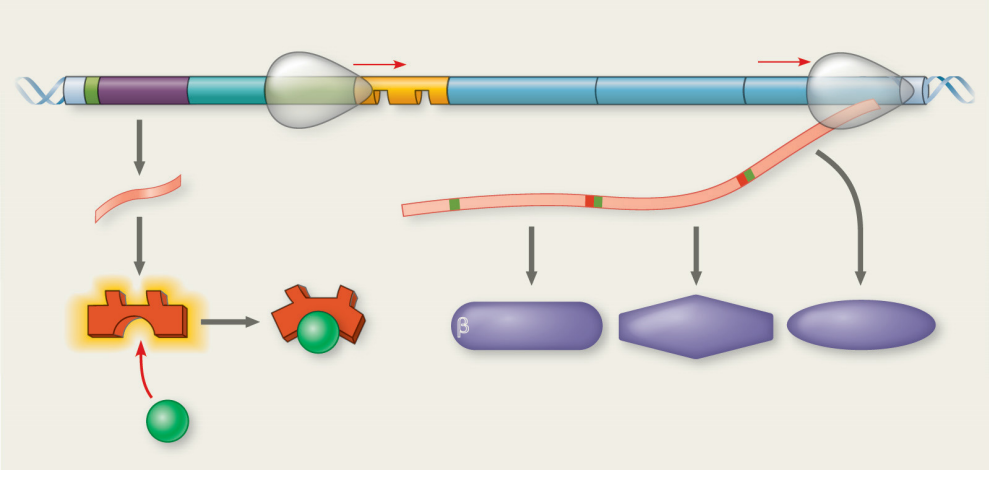
6. Explain how this repressible operon can be turned off. Figure 18.3(b) in the text will help.

7. Distinguish between *inducible* and *repressible operons* and describe one example of each type of operon.

8. What is the fundamental difference between the repressor protein in a repressible operon versus the repressor protein in an inducible operon?

9. Explain why the operon shown in Figure 18.4(a) in your text is off.

10. Refer to text Figure 18.4(b) and label every part of the *lac* operon. As you label the following diagram, review the function of each part.



11. What is the role of the *inducer*? Be sure it is labeled in the figure above.

12. Compare and contrast the *lac* operon and the *trp* operon.

13. When a repressor is bound to the operator of the lac operon, is the operon off or on?

14. To demonstrate you understand how the *lac* and *trp* operon work, let's assume a human host has had a meal of turkey (rich in the amino acid tryptophan) and washed it down with milk. Explain your answer to each of the following:

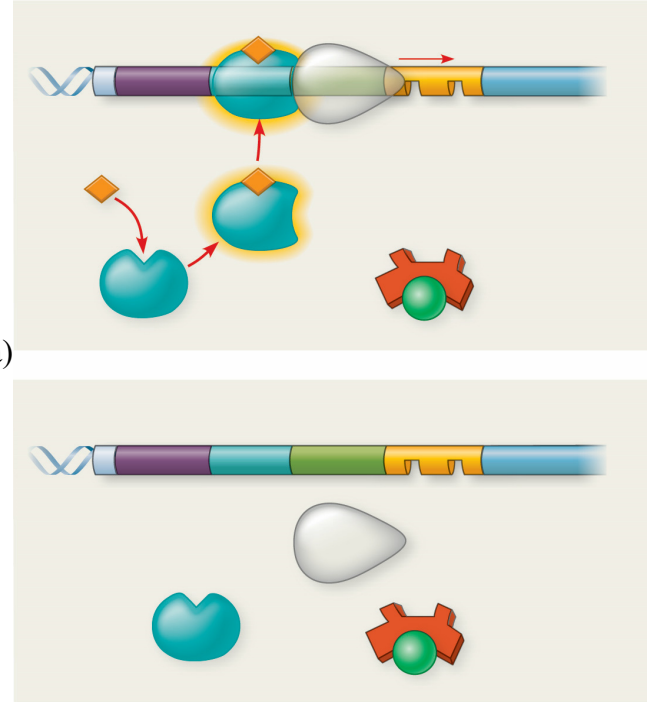
    a. Will the *trp* operon of *E. coli* in the gut of the human be active?

    b. Will the *lac* operon of *E. coli* in the gut of the human be active?

15. Given access to both glucose and lactose, *E. coli* will use the glucose. Describe the relationship between glucose supply, cAMP, and CRP.

16. Figure 18.5 in your text shows that not only can operons be turned on and off, they also may have volume control. Label both figures (a) and (b) and describe how the operon is controlled in both scenarios.

(a)



17. Explain why CRP binding and stimulation of gene expression is *positive regulation*. What is the role of the *activator*?

Concept 18.2 Eukaryotic gene expression is regulated at many stages

LO 18.2: Describe the stages of eukaryotic gene expression and the regulation that can occur at each stage.

18. Even though all cells of an organism have the same genes, there is *differential gene expression*. What does this mean?

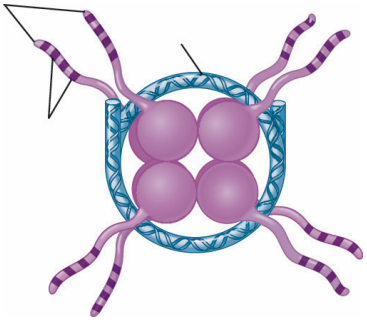
19. What percentage of the genes of a typical human cell is expressed at any given time?

20. One common control point of gene expression for all organisms is at transcription, although for eukaryotes, gene expression can be regulated at other points. Study Figure 18.6 in your text for an overview of the possible points of eukaryotic gene regulation. The rest of this concept is organized around these key areas of regulation.

Regulation of Chromatin Structure

21. Gene expression can be regulated by modifications of the chromatins that affect transcription. Distinguish between *heterochromatin* and *euchromatin* as to their structure and activity.

22. The architecture of how DNA is wrapped around histone proteins to form *nucleosomes* is shown in the figure below. The packaging of DNA in this manner will affect gene expression. Label all the parts of a nucleosome as shown in Figure 18.7(a) of your text.



23. Study text Figure 18.7b. What occurs in *histone acetylation*? How does it affect gene expression?

24. What is *DNA methylation*? What role may it play in gene expression?

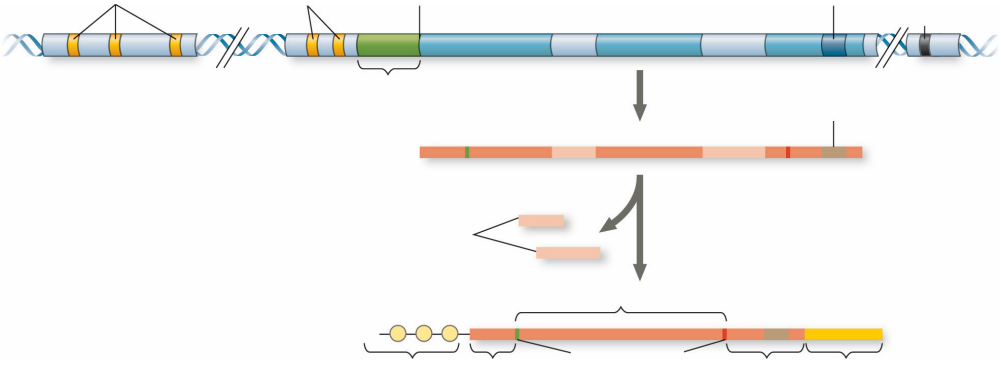
25. The inactive mammalian X chromosome is heavily methylated. What is the result of this methylation?

26. What is *genomic imprinting*, and how is it maintained?

27. Explain what is meant by *epigenetic inheritance* and give an example of epigenetic changes discussed in the text or in class.

Regulation of Transcription Initiation

28. Figure 18.9 in your text reviews some material you are already familiar with by showing what occurs in transcription and RNA processing. However, focus on what is new in this figure. Note the *Enhancer (distal control elements)* and *Proximal control elements*. Completely label the following figure as you study the legend for this figure.



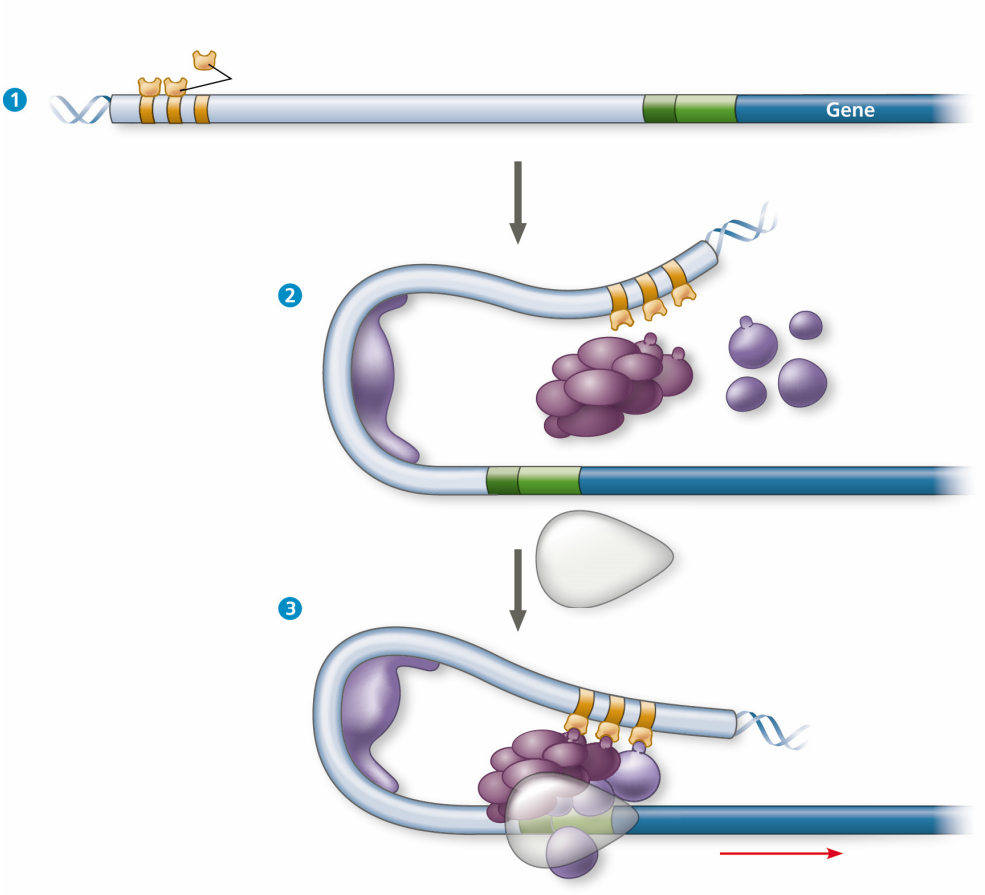
29. What are the respective roles of distal and proximal control elements?

30. What are *general transcription factors*, and how do they function?

32. How can the rate of gene expression be modified by *specific transcription factors* (*activators* or *repressors*)?

33. In prokaryotes, functionally related genes are usually clustered in a single operon. How are coordinately controlled genes in eukaryotes expressed at the same time even when the genes may be on different chromosomes?

34. Use the following sketch to explain how enhancers and activators interact with transcription factors to affect gene expression. Label the following elements: *TATA box, promoter, gene, enhancer, activators, mediator proteins, general transcription factors, transcription initiation complex, DNA-bending protein, RNA polymerase II,* and *DNA.* Then place your explanation, including the three major points in the figure, to the left of the page.



35. The old view that the nuclear contents are like a bowl of chromosomal spaghetti has been replaced with a much more structured vision of chromosomal arrangement. Using Figure 18.13 in your text, explain the current understanding of chromosomal arrangement.

Mechanisms of Post-Transcriptional Regulation

36. How can *alternative RNA splicing* result in different proteins derived from the same initial RNA transcript?

37. *Post-transcriptional control* includes regulation of *mRNA degradation*. Explain how this affects translation.

38. How can proteins be activated, processed, and degraded? Give an example or describe each process.

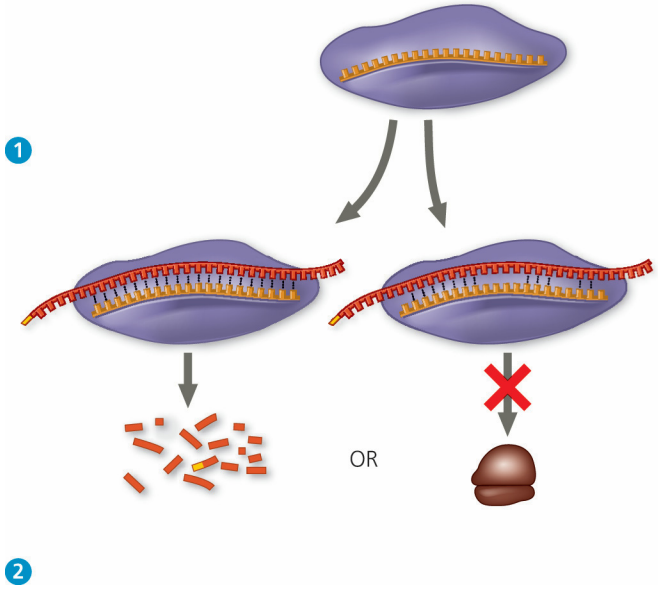
39. An article in *Scientific American* about the giant protein complexes called *proteasomes* was titled "Little Chamber of Horrors." Explain how proteins are targeted for degradation, and give a specific example of when this might occur.

Concept 18.3 Noncoding RNAs play multiple roles in controlling gene expression

LO 18.3: Define "noncoding RNAs" and explain how they participate in regulating gene expression, including their effects on chromatin.

40. It is now known that much of the RNA that is transcribed is not translated into protein. These RNAs are called *noncoding RNAs*. Read carefully to discern a crucial role played by these ncRNAs. What is this role?

41. One of the *noncoding RNAs* that regulate gene expression is *microRNA (miRNA)*. Use the following sketch to label and explain the two modes of action of *microRNAs*.



42. Other classes of small RNAs continue to be discovered. Give an associated function for each:

    a. small interfering RNA (siRNA)

    b. piwi-interacting RNA (piRNA)

    c. long noncoding RNAs (lncRNAs)

This would be a good time to revisit Figure 18.6 in your text. See if you can now cite a specific example of how gene expression is known to be controlled at each stage shown in the figure.

Concept 18.4 A program of differential gene expression leads to the different cell types in a multicellular organism

LO 18.4: Explain how differential gene expression leads to the different cell types in a multicellular organism.

This concept deals with the regulation of gene expression in development. Animal development is also discussed in Chapter 47. Embryonic development is perhaps the ultimate example of precisely regulated gene expression.

43. What three processes lead to the transformation of a zygote into the organism?

44. Explain what occurs in *cell differentiation* and *morphogenesis*.

45. Differential gene expression results from different activators in different cells. How do different sets of activators come to be present in two cells? Explain how each of these occurs:

    a. distribution of *cytoplasmic determinants* (Use Figure 18.17(a) in your text to frame your answer.)

    b. *induction* (Use Figure 18.17(b) to frame your answer.)

46. What is meant by *determination*? Explain what this means within an embryonic cell.

47. What process ensures that all the tissues and organs of an organism are in their characteristic places? Where do the molecular cues that control this process arise?

48. What is controlled by *homeotic genes*? (Don't miss Figure 18.20!)

49. What are *maternal effect genes*? Describe some effects they may control.

50. *Bicoid* is a gene that produces a *morphogen.* What results when there is a high concentration of the *bicoid* protein in a developing embryo?

51. What important understandings about embryonic development resulted from the research into *bicoid?*

Concept 18.5 Cancer results from genetic changes that affect cell cycle control

LO 18.5: Describe how cancer can result from genetic changes that affect cell cycle control.

52. Mutations that alter growth factors, their receptors, or intracellular signaling pathway molecules, or affect regulation of the cell cycle, can lead to cancer in somatic cells. Therefore, genetic mutation is the mechanism involved in the beginning of tumor growth. What are several mechanisms that can result in these cancer-causing mutations?

53. Compare *oncogenes* and *proto-oncogenes*.

54. Explain how each of the four mechanisms listed here are involved in converting a proto-oncogene to an oncogene. Figure 18.23 in your text helps clarify each of the four mechanisms.

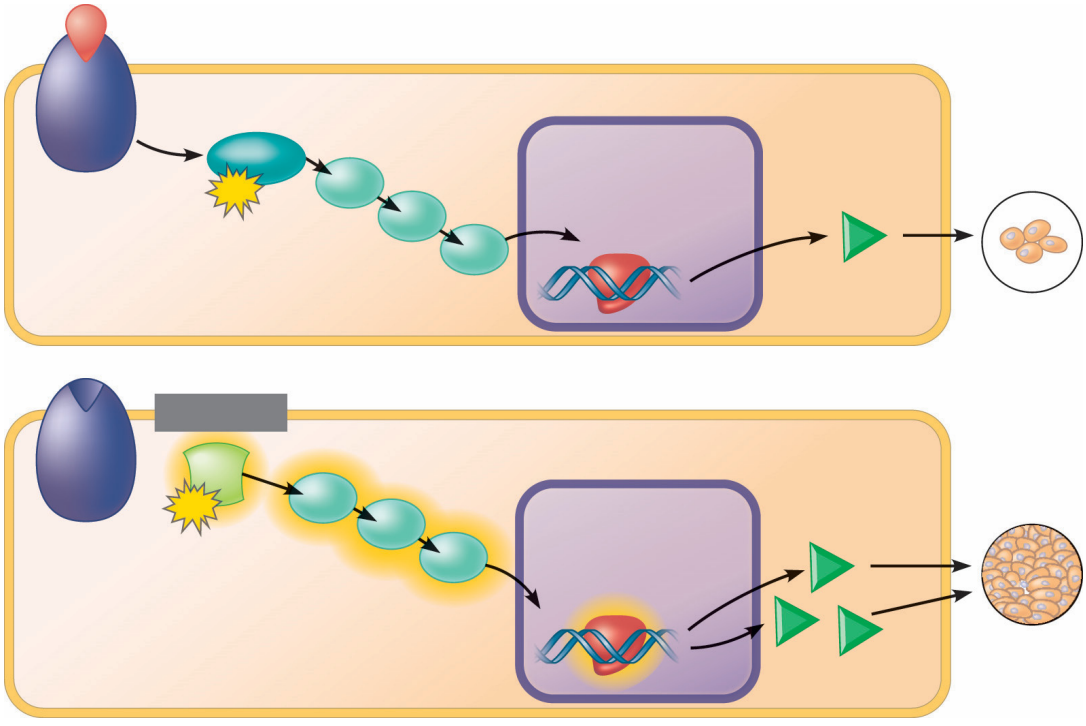
    a. epigenetic modifications:

    b. translocations:

    c. gene amplification:

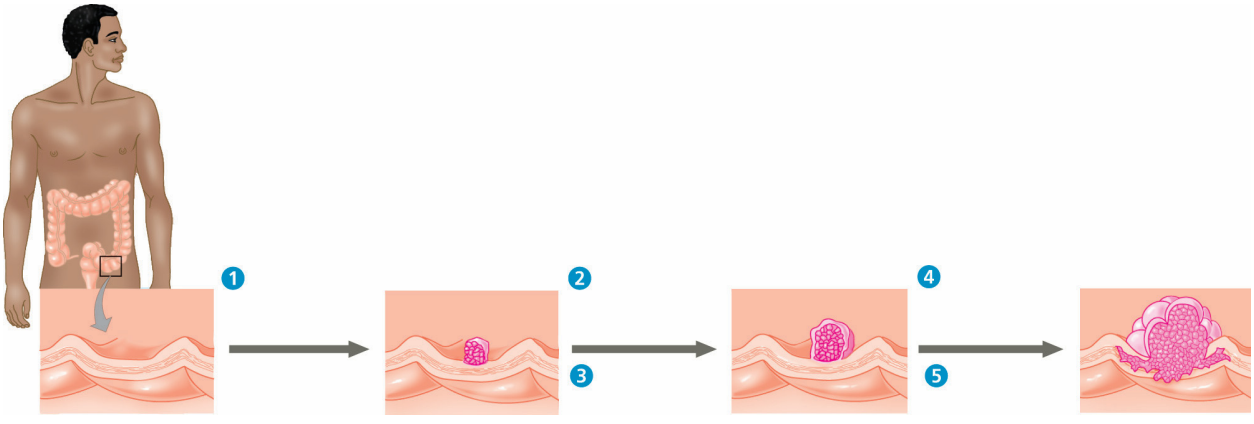
    d. point mutations:

55. There seem to be two categories of genes involved in cancer: *oncogenes*, which code for proteins to regulate cell growth, and should not be stuck "on," much like the accelerator in a car; and *tumor-suppressor genes*, which work like the brakes on a car and must function! Let's begin with a look at the *ras* gene, which codes for a G protein and is an *oncogene*. Label the following two sketches, then explain how a *ras* mutation leads to cancer.



56. *Tumor-suppressor genes* help prevent uncontrolled cell growth. One that is found mutated (and therefore nonfunctional) in more than 50% of human cancer is *p53*. So important is the *p53* gene that it is sometimes called the "guardian angel of the genome." Describe the double whammy that results from mutation of *p53*.

57. Explain the *multistep model of cancer development* by using the specific example of colorectal cancer. Use the following figure to label the five mutation levels leading to this form of cancer.



Make Connections Figure 18.27: Genomics, Cell Signaling, and Cancer

58. You probably know someone who has been treated for breast cancer. Did you realize there were genetically distinct types? Study Figure 18.27 in your text to understand why the treatment varies from woman to woman. Why is it not surprising that signal receptors are over-expressed in most types of cancer?

59. Why do Tamoxifen and Herceptin not work against basal-like breast cancer?

60. Explain how mutations in *BRCA1* and *BRAC2* are associated with an increased risk of breast cancer.

61. Briefly explain how viruses can play a variety of roles in cancer formation.

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Now you should be ready to test your knowledge. Place your answers here:

1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ 7. _____

8. _____ 9. _____ 10. _____