Name _____ **Period** _____

Chapter 18: Regulation of Gene Expression

The overview for Chapter 18 introduces the idea that although all of 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.

Concept 18.1 Bacteria often respond to environmental change by regulating transcription

1. All genes are not "on" all the time. Using the metabolic needs of *E. coli*, explain why not.

2. What are the two main ways of controlling metabolism in bacterial cells?

3. *Feedback inhibition* is a recurring mechanism throughout biological systems. In the case of *E. coli* regulating tryptophan synthesis, is it *positive* or *negative inhibition*? 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 order for this to occur, 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. *repressor*

   d. *regulatory genes*

5. Distinguish between *inducible* and *repressible operons*, and describe one example of each type.

6. Label this sketch of the *lac* operon with the following terms. Know the function of each structure.

operon genes

operon

RNA polymerase

mRNA

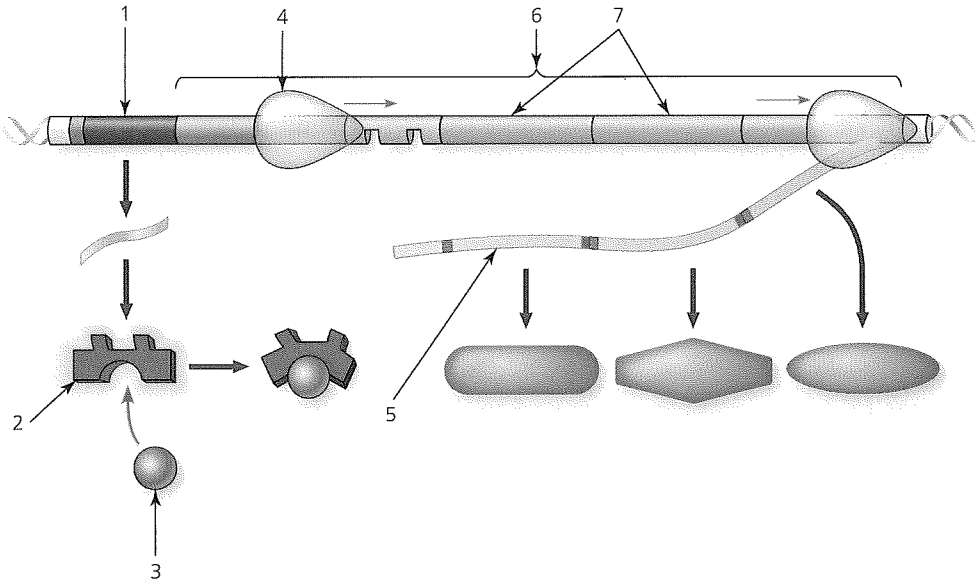
repressor protein

operator

repressor

regulatory gene

inducer



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

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

9. 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 be active?

   b. Will the *lac* operon be active?

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

11. Explain why CAP binding and stimulation of gene expression is *positive regulation.*

12. How can both repressible and inducible operons be *negative regulators*?

***Concept 18.2** Eukaryotic gene expression is regulated at many stages*

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

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

15. The common control point of gene expression for all organisms is at transcription, although for eukaryotes gene expression can be regulated at other points, to be discussed later. Refer to the diagrams on the left side of Figures 18.7, 18.8, and 18.10 to list the three points at which control of transcription occurs.

Regulation of Chromatin Structure

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

17. What occurs in *histone acetylation*? How does it affect gene expression?

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

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

20. What is *genomic imprinting*, and how is it maintained? Give an example discussed earlier in human genetics.

21. 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

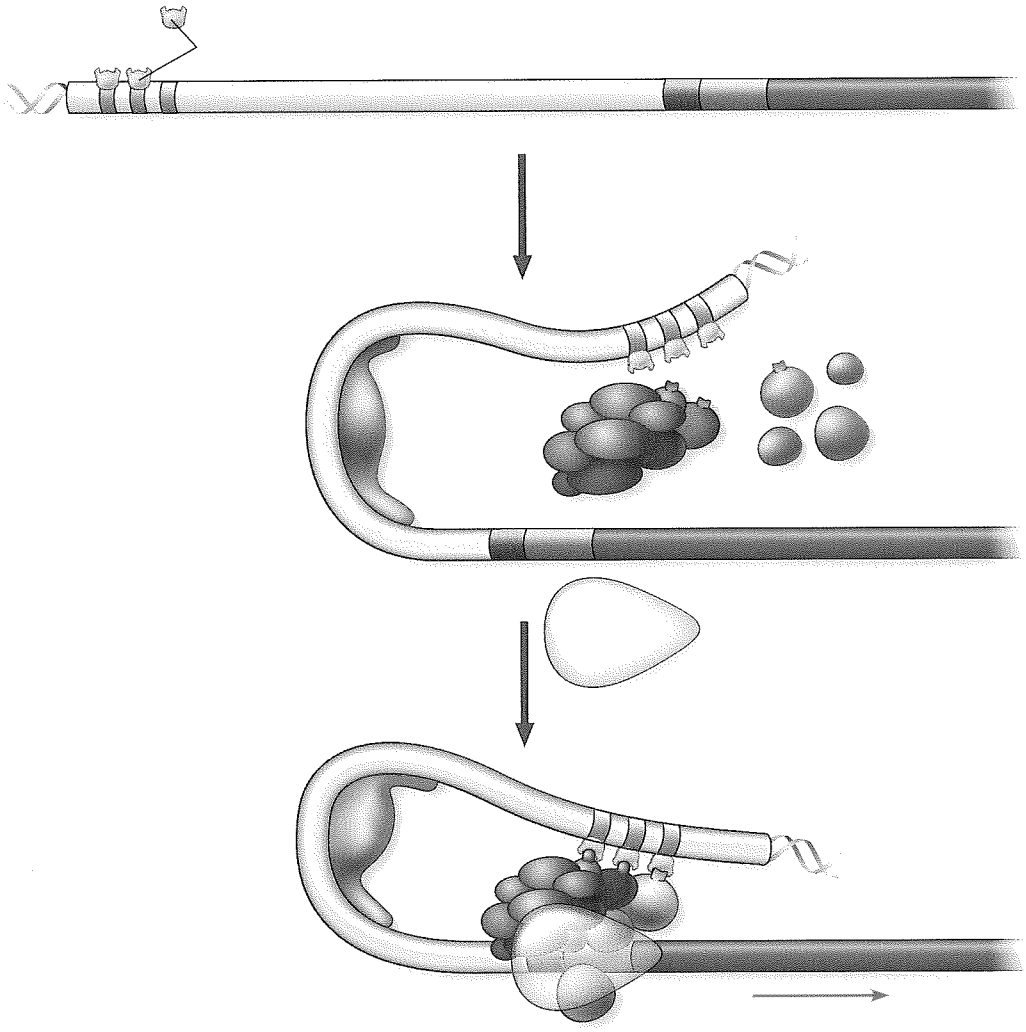
22. Figure 18.8 reviews some material you are already familiar with by showing what occurs in transcription and RNA processing. However, focus on what is new in this figure. Note the *Enhancer (distal control elements)* and *Proximal control elements*. What is the role of each of these?

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

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

25. 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 to the left of the figure.

Explanation



26. In prokaryotes, functionally related genes are usually clustered in a single operon. What has been found to be the case in eukaryotes?

27. With rare exception, operons have not been found in eukaryotic cells, and the genes coding for the enzymes of a particular metabolic pathway are often scattered over different chromosomes. What is a plausible mechanism for the *coordination of gene expression*?

Mechanisms of Post-Transcriptional Regulation

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

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

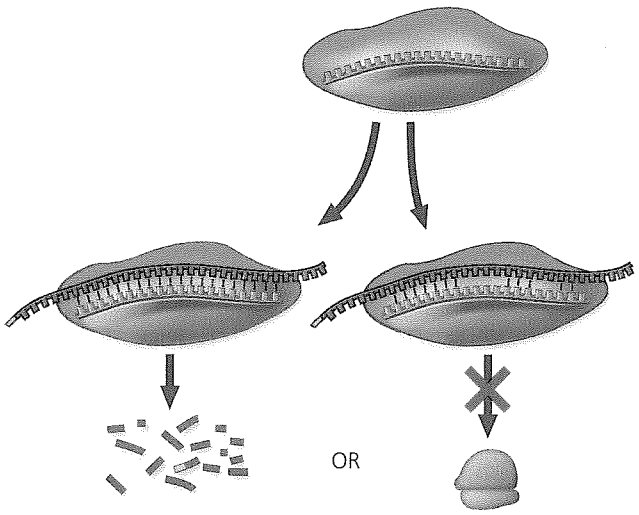
30. How can proteins be activated, processed, and degraded? Give an example or describe each process.

31. An article in *Scientific American* about *proteasomes* was entitled "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

32. 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 RNAs. What is this role?

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



34. 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)

Concept 18.4 *A program of 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.

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

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

37. 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*

    b. *induction*

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

39. 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?

40. What is controlled by *homeotic genes*?

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

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

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

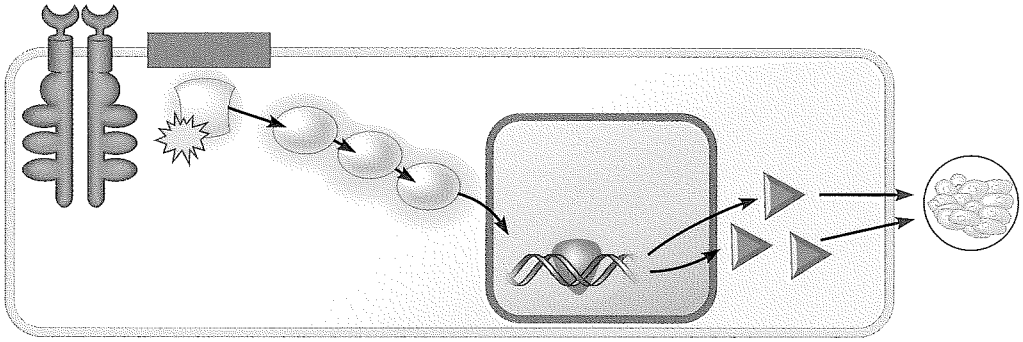
***Concept 18.5** Cancer results from genetic changes that affect cell cycle control*

44. 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 can lead to these cancer-causing mutations?

45. Compare *oncogenes* and *proto-oncogenes*.

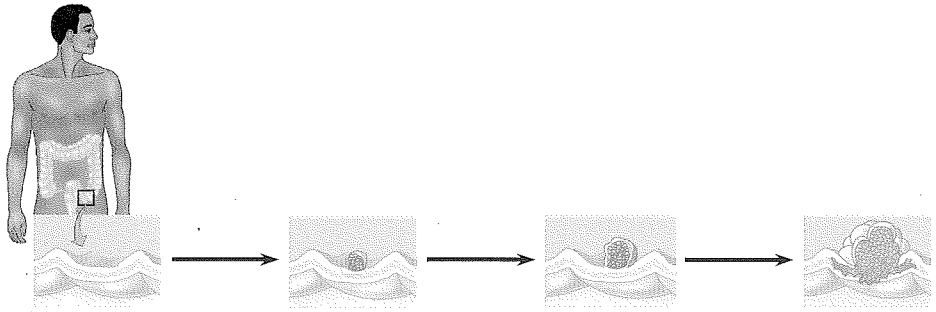
46. What are three mechanisms for converting a proto-oncogene to an oncogene?

47. 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 sketch to explain how a *ras* mutation leads to cancer.



48. *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*.

49. 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*

50. You probably know someone who has been treated for breast cancer. Did you realize there were genetically distinct types? Study figure 18.27 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?

51. Why do Tamoxifen and Herceptin not work against Basal-like breast cancer?

Test Your Understanding Answers

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

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

7. _____ 8. _____ 9. _____ 10. _____