The Control of Gene Expression 11

One of the wonders of biology is how a fertilized egg—a single, relatively generalized cell—can develop into an adult human being—a multicellular organism consisting of hundreds of kinds of specialized cells. The zygote contains all the genes needed to construct and direct the activities of an entire human being. As the zygote divides, different groups of cells differentiate, taking on different shapes and different functions, finally forming the cooperating tissues and organs of the adult body. Muscle cells, bone cells, nerve cells—experiments suggest that these different kinds of cells all contain identical sets of genes. What makes the cells different is that different subsets of genes are expressed in each kind of cell. A sophisticated regulatory system switches genes on and off, responding to environmental changes and shaping the differentiation of various cell lineages. Occasionally, genes escape from their normal controls, producing birth defects or cancer. Scientists are learning to switch genes on and off on command, producing clones for reproduction and therapy. This chapter considers gene regulation, a subject of much mystery and intensive research.

Organizing Your Knowledge

Exercise 1 (Module 11.1)

Web/CD Activity 11A *The* lac *Operon in* E.Coli

A prokaryote can respond to changes in its environment by turning genes on and off. In bacteria, genes are grouped, with control sequences called operators and promoters, into clusters called operons. The *lac* and *trp* operons are two such gene clusters in the bacterium *E. coli*. Study the diagrams in Module 11.1, and then match each of the components of the *lac* and *trp* operon systems with its function.

lac operon:

_____ 1. Regulatory gene
_____ 2. Repressor protein + lactose
_____ 3. Repressor protein without lactose
_____ 4. RNA polymerase
_____ 5. Promoter
_____ 6. Operator
_____ 7. Operon genes
_____ 8. Enzymes

A. Keeps RNA polymerase from attaching to promoter and transcribing genes
B. Transcribes genes into RNA for protein synthesis
C. Repressor protein attaches here
D. Use lactose
E. Information for making repressor protein
F. Where RNA polymerase starts transcribing genes
G. Allows RNA polymerase to transcribe genes
H. Information for making enzymes that use lactose

trp operon:

_____ 1. Regulatory gene
_____ 2. Repressor protein + tryptophan
_____ 3. Repressor protein without tryptophan
_____ 4. RNA polymerase
_____ 5. Promoter
_____ 6. Operator
_____ 7. Operon genes
_____ 8. Enzymes

A. Keeps RNA polymerase from attaching to promoter and transcribing genes
B. Transcribes genes into RNA for protein synthesis
C. Repressor protein attaches here
D. Make tryptophan
E. Information for making repressor protein
F. Where RNA polymerase starts transcribing genes
G. Allows RNA polymerase to transcribe genes
H. Information for making enzymes that make tryptophan

Exercise 2 (Modules 11.2 – 11.4)

In eukaryotic organisms, cells become specialized—differentiated—for different functions. It has been demonstrated in several kinds of plants and animals that differentiated cells retain a complete set of genes for making all the specialized cells in the whole organism. Each differentiated cell *has* all the genes, but *different* genes are *active* in different kinds of cells. Check your understanding of this concept by coloring in the boxes below to show which genes you think would be active in each of the cell types.

	Stomach Gland Cell	*Hair Follicle Cell*	*Stem Cell (Becomes Red Blood Cell)*
Hemoglobin gene	☐	☐	☐
Keratin (hair protein) gene	☐	☐	☐
Krebs cycle enzyme gene	☐	☐	☐
Digestive enzyme gene	☐	☐	☐
Insulin gene	☐	☐	☐

Exercise 3 (Modules 11.2 – 11.5)

Cloning experiments show that differentiated cells retain all of their genetic potential. Stem cells of embryos and adults are able to differentiate into many kinds of cells—useful for reproduction and therapy. Review cloning and stem cells by matching each phrase with a term from the list on the right.

_____ 1. Regrowth of lost body parts
_____ 2. Producing genetically identical organisms for agriculture or research
_____ 3. Cells that give rise to all specialized cells in the body
_____ 4. The process of cell specialization
_____ 5. Growing cells for replacement or repair of damaged or diseased organs
_____ 6. Genetically identical organisms
_____ 7. Replacing the nucleus of an egg or zygote with a nucleus from a differentiated cell
_____ 8. Partially differentiated cells present in mature animals

A. reproductive cloning
B. nuclear transplantation
C. differentiation
D. embryonic stem cells
E. therapeutic cloning
F. adult stem cells
G. regeneration
H. clones

trp operon:

_____ 1. Regulatory gene
_____ 2. Repressor protein + tryptophan
_____ 3. Repressor protein without tryptophan
_____ 4. RNA polymerase
_____ 5. Promoter
_____ 6. Operator
_____ 7. Operon genes
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A. reproductive cloning
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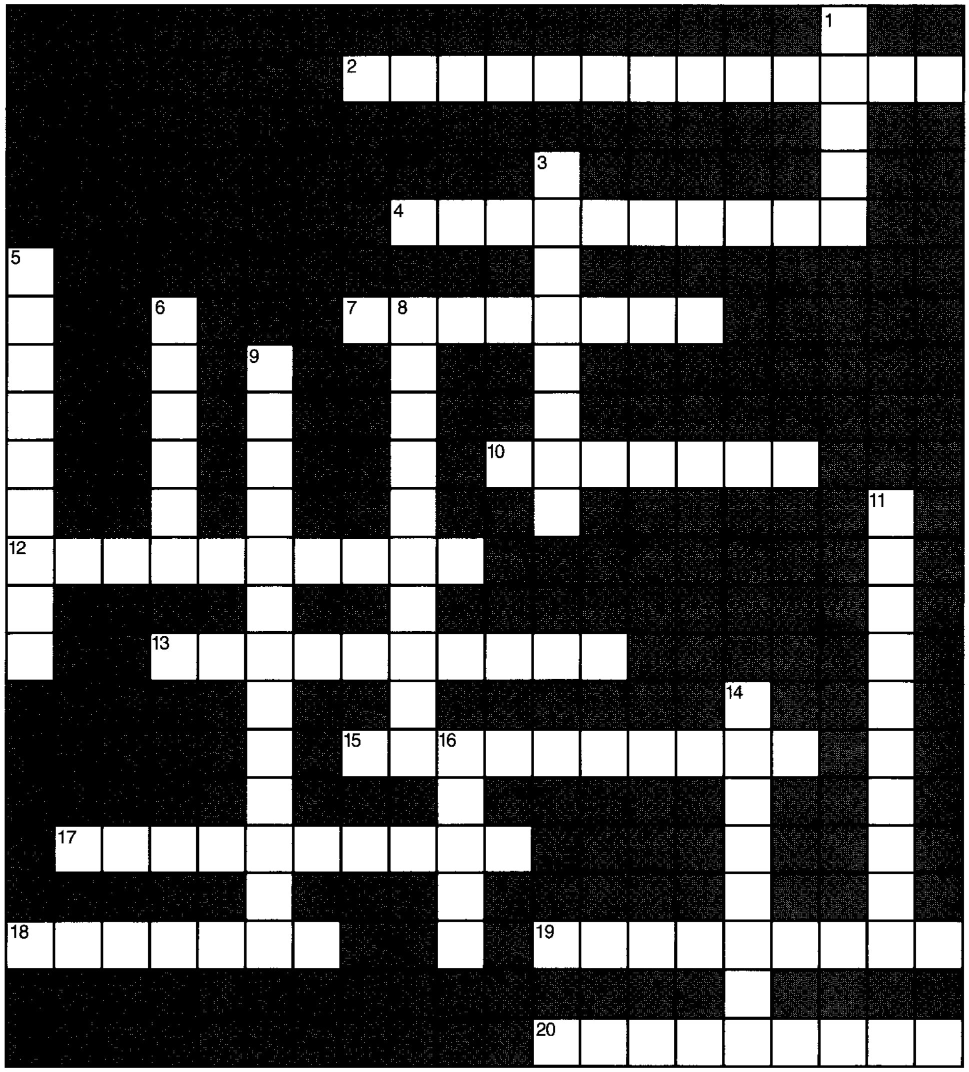
Exercise 4 (Modules 11.6 – 11.8)

Complete this crossword puzzle to review the roles of DNA packing and protein activators in gene expression.



Across

2. The color pattern of a ____ cat reflects the influence of chromosome inactivation.
4. Scientists think most eukaryotic regulatory proteins act as ____.
7. One *X* chromosome in each of a woman's cells is ____.
10. The DNA-histone beaded fiber is further wrapped into a tight ___ fiber.
12. Nucleosomes may control gene ____ by limiting access to DNA.
13. The DNA supercoil is further wrapped and folded into a ____.
15. In eukaryotes, many ____ proteins interact with DNA and one another to turn genes on and off.
17. ____ chromosomal proteins control how tightly the histones bind the DNA.
18. DNA fits into a cell because of a system of folding, or ____.
19. In eukaryotes, structural and regulatory genes are ____.
20. The twisted DNA further coils into a ____ with a diameter of 200 nm.

Down

1. The DNA-histone complex looks like "____ on a string."
3. DNA is wound around small proteins called ____.
5. The first step in initiating gene transcription is binding of activators to sites called ____.
6. A transcription ____ may be involved in turning on a eukaryotic gene.
8. A ____ is a complex of DNA wrapped around eight histone molecules.
9. DNA packing seems to control gene expression at the ____ stage.
11. Activators trigger RNA ____ to begin transcription.
14. An activator may help position RNA polymerase on a gene's ____.
16. In most eukaryotic cells, most ____ are not expressed.

Exercise 5 (Modules 11.9 - 11.10)

Web/CD Activity 11B *Gene Regulation in Eukaryotes*

In eukaryotes, gene expression is also regulated after transcription of genes into mRNA and during and after translation of mRNA into protein. Review these processes by matching each of the processes on the right (listed in order of occurrence) with a description on the left.

A. Altering a protein to form an active final product
B. Retaining or breaking down mRNA molecules, controlling how much they are translated
C. Action of inhibitors that may block synthesis of protein from mRNA message
D. Joining exons in different ways to produce more than one polypeptide from a single gene
E. Removal of noncoding introns from RNA
F. Joining of exons to produce mRNA
G. Retaining or breaking down proteins, depending on cell's needs

_____ 1. First step in RNA splicing
_____ 2. Second step in RNA splicing
_____ 3. Alternative RNA splicing
_____ 4. Selective breakdown of mRNA
_____ 5. Inhibition of translation
_____ 6. Activation of finished protein
_____ 7. Selective breakdown of proteins

Exercise 7 (Modules 11.12 – 11.14)

Web/CD Activity 11D *Development of Head-Tail Polarity*
Web/CD Activity 11E *Signal-Transduction Pathway*

Powerful new methods of molecular biology have enabled scientists to explore how gene regulation controls animal development. Researchers have found that one of the first events in fruit-fly development is a sequence of changes that determine which end of an egg will develop into the fly's 1________________ and which will develop into the 2________________. One of the first 3________________ that "turns on" in the egg cell codes for a protein that leaves the egg and signals nearby cells in its follicle, or egg chamber. The signal protein binds to a specific 4________________ in the membrane of the target cell, which in turn activates a series of relay proteins in the target cell. The last relay protein activates a 5________________ factor that triggers transcription of a specific target cell gene. The mRNA produced is then 6________________ into a protein.

Via this mechanism, the egg cell signals the follicle cells. This 7________________ genes in the follicle cells, and they produce proteins that signal back to the egg cell. One of the egg cell's responses is to localize a type of 8________________ at one end of the egg cell. This marks where the fly's 9________________ will develop. The other end of the egg will become the 10________________. Similar processes establish the other body axes and thus the layout of the overall body plan of the fly.

After the egg is fertilized, the zygote is transformed into a multicellular embryo by repeated 11________________. Translation of the "head" mRNA creates a regulatory 12________________ that is concentrated mostly in the head of the developing fly. This protein in turn influences other genes, and these act to subdivide the embryo into repeating subunits called body 13________________.

Protein products of the axis-forming and segment-forming genes now trigger another round of gene 14________________ that shapes the details of the fly. Master control genes called 15________________ genes determine what body parts—antennae, legs, and so on—will develop in each segment. Every homeotic gene contains a sequence of about 180 nucleotides called a 16________________, which is translated into a protein segment of about 60 17________________. This homeobox polypeptide segment binds to specific 18________________ base sequences, enabling the homeotic protein to turn groups of genes on and off during development.

19________________ in homeotic genes produce flies with spectacular changes in body structure, such as extra pairs of wings, or heads bearing legs instead of antennae. Such changes attracted the attention of researchers, which led to the discovery of homeotic genes and study of their important role in 20________________. Further research has shown that homeoboxes are virtually identical in every eukaryotic organism studied so far—from yeast to plants to chickens to humans. For example, the chromosomes of a mouse and a fruit fly bear similar homeotic genes in the same 21________________, and the genes are ordered from 22"________________" to 23"________________" on the chromosomes. These great similarities suggest that many of the base sequences in genes that control development arose 24________________ in the history of life and have changed little since.

Exercise 8 (Modules 11.15 – 11.18)

Review the causes and mechanisms of cancer by filling in the blanks in the following story.

In the United States, lung cancer kills about 155,000 people per year. About 169,000 Americans will be diagnosed with lung cancer this year. Long the most common kind of cancer in men, lung cancer recently passed breast cancer to become the most frequent cancer in women as well. There has been a 136% increase in lung cancer deaths among women over a 20-year period.

Cancer is uncontrolled multiplication of cells. The [1]________________ control system is responsible for regulating cell [2]________________ and [3]________________. Sometimes cells escape from this control and multiply wildly. The cells form abnormal masses called tumors, which displace nearby normal tissues and can spread through the body.

Because the growing tumors block breathing passages, the first symptoms of lung cancer are usually coughing and difficulty breathing. The tumorous masses show up on chest X-rays, and usually a small sample of lung tissue is taken to examine the tumor cells.

What causes lung cancer? Cancer-causing agents are called [4]________________. Radiation, such as X-rays and UV light, are known to cause some cancers, but most are caused by chemicals. Carcinogens in tobacco smoke appear to be the major cause of lung cancer. An increase in cigarette smoking over the last century has been paralleled by a rise in lung cancer rates. Tobacco has also been linked to other forms of cancer, such as cancer of the throat and stomach.

Scientists have discovered much about the cellular mechanisms of cancer by studying cancers caused by viruses in humans and other animals. They were surprised to find that cancer-causing viruses carry cancer-causing genes, called [5]________________, as part of their genome. When the viruses insert their genes into the chromosomes of a host cell, the cancer-causing genes are inserted as well. Even more surprising, researchers found that oncogenes are simply altered versions of genes normally found in all cells. These genes, called [6]_____________, usually code for proteins called [7]_____________ factors—which normally stimulate cell [8]________________—or for other proteins that affect growth factors. What appears to cause most cancers is a [9]________________ in a proto-oncogene in a body (somatic) cell that changes it into an oncogene.

Changes in genes whose products *inhibit* cell division—so-called [10]____________ genes—can also contribute to the development of cancer. The normal products of proto-oncogenes and tumor-suppressor genes are involved in [11]________________-transduction pathways. Normally, the [12]________________ product of a proto-oncogene (such as one called *ras*) might act to conduct a signal from a [13]________________ factor to the interior of a cell, stimulating [14]________________ to occur. When the proto-oncogene mutates into an oncogene, it might produce a protein that increases cell division even in the [15]________________ of the growth factor.

A tumor-suppressor protein might act as a [16]________________ factor, which normally promotes production of a protein that blocks cell division. A mutation in a tumor-suppressor gene (such as *p53*) could produce a defective transcription factor. In this case, the inhibitory protein would not be transcribed, causing an [17]______________ rate of cell division.

Evidence suggests that more than one somatic [18]________________ is needed to produce cancer. These mutations are cumulative and passed to all of a cell's [19]________________. In most cases studied so far, changes in both proto-oncogenes and tumor-suppressing genes seem to be necessary for a full-fledged tumor to develop. Recent research has also brought to light a different kind of tumor-suppressor gene, like the *BRCA1* gene implicated in breast cancer, whose function is to [20]________________ damaged DNA. If this gene is defective, cancer is more likely to develop.

Exercise 9 (Module 11.19)

Web/CD Activity 11F *Connection: Causes of Cancer*

After reading this module, match each of the following human cancers with the carcinogen(s) implicated as its major cause. (Answers may be used more than once or not at all.)

A. Ultraviolet light
B. Testosterone; possibly dietary fat
C. Cigarette smoke
D. Estrogen; possibly dietary fat
E. Alcohol; hepatitis viruses
F. High dietary fat; low dietary fiber
G. X-rays

_____ 1. Lung
_____ 2. Colon and rectum
_____ 3. Breast
_____ 4. Prostate
_____ 5. Bladder
_____ 6. Kidney
_____ 7. Pancreas
_____ 8. Melanoma (skin)
_____ 9. Liver

Testing Your Knowledge

Multiple Choice

1. Your muscle and bone cells are different because
   a. they contain different sets of genes.
   b. they are differentiated.
   c. they contain different operons.
   d. different genes are switched on and off in each.
   e. they contain different histones.

2. Operons enable bacteria to
   a. function in frequently changing environments.
   b. resist attack by predators.
   c. correct mutations that might interfere with their genetic instructions.
   d. differentiate.
   e. mutate and evolve more rapidly.

3. If the nucleus of a frog egg is destroyed and replaced with the nucleus of an intestine cell from a tadpole, the egg can develop into a normal tadpole. This demonstrates that
   a. intestine cells are fully differentiated.
   b. there is little difference between an egg cell and an intestine cell.
   c. an intestine cell possesses a full set of genes.
   d. intestine cells are not differentiated.
   e. frogs can regenerate lost parts.

4. DNA packing—the way DNA is folded into chromosomes—affects gene expression by
   a. controlling access to DNA.
   b. positioning related genes near each other.
   c. protecting DNA from mutations.
   d. enhancing recombination of genes.
   e. allowing "unpacked" genes to be eliminated from the genome.

5. The genes that malfunction in cancer normally
   a. control RNA transcription.
   b. are responsible for organizing DNA packing.
   c. code for enzymes that transcribe DNA.
   d. are not present in most body cells unless inserted by a virus.
   e. regulate cell division.

6. In most eukaryotic cells most genes are not expressed. This suggests that most eukaryotic regulatory proteins act as
   a. exons.
   b. repressors.
   c. introns.
   d. enhancers.
   e. activators.

7. After an mRNA molecule is transcribed from a eukaryotic gene, portions called ____ are removed and the remaining ____ are spliced together to produce an mRNA molecule with a continuous coding sequence.
   a. operators . . . promoters
   b. exons . . . introns
   c. silencers . . . enhancers
   d. introns . . . exons
   e. promoters . . . operators

8. Which of the following mechanisms of gene regulation operates after mRNA transcription but before translation of mRNA into protein?
   a. mRNA splicing
   b. DNA packing
   c. repressors and activators
   d. protein degradation
   e. all of the above

9. Homeobox polypeptide segments
   a. serve as histones, facilitating DNA packing.
   b. bind to DNA and activate or repress gene transcription.
   c. are vastly different in different organisms.
   d. act as enzymes, carrying out important chemical reactions.
   e. carry out mRNA splicing in the cell nucleus.

10. In a eukaryote, a repressor protein may block gene expression by binding to a DNA site called
   a. an operon.
   b. a histone.
   c. an enhancer.
   d. a promoter.
   e. a silencer.

11. Gene expression in animal development seems to be regulated largely by
   a. controlling gene packing and unpacking.
   b. controlling the transcription of genes into mRNAs.
   c. controlling the translation of mRNAs into protein.
   d. selectively eliminating certain genes from the genome.
   e. selectively breaking down certain proteins so they cannot function.

12. Which of the following is a known or likely carcinogen?
   a. ultraviolet light
   b. cigarette smoke
   c. hormones
   d. X-rays
   e. all of the above

13. Which of the following is the first thing that happens when a signal molecule acts on a target cell?
   a. A transcription factor acts on the DNA.
   b. The signal molecule binds to the DNA.
   c. A new protein is made in the target cell.
   d. A specific gene is transcribed.
   e. The signal molecule binds to a receptor.

Essay

1. In the proper growth medium, a single cell from a Boston fern can be stimulated to grow into an entire plant. What does this signify with regard to cellular differentiation in plants?

2. What are introns and exons? Discuss three possible biological functions of introns.

3. What is a homeotic gene? Why does a mutation in a homeotic gene have a much more drastic effect on the organism than a mutation in other genes?

4. Very similar homeoboxes control gene transcription in the DNA of frogs, flies, and humans. Why do biologists consider this significant?

5. Briefly explain how genes control development of the head-to-tail axis of a fruit-fly embryo.

6. Describe the changes in a cell that can make the cell become cancerous.

7. If a person wishes to avoid cancer, what factors in the environment should he or she try to avoid? What dietary and health habits would you recommend?

Applying Your Knowledge

Multiple Choice

1. When a certain bacterium encounters the antibiotic tetracycline, the antibiotic molecule enters the cell and attaches to a repressor protein. This keeps the repressor from binding to the bacterial chromosome, allowing a set of genes to be transcribed. These genes code for enzymes that break down the antibiotic. This set of genes is best described as
   a. an exon.
   b. regulatory genes.
   c. an operon.
   d. a homeobox.
   e. a nucleosome.

2. A genetic defect in humans results in the absence of sweat glands in the skin. Some men have this defect all over their bodies, but in women it is usually expressed in a peculiar way. A woman with the defect typically has small patches of skin with sweat glands and other patches where sweat glands are lacking. This pattern suggests the phenotypic effect of
   a. a mutation.
   b. chromosome inactivation.
   c. RNA splicing.
   d. an operon.
   e. the homeobox.

3. A bacterium makes the amino acid glycine or absorbs it from its surroundings. A biochemist found that glycine binds to a repressor protein and causes the repressor to bind to the bacterial chromosome, "turning off" an operon. If this is like other operons, the genes of this operon probably code for enzymes that
   a. control bacterial cell division.
   b. break down glycine.
   c. produce glycine.
   d. cause the bacterium to differentiate.
   e. manufacture the repressor protein.

4. In humans, the hormone testosterone enters cells and binds to specific proteins, which in turn bind to specific sites on the cells' DNA. These proteins probably act to
   a. help RNA polymerase transcribe certain genes.
   b. alter the pattern of DNA splicing.
   c. stimulate protein synthesis.
   d. unwind the DNA so that its genes can be transcribed.
   e. cause mutations in the DNA.

5. It is possible for a cell to make proteins that last for months; hemoglobin in red blood cells is a good example. However, many proteins are not this long-lasting. They may be degraded in days or even hours. Why do cells make proteins with such short lifetimes if it is possible to make them last longer?
   a. Most proteins are used only once.
   b. Most cells in the body live only a few days.
   c. Cells lack the raw materials to make most of the proteins they need.
   d. Only cancer cells, which can keep dividing, contain long-lasting proteins.
   e. This enables cells to control the amount of protein present.

6. Dioxin, produced as a by-product of various industrial chemical processes, is suspected of causing cancer and birth defects in animals and humans. It apparently acts by entering cells and binding to proteins, altering the pattern of gene expression. The proteins affected by dioxin are probably
   a. enzymes.
   b. DNA polymerases.
   c. transcription factors.
   d. enhancers.
   e. nucleosomes.

7. Which of the following would be most likely to lead to cancer?
   a. multiplication of a proto-oncogene and inactivation of a tumor-suppressor gene
   b. hyperactivity of a proto-oncogene and activation of a tumor-suppressor gene
   c. inactivation of a proto-oncogene and multiplication of a tumor-suppressor gene
   d. inactivation of both a proto-oncogene and a tumor-suppressor gene
   e. hyperactivity of both a proto-oncogene and a tumor-suppressor gene

8. A cell biologist found that two different proteins with largely different structures were translated from two different mRNAs. These mRNAs, however, were transcribed from the same gene in the cell nucleus. What mechanism below could best account for this?
   a. Different systems of DNA unpacking could result in two different mRNAs.
   b. A mutation might have altered the gene.
   c. Exons from the same gene could be spliced in different ways to make different mRNAs.
   d. The two mRNAs could be transcribed from different chromosome puffs.
   e. Different chemicals activated different operons.

9. Researchers have found homeotic genes in humans, but they are not yet certain how these genes shape the human phenotype. Considering the functions of homeotic genes in other animals, which of the following is most likely to be their function in humans?
   a. determining skin and hair color
   b. regulating cellular metabolic rate
   c. determining head and tail, back and front
   d. determining whether an individual is male or female
   e. regulating the rate and timing of cell division

Essay

1. Mutations sometimes affect operons. Imagine a mutation in the regulatory gene that produces the repressor of the *lac* operon in *E. coli*. The altered repressor is no longer able to bind to the operator. What effect will this have on the bacterium?

2. Describe how three different types of cells in your body are specialized for different functions. How do their differences reflect differences in gene expression? Suggest a gene that might be active in each of the cells but none of the others. Suggest a gene that might be active in all the cells. Suggest a gene that is probably not active in any of the cells.

3. A biochemist was studying a membrane-transport protein consisting of 258 amino acids. She found that the gene coding for the transport protein consisted of 3561 nucleotides. The mRNA molecule from which the transport protein was transcribed contained 1455 nucleotides. What is the minimum number of nucleotides needed to code for the protein? How can the protein be transcribed from an mRNA that is larger than necessary? How can this mRNA be made from a gene that is so much larger?

4. Explain how, in a eukaryotic cell, a gene on one chromosome might affect the expression of a gene on a different chromosome. How might a gene in a certain cell affect expression of a gene in a different cell?

5. A certain kind of leukemia can be caused by a virus, a chemical, or radiation. Explain how these different factors can all trigger identical forms of cancer in the same kind of tissue.

Extending Your Knowledge

1. Pregnant women are advised to avoid unneeded exposure to chemicals from the environment, such as pesticides, alcohol, tobacco smoke, and medications. Does this chapter suggest how these substances might alter fetal development?