

How Genes Are Controlled

Focus on the Concepts

This chapter describes how genes are controlled and how this relates to differentiation, development, cloning, signal transduction, and what can happen when cells escape their normal controls—cancer. Focus on the following concepts:

- The flow of information from genes to proteins is called gene expression. Gene regulation helps organisms respond to environmental changes. In bacteria such as *E. coli*, groups of genes called operons respond to changes. In the absence of the sugar lactose, a repressor protein keeps the operator sequence controlling a group of genes turned off. When lactose is present, it pulls the repressor from the DNA, RNA polymerase attaches to the promoter, the genes are transcribed, and proteins are made that enable the bacterium to use lactose.
- In eukaryotes, differentiation of cells results from differences in gene expression. Regulation can occur at many points from gene to protein: Coiling or “packing” can control access to genes, even inactivating an entire X chromosome. DNA can be chemically altered. The most important level of control is carried out by transcription factors (and other proteins) that enhance or inhibit attachment of RNA polymerase and thus regulate gene transcription. mRNA can be spliced, blocked, or broken down before translation. Finally, polypeptides and proteins may be modified, activated, or destroyed.
- Cascades of gene expression direct animal development. For example, communication between a fruit fly egg and surrounding cells determines where in the egg genes are transcribed, where certain RNAs and proteins accumulate, and as a result, which end of the fly will be the head and which end the tail. Similar changes determine left and right and division of the fly into segments. Master control genes called homeotic genes regulate batteries of other genes that determine where and when appendages and organs develop.
- Signal transduction pathways are important in gene control. Typically, the pathway is activated by a signal molecule that binds to a receptor in the cell membrane. The receptor activates a chain of relay proteins, which activates a transcription factor. The transcription factor triggers a specific gene, which codes for a protein that carries out some function in the cell.
- Cloning demonstrates that differentiated cells may retain all of their genetic potential. Individual plant cells can be made to dedifferentiate and develop into whole plants. Animals are typically cloned via nuclear transplantation—transferring the nucleus of a somatic cell into an egg or zygote. Reproductive cloning can produce genetically identical individuals. Therapeutic cloning generates stem cells, which retain the ability to give rise to all or most kinds of cells in the organism.

- Cancer results from mutations in genes that control the cell cycle, causing uncontrolled multiplication of cells. The affected genes usually code for proteins in signal transduction pathways. Mutation of a proto-oncogene into an oncogene results in manufacture of an overactive protein or excess of a protein that stimulates cell division. Mutation of a tumor-suppressor gene alters a protein that normally activates the production of a cell-division inhibitor.

Review the Concepts

Work through the following exercises to review the concepts in this chapter. For additional review, refer to the activities at www.masteringbiology.com. The website offers a pre-test that will help you plan your studies.

Exercise 1 (Module 11.1)

Natural selection has favored bacteria that express only those genes whose functions are needed by the cell—in other words, bacteria that can turn genes on and off in response to changes in their environment. 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 that enable the bacterium *E. coli* to respond to its environment. 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:

- E 1. Regulatory gene
- G 2. Repressor protein + lactose
- A 3. Repressor protein without lactose
- B 4. RNA polymerase
- F 5. Promoter
- C 6. Operator
- H 7. Operon genes
- D 8. Enzymes

- A. Keeps RNA polymerase from attaching to promoter and transcribing genes
- B. Transcribes genes into mRNA 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

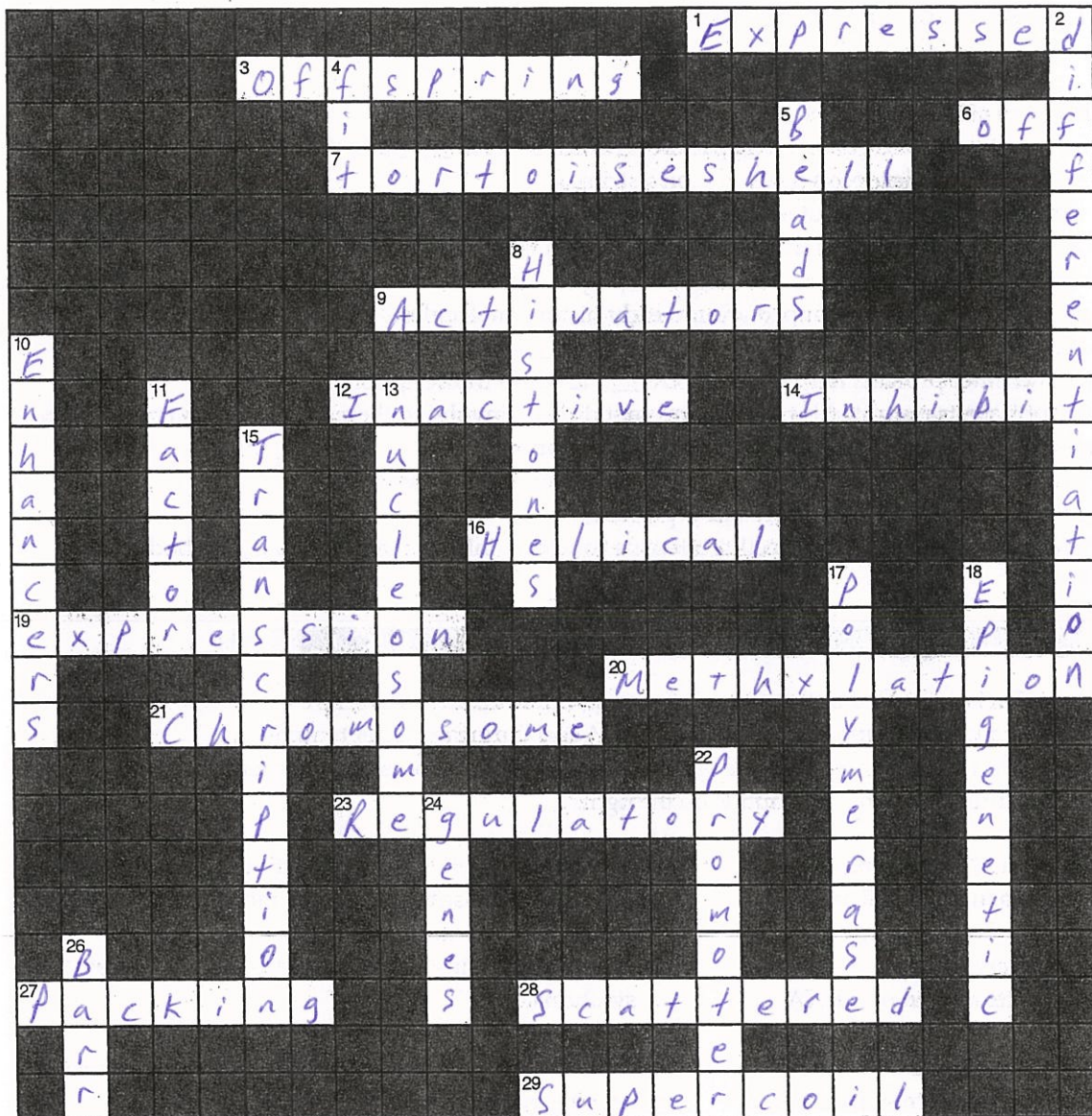
trp operon:

- E 1. Regulatory gene
- A 2. Repressor protein + tryptophan
- G 3. Repressor protein without tryptophan
- B 4. RNA polymerase
- F 5. Promoter
- C 6. Operator
- H 7. Operon genes
- D 8. Enzymes

- A. Keeps RNA polymerase from attaching to promoter and transcribing genes
- B. Transcribes genes into mRNA 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 11.2–11.3)

The first level of genetic control is a variety of mechanisms that can “lock” and “unlock” the DNA itself by controlling access to genes and allowing or disallowing RNA transcription. Complete this crossword puzzle to review the roles of DNA packing and protein activators in gene expression.

**Across**

1. All cells in a eukaryotic organisms have the same genes, but in different kinds of cells different genes are ____.
3. Methylation patterns are passed on to ____.
6. The default setting for most genes seems to be “____.”
7. The color pattern of a ____ cat reflects the influence of chromosome inactivation.
9. Scientists think most eukaryotic regulatory proteins act as ____.
12. One X chromosome in each of a woman’s cells is ____.
14. Proteins called silencers sometimes bind to DNA and ____ transcription.
16. The DNA-histone beaded fiber is further wrapped into a tight ____ fiber.

19. Nucleosomes may control gene ____ by limiting access to DNA.
20. ____ is a chemical modification of DNA that turns genes off.
21. The DNA supercoil is further folded and compacted to form a ____.
23. In eukaryotes, many ____ proteins interact with DNA and one another to turn genes on and off.
25. Epigenetic variations may account for differences between identical ____.
27. The folding and coiling of DNA into a chromosome is called ____.
28. In eukaryotes, genes coding for the enzymes of a metabolic pathway are often ____ around the genome.
29. Twisted DNA further coils into a ____ with a diameter of 300 nm.

Down

2. Specialization of cell structure and function is called ____.
4. Besides helping to regulate genes, DNA packing enables DNA to ____ into the nucleus.
5. The DNA-histone complex looks like " ____ on a string."
8. DNA is wound around small proteins called ____.
10. The first step in initiating gene transcription is binding of activators to sites called ____.
11. A transcription ____ is a protein that assists RNA polymerase.
13. A ____ is a complex of DNA wrapped around eight histone molecules.
15. DNA packing seems to control gene expression at the ____ stage.
17. Activators and other proteins help trigger RNA ____ to begin transcription.
18. Inheritance of traits transmitted by mechanisms not directly involving the nucleotide sequence—such as methylation and histone changes—are called ____ inheritance.
22. Activators and enhancers may help position RNA polymerase on a gene's ____.
24. In most eukaryotic cells, most ____ are not expressed.
26. The inactive X chromosome in each cell of a female compacts into an object called a ____ body.

Exercise 3 (Modules 11.4–11.6)

Often gene expression is controlled at the transcription step, but 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 left (listed in order of occurrence) with a description on the right.

- | | |
|--|---|
| <u>E</u> 1. First step in RNA splicing | A. Altering a protein to form an active final product |
| <u>F</u> 2. Second step in RNA splicing | B. Retaining or destroying mRNA molecules, controlling how much they are translated |
| <u>D</u> 3. Alternative RNA splicing | C. Action of proteins that may control the start of protein synthesis |
| <u>H</u> 4. RNA interference | D. Joining exons in different ways to produce more than one kind of mRNA (and polypeptide) from a single gene |
| <u>B</u> 5. Selective breakdown of mRNA | E. Removal of noncoding introns from RNA |
| <u>C</u> 6. Control of initiation of translation | F. Joining of exons to produce mRNA |
| <u>A</u> 7. Activation of finished protein | G. Retaining or destroying proteins, depending on cell's needs |
| <u>G</u> 8. Selective breakdown of proteins | H. Binding of microRNA (miRNA) to mRNA, blocking translation |

Exercise 4 (Module 11.7)

This module summarizes the major steps in gene expression in eukaryotes and the key mechanisms that regulate gene expression. After reviewing the module, match each of the mechanisms of regulation with the stage of gene expression at which it acts. Choose from: mRNA breakdown, DNA unpacking and changes, cleavage/modification/activation, protein breakdown, addition of cap and tail, TRANSCRIPTION, splicing, TRANSLATION, and flow through nuclear envelope.

#1 → DNA unpacking and changes

#2 → transcription

#3 → Addition of cap and tail

#4 → Splicing

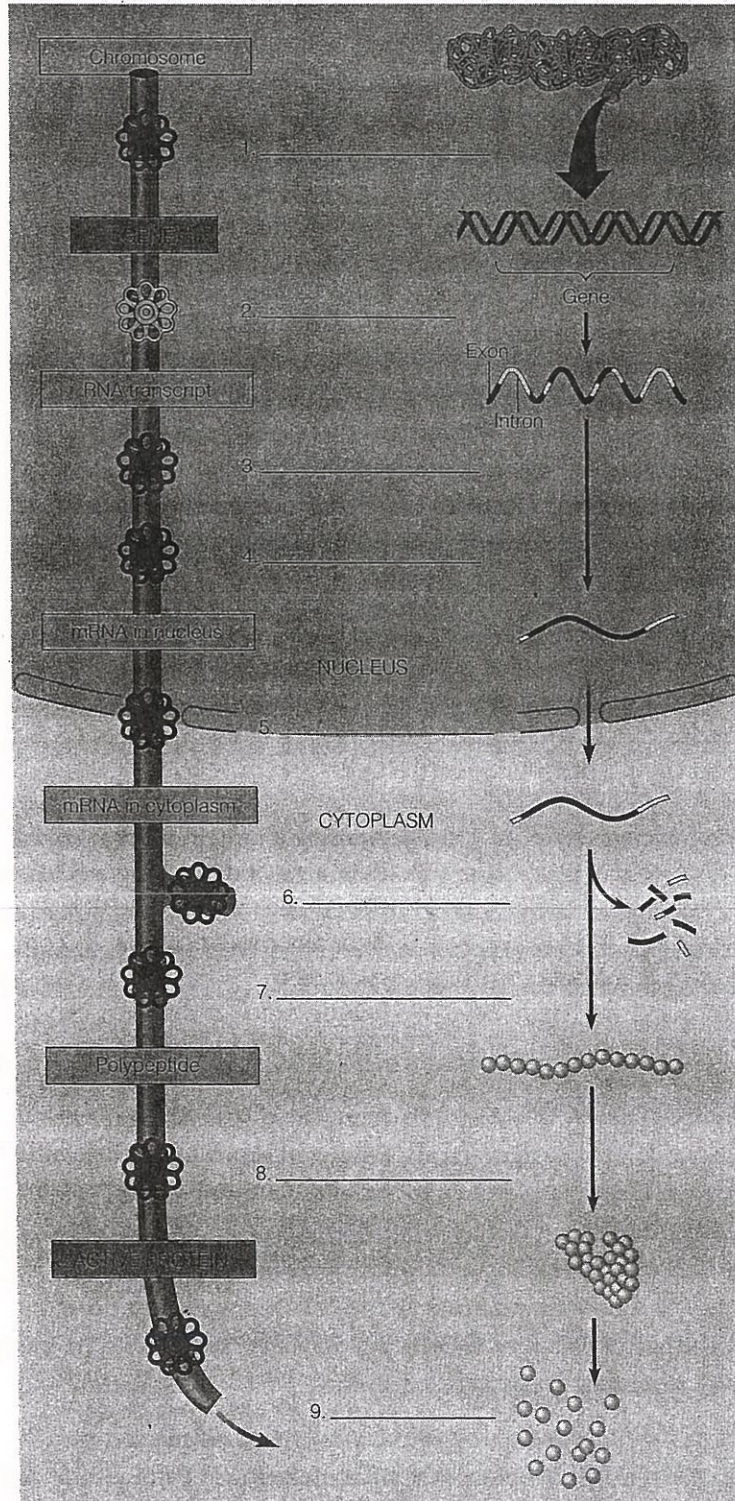
#5 → Flow through nuclear envelope

#6 → mRNA break-down

#7 → translation

#8 → cleavage/modification/activation

#9 → Protein breakdown



Exercise 5 (Modules 11.8–11.11)

As an animal develops, master genes activate other genes, and these genes signal still others. A chain reaction of gene expression shapes the body from head to tail. Review this cascade of gene expression, how cells in a developing embryo signal each other, and how researchers are unraveling this complex process, by filling in the blanks in the story that follows.

Powerful new techniques 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 head and which will develop into the ² tail. One of the first ³ genes 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. In a follicle cell, the egg protein activates a signal-transduction pathway. The signal protein binds to a specific ⁴ receptor in the membrane of a follicle target cell, which in turn activates a series of relay proteins in the target cell. The last relay protein activates a ⁵ transcription factor that triggers transcription of a specific target cell gene. The mRNA produced is then ⁶ translated into a protein.

Via this mechanism, the egg cell signals the follicle cells. The new protein formed in the follicle cells then ⁷ activates follicle cell genes, and they produce proteins that signal back to the egg cell. One of the egg cell's responses is to localize "head" ⁸ mRNA at the opposite end of the egg cell. This marks where the fly's ⁹ head end will develop. The other end of the egg will become the ¹⁰ tail. 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 mitoses. Further signaling and translation creates a cascade of ¹² proteins that diffuse through the cell layers of the fly embryo, activating further signal transduction pathways. One of the outcomes is to subdivide the body into a series of sections, or ¹³ segments.

Protein products of the axis-forming and segment-forming genes now activate another set of ¹⁴ genes that shape the details of the fly. Master control genes called ¹⁵ homeotic genes determine what body parts—antennae, legs, and so on—will develop in each segment. For example, one set of homeotic genes causes ¹⁶ antennae to develop on the head of the fly and ¹⁷ wings on the thorax. Errors in homeotic genes produce ¹⁸ mutant flies with spectacular changes in body structure, such as extra pairs of wings, or heads bearing legs instead of antennae.

How can a researcher know which genes are expressed and which are inactive in particular cells during particular stages of development? One way is to analyze the activity of genes in different cells using a DNA ¹⁹ microarray, also called a DNA chip or gene chip. This is a glass slide that can hold many different ²⁰ single-stranded DNA fragments in a checkerboard array. Each DNA segment on the chip is obtained from a particular gene. There may be thousands of DNA sequences on the chip, perhaps representing every gene in the organism's genome!

To find out which genes are active in a particular cell, for example, a fruit fly follicle cell, a researcher collects all the different mRNAs transcribed by that kind of cell.

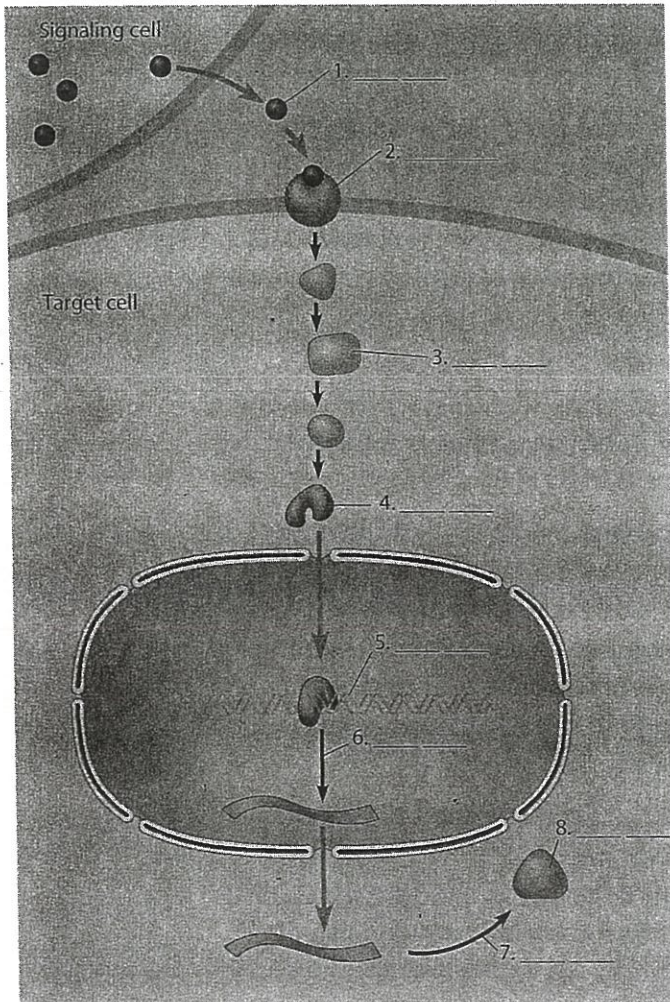
This collection of mRNAs is mixed with ²¹ reverse transcriptase enzyme, which produces a mix of DNA fragments called copy DNAs or ²² cDNAs. These cDNAs are modified so they will fluoresce, or glow. Then a small amount of the cDNA mixture from the cell in question (the follicle cell in this example) is added to each of the DNA fragments on the chip. If a molecule in the cDNA mixture is ²³ complementary to a DNA fragment at a particular spot on the chip, it will bind to it. After nonbinding DNA is rinsed away, the pattern of glowing spots enables the researcher to identify which genes are being ²⁴ transcribed in the cells from which the mRNA was obtained. In this way, one can find out which genes are active in different parts of the organism during different stages in development.

DNA microarrays are valuable tools in other areas of research and medicine. For example, a DNA chip can test for many different kinds of infectious bacteria at one time, or distinguish among different subtypes of ²⁵ leukemia based on the activity of 17 genes.

Exercise 6 (Modules 11.10–11.11)

Cell signaling systems evolved early in the history of life, and the signal transduction pathways of many organisms, from microorganisms to multicellular eukaryotes, show many common features. Review signal transduction by matching each of the parts and processes in the diagram below with its name (A–H) and description (P–W).

#1: H, R
 #2: D, W
 #3: B, S
 #4: E, V
 #5: C, Q
 #6: A, U
 #7: F, P
 #8: G, T



Names

- A. Transcription
- B. Relay protein
- C. Gene
- D. Receptor protein
- E. Transcription factor
- F. Translation
- G. New protein
- H. Signal molecule

Descriptions

- P. Making a new protein
- Q. Information for making target cell protein
- R. Binds to receptor
- S. Conducts message within target cell
- T. Carries out new function in target cell
- U. Synthesis of specific mRNA coding for new protein
- V. When activated, it binds to DNA and "turns on" a gene
- W. Receives signal molecule

Exercise 7 (Modules 11.12–11.15)

Cloning demonstrates 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 treating disease. Review cloning and stem cells by matching each phrase with a term from the list on the right.

- | | | |
|---------------|--|----------------------------|
| <u>F</u> | 1. Partially differentiated cells present in mature animals | A. Reproductive cloning |
| <u>A</u> | 2. Producing genetically identical organisms for agriculture, research, or saving endangered species | B. Nuclear transplantation |
| <u>J</u> | 3. Naturally occurring animal or human clones | C. Differentiation |
| <u>D</u> | 4. Cells that give rise to all specialized cells in the body | D. Embryonic stem cells |
| <u>G</u> | 5. Regrowth of lost body parts | E. Dedifferentiation |
| <u>C</u> | 6. The process of cell specialization | F. Adult stem cells |
| <u>E</u> | 7. Ability of adult cell to reverse specialization | G. Regeneration |
| <u>I</u> | 8. Growing cells for replacement or repair of damaged or diseased organs | H. Clones |
| <u>H or J</u> | 9. Genetically identical organisms | I. Therapeutic cloning |
| <u>B</u> | 10. Replacing the nucleus of an egg or zygote with a nucleus from a differentiated cell | J. Identical twins |

Exercise 8 (Modules 11.16–11.19)

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

In the United States, lung cancer kills about 160,000 people per year. Long one of the most common kinds of cancer in men, lung cancer has passed breast cancer to become the most frequent cancer in women.

Cancer is uncontrolled multiplication of cells. Cancer cells have escaped from the normal ¹ control systems responsible for regulating cell ² division. Cancer cells form abnormal masses called tumors, which displace nearby normal tissues and can spread through the body. The cell changes that lead to cancer are caused by accumulated ³ mutations in genes that ⁴ stimulate cell division and other genes that ⁵ inhibit cell division.

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 ⁶ carcinogens. 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 was paralleled by a rise in lung cancer rates. Tobacco has also been linked to other forms of cancer, such as cancer of the mouth and throat. Chemicals in tobacco smoke act as ⁷ mutagens, triggering mutations in lung cells exposed to the smoke.

Scientists have learned a lot about the cellular mechanisms of cancer by studying cancers caused by viruses in humans and other animals. Researchers were surprised to find that cancer-causing viruses carry cancer-causing genes, called ⁸ oncogenes, 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 normal genes, called ⁹ proto-oncogenes usually code for proteins called ¹⁰ growth factors—which normally stimulate cell ¹¹ division, or for other proteins that affect the cell cycle. Most cancers seem to begin with a ¹² mutation in a proto-oncogene in a body (somatic) cell, turning it into an oncogene. The altered gene may produce a hyperactive growth stimulating protein, or an ¹³ excess of the normal protein.

Changes in genes whose products normally inhibit cell division—so-called ¹⁴ tumor-suppressor genes—also contribute to the development of cancer. One kind of tumor-suppressor gene acts to ¹⁵ repair damaged DNA. Others work through signal-transduction pathways to create inhibitory proteins. It appears that it takes at least ¹⁶ one active oncogene and the mutation or loss of ¹⁷ several tumor-suppressor genes for a cell to become fully cancerous. This may explain why the likelihood of cancer increases with ¹⁸ age.

Generally, the normal products of proto-oncogenes and tumor-suppressor genes are involved in ¹⁹ signal-transduction pathways. Normally, the ²⁰ protein product of a proto-oncogene (such as one called *ras*) might act to conduct a signal from a ²¹ growth factor to the interior of a cell, activating a gene that makes a protein that causes ²² cell division to occur. When the proto-oncogene mutates into an oncogene, it might produce a hyperactive protein that signals an increase in cell division even in the ²³ absence of the growth factor.

Cell division can also be affected by a mutant tumor-suppressor gene. The tumor suppressor gene *p53* produces a protein that acts as a ²⁴ transcription factor, which normally acts at the end of a pathway that promotes production of a protein that blocks cell division. A mutation in *p53* could produce a defective transcription factor, which cannot trigger transcription. In this case, the inhibitory protein is not transcribed, allowing an ²⁵ increased rate of cell division.

We are beginning to understand the genetic and cellular changes that cause cancer to develop. Lifestyle choices can decrease the chances of developing cancer. Regular ²⁶ exams can detect tumors early and increase the chances for successful treatment. Not ²⁷ smoking, avoiding overexposure to the ²⁸ sun, and a ²⁹ high-fiber, low-³⁰ fat diet all reduce cancer risk.

Exercise 9 (Module 11.19)

After reading this module, match each of the following human cancers with the correct associated risk factor(s). Some answers are used more than once.

- | | |
|------------------------------|---|
| <u>C</u> 1. Lung | A. Ultraviolet light |
| <u>F</u> 2. Colon and rectum | B. African heritage, possibly dietary fat |
| <u>D</u> 3. Breast | C. Tobacco smoke |
| <u>B</u> 4. Prostate | D. Estrogen |
| <u>C</u> 5. Urinary bladder | E. Alcohol; hepatitis viruses |
| <u>C</u> 6. Kidney | F. High dietary fat, tobacco smoke, alcohol |
| <u>G</u> 7. Lymphomas | G. Viruses (some types) |
| <u>A</u> 8. Melanoma (skin) | |
| <u>E</u> 9. Liver | |
| <u>D</u> 10. Uterus | |

