CHAPTER 11 REVIEW

Go to the Campbell Biology website (www.campbellbiology.com) to explore an interactive version of the Chapter Review.

Summary of Key Concepts

AN OVERVIEW OF CELL SIGNALING

- **Cell signaling evolved early in the history of life (pp. 197–198, FIGURES 11.1, 11.2)** The evidence is that signaling in microbes has much in common with the process in multicellular organisms.
- **Communicating cells may be close together or far apart (p. 199, FIGURES 11.3, 11.4)** Animal cells signal with nearby cells by secreting local regulators or, if nerve cells, by secreting neurotransmitters at synapses. Both animal and plant cells use hormones for signaling over long distances. Cells can also communicate by direct contact.

  Web/CD **Case Study in the Process of Science:** *How Do Cells Communicate with Each Other?*
- **The three stages of cell signaling are reception, transduction, and response (pp. 200–201, FIGURE 11.5)** Earl Sutherland discovered how the hormone epinephrine acts on cells. The signal molecule epinephrine binds to receptors on a cell's surface (reception), leading to a series of changes in the receptor and other molecules inside the cell (transduction) and finally to the activation of an enzyme that breaks down glycogen (response).

  Web/CD **Activity 11A:** *Overview of Cell Signaling*

SIGNAL RECEPTION AND THE INITIATION OF TRANSDUCTION

- **A signal molecule binds to a receptor protein, causing the protein to change shape (p. 201)** The binding between signal molecule (ligand) and receptor is highly specific. A conformational change in a receptor is often the initial transduction of the signal.
- **Most signal receptors are plasma membrane proteins (pp. 201–204, FIGURES 11.6, 11.8, 11.9, 11.10)** A G-protein-linked receptor is a membrane receptor that works with the help of a cytoplasmic G protein. Ligand binding activates the receptor, which then activates a specific G protein, which activates yet another protein in a signal-transduction pathway. Epinephrine uses this sort of receptor.

  Tyrosine-kinase receptors react to the binding of signal molecules by forming dimers and then adding phosphate groups to tyrosines on the cytoplasmic side of the receptor. Relay proteins in the cell can then be activated by binding to different phosphorylated tyrosines, allowing this receptor to trigger several pathways at once. Growth factors commonly use tyrosine-kinase receptors.

  Specific signal molecules cause ligand-gated ion channels in a membrane to open or close, regulating the flow of specific ions.

  Intracellular receptors are cytosolic or nuclear proteins. Signal molecules that can readily cross the plasma membrane, such as steroid hormones and nitric oxide, use these receptors.

  Web/CD **Activity 11B:** *Reception*

SIGNAL-TRANSDUCTION PATHWAYS

- **Pathways relay signals from receptors to cellular responses (pp. 204–205)** At each step in a pathway, the signal is transduced into a different form, commonly a conformational change in a protein.
- **Protein phosphorylation, a common mode of regulation in cells, is a major mechanism of signal transduction (pp. 205–206, FIGURE 11.11)** Many signal-transduction pathways include phosphorylation cascades, in which a series of protein kinases successively add phosphate groups to the next one in line, activating it. Phosphatase enzymes soon remove the phosphates.
- **Certain small molecules and ions are key components of signaling pathways (second messengers) (pp. 206–209, FIGURES 11.12, 11.13, 11.14, 11.15)** Second messengers, such as cyclic AMP (cAMP) and Ca^{2+}, diffuse readily through the cytosol and thus help broadcast signals quickly. Many G proteins activate adenylyl cyclase, which makes cAMP from ATP. Although continually present in the fluids of organisms, Ca^{2+} can serve as a messenger because protein pumps usually keep it at low concentrations in the cytosol. Many G proteins and tyrosine-kinase receptors activate an enzyme that splits a plasma membrane phospholipid into two second messengers, one of which is inositol trisphosphate (IP_3). IP_3 is the ligand for a gated calcium channel in the membrane of the ER, which stores Ca^{2+} at high concentrations. When IP_3 binds, Ca^{2+} flows into the cytosol, where it activates proteins of many signaling pathways.

  Web/CD **Activity 11C:** *Signal-Transduction Pathways*

CELLULAR RESPONSES TO SIGNALS

- **In response to a signal, a cell may regulate activities in the cytoplasm or transcription in the nucleus (pp. 209–210, FIGURES 11.16, 11.17)** For example, signaling pathways regulate enzyme activity and cytoskeleton rearrangement in the cytoplasm. Other pathways regulate genes; they do this by activating transcription factors, proteins that turn specific genes on or off.

  Web/CD **Activity 11D:** *Cellular Responses*
  Web/CD **Activity 11E:** *Build a Signaling Pathway*
- **Elaborate pathways amplify and specify the cell's response to signals (pp. 210–212, FIGURE 11.18)** Each catalytic protein in a signaling pathway amplifies the signal by activating multiple copies of the next component of the pathway; for long pathways, the total amplification may be a millionfold or more. The particular combination of proteins in a cell gives the cell great specificity in both the signals it detects and the responses it carries out. Scaffolding proteins can increase signal-transduction efficiency by holding multiple components of a pathway together. Pathway branching and cross-talk further help the cell coordinate signals and responses.

Self-Quiz

1. Phosphorylation cascades involving a series of protein kinases are useful for cellular signal transduction because
   a. they are species specific.
   b. they always lead to the same cellular response.
   c. they amplify the original signal many fold.
   d. they counter the harmful effects of phosphatases.
   e. the number of molecules used is small and fixed.

2. Binding of a signal molecule to which type of receptor leads to a change in membrane potential?
   a. tyrosine-kinase receptor
   b. G-protein-linked receptor
   c. phosphorylated tyrosine-kinase dimer
   d. ligand-gated ion channel
   e. intracellular receptor

3. The activation of tyrosine-kinase receptors is characterized by
   a. aggregation and phosphorylation.
   b. IP_3 binding.
   c. calmodulin formation.
   d. GTP hydrolysis.
   e. channel protein conformational change.

4. Cell signaling is believed to have evolved early in the history of life because
   a. it is seen in "primitive" organisms such as bacteria.
   b. yeast cells of different mating types signal one another.
   c. signal-transduction molecules found in distantly related organisms are similar.
   d. signaling can operate over large distances, a function required before the development of multicellular life.
   e. signal molecules typically interact with the outer surface of the plasma membrane.

5. Which observation suggested to Sutherland the involvement of a second messenger in epinephrine's effect on liver cells?
   a. Enzymatic activity was proportional to the amount of calcium added to a cell-free extract.
   b. Receptor studies indicated epinephrine was a ligand.
   c. Glycogen depolymerization was observed only when epinephrine was administered to intact cells.
   d. Glycogen depolymerization was observed when epinephrine and glycogen phosphorylase were combined.
   e. Epinephrine was known to have different effects on different types of cells.

6. Protein phosphorylation is commonly involved with all of the following *except*
   a. regulation of transcription by extracellular signal molecules.
   b. enzyme activation.
   c. activation of G-protein-linked receptors.
   d. activation of tyrosine-kinase receptors.
   e. activation of protein-kinase molecules.

7. Amplification of a chemical signal occurs when
   a. a receptor in the plasma membrane activates several G-protein molecules while a signal molecule is bound to it.
   b. a cAMP molecule activates one protein-kinase molecule before being converted to AMP.
   c. phosphorylase and phosphatase activities are balanced.
   d. numerous calcium ions flow through an open ligand-gated calcium channel.
   e. both a and d occur.

8. Lipid-soluble signal molecules, such as testosterone, cross the membranes of all cells but affect only target cells because
   a. only target cells retain the appropriate DNA segments.
   b. intracellular receptors are present only in target cells.
   c. most cells lack the Y chromosome required.
   d. only target cells possess the cytosolic enzymes that transduce the testosterone.
   e. only in target cells is testosterone able to initiate the phosphorylation cascade leading to activated transcription factor.

9. Signal-transduction pathways benefit cells for all of the following reasons *except*
   a. they help cells respond to signal molecules that are too large or too polar to cross the plasma membrane.
   b. they enable different cells to respond appropriately to the same signal.
   c. they help cells use up phosphate generated by ATP breakdown.
   d. they can amplify a signal.
   e. variations in the signal-transduction pathways can enhance response specificity.

10. Consider this pathway: epinephrine ⟶ G-protein-linked receptor ⟶ G protein ⟶ adenylyl cyclase ⟶ cAMP. Identify the "second messenger."
    a. cAMP
    b. G protein
    c. GTP
    d. adenylyl cyclase
    e. G-protein-linked receptor

11. How do the cellular receptors for water-soluble hormones and lipid-soluble hormones differ?

12. The addition of norepinephrine (a water-soluble hormone) to the solution bathing thyroid cells in culture causes an increase in cytosolic Ca^{2+} levels and the release of thyroxine (another hormone) by these cells. What is the likely mechanism of this effect?

13. In Question 12, would injection of norepinephrine into these cells have the same effect? Explain your answer.

14. How can a target cell's response to a hormone be amplified more than a millionfold?

15. When a signal-transduction pathway involves a phosphorylation cascade, how does the cell's response get turned off?

Go to the website or CD-ROM for more quiz questions.

Evolution Connection

You learned in this chapter that cell-cell signaling is thought to have arisen early in the history of life, because the same mechanisms of signaling are found in distantly related organisms. But why hasn't some "better" mechanism arisen? Is it too difficult to evolve wholly new signaling mechanisms, or are existing mechanisms simply adequate and therefore maintained? Put another way, need superior signaling mechanisms necessarily evolve if existing mechanisms are adequate and effective? Why or why not?

The Process of Science

Cell biologists recently reported the discovery of orexin, a signaling molecule that appears to regulate appetite in humans and other mammals. Orexin concentrations were measurably higher in fasting individuals. Using your knowledge of membrane receptors and signal-transduction pathways, suggest ways in which the understanding of orexin function could lead to treatments for both anorexia and obesity.

Determine the chemical nature of the molecule used for cell communication in the cellular slime mold in the Case Study in the Process of Science, available on the website and CD-ROM.

Science, Technology, and Society

The aging process is thought to be initiated at the cellular level. Among the changes that can occur after a certain number of cell divisions is the loss of a cell's ability to respond to growth factors and other chemical signals. Much research into aging is aimed at understanding such losses, with the ultimate goal of significantly extending the human life span. Not everyone, however, agrees that this is a desirable goal. If life expectancy were greatly increased, what might be the social and ecological consequences? How might we cope with these?

Answers to Self-Quiz: 1. c; 2. d; 3. a; 4. c; 5. c; 6. c; 7. a; 8. b; 9. c; 10. a; 11. Receptors for water-soluble hormones are in the plasma membrane; those for lipid-soluble hormones are inside the cell. 12. Signaling via a plasma membrane receptor, phospholipase C, and IP_3 opens ER channels that release Ca^{2+} into the cytosol; the Ca^{2+} triggers thyroxine release. 13. No, because norepinephrine must bind to the extracellular side of its receptor to activate the signal-transduction pathway. 14. By a cascade of sequential activations in which some of the steps activate numerous molecules. 15. Protein phosphatases reverse the effects of the kinases.

CHAPTER 12 REVIEW

Go to the Campbell Biology website (www.campbellbiology.com) to explore an interactive version of the Chapter Review.

Summary of Key Concepts

THE KEY ROLES OF CELL DIVISION

- **Cell division functions in reproduction, growth, and repair** (p. 215, FIGURE 12.1) Unicellular organisms reproduce by cell division. Multicellular organisms depend on it for development from a fertilized egg, growth, and repair.
- **Cell division distributes identical sets of chromosomes to daughter cells** (pp. 216–217) Eukaryotic cell division consists of mitosis (division of the nucleus) and cytokinesis (division of the cytoplasm). DNA is partitioned among chromosomes, making it easier for the eukaryotic cell to replicate and distribute its huge amounts of DNA. Chromosomes consist of chromatin, a complex of DNA and protein that condenses during mitosis. When chromosomes replicate, they form identical sister chromatids. The chromatids separate during mitosis, becoming the chromosomes of the new daughter cells.

  Web/CD Activity 12A: *Roles of Cell Division*

THE MITOTIC CELL CYCLE

- **The mitotic phase alternates with interphase in the cell cycle: *an overview*** (p. 217, FIGURES 12.4, 12.5) Mitosis and cytokinesis make up the M (mitotic) phase of the cell cycle. Between divisions, cells are in interphase: the G_1, S, and G_2 phases. The cell grows throughout interphase, but DNA is replicated only during the S (synthesis) phase. Mitosis is a continuous process, often described as occurring in five stages: prophase, prometaphase, metaphase, anaphase, and telophase.

  Web/CD Activity 12B: *The Cell Cycle*

- **The mitotic spindle distributes chromosomes to daughter cells: *a closer look*** (pp. 220–221, FIGURE 12.6) The mitotic spindle is an apparatus of microtubules that controls chromosome movement during mitosis. The spindle arises from the centrosomes, organelles near the nucleus that in animal cells include centrioles. Spindle microtubules attach to the kinetochores of chromatids and move the chromosomes to the metaphase plate. In anaphase, sister chromatids separate and move toward opposite poles of the cell. Using motor proteins, each kinetochore moves along shortening microtubules. Meanwhile, nonkinetochore microtubules from opposite poles slide past each other, elongating the cell. In telophase, daughter nuclei form at opposite ends of the cell.
- **Cytokinesis divides the cytoplasm: *a closer look*** (pp. 221–222, FIGURE 12.8) Mitosis is usually followed by cytokinesis, involving cleavage furrows in animals and cell plates in plants.

  Web/CD Activity 12C: *Mitosis and Cytokinesis Animation*
  Web/CD Activity 12D: *Mitosis and Cytokinesis Video*
  Web/CD Case Study in The Process of Science: *How Much Time Do Cells Spend in Each Phase of Mitosis?*
- **Mitosis in eukaryotes may have evolved from binary fission in bacteria** (pp. 223–224, FIGURES 12.10, 12.11) During binary fission, the two daughter bacterial chromosomes actively move apart by a mechanism that is not yet understood.

REGULATION OF THE CELL CYCLE

- **A molecular control system drives the cell cycle** (pp. 224–227, FIGURES 12.13–12.14) Cyclic changes in regulatory proteins work as a mitotic clock. The key molecules are cyclin dependent kinases, complexes of cyclins (whose concentrations build during the cell cycle) and specific protein kinases that are only active when combined with cyclin.
- **Internal and external cues help regulate the cell cycle** (pp. 227–228, FIGURE 12.15) Cell culture has enabled researchers to study the molecular details of cell division. Both internal signals, such as those emanating from kinetochores not yet attached to the spindle, and external signals, such as growth factors, control the cell cycle checkpoints via signal-transduction pathways. Growth factor depletion explains density-dependent inhibition.
- **Cancer cells have escaped from cell cycle controls** (p. 228–229, FIGURES 12.16, 12.17) Cancer cells elude normal regulation and divide out of control, forming tumors. Malignant tumors invade surrounding tissues and can metastasize, exporting cancer cells to other parts of the body.

  Web/CD Activity 12E: *Causes of Cancer*

Self-Quiz

1. During the cell cycle, increases in the enzymatic activity of protein kinases are due to
   a. kinase synthesis by ribosomes.
   b. activation of inactive kinase by binding to cyclin.
   c. conversion of inactive cyclin to the active kinase by means of phosphorylation.
   d. cleavage of the inactive kinase molecules by cytoplasmic proteases.
   e. a decline in external growth factors to a concentration below the inhibitory threshold.

2. Through a microscope, you can see a cell plate beginning to develop across the middle of the cell and nuclei re-forming at opposite poles of the cell. This cell is most likely
   a. an animal cell in the process of cytokinesis.
   b. a plant cell in the process of cytokinesis.
   c. an animal cell in the S phase of the cell cycle.
   d. a bacterial cell dividing.
   e. a plant cell in metaphase.

3. Vinblastine is a standard chemotherapeutic drug used to treat cancer. Since it interferes with the assembly of microtubules, its effectiveness must be related to
   a. disruption of mitotic spindle formation.
   b. inhibition of regulatory protein phosphorylation.
   c. suppression of cyclin production.
   d. myosin denaturation and inhibition of cleavage furrow formation.
   e. inhibition of DNA synthesis.

4. A particular cell has half as much DNA as some of the other cells in a mitotically active tissue. The cell in question is most likely in
   a. G_1.
   b. G_2.
   c. prophase.
   d. metaphase.
   e. anaphase.

5. One difference between a cancer cell and a normal cell is that
   a. the cancer cell is unable to synthesize DNA.
   b. the cell cycle of the cancer cell is arrested at the S phase.
   c. cancer cells continue to divide even when they are tightly packed together.
   d. cancer cells cannot function properly because they suffer from density-dependent inhibition.
   e. cancer cells are always in the M phase of the cell cycle.

6. The decline of MPF at the end of mitosis is caused by
   a. the destruction of the protein kinase (Cdk).
   b. decreased synthesis of cyclin.
   c. the enzymatic destruction of cyclin.
   d. synthesis of DNA.
   e. an increase in the cell's volume-to-genome ratio.

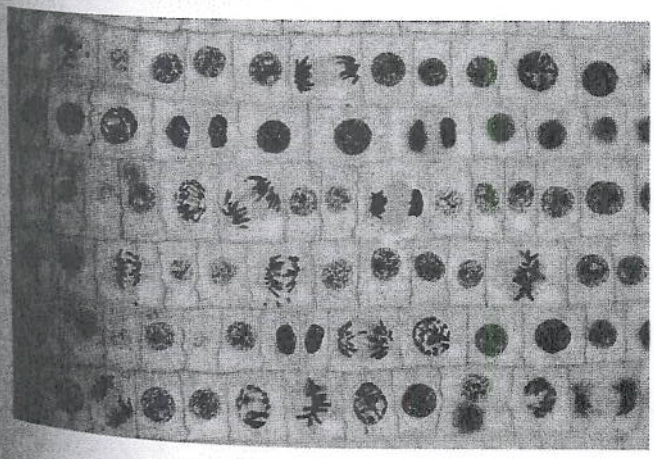
7. A red blood cell (RBC) has a 120-day life span. If an average adult has 5 L (5,000 cm^3) of blood and each cubic millimeter contains 5 million RBCs, how many new cells must be produced each second to replace the entire RBC population?
   a. 30,000
   b. 2,400
   c. 2,400,000
   d. 18,000
   e. 30,000,000

8. In function, the plant cell structure that is analogous to an animal cell's cleavage furrow is the
   a. chromosome.
   b. cell plate.
   c. nucleus.
   d. centrosome.
   e. spindle apparatus.

9. In some organisms, mitosis occurs without cytokinesis occurring. This will result in
   a. cells with more than one nucleus.
   b. cells that are unusually small.
   c. cells lacking nuclei.
   d. destruction of chromosomes.
   e. cell cycles lacking an S phase.

10. Which of the following does *not* occur during mitosis?
    a. packaging of the chromosomes
    b. replication of the DNA
    c. separation of sister chromatids
    d. spindle formation
    e. separation of the centrosomes

11. In the light micrograph below of dividing cells near the tip of an onion root, identify a cell in each of the following stages: interphase, prophase, metaphase, and anaphase. Describe the major events occurring at each stage.



12. Starting with a fertilized egg (zygote), a series of five cell divisions would produce an early embryo with how many cells?
13. Based on what you've read in this chapter, list three similarities between bacterial chromosomes and eukaryotic chromosomes. Consider both chromosome structure and chromosome behavior during cell division.
14. When would a chromosome consist of two identical chromatids?
15. A researcher treats cells with a chemical that prevents DNA synthesis from starting. This treatment traps the cells in which part of the cell cycle?

Go to the website or CD-ROM for more quiz questions.

Evolution Connection

During the mitotic cell cycle, cells double their chromosomes and then return to their original state by mitosis and cell division. The result is that the daughter cells end up with the same number of chromosomes as the parent cell had. Another way to maintain the number of chromosomes would be to carry out cell division first and then replicate the chromosomes in each daughter cell. What would be the problems with this alternative? Or do you think it would be an equally good way of organizing the cell cycle?

The Process of Science

Microtubules are polar structures in that one end (called the "+" end) polymerizes and depolymerizes at a much higher rate than the other end (the "−" end). The experiment shown in FIGURE 12.7 clearly identifies these two ends.

a. From the results, identify the "+" end and explain your reasoning.
b. If the opposite end were the "+" end, redraw part 3 of FIGURE 12.7b to show what the result would have been.
c. Redesign the model in FIGURE 12.7a to reflect these new data.

In the Case Study in the Process of Science on the CD-ROM and website, count cells in different phases of the cell cycle to calculate the percentage of time these cells spend in each phase.

Science, Technology, and Society

Hundreds of millions of dollars are spent each year in the search for effective treatments for cancer; far less money is spent on preventing cancer. Why do you think this is true? What kinds of lifestyle changes could we make to help prevent cancer? What kinds of prevention programs could be initiated or strengthened to encourage these changes? What factors might impede such changes and programs?

Answers: 1. b; 2. b; 3. a; 4. a; 5. c; 6. c; 7. c; 8. b; 9. a; 10. b 11. See Figure 12.5. 12. 32 cells. 13. Each type of chromosome consists of a single molecule of DNA with attached proteins. If stretched out, the molecule of DNA would be many times longer than the cell in which it resides. During cell division, the two copies of a chromosome actively move apart, and one ends up in each of the two daughter cells. 14. After the chromosome replicates during S phase of interphase, throughout G_2, and during prophase, prometaphase, and metaphase of mitosis. 15. G_1