

# 10

## Cell Communication and Signaling

### Learning Objectives

In this chapter, you will learn:

- Types of Cell Signaling
- Signal Transduction
- Disruptions in Signal Transduction Pathways
- Feedback Mechanisms

### Overview

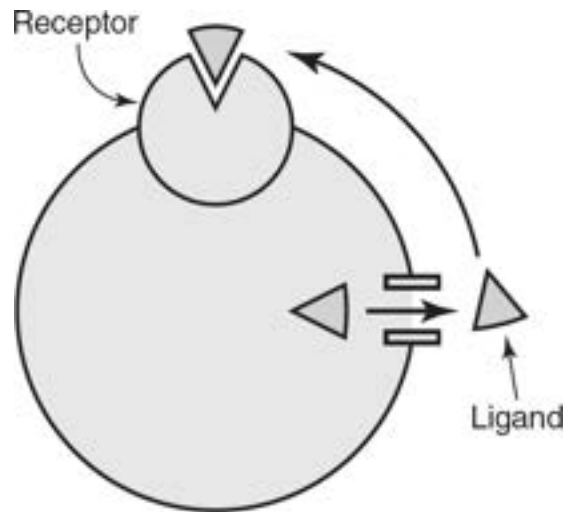
Biological systems interact, exchange information about their environments, and respond to this information. Life often depends on responding quickly to changing environmental conditions. This chapter reviews the basics of cell communication and the process of signal transduction.

### Types of Cell Signaling

The survival of a living organism depends on the ability of its cell, or cells, to communicate by sending, receiving, and responding to chemical signals. These chemical signals are called **ligands**. Figures 10.1–10.4 show four general types of cell signaling:

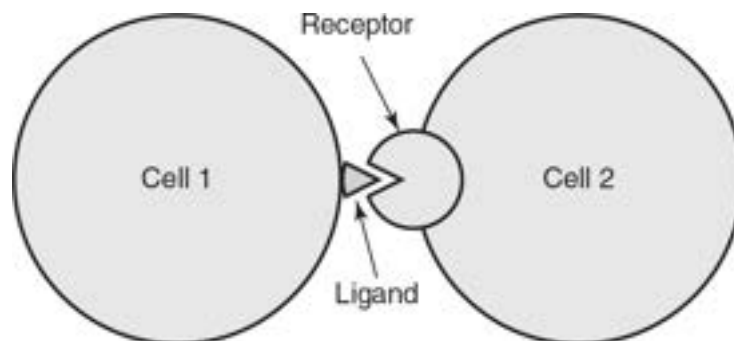
1. **Autocrine signaling**—In autocrine signaling, the cell secretes a ligand. This ligand then binds to a receptor on the cell that secreted the ligand, triggering a response within that same cell. The root word

*auto* means “self,” so this process can be thought of as a cell signaling itself to generate a response. An example of this is a cancer cell, which releases its own growth hormones (the ligands) that stimulate the cancer cell to grow and divide.



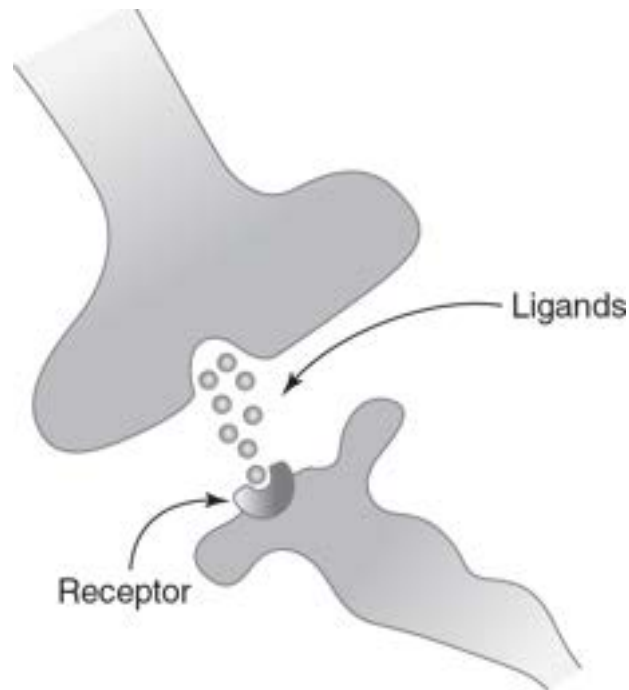
**Figure 10.1** Autocrine Signaling

- 2. Juxtacrine signaling**—This is signaling that depends on direct contact between the cell that is sending the ligand and the cell that is receiving and responding to it via a surface receptor. Examples of juxtacrine signaling include plasmodesmata in plants (which involve the ligand traveling between channels that connect adjacent cells) and antigen-presenting cells in the human immune system (which signal helper T cells through direct cell-to-cell contact).



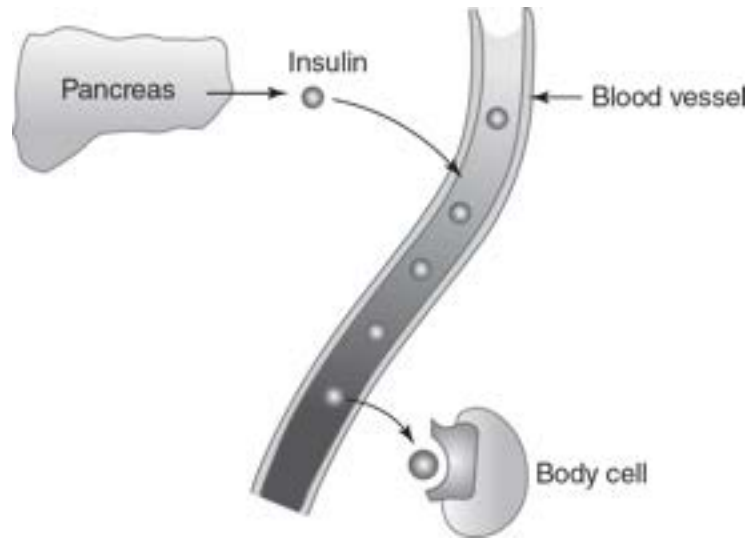
**Figure 10.2** Juxtacrine Signaling

- 3. Paracrine signaling**—In paracrine signaling, the cell secretes a ligand that travels a short distance, eliciting an effect on cells in the nearby area. These ligands are sometimes referred to as local regulators since they only affect cells in the immediate vicinity of the cell that is sending the signals. Neurotransmitters are local regulators that travel the short distance across a synapse to communicate with nearby cells.



**Figure 10.3** Paracrine Signaling

- 4. Endocrine signaling**—Some ligands travel a long distance between the sending and receiving cells; this is called endocrine signaling. Ligands that travel a long distance are called **hormones**. Insulin, a hormone that is produced and released by the pancreas, travels through the circulatory system to trigger responses in cells all over the body.



**Figure 10.4** Endocrine Signaling

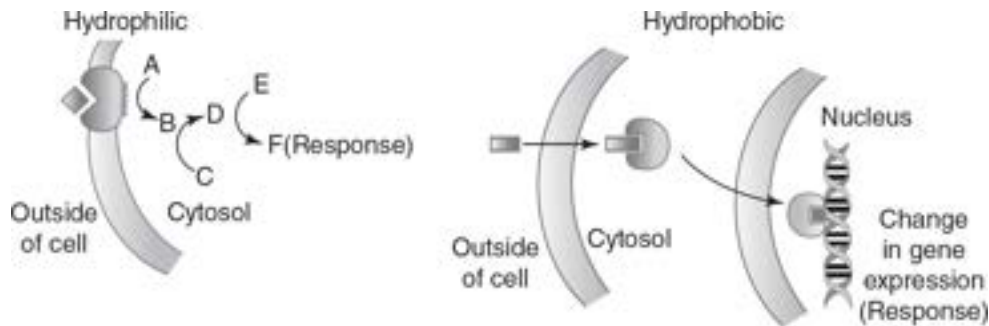
There are many examples of endocrine signaling in everyday life. For example, the hormone ethylene can travel through the air to trigger the ripening of fruits. Another example is the release of hormones called pheromones into the air by some animals and moths, which help them locate and attract mates over long distances.

## Signal Transduction

**Signal transduction** determines how a cell responds internally to a signal in its environment. Important processes, such as gene expression, cell growth and division, and the release of hormones, depend on signal transduction.

Signal transduction begins with a chemical message or **ligand**. Ligands interact with specific **target cells**, which respond to the presence of the ligand. Ligands may be hydrophilic or hydrophobic. Hydrophilic ligands cannot cross the phospholipid bilayer of the cell membrane and enter the cell. Consequently, hydrophilic ligands interact with receptors located on the cell membrane (**cell membrane receptors**), as shown in [Figure 10.5](#). The binding of the ligand to the cell membrane receptor then triggers a series of chemical reactions inside the cell (the series of chemical reactions are shown as  $A \rightarrow B$ ,  $C \rightarrow D$ , and  $E \rightarrow F$  in [Figure 10.5](#)). Hydrophobic ligands may enter the cell by sliding between the phospholipids of the cell

membrane. These hydrophobic ligands then bind to **intracellular receptors** in the cytosol of the cell, as shown in [Figure 10.5](#). Once bound to the intracellular receptor, the ligand can then cross the nuclear membrane and bind to DNA in the nucleus, changing the expression of genes.



**Figure 10.5** Hydrophilic Ligands vs. Hydrophobic Ligands

Signal transduction has three major steps:

1. **Reception:** The ligand binds to a specific receptor on or in the target cell. The receptor may be located on the cell membrane (as is the case for hydrophilic ligands) or in the cytosol of the target cell (as is the case for hydrophobic ligands). Receptors contain ligand-specific binding domains. If a cell does not have the receptor for a specific ligand, the cell will not respond to that ligand. Upon the binding of the ligand to the receptor, the receptor undergoes a conformational (shape) change, which triggers the next step in the process on the inside of the cell. Examples of receptors include G-protein-coupled receptors and receptor tyrosine kinases.
2. **Transduction:** This is the series of chemical reactions (triggered by the binding of the ligand to its receptor) that helps the cell choose the appropriate response. This is often the most complicated part of signal transduction. Possible components of transduction include:
  - Signaling cascades, a series of chemical reactions in which one molecule activates multiple molecules, amplifying the cell's response to a signal (a process called **signal amplification**)
  - **Kinases**, which can transfer phosphate groups to other molecules (which activates those molecules)

- **Phosphatases**, which can remove phosphate groups from other molecules (which inactivates those molecules)
  - Enzymes, which produce **secondary messengers**; an example of this is the enzyme **adenylyl cyclase**, which produces the secondary messenger cyclic AMP (cAMP) from ATP
- 3. Response:** This is the final step of signal transduction and the ultimate result generated by the ligand. Examples of cellular responses include the activation of genes by steroid hormones, the opening of ligand-gated ion channels, and the initiation of cell processes, such as apoptosis (programmed cell death).

## Disruptions in Signal Transduction Pathways

**Signal transduction pathways** refer to the series of chemical reactions that mediate the sensing and processing of stimuli. Disruptions in signal transduction pathways can have profound effects on cells. Since receptors are specific to certain ligands, a mutation in a gene that is coding for a receptor protein could result in a change in shape of the receptor such that it would no longer bind to its specific ligand. Without a functional receptor for the ligand, the cell with the mutated receptor protein would no longer be able to respond to the ligand. Examples of disorders caused by mutations in receptor proteins include androgen insensitivity syndrome (AIS), in which the receptor for testosterone is nonfunctional in gonadal tissue (causing it not to form into gonads during embryonic development), and nephrogenic diabetes insipidus (NDI), in which portions of the structure of the kidneys are insensitive to antidiuretic hormone (ADH) and urine production is affected.

Signal transduction pathways may also be disrupted when molecules in the environment interfere with a ligand's ability to bind to its receptor. For example, the cholera toxin binds to G-protein-coupled receptors in the cell membrane, leading to disruptions in a cell signaling pathway that can cause life-threatening dehydration.

Mutations in the gene for adenylyl cyclase can interfere with a cell's ability to produce the secondary messenger cAMP, disrupting all steps in the signal transduction process that are dependent on that secondary messenger. A disruption to any step in the signal transduction process will affect not only

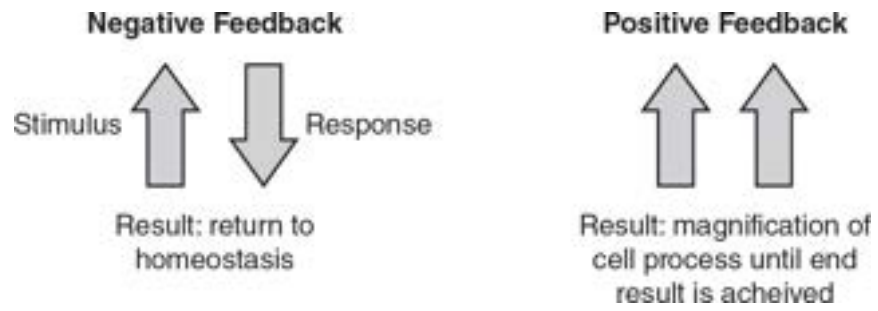
that step but will also affect any subsequent steps in the process that are dependent on the products of the previous steps.

## Feedback Mechanisms

Feedback mechanisms are important to living organisms because they help living organisms respond to changes in the environment while maintaining the internal environment of the cell. (See [Figure 10.6](#).) Cell communication and signaling are crucial in feedback mechanisms.

**Negative feedback** returns a system to its original condition and helps maintain **homeostasis** (the maintenance of a stable state). For example, if the body temperature becomes too elevated, cell signaling processes will trigger skin cells to release sweat, which will cool the body and help return it to its normal body temperature. Another example of negative feedback is the control of blood glucose levels by insulin and glucagon. After a sugary snack, if blood sugar levels get too high, the pancreas releases the ligand (hormone) insulin, which causes body cells to absorb glucose from the blood, returning blood glucose levels to the normal range. Conversely, if blood sugar levels get too low, the pancreas releases the ligand (hormone) glucagon, which stimulates liver cells to break down glycogen into glucose, releasing glucose into the blood and again returning blood glucose levels to the normal range. Since insulin and glucagon travel long distances in the bloodstream, this is an example of endocrine signaling.

**Positive feedback** magnifies cell processes. For example, the hormone oxytocin stimulates contractions of the uterine muscles in labor contractions during childbirth. The contraction of the uterine muscles triggers the production of even more oxytocin, which in turn increases the contractions of the uterine muscles. This positive feedback process causes labor contractions to amplify, getting stronger and stronger during childbirth.



**Figure 10.6** Negative Feedback vs. Positive Feedback

# Practice Questions

## Multiple-Choice

1. Auxin is a plant hormone that triggers cell division. A mutation occurs that deletes the gene for the auxin receptor. Which of the following is the most likely result of this mutation?
  - (A) The cells will still divide but at a faster rate.
  - (B) The cells will not be able to divide.
  - (C) The cells will develop a new receptor for the signaling molecule.
  - (D) The cells will not be affected by the lack of the auxin receptor.
2. Cortisol is a hormone produced in response to stress. Hunger is a stressor that can increase cortisol levels. Which of the following is most likely an effect of increased cortisol levels in response to hunger?
  - (A) increased activation of the immune response
  - (B) increased storage of calcium in bones
  - (C) increased reabsorption of water by the kidneys
  - (D) increased hydrolysis of glycogen to glucose
3. How do small ligands move between plant cells?
  - (A) Receptor proteins on plant cell membranes transport the ligands.
  - (B) Ligands pass through plasmodesmata that connect plant cells.
  - (C) Ligands can pass through the plant cell membrane unassisted.
  - (D) Active transport transfers ligands across the plant cell wall.
4. How do growth factors stimulate cell division?
  - (A) Growth factors bind to multiple cells, grouping them in multicellular structures.
  - (B) Growth factors bind to cyclic AMP, removing it from the cytosol.

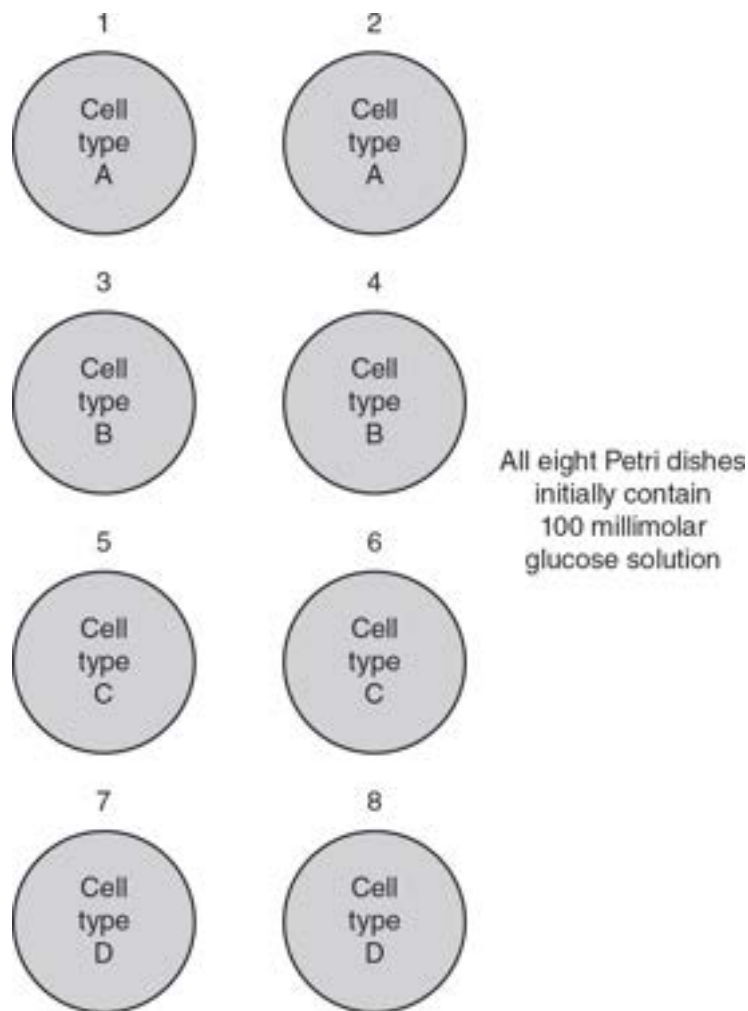
- (C) Growth factors bind to cell membrane receptors, triggering a signal transduction pathway.
  - (D) Growth factors bind to cell membrane phospholipids, which results in increased cell division.
5. In some autoimmune disorders, the body produces antibodies that bind to cell surface receptors on target cells, blocking them from interacting with other molecules. Which of the following is the most likely effect of the binding of the antibodies to the receptors?
- (A) increased stimulation of the target cell
  - (B) the target cell's inability to respond to ligands
  - (C) no effect on the target cell
  - (D) stimulation of gene expression in the target cell
6. Which of the following best describes the roles of calcium ions and cyclic AMP in the signal transduction process?
- (A) They act as ligands.
  - (B) They act as receptor proteins.
  - (C) They act as secondary messengers.
  - (D) They act as protein kinases.
7. Which of the following removes phosphate groups from other molecules?
- (A) cyclic AMP
  - (B) protein kinase
  - (C) protein phosphatase
  - (D) adenylyl cyclase
8. The hormone insulin travels through the circulatory system to reach target cells. Insulin is involved in which type of cell signaling?
- (A) autocrine signaling

- (B) juxtacrine signaling
  - (C) paracrine signaling
  - (D) endocrine signaling
9. Neurotransmitters travel short distances across synapses. This is an example of which type of signaling?
- (A) autocrine signaling
  - (B) juxtacrine signaling
  - (C) paracrine signaling
  - (D) endocrine signaling
10. Which of the following is the most likely reason why some cells do not respond to certain ligands?
- (A) Nonresponsive cells lack cyclic AMP.
  - (B) Nonresponsive cells lack receptors for the ligand.
  - (C) Nonresponsive cells lack the gene for the ligand.
  - (D) Nonresponsive cells cannot metabolize the ligand.

### Short Free-Response

11. The ligands in signal transduction pathways may be hydrophobic or hydrophilic.
- (a) **Describe** where in a cell the receptors for hydrophilic ligands and the receptors for hydrophobic ligands are located.
  - (b) **Explain** why hydrophobic ligands can cross the cell membrane unassisted.
  - (c) A mutation in the gene for adenylyl cyclase renders the enzyme ineffective. **Predict** the effect this would have on the cell.
  - (d) **Justify** your prediction from part (c).

12. An experiment is performed to measure how different cell types respond to a hormone that causes cells to absorb glucose from their environment. Four different cell types (A, B, C, and D) are used. At the start of this experiment, there are eight Petri dishes, each of which contains 100 millimolar glucose solution. Two dishes each contain cell type A, two dishes contain cell type B, two dishes contain cell type C, and the final two dishes contain cell type D, as illustrated in the following figure.



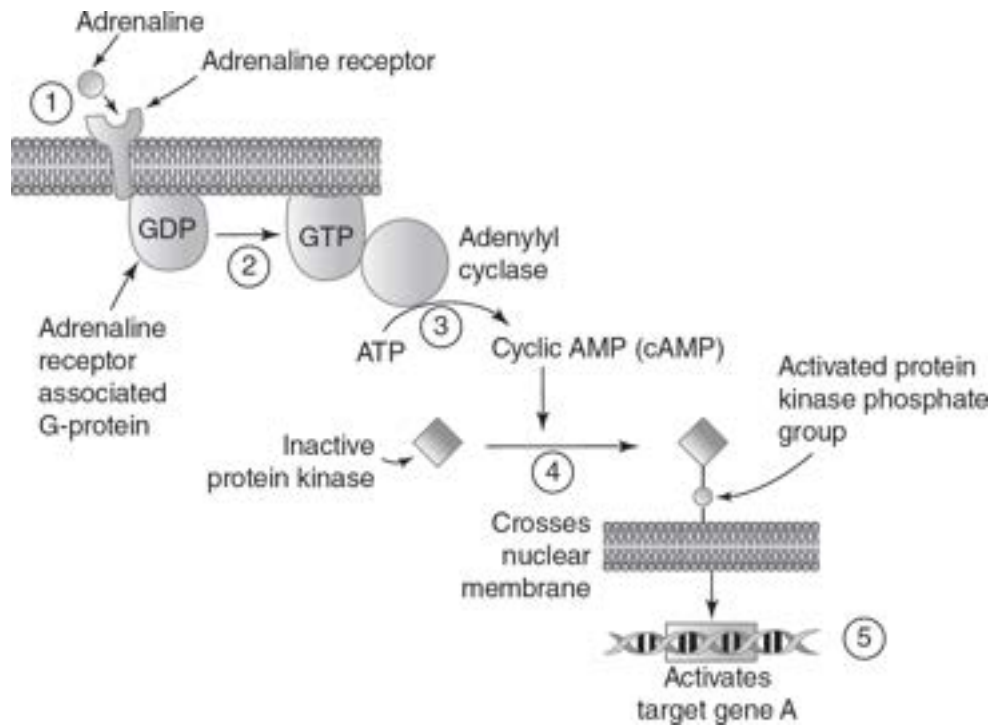
The hormone is added to four of the Petri dishes, one of each cell type. Glucose levels are measured in all eight Petri dishes 30 minutes after the addition of the hormone, and those glucose levels are listed in the following table.

Glucose Levels In Four Cell Types								
Petri Dish	1	2	3	4	5	6	7	8
Cell Type	A	A	B	B	C	C	D	D
Hormone Present (+) or Absent (0)	0	+	0	+	0	+	0	+
Glucose Levels 30 Minutes After the Addition of the Hormone (in millimolars)	100	50	100	50	100	100	100	100

- (a) **Describe** the most likely reason why cell types C and D did not respond to the presence of the hormone.
- (b) **Identify** the function of Petri dishes 1, 3, 5, and 7 in the experimental procedure.
- (c) A molecule is added to Petri dish 4 before the hormone is added. This molecule irreversibly binds to this hormone, preventing the hormone from binding to any receptor. The hormone is then added to Petri dish 4. **Predict** the effect this molecule will have on the glucose concentration in Petri dish 4 at 30 minutes after the addition of the hormone.
- (d) **Justify** your prediction from part (c).

### Long Free-Response

13. A signaling pathway for adrenaline is shown in the following diagram.



Researchers wanted to measure the effects of three different molecules on the adrenaline signaling pathway. Data are shown in the following table.

	Adrenaline (Alone)	Adrenaline (plus Molecule X)	Adrenaline (plus Molecule Y)	Adrenaline (plus Molecule Z)
G-Protein Activation	Yes	Yes	No	Yes
cAMP Production	Yes	No	No	Yes
Activation of Transcription of Target Gene A	Yes	No	No	No

- Describe** the parts of the cell signaling process that are represented in each of the five numbered steps in the diagram.
- Identify** the control, the independent variable, and the dependent variables in this experimental procedure.
- Analyze** the data, and **identify** which molecule(s) most likely interferes with the enzyme adenylyl cyclase.
- Cyclic AMP–dependent phosphodiesterase is an enzyme that breaks down cyclic AMP. **Predict** the numbered step in the diagram

that would be most directly affected by adding cAMP-dependent phosphodiesterase to the cell. **Justify** your prediction.

# Answer Explanations

## Multiple-Choice

1. **(B)** If the target cell lacks receptors for the signaling molecule, it will not be able to initiate the signal transduction pathway that triggers cell division. Choice (A) is incorrect because the cells will not divide if they lack the appropriate receptor for the ligand; the signaling pathway for cell division will not be triggered. Choice (C) is incorrect because individual cells do not evolve new receptors. If the cell lacks the receptors for the signaling molecule, the cell will not be able to respond to the signal, so choice (D) is incorrect.
2. **(D)** Cortisol would stimulate the breakdown of glycogen into glucose. This would provide energy, alleviating one of the symptoms of hunger. Choices (A), (B), and (C) are incorrect because the activation of the immune response, increased storage of calcium in bones, and increased reabsorption of water by the kidneys would not increase the energy available to cells.
3. **(B)** Small molecules pass between plant cells through channels called plasmodesmata, an example of juxtacrine signaling. Choices (A) and (C) are incorrect because plant cells have a cell wall surrounding the cell membrane. So molecules cannot pass through plant cell membranes unassisted nor can they bind to cell membrane receptors unless they can pass through the cell wall first. Choice (D) is incorrect because not all ligands require active transport.
4. **(C)** Growth factors bind to receptors, which triggers a signal transduction process that stimulates cell division. Grouping cells together would not trigger cell division, so choice (A) is incorrect. Removing cyclic AMP from the cytosol would most likely disrupt the signaling process that is required to trigger cell division, so choice (B) is incorrect. Choice (D) is incorrect because growth factors bind to receptor proteins, not to membrane phospholipids.
5. **(B)** If an antibody binds to the receptor, the ligand will be prevented from binding to the receptor, and the signaling process will not occur.

Choice (A) is incorrect because the result will be decreased, not increased, stimulation of the target cell. The effect of the antibody will be decreased stimulation of the target cell, so choice (C) is also incorrect. Since the antibody is preventing the ligand from binding to the receptor, no stimulation of gene expression could be triggered, making choice (D) incorrect as well.

6. **(C)** Both calcium ions and cyclic AMP function as secondary messengers during cell signaling. Ligands bind to the receptor to start the cell signaling process; neither calcium ions nor cAMP do this, so choice (A) is incorrect. Receptor proteins and protein kinases are proteins, but neither calcium ions nor cAMP are proteins. So choices (B) and (D) are incorrect.
7. **(C)** Protein phosphatases remove phosphate groups from other molecules. Choice (A) is incorrect because cyclic AMP functions as a secondary messenger. Protein kinases add phosphate groups to molecules, so choice (B) is incorrect. Choice (D) is incorrect because adenylyl cyclase is the enzyme that catalyzes the formation of cAMP.
8. **(D)** Insulin travels long distances through the circulatory system, so this is an example of endocrine signaling. Choice (A) is incorrect because autocrine signaling involves a cell that produces a ligand, and the ligand then binds to a receptor on the same cell that produced the ligand. Juxtacrine signaling is between cells that are in direct contact, so choice (B) is incorrect. Choice (C) is incorrect because paracrine signaling occurs over short distances.
9. **(C)** Signaling over short distances is paracrine signaling. Choice (A) is incorrect because autocrine signaling involves a cell that produces a ligand and the ligand then binds to a receptor on the same cell that produced the ligand. Juxtacrine signaling is between cells that are in direct contact, so choice (B) is incorrect. Endocrine signaling occurs over long distances, so choice (D) is incorrect.
10. **(B)** If a cell lacks the receptor for a ligand, the signal transduction process cannot start. Choice (A) is incorrect because if cAMP was lacking, the cell might still be able to mount an incomplete response if

the ligand could bind to a receptor and trigger steps in the signal transduction process that do not depend on the presence of cAMP. Ligands are usually not produced in their target cells, so lacking a gene for the ligand would likely have no effect on the target cell, making choice (C) incorrect. Choice (D) is incorrect because the inability to metabolize a ligand would likely not affect the target cell's ability to respond to the ligand.

### Short Free-Response

11. (a) Receptors for hydrophilic ligands are found on the cell membrane. Receptors for hydrophobic ligands are found in the cytosol.
  - (b) The cell membrane is made of a phospholipid bilayer. Hydrophobic ligands can slide between the hydrophobic phospholipids of the bilayer and enter the cell.
  - (c) A mutation in the enzyme adenylyl cyclase (that rendered it ineffective) would result in a cell that could not make the secondary messenger cyclic AMP. This would disrupt any cell signaling process that contains a step that requires cyclic AMP.
  - (d) Adenylyl cyclase catalyzes the conversion of ATP into cAMP, so an ineffective adenylyl cyclase would result in no cAMP production.
12. (a) Cell types C and D did not respond to the presence of the hormone because they most likely did not have the receptor for the hormone.
  - (b) Petri dishes 1, 3, 5, and 7 are the experimental controls for each of the four cell types in the experiment.
  - (c) If a molecule that irreversibly binds to this hormone was added to Petri dish 4 before the hormone was added, the level of glucose in the Petri dish would most likely remain unchanged after 30 minutes.
  - (d) The irreversible binding of the molecule to the hormone would prevent the hormone from binding to its receptor in the cell. Without the binding of the hormone/ligand, the signal to absorb glucose from

the Petri dish would not occur, and the glucose level in the Petri dish would remain unchanged.

## Long Free-Response

13. (a) Step 1 represents reception of the signal. Steps 2, 3, and 4 represent transduction. Step 5 represents the response.
- (b) The control is the cell in which adrenaline alone has been added. The independent variable is the presence or absence of molecules X, Y, or Z. The dependent variables are the activation of the G-protein, the production of cAMP, and the activation of transcription of target gene A.
- (c) Molecule X and molecule Y most likely interfere with adenylyl cyclase because no cAMP was produced when those molecules were added to the cells. Molecule Y also most likely interferes with the GDP on the G-protein receptor since it was never activated.
- (d) If cAMP-dependent phosphodiesterase was added to the cell, the conversion of the inactive protein kinase to activated protein kinase (step 4) would most likely be affected since that step is dependent on the presence of cAMP.