Unit 4: Cell Communication and Cell Cycle

Topic	Learning Objective(s)
4.1 Cell Communication	**IST-3.A** Describe the ways that cells can communicate with one another.
	IST-3.B Explain how cells communicate with one another over short and long distances.
4.2 Introduction to Signal Transduction	**IST-3.C** Describe the components of a signal transduction pathway.
	IST-3.D Describe the role of components of a signal transduction pathway in producing a cellular response.
4.3 Signal Transduction	**IST-3.E** Describe the role of the environment in eliciting a cellular response.
	IST-3.F Describe the different types of cellular responses elicited by a signal transduction pathway.
4.4 Changes in Signal Transduction Pathways	**IST-3.G** Explain how a change in the structure of any signaling molecule affects the activity of the signaling pathway
4.5 Feedback	**ENE-3.A** Describe positive and/ or negative feedback mechanisms.
	ENE-3.B Explain how negative feedback helps to maintain homeostasis
	ENE-3.C Explain how positive feedback affects homeostasis.
4.6 Cell Cycle	**IST-1.B** Describe the events that occur in the cell cycle.
	IST-1.C Explain how mitosis results in the transmission of chromosomes from one generation to the next.
4.7 Regulation of Cell Cycle	**IST-1.D** Describe the role of checkpoints in regulating the cell cycle.
	IST-1.E Describe the effects of disruptions to the cell cycle on the cell or organism.

Free Response Practice

2022 #1

The binding of an extracellular ligand to a G protein-coupled receptor in the plasma membrane of a cell triggers intracellular signaling (Figure 1, A). After ligand binding, GTP replaces the GDP that is bound to Gsα , a subunit of the G protein (Figure 1, B). This causes Gsα to activate other cellular proteins, including adenylyl cyclase that converts ATP to cyclic AMP (cAMP). The cAMP activates protein kinases (Figure 1, C). In cells that line the small intestine, a cAMP -activated protein kinase causes further signaling that ultimately results in the secretion of chloride ions (Cl^-) from the cells. Under normal conditions, Gsα hydrolyzes GTP to GDP, thus inactivating adenylyl cyclase and stopping the signal (Figure 1, A).

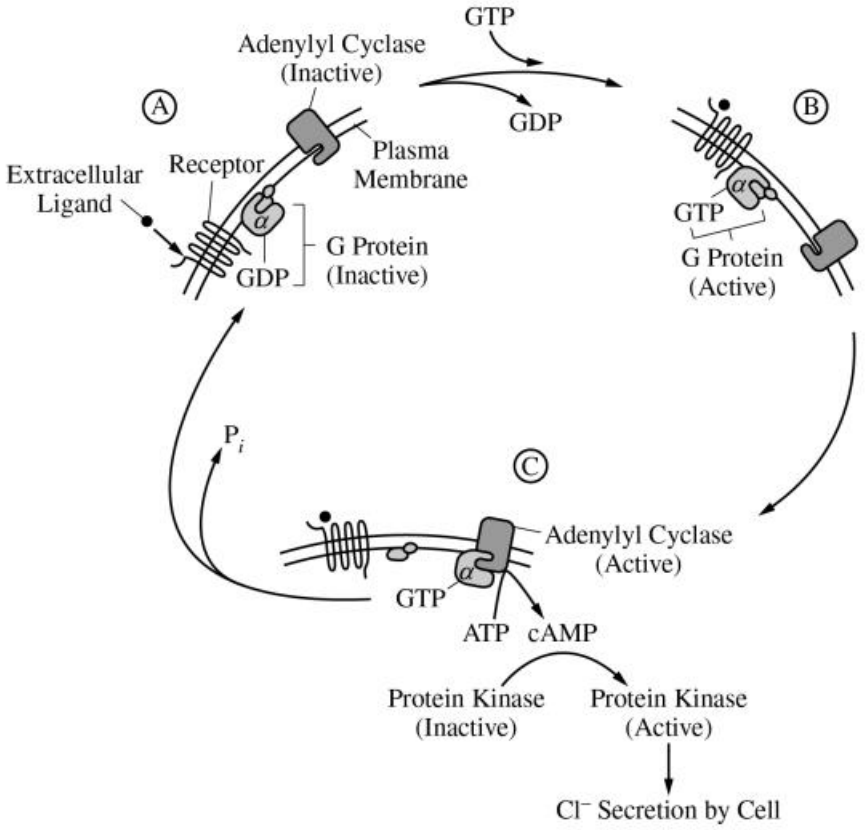


Figure 1. Under normal conditions, ligand binding to a G protein-coupled receptor results in chloride ion transport from an intestinal cell.

Individuals infected with the bacterium Vibrio cholerae experience severe loss of water from the body (dehydration). This is due to the effects of the bacterial cholera toxin that enters intestinal cells. Scientists studied the effects of cholera toxin on four samples of isolated intestinal cell membranes containing the G protein-related signal transduction components shown in Figure 1. GTP was added to samples II and IV only; cholera toxin was added to samples III and IV only. The scientists then measured the amount of cAMP produced by the adenylyl cyclase in each sample (Table 1).

TABLE 1. AMOUNT OF cAMP PRODUCED FROM INTESTINAL CELL MEMBRANES IN THE ABSENCE OR PRESENCE OF CHOLERA TOXIN

Sample	GTP	Cholera Toxin	Rate of cAMP Production (pmol per mg adenylyl cyclase per min)
I	–	–	0.5
II	+	–	10.0
III	–	+	0.5
IV	+	+	127.0

present, +; absent, –

(a) **Describe** one characteristic of a membrane that requires a channel be present for chloride ions to passively cross the membrane. **Explain** why the movement of chloride ions out of intestinal cells leads to water loss.

(b) **Identify** an independent variable in the experiment. **Identify** a negative control in the experiment. **Justify** why the scientists included Sample III as a control treatment in the experiment.

(c) Based on the data, **describe** the effect of cholera toxin on the synthesis of cAMP. **Calculate** the percent change in the rate of cAMP production due to the presence of cholera toxin in sample IV compared with sample II.

(d) A drug is designed to bind to cholera toxin before it crosses the intestinal cell membrane. Scientists mix the drug with cholera toxin and then add this mixture and GTP to a sample of intestinal cell membranes. **Predict** the rate of cAMP production in pmol per mg adenylyl cyclase per min if the drug binds to all of the toxin. In a separate experiment, scientists engineer a mutant adenylyl cyclase that cannot be activated by Gsα . The scientists claim that cholera toxin will not cause excessive water loss from whole intestinal cells that contain the mutant adenylyl cyclase. **Justify** this claim.

2021 #1

Polycystic kidney disease (PKD) is an inherited disease that causes water loss from the body and affects cell division in the kidneys. Because water movement across cell membranes is related to ion movement, scientists investigated the role of Na^+/K^+ ATPase (also known as the sodium/potassium pump) in this disease. Ouabain, a steroid hormone, binds to the Na^+/K^+ ATPase in plasma membranes. Individuals with PKD have a genetic mutation that results in an increased binding of ouabain to the Na+/K+ ATPase. The scientists treated normal human kidney (NHK) cells and PKD cells with increasing concentrations of ouabain and measured the number of cells (Figure 1) and the activity of the Na^+/K^+ ATPase (Figure 2) after a period of time. The scientists hypothesized that a signal transduction pathway that includes the protein kinases MEK and ERK (Figure 3) may play a role in PKD symptoms.

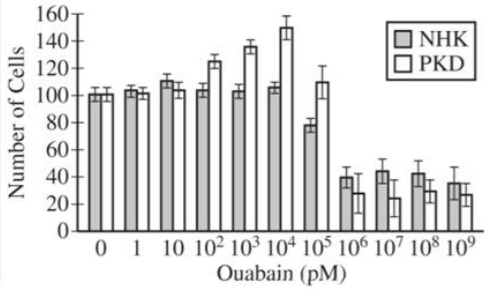


Figure 1. Cell number compared with the number of cells at 0 pM ouabain. Normal human kidney (NHK) cells and polycystic kidney disease (PKD) cells were treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$.

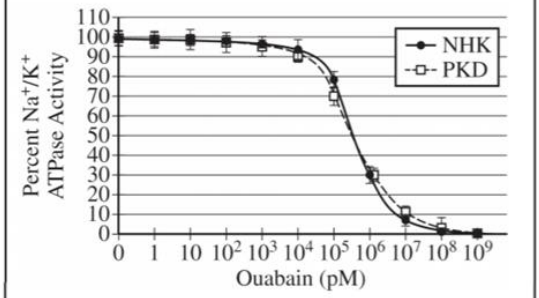


Figure 2. Percent Na^+/K^+ATPase activity of NHK and PKD cells treated with increasing concentrations of ouabain. Error bars represent $\pm 2SE_{\bar{x}}$.

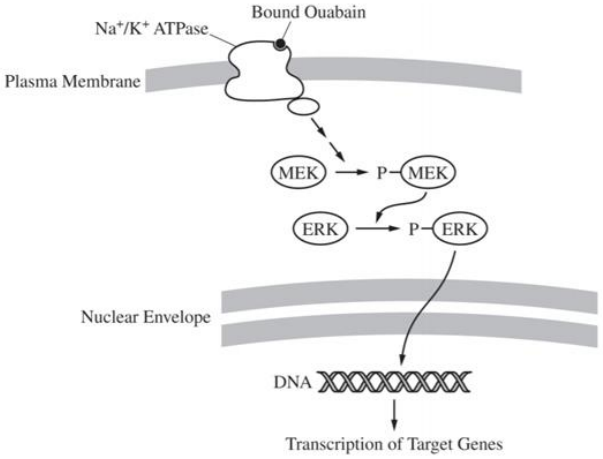


Figure 3. Signal transduction pathway hypothesized to play a role in the increased number of PKD cells

(a) **Describe** the characteristics of the plasma membrane that prevent simple diffusion of Na^+ and K^+ across the membrane. **Explain** why ATP is required for the activity of the Na^+/K^+ ATPase.

(b) **Identify** a dependent variable in the experiment represented in Figure 1. **Justify** the use of normal human kidney (NHK) cells as a control in the experiments. **Justify** the use of a range of ouabain concentrations in the experiment represented in Figure 1.

(c) Based on the data shown in Figure 2, **describe** the relationship between the concentration of ouabain and the Na^+/K^+ ATPase activity both in normal human kidney (NHK) cells AND in PKD cells. The scientists determined that Na^+/K^+ ATPase activity in PKD cells treated with 1 pM ouabain is 150 units of ATP hydrolyzed/sec. **Calculate** the expected Na^+/K^+ ATPase activity (units/sec) in PKD cells treated with 10^6 pM ouabain.

(d) In a third experiment, the scientists added an inhibitor of phosphorylated MEK (pMEK) to the PKD cells exposed to 10^4 pM ouabain. Based on Figure 3, **predict** the change in the relative ratio of ERK and pERK in ouabain-treated PKD cells with the inhibitor compared with ouabain-treated PKD cells without the inhibitor. Provide reasoning to **justify** your prediction. Using the data in Figure 1 AND the signal transduction pathway represented in Figure 3, **explain** how the concentration of cyclin proteins may increase in PKD cells treated with 10^4 pM ouabain.

2019 #4

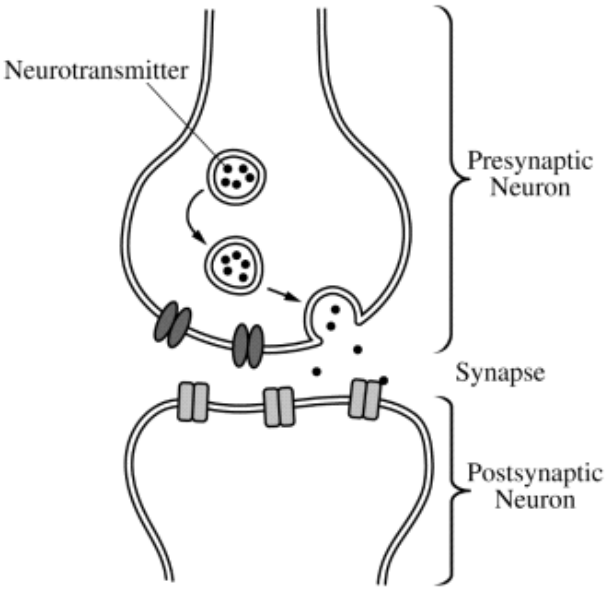


Figure 1. Release of neurotransmitters into the synapse in response to an action potential

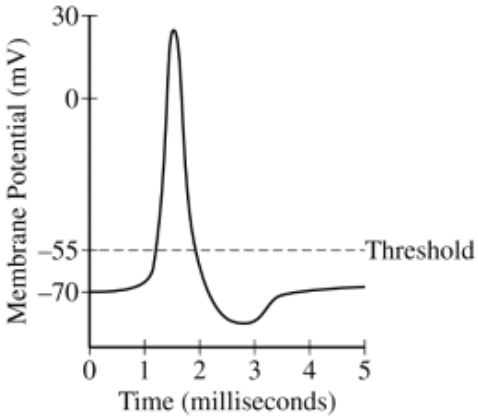


Figure 2. Model of a typical action potential in a neuron

Acetylcholine is a neurotransmitter that can activate an action potential in a postsynaptic neuron (Figures 1 and 2). A researcher is investigating the effect of a particular neurotoxin that causes the amount of acetylcholine released from presynaptic neurons to increase.

(a) **Describe** the immediate effect of the neurotoxin on the number of action potentials in a postsynaptic neuron. **Predict** whether the maximum membrane potential of the postsynaptic neuron will increase, decrease, or stay the same.

(b) The researcher proposes two models, A and B, for using acetylcholinesterase (AChE), an enzyme that degrades acetylcholine, to prevent the effect of the neurotoxin. In model A, AChE is added to the synapse. In model B, AChE is added to the cytoplasm of the postsynaptic cell. **Predict** the effectiveness of EACH proposed model. **Provide reasoning** to support your predictions.

2018 #2

Some pathogenic bacteria enter cells, replicate, and spread to other cells, causing illness in the host organism. Host cells respond to these infections in a number of ways, one of which involves activating particular enzymatic pathways (Figure 1). Cells normally produce a steady supply of inactive caspase-1 protein. In response to intracellular pathogens, the inactive caspase-1 is cleaved and forms an active caspase-1 (step 1). Active caspase-1 can cleave two other proteins. When caspase-1 cleaves an inactive interleukin (step 2), the active portion of interleukin is released from the cell. An interleukin is a signaling molecule that can activate the immune response. When caspase-1 cleaves gasdermin (step 3), the N-terminal portions of several gasdermin proteins associate in the cell membrane to form large, nonspecific pores.

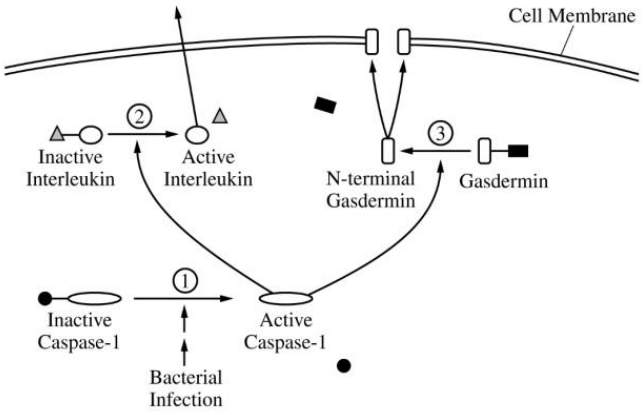


Figure 1. Cellular response to infection by pathogenic bacteria

Researchers created the model in Figure 1 using data from cell fractionation studies. In the experiments, various parts of the cell were separated into fractions by mechanical and chemical methods. Specific proteins known to be located in different parts of the cell were used as markers to determine the location of other proteins. The table below shows the presence of known proteins in specific cellular fractions.

CELL FRACTIONS CONTAINING DIFFERENT CELLULAR PROTEINS

	Aconitase (Krebs cycle protein)	DNA polymerase	GAPDH (glycolytic protein)	Sodium-potassium pump	NF-κB (Immune response protein)
Whole cell sample	+	+	+	+	+
Fraction 1	+				
Fraction 2		+			+
Fraction 3			+		+
Fraction 4				+	
+ = presence of protein					

(a) **Describe** the effect of inhibiting step 3 on the formation of pores AND on the release of interleukin from the cell.

(b) **Make a claim** about how cleaving inactive caspase-1 results in activation of caspase-1. A student claims that preinfection production of inactive precursors shortens the response time of a cell to a bacterial infection. **Provide ONE reason** to support the student's claim.

(c) A student claims that the NF-kB protein is located in the cytoplasm until the protein is needed for transcription. **Justify** the student's claim with evidence. **Identify TWO** fractions where N-terminal gasdermin would be found in cells infected with pathogenic bacteria.

(d) **Describe** the most likely effect of gasdermin pore formation on water balance in the cell in a hypotonic environment.

(e) **Explain** how gasdermin pore formation AND interleukin release contribute to an organism's defense against a bacterial pathogen.

2018 #8

Acetylcholine receptor (AChR) proteins are found at the synapse between neurons and skeletal muscle cells. Acetylcholine released from neurons binds to a specific site on the receptor proteins, which causes an ion channel in the receptors to open and allow sodium ions (Na^+) to enter muscle cells. The resulting depolarization of muscle cells initiates muscle contractions. Another molecule, nicotine, can also bind to certain types of AChR proteins and activate the receptors.

A researcher is investigating two different types of AChR proteins: type 1 and type 2. To determine which stimuli activate the receptors, the researcher exposes muscle cells expressing the different types of receptor proteins to stimuli and observes the result indicated in Table 1.

TABLE 1. RESPONSE OF AChR PROTEINS TO DIFFERENT STIMULI

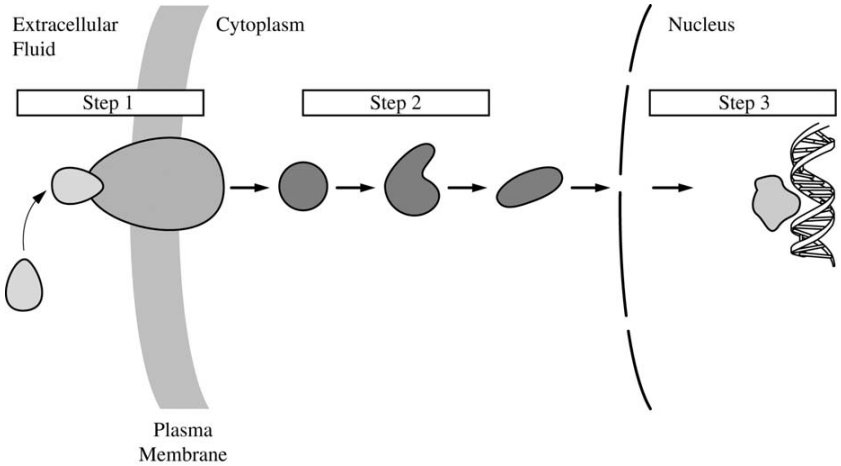
AChR Protein Type	Acetylcholine	Nicotine
Type 1	+	+
Type 2	+	–

+ indicates activation
– indicates no activation

(a) **Describe** the difference in the structure AND function between AChR type 1 and AChR type 2.

(b) Acetylcholinesterase is an enzyme that breaks down acetylcholine in the synapse. **Describe** the effect of inhibiting acetylcholinesterase on the muscle cells with AChR type 2.

2013 #8



The figure above represents a generalized hormone-signaling pathway. Briefly **explain** the role of each numbered step in regulating target gene expression.

Free Response Scoring Guidelines

2022 #1		
Part	Scoring Guidelines	Topic
(a)	**Describe** one characteristic of a membrane that requires a channel be present for chloride ions to passively cross the membrane. Accept one of the following: • The interior of the membrane/phospholipid tail is nonpolar. • The interior of the membrane/phospholipid tail is not charged. • The interior of the membrane/phospholipid tail is hydrophobic. **Explain** why the movement of chloride ions out of intestinal cells leads to water loss. Accept one of the following: • The space outside of the cells becomes hypertonic/hyperosmotic compared with the cells, so water moves out of the cells. • The space outside of the cells would have a lower water potential compared with the cells, so water will move out of the cells.	2.5 2.8
(b)	**Identify** an independent variable in the experiment. Accept one of the following: • The presence or absence of cholera toxin • The presence or absence of GTP **Identify** a negative control in the experiment. Accept one of the following: • The sample lacking both cholera toxin and GTP /sample I • The samples that lack cholera toxin /samples I and II • The sample that lacks cholera toxin but contains GTP /sample II • The samples that lack GTP /samples I and III **Justify** why the scientists included Sample III as a control treatment in the experiment. Accept one of the following: • (Sample III serves as a control) to compare cAMP production with that of the sample having cholera toxin and GTP /sample IV. • Comparing sample III and sample IV enables the scientists to evaluate whether the activity of cholera toxin requires GTP/acts via the G protein pathway.	
(c)	Based on the data, **describe** the effect of cholera toxin on the synthesis of cAMP. Accept one of the following: • Cholera toxin increases the production of cAMP in the presence of GTP (IV vs II). • Cholera toxin has no effect on the production of cAMP in the absence of GTP (III vs I). **Calculate** the percent change in the rate of cAMP production due to the presence of cholera toxin in sample IV compared with sample II. • 1,170% [(127−10)/10 = 11.7 × 100]	4.2

(d)	A drug is designed to bind to cholera toxin and prevent the toxin from crossing the intestinal cell membrane. Scientists mix the drug with cholera toxin and then add this mixture and GTP to a sample of intestinal cell membranes. **Predict** the rate of cAMP production in pmol per mg adenylyl cyclase per min if the drug binds to all of the toxin. • The rate will be 10 (pmol per mg adenyl cyclase per min). In a separate experiment, scientists engineer a mutant adenylyl cyclase that cannot be activated by $Gs\alpha$. The scientists claim that cholera toxin will not cause excessive water loss from whole intestinal cells that contain the mutant adenylyl cyclase. **Justify** this claim. • (Even in the presence of the toxin) cAMP will not be produced (by this pathway), the protein kinases will not be activated, and Cl^- ions will not be secreted (and less water will leave the intestinal cells).	4.2

2021 #1		
Part	Scoring Guidelines	Topic
(a)	**Describe** the characteristics of the plasma membrane that prevent simple diffusion of Na^+ and K^+ across the membrane. Accept one of the following: • The interior of the plasma membrane is hydrophobic/nonpolar. • The phospholipid tails are hydrophobic/nonpolar. • The exterior of the plasma membrane is hydrophilic/polar. • The phospholipid heads are hydrophilic/polar. **Explain** why ATP is required for the activity of the Na^+/K^+ ATPase. • The Na^+/K^+ ATPase pumps ions against their concentration gradients. This requires an input of (metabolic) energy.	2.4 2.7
(b)	**Identify** a dependent variable in the experiment represented in Figure 1. • The number of cells **Justify** the use of normal human kidney NHK cells as a control in the experiments. Accept one of the following: • It allows the scientists to determine the effect of PKD on the cells' responses to (various concentrations of) ouabain. • It allows the scientists to compare the responses of PKD cells and normal cells (to ouabain). **Justify** the use of a range of ouabain concentrations in the experiment represented in Figure 1. Accept one of the following: • The scientists need to determine whether different concentrations have different effects on the cell numbers. • The scientists did not know at which concentration of ouabain there would be an effect.	2.4 2.7

(c)	Based on the data shown in Figure 2, **describe** the relationship between the concentration of ouabain and the Na^+/K^+ ATPase activity both in normal human kidney (NHK) cells AND in PKD cells. Accept one of the following: • Increasing concentrations of ouabain result in decreasing ATPase activity (in both types of cells). • There is an inverse relationship/negative correlation between the concentration of ouabain and the ATPase activity (in both types of cells). The scientists determined that Na^+/K^+ ATPase activity in PKD cells treated with 1 pM ouabain is 150 units of ATP hydrolyzed/sec. **Calculate** the expected Na^+/K^+ ATPase activity (units/sec) in PKD cells treated with 10^6 pM ouabain. • 45 (Accept between 40 and 50)	4.2 4.4
(d)	In a third experiment, the scientists added an inhibitor of phosphorylated MEK (pMEK) to the PKD cells exposed to 10^4 pM ouabain. Based on Figure 3, **predict** the change in the relative ratio of ERK to pERK in ouabain-treated PKD cells with the inhibitor compared with ouabain-treated PKD cells without the inhibitor. Accept one of the following: • Option 1: The ratio of ERK to pERK will increase in the cells with the inhibitor. • Option 2: The ratio of ERK to pERK will stay the same in the cells with the inhibitor. Provide reasoning to **justify** your prediction. • The justification must indicate that the pMEK inhibitor blocks further phosphorylation of ERK AND one of the following: Option 1: • The amount of pERK will not increase as it does in cells without the inhibitor. • The amount of ERK will not decrease as it does in cells without the inhibitor. • The cell continues to synthesize ERK. • Phosphorylated ERK is being dephosphorylated to ERK. Option 2: • No additional ERK is synthesized/pERK is not being dephosphorylated. Using the data in Figure 1 AND the signal transduction pathway represented in Figure 3, **explain** why the concentration of cyclin proteins may increase in PKD cells treated with 10^4 pM ouabain. • The cell number increases to a maximum at 10^4 pM ouabain. The signaling pathway stimulates transcription of genes involved in cell division. The target genes likely include those for cyclins because cyclins regulate the cell cycle.	4.2 4.4

2019 #4

<table>
<tr><th>Part</th><th>Scoring Guidelines</th><th>Topic</th></tr>
<tr><td>(a)</td><td>Description (1 point)
• It will increase the number of action potentials.

Prediction (1 point)
• It will stay the same.</td><td>4.2</td></tr>
<tr><td>(b)</td><td>(1 point per row; 2 points max.)
<table><tr><th></th><th>Prediction</th><th>Reasoning</th></tr><tr><td>Model A</td><td>Effective</td><td>Acetylcholine is in the synapse.</td></tr><tr><td>Model B</td><td>Not effective</td><td>Acetylcholine is not in the cytoplasm of the postsynaptic cell.</td></tr></table></td><td>4.2</td></tr>
</table>

2018 #2

<table>
<tr><th>Part</th><th>Scoring Guidelines</th><th>Topic</th></tr>
<tr><td>(a)</td><td>Description (2 points)
• Pores will not form.
• Interleukin release will not be affected/interleukin release continues.</td><td>4.2</td></tr>
<tr><td>(b)</td><td>Claim (1 point)
• Removes inhibitor/repressor/inhibitory domain of protein
• Changes the shape/protein structure

Reasoning (1 point)
• Cleaving a precursor/protein/molecule is faster than making one upon infection.
• Cells do not have to wait for transcription and translation/protein synthesis.</td><td>4.2</td></tr>
<tr><td>(c)</td><td>Justification (1 point)
• NF-kB and glycolytic enzymes/GAPDH are found together (in the cytoplasm).

Identification (2 points)
• Fraction 3
• Fraction 4</td><td>4.2</td></tr>
<tr><td>(d)</td><td>Description (1 point)
• Water enters the cell.</td><td>2.8</td></tr>
<tr><td>(e)</td><td>Explanation (2 points)
• Cell lysis destroys infected cells OR cell lysis prevents bacteria from replicating.
• Interleukin signaling will stimulate immune cells/components of the immune system (to destroy the infected cells or bacteria).</td><td>4.2</td></tr>
</table>

2018 #8

<table>
<tr><th>Part</th><th>Scoring Guidelines</th><th>Topic</th></tr>
<tr><td>(a)</td><td>
Description (2 points)

Points may be earned from only one row.

<table>
<tr><th>Structure (1 point maximum)</th><th>Function (1 point maximum)</th></tr>
<tr><td>Binding sites differ in shape/ specificity/number</td><td>• Differential binding of molecules to type 1 and type 2 receptors
• Activated by one (ACh) molecule or both (ACh and nicotine) molecules
• No difference in response (both open channels OR both result in depolarization OR both cause muscle contraction)</td></tr>
<tr><td>Differential binding of molecules to type 1 and type 2 receptors</td><td>• Activated by one (ACh) or both (ACh and nicotine) molecules
• No difference in response (both open channels OR both result in depolarization OR both cause muscle contraction)</td></tr>
<tr><td>Receptors activated by one (ACh) or both (ACh and nicotine) molecules</td><td>• No difference in response (both open channels OR both result in depolarization OR both cause muscle contraction)</td></tr>
</table>
</td><td>4.4</td></tr>
<tr><td>(b)</td><td>Description (1 point)
• Continued activation
• Repeated opening of sodium channels OR repeated depolarization OR muscle spasms</td><td>4.4</td></tr>
</table>

2013 #8

Part	Scoring Guidelines	Topic
	The figure above represents a generalized hormone-signaling pathway. Briefly **explain** the role of each numbered step in regulating target gene expression. (**3 points maximum**) • Step 1 = hormone/ligand binding to receptor to initiate/trigger/induce signaling OR signal reception • Step 2 = an intracellular cascade that transduces/amplifies/transfers the signal from plasma membrane to nucleus (or other cellular effectors) • Step 3 = transcription/expression of target genes is stimulated/repressed	4.2