Understanding Immunity through Cell Communication

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Teacher Guide

I. Science Background

- Cells are constantly able to detect what is going on around them and respond to cues within their environment and with neighboring cells. Typically, cells communicate with each other via chemical messengers to produce a chain of reactions within the cell to produce a response. For example, when your body temperature is rising, your cells can relay this message via a chemical messenger, causing your body to produce sweat and cool your temperature down.
- Immunology is the study of the immune system and an important part of all medical and biological sciences. The immune system helps protect us from infection through various lines of defense and involves multiple cellular components to help protect our bodies from the infectious agents. One particular line of defense is granuloma formation. A granuloma is a structure formed during inflammation that is found in many diseases, as a way to wall off foreign substances the body is unable to eliminate. Granuloma formation involves a collection of immune cells, such as macrophages that produce chemical messages to help produce the specific immune response.
- The goal of this unit is to allow students to apply the concepts of cell communication, as well as immunology, to explore how cells communicate with each other in various ways and are able to use their chemical messages to produce an immune response. Students will use real world examples of an immune response to better understand how these cells communicate with each other. In addition to exploring immune responses students will explore one particular laboratory technique to investigate components of the immune system, by working their way through an ELISA assay.
- ELISA, or Enzyme-linked immunosorbent assay, is a plate-based technique used in immunology. It is designed to detect and quantify peptides, proteins, antibodies, and hormones present within a sample. In order for detection to take place, an antigen is bound to the surface of a plate, followed by an antibody that is linked to an enzyme that can bind to our particular substrate. Once bound and modified by the enzyme, the substrate will change color to be quantified.

II. Student Outcomes

- Lesson will occur in a High School AP Biology course
- Students will cover the concepts of cell communication, as well as how these concepts relate within the immune system.

- AP Alignment
  - Topic 4.1 Cell communication
    - IST-3: Cells communicate by generating, transmitting, receiving, and responding to chemical signals.
      - IST-3.A.1: Cells communicate with one another through direct contact with other cells or from a distance via chemical signaling.
      - IST-3.B.1: Cells communicate over short distances by using local regulators that target cells in the vicinity of the signal-emitting cell.
      - IST-3.C.1: Signal transduction pathways link signal reception with cellular responses.
      - IST-3.C.2: Many signal transduction pathways include protein modification and phosphorylation cascades.
      - IST-3.D.1: Signaling begins with the recognition of a chemical messenger-a ligand-by a receptor protein in a target cell.
      - IST-3.D.2: Signaling cascades relay signals from receptors to cell targets, often amplifying the incoming signals, resulting in the appropriate responses by the cell, which could include cell growth, secretion of molecules, or gene expression.
      - IST-3.E.1: Signal transduction pathways influence how the cell responds to its environment.
      - IST-3.F.1: Signal transduction may result in changes in gene expression and cell function, which may alter phenotype or result in programmed cell death (apoptosis).
      - IST-3.G.1: Changes in signal transduction pathways can alter cellular responses.

- NGSS alignment
  - A: Structure and Function
    - HS-LS1-1: Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins which carry out the essential functions of life through systems of specialized cells.
    - HS-LS1-2: Multicellular organisms have a hierarchical structural organization, in which any one system is made up of numerous parts and is itself a component of the next level.
    - HS-LS1-3: Feedback mechanisms maintain a living system's internal conditions within certain limits and mediate behaviors, allowing it to remain alive and functional even as external conditions change within some range. Feedback mechanisms can encourage or discourage what is going on inside the living system.

- What students will do and what technical skills they will learn
  - Students will learn how to use an ELISA assay to quantify the amount of cellular components in a sample.
  - NGSS Science Practices
    - Developing and using models
    - Analyzing and interpreting data
    - Constructing explanations and designing solutions
    - Engaging in argument from evidence
    - Obtaining, evaluating, and communicating information

- Relevance to other science concepts and students' lives
  - Immune system responses and other information will be applicable and transferrable into many aspects of the student's lives. Using real-world examples and examples of infectious diseases, students should be able to apply these concepts.

III. Learning objectives

- Observable and measurable
  - Students will create models and demonstrate how cells communicate by generating, transmitting, and receiving signals.
  - Students will describe how immune cells are involved in producing an immune response.
  - Students will apply how the concept of cell communication is connected to the functioning immune system.
- How students will demonstrate specific knowledge and skills
  - Through the "Modeling Cell Communication Activity," students will demonstrate how cells communicate through creating and describing models, showing the signal, transduction, and response cascade.
  - Through the understanding immunity activity, students will make connections amongst their peer's models to describe common aspects within the immune system that contribute to an immune response and protecting ourselves against foreign substances.
  - Through the online and laboratory ELISA simulations, students should be able to explain how the immune system involves cells that are able to communicate with each other via different mechanisms to produce a specific immune response.

IV. Time requirements

- Class periods are 85 minute block schedule
    - Estimated time= 6 block periods.

V. Advance Preparation

- List of equipment and materials
    - Large white boards or lab bench as chalk board
    - White board markers
    - Lab handouts
    - Computers with online access
    - Paper cutouts, if necessary
    - Giant Panda ELISA Kit from Biorad
- Directions for preparing solutions and other reagents
    - See Biorad kit for preparation of solutions for kit
- Approximate preparation time
    - About 60 minutes

VI. Materials and Equipment

- Student Computers for Notes/PowerPoint/online ELISA simulation (1 per person)
- Student handouts (1 per person)
- Playdoh (as needed)
- 3D models (as needed)
- Large whiteboards/whiteboard markers for cell communication activity and understanding immunity activity (1 set per group of 3 or 4)
- No safety equipment (goggles, aprons, etc.) needed at this time

VII. Student Prior Knowledge and Skills

- Expected prior content knowledge
    - Students should have taken a basic biology class and have a basic understanding of biological concepts, related to cells and the human body. Students should have already learned about cells and cell components and should understand the basic components of a cell as well as the function of the organelles. Students will also have learned about cell differentiation and how cells can become specialized in order to perform a specific function. This will allow the students to have a better understanding of the cells of the immune system and how there are multiple cells within the immune system that can perform various roles.
    - Students should have a general understanding of the immune system, its role in the human body and function against infectious material.
- Expected prior technical skills
    - For ELISA laboratory experiment, students should have a background understanding of certain laboratory equipment such as micropipettes, centrifuges, and 96 well plates including their functions and uses.

VIII. Unit Plans

A. Overview/outline of unit

- Engage: "Everything you didn't want to know about snot" video
  - As students watch the video, they can use the guided discussion questions to brainstorm and discuss following the video (See Appendix A)
  - Ask students what happens when bacteria or viruses pass this first line of defense.

- Explore: Notes/overview of cell communication
  - Students will work through notes with the teacher, on the three main parts involved in all cell communication processes (signal, transduction, response). Through the notes, as well as interactive activities, students will learn real world applications of how our cells are able to communicate with each other. Real world examples will include the Growth Factor response, Apoptosis, as well as Testosterone

- Explain: Modeling Cell Communication
  - Students will use playdoh to model the three main parts of cell communication. Through these models and activities, students will be able to visualize the aspects of cell communication. Additionally, through this activity, students will receive real world examples of cell communication (ex. Touching a hot stove), and will be asked to use their models to help explain how the aspects of cell communication apply to these examples. (See Appendix B)

- Explore: Notes/overview of immune system
  - Students will work through notes and collaborative worksheets (POGIL-Immunity) with the teacher. Through the notes and worksheets, students will learn about the innate and adaptive immune systems, as well as the roles of each cell type within those systems.

- Elaborate: Understanding Immunity, a Modeling Activity
  - Students will understand key players and their functions in different types of immune responses (innate, and adaptive, including humoral and cell-mediated). They will relate the structures and functions of the different proteins involved in immune pathways.
  - Working in small groups, students will become the expert for one of the following types of

immune responses (innate, humoral, cell-mediated). They will then develop a dynamic model of the assigned immune response and show how it works. They will use the model to explain the response to the other groups. When designing the model, they will be assigned components that should be represented in their models and should demonstrate the structures, as well as the functions, of the proteins involved. Models should also show the spatial reference (where these events occur). (See Appendix C)

- Evaluate: ELISA
  - https://www.biointeractive.org/classroom-resources/immunology-virtual-lab
  - Students will work through an online ELISA simulation to investigate how antibodies are involved in the immune system. Through the online simulation students will explore the fundamental principles of an ELISA, as well as be able to explore a particular immunology laboratory technique. While the online simulation explores Systemic Lupus Erythematosus (SLE), following the laboratory investigation, students will be asked to explore additional antibodies and their involvement in a particular immune response. This will allow the students to connect and see how the aspects of the immune system explored in this lab apply to cell communication.
  - Students will then complete an actual ELISA using the following kit from Biorad: Giant Panda Problem Kit. This kit provides tools for students to examine simulated urine samples from giant pandas to determine which panda(s) show evidence of a pregnancy-related complication (pre-eclampsia) through the presence of anti-phospholipid antibodies. Then, in a flexible, guided, or open inquiry investigation, students will design their own ELISA to determine which of four pandas is nearing ovulation to increase the chances of pregnancy in captivity.

Overview of plans for each day of the unit

Day 1: **Immune System Preview-Appendix A** **Cell Communication Notes/POGIL**
Materials: • Video Handout (Appendix A) • Signal Transduction POGIL[1] https://www.flinnsci.com/pogil-activities-for-ap-biology/fb2047/
Description: Students will start out by viewing a short video entitled "Everything You Didn't Want to Know About Snot." This video will provide a short introduction into the immune system to engage the students and allow the students to begin thinking about how our bodies avoid foreign invaders, and what can happen when microbes are still able to invade. As students watch the video, they can think about, and answer, the questions listed in Appendix A. Following the video, a class discussion can allow the students to hear various ideas and help build a class consensus on their understanding of our immune system. With the assistance of the teacher, students will work through the POGIL Activity "Signal Transduction Pathways."[1] Following completion of the POGIL activity, students will share and compare responses with other group's members, and the class will discuss the results found. Students can also work though guided notes with the teacher to help understand and apply the topic of cell communication and avoid misconceptions. For example, students can discuss how the pituitary gland releases growth hormones that can bind to cells, such as cartilage cells, to stimulate cell division.

Day 2: **Modeling Cell Communication** **Appendix B**
Materials: • Modeling Cell Communication Handout (Appendix B) • Large White Boards or Tabletop • White Board Markers/Chalk • Playdoh

- Cell Communication cutouts

Description:

Students will work through "Modeling Cell Communication Activity."[2] Students will work in groups, use Playdoh and cutout models to develop a dynamic representation of cell communication that involves either a G-protein receptor or a tyrosine kinase receptor. Students will then share their models with other groups to compare and contrast the different receptors and actions produced through their models.

Day 3: Immune System Notes/POGIL

Materials:

- Immunity POGIL[1]

https://www.flinnsci.com/pogil-activities-for-ap-biology/fb2047/

Description:

With the assistance of the teacher, students will work through the POGIL activity "Immunity."[1] Following completion of the POGIL activity, students will share and compare responses with other group's members, and the class will discuss the results found. Students can also work though guided notes with the teacher to help understand and apply the topics of the immune system and avoid misconceptions. For example, students can discuss the differences between the innate and adaptive responses, as well as identifying similarities amongst all of the immune responses.

Day 4: Understanding Immunity Modeling
Appendix C

Materials:

- Understanding Immunity Modeling Handout (Appendix C)
- Large White Boards or Tabletop
- White Board Markers/Chalk
- Playdoh
- Immune System cutouts

Description

Students will apply their knowledge of cell communication and the immune system to work through "Understanding Immunity-A modeling Activity." Again, students will develop a dynamic model of an assigned immune response. Responses include the innate response, humoral response, and cell-mediated response. Students will then demonstrate their models to another group to allow students to make connections amongst the different immune responses and see how cell communication applies to the immune system.

Day 5: ELISA Online Simulation

Materials:

- Computer or device with internet access

Description:

https://www.biointeractive.org/classroom-resources/immunology-virtual-lab

This virtual laboratory will demonstrate how such a test, termed an enzyme-linked immunosorbent assay (ELISA), is carried out and some of the key experimental problems that may be encountered. Students will learn about the assay procedure and the equipment and materials that are needed. By completing this exercise, students will gain a better understanding of experimental design, key concepts in immunological reactions, and interpretation of data. As students work thought the completed online ELISA, they can be provided with a guided worksheet to help guide their thinking and record/analyze their results.

Day 6-8: Giant Panda Problem Kit-ELISA Lab from Biorad

Materials:

- https://www.bio-rad.com/en-us/product/giant-panda-problem-kit-for-ap-biology?ID=OM5OWJE8Z
  (See Biorad Kit for components)

Description:

Students will use this kit to practice the basic technique and biochemical interactions as they learn about humoral immune responses. In this investigation students will learn the technique of conducting an ELISA while determining if simulated urine samples from giant pandas contain disease antibodies. If time permits, students can support their knowledge by designing an ELISA to test for the presence of a panda hormone.

IX. Summative Assessments

B. Discussion/Analysis

- Questions to guide data interpretation, Questions that link data to concepts, Probes for analyzing results, Probes for students to ask extension questions
    - Modeling Cell Communication
        - What are the three main components of cell communication?
        - What are the roles of secondary messengers?
        - How would a cell be able to respond to a signal without the signal actually entering the cell?
        - How are proteins involved in the signal transduction stage?
    - Understanding Immunity-A modeling Activity
        - What are some key differences between the innate, humoral, and cell-mediated responses?
        - What makes up the body's first and second lines of defense in the immune system?
        - How do vaccines work?
        - How are the topics of cell communication coming into play in the immune system?
    - Online ELISA
        - What are the components of the immune system and how do they work?
        - How can testing for antibodies help inform a medical diagnosis?
        - What is the purpose of an ELISA?
        - What are some limitations of an ELISA?
    - Bio-rad Giant Panda Simulation
        - What hormones can influence the ovulation cycle of a panda?
        - How do antigens and antibodies interact within the immune system?
        - How can antibodies be engineered to detect the presence of a molecule that does not cause disease, such as a hormone?
        - What is the purpose of controls in an ELISA?

- Possible modes
  (See Appendix B and C)
    - Cell Communication models and explanations
    - Immune System models and explanations
    - Online ELISA Simulation Data Analysis and Questions
    - Giant Panda ELISA Data Analysis and Questions

- Possible rubrics and/or answer keys
  (See Appendix B and C)
  - Rubric for Modeling Cell Communication
  - Rubric for understanding immunity
  - Answer Keys for Online Elisa Lab Simulation
  - Answer Key for Giant Panda Elisa Lab

Student Materials

***Appendix A**

Everything You Didn't Want to Know About Snot

As you watch the video entitled "Everything You Didn't Want to Know about Snot," think through the following questions and use them to help guide our class discussion.

1. Why is mucus important?

2. Describe why snot is considered a "first line of defense?"

3. Explain what goblet cells are and why they are important to snot.

4. Predict what happens when bacteria or viruses pass this first line of defense.

***Appendix B**

Name_____ **AP Biology**

Modeling Signal Transduction Pathways[2]

Purpose:
In this modeling activity, you will compare different signal transduction pathways by building models with clay. The focus of the activity is primarily transduction, but we will review signals and introduce responses as well.

Background:
We have identified at least four classes of signal transduction pathways. G-protein linked receptors, tyrosine kinase receptors, and ligand gated ion channels involve receptors located in the cell membrane. There are also receptors for cell signals located in the cytoplasm or nucleus of the cell. *Note: you will not need to memorize all of the parts of all of these pathways, but by modeling the pathways you will better understand the idea of:*
"Signal → Transduction → Response"

Signal transduction pathways are initiated when the cell receives a signal, for example a hormone signal, from another cell. This signal initiates a series of changes in the cell (transduction) that allows cells to respond appropriately to the signal. The process of transduction is a relay of the message carried by the original signal. When the cell receives the initial signal, the receptor for the signal is either located in the cell membrane OR in the cytoplasm or nucleus of the cell. Think about the chemical composition of the signal and describe the properties of a signal that uses a membrane-based receptor compared to an intracellular receptor. How would they compare?

Once the signal interacts with the receptor multiple things can happen inside the cell. Ultimately, the cell will respond. Responses include, but are not limited to, dividing, creating particular proteins, or changing gene expression. In your group, you will build models of two different classes of transduction pathways. Both involve signals that bind to receptors in the cell membrane.

Procedure:
In your groups, choose one of the signal transduction pathways below to build. Use the large whiteboards, cut outs, and clay materials provided. If time allows, create a "real-time" video to demonstrate your model.

G-protein

- Signal protein
- G-protein linked receptor
- Cell membrane
- GTP and GDP
- Inactive and active G protein
- Second messengers
- Response: Cell releasing Ca^{2+} from the endoplasmic reticulum

Tyrosine Kinase

- Signal Protein
- Tyrosine Kinase receptor
- Cell membrane
- Inactive and active relay protein (phosphorylation cascade)
- ATP and ADP
- Response: Cell releasing Ca^{2+} from the endoplasmic reticulum

Check your understanding:

1. Find another group with the alternate pathway.
2. Share the two pathway models with each group.
3. Both pathways start with a signal protein and end with the cell releasing calcium ions from the ER. Specifically explain how the two pathways differ in the transduction of the signal.

4. Both of these pathways begin with a signal protein. How would the models change if you were to instead use a steroid signal? Explain your answer.

5. What is the role of a second messenger in transduction? Chemically describe second messengers, and explain how their structure suits their function.

6. What is the purpose of the phosphorylation cascade in transduction? Explain

7. It is very important to note that some G-protein linked receptors initiate phosphorylation cascades and some tyrosine kinase receptors initiate second messengers. The point of this modeling activity is to let you see how a signal can remain outside of a cell, yet still cause an intracellular change. So, how would you summarize the ability of a cell to respond to a signal without the signal actually entering the cell?

8. Thinking ahead: Consider the following scenario:
    a. What if one of the proteins in the “transduction” part of the pathway had an abnormal shape (due to a gene mutation) that caused the pathway to be permanently “on” or permanently “off”? What would this mean for the cell? If you need help with this, look up the Ras subfamily of proteins online to get you started.

***Appendix C**

Name_____

Understanding Immunity: A Modeling Activity

Purpose: In this activity, you will investigate the workings of innate immunity, the humoral response and the cell-mediated response.

Learning Objectives:
1. Understand key players and their functions in different types of immune responses (innate, and adaptive, including humoral and cell-mediated).
2. Relate the structures and functions of the different proteins and involved in immune pathways.

Directions:
Working in small groups, you will become the expert for one of the following types of immune responses assigned to you:
1. Innate response
2. Humoral response
3. Cell-mediated response

Your task is to make a dynamic model of the immune response assigned to you. You must show how it works and then use the model to explain the response to the other groups. When designing the model, you should demonstrate the structures as well as the functions of the proteins involved. Key cells, structures and proteins for each of the immune responses are listed below. You may include additional relevant terms that are not listed here. Models should also show the spatial reference, in other words, you need to show where these events are occurring.

Key terms that must be included in your model:

Innate Response	Humoral Response	Cell-mediated response
Pathogen Histamines Cytokines Lysozymes Neutrophils Macrophages Eosinophils Mast-cells Toll-like-receptors Skin Phagocytosis	Pathogen Antibodies Memory B cells Antigen Plasma cells B cell antigen receptor Clonal selection	Pathogen Antigen-presenting cells Memory T cells Cytotoxic-T-cells T cell antigen receptor MHC-I MHC-II

After the model is assembled, you should practice your presentation, first in your small group and then to other groups that share the same immune response. We will be presenting these to the class to better understand the various defenses against pathogens.

When all presentations are completed, summarize the immune response with the activity on the following page.

After viewing the models of all the immune responses, complete the following:

1. General Comparison of the three types of immune responses:

	Innate Response	**Humoral Response**	**Cell-Mediated Response**
How it is initiated: what starts the process?			
Speed of response			
Types of cells involved			
Types of protein molecules involved			
Is memory acquired? If so, what cells?			

2. Compare and contrast MHC I and MHC II. What is the significance of each? Which cells have MHC II? How does the presence of MHC II relate to the functions of these cells?

3. The innate immune response involves the body's first and second lines of defense and is considered a nonspecific response. However, the third line of defense is considered specific. Explain why these statements are true.

4. Discuss how vaccines/immunizations provide active immunity to a particular disease.

5. An individual receives the BCG vaccine, a vaccine used in areas with high rates of tuberculosis. Explain why this person may have received a false-positive on a skin test for tuberculosis.

6. How does cell communication play a role in our immune response? Give an example from one of the models.

7. You have a respiratory infection and the culprit is an adenovirus. Using a flow chart or infographic, show how the immune system responds to the virus.

References

[1]Trout, L., & High School POGIL Initiative. (2012). *POGIL activities for AP biology*.

[2]Freeman, S. (2014). *Biological science*

[3]Reece, J. B., & Campbell, N. A. (2011). *Campbell biology*. Boston: Benjamin Cummings / Pearson