Mind the Gap: Utilizing *Borrelia burgdorferi*, causative agent of Lyme Disease, as a model to study cells bridging innate and adaptive immunity

Author:
Sarah Peterson, Denver Public Schools, Denver, CO

Mentor:
Dr. Mark Soloski, Johns Hopkins University, Baltimore, MD

Table of Contents

INTRODUCTION:

Immunology is a topic that affects every single student in school, regardless of who they are, what their background is, and what they want to be when they grow up. Despite this, the immune system is taught to a very select group of high school students, if at all. The large majority of students never get to learn the wonders of how we stay so healthy, and why some people get cancer, and how hard a virus or bacteria has to work in order to make us sick. This unit serves to teach immunology in a three-week unit, and gives the students time to apply their learning in both a laboratory and debate setting.

Scientists have long broken down the immune system into adaptive and innate, with each cell fitting neatly into one of those two categories. However, as time has progressed, there have been a number of cells discovered that do not fit as perfectly into a category. Many of these cell types find a place to land, but they certainly don't fit into the neat categories like the others. One such cell is the Mucosal-Associated Invariant T Cell, or MAIT cell. This subset of the immune system was discovered in 1999, and was classified as an innate immune cell. However, the more that scientists learn about this cell, the less clear this classification becomes. While there are certainly characteristics that are innate-like, there are also those that are more adaptive in nature.

This debate serves as a perfect place for student inquiry to live. In order for scientists to make an argument for why MAIT cells should be categorized in the adaptive or innate immune systems, they must understand the different characteristics of each part of the immune system. They also must understand what cells currently make up the adaptive and innate immune system, and why those are placed where they are.

This summer I had the opportunity to help conduct research in the lab of Dr. Mark Soloski at Johns Hopkins University in Baltimore, Maryland. Dr. Soloski is a faculty member in the Lyme Research Center of JHU, where studies are currently being conducted on both acute and chronic Lyme patients to determine the immune response in each. My portion of the work looked specifically at identifying MAIT cells in blood samples of Lyme patients to determine if levels of MAIT cells varied in acute versus chronic patients. It involved creating a panel of antibodies for use in flow cytometry, and then a cellular analysis of each sample to determine the MAIT cell population present.

TEACHER GUIDE:

SCIENCE BACKGROUND:

Innate and Adaptive Immunity

The immune system is the body's way of keeping itself healthy. The immune system is comprised of a variety of different cells with a variety of different functions. Together, the different cells ensure that the body stays as healthy as possible. These cells function to communicate, to attack potential pathogens, and to ensure that foreign substances are cleared out of the body.

The innate immune system is the first line of defense for the body when it feels under attack. This form of immunity is more general, and it is also a faster response. It typically responds to a foreign particle in hours. The benefit to this is that the body can quickly respond to an attack and attempt to quell it. The detriment is that the response is less specific, so it is easier for a bacteria or virus to selectively adapt to avoid it. This part of the immune system successfully removes over 90% of foreign objects from the body.

When a pathogen survives the innate immune system, the adaptive immune system is activated. This part of the immune system is significantly more specific than the innate immune system, and it takes longer to activate than the innate. It typically responds to an infection in days. The adaptive immune system is capable of forming "memory," so that once the body fights a given pathogen, it is capable of recognizing that pathogen for many years or the remainder of the life of the individual, providing a faster response to the pathogen. This is the reason that vaccines are given to young children, and the vast majority of those children will never get the disease throughout their entire lifetime.

MAIT Cells

Mucosal Associated Invariant T cells are a subset of cells in the immune system that are found in mucosal surfaces. When they were first discovered in the end of the twentieth century, the thought was that they were a subset of Natural Killer cells. However, as research has progressed, it has become clear that this designation has more nuances than first believed. Originally the cells were thought to be completely invariant, but now this designation has been corrected to semi-invariant, as it is clear that cell modification occurs during the life of the MAIT cell.

Lyme Disease

Lyme Disease is a bacterial infection carried by the blacklegged tick. The bacteria is transmitted from the tick to the human through a tick bite, and it results in a range of symptoms including fatigue, fever, and the characteristic bulls eye rash also known as erythema migrans. The bacteria are most commonly found across the east coast of the United States, as well as

north central United States such as Minnesota and Wisconsin. However, as the climate changes the range of the vector has spread, bringing Lyme disease with it.

Originally, the assumption was that the disease was an acute bacterial infection that could be cleared with one round of antibiotics; however, as the number of cases has increased, a clear subset of patients has emerged that have reoccurring symptoms long after the antibiotics have been stopped. There is current debate on whether this is a result of the bacteria living in a dormant phase and reappearing periodically, or whether it is a case of an autoimmune response that develops as a result of the infection.

STUDENT OUTCOMES:

Students will gain a basic understanding of the immune system and how it functions. More specifically, students will learn about the two different branches of the immune system through a test cell, the MAIT cell, and, at the end of the unit, will decide whether they believe the MAIT cell is more innate-like or adaptive by looking at the way that it functions in the body. Students will utilize data from flow cytometry as well as a case study on Lyme disease to further study the cells of the immune system and comprehend how they function together to keep a person healthy.

LEARNING OBJECTIVES:

At the completion of this unit students will be able to:

- Explain the adaptive and innate immune system
- Explain the cellular features of each type of cell
- Describe the MAIT cell and its role in immunity
- Defend a position on whether the MAIT cell should be categorized in the adaptive or innate immune system
- Analyze data from FACS flow cytometry
- Utilize data to form a position
- Write an argument discussing the position named above

STANDARDS:

The following Common Core and Next Generation Science Standards can be assessed from this unit:

- NGSS HS-LS1-2: Develop and use a model to illustrate the hierarchical organization of interacting systems that provide specific functions within multicellular organisms.
- CCSS.ELA-LITERACY.W.11-12.1: Write arguments to support claims in an analysis of substantive topics or texts, using valid reasoning and relevant and sufficient evidence.
- CCSS.ELA-LITERACY.SL.11-12.1: Initiate and participate effectively in a range of collaborative discussions (one-on-one, in groups, and teacher-led) with diverse partners

on grades 11-12 topics, texts, and issues, building on others' ideas and expressing their own clearly and persuasively.

- CCSS.ELA-LITERACY.SL.11-12.2: Integrate multiple sources of information presented in diverse formats and media (e.g., visually, quantitatively, orally) in order to make informed decisions and solve problems, evaluating the credibility and accuracy of each source and noting any discrepancies among the data.
- CCSS.ELA-LITERACY.RST.I.11-12.1: Cite specific textual evidence to support analysis of science and technical texts, attending to important distinctions the author makes and to any gaps or inconsistencies in the account.
- CCSS.ELA-LITERACY.RST.11-12.8: Evaluate the hypotheses, data, analysis, and conclusions in a science or technical text, verifying the data when possible and corroborating or challenging conclusions with other sources of information.

TIME REQUIREMENTS:

The following amount of time is recommended for the sequence in order to teach the unit in a depth that allows for student retention:

- 1 week pre-teaching innate and adaptive immune system
- 1 week learning the basics of the MAIT cell, and discussing the Lyme Disease application. As we learn, do we think that research should look at MAIT Cells as a potential indicator for Lyme Disease immune response? Why or why not?
- 1 week lab experience with local scientist and data analysis
- 1 week to prepare for Socratic seminar using a graphic organizer explaining the claim, counter claim, and supporting evidence, and then submit a final written opinion citing scientific evidence from readings, the lab experience, and the Socratic seminar.

ADVANCE PREPARATION:

Pre-teaching Immunology:
First, it is important for the teacher to be comfortable with the material being presented in the upcoming lessons. If the teacher did not teach immunology prior to this, it is a good idea to go through the lessons before teaching students. The terminology and relationships can be complex, and the research is also continuously evolving. Therefore, being comfortable with the information and its evolution is helpful for the teacher.

MAIT Cells:
To teach MAIT cells, there are notes connected to the topic below. The key here is to fully understand the characteristics that make them adaptive-like, and the main characteristics that make them innate-like. Lyme Disease can be used as a model to discuss the cells to get at the idea of where the cells are typically found, what the function is in the body, how they fit into the bigger picture of the immune system, and how they seem more innate-like or more adaptive-like.

Scientist and Data Analysis:
Prior to starting this unit, it is important to begin the search for a local scientist. This is by no means required for the unit, but it can add a nice dimension and allow students to see a potential career path. Many local scientists are very willing to partner with schools; they just don't always know how best to help. The further ahead of time that you can schedule this, the more luck you will have. Places to look include local hospitals (if they have a research component) or a local university. Ideally, the scientist will come to your classroom to work with your students for a day, and then your students can visit the lab and see how the data is produced.

Socratic Seminar and reading preparation:
For this portion of the unit, the major component is ensuring that readings are ready and anticipated student needs are noted. If students are on grade level, they will likely be able to handle the reading with little struggle. If they are below grade level, a number of scaffolds may need to be put in place to guarantee success. Examples of this include text-dependent questions, collaborative grouping, or providing a glossary of terms to accompany the text. It is not recommended that the text be altered, as standards specifically note that students should be exposed to grade level texts.

SUMMATIVE ASSESSMENT

The summative assessment for this assignment is a final paper in which the student argues to the following task.

Should the MAIT cell belong in the Adaptive or Innate Immune System? After reading current research and infographics on the immune system, write an essay in which you argue where the MAIT cell belongs in the current breakdown of the immune system. Defend your position with scientific evidence from the text.
Optional Extension: Use Lyme disease as an example when making your argument.

Under the teacher materials there are suggested scaffolds to help build a student's ability to write a scientific essay. There is also a suggested rubric that can be used to assess the papers.

MATERIALS AND EQUIPMENT:

- Hand outs
- Articles
- Rubric
- Flow data
- Scientist
- Flow machine at local lab
- Access to FlowJo to look at different results or printed by the scientist partnering

STUDENT PRIOR KNOWLEDGE:

Prior to beginning this unit, students should have a basic understanding of cells and the way that they function in the body. The immune system is typically taught at the end of an advanced biology or anatomy and physiology class. Therefore, students should have a basic understanding of best practices in the lab, and should have been exposed to multiple types of data for evaluation.

TEACHER FACING MATERIALS:

Document 1: Overview of the reading and writing process:

Immune System, NAIAD	Goal is to introduce students to the basics of immunology.	**Text Dependent Questions:** Student answers the attached questions while exploring the NIAID website to increase understanding around the immune system.
Clarifying notes	Used after website exploration before reading.	This ensures that all students have basic information written in notes prior to the start of the readings.
Socratic seminar	Get students to think and question what they are going to be reading about and what their wonderings are in this manner. Sample MAIT Cell Flow Cytometry Diagram of a MAIT Cell interaction	Give students the picture of a MAIT cell and a FACs plot. Have students write down at least 3 questions on each picture as homework. They can be basic "What is CD4?" or about the picture "Why is that box surrounding one area of the graph?" Have a doc open where students who are not speaking can catch all of the questions. It is important to verbalize to see if the questions build on each other and to see if additional wonderings come.
Post reading after the Socratic seminar	Mucosal-associated invariant T-cells: new players in anti-	

	bacterial immunity MAIT Cells Detect and Efficiently Lyse Bacterially-Infected Epithelial Cells	

Reading process:

Immune Cell 'Defenders' Could Beat Invading Bacteria	Overview of the Nature article that notes the discovery and overview of MAIT cells.	**Double-entry journal.** Have students read the article, summarizing the research on the left side and making personal connections or connections to notes from previous days on the right side. Should establish why students should care about this research and how it impacts them.
MAIT cells are licensed through granzyme exchange to kill bacterially sensitized targets	Original publication on the discovery of MAIT cells (frame this as "this is the journal where a lot of groundbreaking research gets published. Many Nobel prize winners have published their research in this journal. Watson and Crick first published the shape of the double helix here").	**Annotate** the article by circling unknown words, underlining the main idea of each paragraph, and annotating (on the side of the paper) how this article goes into more detail on the previous day's article. This can be done in groups so that students can work together to compare the two.
CD161++CD8+ T cells, including the MAIT cell subset, are specifically activated by IL-12+IL-18 in a TCR-independent manner	Optional	
MAIT cells are critical for optimal mucosal immune responses during in vivo pulmonary bacterial infection	Optional	
MAIT cell alterations involved in obesity, diabetes	Link between obesity, type 2 diabetes, and MAIT cells/the immune system.	**Annotate:** Annotate this article by underlining the main claim of each paragraph. In the margins, write answers to the

		questions 1. What is the research? 2. Who does it help? 3. Why is this important to me? These questions should be answered in summary form. **Text-dependent questions:** Use as a connection to discuss how the immune system plays a role in so many diseases. What are all of the different areas that we think of inflammation?

Transition to writing:

Repeat the Socratic seminar	Have students determine what constitutes whether a cell belongs to innate or adaptive immunity.	Give students the same two pictures, this time asking them to focus on their notecatcher and what makes an adaptive vs. innate immune cell. Knowing this, have a discussion grounded in the picture and the data, referencing both in making an argument to either place MAIT cells in the innate or the adaptive immune system.

Writing process:

Create an outline	Begin thinking through what is needed in the paper.	Have students brainstorm what pieces of information are important for a reader to fully understand what makes the adaptive and innate immune systems and where the MAIT cell falls. Be sure to point out what background information is necessary and why it is important that students fully explain the two different parts before going into convincing the reader.

Fill in the outline	Use notes from the two notecatchers (preparing for the task and reading process).	There is a sample outline provided in the teacher guide. At this point, students should make something similar in format to the outline given, providing sound evidence from the readings to support their stance on MAIT cells. A word of caution about use of the outline. You may consider not showing it to students to avoid getting a class full of papers that look very similar to that outline.
Peer Edit	Allow students to help one another increase writing level by allowing for targeted feedback.	Provide students with the grading rubric and review what makes good feedback and poor feedback. Things such as "Good paper" may be nice, but they don't help a person improve the writing. Give examples of feedback that could be helpful for students to hear to improve writing.
Citations	Insert citations into the paper.	

Document 2: Socratic Seminar One Pager

The Socratic Seminar: Are MAIT Cells Part of the Adaptive or Innate Immune System?
This is based off of the AVID Socratic Seminar method. It involves all students having a discussion surrounding a piece of text. All students should enter the seminar space with two questions prepared based on the text. Students should work in partners, with one partner sitting on the inside of the circle and one partner standing on the outside of the circle at all times.

The text:
Typically a Socratic Seminar is based off of a specific text. For this adaptation, rather than a text, students are using the data that they have either collected from the lab or that the teacher has provided. Students should know background on what makes an innate vs. an adaptive immune cell. If this has not been explicitly pre-taught then a supplemental reading can be used as another source of evidence for students.

The question:
Prior to the start of the seminar, each student should prepare two questions based on the text.

These questions should relate to the overall question and come directly from the text. The seminar begins with a few students stating one of their questions, and the class noticing trends that exist from the questions listed. The seminar begins around that consensus question that comes from the trends.

The Leader:
This can be the teacher or a responsible student in the class. If you have never done this type of speaking exercise before, it is best to have the teacher lead the first round. This person is in charge of timing (typically around 5 minutes per question unless the conversation stalls), and in charge of ensuring that the discussion is text based.

Sentence starters if the seminar gets away from the data:
1. What in the text leads you to think…..
2. How does the data support….

The Inner Circle Participants:
The only people who are allowed to speak are those sitting in the inner circle. These students should have the data in front of them as well as the questions for both them and their partner. They speak on behalf of their team of two when sitting in the inner circle.

The Outer Circle Participants:
The outer circle participants serve as teammates to those in the inner circle. They can give advice and contribute to the conversation by writing on sticky notes and passing them into the partner on the inside. This allows them to be active listeners, and it gives an element of safety to the students, since there are two of them contributing ideas at all times.

Modifications:
1. If needed have an object that represents who is speaking. This object can be passed around to whomever wants to speak, and it helps to ensure that only one person is speaking at a time.
2. Give each student two or three "tickets" that they are allowed to use to speak. Once they have spent their tickets, they tag out and their partner tags in. This ensures that everyone is getting a turn to speak and that no one is dominating the conversation.

Grading:
Students can be graded on participation, or the teacher can request a written piece at the conclusion of the seminar.

<u>Document 3: Obtaining Lab Data from a Local Scientist:</u>

This unit looks at flow cytometry data as evidence that the MAIT cells express certain features of innate immune cells, and certain features of adaptive immune cells. One recommendation on how to teach flow cytometry to students is to partner with a local scientist who has access to a

flow machine. The benefit of this is that it allows an opportunity to create a partnership between the high school and local university.

Recommendation for reaching out:
Roughly a month before the unit begins, research (or assign a student to research) work being done at local universities that relates to immunology. Most PIs are more than happy to discuss their work with teachers and students, and many enjoy sharing in their excitement for immunology. One option is to ask the scientist to come out to the classroom and spend a day explaining their research to students, and to allow students to go through the experimental process of exposing Peripheral Mononuclear Blood Cells (PMBCs) to antibodies which will then be evaluated in flow cytometry. This would help students comprehend what exactly flow cytometry is, and what information it provides to a scientist using it in research. One optional extension to this is to then schedule a fieldtrip to the lab of the scientist, taking students to see what research looks like at that level and make connections to the students' future plans.

A second option is to communicate with the scientist and ask for flow cytometry data that they have gathered. This still allows for an opportunity of collaboration between students in the classroom and the local scientist, and it gives the students the chance to see real data when interpreting it to make an argument. There are also data attached to this curriculum that can be used if needed.

Document 4: Sample Outline for the final paper

I. Introduction
    A. What is the immune system?
    B. How does it help the body?
    C. What are the different parts, and how do they support human health?
    D. Thesis statement (the MAIT cell belongs in the innate immune system)
    E. Points to cover (the cell receptor does not change, can cause cytokine secretion, cells do not originate in the thymus)
II. Body paragraph 1:
    A. Main point: Ex. cell receptor does not change
    B. Evidence: (cite reading)
    C. Reasoning: Adaptive immune cells literally adapt to become more specific, MAIT cells do not
        1. Explain more details about traditional T cells to support point
    D. Counter argument: Some say because T cell Receptor exists it should be in same category as T cells, but because the T cell Receptors do not change, they should not be automatically put together.
III. Body Paragraph 2:
    A. Main point: Ex. MAIT cells do not mature in the thymus
    B. Evidence: The MAIT cell matures outside of the thymus in the tissue, while traditional T cells are produced in the thymus. Even Natural Killer T cells come

from the thymus, making them closer to the T cell than MAIT cells are. (Ussher et al., 2014)

C. Counter argument: One argument against this is that MAIT cells originate in the thymus, but the maturation occurs outside of it. While this is true, the maturation and recombination that occurs in the thymus is critical to the designation of adaptive cells.

IV. Body Paragraph 3:
   A. Main point: Ex. MAIT cells produce a cytokine response that recruits other cells to the site of the infection.
   B. Evidence: According to Cosgrove et al. (2013), MAIT cells produce IL17, which is a cytokine used in the inflammatory response and characteristic of innate immune cells.
   C. Counter argument: While the MAIT cell also contains receptors that are traditionally associated with the adaptive immune system, their cytokine response indicates an innate characteristic.

V. Optional Extension: Body Paragraph 4:
   A. From what you know, should MAIT cells be investigated further in relation to Lyme Disease? Why or why not?

VI. Conclusion
   A. MAIT cells are a unique subset of cells that contain features of both the adaptive and innate immune system. While they theoretically could be members of either part of the system, the innate system is the more logical choice because of the characteristics of these cells, such as their limited adaptations, their location of origin, and their production of cytokines.

References

Cosgrove et al. (2013) Early and nonreversible decrease of CD161++ /MAIT cells in HIV infection. Blood. 121:951-61.

Ussher et al. (2014) Mucosal-associated invariant T-cells: new players in anti-bacterial immunity. Front Immunol. 5:450.

Videos to Assist:

It can be helpful to utilize videos, particularly in support of visual learners. The following videos can be used in conjunction with the readings above to help students visualize the processes being discussed.

TLRs: https://www.youtube.com/watch?v=94emS00OIHc

Antigen presentation: https://www.youtube.com/watch?v=LwLYGTS_3EI

B cells and antibodies: https://www.youtube.com/watch?v=548wQ5C6ufQ

T cells: https://www.youtube.com/watch?v=V5wXrxupQmA

STUDENT GUIDE:

RATIONALE:

You know what happens when you get sick, right? If you have a cold, you might get a runny nose, a little bit of a cough, maybe a fever. Do you ever wonder why that is? What happens that makes you feel these that way?

The next four weeks we will begin to explore this topic and find answers. You will understand at the cellular level what is occurring in your body that keeps you healthy and safe from foreign pathogens.

SCIENCE BACKGROUND:

Innate and Adaptive Immunity

The immune system is the body's way of keeping itself healthy. The immune system is comprised of a variety of different cells with a variety of different functions. Together, the different cells ensure that the body stays as healthy as possible. These cells function to communicate, to attack potential pathogens, and to ensure that foreign substances are cleared out of the body.

The innate immune system is the first line of defense for the body when it feels under attack. This form of immunity is more general, and it is also a faster response. It typically responds to a foreign particle in hours. The benefit to this is that the body can quickly respond to an attack and attempt to quell it. The detriment is that the response is less specific, so it is easier for a bacteria or virus to selectively adapt to avoid it. This part of the immune system successfully removes over 90% of foreign objects from the body.

When a pathogen survives the innate immune system, the adaptive immune system is activated. This part of the immune system is significantly more specific than the innate immune system, and it takes longer to activate than the innate. It typically responds to an infection in days. The adaptive immune system is capable of forming "memory," so that once the body fights a given pathogen, it is capable of recognizing that pathogen for many years or the remainder of the life of the individual, providing a faster response to the pathogen. This is the reason that vaccines are given to young children, and the vast majority of those children will never get the disease throughout their entire lifetime.

MAIT Cells

Mucosal Associated Invariant T cells are a subset of cells in the immune system that are found in mucosal surfaces. When they were first discovered in the end of the twentieth century, the thought was that they were a subset of Natural Killer cells. However, as research has

progressed, it has become clear that this designation has more nuances than first believed. Originally the cells were thought to be completely invariant, but now this designation has been corrected to semi-invariant, as it is clear that cell modification occurs during the life of the MAIT cell.

Lyme Disease

Lyme Disease is a bacterial infection carried by the blacklegged tick. The bacteria is transmitted from the tick to the human through a tick bite, and it results in a range of symptoms including fatigue, fever, and the characteristic bulls eye rash also known as erythema migrans. The bacteria are most commonly found across the east coast of the United States, as well as north central United States such as Minnesota and Wisconsin. However, due to changes in climate, the range the vector has spread, bringing Lyme disease with it.

Originally, the assumption was that the disease was an acute bacterial infection that could be cleared with one round of antibiotics; however, as the number of cases has increased, a clear subset of patients has emerged that have reoccurring symptoms long after the antibiotics have been stopped. There is current debate on whether this is a result of the bacteria living in a dormant phase and reappearing periodically, or whether it is a case of an autoimmune response that develops as a result of the infection.

STUDENT HANDOUTS

Student Handout 1: Graphic organizer to capture learning from the NIAID website.

Pre-reading questions based on website:
What is NIAID?:

Describe 3 ways the NIAID has impacted your life according to what you know about the agency:

1. _
2. _
3. _

Innate Immune System:
Cells:
What is the main role of the innate immune system, according to the definition of what all of the cells do?

Write an analogy of the innate immune system.

Compare and contrast the different cells of the innate immune system. How do they all work together to create an effective response?

Inflammation:
Describe the mechanisms of inflammation. What is the purpose?

Describe the cells and chemicals involved in inflammation.

Describe the mechanism of fever and the roles of pyrogens.

Adaptive Immune System:
Cells:
Define immunocompetence and self-tolerance, and distinguish between naive and activated immune cells.

Compare and contrast B cells and T cells in the location where they originate and the location where they end up in the body.

Compare and contrast the defense mechanisms of each cell. When are they most effective, and why?

What is the structure of the antibody, and how does its structure relate to its function?

What differs between the adaptive and innate immune systems?

Vaccinations:
How do vaccines utilize the immune system to create immunity?

Is this immunity adaptive or innate? Explain your answer.

Communication:
A person has a disorder in which the complement system never activates. What would that person expect to see in terms of both intercellular and whole body symptoms?

What are cytokines and how do they function in the immune system?

What are MHCs and how do they assist in intercellular communication?

What are examples of Antigen Presenting Cells and where are they found?

Research frontiers:
Jigsaw the research frontiers and have students teach each other (in table groups of 4, each person picks one of the research frontiers).

Student Handout 2: Evidence Note Catcher to be used throughout the unit

As you complete your reading, utilize this chart to gather evidence of how MAIT cells have characteristics of the innate immune system, and how MAIT cells have characteristics of the adaptive immune system.

	Evidence that MAIT cells belong in innate	**Evidence that MAIT cells belong in adaptive**
Source Title: Source Author: Source Publication: Source Date:		
Source Title: Source Author: Source Publication: Source Date:		
Source Title:		

Source Author: Source Publication: Source Date:		
Source Title: Source Author: Source Publication: Source Date:		

Resources used:
http://missinglink.ucsf.edu/lm/immunology_module/prologue/objectives/obj02.html