The Immune System as an Illustrative Example

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The American Association of Immunologists
Teacher Research Program

in collaboration with mentor
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and

Recommended Audience: AP Biology Teachers

Class Schedule: 3 quarters, 85 minutes/day

Curriculum Outline: This is not intended to be a stand-alone immunology unit, though it could be modified for that purpose. Instead, it is a method for incorporating immune system concepts within other units. Therefore, aspects of the immune system will be shared with students over multiple units. During the immune system unit, students put their prior learning together with additional learning culminating in a project that requires them to demonstrate their comprehensive understanding of immune topics.

To do this successfully, it will be helpful to set the stage for investigating the immune system early in the year. This can be done in a variety of ways, listed below:

- Brainstorming – Provide students with a list of questions, such as, "How does your body fight an infection? How do vaccines work? What are autoimmune disorders?" Give students a chance to discuss and then share ideas with the class. Record ideas and questions on posters placed around the classroom so they can be referred to later.
- Video and discussion – Show a video clip that highlights an interesting immune-based scenario. Provide students an opportunity to discuss what they watched and find out what questions the video prompted.
- Article and discussion – Same as above, but with reading an article.

In each unit, refer back to the conversation and questions that were discussed as a way to engage students with the current learning.

AP Biology Curriculum Framework Objectives: These are written in the style of the Curriculum Framework. Enduring Knowledge benchmarks are abbreviated to E.K. and L.O. stands for Learning Objectives. Science Practices are abbreviated S.P.

Background Knowledge:

This lesson is meant to be an illustrative example of the concepts students have learned during the biochemistry unit. They will demonstrate their understanding of those concepts in this applied example. Therefore, students should have ample background information. They should be familiar with basic chemistry including composition of atoms, types of bonds and how they form (covalent, hydrogen, disulfide bridges). They should have already learned about the major macromolecu

d. Proeins hav primar y srcur deermined b y he seqence order of heir consien amino acids, secondar y srcur ha arises hrogh local folding of he amino acid chain ino elemens sch as alpha- helices and bea- shees, eriar y srcur ha is he ovrall hree- dimensional shape of he proein and ofen minimi z es free energ y , and qaernar y srcur ha arises from ineracions beeen mliple pol y pepide nis. The fon elemens of proein srcur deermine he fncion of a proein.

Lesson Deails:

Sdens ill need a deice o access he ideo, or i can be shon o he class as a grop.

Sdens ill also need a deice o access he 1hsa file a rcsb.org. The ebsie orks bes on a compr. If sing an iPad, sdens ill be nable o mose ovr he srcr hich prevens hem from ansering qsions 13, 14, and 18.

I is impora o proide sdens ih a lile backgrond on ho he srcr of proeins has been inesigaed. Thogh x -ra y cr y sallograph y is no a reqired componen of he AP Biolog y crricl, i helps o gie sdens cone x for he models ha are sed in his aciiy . If y ohae sdens ho e x press an ineres in he area of x -ra y cr y sallograph y , I recommend he book The Gene Machine b y Venki Ramakrishnan hich is abo he discoer y of he srcr of he ribosome.

As ih all sden- led aciiies in his docmen, i is recommended ha y obring sdens back as a grop a he end of he class or a he sar of he ne x class o discss heir ansers, or collec heir responses and proide personali z ed feedback in some oher a y .

Possible discssion qsions:

Ho did his aciiy help deepen y onnderstanding of proein srcr?

Wha are y oncrios abo no ha y okno ho MHC holds pepides?

If sdens press o kno he deails of he immne s y sem, a his poin, i is bes o kee p hem engaged ih open- ended qsions sch as:

Based on y oncren nderstanding, ha do y ohink?

is not included in the structure and is shown schematically.
Download high quality TIFF image

displa y ed b y he MHC molecle on he srface of he cell. Wha secondar y srcre appears o be gripping he pepide from he sides?
alpha helices

11. Which secondar y srcre is holding he gra y pepide from belo?
bea shees

12. These 2 secondar y srcres are ha form he "grip" on he iral pepide ha as described in he aricle abov. H y pohesi z e ho his pocke is able o "grip" he gra y pepide.
Ansers ill var y ; perhaps h y drogen bonds disfide bridges, ionic bonding, or h y drophobic ineracions beeen he MHC and pepide hold i in place.

13. Mose ov r he srands and pase nil a label pops p. The label shos he amino acid a ha posiion and liss he y pe of amino acid in brackes, he nmber of he amino acid in seqence saring ih he N -ermins, and hen some oher coding z id

-

16. Disulfide bridges are involved in the tertiary level of protein folding. This means the y form between which
    - the backbone structure of a polypeptide or
    - the R groups of a polypeptide?

17. Describe the location of those disulfide bridges. What role do the y seem to be playing in the structure of the molecule?
    The y join 2 beta sheets together or the y join an alpha helix with a beta sheet. It appears the role of disulfide bridges in this protein are to stabilize its 3D structure.

18. In the Display Options window, click on H -Bonds. The dotted lines represent hydrogen bonds. In an alpha helix, every hydrogen bond occurs between amino acids that are separated by how many amino acids? (count by moving over the structure)
    4

19. Is the same true for beta sheets? Are the amino acids joined by a hydrogen bond separated by the same number of amino acids?
    No, the number of amino acids between here 2 are joined by hydrogen bonds varies.

20.

Now that you've learned about protein structure, let's investigate a protein that is important in the immune system. But first, how do we know about the structure of proteins? And how is the MHC molecule important in our immune system?

Background on x-ray crystallography: https://youtu.be/watch?v=qQlY8VQI

This is an excerpt that has been slightly modified from the Molecule of the Month feature on MHC from the Educational Portal of the Protein Data Bank (PDB).

Major Histocompatibility Complex

MHC displays peptides on the surfaces of cells, allowing the immune system to sense the infection inside

Viruses are insidious enemies, so we must have numerous defenses against them. Antibodies are

1. According o p

18. In the Display Options window, click on H-Bonds. The dotted lines represent hydrogen bonds. In an alpha helix, every hydrogen bond occurs between amino acids that are separated by how many amino acids? (count by moving over the structure)

19. Is the same true for beta sheets? Are the amino acids joined by a hydrogen bond separated by the same number of amino acids?

20. Does MHC exhibit quaternary structure? What evidence do you have to support your answer?

21. As mentioned above, the transmembrane portion (the part that anchors MHC in the membrane) is too flexible for study by x-ray crystallography, so it has been removed. Given what you know about the structure of the cell membrane, predict the characteristics (acidic, basic, polar, or nonpolar) of the amino acids in the transmembrane portion of the protein and explain your prediction.

Students may wonder how the viral genome is replicated since it isn't described in the animation. The virus either contains enzymes for synthesizing the negative sense DNA or has genetic information that results in synthesis of those enzymes.

5. How is the process of releasing viruses important to their structure?

Since viruses had leaved by exocytosis end up coated in the cell's plasma membrane, any viral proteins that were incorporated into the plasma membrane will end up on the surface of the virus.

6. Hypothesize methods we could use to interfere with viruses. What could be a target? What would we have to avoid targeting?

Antigens (or viral proteins, if you don't want to introduce the vocabulary term here). Depending on your students' background knowledge you could ask what molecules are made by specialized immune cells that travel in the blood and attach to antigens, or explain antibodies. Guide students to understand that this targets the viruses that are traveling in our bodies OUTSIDE of cells, which isn't enough. Explain that we must also target viral reproductive cycle to stop the manufacture of new viruses. This sets the stage for understanding the 2 different branches of our adaptive immune system, humoral and cell-mediated, without necessarily going into all the details yet.

You don't usually target the cell's machinery itself. To do that, you'd need to give a person a drug that interfered with the basic cellular processes needed to keep cells alive and functioning. This would be toxic.

So how do we interfere with the viral reproduction cycle?

You might remember the images on the right. There are 2 different ways of representing the MHC molecule we studied in a previous unit. Answer the questions below to jog your memory about this molecule.

7. To which macromolecule category does it belong?
   protein

8. The MHC molecule plays an important role in which system?
   immune

9. The red molecule on the left image and the gray molecule in the right image represents what?
   viral protein (or cytosolic protein that's native to the cell itself)

Read this excerpt from the Molecule of the Month on MHC to further refresh your memory:

> Each cell has another type of defense that it uses to signal to the immune system when something goes wrong inside. Cells continually break apart a few of their old, obsolete proteins and display the pieces on their surfaces. The small peptides are held in MHC, the major histocompatibility complex, which grips the peptides and allows the immune system to examine them. In this way, 1 (a)11.8 0 g8naaom11.5 0 and a ht h.6 (l)21.9 (e)66.1 (mes)1 ((l)7.1 (i)-4.3oei)-4


Chromosomes
1
membrane fusion or endocytosis
9 Exocytosis
Receptor
Ribosome

Now that we've learned about the inner workings of a cell, how can a cell be hijacked by a virus in order to make more virus particles? How does our body defend against these invaders?

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If you are interested…

Below is a visual explains the reproductive cycle of SARS-CoV2.

Cell Signaling Uni

Backgrond informaion: Sdens should have learned abo signal ransdcion pahas as an earlier par of his ni. The y should be familiar ih he y pes of recepors, roles of kinases, phosphaases, second messengers, and y pes of responses. The y shold also kno he difference beeen aocrine, paracrine, and endocrine signaling.

Lesson Draion: 1 /2 block (40 mines)

Objecives:

Sdens ill se a specific immne cell e x ample o idenif y he componens of a signal ransdcion pahay and e x plain heir roles .

AP Biolog y Crricln Frameork Learning Objecives:

E.K. IST-3 Cells commnicae b y generaing, ransmiing, receiing, and responding o chemical signals.

L.O. IST-3.A Describe he a y s ha cells can commnicae ih one anoher.

E.K. IST-3.A.1 Cells commnicae ih one anoher hrogh direc conac ih oher cells or from a disance ia chemical signaling –a. Cells commnicae b y cell -o -cell conac.

L.O. IST-3.D Describe he role of componens of a signal ransdcion pahay in prodcing a celllar response.

E.K. IST-3.D.1 Signaling begins ih he recogniion of a chemical messengera ligand –b– y a recepor proein in a arge cell –a. The ligand -binding domain of a recepor recogni z es a specific chemical messenger, hich can be a pepide, a small chemical, or proein, in a specific one-o -one relaionship.

E.K. IST 3.D.2 Signaling cascades rela y signals from recepors o cell arges, ofen amplif y ing he incoming signals, resling in he appropriae responses b y he cell, hich cold incde cell grh, secreion of molecles, or gene e x pression— a. Afer he ligand binds, he inracellar domain of a recepor proein changes shape iniiaing ransdcion of he signal. b. Second messengers (sch as c y clic AMP) are molecles ha rela y and amplif y he inracellar signal.

Lesson Deails:

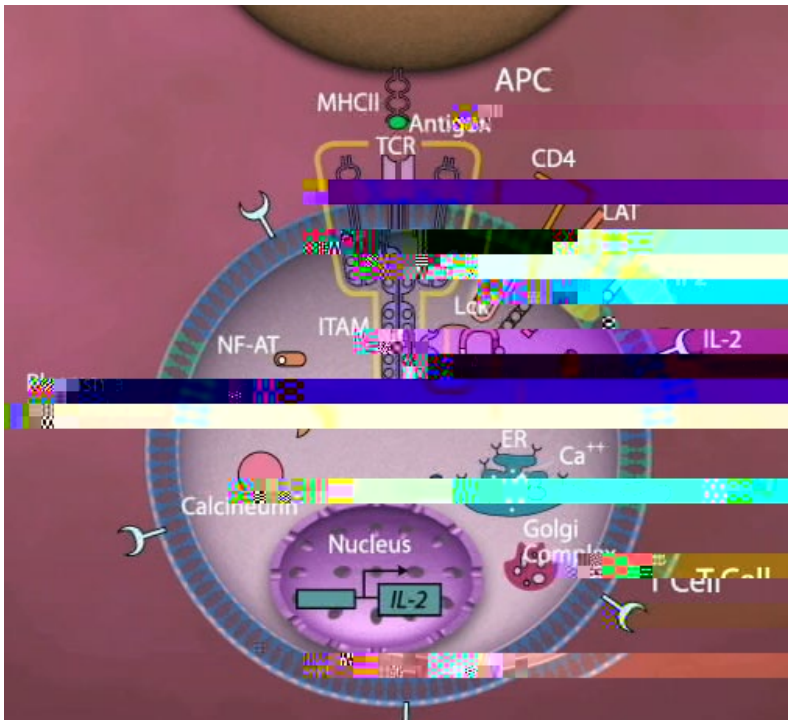
Remember he immne s y sem? Wee learned abou MHC molecles and ho he y can displa y iral proeins on cells. As i rns ou, hen an immne cell ineracs ih he displa y ed proein, i iniiaes a signal ransducion pah a y . Wee going o learn more abou ho a paricular ineracion beeen 2 immne cells orks. Thogh his e x ample has been simplified, i is sill er y comple x . Here are a fe erms o ge y ou on he righ rack.

Remember he immune s y sem? We've learned abou MHC molecules and ho he y can displa y viral pro eins on cells. As i urns ou, hen an immune cell ineracs i h he displa y ed pro ein, i iniiaes a signal ransduion pa ha y . We're going o learn more abou ho a paricular ineracion be een 2 immune cells orks. Tho gh his e x ample has been simplified, i is sill ver y comple x . Here are a fe erms o ge y ou on he righ rack.

anigen – This is an y sbsance ha cases an immune response. In ou previos lessons, e discssed iruses as he pahogen. We learned ha iruses are broken don into viral proeins hich can be displa y ed b y MHC molecles. In he image, ha color is he anigen?

APC – This is an anigen -presening cell. In he image, ha color is he APC?

MHCII – This is a specific y pe of MHC molecle. I i sn' he one sed b y infeced cells o aler immune cells o kill i. Instead, MHCII are sed b y special immune cells ha can simlae oher immune cells, in his e x ample, a T cell. In he image, ho man y nis make p he MHCII molecle?



TCR – TCR sa nds for T cell recepor. The ideo is highlighing ho a T cell responds o a cell ha's displa y ing viral proein. Wha color is he TCR in he image?

Open he T Cell aciation ideo : hp://.hhmi.org/bioineracive/cloning -arm y--cells-immune -defense.

1. Wha does a kinase do (b y definiion)?

2. Which of the proteins in the animation could be classified as kinases?

3. What does a phosphatase do (by definition)?

4. Which of the proteins in the animation could be classified as phosphatases?

5. Which of the following components are present in this signal transduction pathway?

Reception – Tyrosine kinase receptor G-Protein coupled receptor

Transduction – Which second messenger is used? cAMP IP3 and Calcium

Response – changes in: cytoskeleton enzyme activity gene expression

6. What are the effects of this cell producing IL-2?

7. Is the release of the IL-2 chemicals an example of endocrine signaling or paracrine signaling? Explain why.

8. Now that you've seen an example of a signal transduction pathway in an immune cell, what questions do you now have about cell signaling or the immune response?

Spiderman, and a varie y of props. In Par 3, folloing he sk

Immune System Unit: Lesson 1, Part 1 TEACHER NOTES

Students read Chapter 43.1 from Campbell Biology, 9e or a similar introduction to innate vs adaptive immunity. This should be an overview only.

Then use [these Powerpoint slides](#) and direct instruction to introduce innate and adaptive immunity.

Deepen the discussion by mentioning PAMPs, which are pathogen-associated molecular patterns that are commonly exhibited on pathogens. Our innate immune system can recognize these motifs as foreign and defend against them.

Vaccines use the adaptive immune response to protect us against future infections of the same pathogen.

A common misconception is that animals have immune defenses but other organisms don't. This is a great opportunity to mention that plants have defenses, too, including epithelial surfaces that are often reinforced with strong proteins, sugars.

To help students correcar [illegible] Toelpi (ents)2 (c)3 (o)3 (r)6 (r)6 (ecar)6 (

1. The esophagus produces a fluid that is rich in mucin and bicarbonate. This fluid provides protection. What type of defense is this? Innate, Barrier: mucous membrane

2. A vaccine prompts your immune response to respond to future infections of that particular pathogen. If you encounter a pathogen for which you've been vaccinated, that response is activated? Adaptive: both humoral and cell-mediated

3. What part of that response refers to the molecules that are released in mass quantity in the bloodstream? Adaptive: humoral (the molecules are called antibodies)

Immune System Unit: Lesson 1, Part 2 TEACHER NOTES

As students begin working on the questions from Part 1, ask for 9 volunteers to participate in a skit. (They can finish the questions on their own time.)

Bring them into a separate area where you can assign roles, distribute props, and direct the skit while students read it.

(if the prop represents an immune component, it has been listed in caps) :

Spiderman mask – Available online or in the party section of some stores

Batman mask - Available online or in the party section of some stores

Boomerang – (beyond the scope, but this represents perforin and granzyme which initiate apoptosis of the infected cell). This can be made of paper.

Bandanas (4) – ANTIGEN. Any bandana will do, though it is helpful if all 4 look identical.

Badge – MHC-II. A sleeve for a teacher badge on a lanyard works well, or it could be made with paper.

Brain – MEMORY B CELL. A printed picture of a brain will do, but use a brain model I have in the classroom.

Basketball – INTERLEUKIN-2. Print a Batman outline from the internet and cut so the paper is in the shape of the symbol

Flood lamp or flashlight – any type of light will do; a student will hold the basketball in front of it to show the basketball as a shadow on the wall.

White flag – MHC-I. Attach a triangle of white paper to a dowel or popsicle stick.

CD – (not shown in the Cmap, but this represents MEMORY HELPER T CELL.) An old CD works well as a memory because CDs can be used to store things. Alternatively, you could use a memory stick, it's just harder to see. NOTE: this does not appear in the Cmap activity.

Silly string – ANTIBODIES. This part is optional, but is intended to represent antibodies which neutralize, opsonize, and activate the complement system. It's a nice visual to imagine silly string as the webbing that Spiderman uses to neutralize the bad guy. Note: Avoid silly string with dyes as it may stain student clothing! Also, instruct to point at waist level to avoid getting it in the eyes. Goggles could be worn for that reason.

Glasses and clipboard – any old readers will do. The idea with these 2 props is to help the student who is playing Alfred the Butler to feel more involved!

Actors are in green. Props are in blue.

Narrator reads italicized text

SCENE 1

Gang members (2)	wearing bandanas (gang symbols), carrying a couple more bandanas
Watch Group member	wearing a badge to identify him/herself
Innocent bystander	has a white flag that is hidden

It's a warm, muggy night.

Gang members prowl around, looking for trouble. They flash their gang symbols multiple times. Check out their goofy handshake. <Pause for flashing of bandana and handshake; both gang members move through crowd>

One gang member recruits an innocent bystander to become part of the gang. He gives them a bandana to affirm membership to the gang. <Gang member solicits bystander and hands him the bandana. Bystander reluctantly takes it.>

The innocent bystander may be reluctant, but he takes the bandana.

A local member of a Watch Group enters the scene. Seeing one of the gang members, he stares at him until he crumples to the ground. The Watch Group snatches the bandana and displays it and his badge to the world. <The watch group takes 1 bandana and uses the badge to hold it up. This gang member will quietly exit the stage and will be used again as a different gang member shortly.>

SCENE 2

Watch group member	wearing a badge
Police dispatch	has the bass symbol and flood light; CD is hidden

He approaches police dispatch and realizes he's found a match!

Wach grop: "YOURE A MATCH! And look a m y badge - Im he good guy , no he bad guy !"<CLEARLY SHOW police dispach he bandana, sing he badge o hold i p.>

The police dispatch acknowledges it, but doesn't seem to be taking the threat seriously! The watch group shows frustration and starts yelling!

Wach grop y ells: "DO SOMETHING ABOUT THIS! WE HAVE A PROBLEM! COME ON!"

Finally, the police dispatch jumps into action by displaying the bat signal.<Ba signal shold sho p on he all. Hold p ba s y mbol a fe fee from he all, hen n on he flood ligh o see he ba signal. LEAVE BAT SIGNAL ON!>

SCENE 3

Spiderman	earing mask, holding sill y sring, keeping a brain hidden
Gang member	earing bandana

Spiderman appears on the scene, noticing the bat signal, YETBut he does see a gang member. Just like the Watch Group, Spiderman stares at him until he crumples to the ground, and takes his bandana away.<This gang member sa y s pu and doesn'ren n o he ski.>

Wandering around, Spiderman comes across the police dispatch and shows him the bandana. Alerted by the bat signal, he realizes he's an expert at identifying gang members. He prowls around looking for moreFinding one, he sprays silly string at the gang member. This immobilizes the gang member! <DO NOT spra y sill y sring in a person's face.>

Spiderman then uses his super spidey sense to store a memory of the gang member and symbol in his brain.<Spiderman holds p he brain and makes i clear ha memories are sored h ere.>

SCENE 4

Baman	earing mask, boomerang is hidden
Innocen b y sander	holding hie flag ih a bandana
Wach grop	holding he bandana along ih his badge
Alfred he bler	earing glasses and holding clipboard

Police dispach holding he CD

Actors are in green. Props are in blue.

Narrator reads italicized text

SCENE 1

Gang members (2)	Wearing bandanas (gang symbols), carrying a couple more bandanas

He approaches police dispatch and realizes he’s found a match!

Wach grou p: “YOURE A MATCH! And look a m y badge -I’m he good guy , no he bad guy !”

Immune System Unit: Lesson 1, Part 3 TEACHER NOTES

The concept map included here was created using CMap, which is a free concept-mapping program that works on PCs and iPads.

CMap file of student handout – this will only open in the CMap software

CMap file of KEY –