Instructor Version

A. Classroom preparation.

Before the play:

a. The class period before the play, assign the roles and have students learn about the characters. If doing the human immunodeficiency virus (HIV) extension, have all students answer these questions specifically for HIV as well.
    i. Where do I "live"?
    ii. What is my "job"?
    iii. With whom do I typically "hang-out"?

b. Make copies of the student version of the play (one per student) and assessment tool (two per student).

c. Make props (~20 minutes).

Some weblinks are included in the References portion of this activity for the instructor to review if necessary.

The day of the play:

d. Have each student complete the preassessment self-report.

e. Provide each student with a copy of the play.

f. Have all props ready to hand out to their respective actors when directed.

g. If you have a larger class (>20 students), you may want to set up multiple versions of the play to create more student engagement. For example, in a smaller class, you can make more cytokine sheets to include more students or let a student serve as narrator. For a class of 48, you can run the play simultaneously on two sides of the room with two identical sets of materials. You can have each class do the play twice and change the actors playing the roles so that each student has a chance to be in the play as well as be an audience member observing the play. Pausing after each scene allows for visual assessment of actor and prop placement.

h. Have assessment tools copied. (Two copies of the survey per student if using the tool provided with this activity; one handed out before the activity and one after it.)

i. Direct the play (and serve as the narrator or assign this to a student as well) and assign a student as the props manager. For nonmajor students, it may work best for you to be both the director and props manager with a student narrator at least the first time through the activity. Students like to share these roles as they gain more confidence with the activity and content

j. Notes to the director are included in ***bold italic*** font to the right of the script. These will aid in the direction of actors, use of props, and general placement on the stage, as well as serve as answers to the student version questions.

k. Have each student complete the postassessment self-report.

l. Each student should turn in their script with the questions answered or answering the questions can be assigned as reflective homework to turn in during the next class period.

Much Ado about Infection

The Cast:

INSTRUCTOR VERSION

T cells: major players in cell-mediated immunity, regulators and effectors of the immune system, respond to antigen (Ag) fragments exposed on the surfaces of antigen-presenting cells (APCs), expressed on plasma membrane.
Subpopulations of T cells:
$CD8^+$ cells
Role: "The Attackers"
$CD4^+$ cells, also known as helper T cells
Role: "The Stimulators"

Macrophages: phagocytic cells and APC.
Role: "The Engulfers"

B cells: proliferate and differentiate into plasma or memory cells. Plasma cells respond to antigen by making and secreting antibodies (Ab). Memory cells "remember" the infectious agent and will differentiate into plasma cells during future exposure to the same Ag. They can act as APCs.
Role: "The Humoralists"

Virus: the infectious agent.
Role: "The Infector Gadget"

Host cell: an epithelial cell.
Role: "The Infectee"

Important Props:

Major histocompatibility complex (MHC): assembled in endoplasmic reticulum.
Class I MHC: expressed by all cells except erythrocytes, bind and present internal peptides.
Role: "The Presenters" (Act 1)

Class II MHC: expressed by APCs involved in cell-mediated immunity (mainly macrophages, B cells, and other APCs), bind and present exogenous peptides.
Role: "The Presenters"(Acts 1 and 2)

Cytokines: secreted proteins.
Role: "The Signalers"
Chemokines: secreted proteins.
Role: "The Recruiters"

Antibodies: proteins made in response to antigen.
Role: "The Protectors"

INSTRUCTOR VERSION

Page set-up: narrator reads left side.....director's cues on right side

Act 1. The Cell-Mediated Response

Cell-cell killing

Scene 1: The Recognition

<**Enter virus, cell**> Virus infects host cell. Virus starts its replication cycle inside of the cell. Viral proteins synthesized in the cytoplasm are degraded by proteasome complexes. The viral peptides (Ag) are transported to the endoplasmic reticulum where they associate with class I MHC. The Ag-MHC complexes are then transported to the cell surface where $CD8^+$ T cells recognize the peptide as foreign.

Allow virus to touch cell.

The cell's function is now to be a virus factory making more viruses.

This is how your immune system recognizes an infected cell.

<**Enter Class I MHC with viral Ag on cell surface**>
<**Enter $CD8^+$ T cells with T cell receptor**>
$CD8^+$ T cells recognize and bind the Ag-class I MHC complex via the T cell receptor (TCR). The $CD8^+$ T cell needs several signals to become activated, one is binding the Ag-MHC class I complex. The other signal comes from the $CD4^+$ T cell…

Have student hold MHC-Ag (one per hand).

The TCR links with the MHC-Ag complex. These two cells remain linked together through Act I.

Scene 2: The Helper Cometh Forth!

<**Enter macrophage and newly made virus**>
Macrophage engulfs newly made virus, degrades the virus, processes its proteins, and presents them on the macrophage cell surface in association with class II MHC.

The macrophage is a "big eater" and kills the virus, taking pieces of it to present on Class II MHC.

<**Enter class II MHC with viral Ag**>
<**Enter $CD4^+$ T cell with TCR**>
The $CD4^+$ T cell binds to MHC II-Ag complexes. The class II MHC-Ag–TCR interaction activates the T helper cell, which then releases large amounts of cytokines to activate other cells.

Student holds one MHC-Ag in each hand.

These cells stay together.

Scene 3: The Killing Begins!

<**Enter virus-infected cell, $CD8^+$ T cell**>
$CD8^+$ T cells receive cytokine stimulation from activated $CD4^+$ T cells (thus the name helper T cell), signaling the $CD8^+$ T cell to differentiate into a cytotoxic T lymphocyte (CTL).

Scan back to this infection…. How will we get rid of the infected cell (a virus factory)? By throwing toxic granules at it!

<Enter cytokines who "exchange" CD8+ T cell with CTL>
<**Enter CTL with granules**> The CTL kills the virus-infected cell by releasing toxic granules near the virus-infected cell.
<**Exit all cast**>

The infected cell tragically dies.

Act 2. The Humoral Response

Antibody response

Scene 1: The Recognition
<**Enter macrophage with MHC II-Ag, CD4+ cell**>
Meanwhile, the other CD4+ T cells recruited to the area also bind the MHC class II–viral Ag and become activated, releasing many cytokines.
<Enter chemokines who go and get the B cell>
<**Enter B cell**>
B cells also act as APC, presenting viral Ag on class II MHC.
<Enter class II MHC and viral Ag>

The B cell can also present viral antigen on Class II MHC. The interaction with the CD4+ T cell is similar to that with the macrophage.

Student holds one MHC-Ag in each hand.

Scene 2: The Response
CD4+ T cells then interact directly with B cells by binding to the viral Ag-class II MHC complex on the B cell surface. These interactions cause B cell proliferation and differentiation into plasma cells.
<**Enter CD4+ T cells with TCR**>
<Enter cytokines who "exchange" B cell with plasma cell>
<**Enter plasma cell with antibodies**>
Typically IgM is produced if this is the primary response to the virus.

The plasma cell should attach the antibodies onto the spikes of the virus. This neutralizes the virus—it can no longer bind to cell receptors effectively. Antibodies also opsonize the virus or tag it for degradation.

Typically IgG is produced if this is the secondary response to the virus.
The antibodies can bind to the virus and neutralize it, not permitting it to attach to any uninfected cells, or enhance phagocytosis of the virus by binding to its surface, thus marking it for degradation by phagocytes, a process called opsonization.
<**End Act 2: Exit all cast**>

Antibodies are big and bulky, not allowing spikes to bind to cell receptors for infection.

Macrophages love antibody-coated pathogens! Yum!

The viral infection is now cleared, and the immune system has memory of this pathogen to mount a quicker and more efficient response the next time it detects this virus! THE END

The immune system has killed the virus-making factory and the virus!

HIV extension activity—**INSTRUCTOR VERSION**

But, with human immunodeficiency virus or HIV, this whole process doesn't go as smoothly as stated in this play. Why? Let's find out!

> ***HIV can infect CD4+ T cells, macrophages, and other cells derived from macrophage precursors. HIV alters the function of these cells. Macrophages are one of the major reservoirs of HIV and allow the virus to be distributed to various tissues such as the brain and lungs.***

In small groups, make a prediction about what the impact would be if CD4+ T cells were the cells being infected in the play.

> ***By infecting the CD4+ T cell, this cell is now a virus factory that doesn't function properly and is targeted for killing by the CTL. As this occurs, there are fewer and fewer CD4+ T cells to provide the "help" to immune cells in both the cell-mediated and humoral responses. A more detailed discussion could also include how HIV-infected cells can fuse with noninfected CD4+ T cells, resulting in syncytia formation and further reducing the CD4+ T cell counts and function.***

Now re-run the play, this time inserting a CD4+ T cell as the original infected cell and HIV as the virus. What do you notice?

> ***After the initial infection, the CD4+ T cell will be killed by the CTL. With only limited numbers of CD4+ T cell actors, it will become clear the immune system's response is impeded for both the cell-mediated and humoral responses.***

How does an HIV infection act differently than just a typical virus infection like in the play?

> ***As HIV infection progresses, instead of a better immune response and clearing of the infectious agent, the immune response weakens and HIV is prevalent.***

Notes: this activity can serve as a springboard for discussion on how HIV patients are prone to infection by multiple types of infectious agents. This activity can easily be adapted for infections caused by bacteria, fungi, or parasites and can address items such as immune evasion or memory.