

Much Ado about Infection



The Cast: STUDENT 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”

Act 1. The Cell-Mediated Response STUDENT VERSION

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.

<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...

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.

<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 CD4⁺ T cell, which then releases large amounts of cytokines to activate other cells.

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).

<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>

Notes and Questions

Why would a virus need to be inside a host cell?

Why is it important that the CD8⁺ T cell recognizes the Ag-MHC complex?

What two purposes does the macrophage serve during a viral infection?

Why would the CTL attack the virus-infected cell and not the virus itself?

Act 2. The Humoral Response STUDENT VERSION

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>

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; some cells remain as memory 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.

Typically IgG is produced late in the primary response and during 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>

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

Notes and Questions

A small amount of B cells become memory cells, which do not secrete Ab but will be ready to recognize the virus the next time it infects. Why would “memory” also be important for an immune response?

Why are the cell-mediated and humoral responses both necessary to clear the viral infection?

HIV extension activity **STUDENT 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.

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?

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