Student Activity

Armed and Dangerous: The Activation of Killer T-Cells

I. Rationale:

Understanding the nature and functioning of the immune system is of essential importance in our increasingly complex and dangerous modern world. New diseases such as AIDS, West Nile, and others regularly surface in the news. At the same time "old" pathogens like smallpox, anthrax, tuberculosis, and many others threaten to make an alarming comeback as a result of bioterrorism, genetic engineering, and antibiotic resistance.

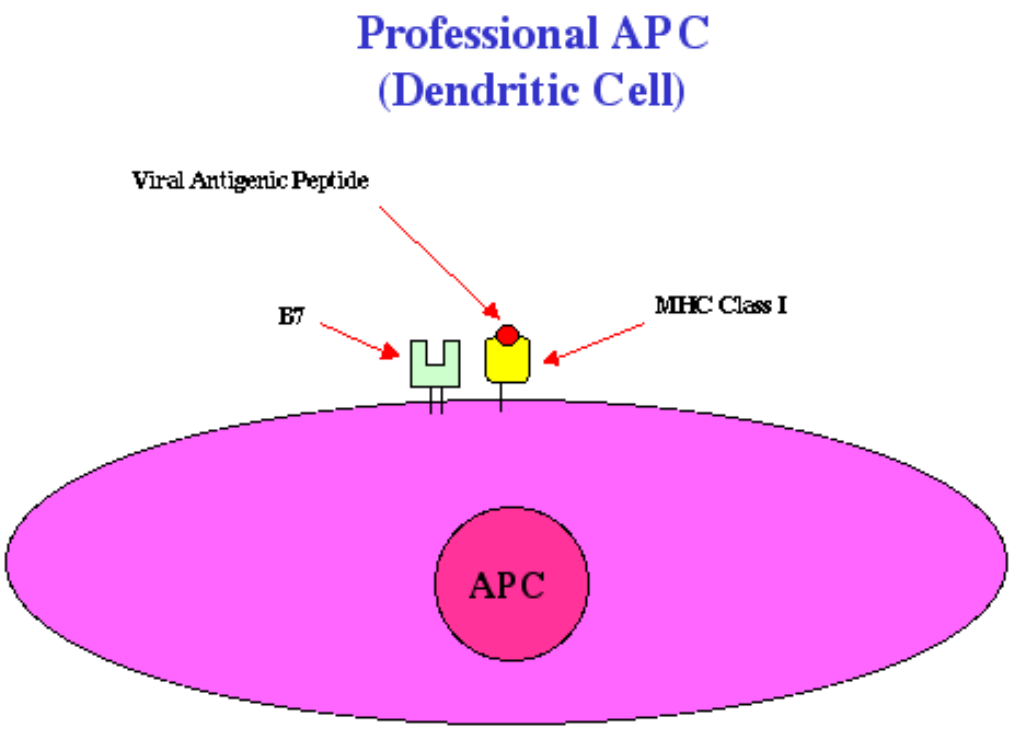
II. Introduction:

The Immune System is a complex association of numerous specialized cells, tissues, and cell products that interact collectively to keep us alive in a world where we constantly encounter microorganisms. These cells originate in the bone marrow and eventually migrate to the tissues where they circulate in specialized vascular tissue called the **lympahtic system**.

The immune response may be innate (inborn), or adaptive (acquired during an individual's lifetime as a response to encountering pathogens). Inflamation is an example of the action of innate immunity, while the production of antigen specific antibodies is an example of the action of adaptive immunity. One of the responses of adaptive immunity involves the ability of special white blood cells, called **Killer T-Cells**, to destroy cells infected by virus.

Dendritic Cells:

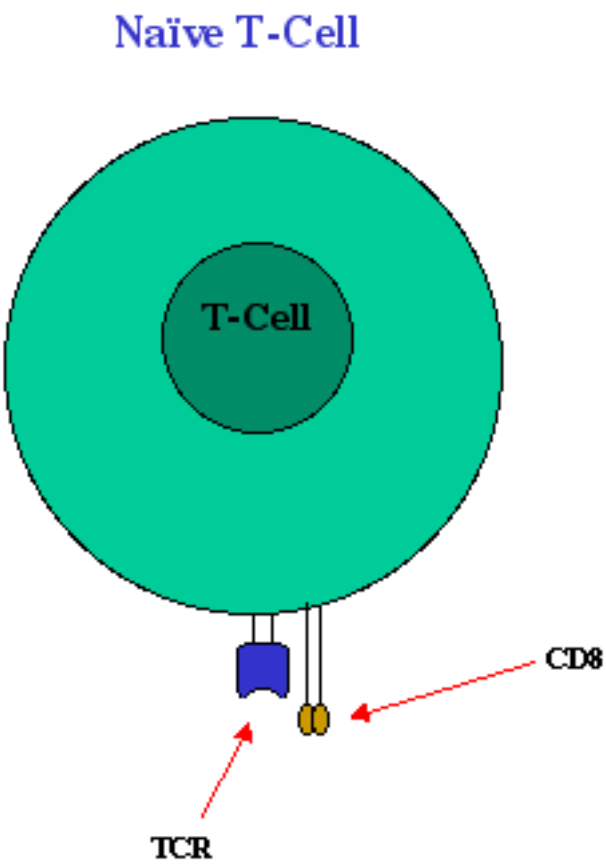
The adaptive immune response begins when specialized immune cells in infected tissue, called **derndritic cells**, ingest pathogens (bacteria) by **phagocytosis**, or take them (viruses) in through a process called **macropinocytosis.** Infected dendritic cells migrate to peripheral lymphoid tissues, such as **lymph nodes**, where they mature into professional **antigen-presenting cells (APC)**. Small protein fragments of the pathogen **(antigenic peptides)** become associated with special cell proteins known as **MHC Class I**.



MHC stands for major histocomatibility complex, and these molecules act as cellular flags identifying "self." Antigenic peptides become associated with a groove in the MHC Class I "flags" and are transported to the cell surface where they are displayed. Here they signal other immune cells to spring into action and destroy infected cells.

T-Cells:

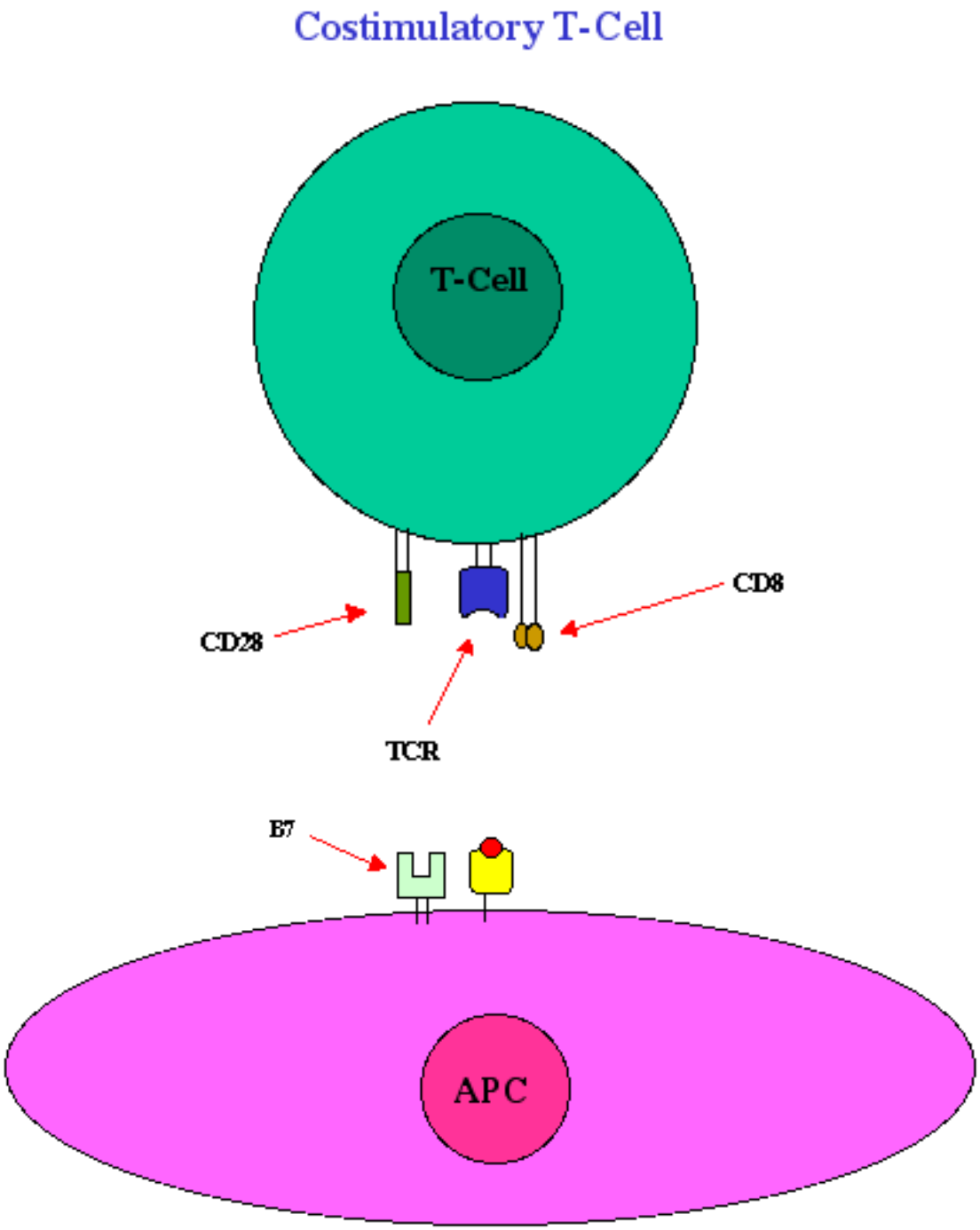
The immune cells activated by contact with APC displaying the MHC:peptide flag are members of a group of white blood cells known as **T-lymphocytes**, or T-cells. Certain T-cells carry their own protein surface flag (**CD8**) in addition to a T-cell receptor (**TCR**).



Naïve CD8 T-cells (those that have not previously encountered antigen) become activated by interacting with dendritic cells that display the MHC Class I:peptide flag. The TCR of a naïve CD8 T-cell must recognize the pathogen specific flag complex on the APC surface to become activated.

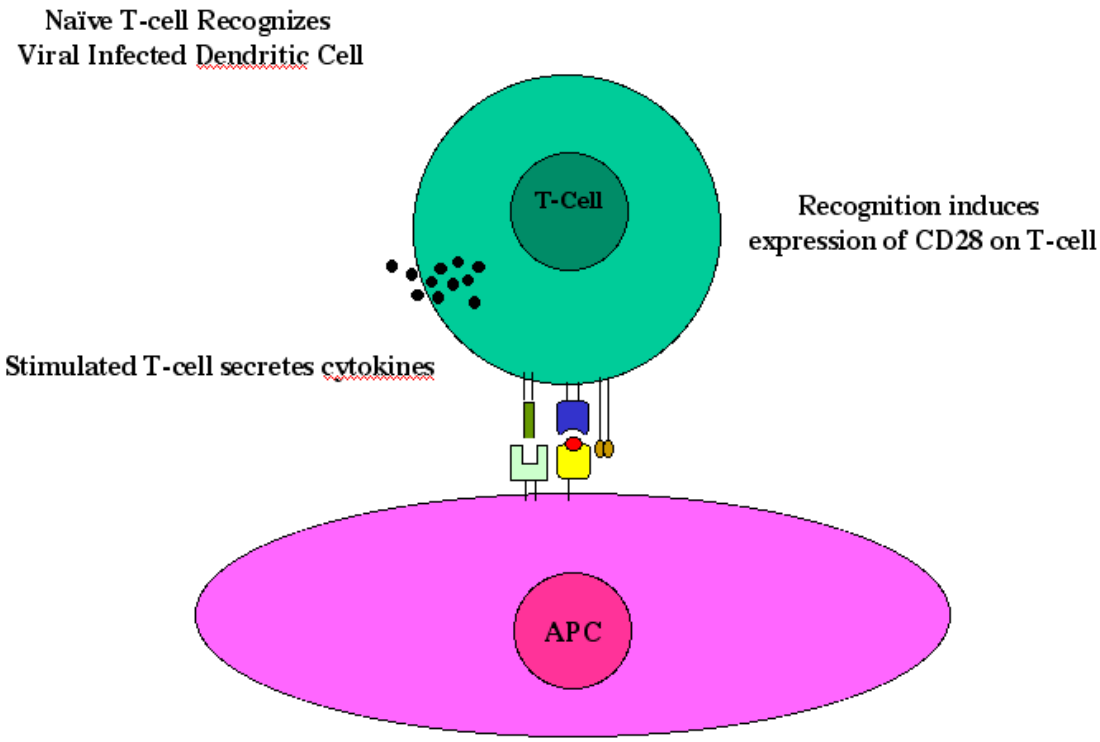
Costimulation:

As a safeguard, the activation process cannot occur unless there is an additional costimulation event involving the recognition of another APC protein flag (**B7**) by a T-cell protein called **CD28**.



Activation:

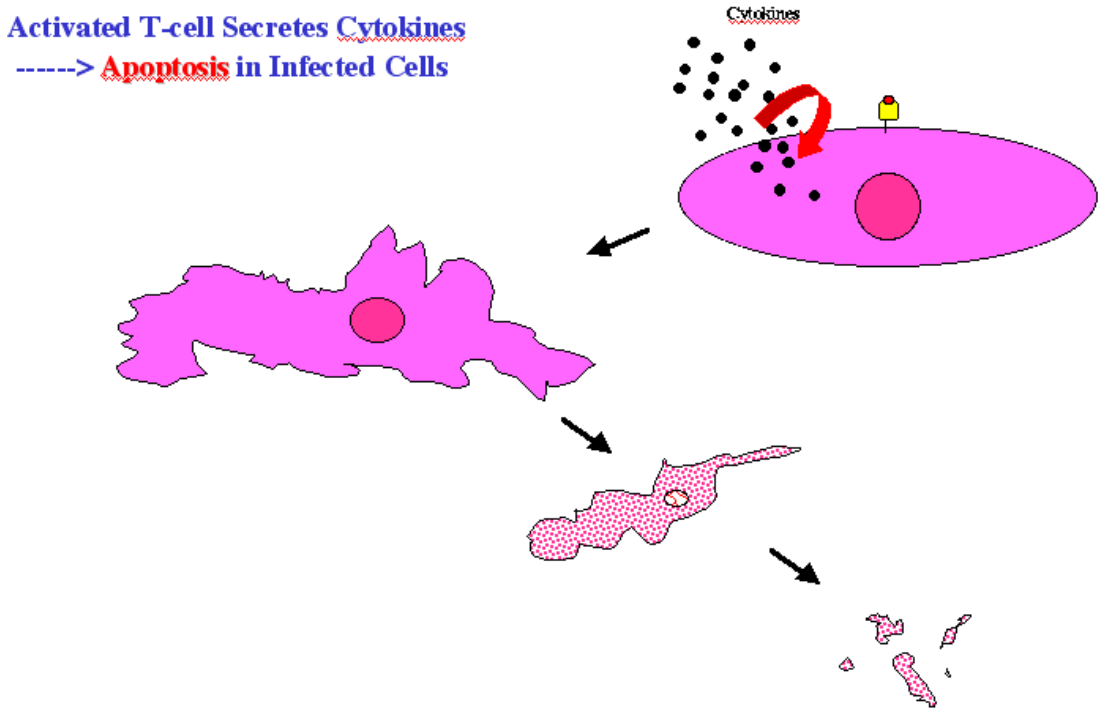
The two cells will "dock" such that they both bind to the pathogen peptide fragment held by MHC Class I complex. During the docking CD8 will also bind to the MHC Class I:peptide complex.



This docking procedure signals the CD8 T-cell to become an effector T- cell producing chemicals (**cytokines**) that induce it to proliferate and destroy infected cells by inducing **apoptosis**, or programmed cell death. These (activated) effector T- cell s are known as **cytotoxic T-cells** , or Killer T-Cells.

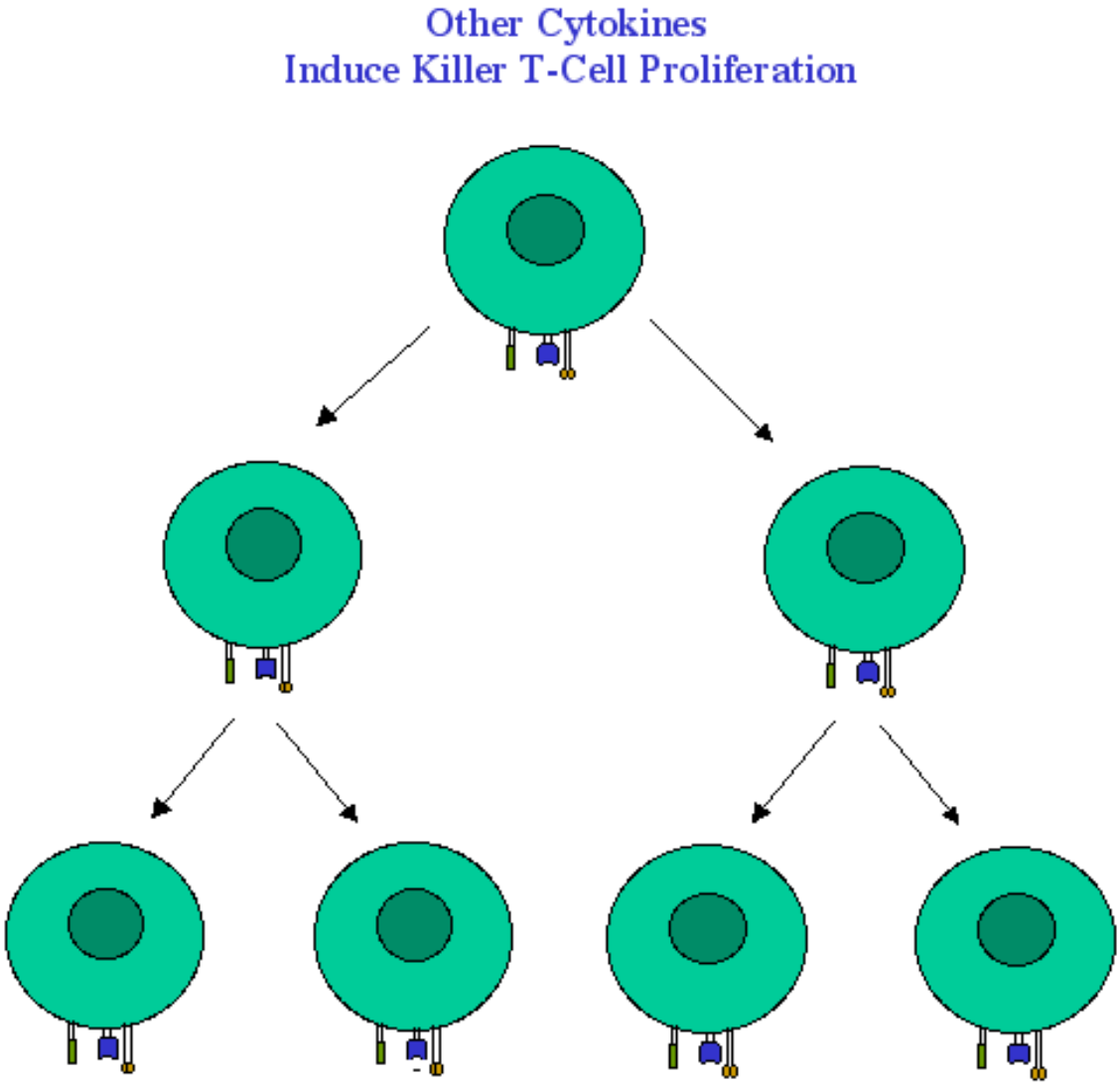
Cytotoxicity:

There are many different types of cytokines. Activated CD8 T-cells produce several. Some of these are responsible for the cytotoxic effects of Killer T-Cells by binding to infected target cells, punching holes in them, and activating apoptosis. This will result in the death of the infected cell.



Proliferation:

Another group of cytokines produced by activated CD8 T-Cells results in differentiation and proliferation. The proliferation of these antigen specific killer cells is an important step in building a standing army of armed Killer T-Cells. These immune "soldiers" will then fight the invading pathogen by killing infected cells and overcome the infection (hopefully).



Objectives

In this activity you will learn about the activation of naïve CD8 T-cells to become killer T-cells. You will work in groups to develop and construct models that demonstrate your understanding of this T-cell activation process. Each group is challenged to be as creative as possible, and to produce a product that reflects a synergistic effort. This means that the final product is better than the total individual efforts.

Your project must involve construction of models of an activated CD8 T-cell, and professional APC with processed antigenic peptide. These cells must also have the appropriate cell surface molecules (as described in the introduction). *Both cell models must be made completely of non-toxic edible materials*.

As a summary activity, each group will make a class presentation (utilizing your edible models) that demonstrates your understanding of the process. At the post presentation "cocktail party" all participants will have an opportunity to celebrate their accomplishments while dining on the edible projects. A poster of each project will be displayed as a permanent record of the activity.

III. Materials:

You and your partners must decide what materials will be appropriate within the guidelines described above. The more creative your selections are, the better.

IV. Procedure:

1. Discuss the process of CD8 T-Cell activation with the members of your group. Work collaboratively to make sure everyone in your group has a thorough understanding of the overall process and the role of each cell type.
2. Brainstorm to get suggestions regarding what edible materials have potential use in your group's models.
3. Make a list of these materials and how they would be used (i.e. what each represents).
4. Narrow your list until there is consensus regarding what materials will be used and what they will represent.
5. Acquire the materials and meet as a group to construct your models.
6. Construct a poster that will serve as a permanent record of your project to be displayed at your presentation and the post presentation party.
7. Enjoy interacting with the other participants at the post presentation "cocktail party." This is an opportunity to celebrate your creativity and accomplishments in much the same way as artists do at an art show opening.

You may wish to invite special guests, take pictures for the yearbook or school newspaper, or do other things to enhance the event. Some may wish to award prizes for the most creative project and/or other categories. Have fun and be creative!

V. Discussion:

Bring your completed models to class on the assigned date and make a formal presentation to your peers. Your presentation must demonstrate all the steps involved with the activation of CD8 T-cells to become mature Killer T-cells. It

must also demonstrate your understanding of the role of each of the following:

naïve CD8 T-cells, APC, MHC Class I, CD8, TCR, B7, CD28, cytokines, and antigenic peptides.

Part of your presentation must include a poster that will also be displayed at the post presentation party as described above.

Group presentations simulate the peer review process in science. All students have shared this creative problem solviing experience and are therefore "experts." Students are therefore expected to engage presenters in meaningful exchanges, much as scientists would do in defending their own research. Remember, it is important that your project is creative, and that you demonstrate insight and understanding of the subject matter.

The following are some questions to help guide your effort:

1. What role do CD8 T-cells play in the adaptive immune response?
2. How do CD8 T-cells differ in *structure* from other T-cell populations?
3. How do CD8 T-cells differ in f*unction* from other T-cell populations?
4. How do a naïve CD8 T-cells differ from an activated CD8 T-cells?
5. Discuss the role of the MHC Class I in CD8 T-cell activation.
6. Formulate an hypothesis concerning the need for a costimulatory event before full CD8 T-cell activation can occur.
7. What are cytokines?
8. Name two effects resulting from the production of cytokines from activated CD8 T-cells.
9. Explain what apoptosis is and how it is related to CD8 T-cell activation and the adaptive immune response.
10. Formulate an hypothesis relating an understanding of apoptosis to cancer?