Armed and Dangerous: The Activation of Killer T-Cells

by

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Teacher Guide

Armed and Dangerous: The Activation of Killer T-Cells

I. Overview:

The Immune System is a complex association of numerous specialized cells, tissues, and cell products that interact collectively to keep us alive. 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.

Armed and Dangerous: The Activation of Killer T-Cells is a student driven supplemental activity designed to be used as a s enrichment when teaching the immune system. The activity actively engages students as they design and construct edible models of cell types involved in the production of Killer T-cells. After groups explain their models in formal presentations they and consume the projects at a special celebratory "cocktail party." The celebration can be turned into a special event by inviting dignitaries and other guests.

II. Science Background:

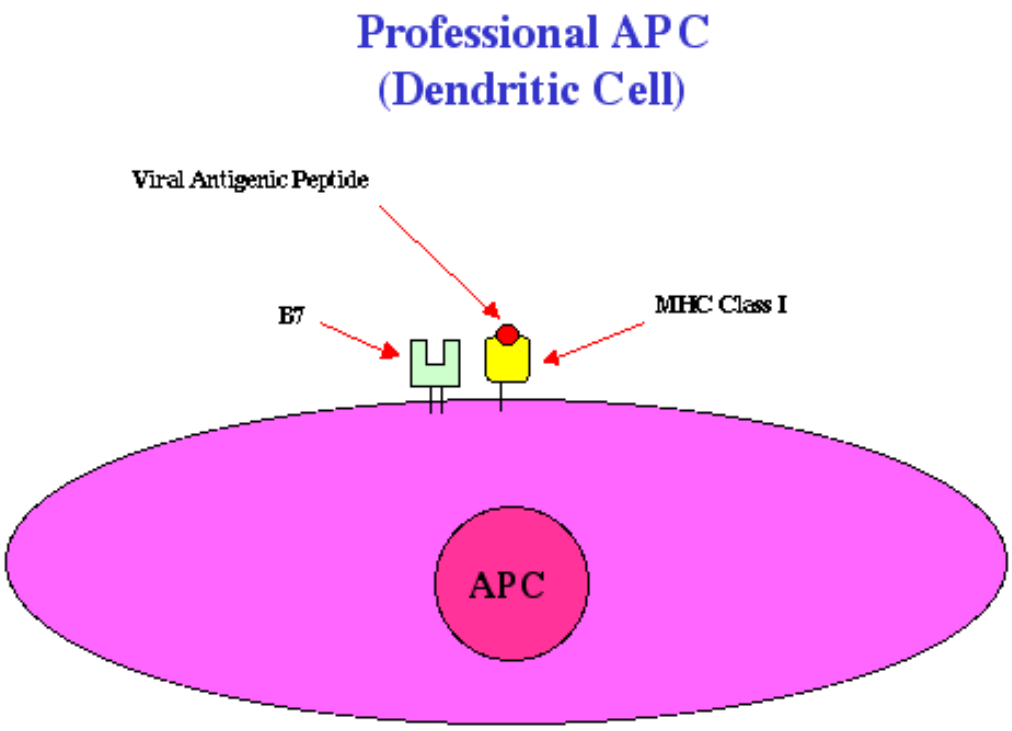
Teachers unfamiliar with the immune system are encouraged to consult additional sources, such as various college biology texts, but a general introductory background appears below. It is anticipated that students will be familiar with innate vs. adaptive immunity, the adaptive immune response, and have a general understanding of the role of its major cell populations prior to this activity.

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:

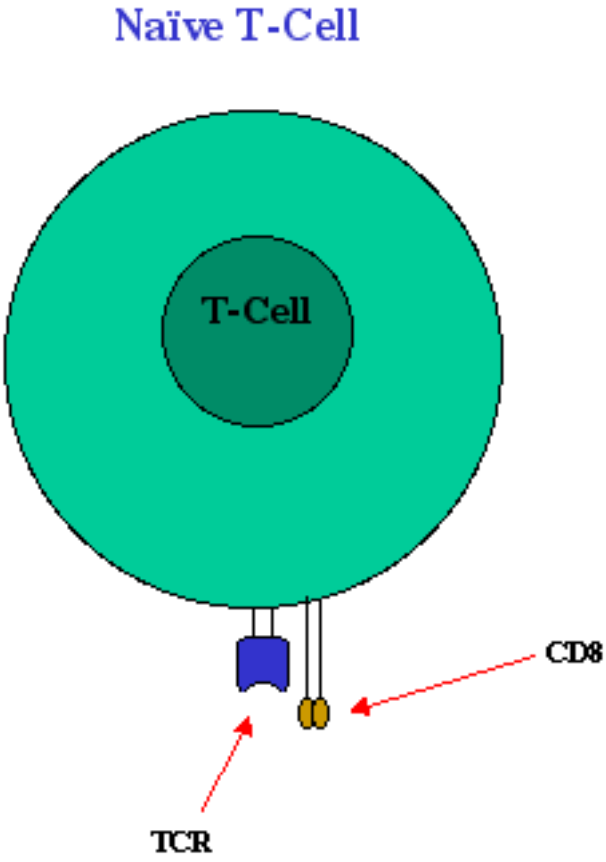
The adaptive immune response begins when specialized immune cells in infected tissue, called **derndritic cells**, ingest pathogens (bacteria) by **phagocytosis**, or take them (viruses) in through a process called **macropinocytosis.** Infected dendritic cells migrate to peripheral lymphoid tissues, 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:

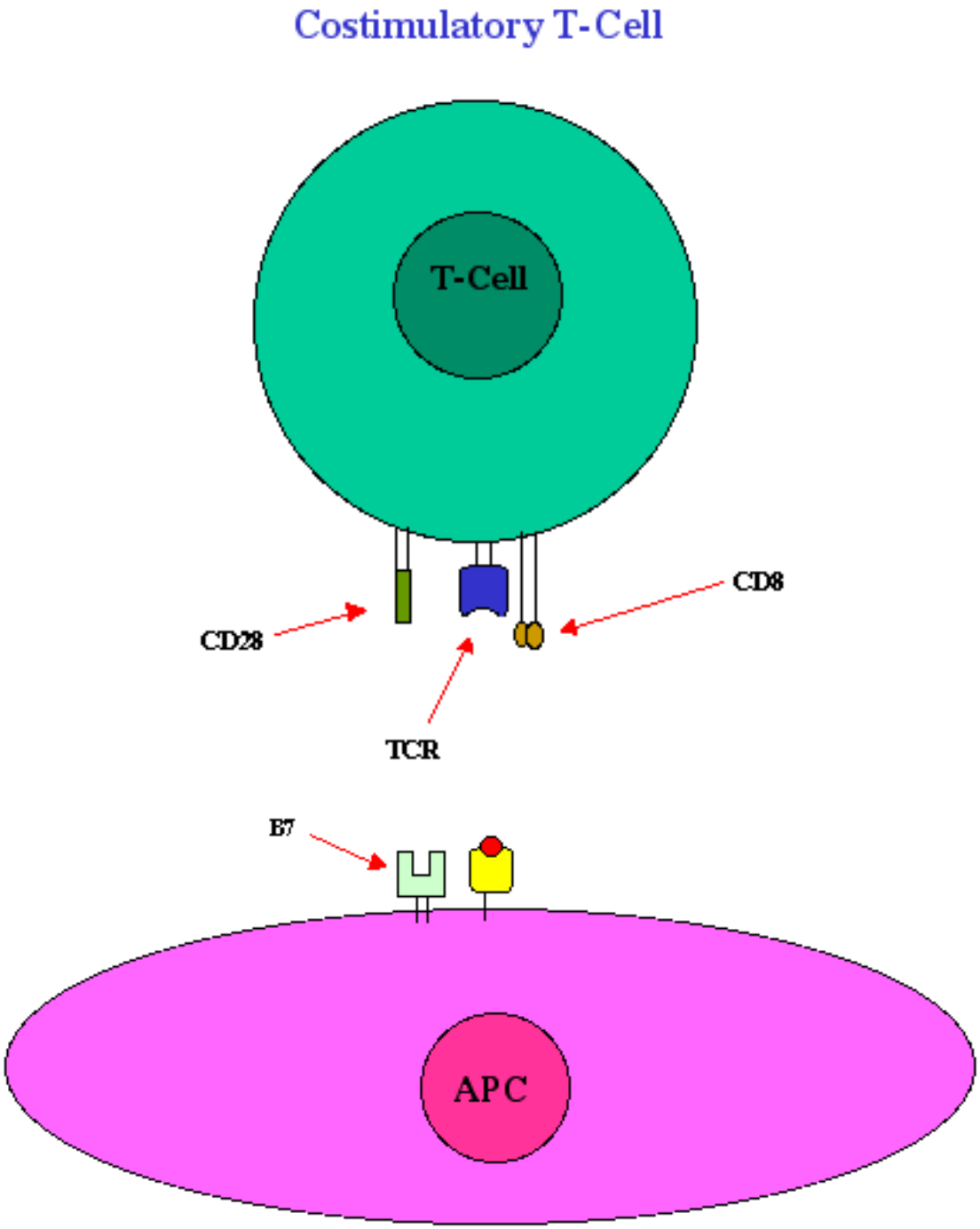
The immune cells activated by contact with APC displaying the MHC:peptide flag are members of a group of white blood cells known as **T-lymphocytes**, or T-cells. Certain T-cells carry their own protein surface flag (**CD8**) in addition to a T-cell receptor (**TCR**).



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.

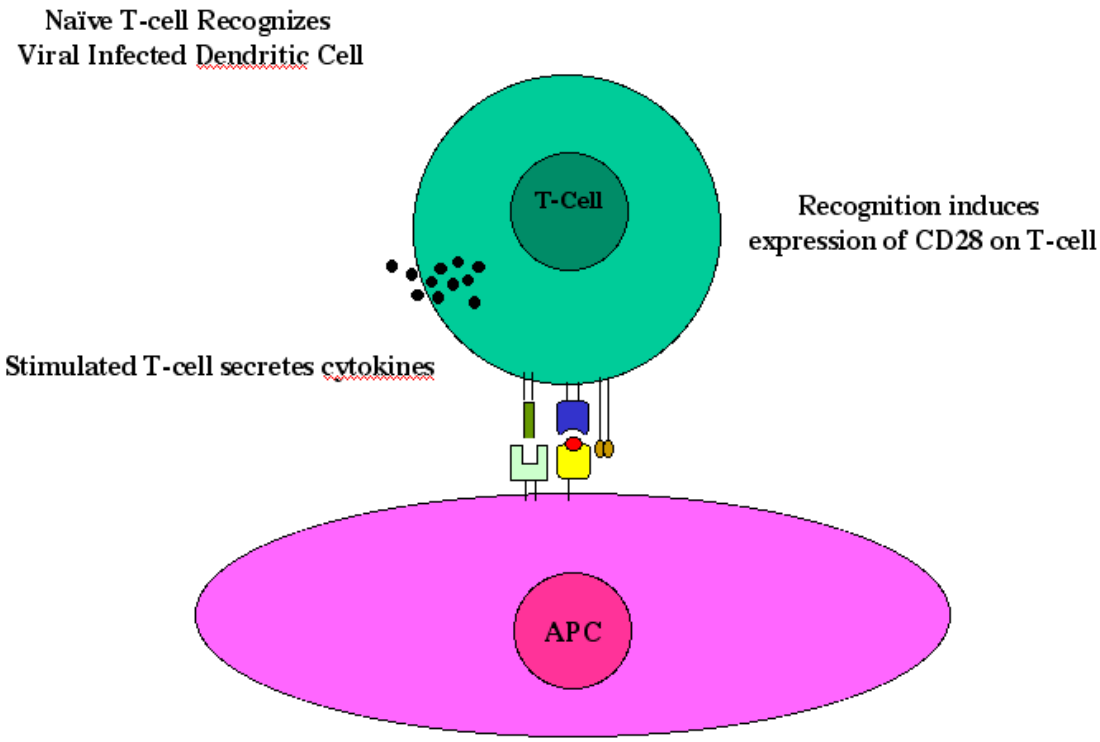
Costimulation:

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:

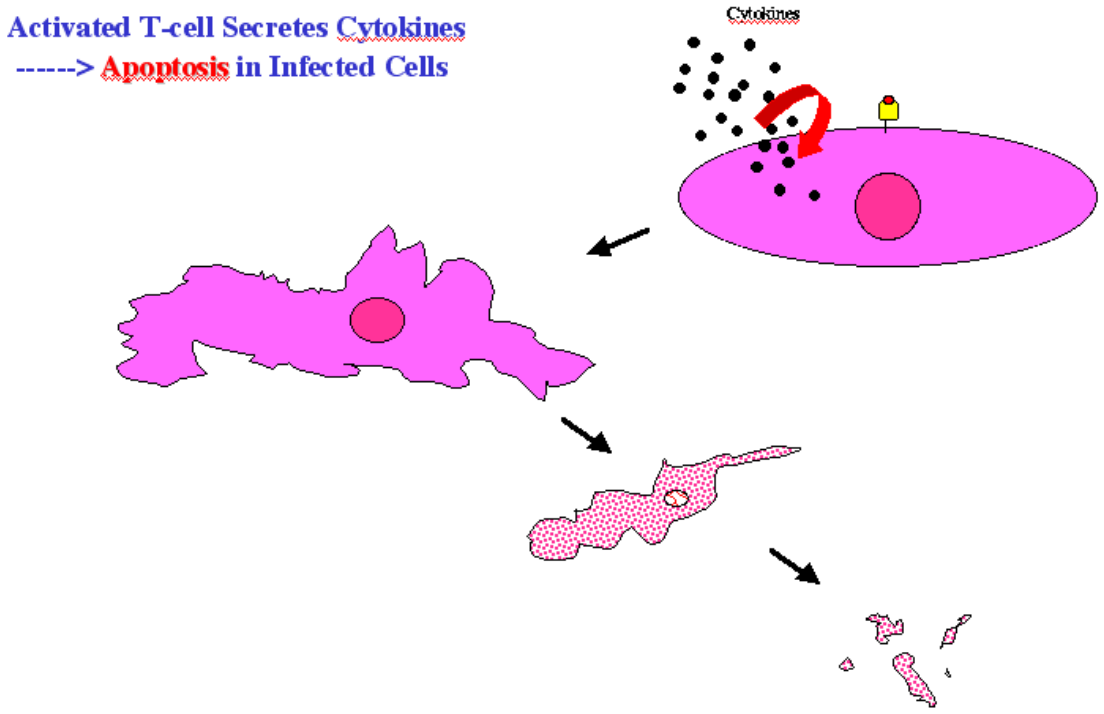
The two cells will "dock" such that they both bind to the pathogen peptide fragment held by MHC Class I complex. During the docking CD8 will also bind to the MHC Class I:peptide complex.



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.

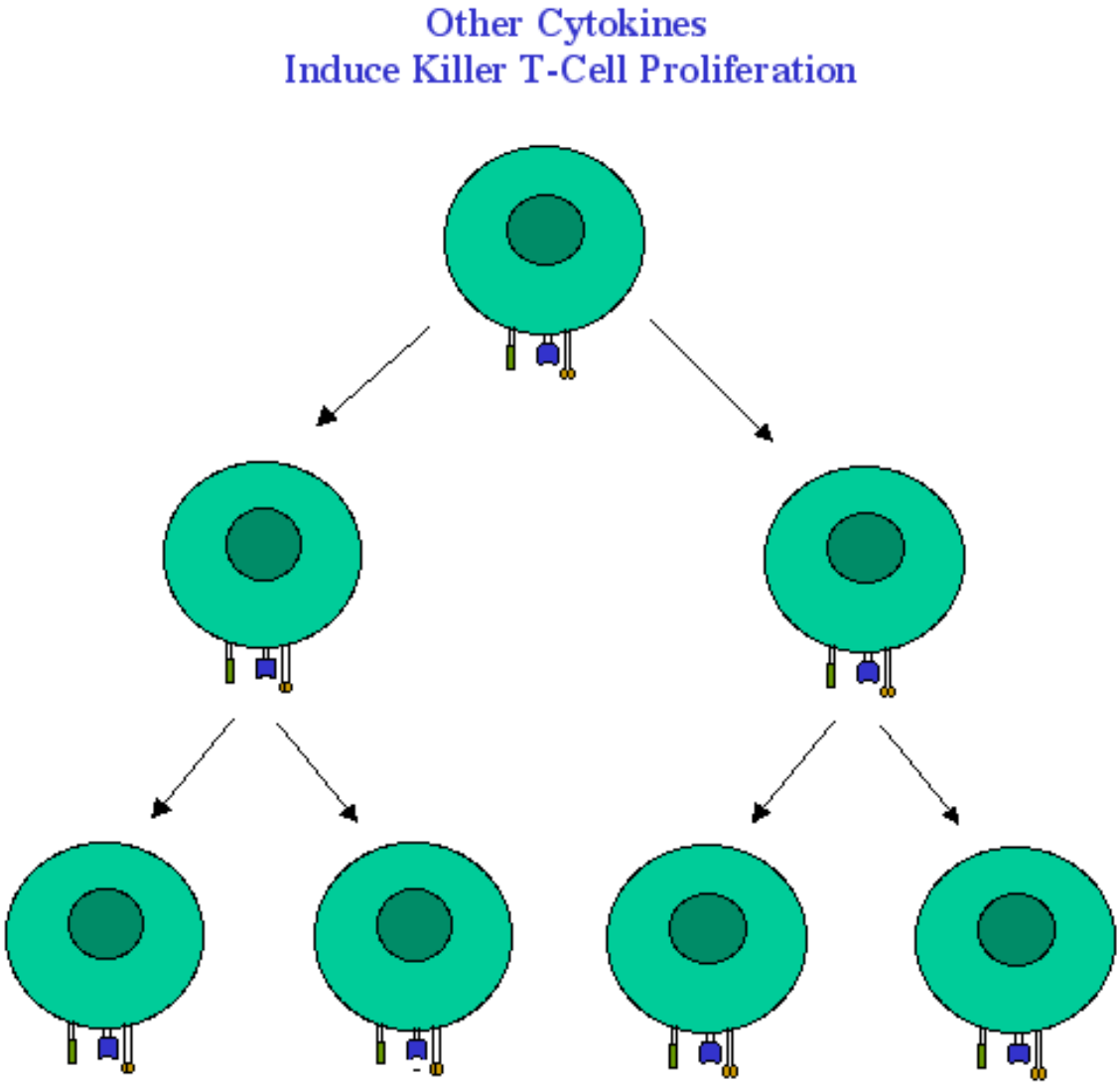
Cytotoxicity:

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).



III. Student Outcomes:

It is reasonable to expect that students who have participated in this activity will have an increased understanding of the mechanism of T-Cell activation, the interactions between various cell populations and chemical mediators, and a deeper understanding and appreciation of the immune system.

Additionally, the group presentations serve as an analog of the scientific peer review process and can thus be used to augment teaching the nature of science. Students will share a common experience in which *they* are the "experts," yet have taken different problem solving pathways to the endpoint. Furthermore, the post presentation "cocktail party" should create an interesting social dynamic that can foster interpersonal relations and strengthen classroom cohesiveness and unity.

IV. Learning Objectives:

Students will demonstrate specific content knowledge of this activity by working in small groups to build *edible* models of CD8 T-cells and antigen presenting cells. Each group will then make a class presentation that explains the process of CD8 T-cell activation to become cytotoxic (killer) T-cells that destroy virus infected cells as part of the adaptive immune response. It is important to challenge students to demonstrate creativity in the selection of edible materials and in construction of their models. Additionally, each group will produce a poster of their models to serve as a permanent record and be displayed at the post presentation "cocktail party."

At the completion of group presentations, students will further interact by consuming the projects at a post presentation "cocktail party". In addition to celebrating collective accomplishments, the party serves to reinforce core knowledge, foster interpersonal relationships, and boost classroom morale.

V. Time Requirements:

This activity can be adapted to suit the individual needs of teachers. A detailed general study of the immune system is a recommended prerequisite. The following is only one possible timetable :

Introduction – 1 period
Group Brainstorming – 1 period
Discussion of Proposals – 1 period
Group Presentations – 1 (or more) periods
Post Presentation Feast – 1 period

VI. Materials and Equipment:

Students are expected to provide heir own project materials.

VII. Student Prior Knowledge and Skills

Teach basic immunology unit.

VIII. What Is Expected From Students:

Work together and be creative
Submit proposal
Obtain all materials for project construction
Get together outside class to plan, construct, and produce models and poster
To be actively involved in the group presentations and discussions
Attend post presentation celebration party

IX. Anticipated Results:

If initially presented in an enthusiastic way, students will accept the challenge to creatively demonstrate their understanding of this complex biological process while enjoying a break from normal classroom routine.

The post presentation party is an opportunity to promote interest in the subject mater and boost class unity and morale. The invitation of outside guests is a way to boost enthusiasm and increase student recognition.

X. Classroom Discussion:

The bulk of class discussion may occur during the student presentations that simulate the scientific peer review process. The teacher may decide that formal "discussion questions" are not necessary in this context. It is suggested, however, that each group be held accountable for demonstrating that it fully understands the nature and function of the following in the production of killer T-cells:

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

Possible discussion questions:

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?

XI. Assessment:

Teachers are encouraged to devise their own assessment criteria. One possible rubric is shown below:

	Unsatisfactory	**Acceptable**	**Superior**
Brainstorming	ineffective use of time; few or no contributions	some contribution to overall group effort	uses time effectively and makes significant contributions
Proposal	submission is late or missing	submission is on time, but needs revision and resubmission	submission is on time and acceptable.
Presentation	incomplete, inaccurate, or significantly flawed	acceptable, but lacking in some respect	clearly presented, cohesive, and complete
Poster	not submitted or does not meet minimum requirements	meets minimum requirements	exceeds minimum requirements; exceptional effort
Creativity	effort is unacceptable	demonstrates acceptable effort and moderate creativity	demonstrates quality effort and high creativity
Discussion	unable to demonstrate acceptable knowledge base	demonstrates acceptable knowledge base	demonstrates insight and mastery of knowledge base

XII. References

Arousing The Fury Of The Immune System - New Ways To Boost The Body's Defenses. A Report From The Howard Hughes Medical Center. Chevy Chase: Howard Hughes Medical Center, 1998.

Janeway. Charles A; Travers, P.; Walport, M.; Shlomchik, M. Immunobiology. New York: Garland Publishing, 2001.

XIII. Acknowledgements

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