

Lecture Outline

T Cell Immunity

Jan 26, 2001

T cell immunity involves initial activation of T cells in secondary lymphoid organs followed by T cells leaving lymphoid tissue and traveling throughout body to find pathogens to kill or cells to activate.

Antigen presenting cells (APCs). T cells will only bind antigen when it is presented by MHC molecules. APCs are immune cells capable of presenting antigen and activating T cells. APCs must take up antigen and process it (cleave with enzymes) and present small fragments (epitopes) of the larger pathogen to the T cells.

Cell adhesion molecules (CAMs). CAMs are surface receptors that help bind cells to endothelium lining in bloodstream and target cells to locations throughout the body. CAMs also function to establish binding between T cells and APCs or CTLs and target cells.

I. T cell populations can be determined by the surface expression of CAMs.

1. Naive or resting T cells have not encountered antigen.
2. Effector T cells have been activated and now have increased CAMs, and cytokine receptors.
3. Memory T cells will be activated more quickly to initiate a secondary immune response.

II. T cell activation is a series of cellular events that are in response to TCR binding antigen plus MHC with costimulation required for full T cell activation. 2 signal concept

- 1' signal TCR and CD4 or CD8 binding antigen in MHC.
- 2' signal CD28 on T cell binding to B7 on APC.

T cell activation includes the following:

1. Upregulation of many genes: cytokines, CAMs, cytokine receptors.
3. Expression of new cell surface molecules.
4. Secretion of cytokines (especially IL-2).
5. Induction of proliferation. (The amount of proliferation is determined by the amount of IL-2).

III. T cell effector functions

T helper cells (CD4⁺ T cells)

The primary effector function for CD4 T cells is cytokine production.

Helper cells are subdivided into 2 subsets based on their cytokine secretion profile.

Subset	Pivotal CK	Secrete	Function
Th1 cells	IL-12	IL-1, IFN- γ , TNF- α	Activate macrophages, CTLs.
Th2 cells	IL-4	IL-4, IL-10, IL-6	Activate B cells.

T cytotoxic cells (CD8⁺ T cells)

The effector function of activated cytotoxic T cells (CTLs) is lysis of antigen bearing target cells.

CTLs can kill through 2 pathways

1. Perforin/Granzyme B pathway.

TCR binds antigen presented in Class I MHC and with costimulation CTLs will release granules containing perforin and Granzyme B. Perforin pokes holes in the target cell membrane and the granzymes enter the cell and chew up DNA which causes cell death.

2. Fas-Fas Ligand (FasL) pathway. FasL on T cells binds to Fas on target cell. Binding of Fas initiates apoptosis of target cell.

Apoptosis or programmed cell death is an active form of cell suicide. The target cell turns on internal proteases that activate DNA degradation and nuclear condensation. Apoptosis is a normal part of immune development and lymphocyte proliferation as well as the primary mechanism to kill infected cells by CTLs.

Necrosis contrasts with apoptosis as an uncontrolled cell death resulting from poisoning or cell injury.