

**Antigen Processing and Presentation****Feb. 2-5, 2001****I. APCs control the activation of Naive T cells****A. Activation of helper T cells.**

APCs will determine what peptides or epitopes will be presented on Class II MHC to Thelper cells.

**Characteristics of APCs for Th cell activation.**

1. Express high levels of Class II MHC.
2. Ability to capture and take up particulate antigen.

Antigen Uptake for Different Types of APCs

1. Dendritic cells capture antigen in tissue and migrate to lymphoid organs to present antigen to lymphocytes. Uptake of antigen through phagocytosis.
2. Macrophages. Uptake of antigen through phagocytosis.
3. B cells bind antigen with surface antibody/B cell receptor. Uptake of antigen through receptor mediated endocytosis.

**B. Activation of naive cytotoxic T cells.**

Primary activation of Tc cell is thought to be done by dendritic cells in lymph nodes and spleen. Characteristics of dendritic cells that allow them to activate Tc cells.

1. Easily infected by viruses.
2. Abundant Class I MHC.

After they are activated, Tc become armed effector cells (CTLs) which leave the lymphoid tissue and go to the rest of the body to look for target cells (infected cells) to kill.

**II. Activation of armed effector T cells in tissues to get effector function.****A. Th cells are only activated by Class II expressing cells (APCs).**

Th1 cells are activated by macrophages.

Th2 cells are activated by B cells.

**B. CTLs kill target cells expressing foreign antigen presented by Class I MHC.**

Target cells are usually virally infected cells. Almost all cells express Class I MHC and theoretically almost any cell including APCs can be a target cell for CD8+ T cell mediated cell lysis.

**III. Antigen processing** is the metabolic process of degrading proteins into peptide portions that are capable of binding MHC cleft and being presented on the cell surface for T cell recognition. Proteins are broken down by enzymes inside the cell.

Many different peptides can bind to same MHC molecule and one cell can present many different peptides from different pathogens. A sampling of peptides from the cell will be presented on MHC molecules. This includes self proteins which are presented by cells but hopefully will not activate T cells because the T cells will not respond to self antigens.

#### **IV. Antigen Processing Pathways**

##### **EXOGENOUS PATHWAY**

Exogenous antigen --> Endocytic processing pathway---> Endosome/lysosome fuses with vesicle containing Class II molecules ---> Foreign antigen peptide binds Class II-MHC.

Class II molecules come from endoplasmic reticulum to golgi to endocytic pathway fuses with endosome.

Foreign peptide antigen from digested endocytosed proteins exchanges with self peptide in cleft of MHC and returns to cell surface to stimulate T cell.

##### **ENDOGENOUS PATHWAY**

Endogenous antigen ---> Cytosolic processing pathway  
----> Peptide Binds Class I MHC

Proteins produced internally inside cell are degraded into peptides and without leaving the cell will find Class I MHC internally and get exported to cell plasma membrane.

Peptides produced by enzymatic degradation in cytoplasm are selectively transferred into the ER where they bind to class I MHC.

From the ER they migrate to golgi and then out to cell surface.

#### **Why two pathways?**

The distinct pathways with proteins from different origins maintain segregated pathways inside the cell. The routing of the class I MHC and class II MHC molecules to separate intracellular compartments determines what peptides they interact with.

#### **CD4+ Th**

Thelper cells are especially important in the turning on of the immune system in general. The foreign antigens from infections need to be taken up by APCs to get noticed by immune system which in turn can activate the Th cells.

#### **CD8+ Tc**

CTLs are primarily needed for killing in infected cells. Viruses must replicate inside cells and many bacteria and parasites live inside host cells. Therefore the antigens for stimulating CTLs come from inside the cell because they will indicate an intracellular infection.