

S. No	Topic	Class No	Date
1	Introduction	1	27/1
		2	29/1
2	Fundamentals of Immunology <ul style="list-style-type: none"> • Definitions and basic terms • Types of immunity • Organs of immune system • Cells of immune system 	3	3/2
		4	5/2
3	Innate immunity <ul style="list-style-type: none"> • PAMPs • PRRs • Phagocytosis 	5	10/2
		6	12/2
4	Antigens <ul style="list-style-type: none"> • Characteristic features of antigens • Types of antigens • Super antigens 	7	17/2
		8	19/2
5	Humoral Immunity <ul style="list-style-type: none"> • Antibody – structure and functions 	9	24/2
		10	26/2
6	Ig Biosynthesis <ul style="list-style-type: none"> • Monoclonal antibody production 	11	3/3
		12	5/3
7	Complement system <ul style="list-style-type: none"> • 3 pathways of complement system 	13	10/3
		14	12/3
		15	17/3
		15	19/3
	First mid term (25 marks)	16	17/3 or 19/3
8	Cell mediated immunity <ul style="list-style-type: none"> • Macrophages • T cells • Th1 and Th2 response 	17	24/3
		18	26/3
9	MHC and transplantation immunity	19	31/3
		20	2/4
10	Disorders of Immune system <ul style="list-style-type: none"> • Hypersensitivity • Immunodeficiency 	21	7/4
		22	9/4
11	Tumor immunology <ul style="list-style-type: none"> • Tumor specific antigens • TIL 	23	14/4
		24	16/4
12	Tolerance and autoimmunity	25	21/4
	Antigen and Antibody reactions	26	23/4
	Reserve	27	28/4
		28	30/4
	Second mid term(25 marks) (submit literature review – 10 marks)	27/28	27/4 or 28/4
	Final (40 marks)		

Cell mediated immunity

By
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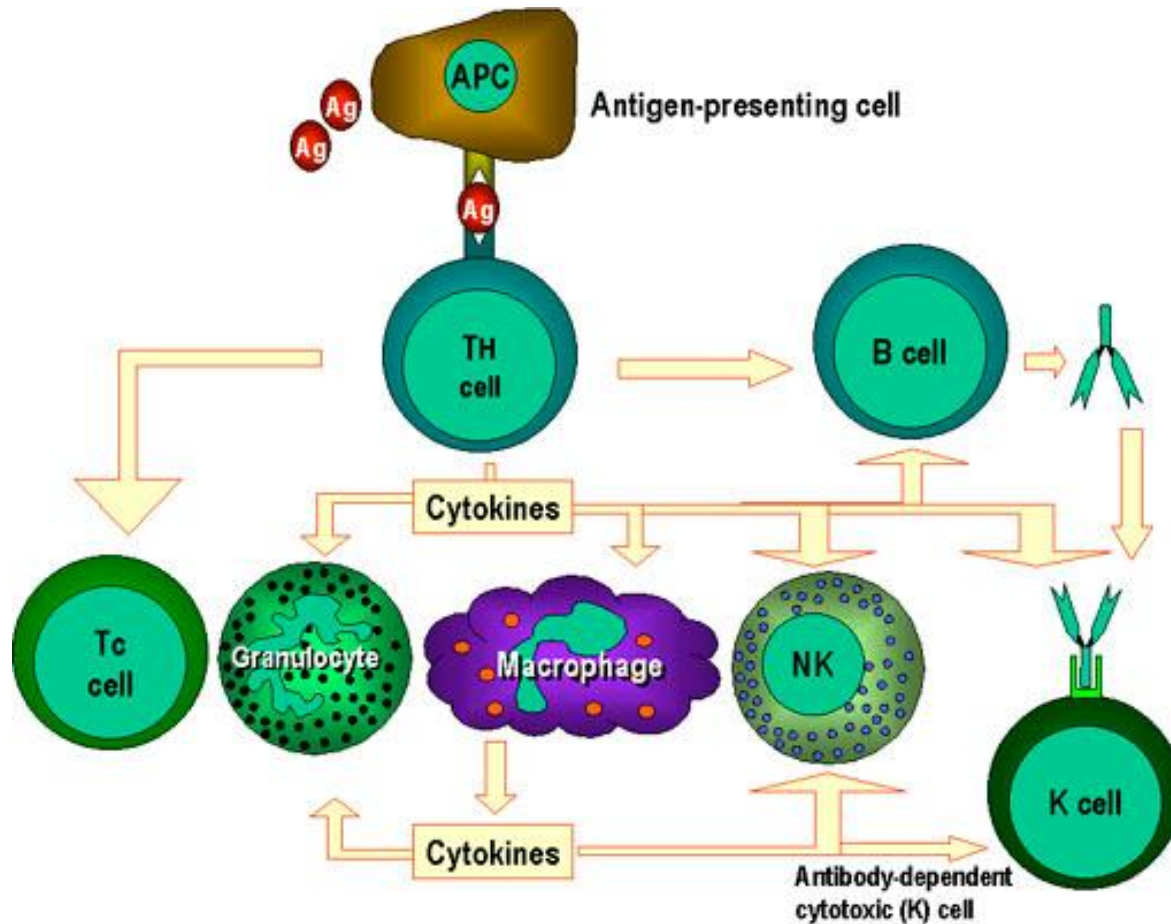
Cell mediated immunity

- This is specific immune response
- Involves mainly T Cells, APC (macrophage), NK cells
- T cells are of 2 types Th (helper) and Tc (cytotoxic)
- Th and Tc cells are called effector cells
- Th cells are of 2 types Th1 and Th2

Role of Th cells

- Th cells are CD4 +ve and recognize MHC class II
- Th cells play a central role in deciding which type of immune response to initiate (Humoral or cell mediated)
- Select effector mechanisms
- Induce proliferation of effector cells
- Enhance function of effector cells

Role of Th cells

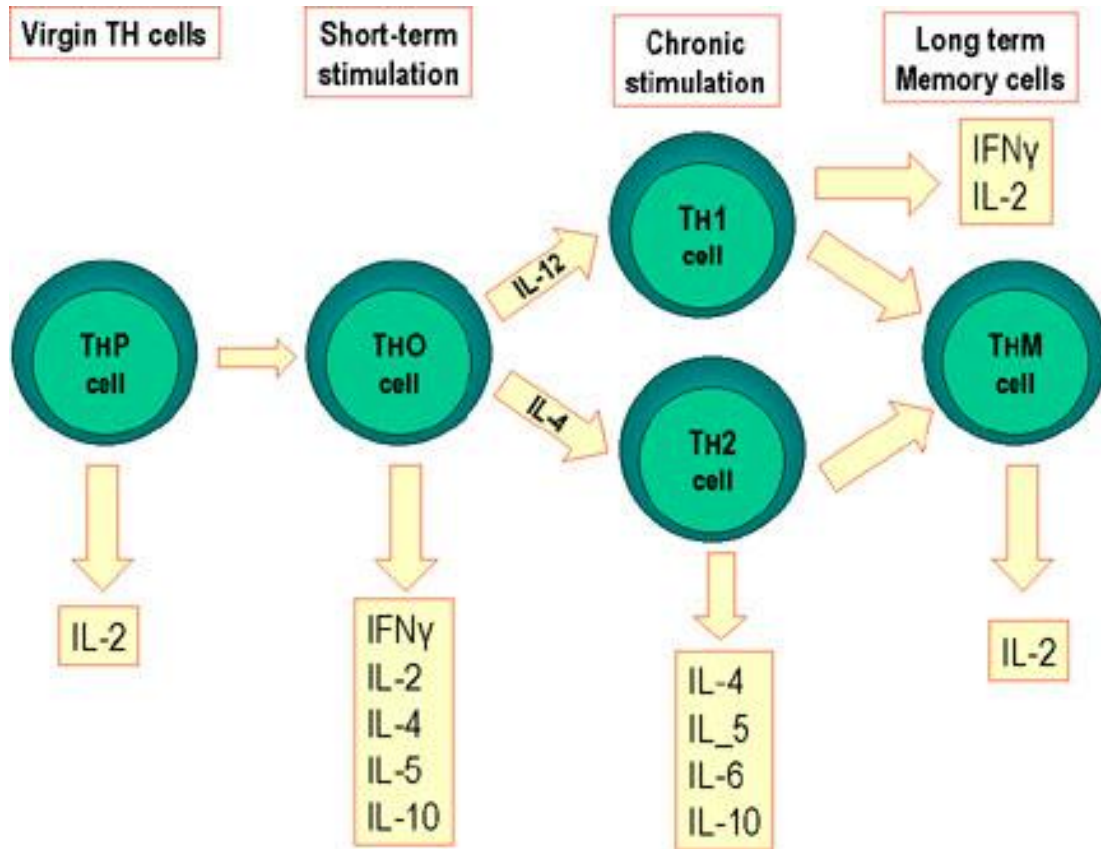


Th cells are at the center of cell-mediated immunity. The antigen-presenting cells present antigen to the T helper (Th) cell. The Th cell recognises specific epitopes which are selected as target epitopes. Appropriate effector mechanisms are now determined. For example, Th cells help the B cells to make antibody and also activate other cells. The activation signals produced by Th cells are cytokines (lymphokines) but similar cytokines made by macrophages and other cells also participate in this process

Th cells are of 2 types

- Th cells differentiate into two sub sets
- Th1 or Th2
- During differentiation they pass through phases (Th0)
- In each phase they secrete different cytokines
- Mainly Th1 response leads to Cell mediated immune response
- Th2 response leads to humoral immune response

Role of Th cells



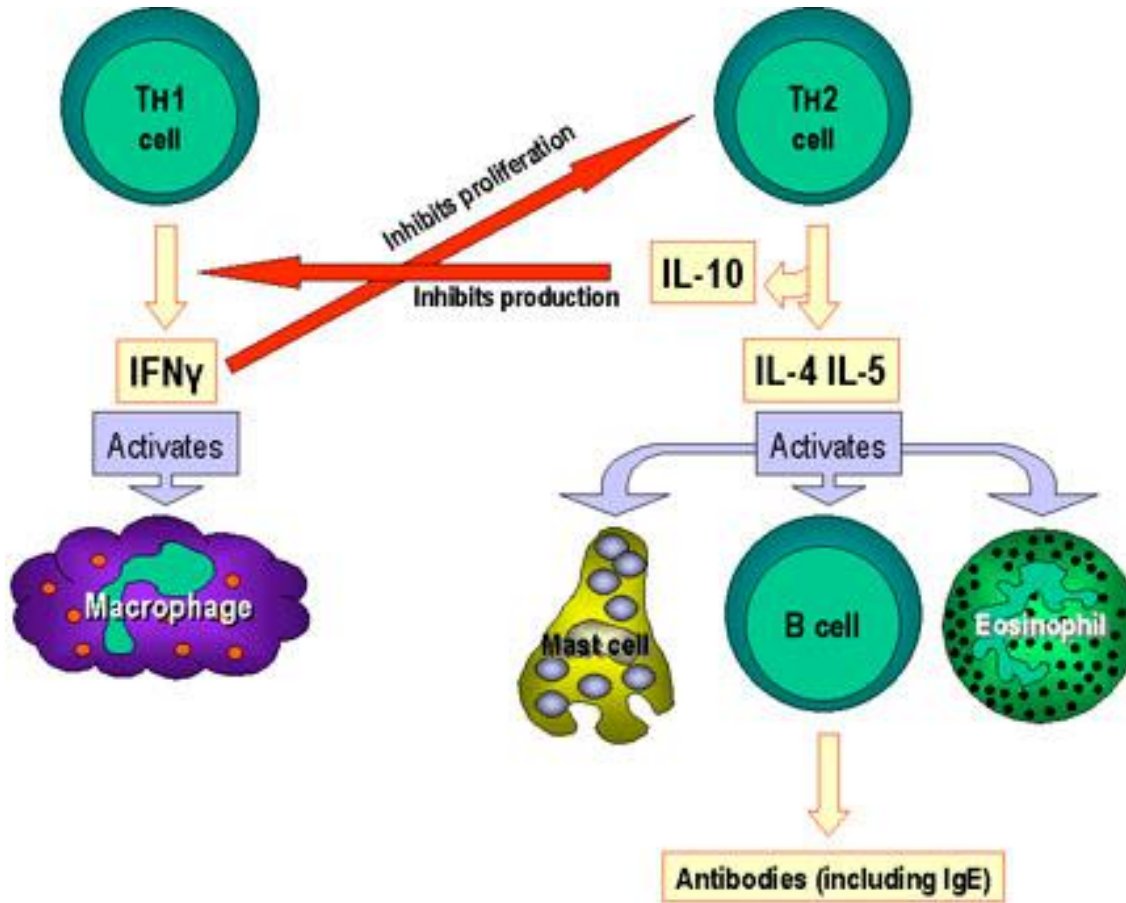
Differentiation of murine Th cells. Mouse Th cells differentiate into subsets that synthesize different patterns of lymphokines. This also occurs in humans

Th1 response leads to Cell mediated immunity
Th2 response leads to Humoral immunity

Regulation of Th cells

- There is cross regulation of Th1 and Th2 cells
- Th1 cells secrete cytokines that inhibit the function of Th2 cells
- Vice versa occurs
- Useful in not wasting energy and resources

Role of Th cells

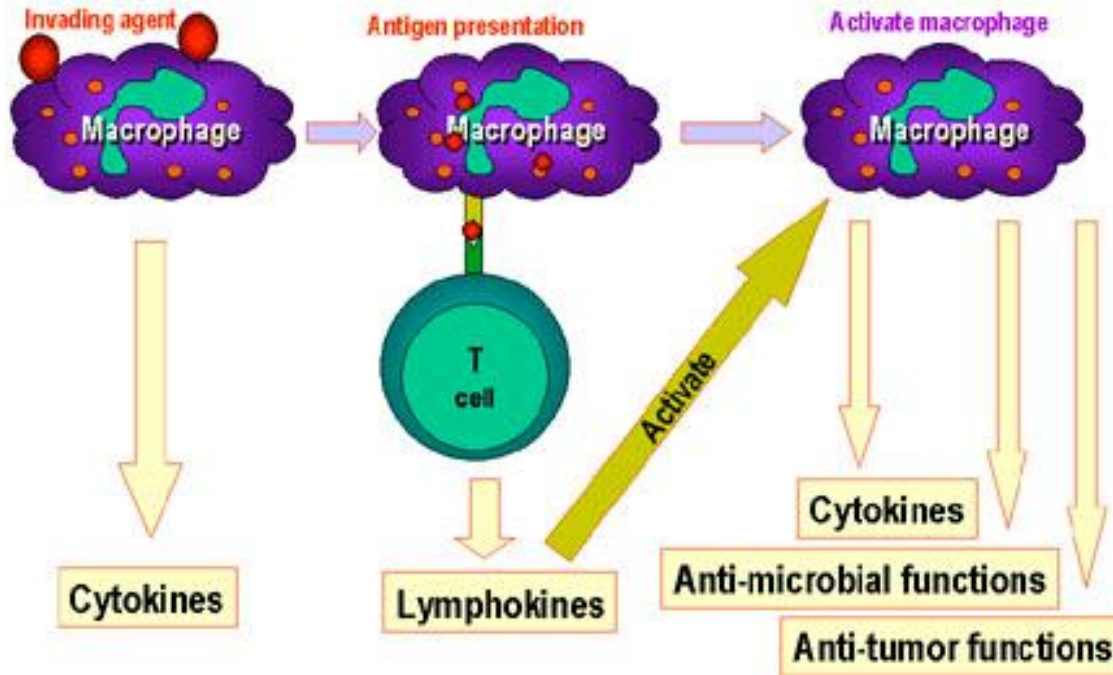


Selection of effector mechanisms by Th1 and Th2 cells. In addition to determining various effector pathways by virtue of their lymphokine production, Th1 cells switch off Th2 cells and vice versa

Role of macrophages

- Macrophages play central role in natural and specific immunity
- Involved in initial defense and antigen presentation and have effector functions
- Macrophages engulf invading pathogens leading to activation and production of cytokines
- Works as APC

Role of macrophages



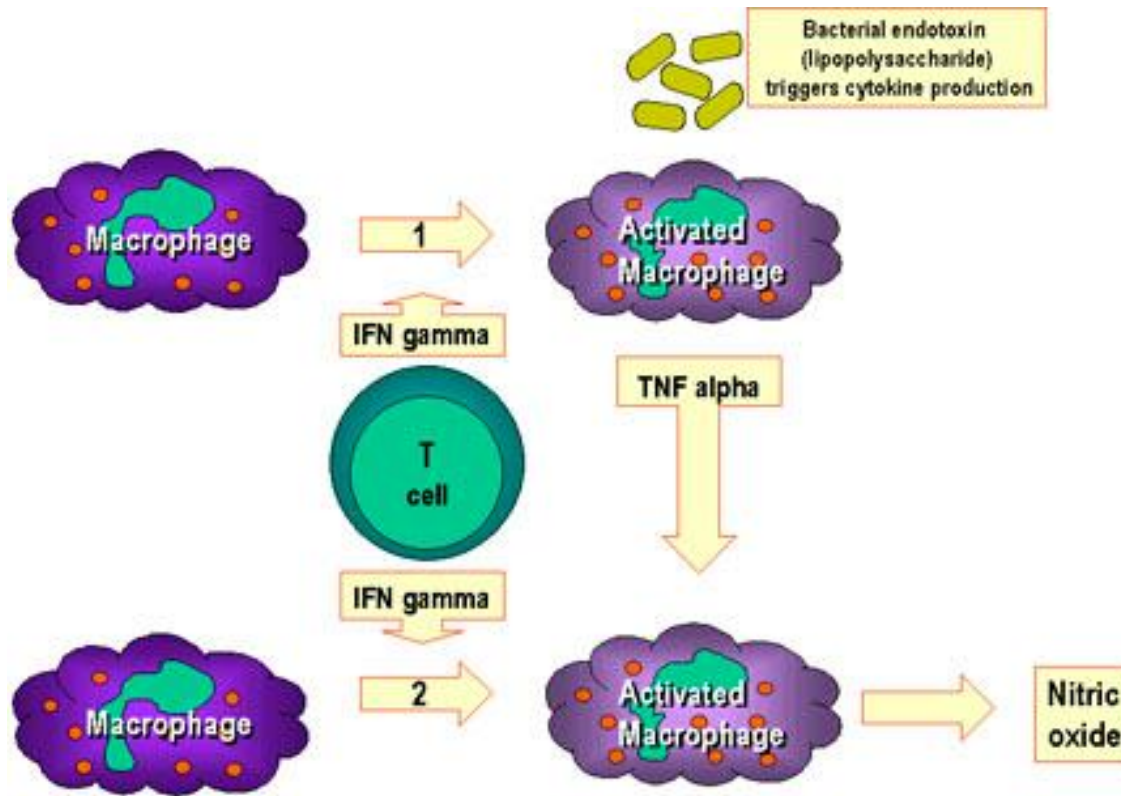
Macrophages play a central role in the immune system. before T and B-cell immunity starts. Macrophages process antigens and present them to T cells which then release lymphokines which activate the macrophages to perform various other functions including the production of more cytokines

Ovelaps both natural and specific immune response

Activation of macrophages

- INF- γ plays critical role
- Two major mechanisms that activate macrophages
- INF- γ produced by Th1 cells plus bacterial endotoxin (LPS)
- INF- γ produced by Th1 cells plus TNF- α

Activation of macrophages



Macrophage activation results from the interaction of multiple cytokines and other factors.

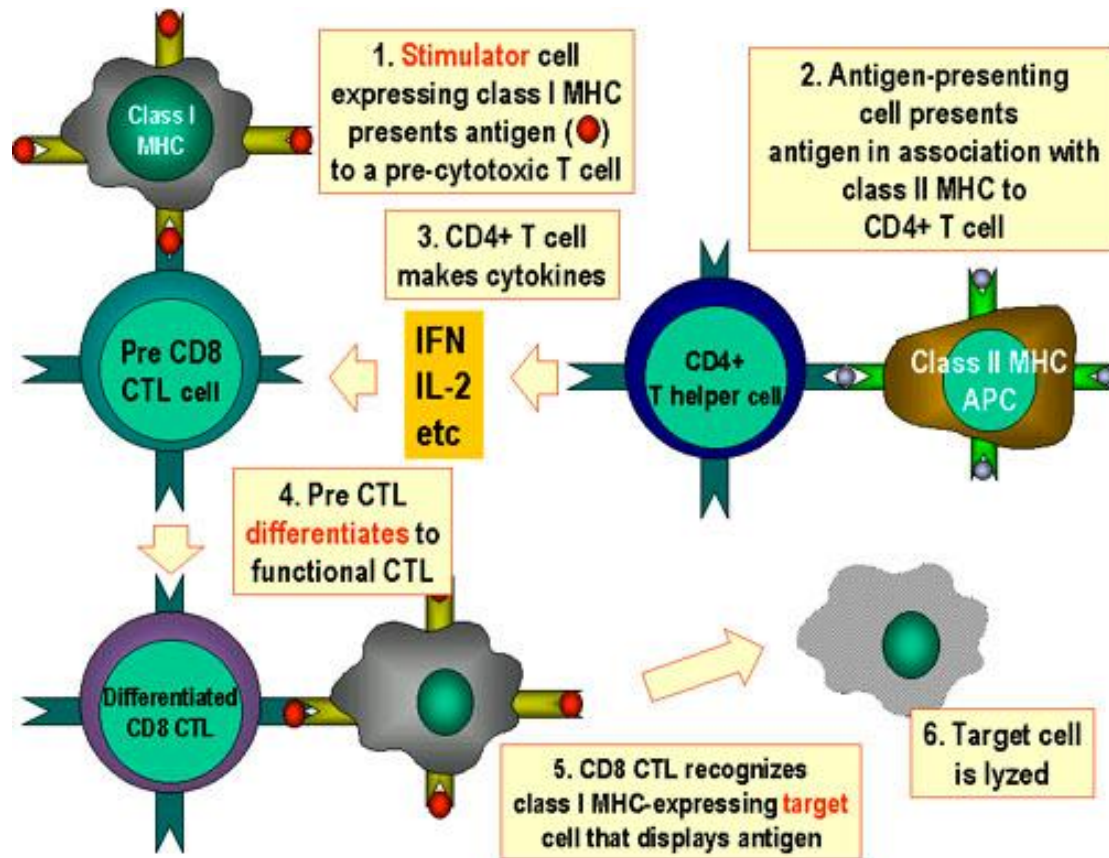
In pathway 1, TNF-alpha is released from macrophages as a result of activation by interferon gamma and interaction with bacterial components that trigger cytokine production. An example of such a triggering component is bacterial lipopolysaccharide. The TNF-alpha from pathway 1 leads to the production of nitric oxide by the interferon-activated macrophage in pathway 2.

INF- γ can bind to LPS or TNF α

Tc cells (cytotoxic T cells)

- Tc cells are CD8 +ve and recognize MHC class I. Also called Cytotoxic T lymphocytes (CTL)
- Tc produced by thymus are pre-Tc cells
- Pre-Tc cells are not mature and can not kill until armed. They have T Cell Receptor (TCR)
- Tc maturation requires two signals
- 1. Recognition by TCR of specific Ag in association with MHC class I
- Exposure to cytokines (IL-2, INF- γ)

Activation of CTL



CTL cells must differentiate in response to antigen. In order to differentiate into functional cytotoxic T lymphocytes, pre-CD8+ CTLs must receive two different signals. First, they must recognize antigen presented by MHC-I expressing cells (the stimulator cells) and, second, they must be stimulated by cytokines. IL-2, interferon-gamma and others are made by CD4+ helper T cells as a result of their interaction with class II MHC-expressing antigen presenting cells. As a result of these two signals, the pre-CTL differentiates into an active CTL that can then lyse target cells that bear the same antigen.

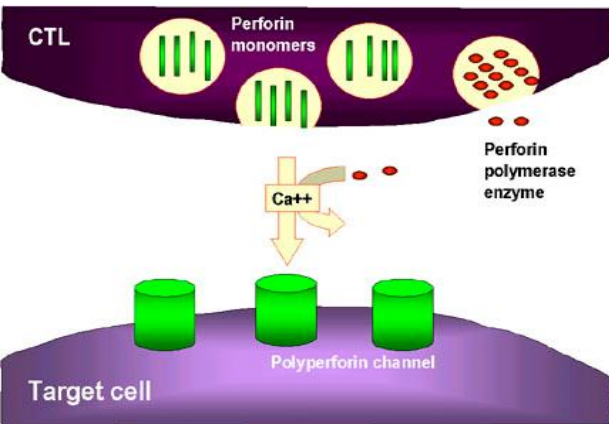
Tc Killing

- Antigen specific
- Requires cell to cell contact
- Each Tc can kill many target cells
- Two mechanisms are used for Tc activity
 - Direct cell to cell signaling via surface receptors
 - Indirect signaling via cytokines

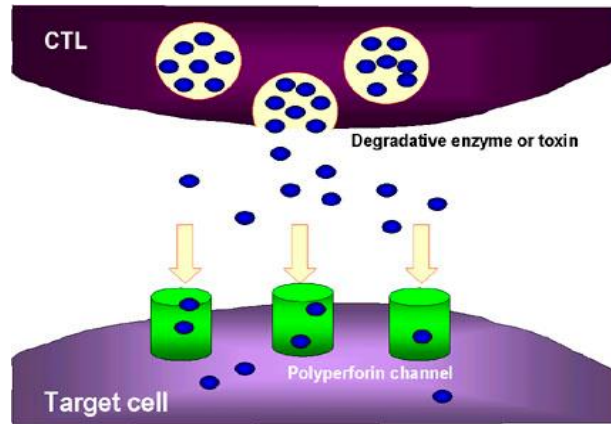
Tc Killing

- Tc killing mainly uses granules that contains perforins and granzymes
- Upon contact with target cell granules are released
 - Perforin polymerizes and forms pores
 - Granzymes (ser proteases) enter the cell and induce apoptosis by activating caspases and nucleases
- Apoptosis is very important in limiting viral spread

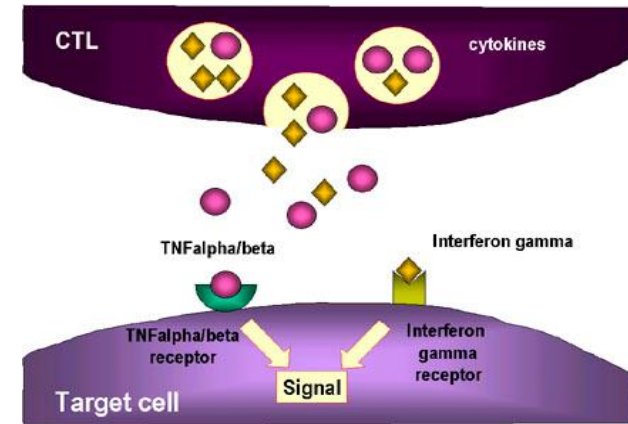
Mechanism of CTL killing



CTL degranulates and releases perforin monomers into the surroundings. Enzymes that polymerize perforin to form polyperforin channels are also released and these along with Ca^{++} catalyze channel formation in the membrane of the target cell



The CTL may also release degradative enzymes and toxins which travel through the perforin channels and damage the target cell

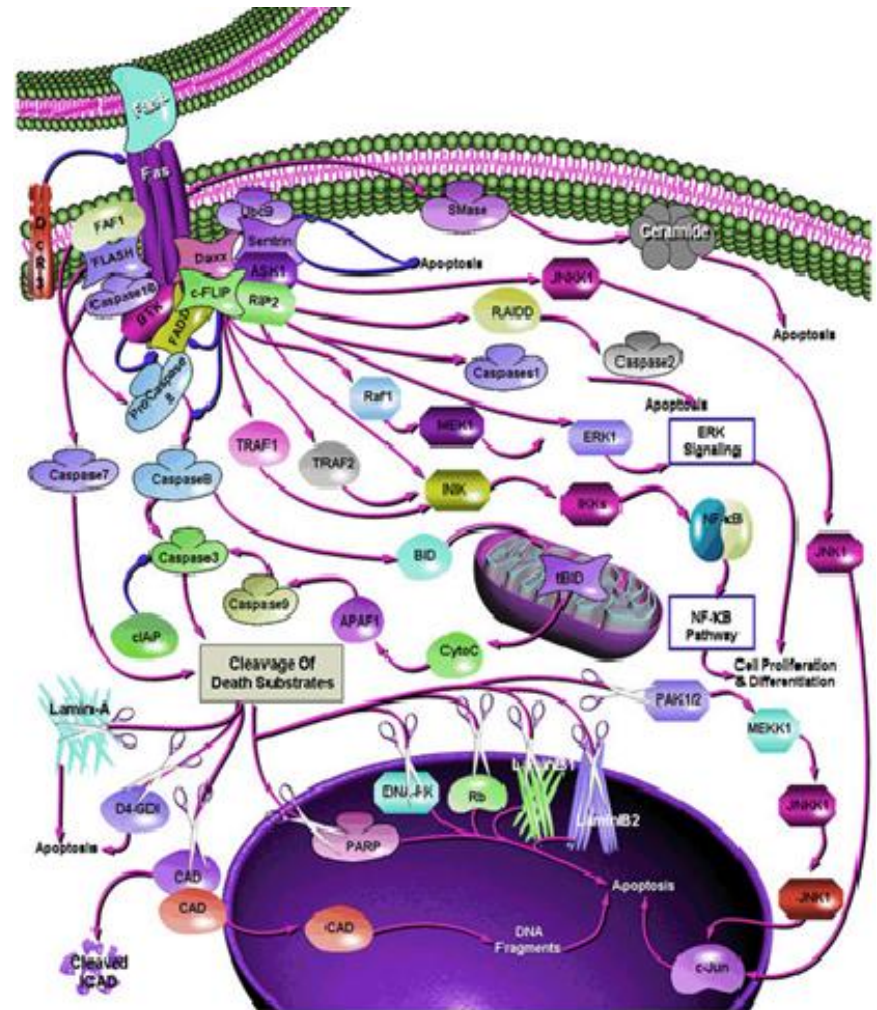
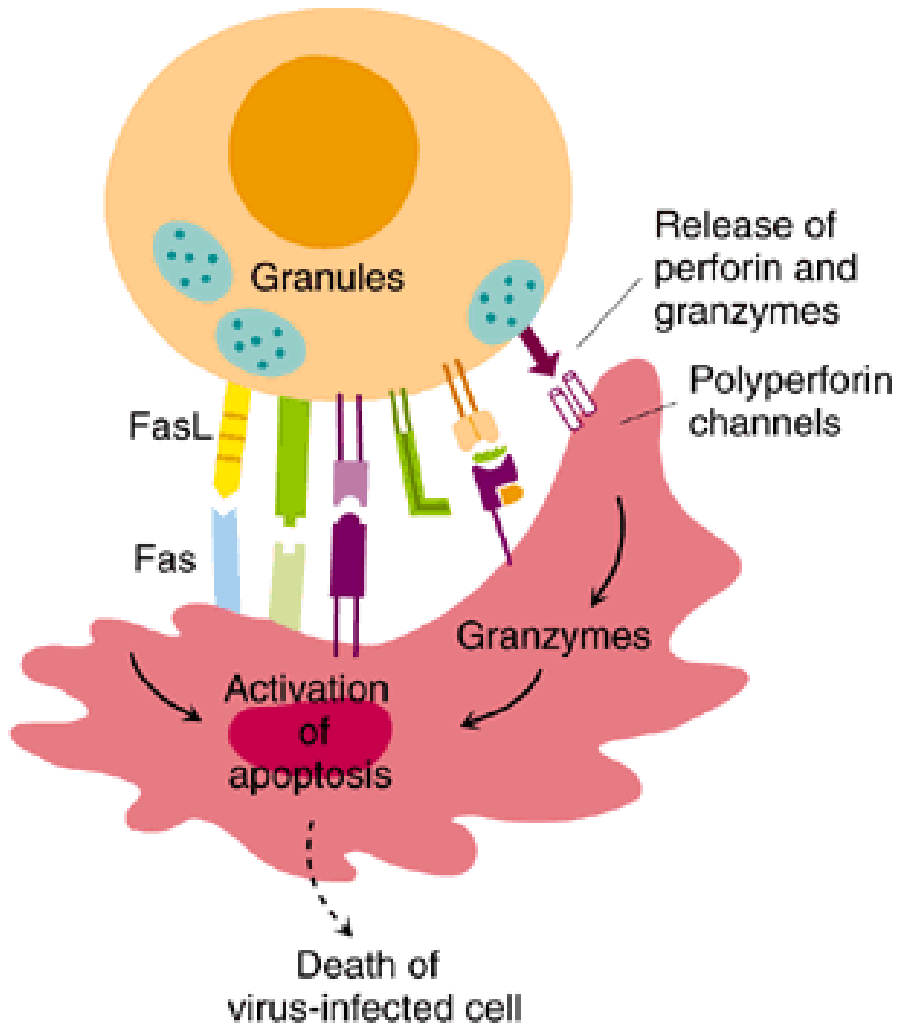


Cytokines such as TNF alpha and TNF beta are released from the CTL or nearby macrophages. Interferon gamma may also be released from the CTLs or from other nearby lymphoid cells. These bind to receptors on the target cell and trigger apoptosis

Mechanism of Tc killing

- Tc can kill via Fas ligand and Tumor Necrosis Factor (TNF) receptor on target cells
- Signaling through Fas or TNF receptor
- CTLs express Fas ligand on surface
- TNF can be secreted by Tc
- Binding of ligand to receptor leads to apoptosis through death domain.

Mechanism of Tc killing



Next class.....

- MHC and transplantation immunity