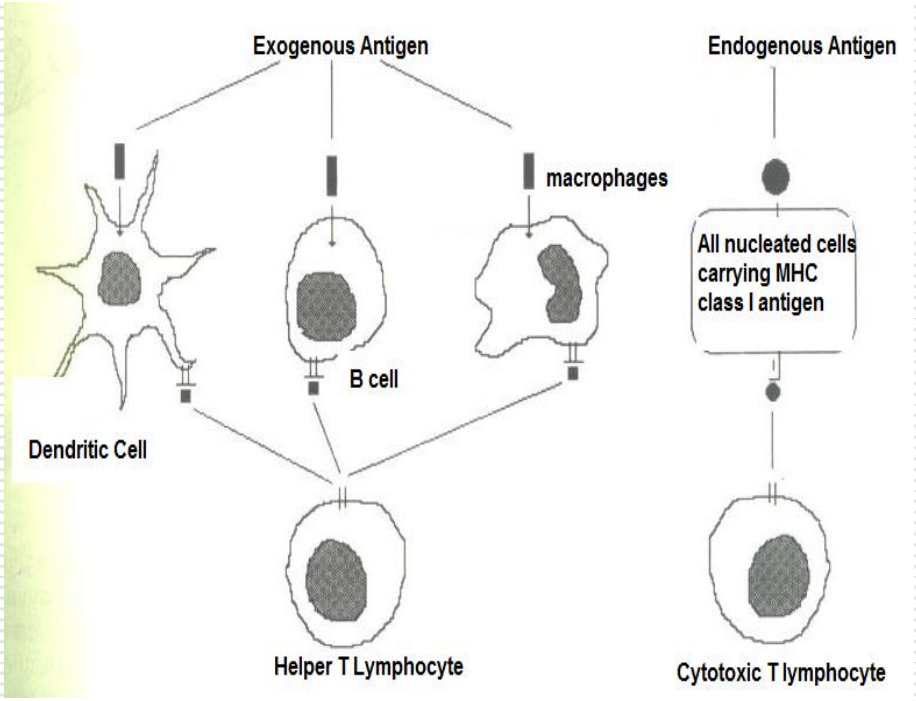
Cellular Immune Response

Cellular Immune Response

- It is the immunity to antigenic molecules or cells with abnormal structure in / living cells.
- Endogenous antigens are introduced into cytotoxic T-lymphocytes with the MHC class I molecule found in all nucleated cells — cellular immunity occurs
- Some antigens stimulate cellular immunity by introducing them into Th1 with MHC class II molecule

Cellular Immune Response

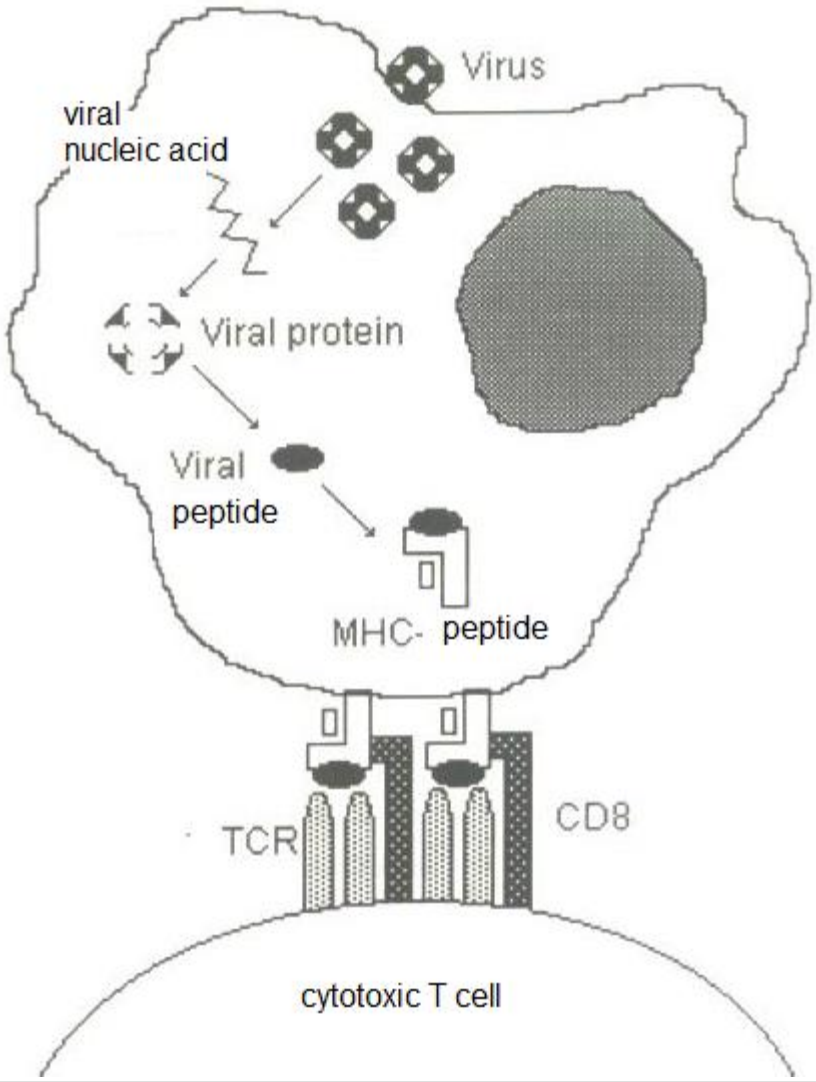


- Endogenous antigens are introduced to cytotoxic T-lymphocytes with the MHC class I molecule found in all nucleated cells — cellular immunity occurs

Cellular Immune Response

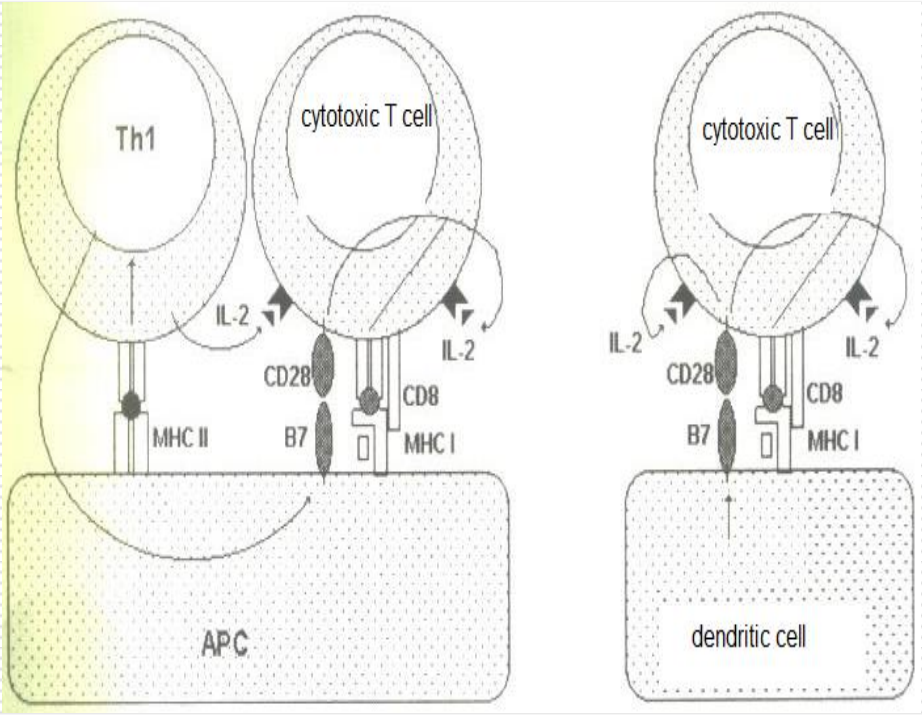
- T cell cytotoxicity
- NK cell cytotoxicity
- Macrophage Activation

Cellular Immune Response (T cell cytotoxicity)



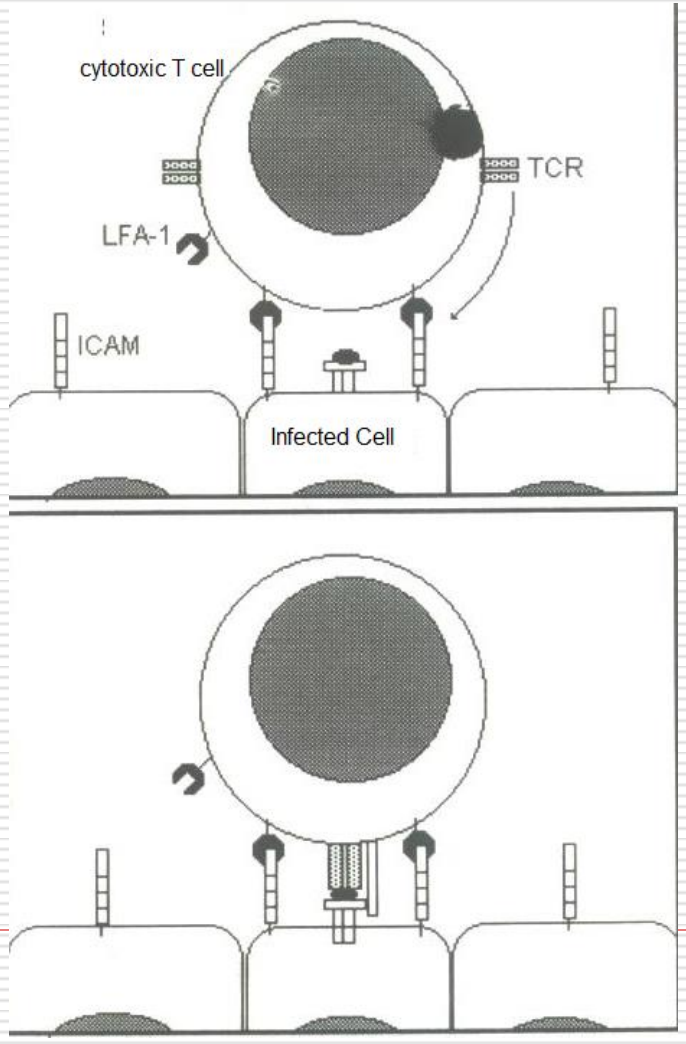
- Presentation of endogenous antigens to cytotoxic T-lymphocytes with MHC class I molecule
- Peptide-TCR connection
- MHC class I-CD8 connection

Cellular Immune Response (T cell cytotoxicity)



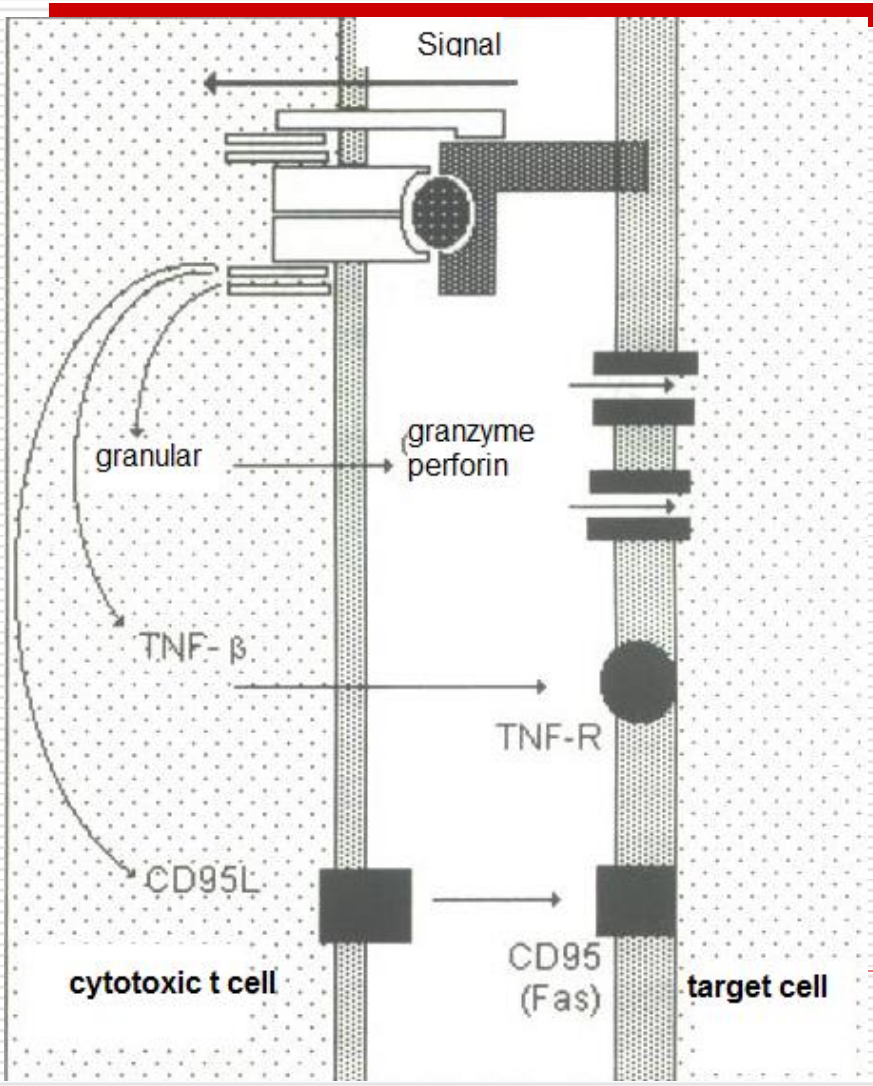
- There are two important stimulants in cytotoxic T-lymphocyte activation
- **1.** TCR linkage with endogenous antigen presented with MHC class I
- **2.** IL2 stimulation secreted from Th1
- Cytotoxic T-lymphocytes receiving these stimuli rapidly, divide and multiply. Part of it turns into memory T-cell

Cellular Immune Response (T cell cytotoxicity)



- Adhesion of cytotoxic T-lymphocytes to target cells
- T-lymphocytes should be specific to the target cell
- CD8-MHC class I molecular bond
- Adhesion molecules

Cellular Immune Response (T cell cytotoxicity)



- Killing the target cell «***apoptosis*** «
- ” Apoptosis is stimulated by three different mechanisms

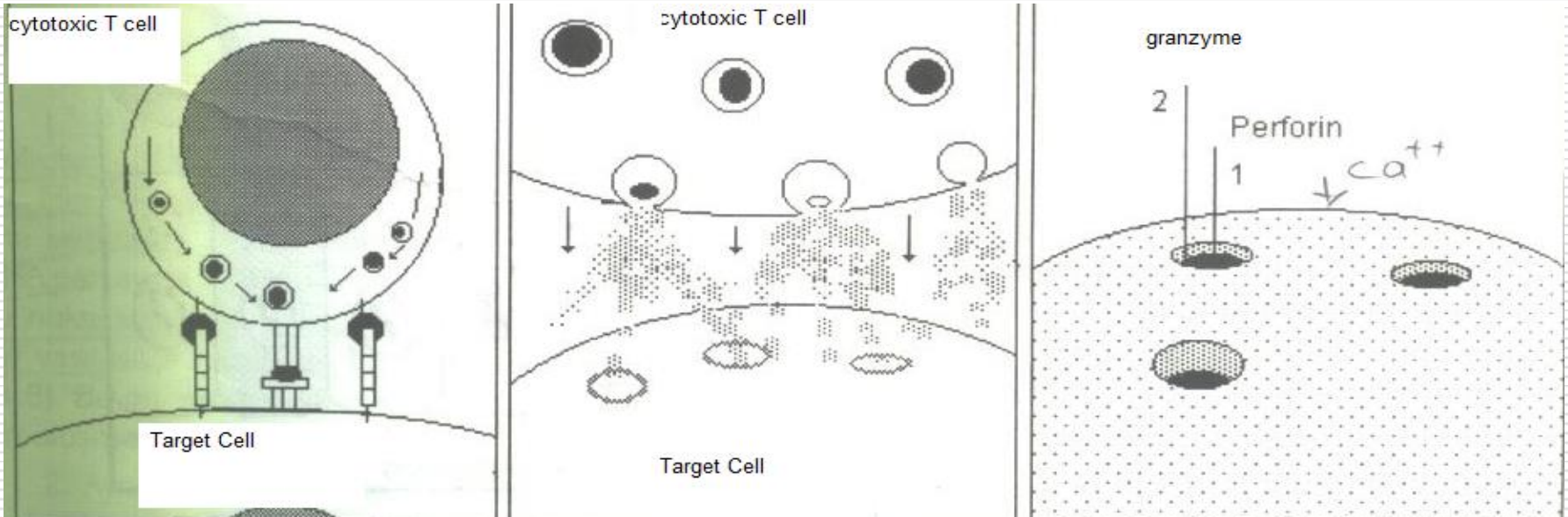
1- Perforin pathway

2-CD95 pathway

3-TNF-beta pathway

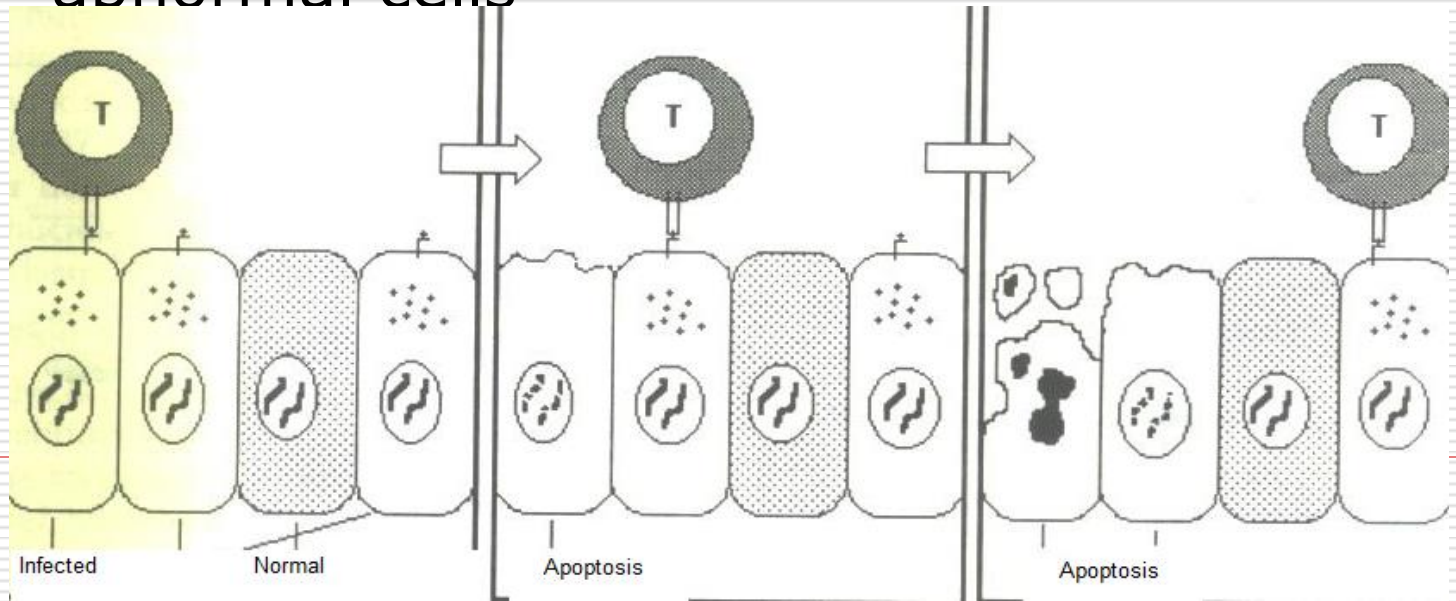
Cellular Immune Response (T cell cytotoxicity)

- Stages of the perforin pathway
- -enzyme granules (perforin and granzyme-perforin:
- Opens pores in lipid layer on target cell surface -granymes: penetrate through the pores into the target cell, increase intracellular Ca ++ concentration and activate endonucleases
- -endonucleases dissect target cell DNA into 200 base segments and the cell dies



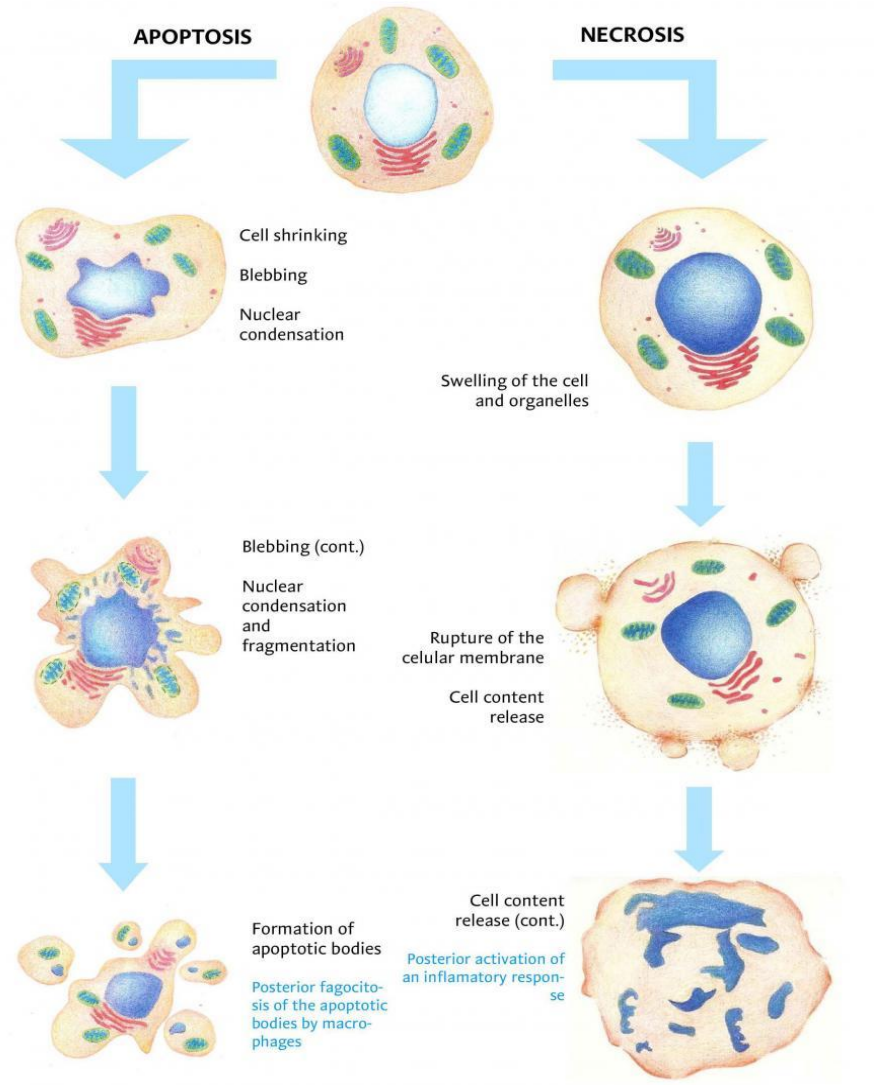
Cellular Immune Response (T cell cytotoxicity-Apoptosis)

- Both target cell and intracellular viruses are killed by apoptosis
- After the cytototoxic T-lymphocyte is bound to the target cell 5m. Kills the cell inside and immediately moves to the new target cell
- Cytototoxic T-lymphocyte has the ability to distinguish between normal and infected / abnormal cells



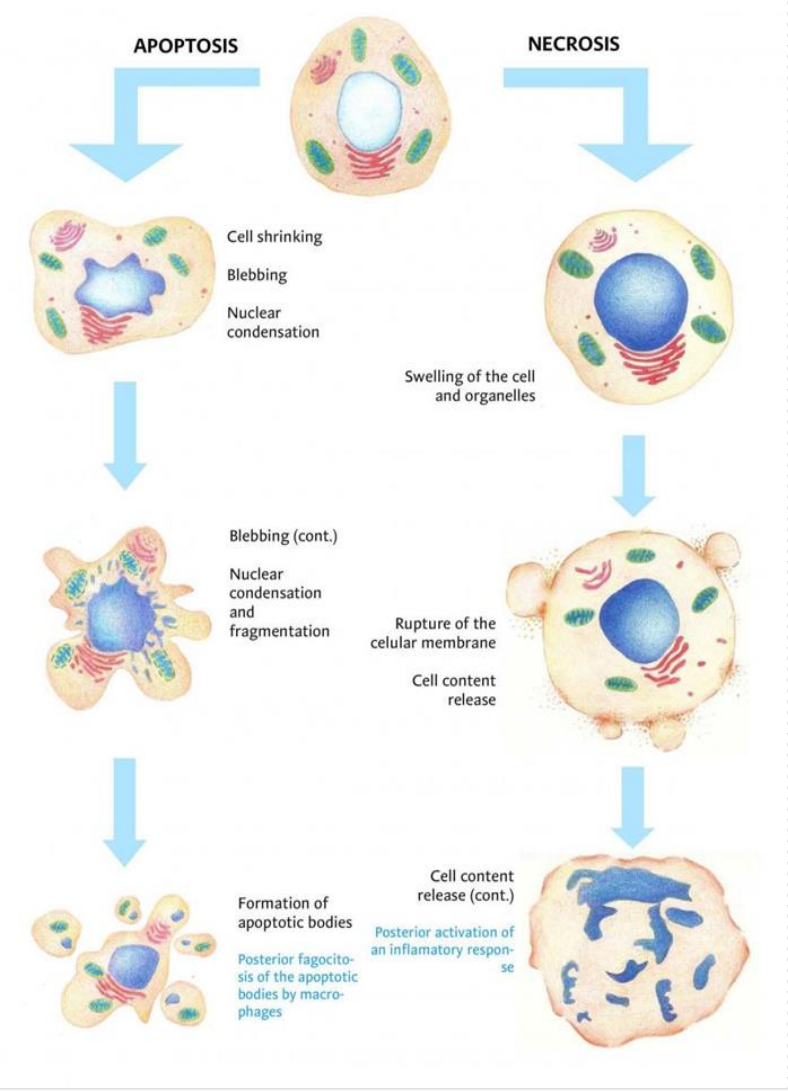
Cellular Immune Response (T cell cytotoxicity-Apoptosis)

- Apoptosis (other than cellular immunity) is a physiological event (embryogenesis, autoreactive cell deaths, etc.) necessary for the maintenance of normal body functions.



Cellular Immune Response (T cell cytotoxicity-Apoptosis)

- Apoptosis is different from cell lysis
- Fragmentation of histones (200 base pair DNA fragments) with endonucleases
- Production of enzyme degrading cell cytoplasm and disruption of cell skeleton
- Formation of apoptotic bodies



Functions of Cytotoxic T-lymphocytes

- Death of virus-infected cells
- Death of intracellular bacteria
- Death of tumor cells
- Rejection of tissue transplantation
- Death of autoreactive T-lymphocytes
- Macrophage activation and prevention of viral replication by synthesized cytokines

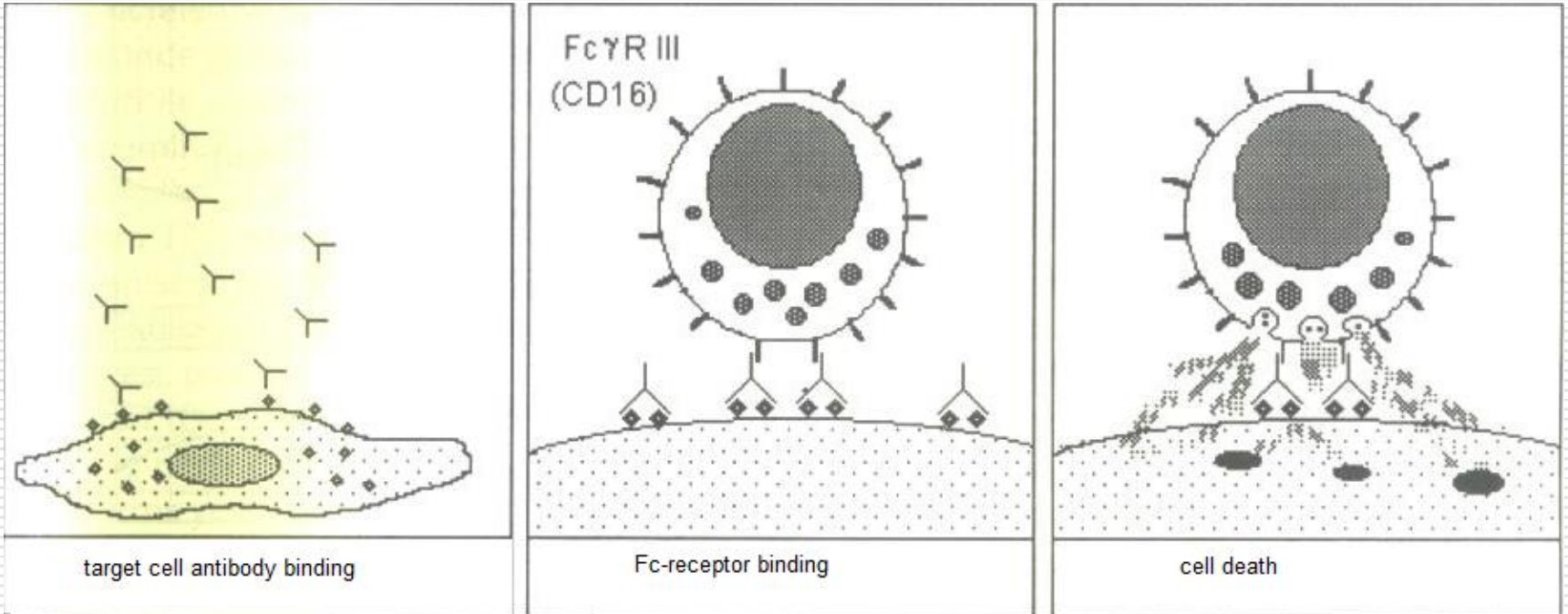
Cellular Immune Response (NK Cell Cytotoxicity)

- NK cells are an important element of cellular immunity
- NK cells do not carry antigen receptors – nonspecific
- The way NK cells recognize and bind the target cell is different
- Kills target cell with apoptosis

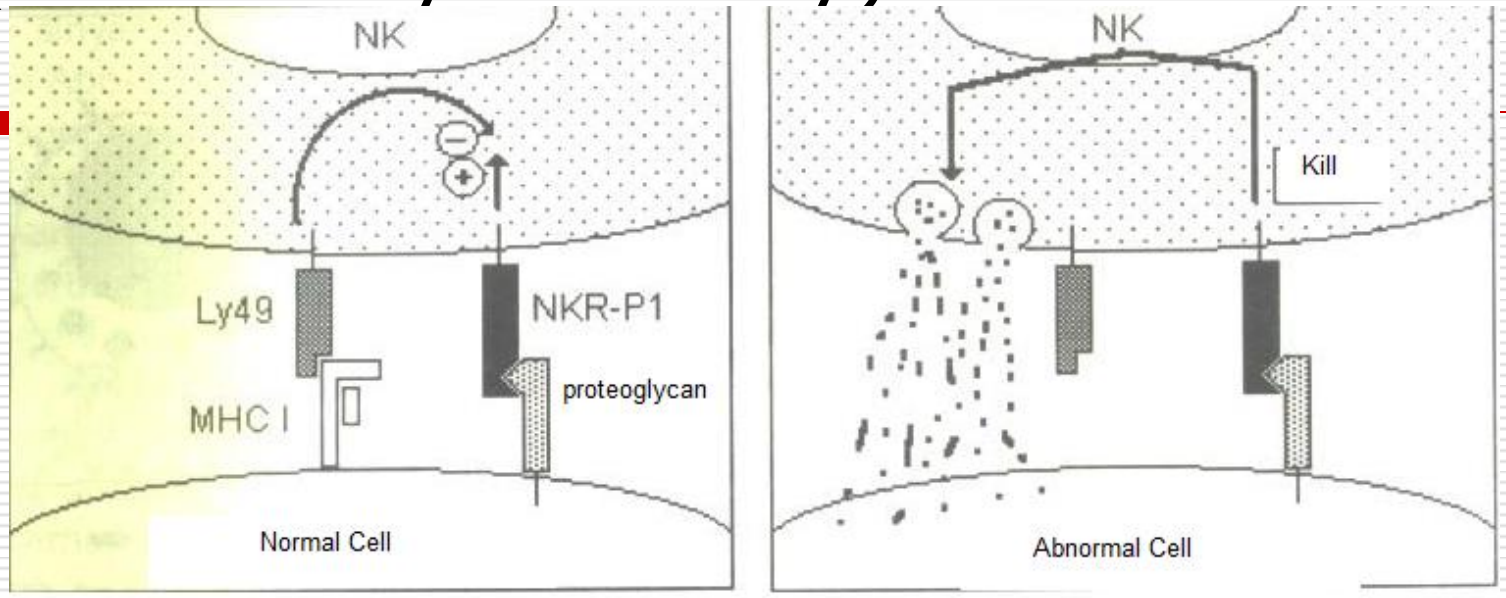
Cellular Immune Response (NK Cell Cytotoxicity)

Antibody Dependent Cellular Cytotoxicity(ADCC)

- NK cells carry Fc-gamma receptor and can bind with Ig G molecules
- Main target virus-infected cells
- ADCC; Develops more slowly than T cell cytotoxicity



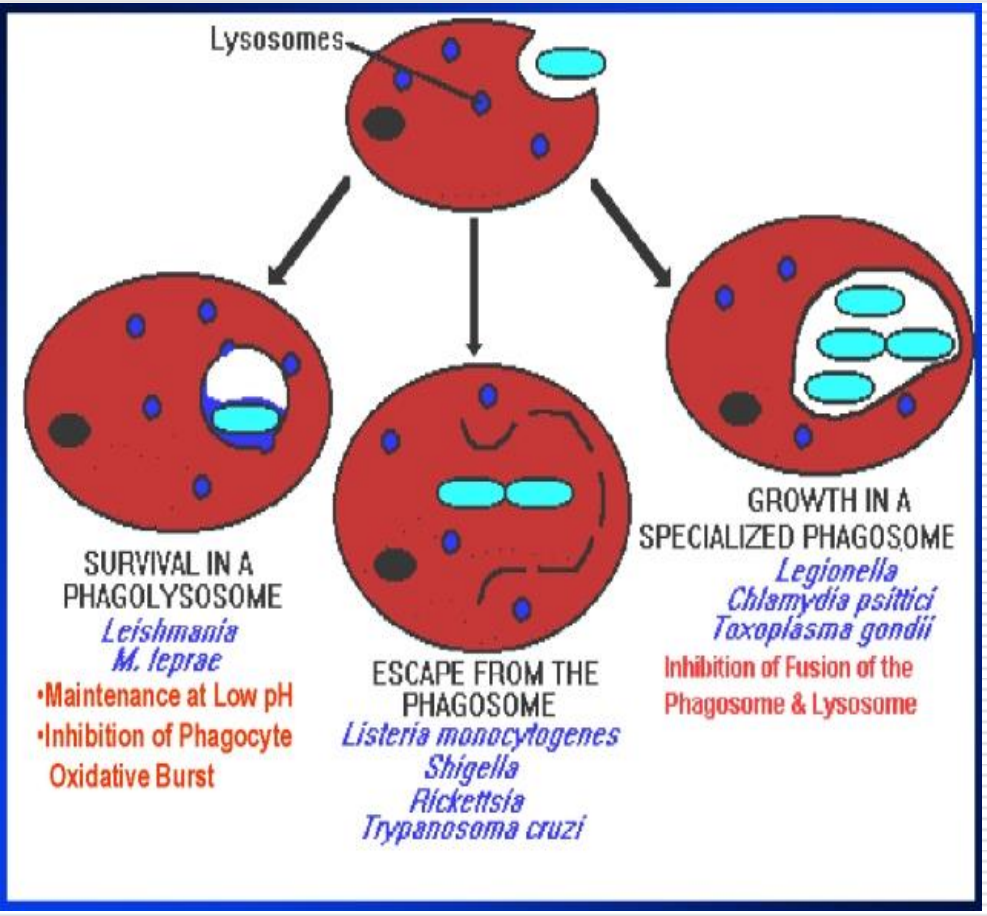
Cellular Immune Response (NK Cell Cytotoxicity)



Direct NK Cell Cytotoxicity

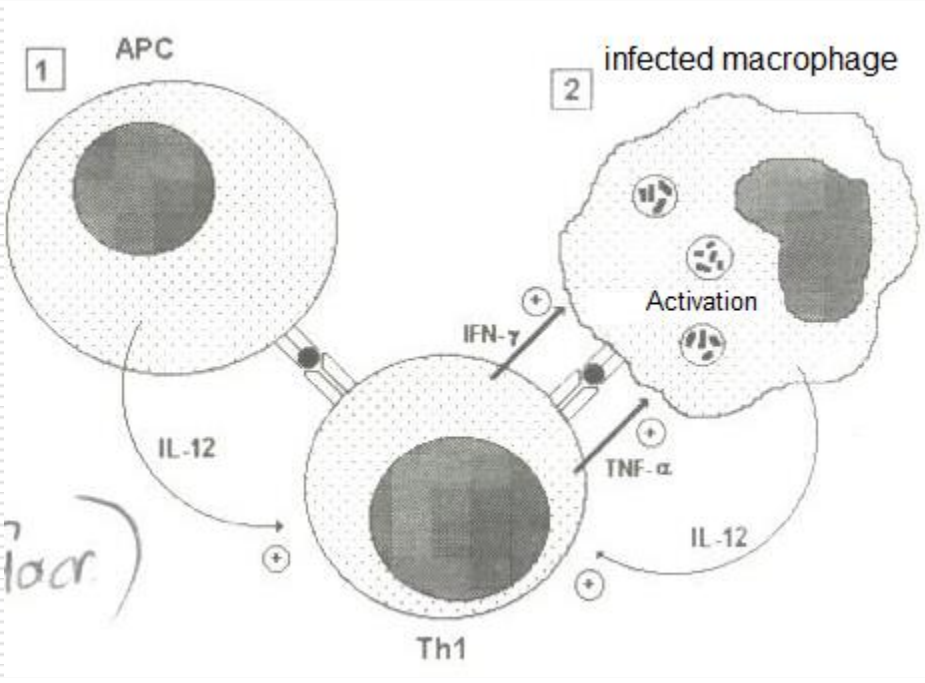
- Occurs early in cellular immunity
- Viral infections-tumor cell defenses
- Cytokine stimulation (IL12, IFN-alpha, IFN-beta) from macrophages is important in the early stage of infection
- Normal-abnormal body cell separation
- NKR-P1 receptor: binds to proteoglycans present in all cells - **death warrant**
- Ly49 receptor: binds to MHC class I molecule found in normal cells - **death warrant cancellation**
- This double bonding is normal and occurs in all healthy living organisms
- Abnormal cells do not have MHC class I molecule or have been altered - **death order cannot be canceled - apoptosis begins**

Cellular Immune Response (Macrophage Activation)



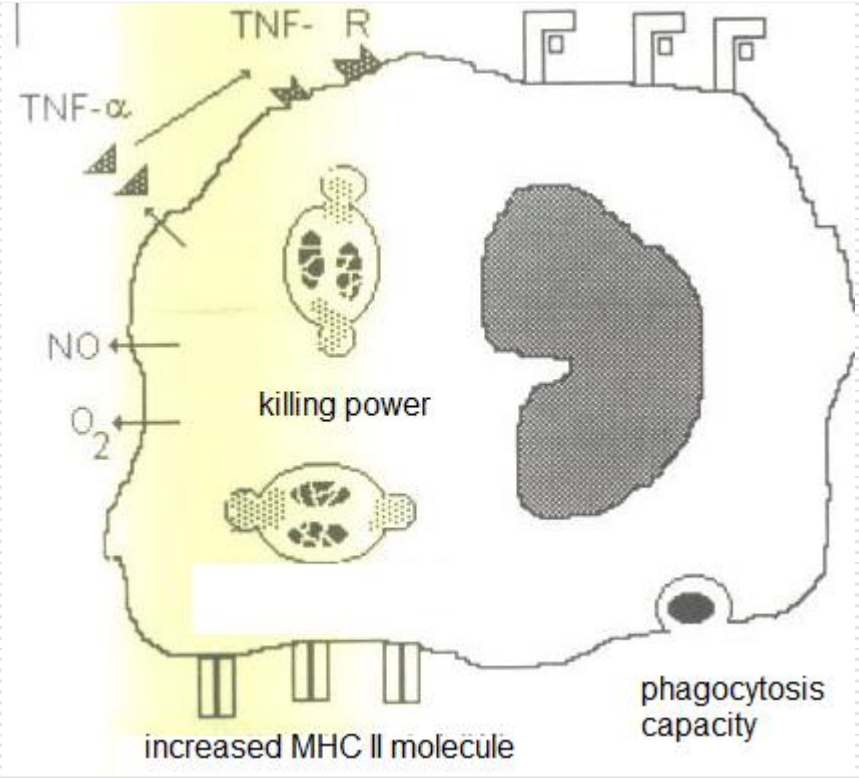
- Some bacteria, fungi and protoozoa are resistant to phagocytosis !!!!
- ‘’Macrophage activation ”is important for such microorganisms

Cellular Immune Response (Macrophage Activation)



- Antigen presentation to Th 1 cells by MHC class II by APC or infected macrophage
- Cytokine release from Th1 cells (IFN-gamma and TNF-alpha)
- Macrophage activation

Cellular Immune Response (Macrophage Activation)



Macrophage Activation

-Increases Cytokine Synthesis

- Increases MHC Class II Synthesis

-Membrane activity increases

-Increases ability to create pseudopod

-Increases ability of pinocytosis

-Increases intracellular killing capacity