

## ***Cell mediated immune response***

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#### **Naive T cells:**

Mature cells that have not yet encountered their specific Ag

#### **priming**

The activation and clonal expansion of a naive T cell on its initial encounter with Ag

#### **effector T cells**

The T cells that perform the functions of an immune response: cell killing, cell activation that clear the infectious agent .

#### **Target cells:**

The cells on which effector T cells act

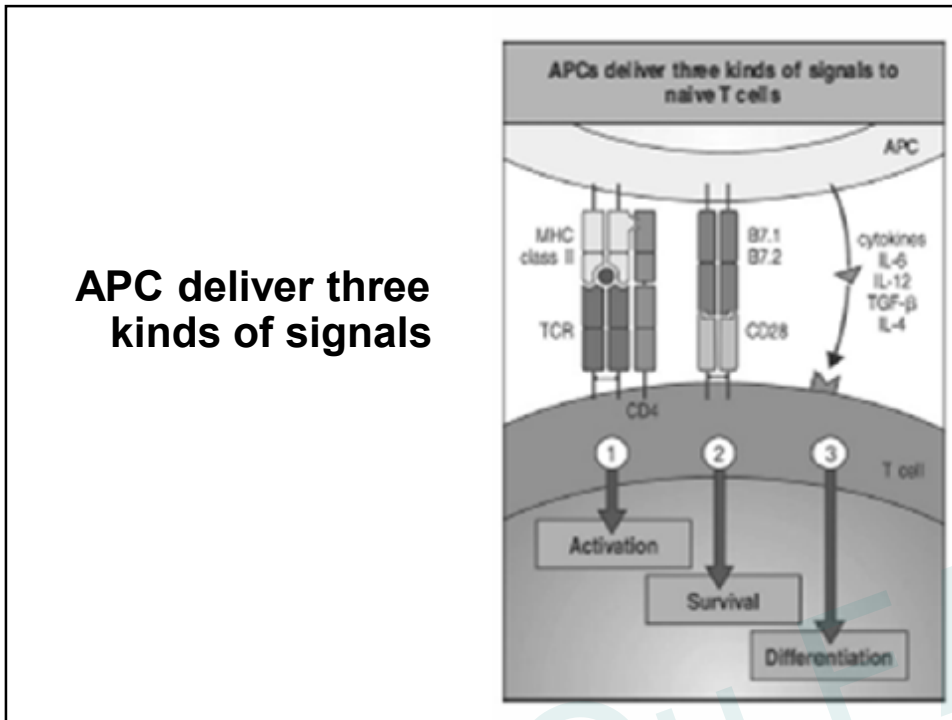
### **T cell activation**

- Naive T cell recognizes its specific antigen on the surface of a mature DC, it ceases to migrate. proliferates for several days
- Clonal expansion/differentiation: effector T cells and memory cells of identical Ag specificity
- the effector T cells exit into the efferent lymphatics and reenter the bloodstream, migrate to the sites of infection

### **Key steps in T cell activation**

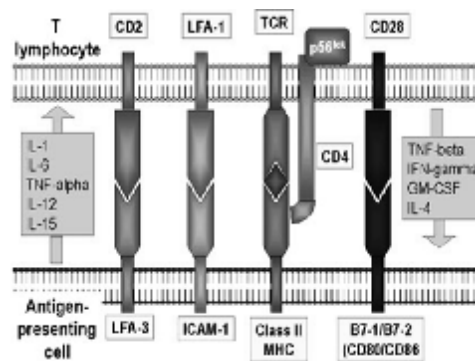
- APC must process and present peptides to T cells
- T cells must receive co-stimulatory signal
- Accessory adhesion molecules stabilize binding of TCR and MHC
- Signal from cell surface is transmitted to nucleus
- Cytokines produced help drive cell proliferation

**APC deliver three kinds of signals**



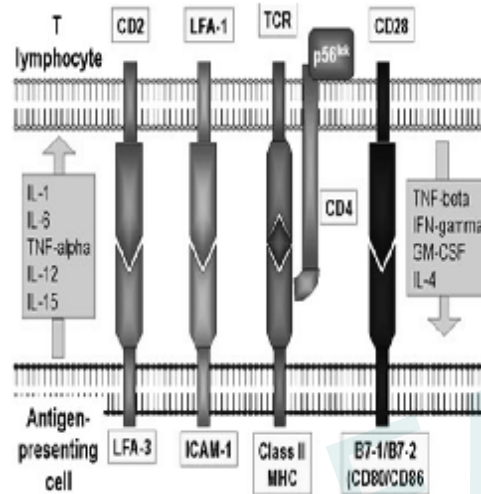
**The “immunological synapse”**

- TCR-MHC interaction is not strong
- Accessory molecules stabilize interaction
  - CD4/MHC class II or CD8/MHC class I
  - CD2/LFA-3
  - LFA-1/ICAM-1



### The “immunological synapse”

- Specificity for Ag is solely in TCR
- Accessory molecules are invariant, necessary for activation of T cells
- Cytokines change expression levels



### Costimulation

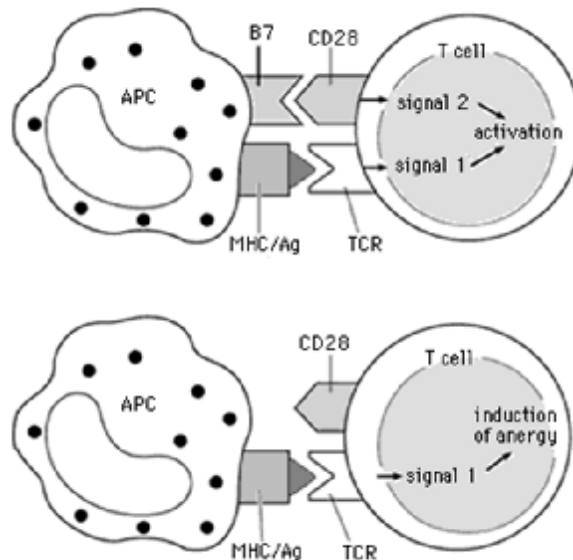
- the signals delivered by the TCR are insufficient to fully activate T cells.
- A second set of signals generated by costimulatory molecules is required for T-cell activation

## CD28

- A glycoprotein that is expressed as a homodimer on T cells
- **CD28** binds two distinct cell surface molecules, **B7.1 (CD80) / B7.2 (CD86)**, found on APCs.
- TCR stimulation and the interaction CD28:B7 activate T cells and results in great lymphokine production.

### Costimulation by CD28

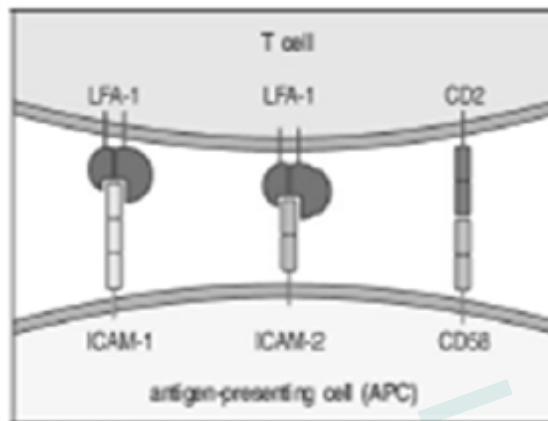
***Anergic T cell: viable but is refractory to stimulation by antigen***



Cell-adhesion molecules mediate the initial interaction of naive T cells with antigen-presenting cells.

*Leukocyte Functional Antigens (LFAs)*

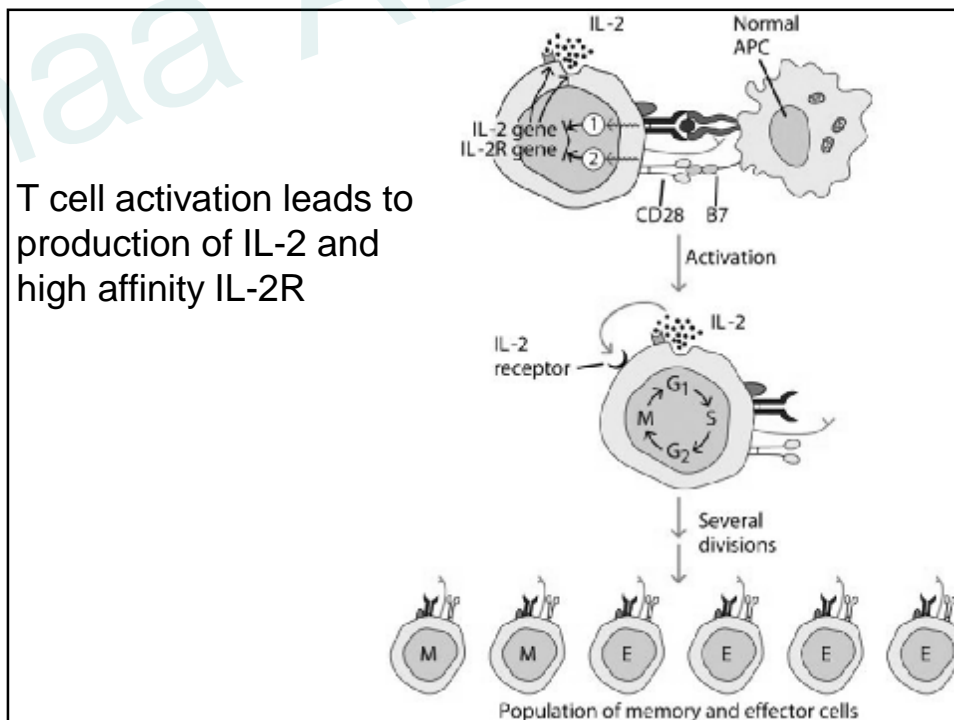
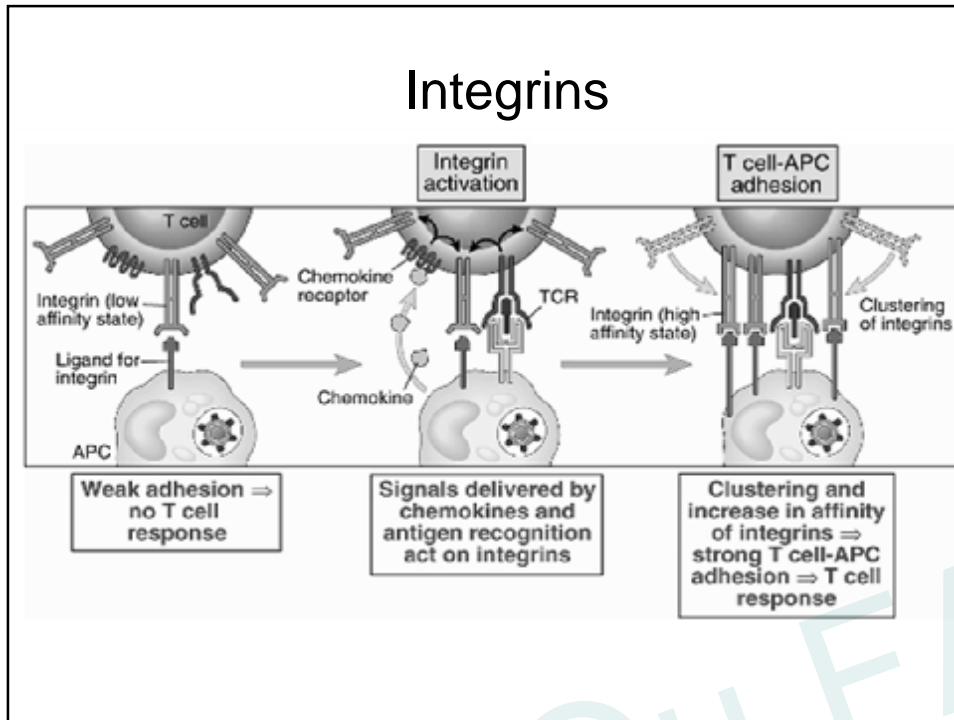
***LFA-1 is important in T-cell adhesion to endothelial cells and antigen presenting cells.***



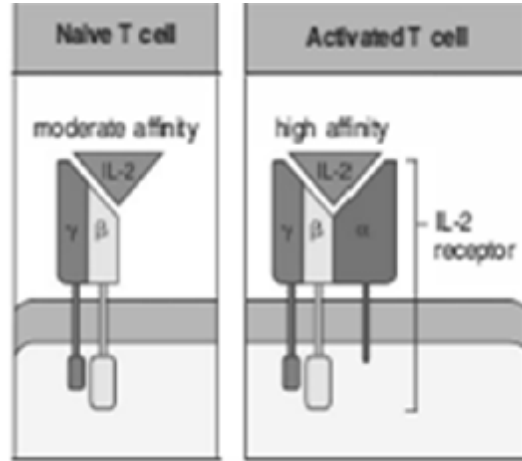
intercellular adhesion molecules (ICAMs)

## Integrins

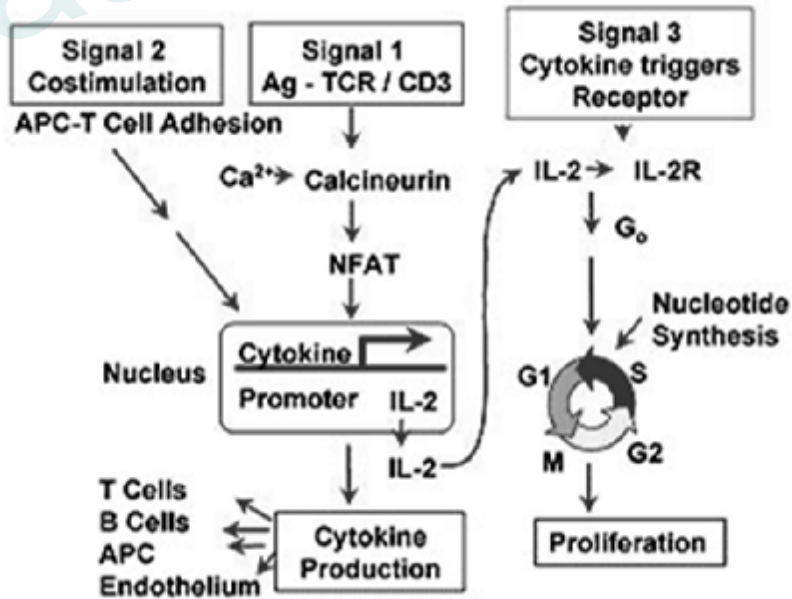
- T-cell integrins are to mediate adhesion to APCs, endothelial cells, and extracellular matrix proteins.
- The avidity of integrins for their ligands is increased rapidly on exposure of the T-cells to chemokines and after stimulation of T-cells through the TCR.



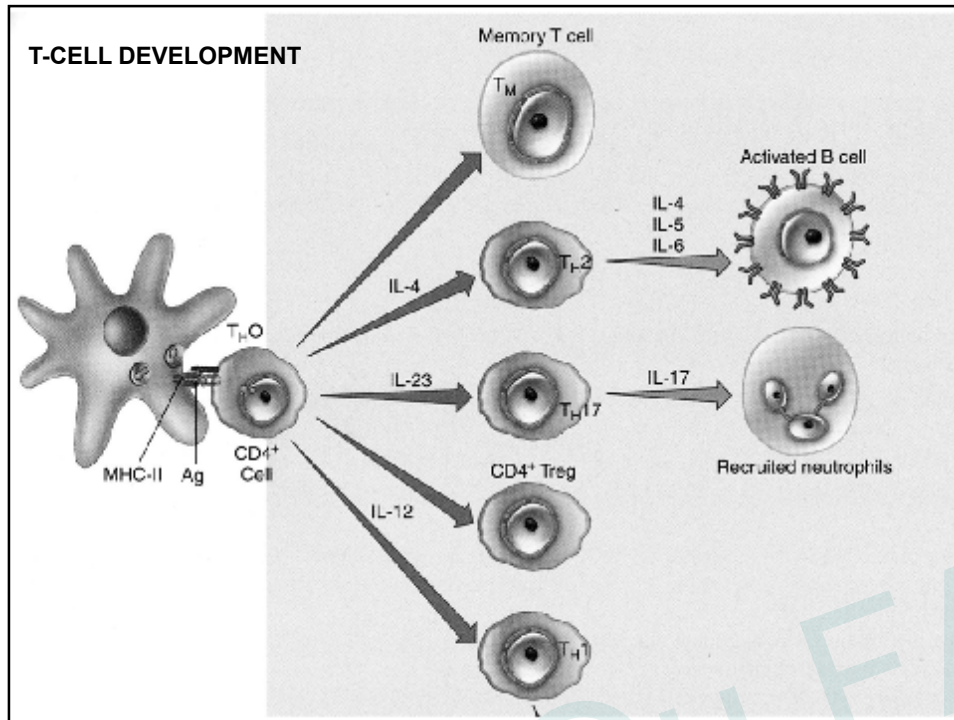
*High-affinity IL-2 receptors are three-chain structures that are present only on activated T cells.*



**Three Steps to Activation**





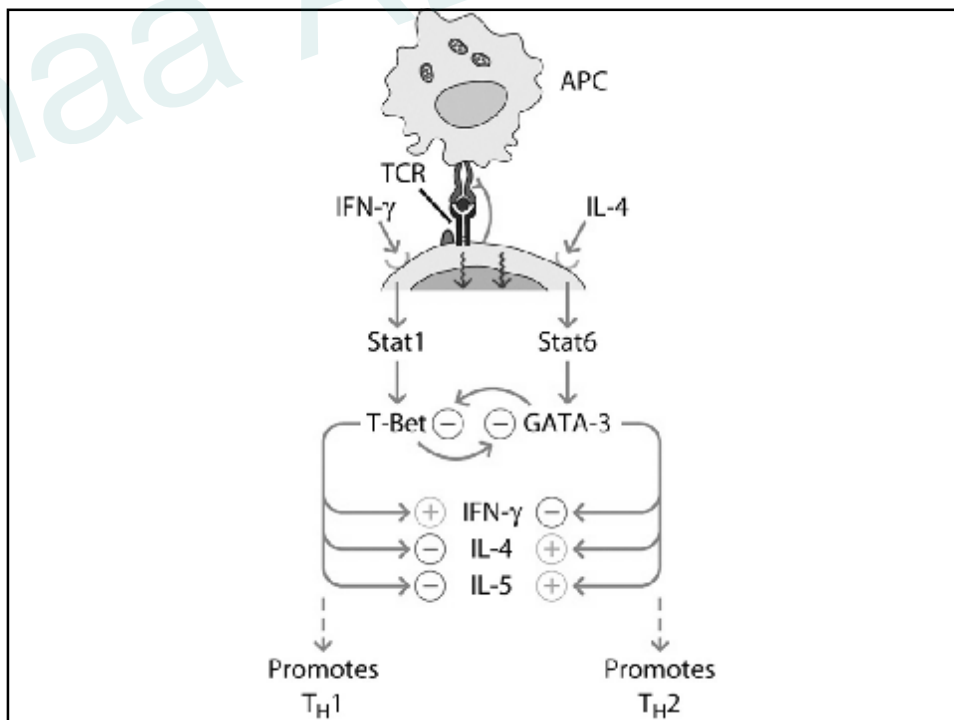
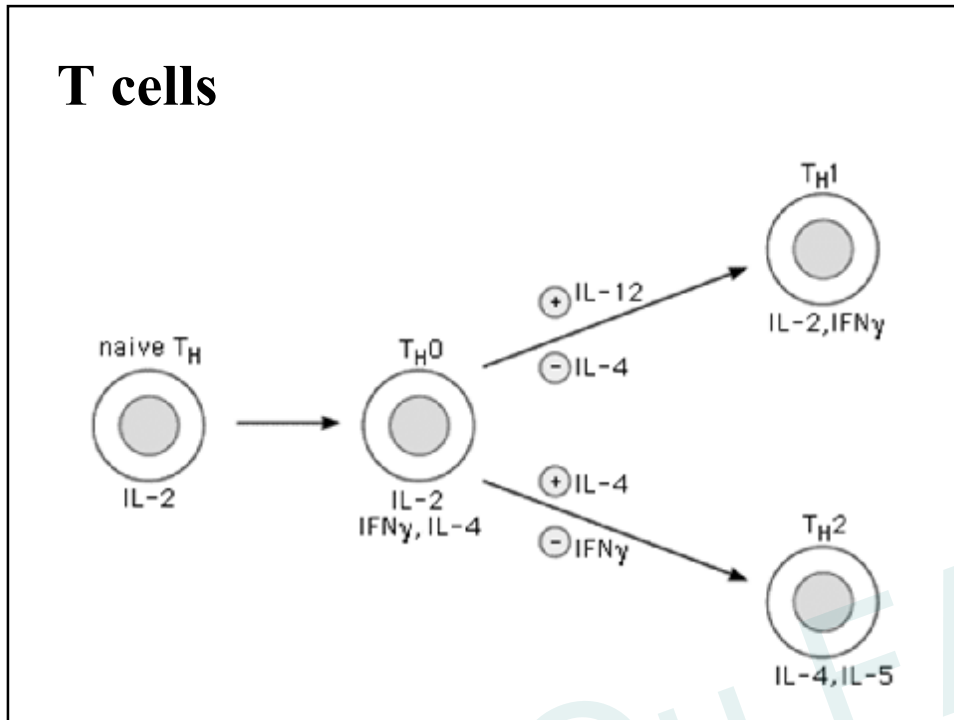


## *Types of T cells*

### **T Helper (T<sub>H</sub>) Cells**

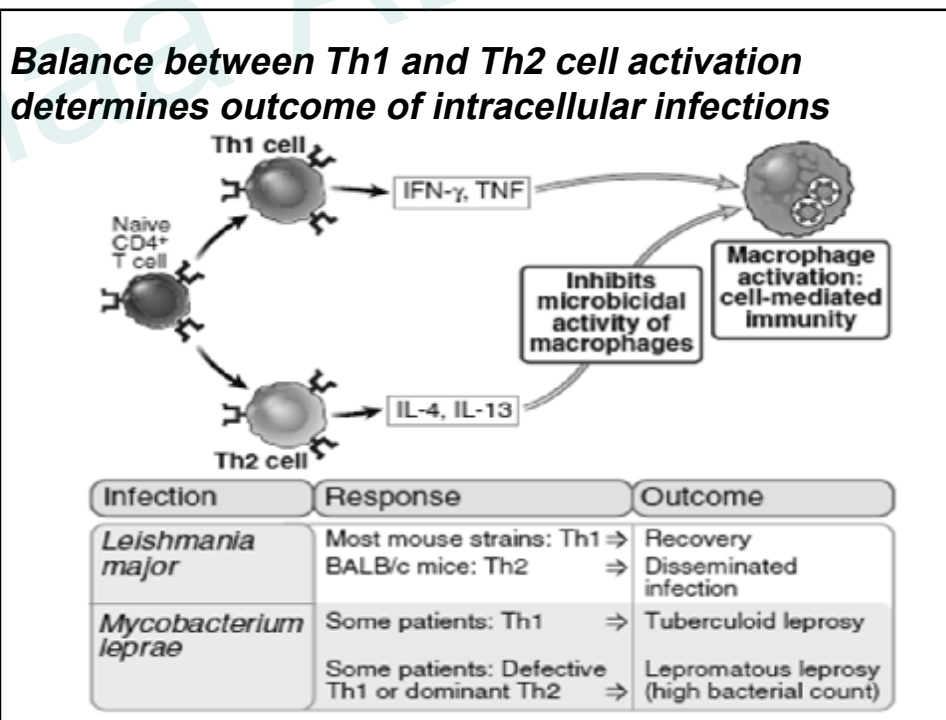
- Central role in immune response
- are CD4<sup>+</sup>
- Recognize antigen on the surface of antigen presenting cells
- Activate macrophages
- Induce formation of cytotoxic T cells
- Stimulate B cells to produce antibodies.

# T cells

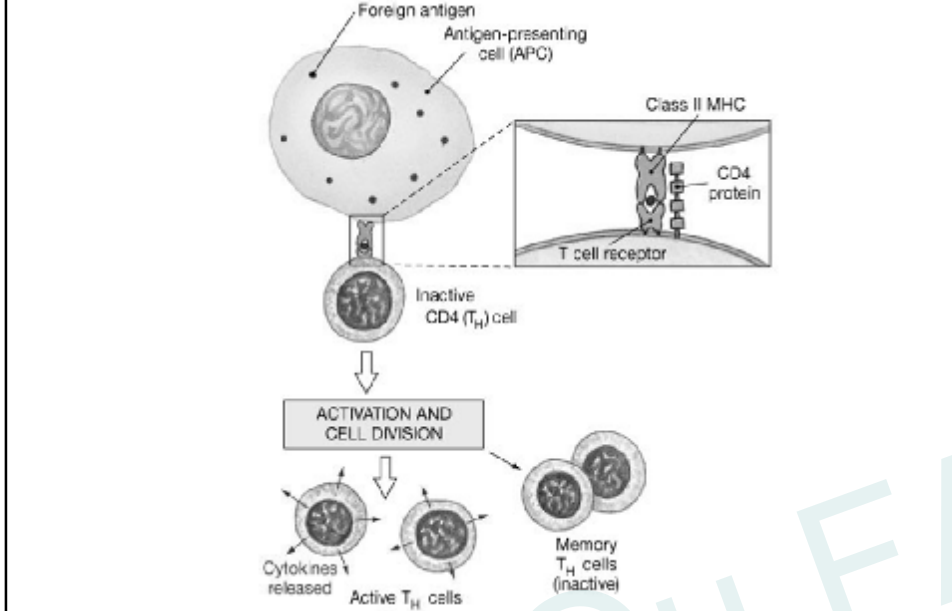


### Subsets of T helper Cells

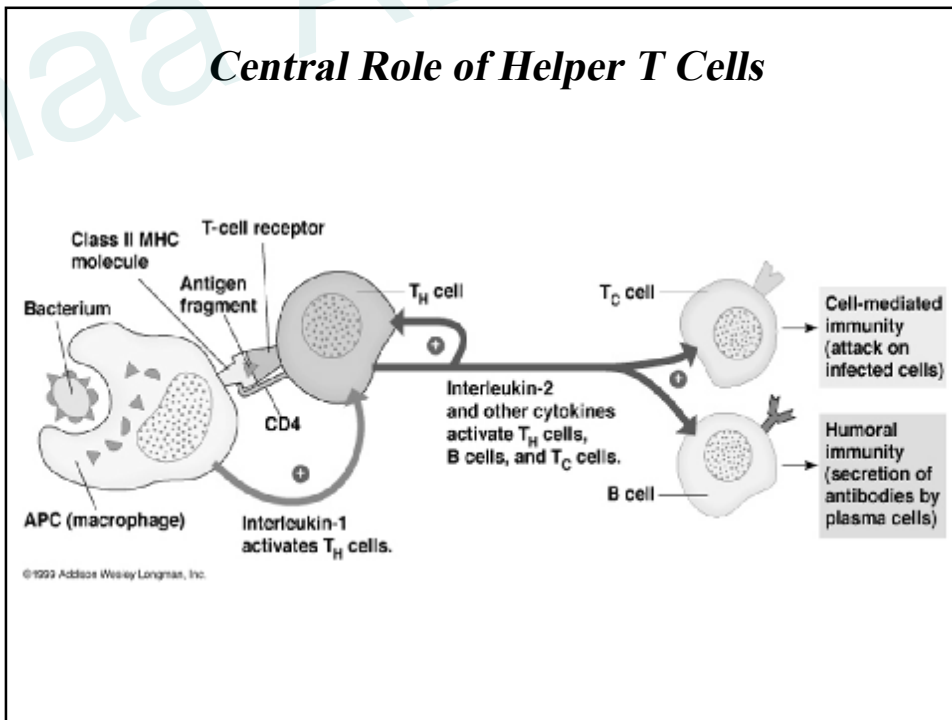
- T helper 1
  - IgG production/Complement fixation
  - Macrophage activation
  - DTH
  - CTL production
  
- T helper 2
  - IgE production
  - Eosinophils



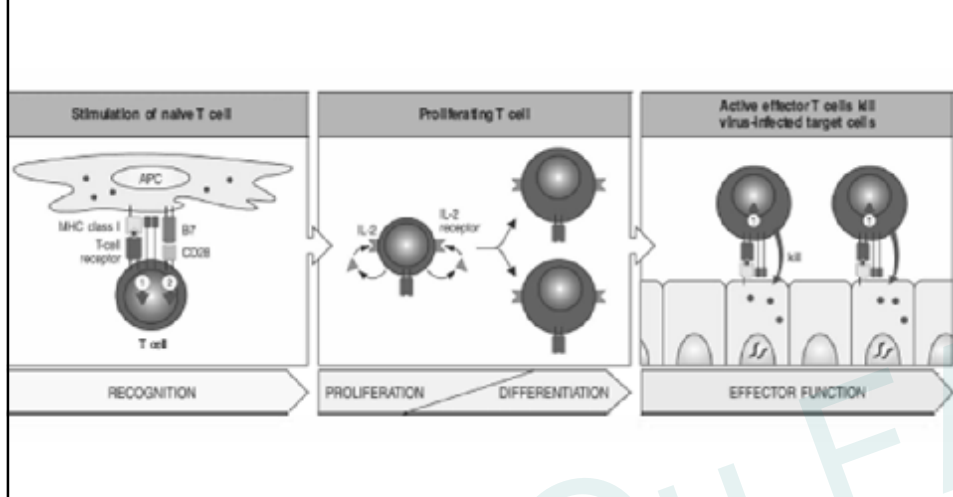
## Antigen Recognition and Activation of Helper T cells



## Central Role of Helper T Cells



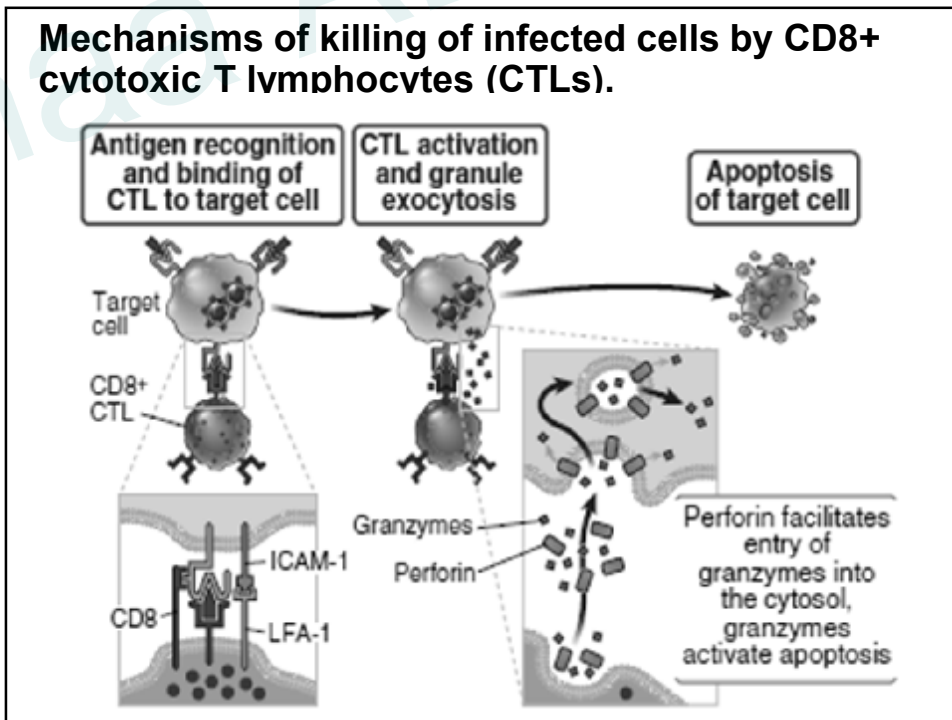
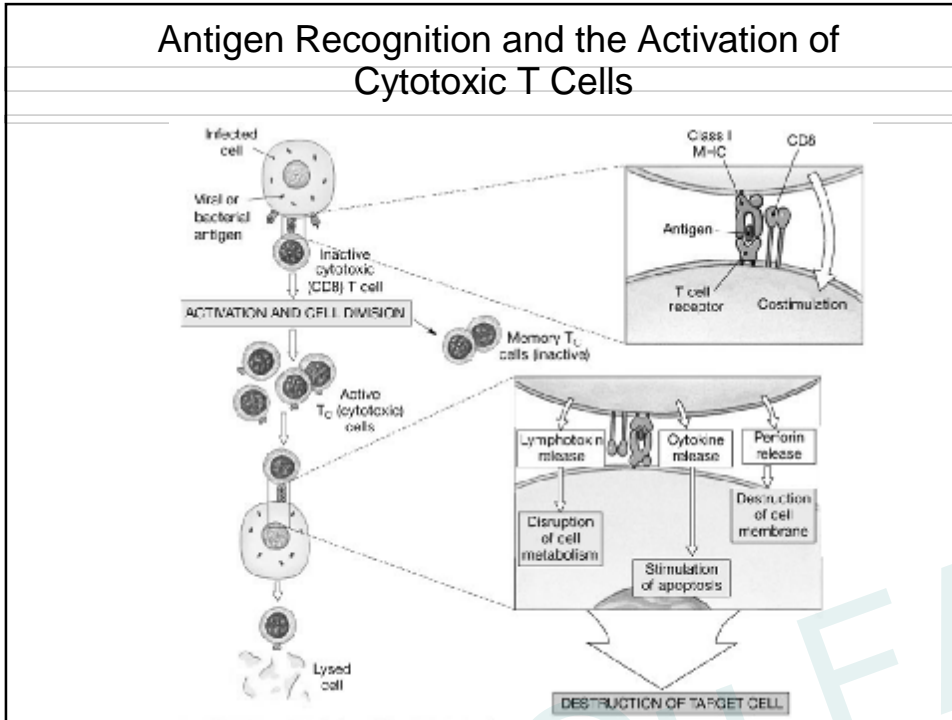
*Proliferating T cells differentiate into effector T cells that do not require co-stimulation to act.*

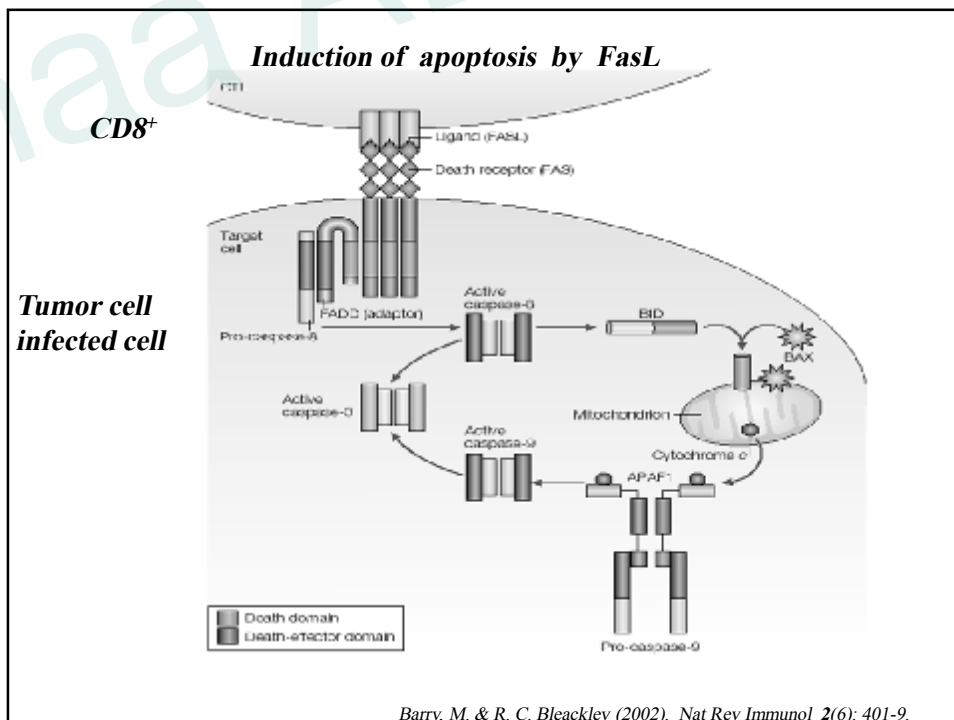
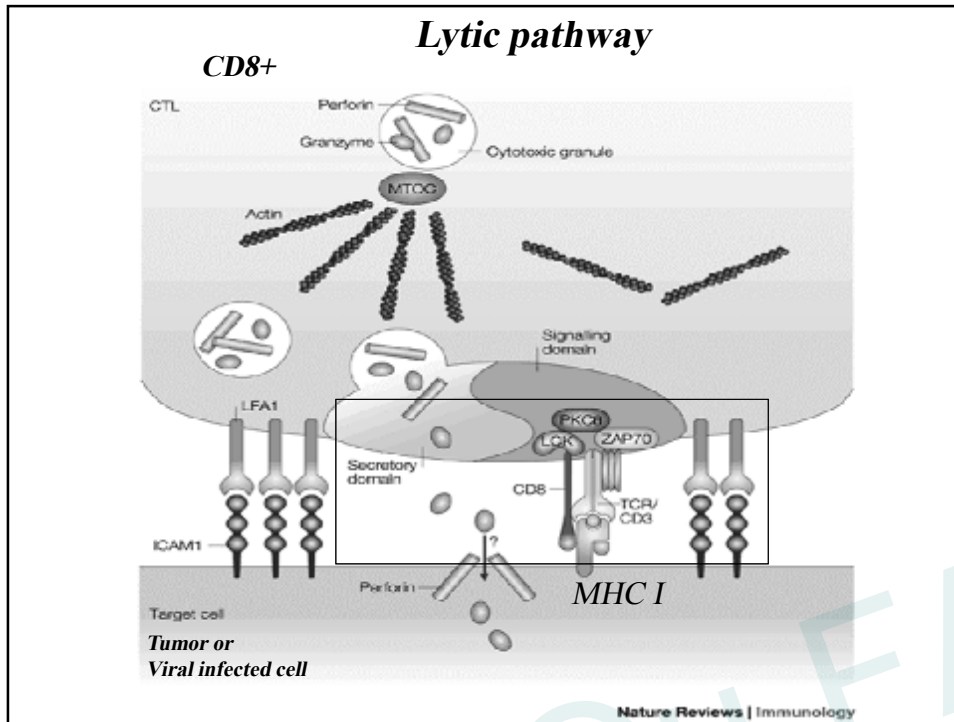


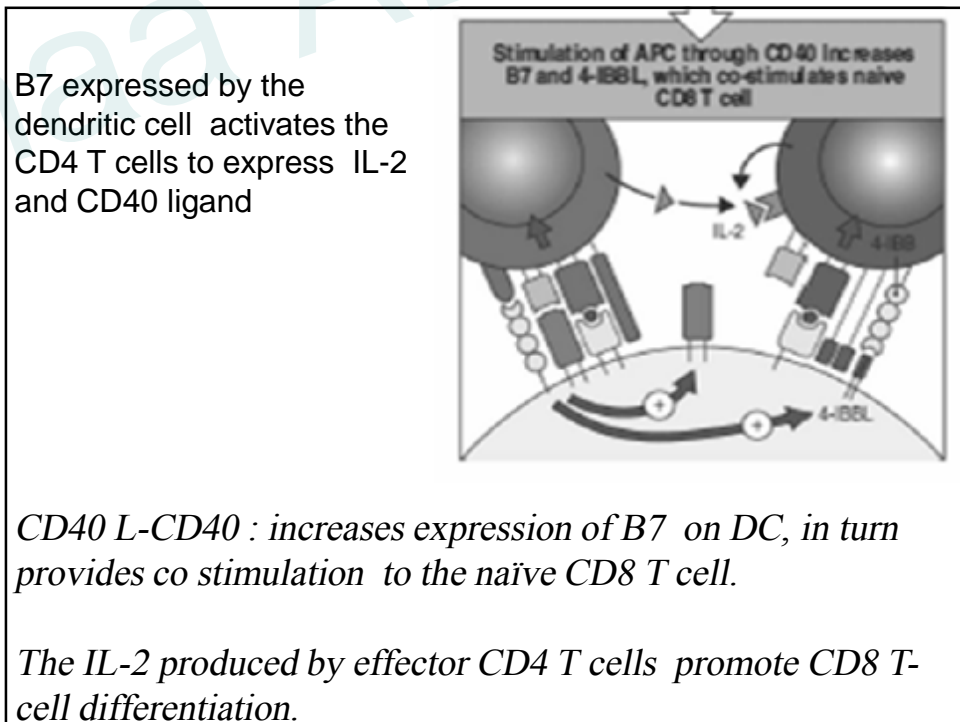
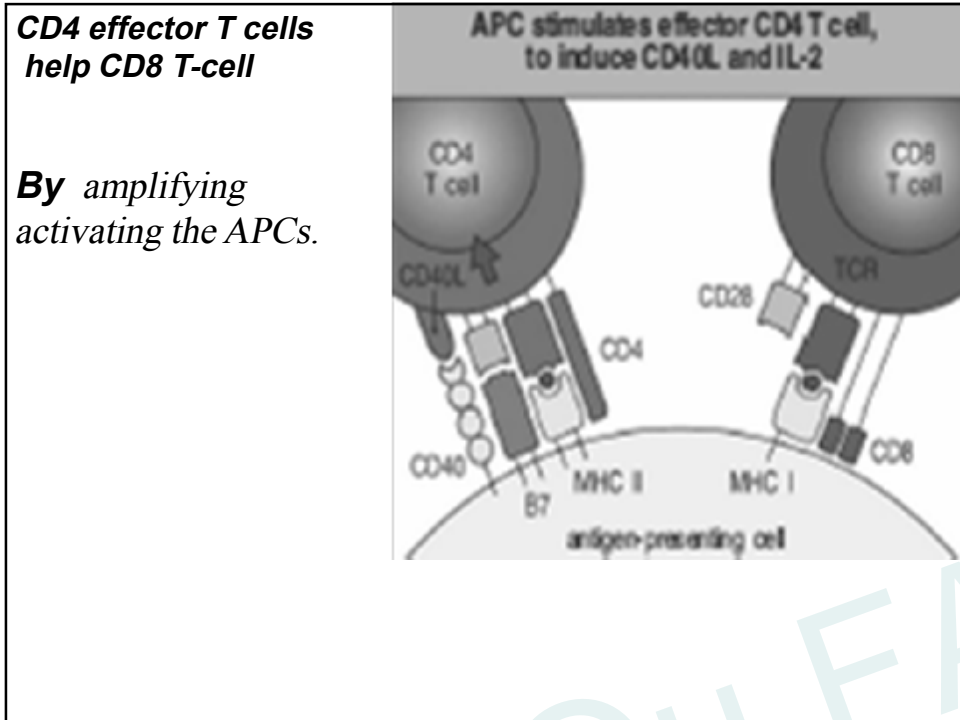
## **Types of T cells**

### ***Cytotoxic T (Tc) Cells (CD8):***

- Naïve CD8 T cells require more co-stimulatory activity to drive them to become activated effector cells than do naïve CD4 T cells.
- Kill host cells that are infected with viruses or bacteria.
- Recognize and kill cancer cells.
- destroy transplanted tissue.
- Release *perforin* causing lysis of infected cells.
- Undergo *apoptosis* when stimulating antigen is gone.









## Regulation of T cell Responses

- **Inhibition by Treg cells**
  - T reg cells inhibit in an antigen specific manner
  - Inhibit both CD4 and CD8 cell activation
- **Activation induced regulation**
  - Induction of CTLA-4
  - Induction of FasL
- **Inhibition by dendritic cells**
  - Immature DC inhibit/tolerize T cells
  - CTLA-4 induction of tolerance

### CTLA-4

#### **cytotoxic T lymphocyte-associated antigen 4-Ig**

- (CTLA41g) The cell-surface protein CTLA-4 is produced by activated T cells and is an inhibitory receptor for B7 (Negative regulator of T-cell activation)
- a T-cell surface molecule induced on activation and not found on resting cells.
- **CTLA-4** shares considerable sequence homology with CD28 and, like CD28, binds B7.1 and B7.2 on the APC.
- Unlike CD28, CTLA-4 delivers **inhibitory signals** to T cells, so that engagement of CTLA-4 tends to strongly diminish T-cell responses.

