Lecture eight Dr. wurood &Dr. Zaid

T-Cell Activation, and Memory

T-Cell Activation

T cells are essential for adaptive immunity. However, they exist in a **resting (naïve)** state until they encounter their specific antigen.

T-cell activation occurs mainly in **lymph nodes**, where T cells interact with antigen-presenting cells (APCs), especially **dendritic cells**.

Activation requires **three main signals**:

Three phases

- Antigen recognition phase
- Activation and differentiation phase
- Effector phase

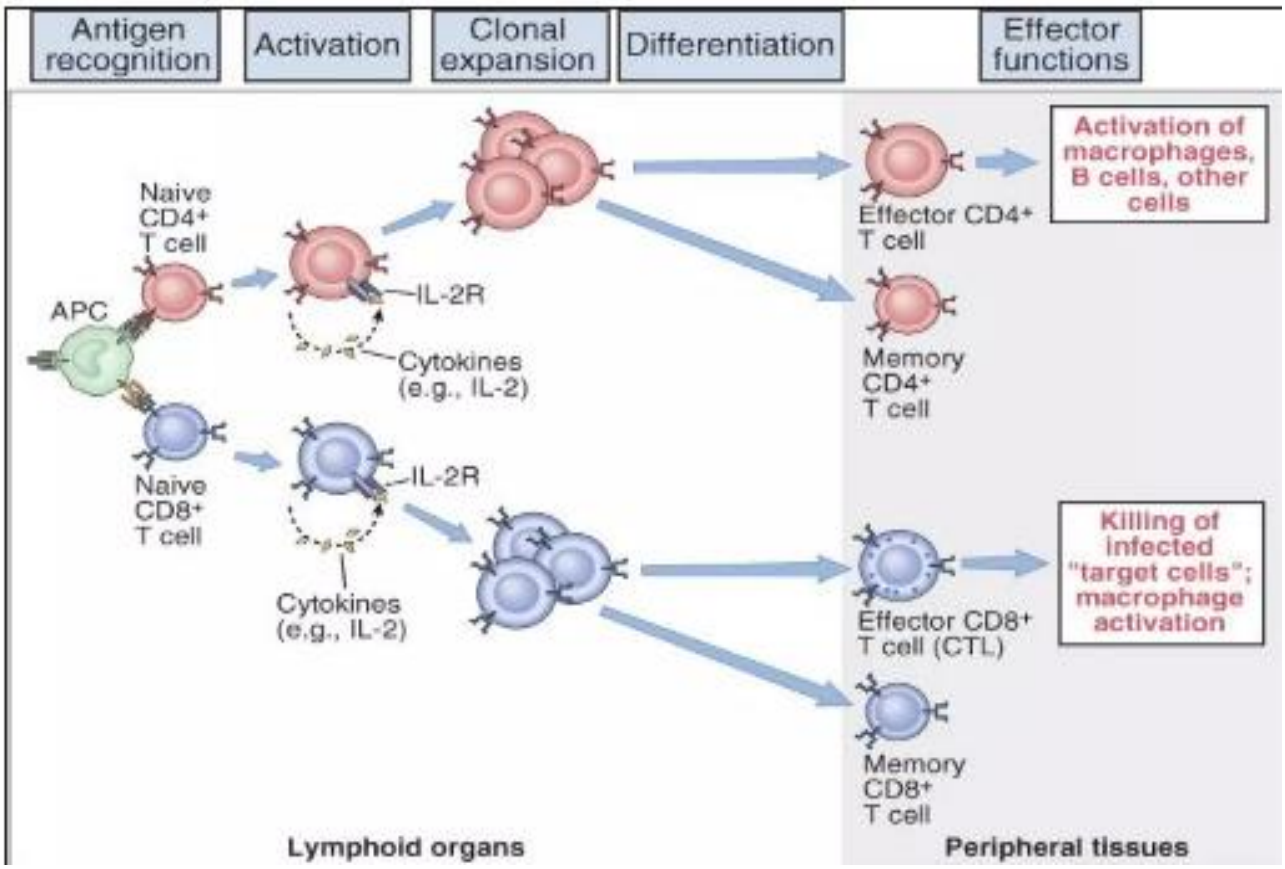

Fig (1) **activation of T-Cell Activation**

Step 1: Antigen Recognition

T cell activation begins with antigen recognition. T cells, using their T cell receptors (TCRs), specifically recognize antigens presented on major histocompatibility complex (MHC) molecules by antigen-presenting cells (APCs) like macrophages.

MHC molecules are crucial for immune function, displaying antigen-derived peptide fragments for T cell surveillance. This recognition ensures that T cells accurately identify and respond to specific antigens, a fundamental step for targeted immune response.

Step 2: Costimulatory Signals

T cells require a second signal from costimulatory molecules on APCs following antigen recognition. These molecules, including CD28 and CD3, are essential for full activation. CD28 amplifies the TCR signals, while CD3 transduces these signals into the cell, leading to T cell activation. This step ensures that T cells are fully equipped and committed to responding to the antigen.

Step 3: Cytokine Secretion and Response

Once activated, T cells secrete cytokines, which are critical for modulating the immune response. These proteins have various effects, from stimulating further T cell activation to controlling inflammation. This phase is pivotal in dictating the scope and scale of the immune response, fine-tuning the body’s defense against specific microbes and diseases.

Cytokines play a crucial role in eliminating infections by inducing collective cell death. This makes them an important tool in cancer research and fighting cancer within the body. However, it's important to control cytokine activity during adoptive cell therapy to prevent cytokine release syndrome in patients. This syndrome can rapidly damage healthy tissues, hence the imperative need for its prevention.

Proliferation and Differentiation

During the final stage of the immune response, T cells undergo proliferation and differentiation. The activated T cells multiply rapidly and transform into various types, such as helper T cells or cytotoxic T cells, each with a specialized function in the immune system. This phase is essential for amplifying the immune response and ensuring a robust defense against diseases.

Differentiation of Helper T Cells ($CD4^+$ T Cells)

Subset	Function	Main Cytokines	Key Role
Th1	Fight intracellular pathogens (viruses, bacteria)	IFN-γ	Activates macrophages & cytotoxic T cells
Th2	Defend against extracellular parasites (helminths)	IL-4, IL-5, IL-13	Promotes B cell antibody production (IgE) & eosinophil activation
Th17	Protect mucosal surfaces from bacteria & fungi	IL-17, IL-22	Recruits neutrophils, enhances inflammation
Tfh	Help B cells in lymphoid follicles	IL-21	Promotes germinal center formation & high-affinity antibody production
Treg	Suppress immune responses, maintain tolerance	TGF-β, IL-10	Limits inflammation, prevents autoimmunity

Formation of Memory T Cells

After the immune response ends, most effector T cells die by apoptosis.

A smaller population survives to form **long-lived memory T cells**.

Types of Memory T Cells

1. Central Memory T Cells (Tcm)

- Located in lymph nodes
- Express **CCR7** and **CD62L**
- Respond quickly when re-exposed to antigen

2. Effector Memory T Cells (Tem)

- Circulate in blood and tissues
- Rapidly produce cytokines
- Provide immediate protection

3. Tissue-Resident Memory T Cells (Trm)

- Remain in tissues (skin, gut, lungs)
- Provide frontline defense
- Important in viral infections (e.g., HSV)

How Memory T Cells Form

Factors include:

- IL-7 and IL-15 for survival
- Reduced activation strength
- Changes in metabolism (switch to fatty-acid oxidation)

Advantages of Memory T Cells

- Faster and stronger response
- Less dependence on co-stimulation
- Basis of long-term immunity after infection or vaccination