# Major Histocompatibility Complex (MHC) & Antigen presenting cell (APC)

# Learning outcome

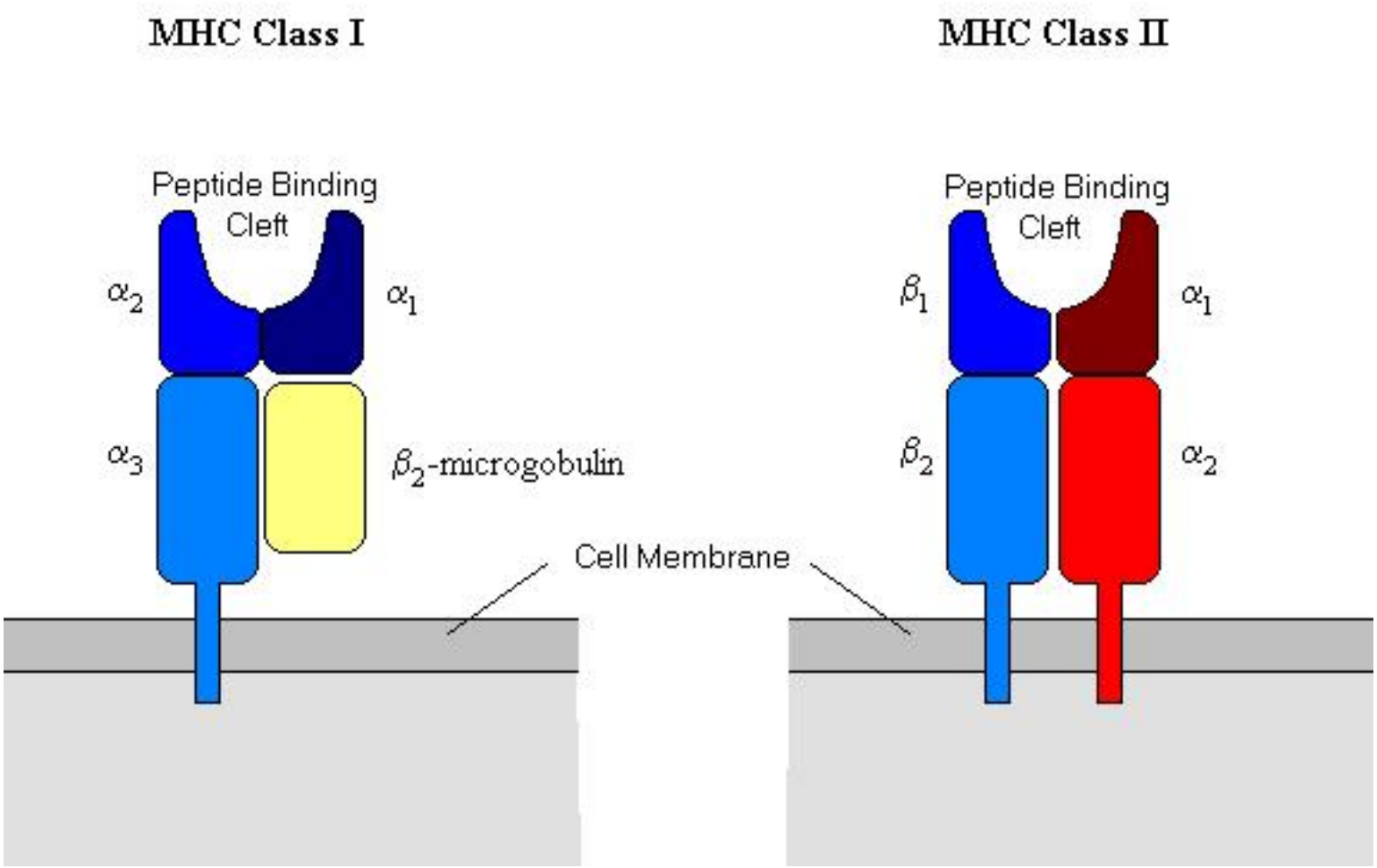
You should be able to:

1. Understand the structure and function of MHC molecules

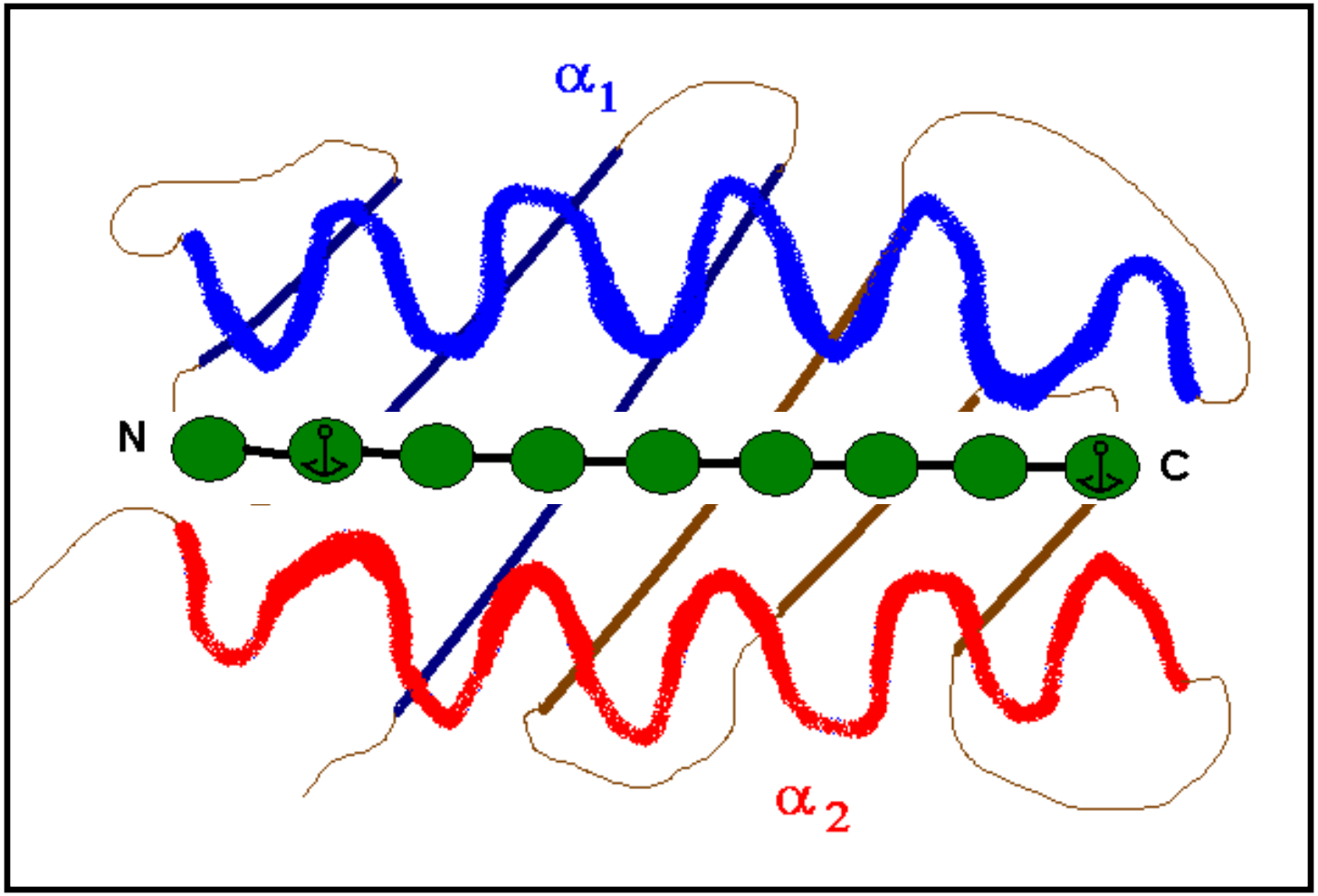
2. Differentiate between different types of APCs and their function

3. Explain how T cell response is induced by APC

# Structure of MHC Molecules



# MHC peptide binding groove



# MHC Class II molecule

- Expressed by ‘professional’ APCs:

  MΦ, DCs, B cells.

- Bind peptides from *exogenous* antigens.
- Peptides are 12-20 amino acids in length.
- Restriction element for $CD4^+$ T cells.

# MHC class I molecule

- Expressed by most nucleated cells.
- Bind peptides from endogenously-synthesised antigens.
- Peptides are 8-11 amino acids in length.
- Restriction element for $CD8^+$ T cells.

# Antigen Presenting cell (APC)

- Ability to ingest, process and present antigen
- Express MHC class II, co-stimulatory molecules

For example:

1. Langerhans cells
2. Macrophages (MΦ)
3. Dendritic cells (DC)
4. B cells

# Macrophages (MΦ)

- Presenting antigens from bacteria and parasites
- Has important role in primary immune response
- Also present antigen during secondary response via ingestion of opsonised bacteria
- Class II expression up-regulated by TLR triggering but not always by phagocytosis

# Macrophage Receptors

| Ligands | Receptors |
| --- | --- |
| Lipopolysaccharide | CD14 etc. |
| Other PAMPs | Other PRRs (TLRs etc.) |
| Leishmania<br>Bordetella<br>Yeast etc. | CR3 (CD11b/CD18) |
| Antibody coated antigens | FcR |

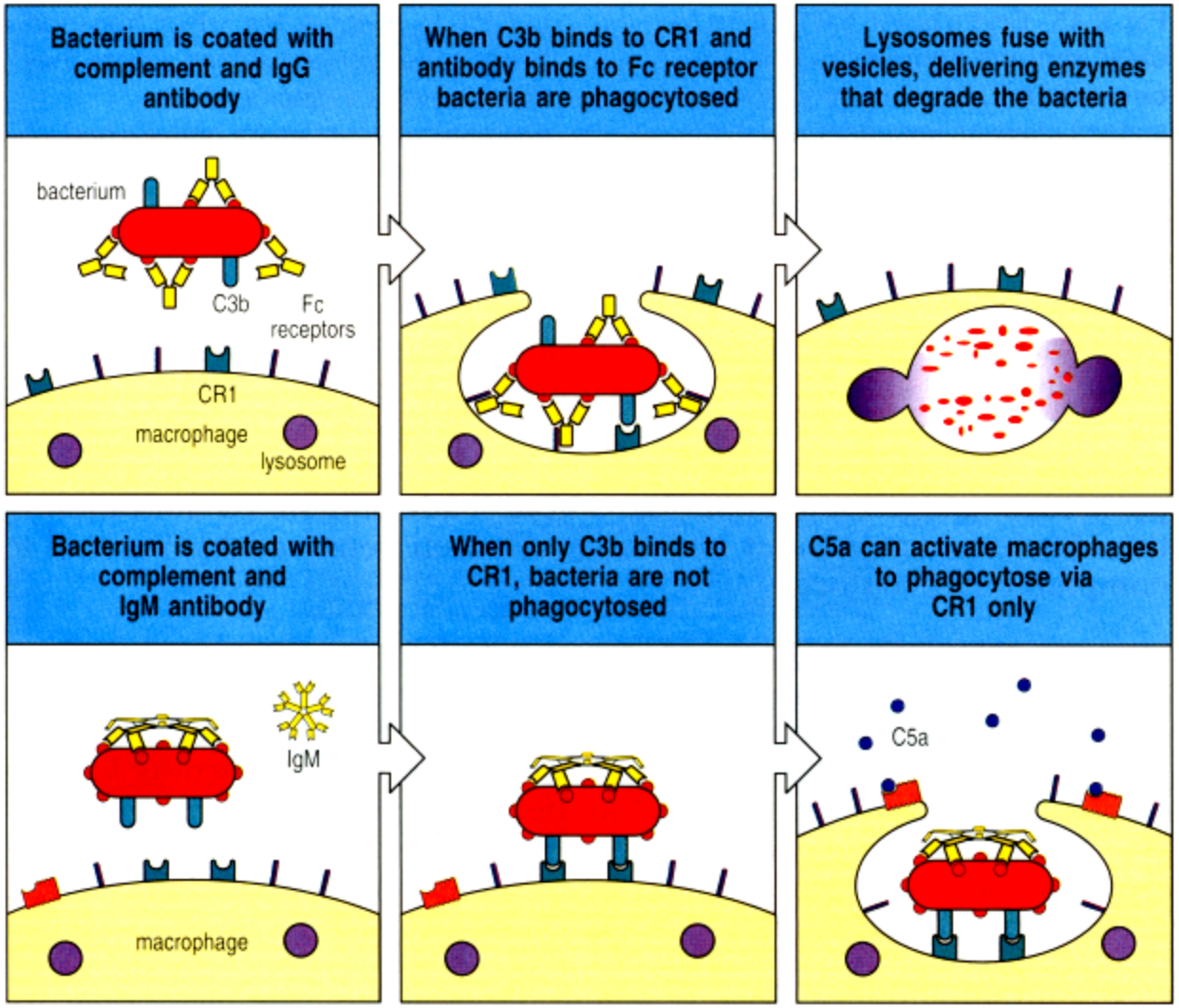
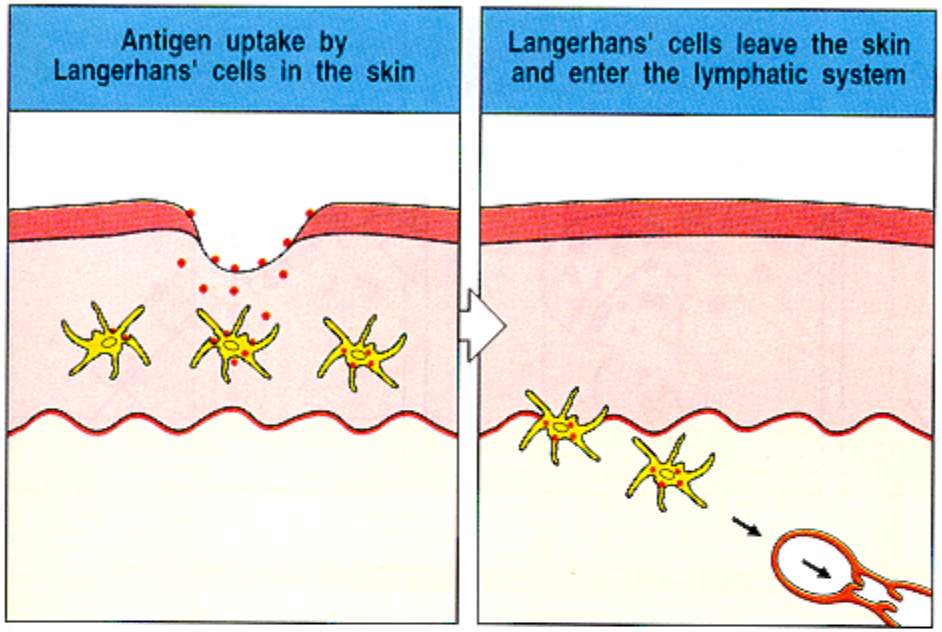
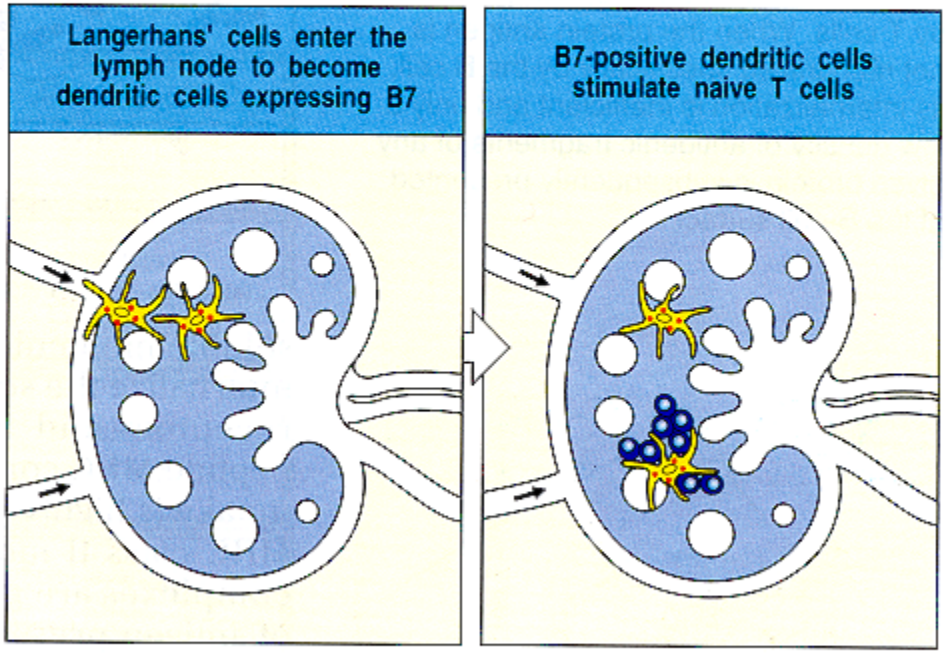



**Fig. 8.44 Complement CR1 receptors require ancillary activating signals to participate in phagocytosis.**
Fc receptors and complement receptors synergize in inducing phagocytosis, and bacteria coated with IgG antibody and complement are therefore more readily ingested than those coated with IgG alone (upper panels). When bacteria are coated with IgM antibody and complement, however, they cannot be ingested unless the phagocyte is pre-activated, for example by T cells or by C5a, as phagocytes do not have Fc-receptors for IgM (lower panels).

# Dendritic cells

- Most potent initiators of the primary immune response
- Less strongly phagocytic than macrophages
- Distributed in surface epithelia, solid organs and lymphoid tissues
- Develop from myeloid (or lymphoid) lineage precursors




LCs pick up antigen in epidermis and in response to TNFα migrate to draining LN to become DCs

# B cells

- Not phagocytic
- Express co-stimulatory molecules only when activated, e.g. by infection.
- Antigen-specific B cells highly efficient APC.
- Become more important with each subsequent encounter with antigen.

# B cells

- Bind specific soluble molecules through cell surface Ig.
- Very efficient cell in antigen uptake + high levels of Class II HLA.
- Leads to high levels of specific peptide : Class II HLA on surface

## APC express :-

## Ligands on T cells :-

**Class II MHC molecules** ⟷ **CD3-T cell receptor/CD4**

**Co-stimulatory molecules:**

**CD80 (B7.1)**
**CD86 (B7.2)**
} ⟷ {
**CD28 (native & activated)**
**CD152; CTLA-4(activated)**

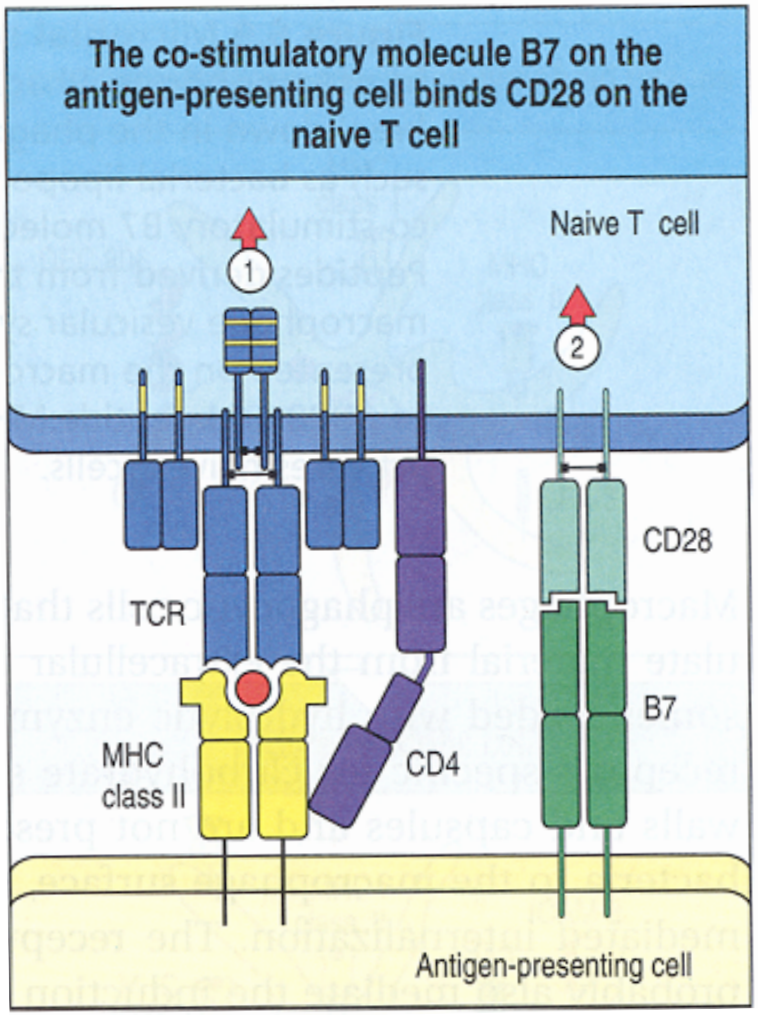
**CD40** ⟷ **CD40L (CD154)**

T cells require 2 signals for activation:

1. TCR: MHC-peptide interaction
2. CD28 interaction with B7 (CD80/86) on APC

Note:

In the absence of B7, T cells are switched off

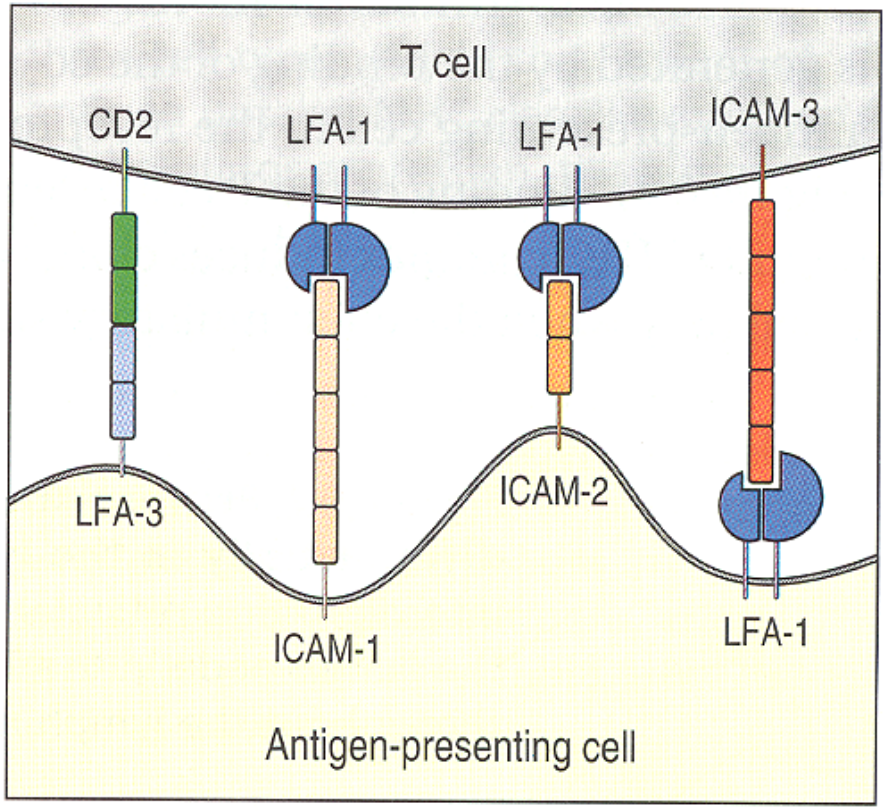


# APC also express:- Ligands on T cells :-

**Adhesion molecules**

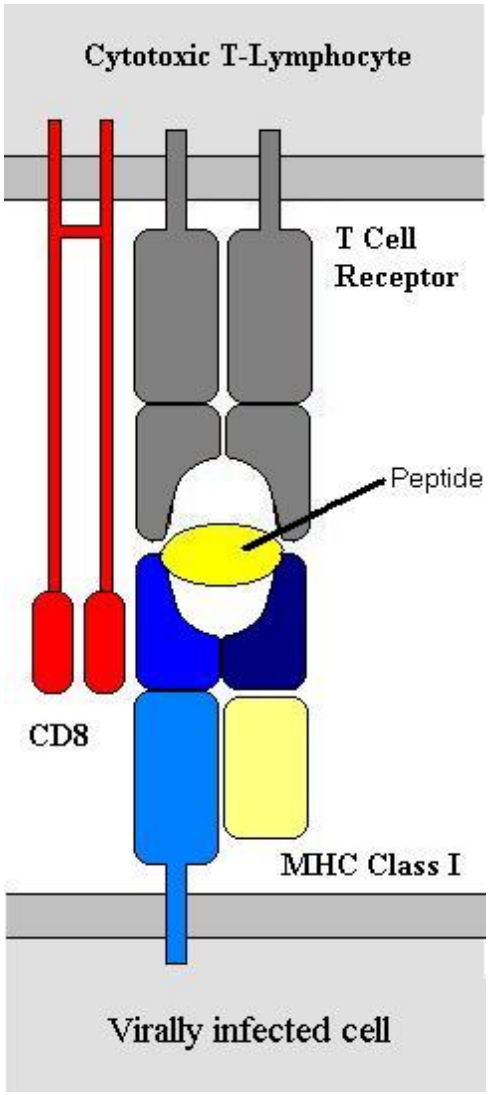
| | | |
|---|---|---|
| **ICAM-1 (CD54)** | ⟷ | **LFA-1 (CD11a/CD18)** |
| **ICAM-2 (CD102)** | ⟷ | **LFA-1** |
| **ICAM-3 (CD50)** | ⟷ | **LFA-1** |
| **LFA-3 (CD58)** | ⟷ | **CD2** |
| **CD11b/CD18 (CR3)** | ⟷ | **ICAM-1** |

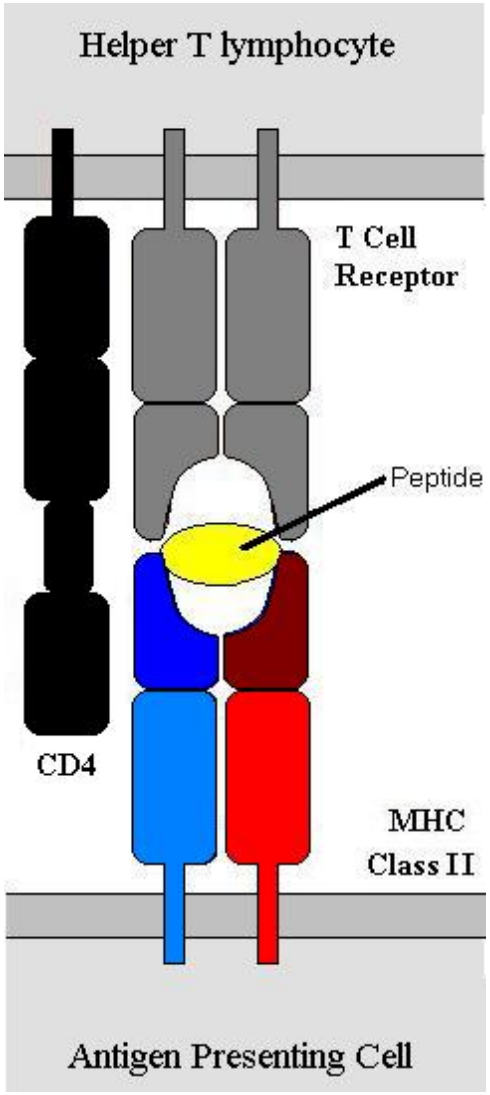
**ICAM 1 = Intercellular Adhesion Molecule-1**
**LFA 1 = Lymphocyte function-associated antigen 1**




**Synergistic binding of invariant adhesion molecules strengthens interaction between T cell and APC**

# Interaction between T cells and MHC-peptide complex



# Summary:

- Antigens taken up by APCs and sensed via PRRs
- Triggers activation and maturation of APCs
- Antigen process and presentation on MHC I or MHC II
- Stimulates T cell activation via TCR complex and MHC-peptide and therefore the adaptive immune response.

## By the end you will be able to answer these questions

- Compare between MHC I and MHC II?
- What are the differences between DC, B cells and Macrophage?
- How APC induce the activation of T cell response ?