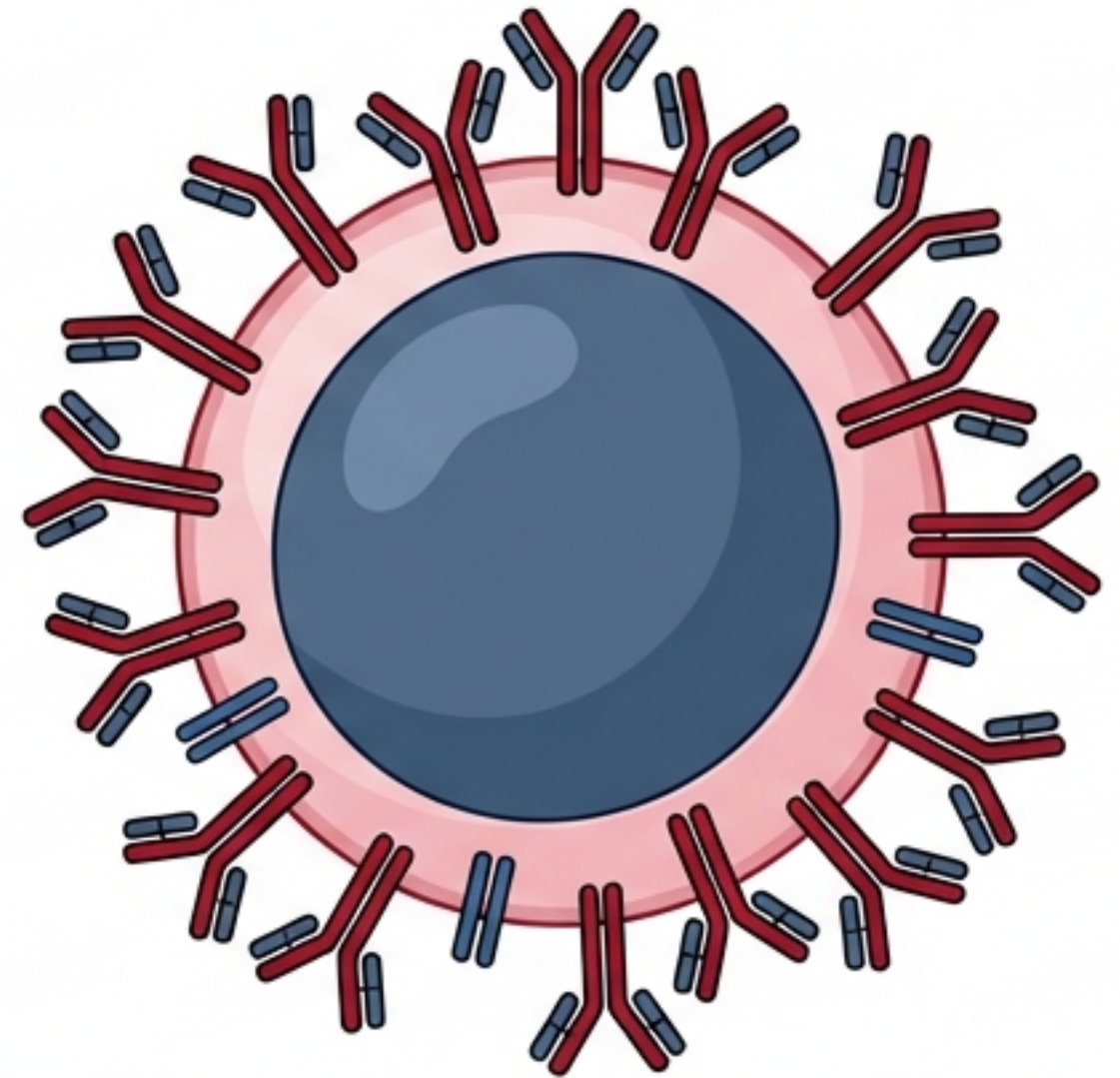
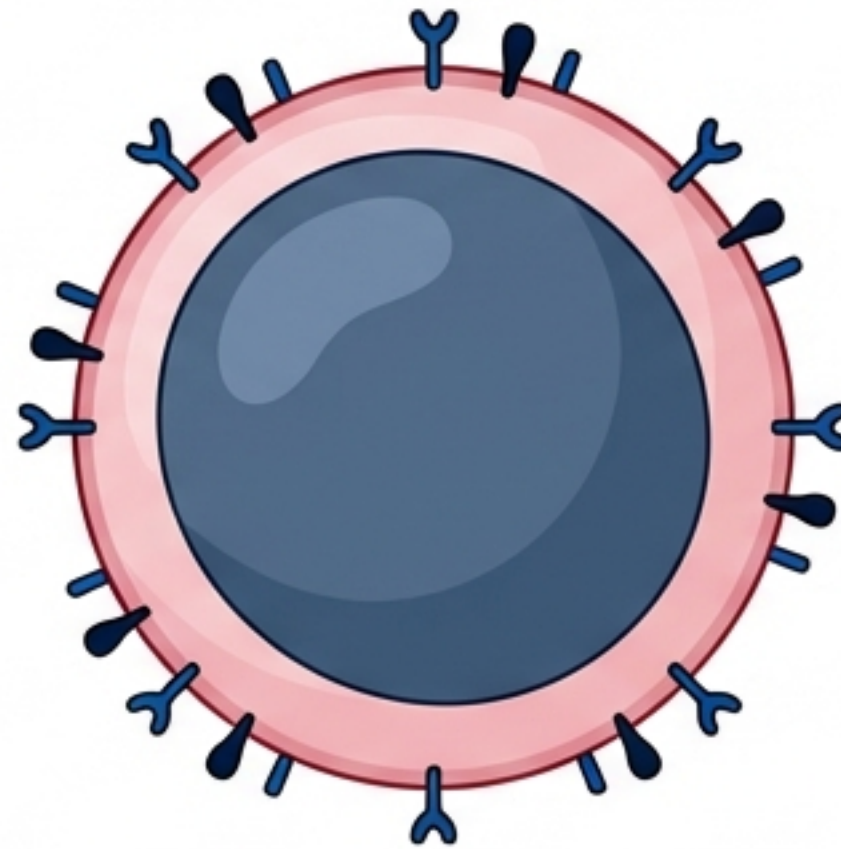
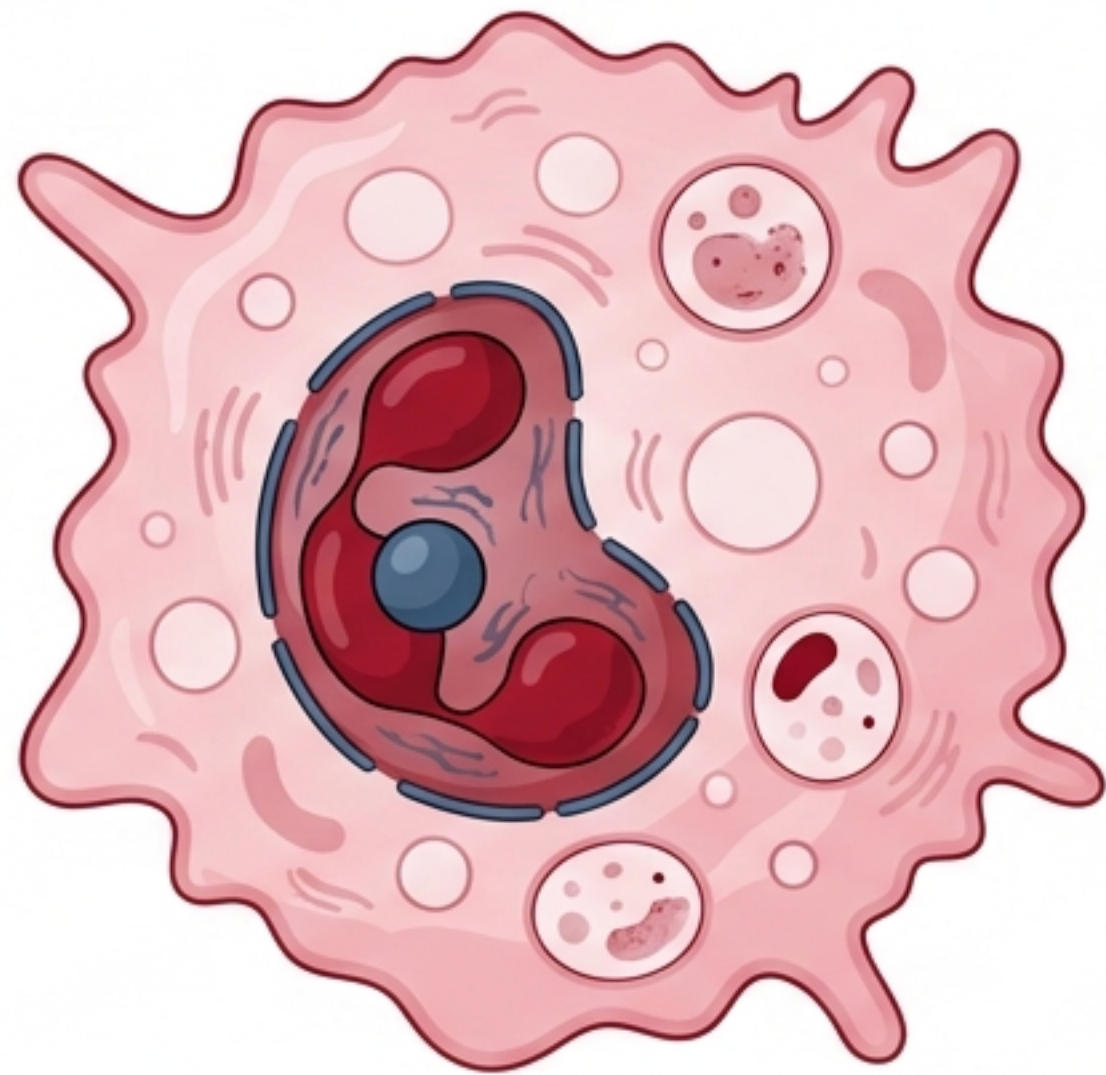


# The Architecture of Chronic Inflammation

Mechanisms of Adaptive Immunity and Granulomatous Pathology



T Lymphocyte



B Lymphocyte

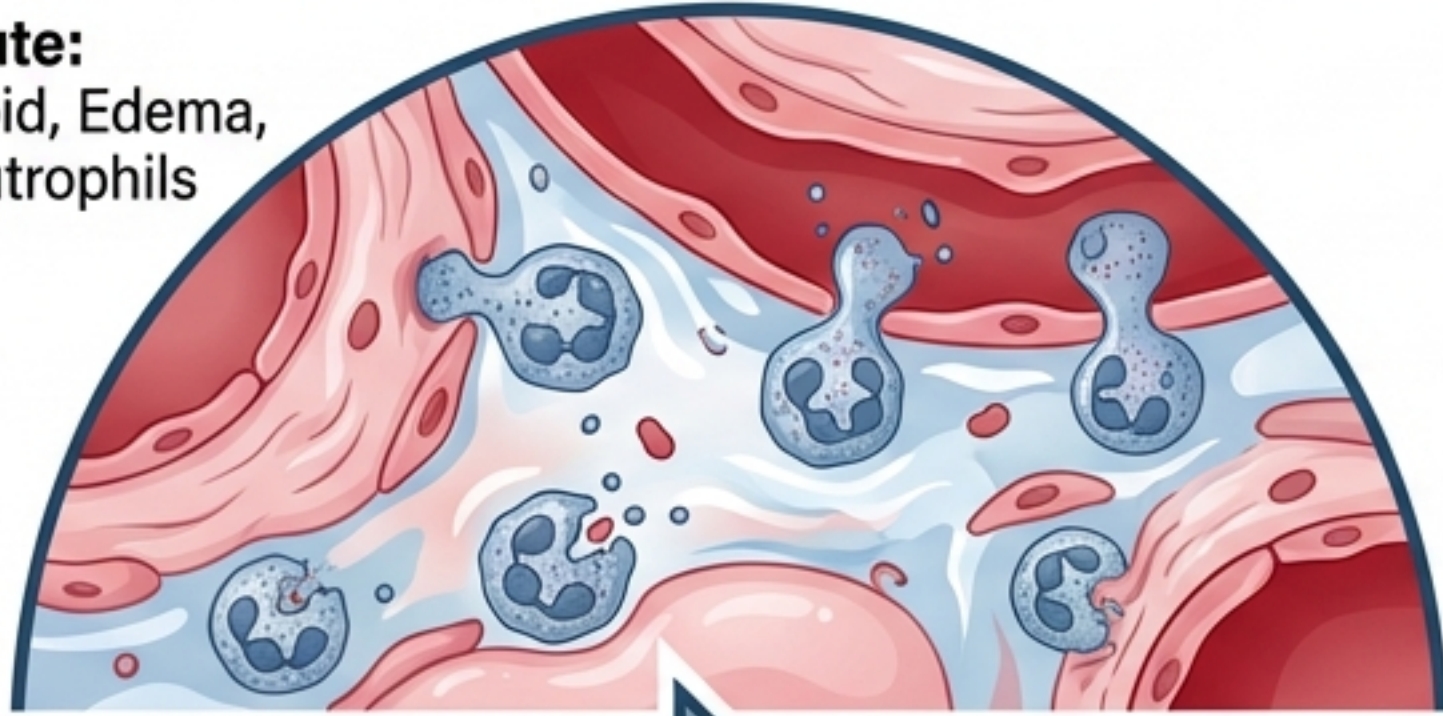


Macrophage

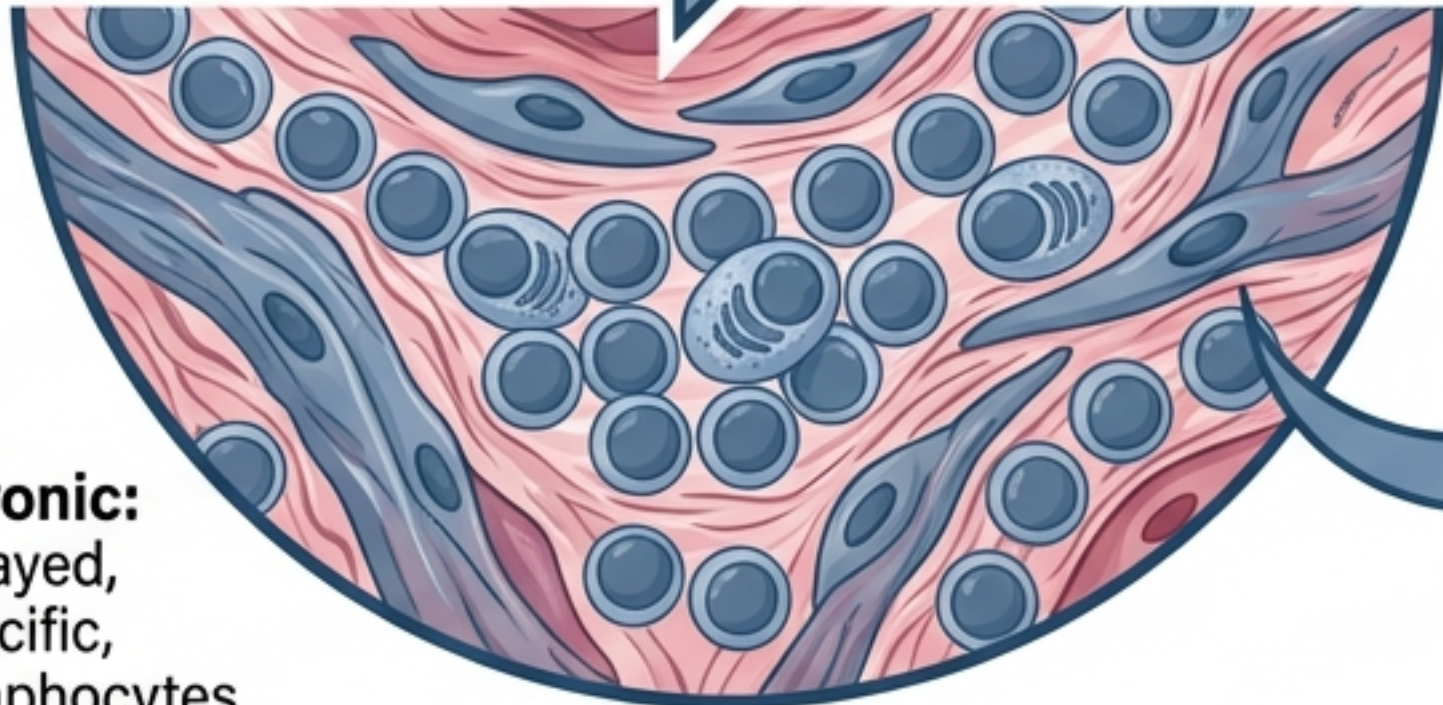
# The Shift from Acute to Chronic Response

## Comparison of Inflammatory States

**Acute:**  
Rapid, Edema,  
Neutrophils



**Chronic:**  
Delayed,  
Specific,  
Lymphocytes

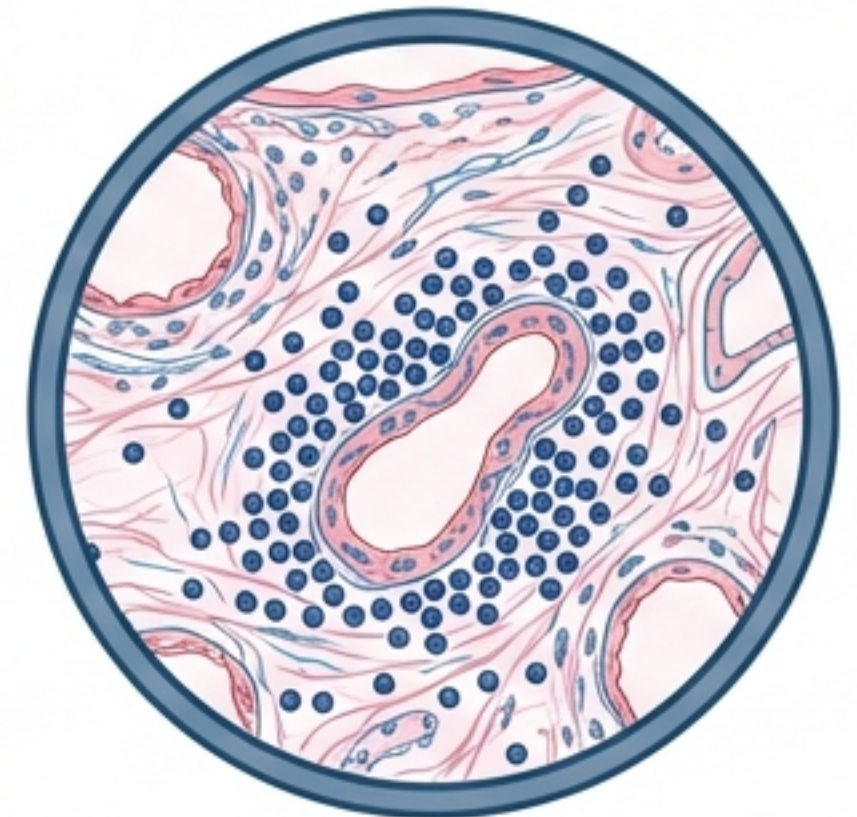


Chronic inflammation is a specific, adaptive immune response to persistent threats.

## The 5 Triggers

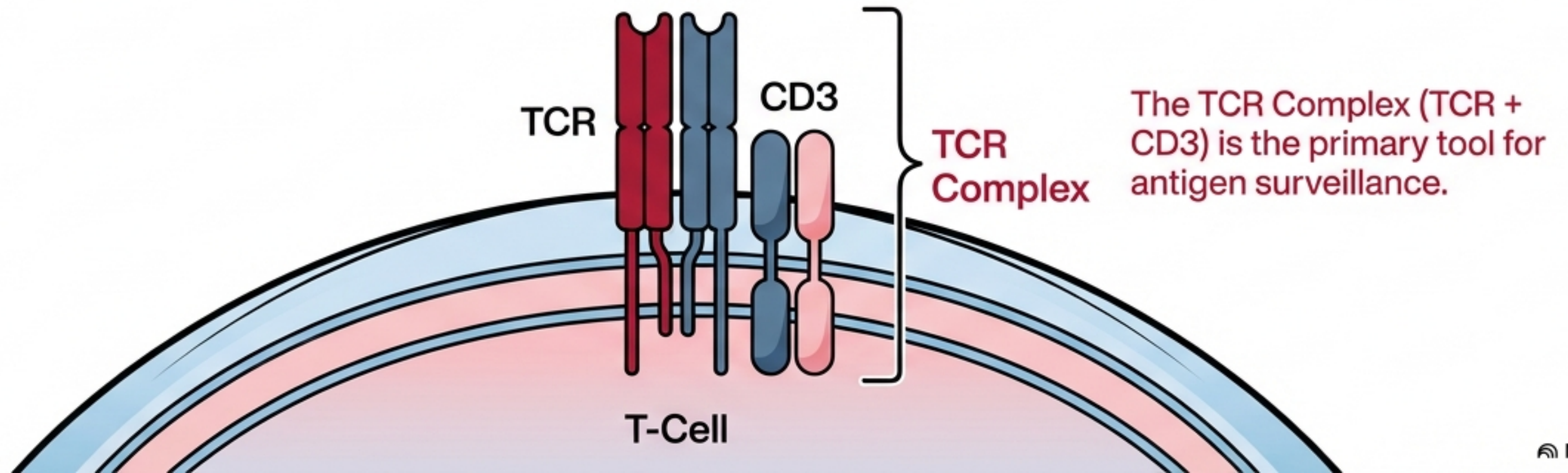
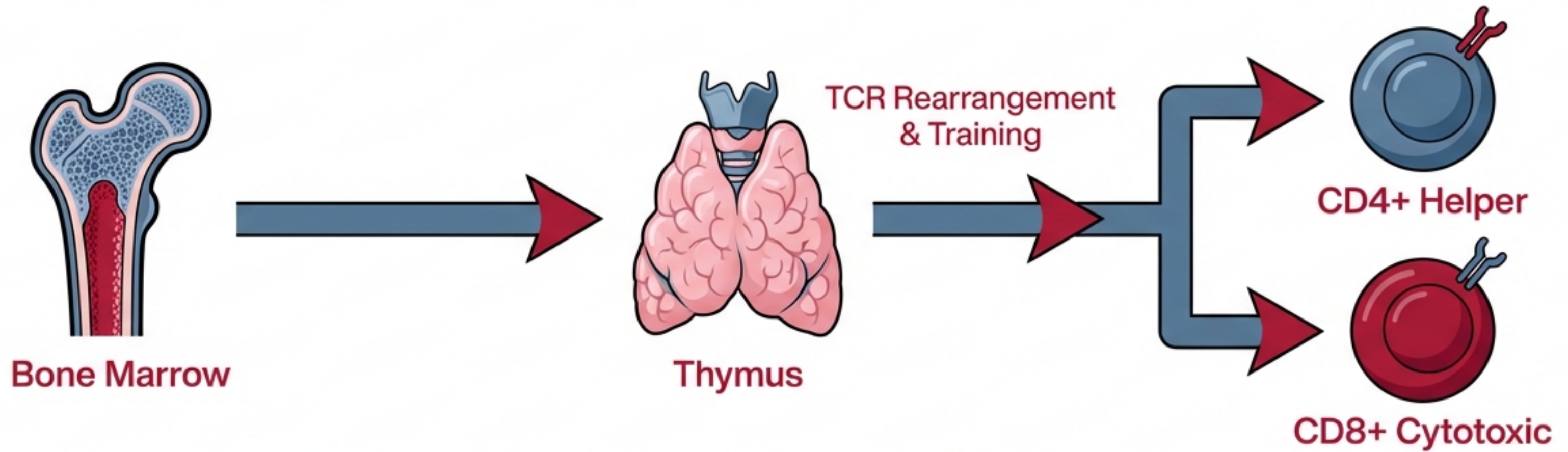
- ✓ 1. Persistent infection (Most common)
- ✓ 2. Specific pathogens (Viruses, Mycobacteria, Parasites, Fungi)
- ✓ 3. Autoimmune disease
- ✓ 4. Foreign material
- ✓ 5. Malignancy

**Chronic inflammation is a specific, adaptive immune response to persistent specific adaptive response**



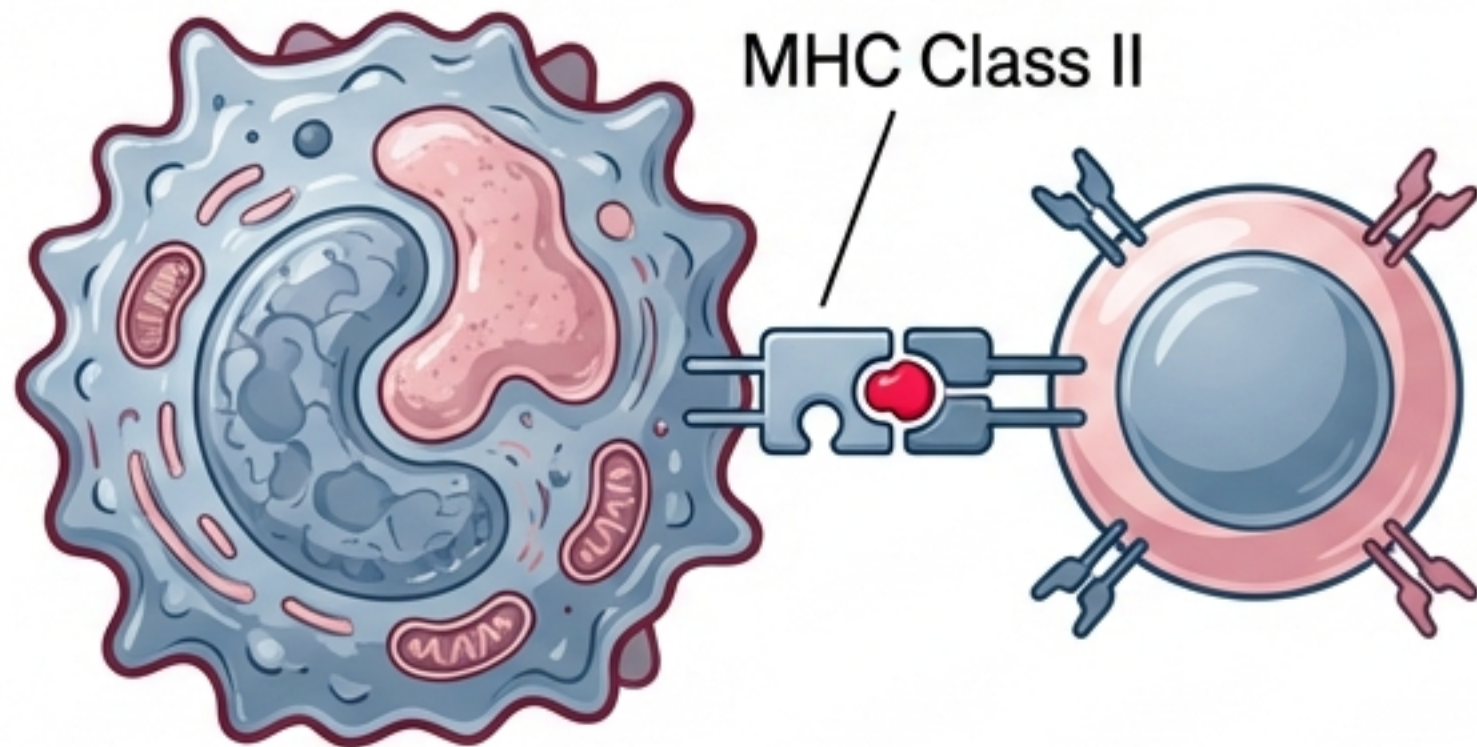
**Hallmark:  
Lymphocytic Infiltration**

# T Lymphocyte Maturation and Surveillance



# The Rules of Recognition: MHC Restriction

## CD4+ Helper T Cells

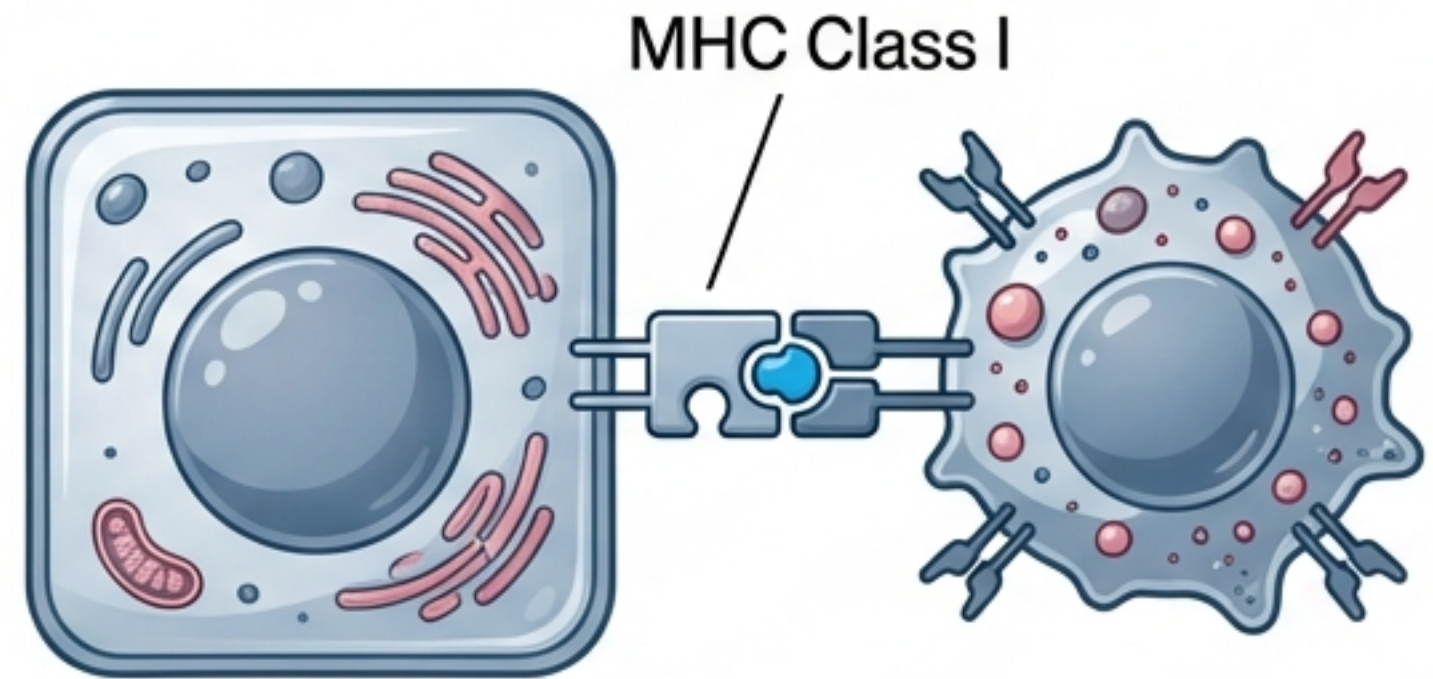


Macrophage (APC)

**Binding Partner:** MHC Class II

**Context:** Extracellular antigens (e.g., foreign proteins).

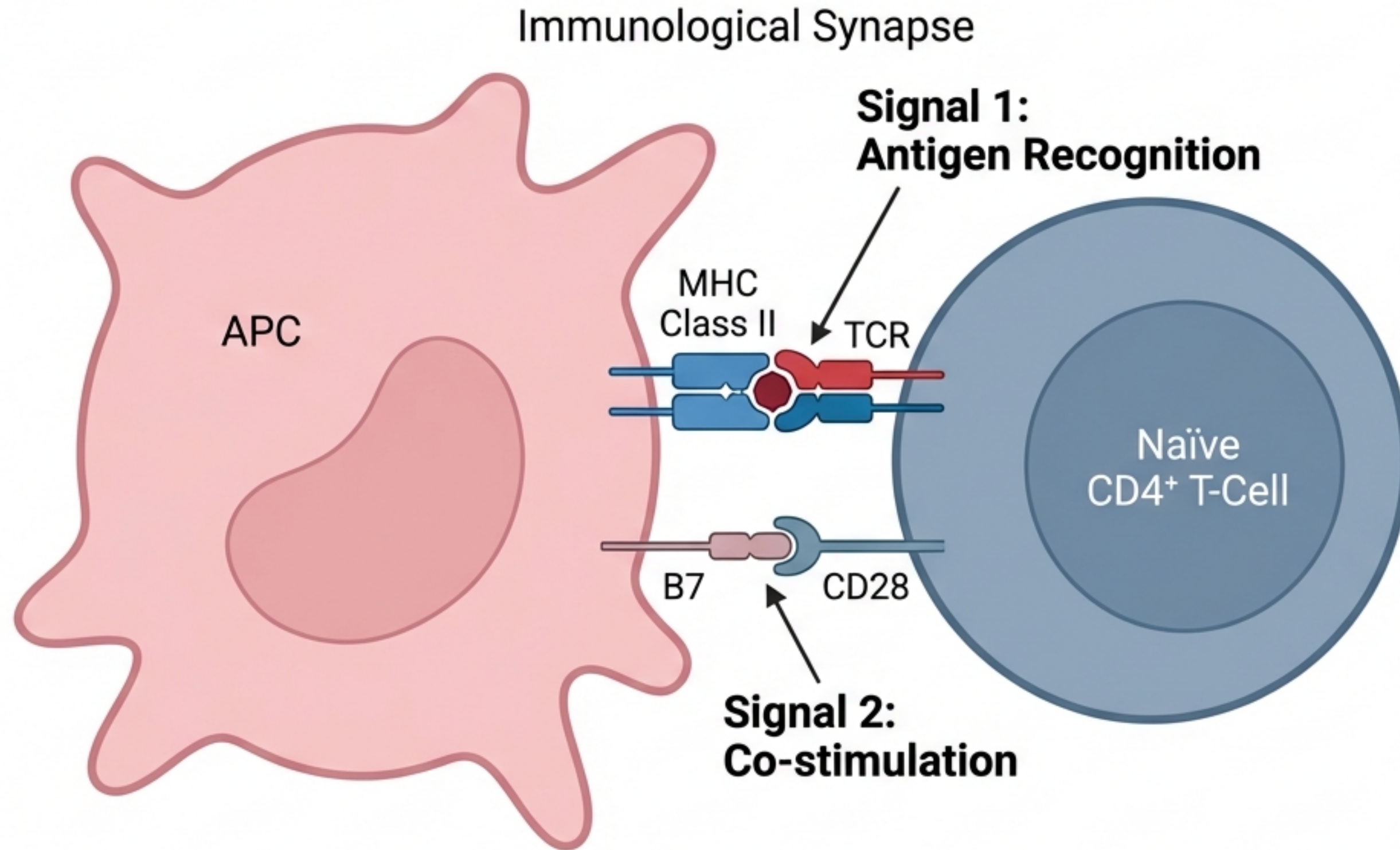
## CD8+ Cytotoxic T Cells



**Binding Partner:** MHC Class I

**Context:** Intracellular antigens (e.g., cytoplasmic proteins).

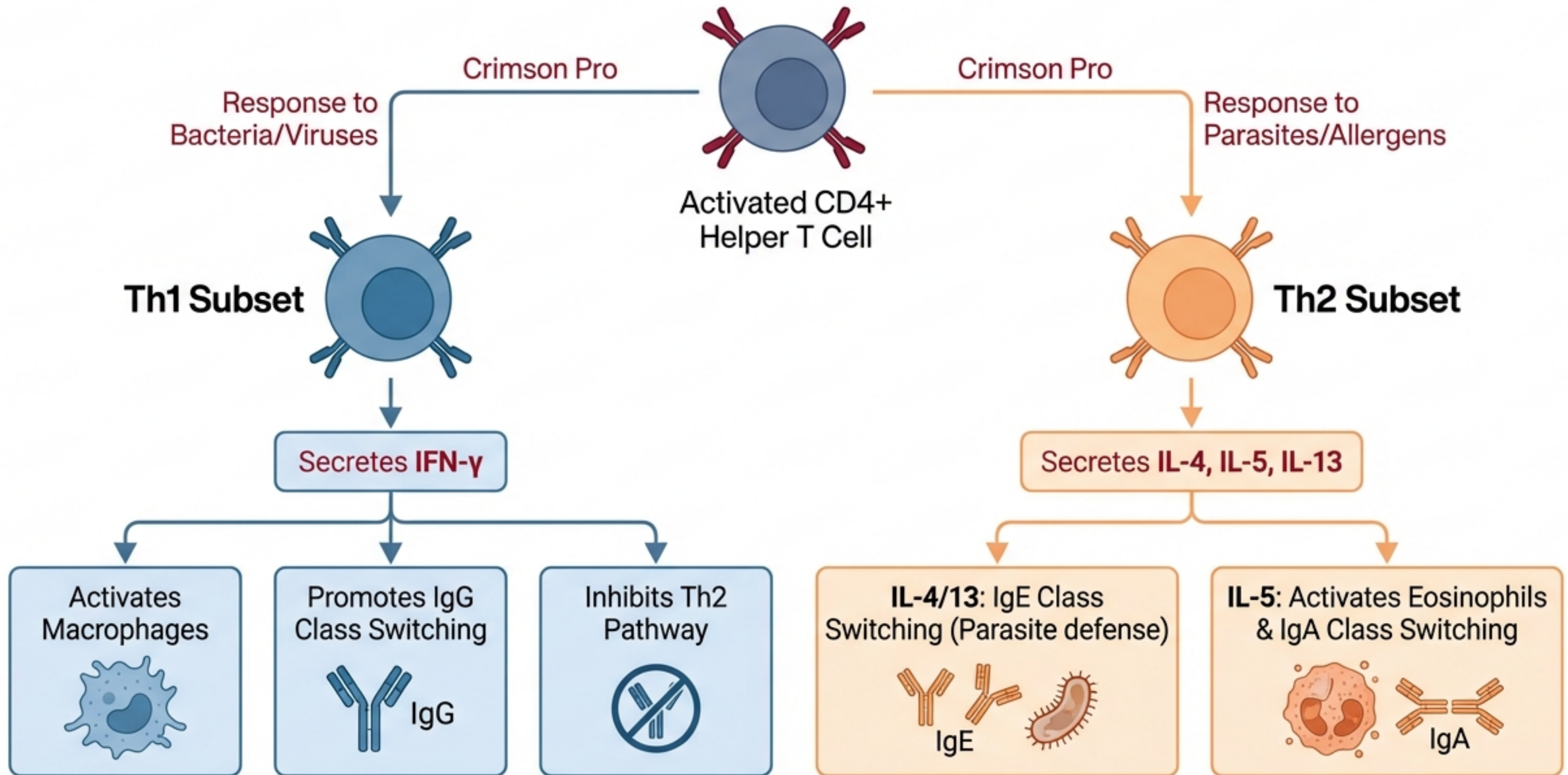
# CD4+ Activation Requires Two Signals



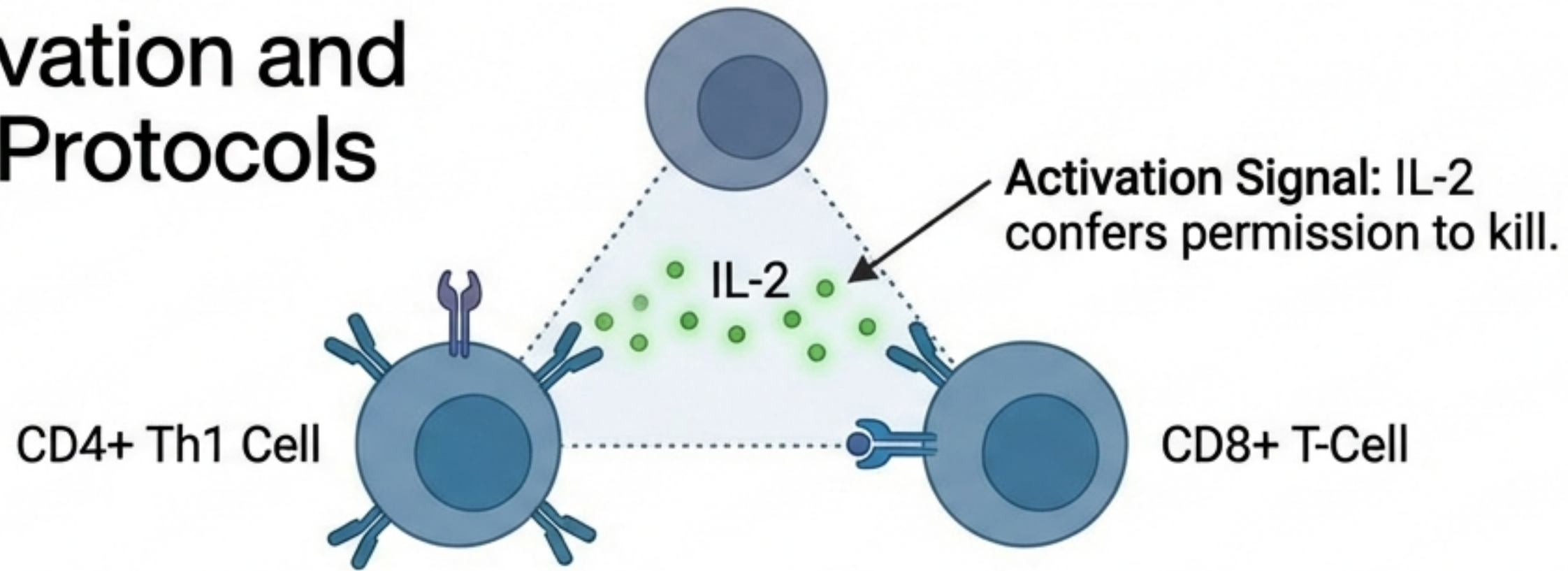
Without Signal 2, the T-cell remains dormant (anergy).

Both keys must turn simultaneously to initiate the adaptive response.

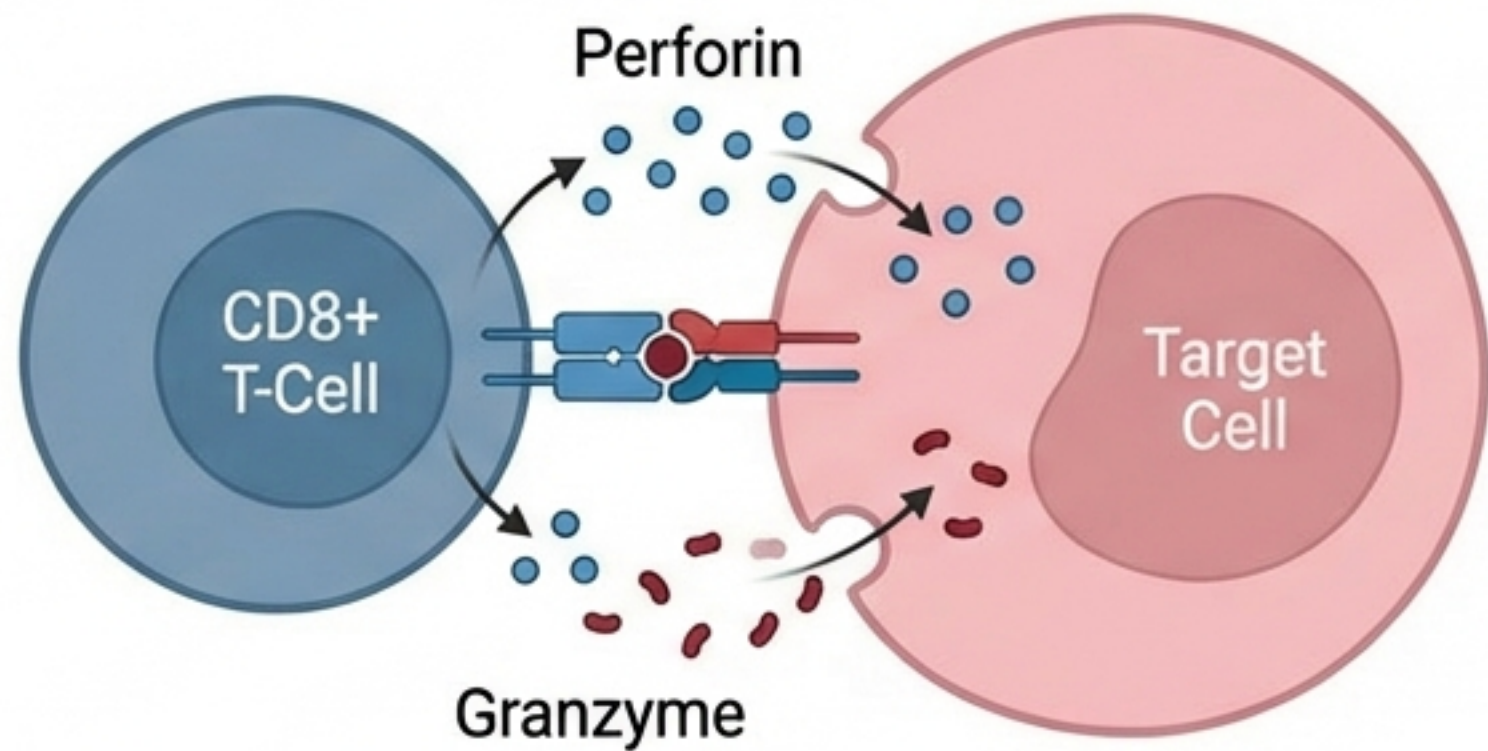
# Strategy Selection: Th1 vs. Th2 Subsets



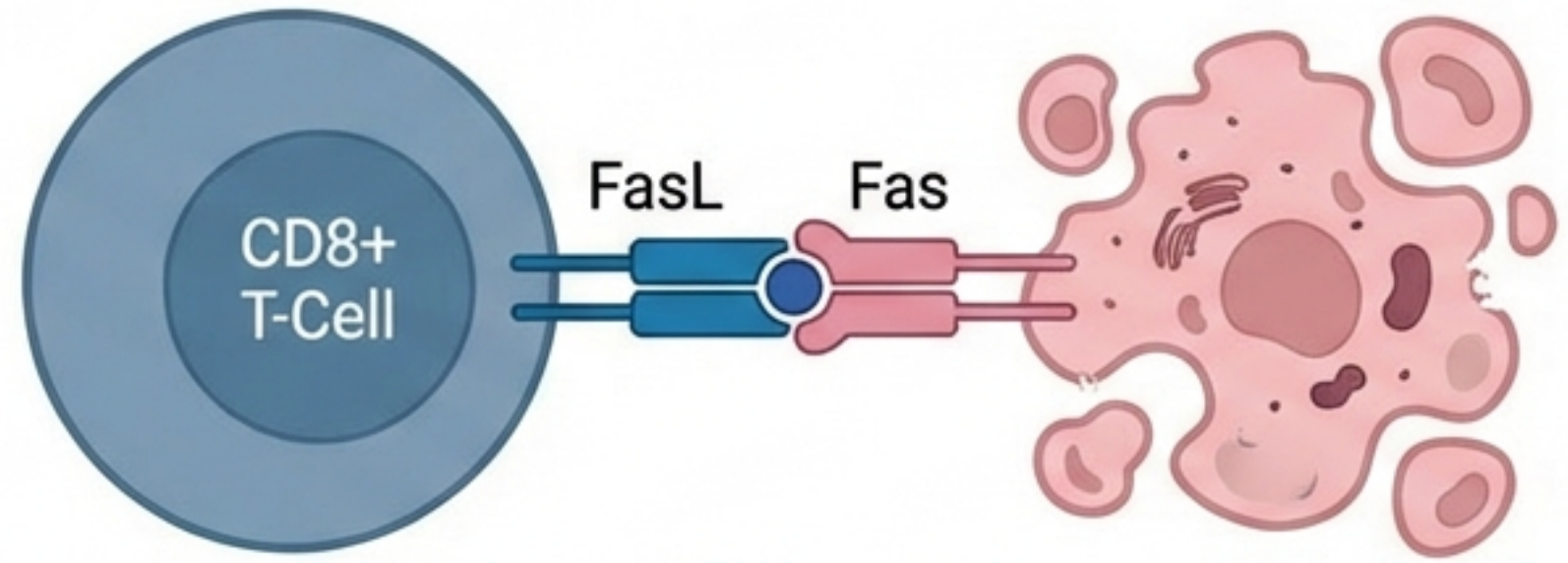
# CD8+ Activation and Execution Protocols



## Perforin/Granzyme Pathway

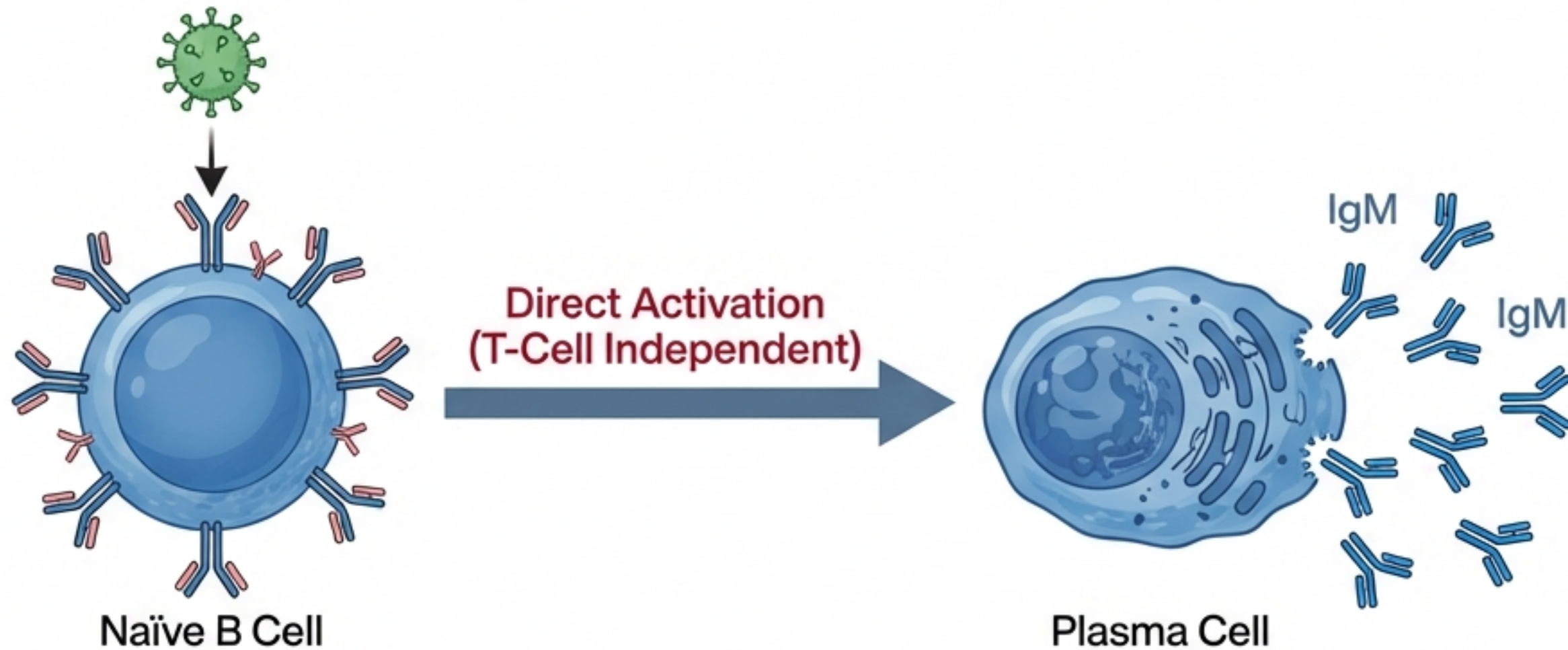
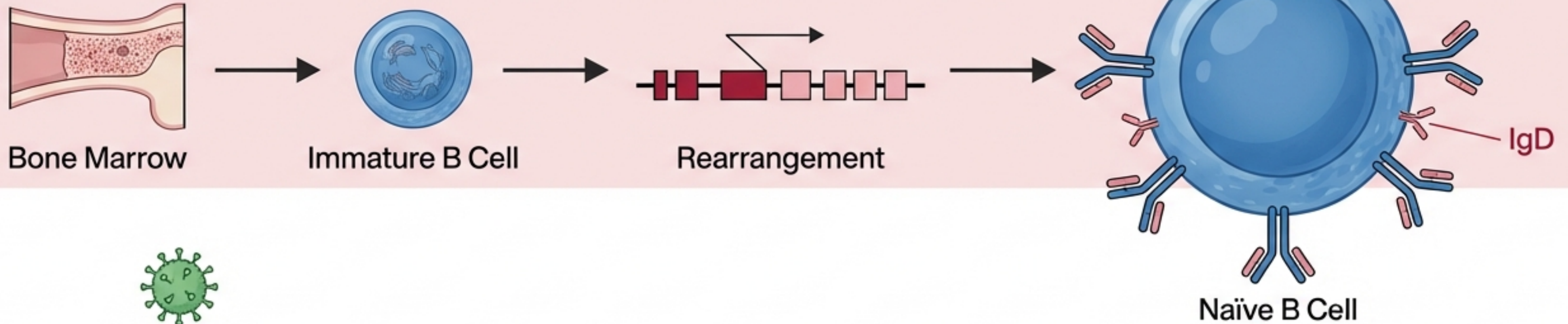


## Fas Ligand Pathway



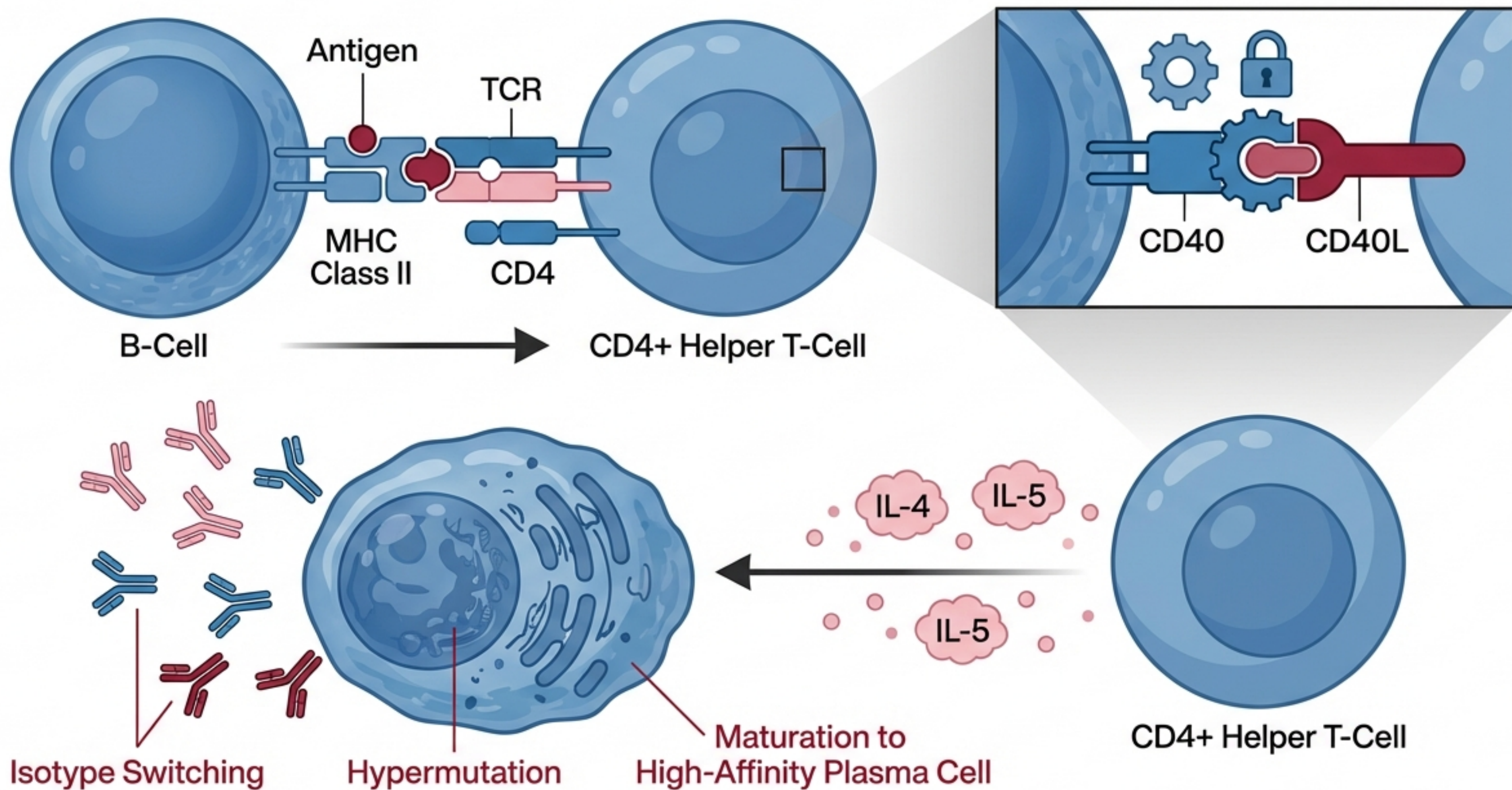
Apoptosis: Controlled Cell Death

# B Lymphocyte Mobilization

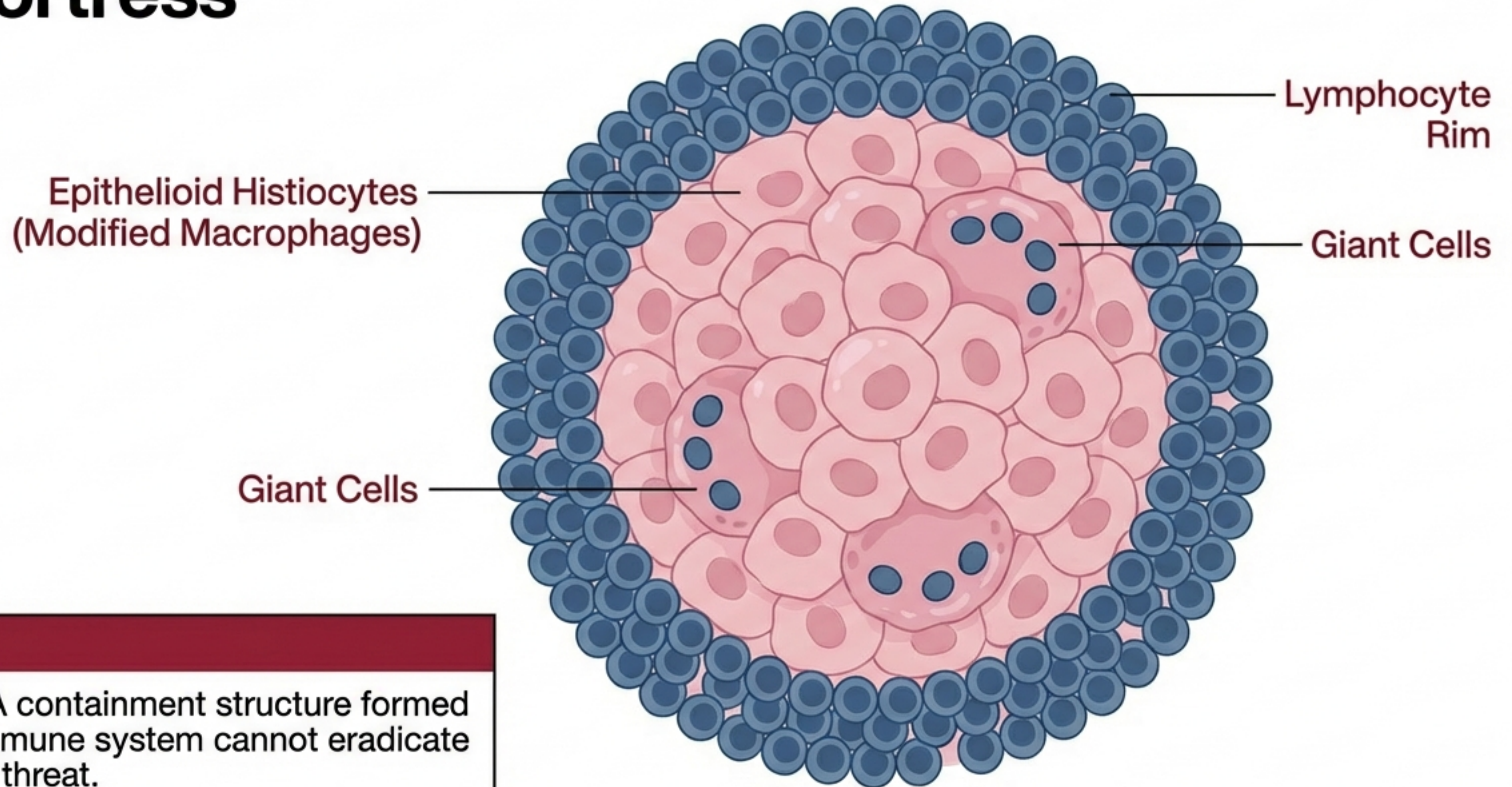


**Direct activation is fast but limited. For advanced weaponry, B-cells require T-cell assistance.**

# The T-Cell / B-Cell Alliance

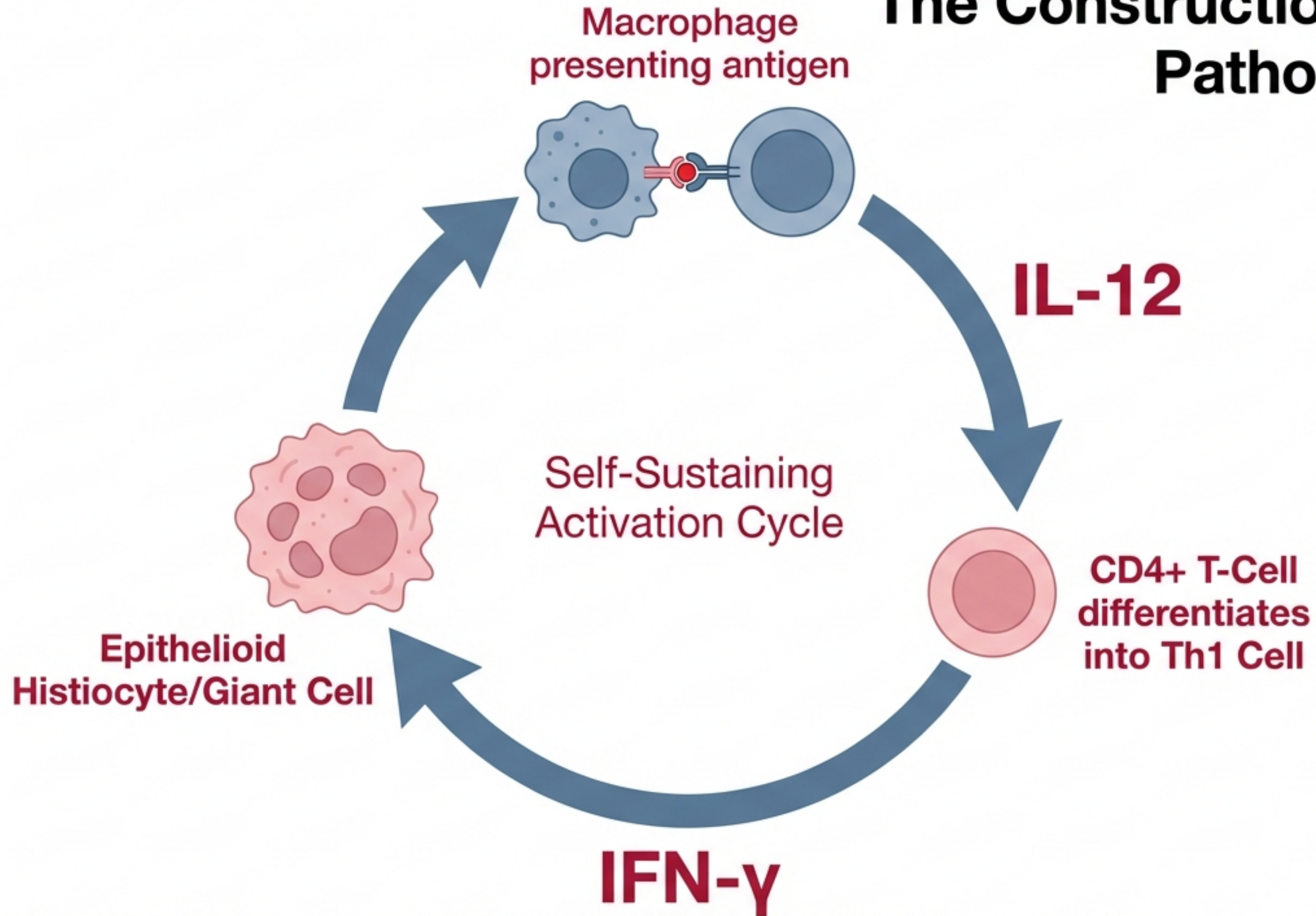


# Granulomatous Inflammation: The Fortress



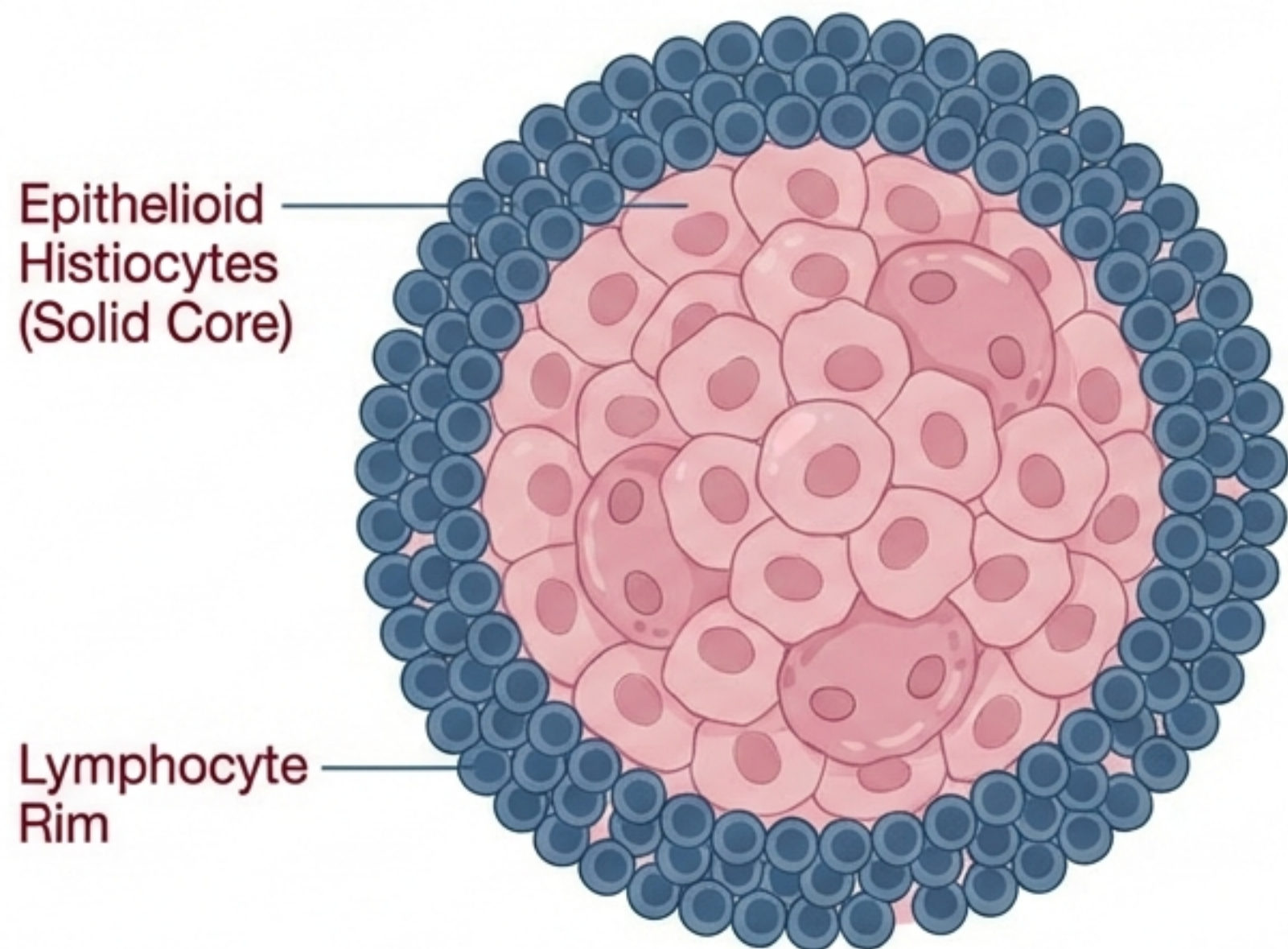
**Definition:** A containment structure formed when the immune system cannot eradicate a persistent threat.

# The Construction Loop: Pathogenesis



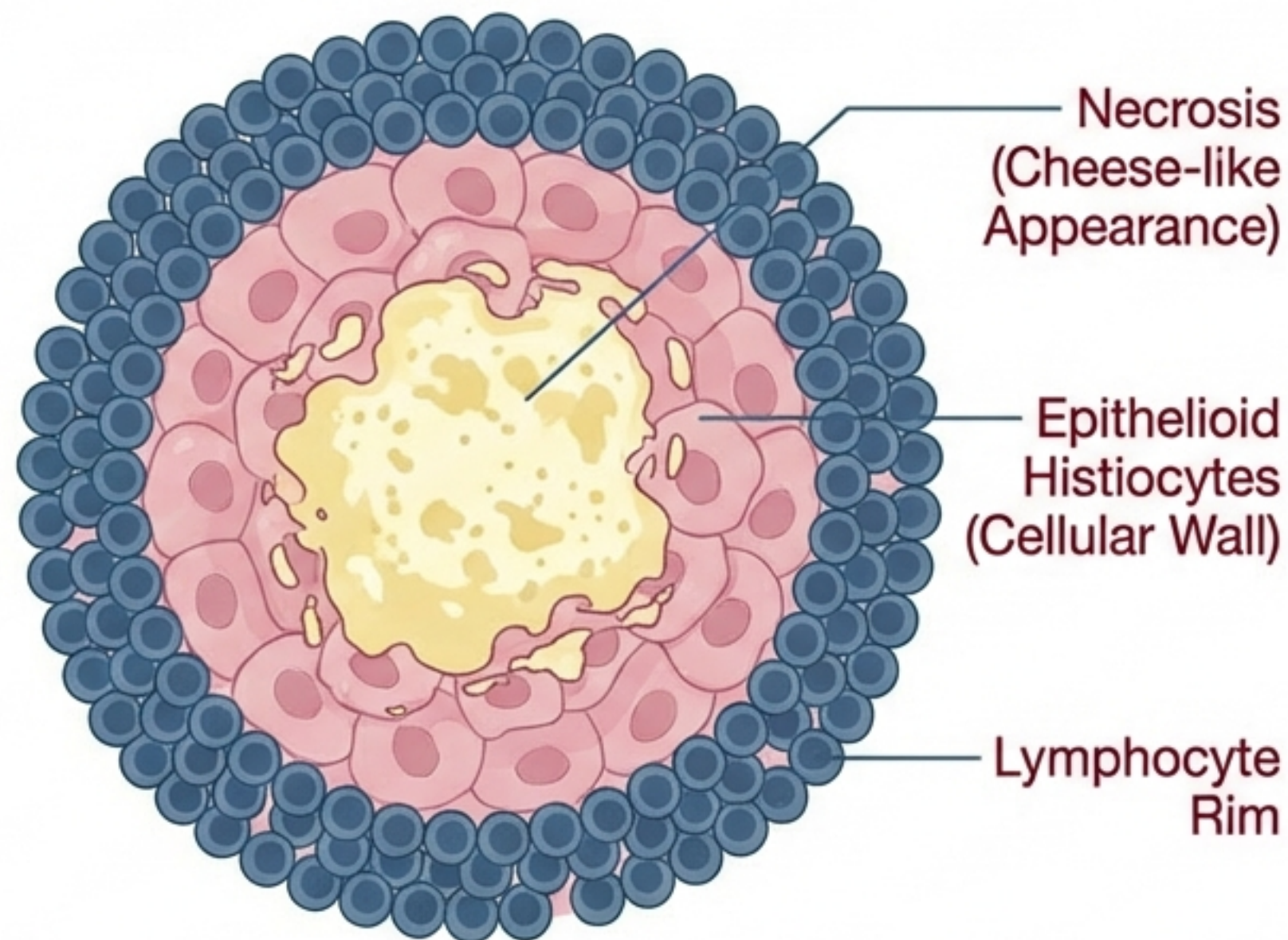
# Granuloma Classifications

## Noncaseating Granuloma









- Foreign material
- Sarcoidosis
- Beryllium exposure
- Crohn disease
- Cat scratch disease

## Caseating Granuloma



- Tuberculosis (TB)
- Fungal infections

# Tactical Summary: Cells and Signals

Cell Type	Binding Partner	Key Signal 2	Primary Output
CD4+ Helper 	MHC Class II	B7 binds CD28 	IFN- $\gamma$ (Th1) or IL-4/5 (Th2)
CD8+ Cytotoxic 	MHC Class I	IL-2 (from Th1)	Perforin, Granzyme, FasL
B-Cell 	Antigen or T-cell	CD40 binds CD40L 	Plasma Cells, Antibodies
Macrophage 	Antigen (as APC)	IFN- $\gamma$ (activator)	IL-12, Epithelioid transformation

*Chronic inflammation is a precise, coordinated conversation between these agents. Disruption of these signals leads to pathology.*