

# **Immunology and Immunotherapy 101 for the Non-Immunologist**

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Society for Immunotherapy of Cancer

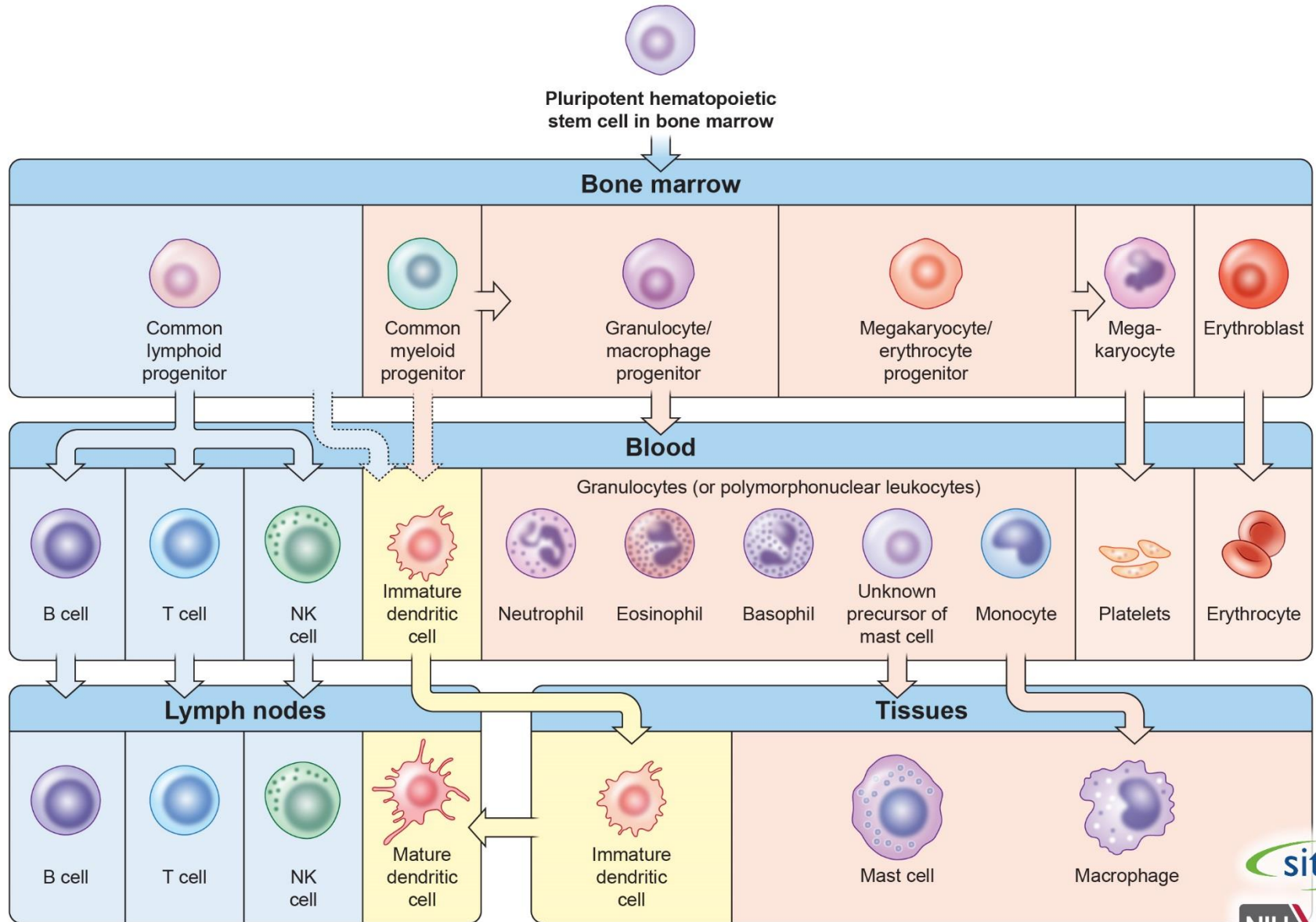
# Disclosures

- Consulting Fees: AstraZeneca, Pfizer, Regeneron Pharmaceuticals, Inc.
- Contracted Research: Bristol-Myers Squibb
- I will be discussing non-FDA approved treatments during my presentation.

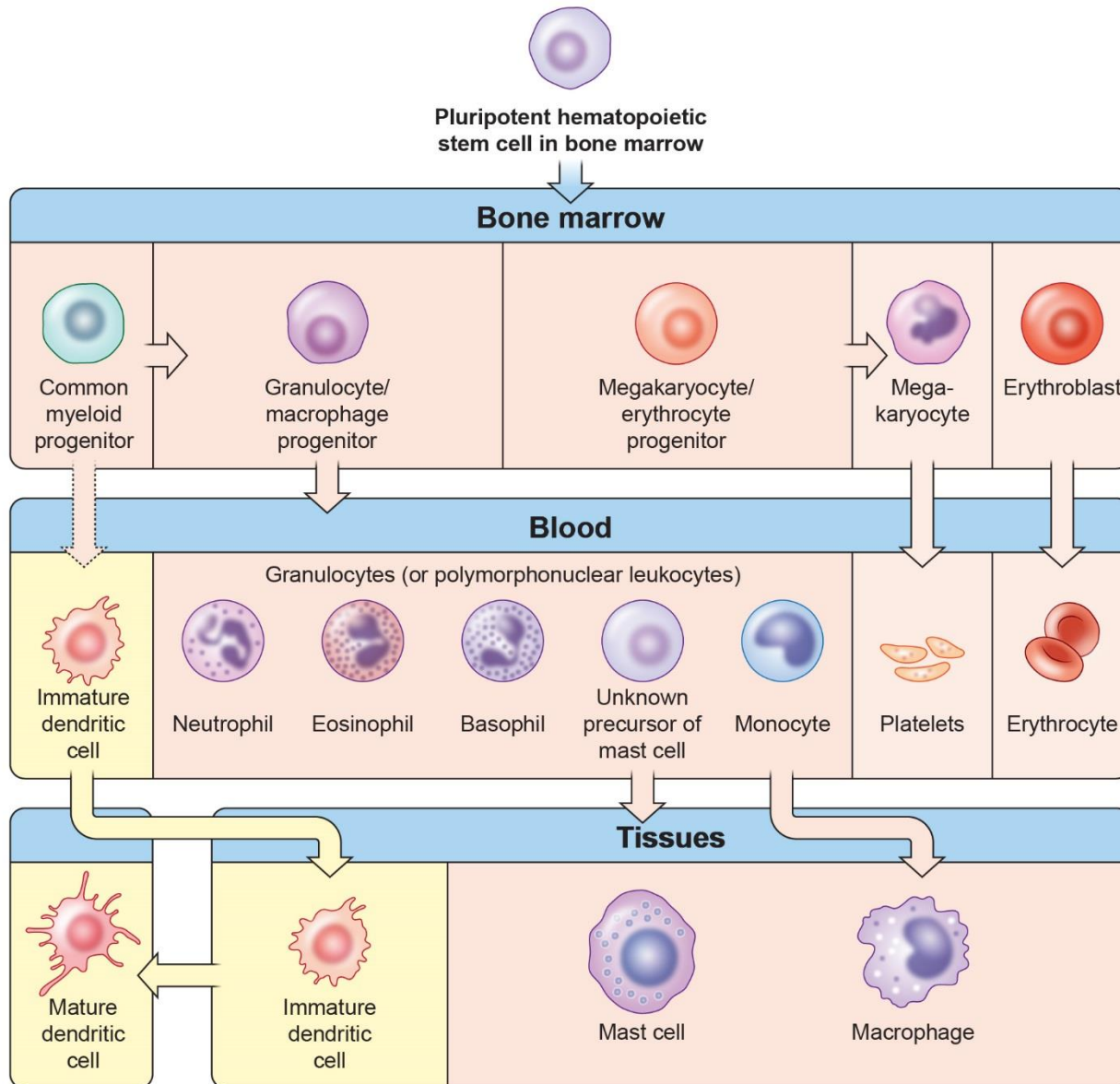


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# Immune cells are derived from stem cells in the bone marrow




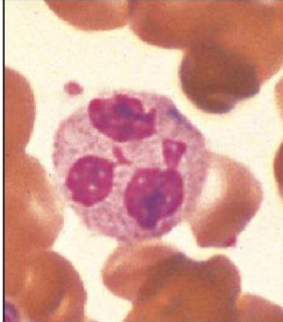
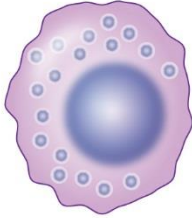
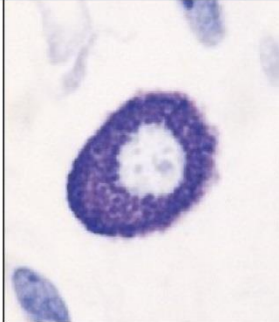
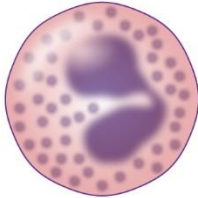
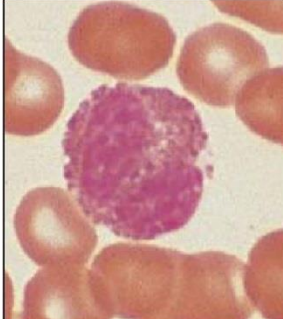
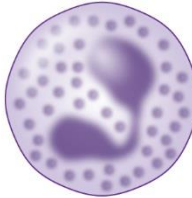
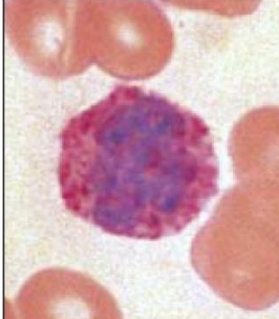
# Myeloid cells



- Derived from a common progenitor
- Comprises most of the cells of the innate immune system
- Functional maturation may happen in tissue in response to danger signals

# Granulocytes

Short-lived cells that possess granules containing degradative enzymes and anti-microbial substances

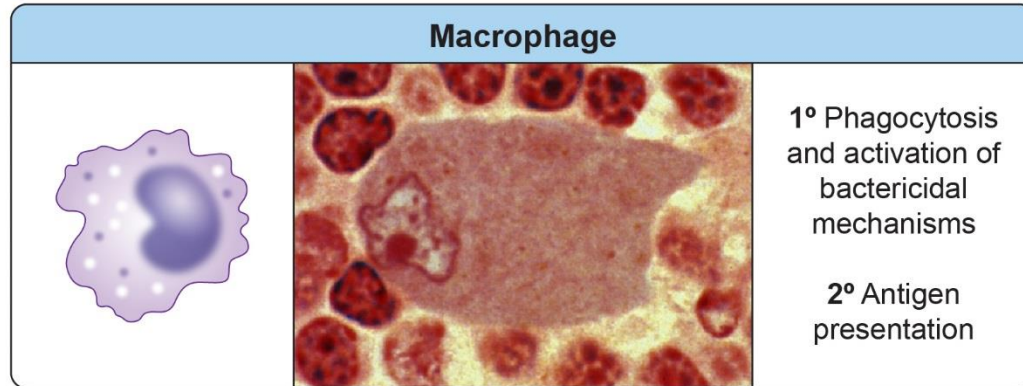
Neutrophil		
		Phagocytosis and activation of bacterial mechanisms
Mast cell		
		Release of granules containing histamines and other inflammatory mediators
Eosinophil		
		Killing of antibody-coated parasites
Basophil		
		Promotion of allergic responses and augmentation of anti-parasitic immunity (Blood mast cells)

Neutrophils, eosinophils and basophils are sometimes referred to as polymorphonuclear leukocytes (PMNs)

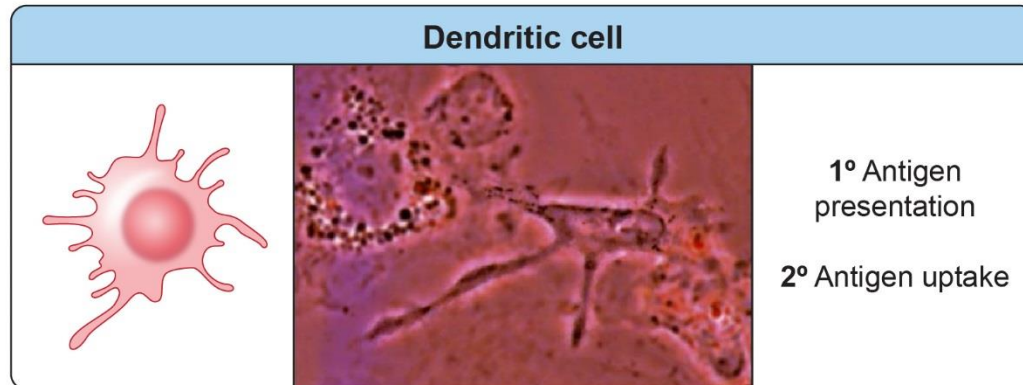


# Phagocytes

Neutrophils, macrophages and dendritic cells



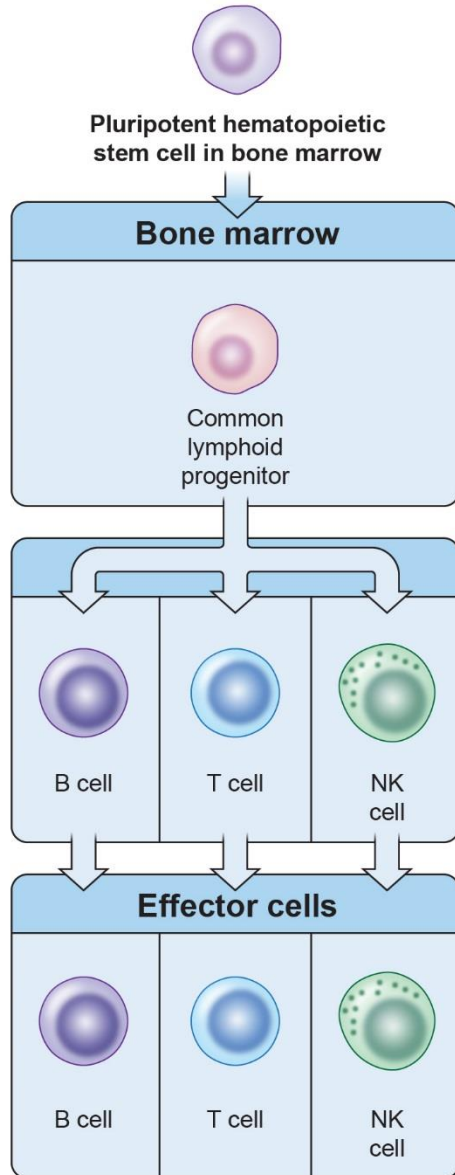
Reside in tissues



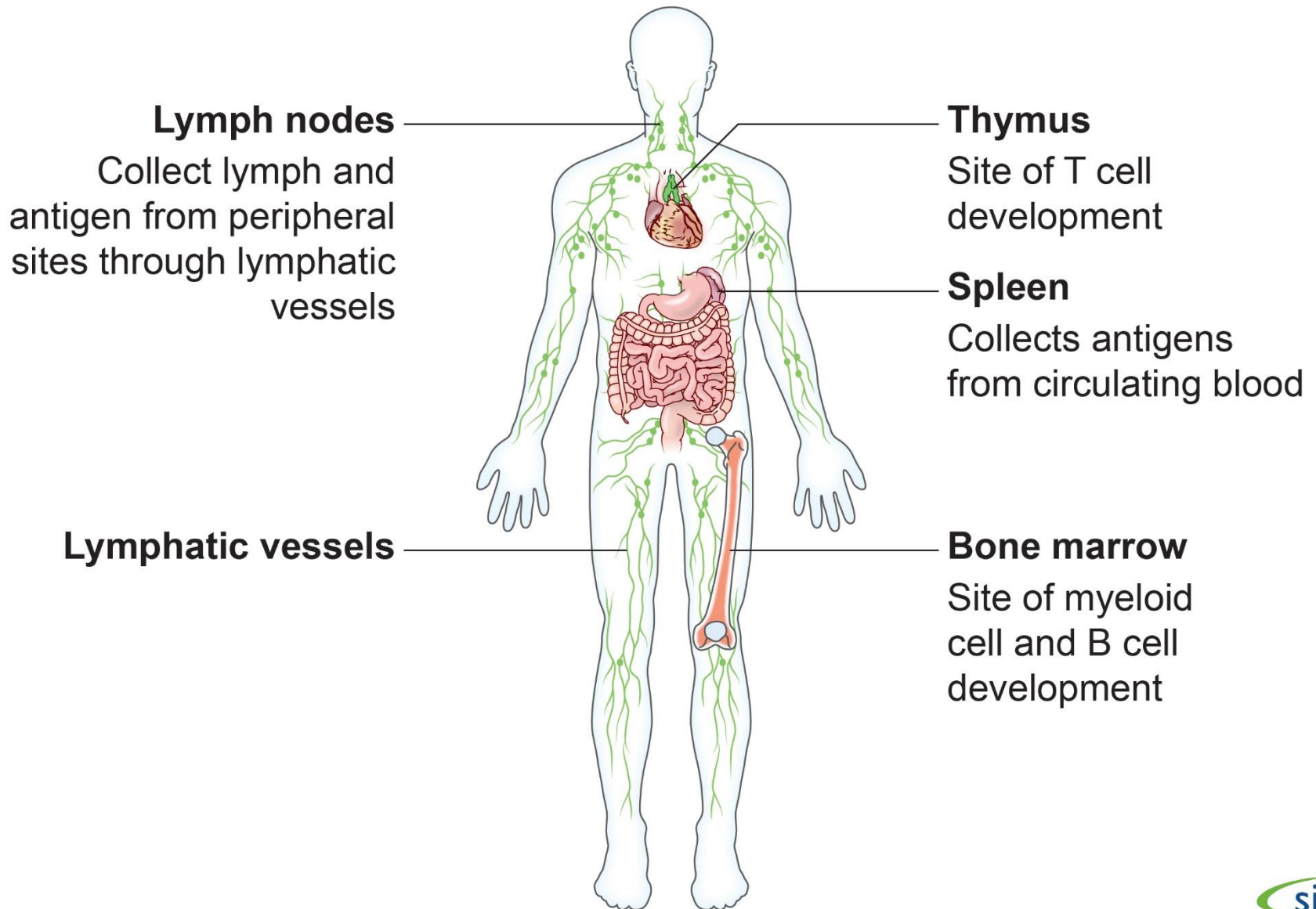
Main role is not clearance of pathogen but rather immune cell activation; patrolling population in lymphoid tissues as well as non-lymphoid tissues

Dendritic cells and macrophages are two types of professional antigen presenting cells (APCs)

# Lymphocytes



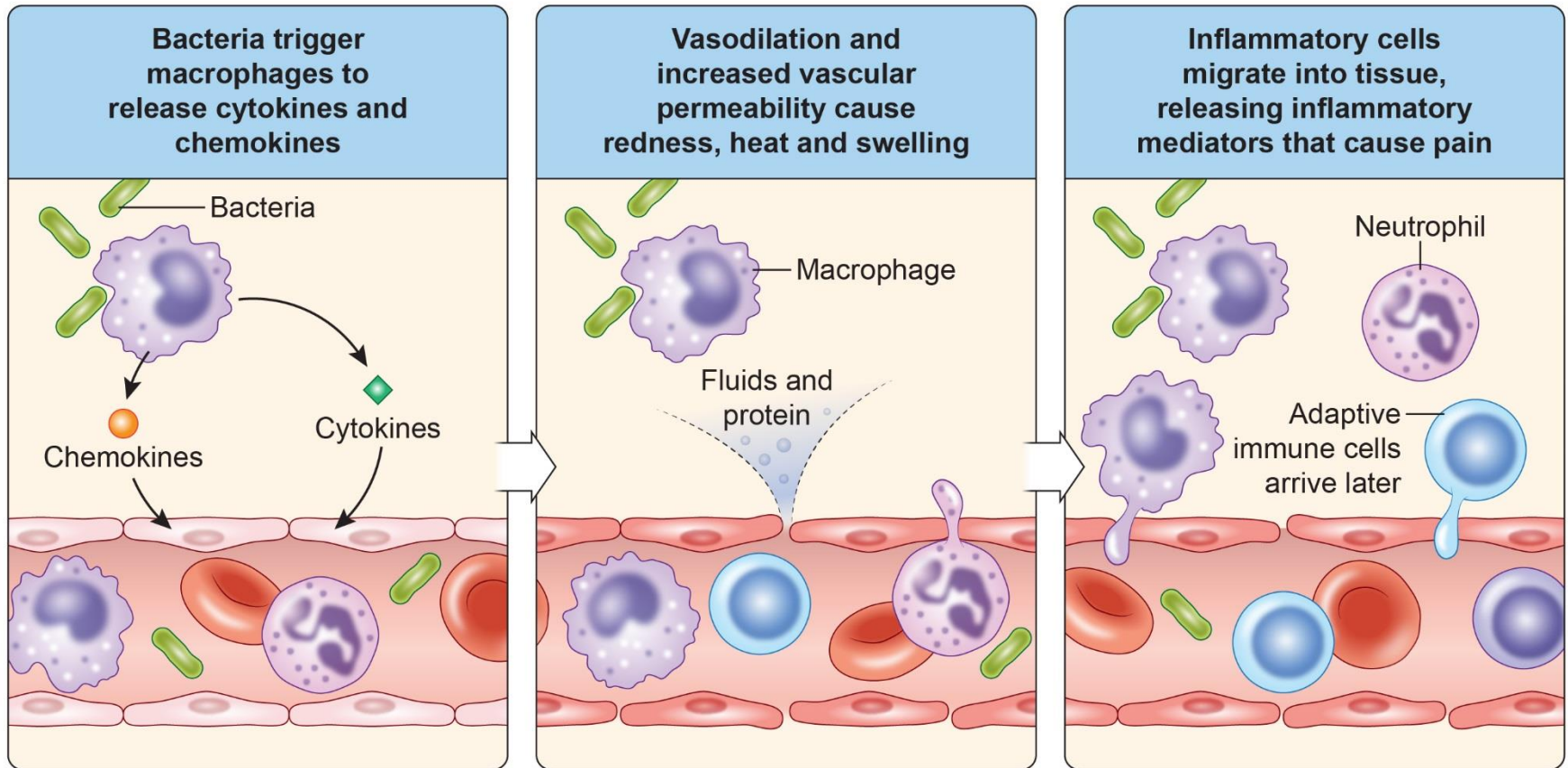
# Lymphoid organs



Note: Immune cells and lymphoid aggregates are also found throughout the body



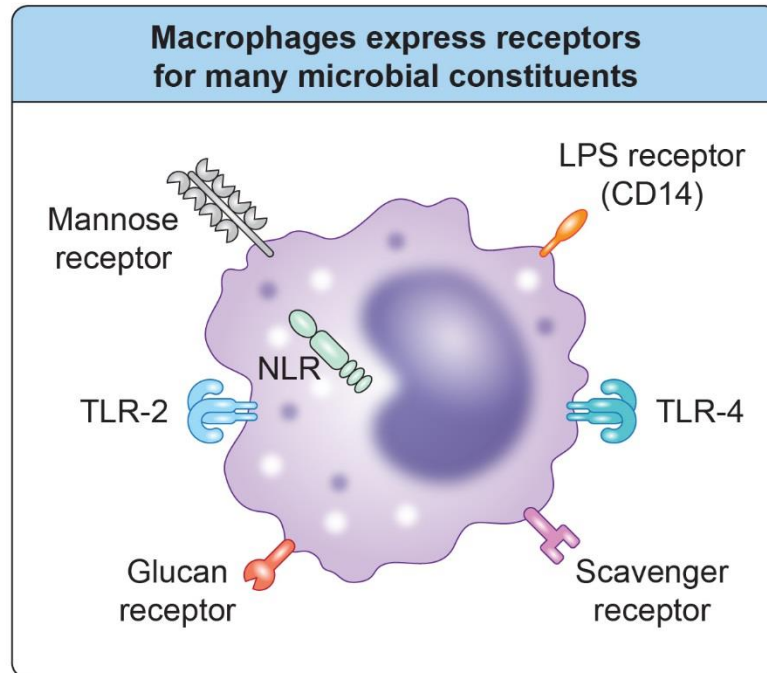
# Infectious agents first activate innate immune cells resulting in an inflammatory response



Cytokines are proteins that immune cells use to communicate/regulate other immune cells, not all cytokines are inflammatory

Chemokines are a group of cytokines that attract other immune cells

# Innate responses are initiated upon recognition of “danger signals” by pattern recognition receptors (PRRs)



## “Danger signals”

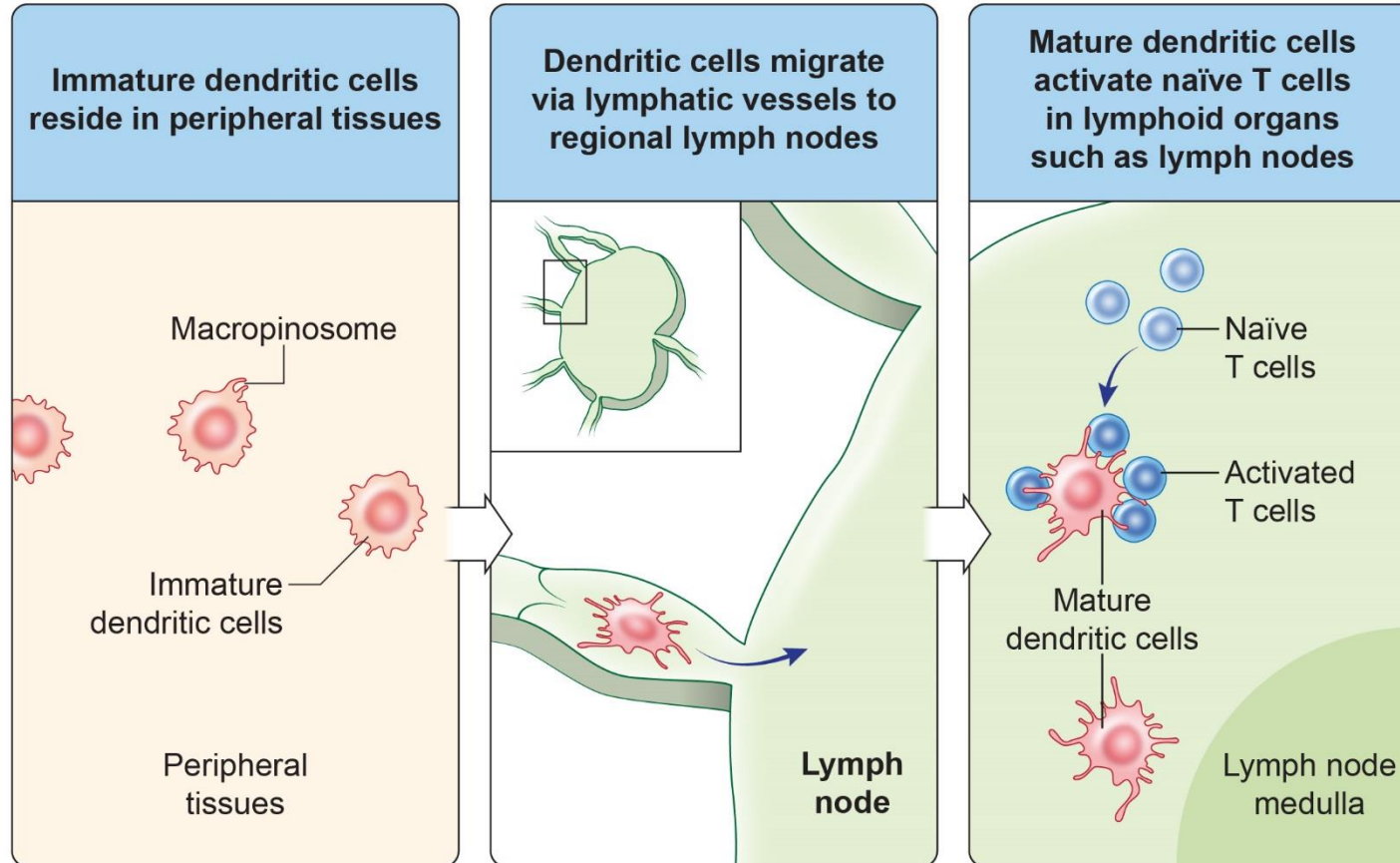
- Pathogen-associated molecular patterns (PAMPs)
  - Bacteria proteins
  - viral DNA/RNA
- Damage-associated molecular patterns (DAMPs)
  - Products of dying cells

## Types of PRRs

- Toll-like receptors (TLR)
- C-type lectin receptors
- NOD-like receptors (NLRs)
- RIG-I-like receptors

Receptors can be on the cell surface or intracellular (NLRs)

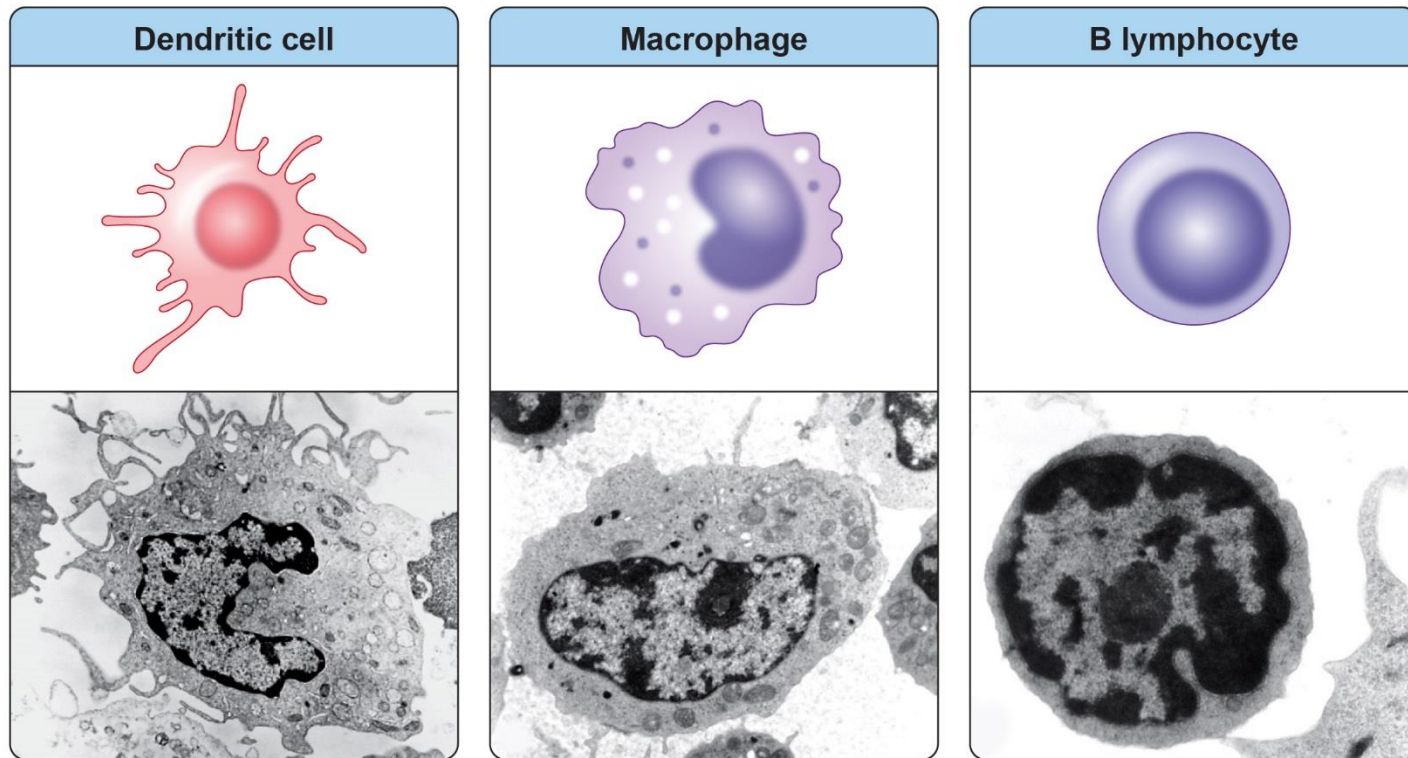
# DCs are important for initiating adaptive immune responses



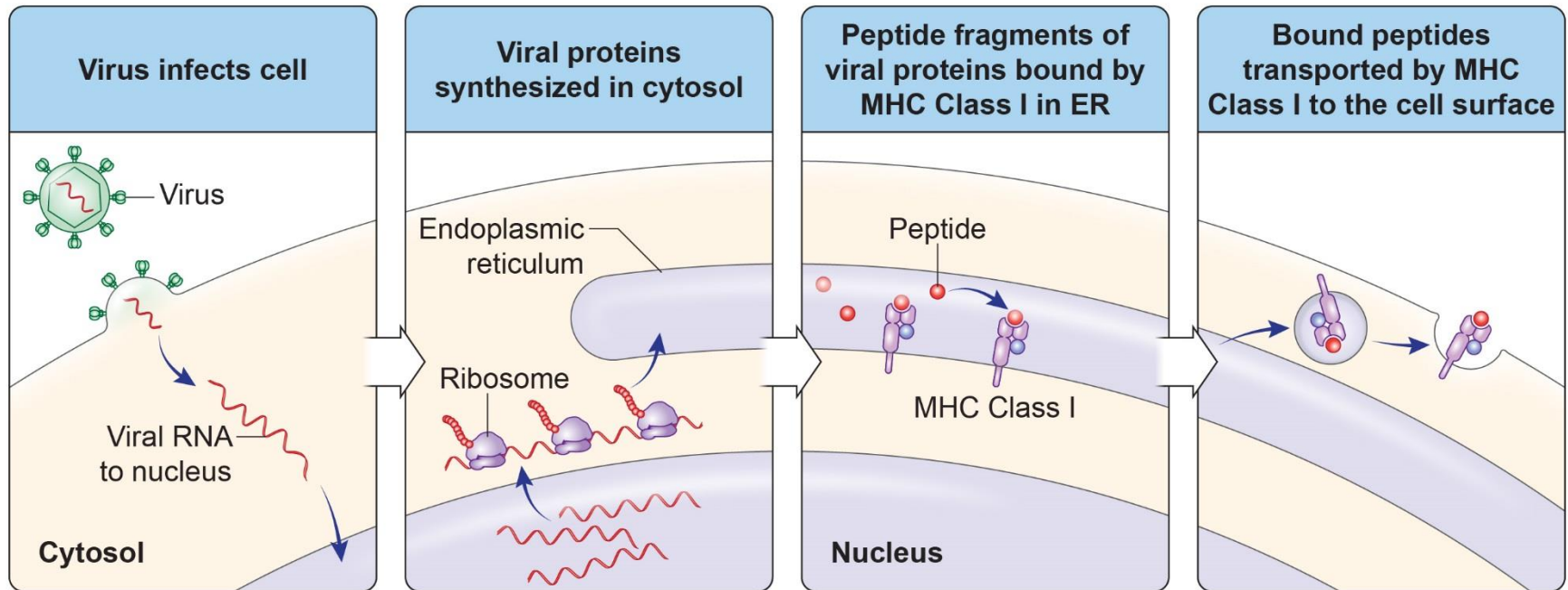


# Antigen processing and presentation

Professional APCs present Ag to naïve T cells and induce activation



# MHC Class I presents peptide antigens to CD8 T cells

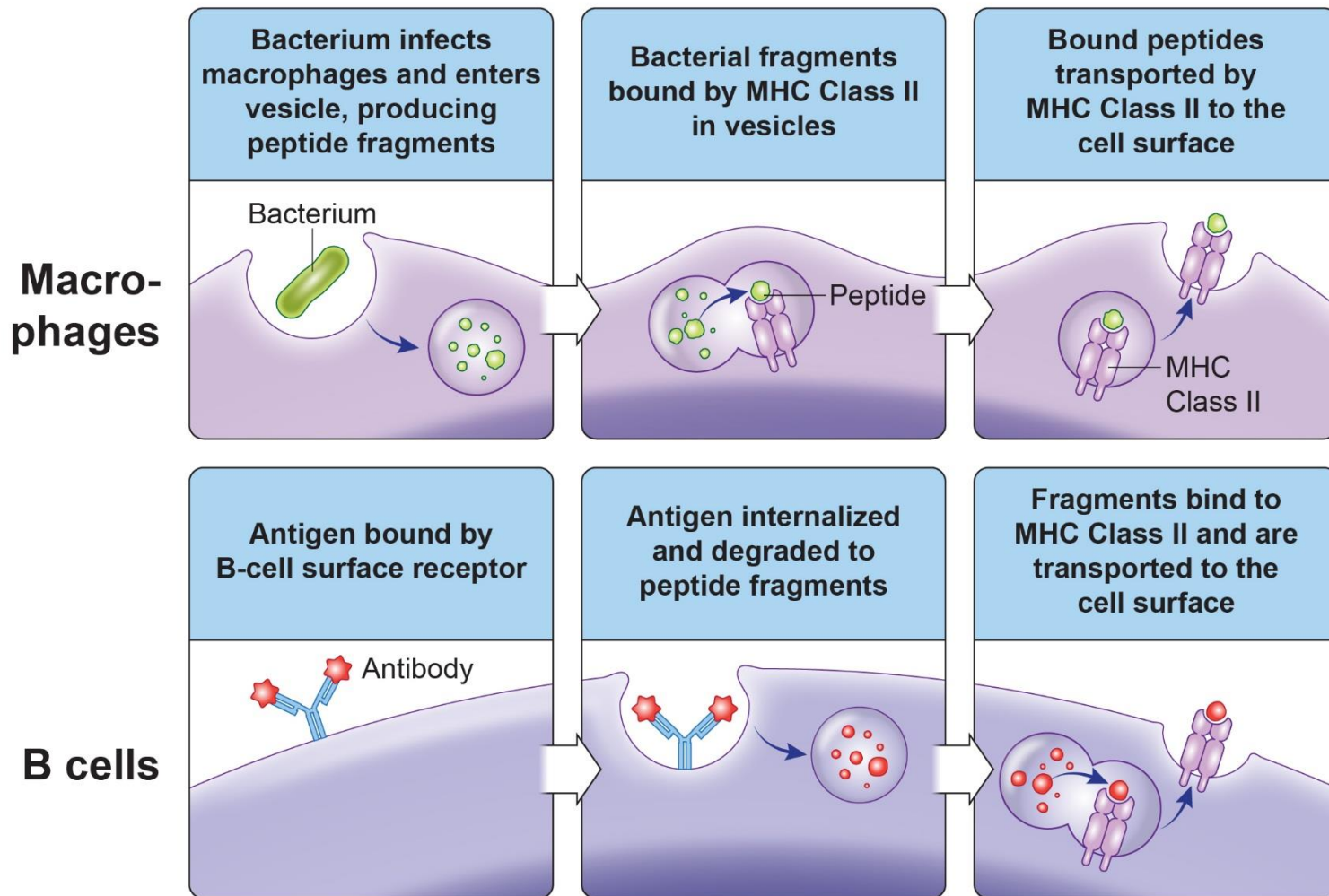


## Major Histocompatibility Complex (MHC) Class I

- Expressed by all nucleated cells
- Presents peptides derived from endogenous proteins
- MHC Class I proteins are also recognized by NK cells



# MHC Class II presents antigens to CD4 T cells



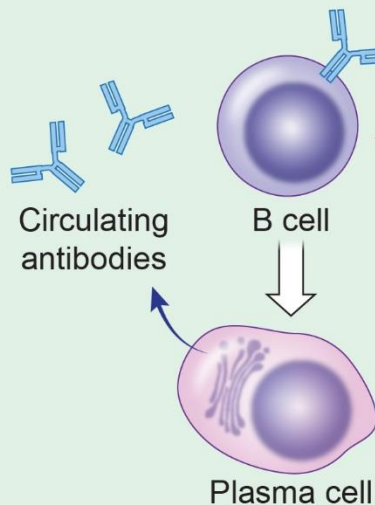
## Major Histocompatibility Complex (MHC) Class II

- Typically expressed by professional APCs
- Presents peptides derived from exogenous proteins

# Adaptive immune responses

## Humoral response

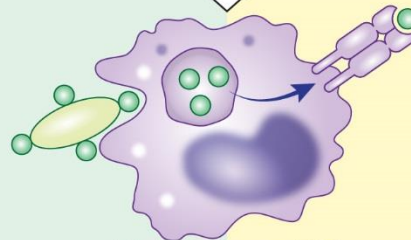
Antibodies present in blood allow immunity to be transferred via proteins



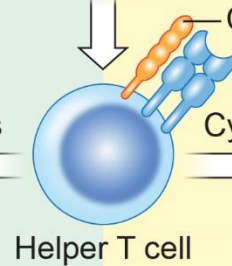
## Cellular response

Immunity is mediated by T cells

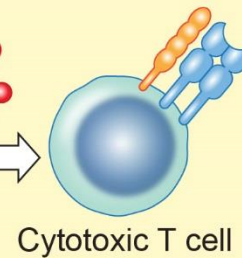
Foreign body



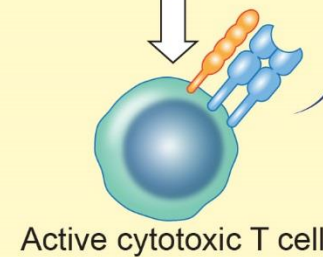
Macrophage/DC



Helper T cell



Cytotoxic T cell

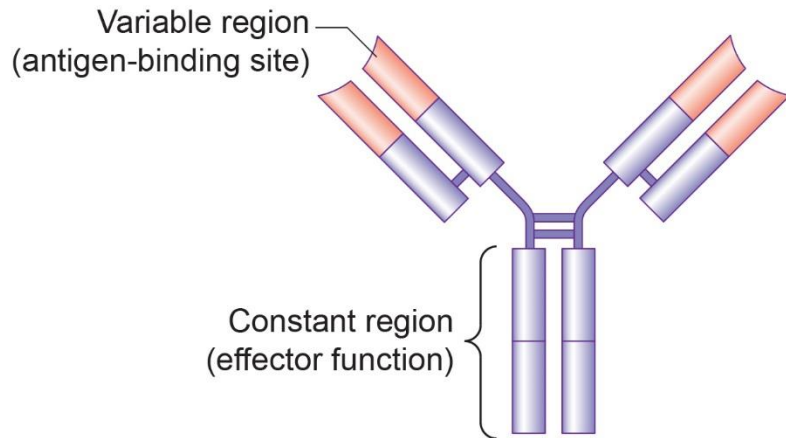


Circulating T cells

# Antigen receptors

## Antibody (Ab)

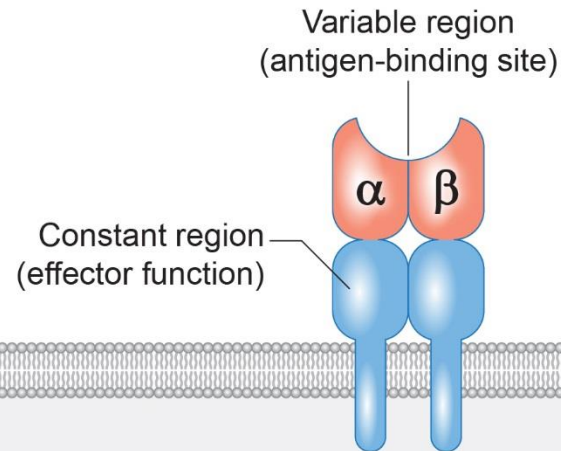
Schematic structure of an antibody molecule



Cell surface and secreted

## T cell receptor (TCR)

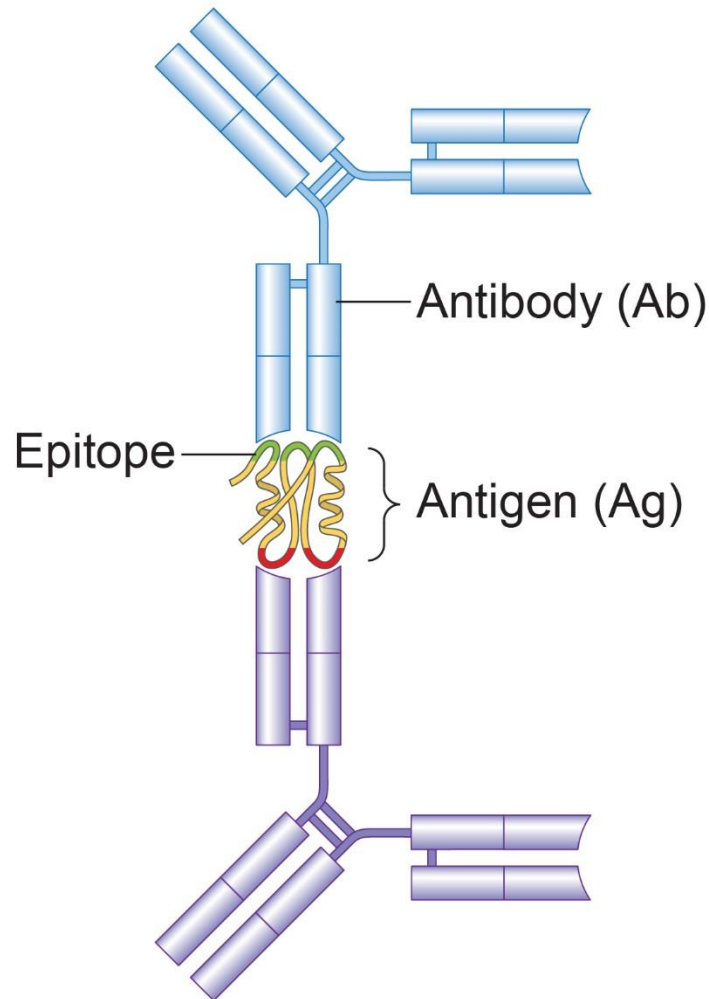
Schematic structure of the T cell receptor



Cell surface only

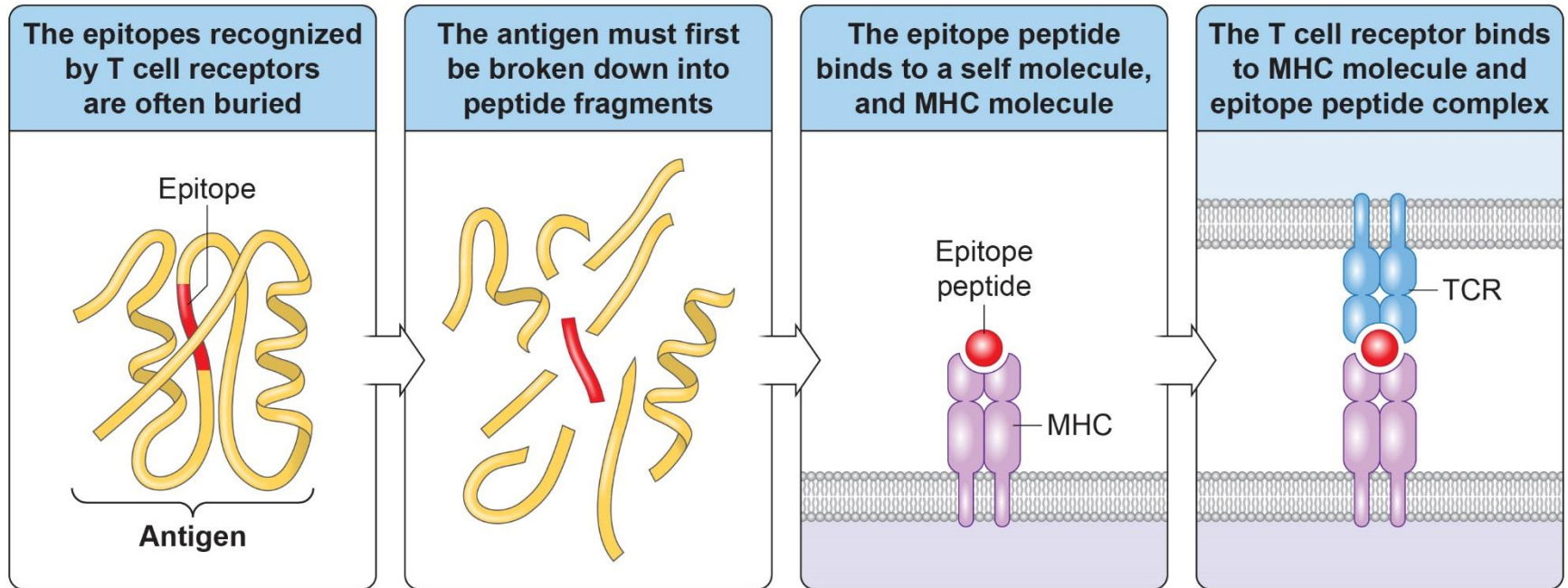
# Antigen recognition by antibodies

Ab recognizes portions of proteins in native structures, not processed proteins (may not be continuous portion of protein)





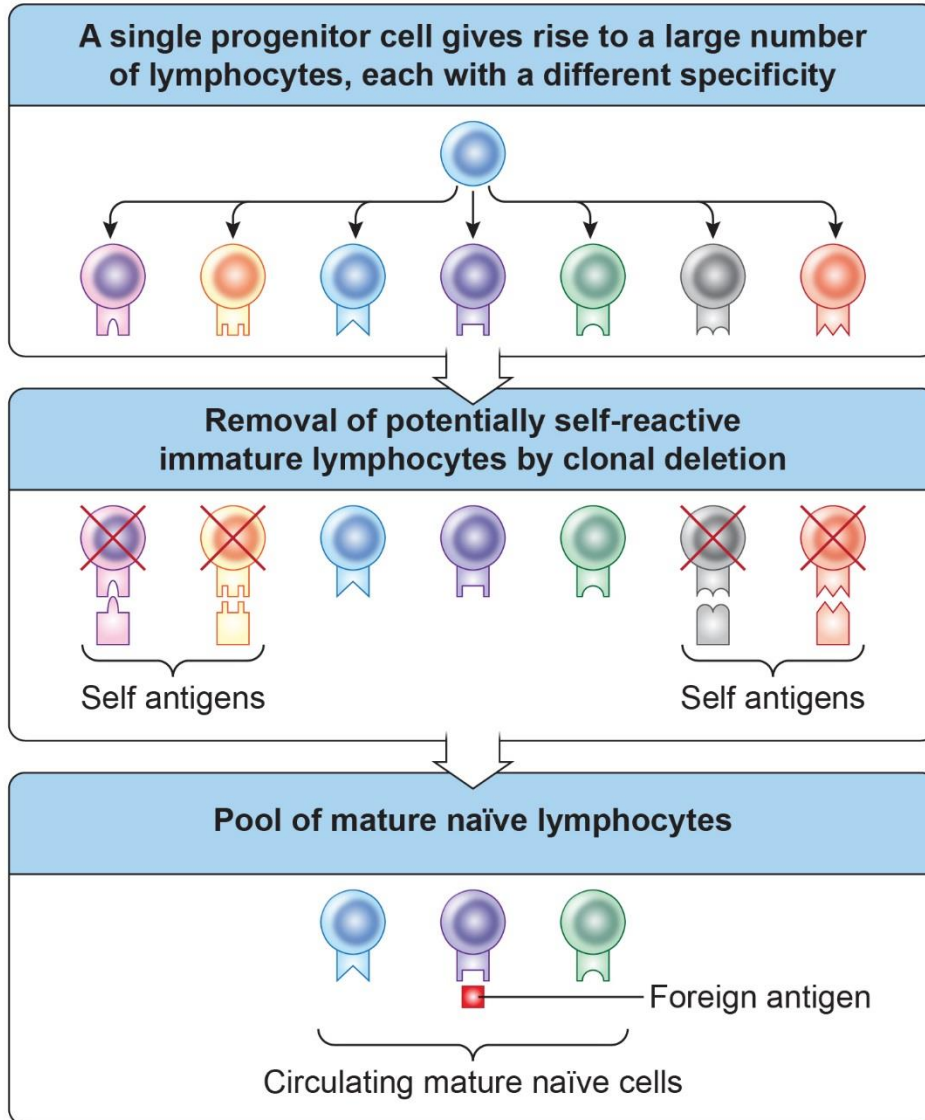
# T cell receptors (TCRs) recognize processed proteins presented by MHC



MHC = Major Histocompatibility Complex



# Generating lymphocytes that each have a unique specificity



## Generation of vast pool of cells

- Immature cells (non-functional)

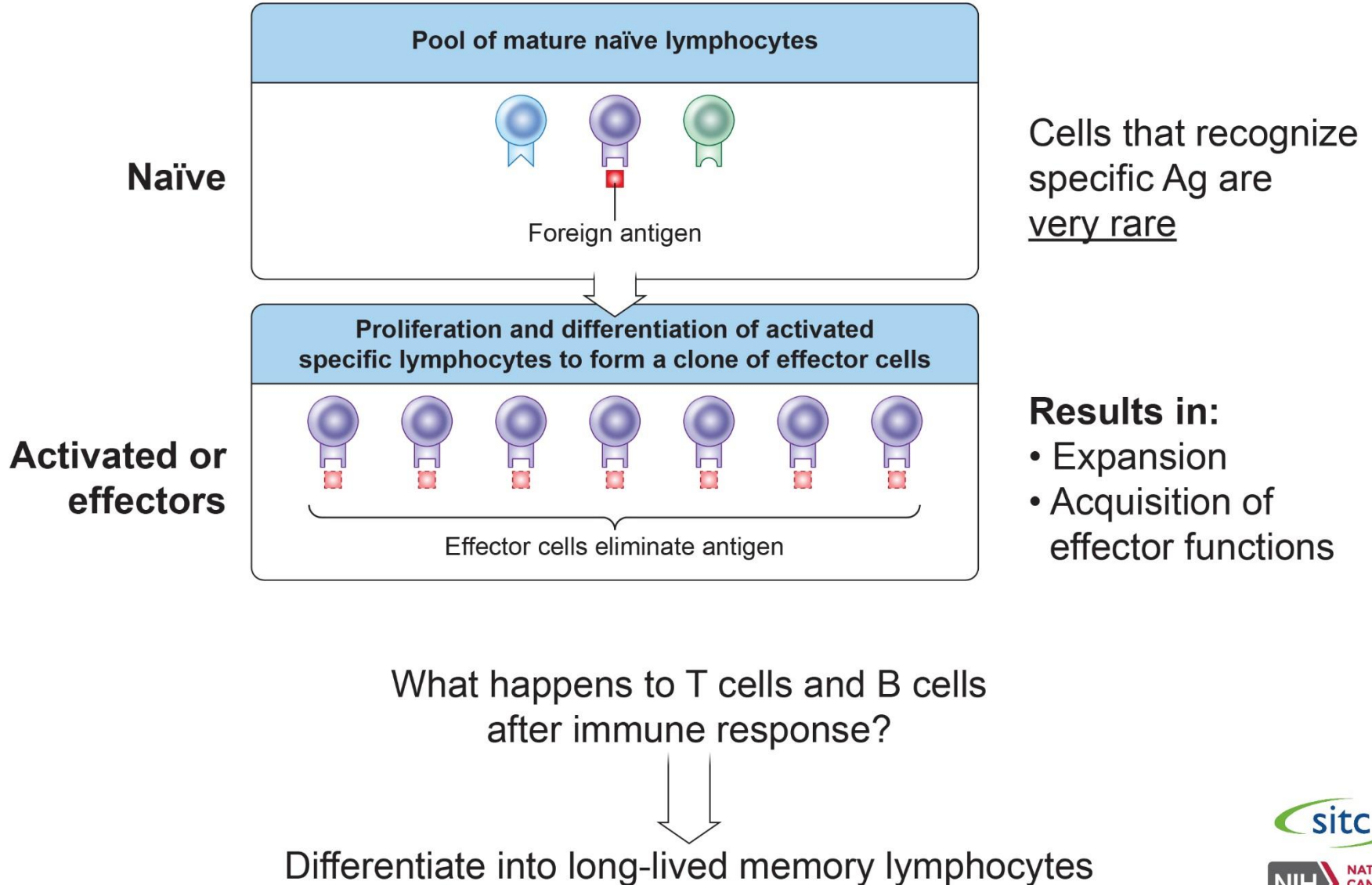
## Elimination of cells that can recognize self Ags

- One barrier to inducing responses against tumor cells

## Mechanism of central tolerance

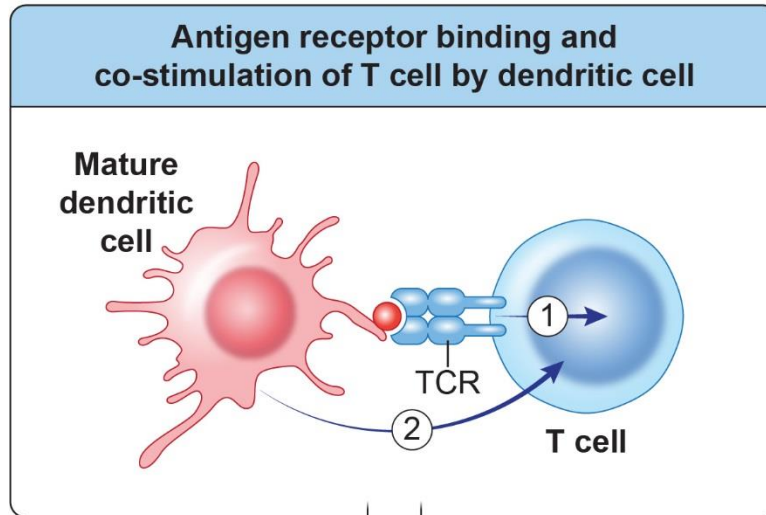
- Circulating mature naïve cells

# Lymphocyte activation

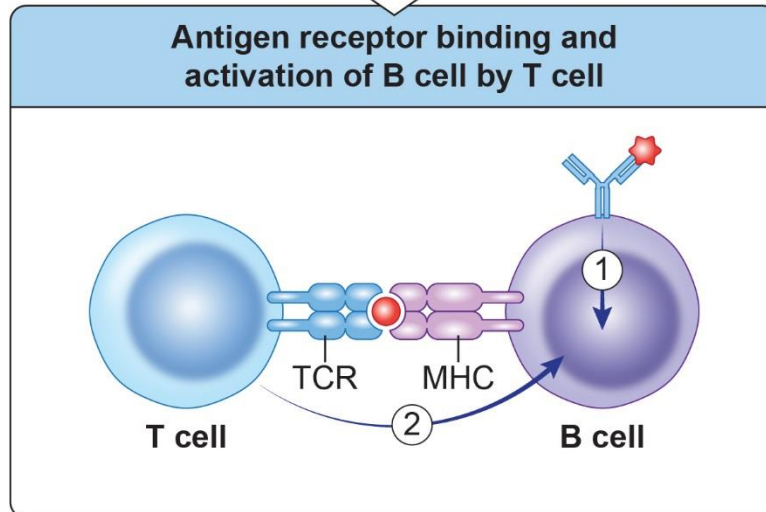


# Lymphocyte activation

T cells



B cells



**Activation of T and B cells requires stimulation via:**

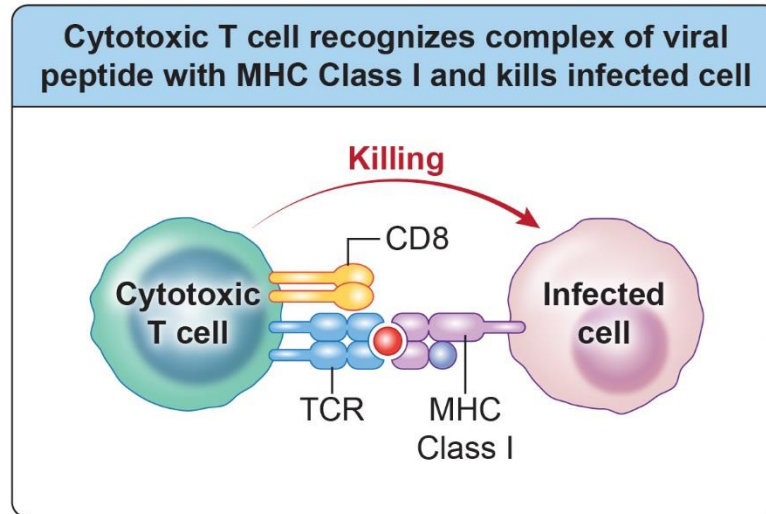
- Antigen receptor (Signal 1)
- Costimulatory molecules (Signal 2)

Absence of co-stimulation leads to unresponsiveness

Peripheral tolerance

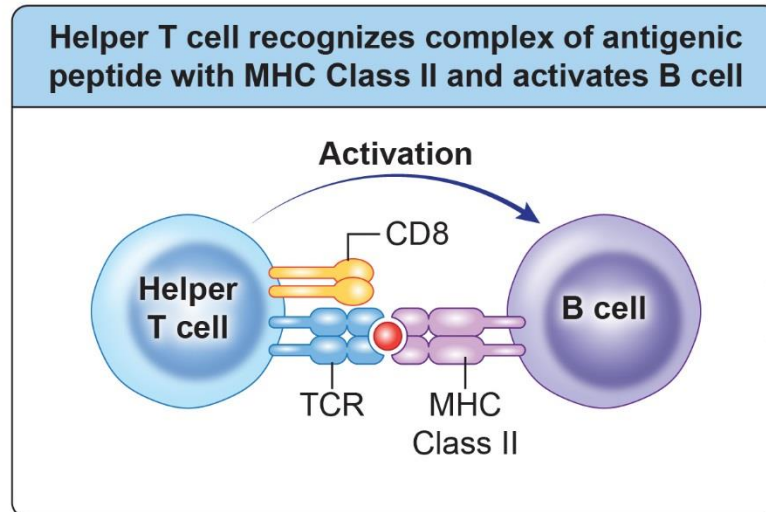
# Effector mechanisms of adaptive immunity

## CD8+ T cells (Cytotoxic T cells)



Produce proteins that lyse cells

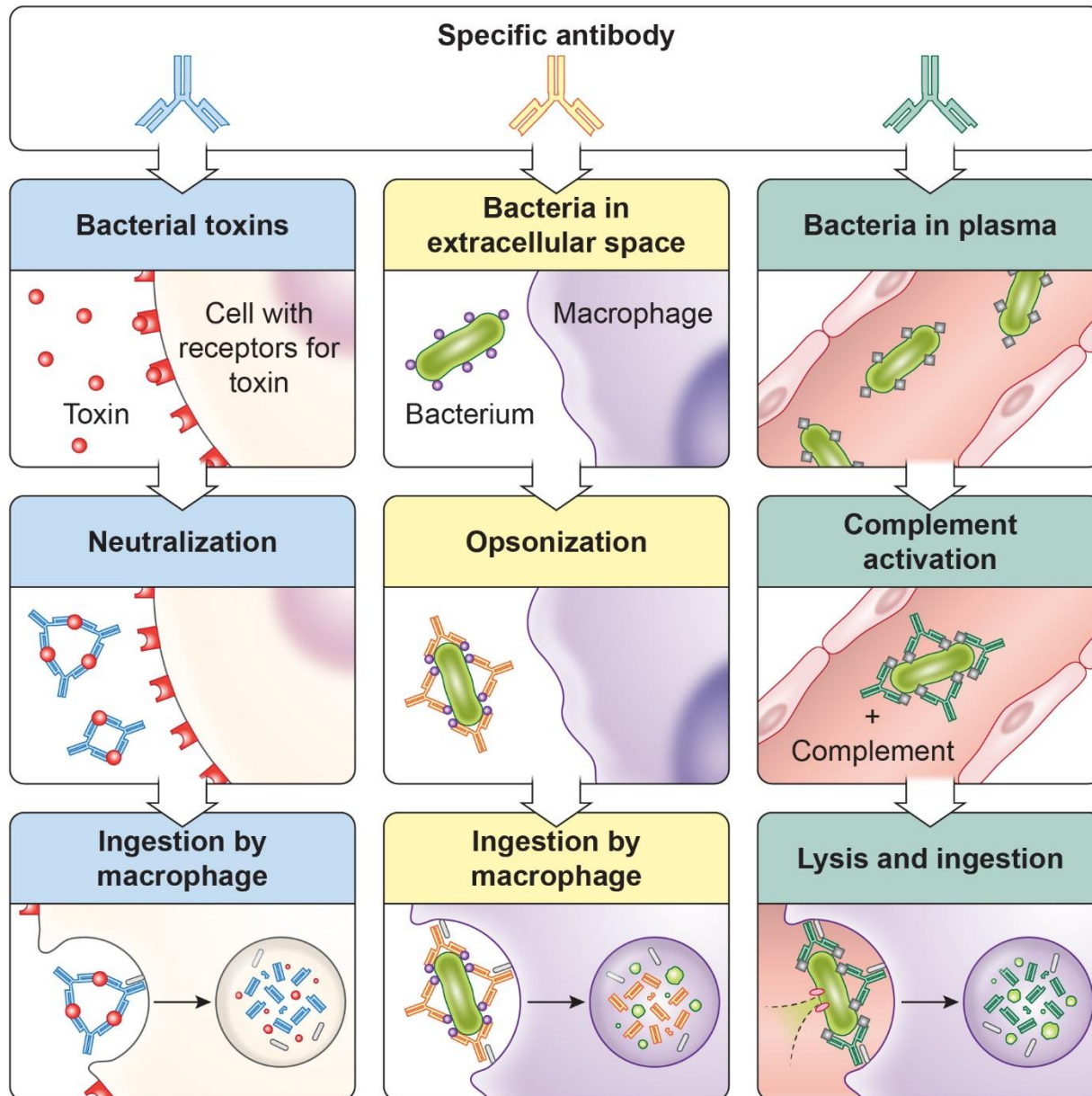
## CD4+ T cells (Helper T cells)



Different subtypes:  
Th1, Th2, Th17, Tregs



# Effector mechanisms of adaptive immunity



## B Cells

### Ab function:

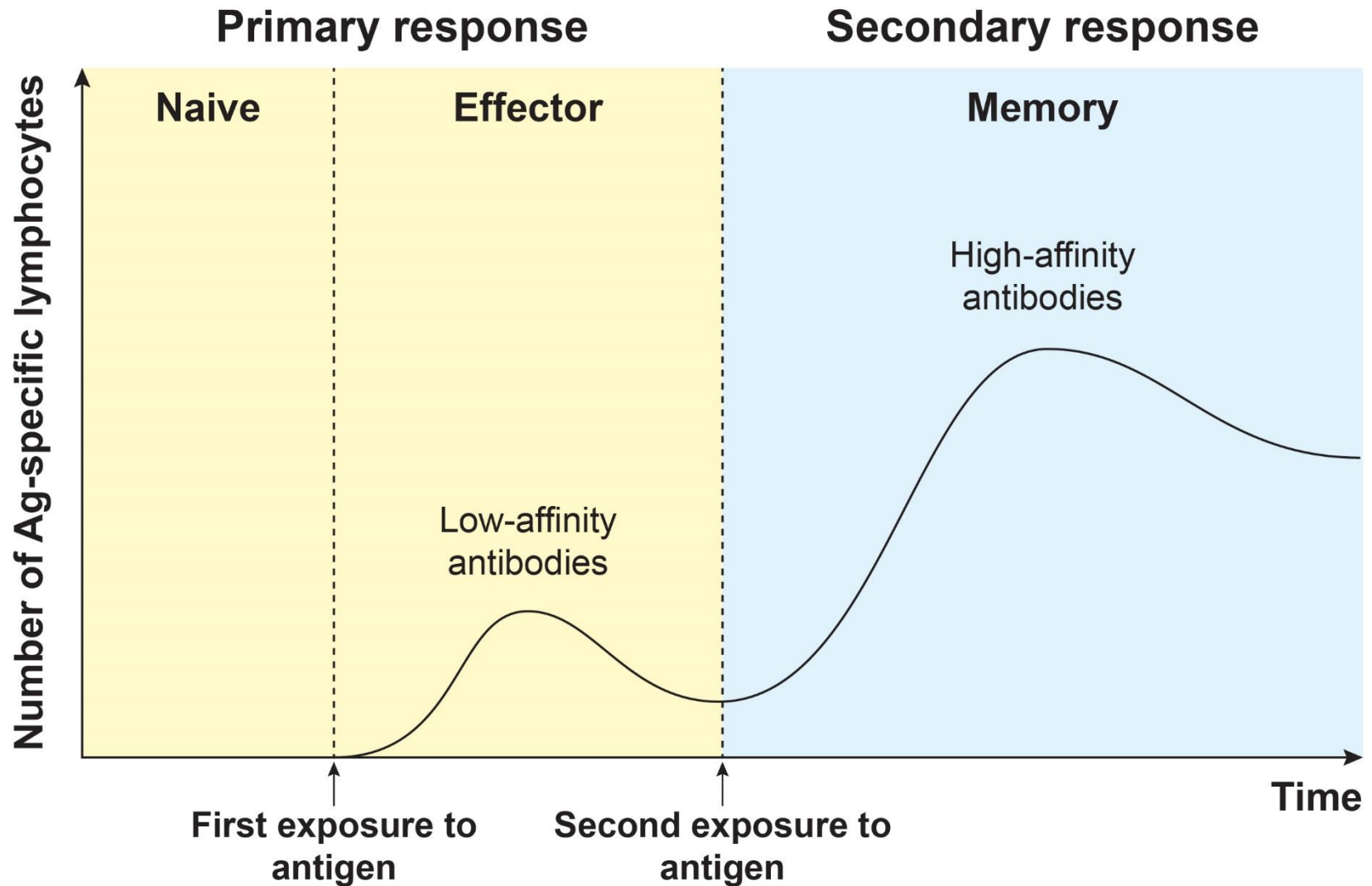
- Neutralize
- Block protein functions
- Promote engulfment
- Induce complement-mediated cell lysis

### Different classes (isotypes) of Ab

- IgM
- IgG
- IgE
- IgA



# Significance of immunological memory



- Typically expressed by professional APCs
- Presents peptides derived from exogenous proteins

To exist, tumors must evolve mechanisms to locally disable and/or evade the immune system.

The goal of immunotherapy, then, is to restore the capacity of the immune system to recognize and reject cancer.