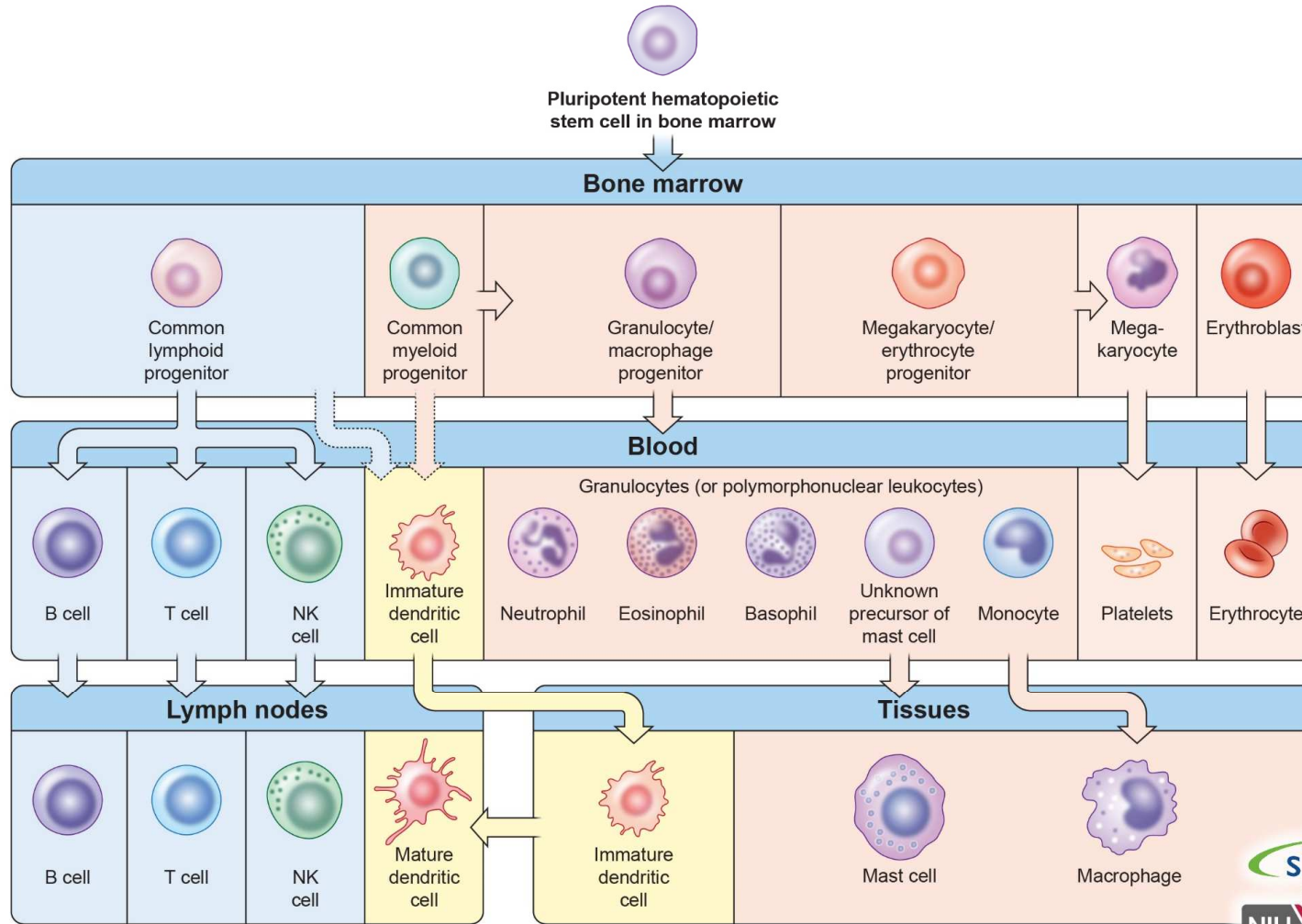
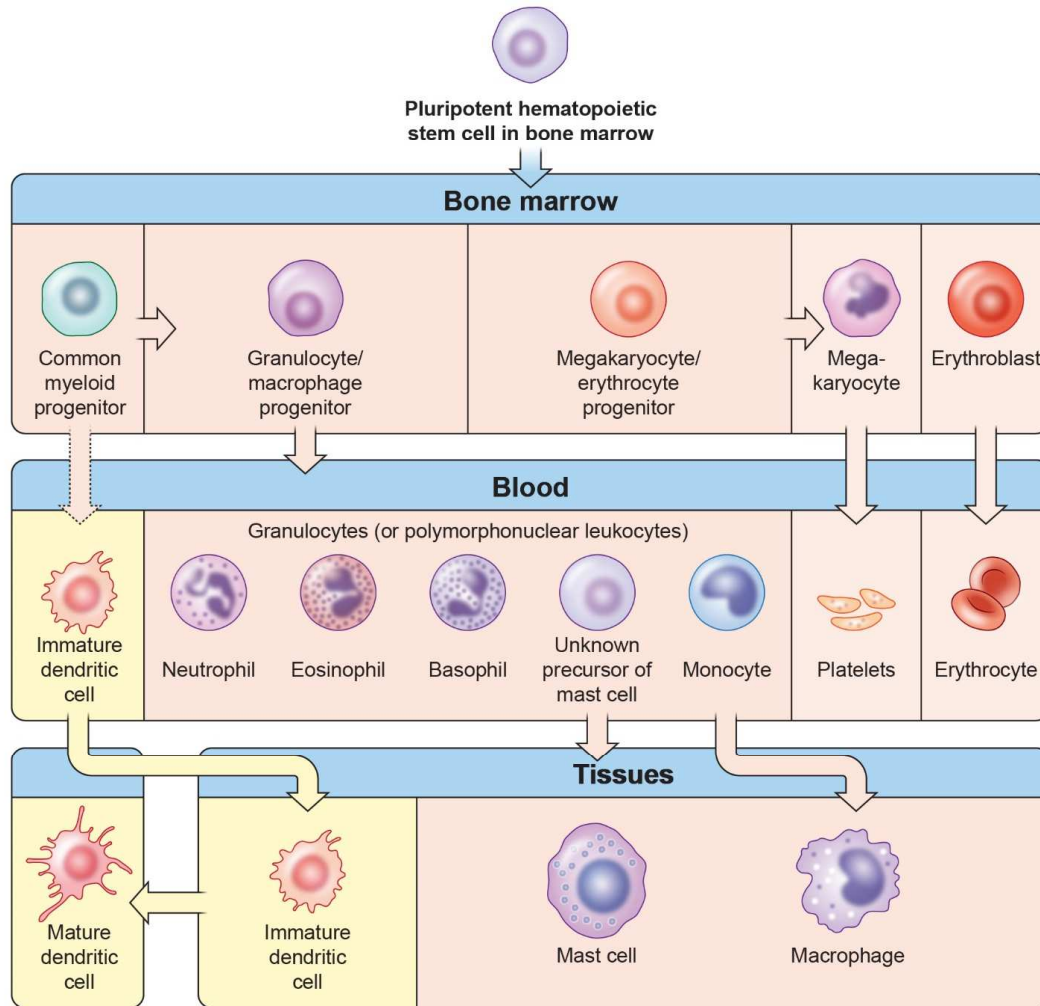


Immune cells are derived from stem cells in the bone marrow





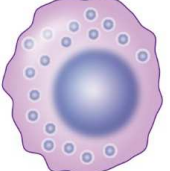

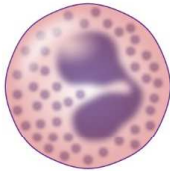



Myeloid cells



- 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

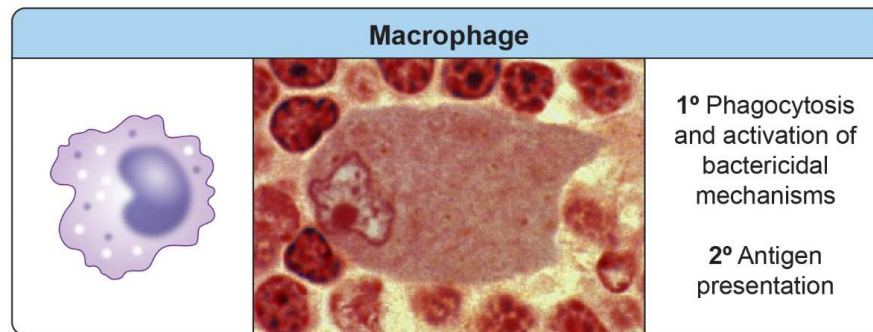
Short-lived cells that possess granules containing degradative enzymes and anti-microbial substances

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

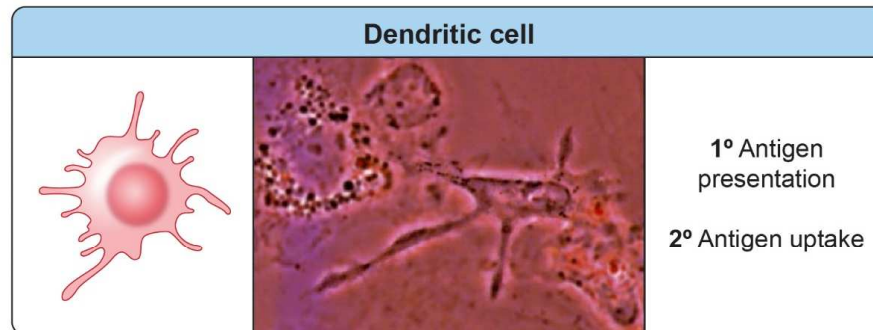
Neutrophils, eosinophils and basophils are sometimes referred to as polymorphonuclear leukocytes (PMNs)

Phagocytes

Neutrophils, macrophages and dendritic cells



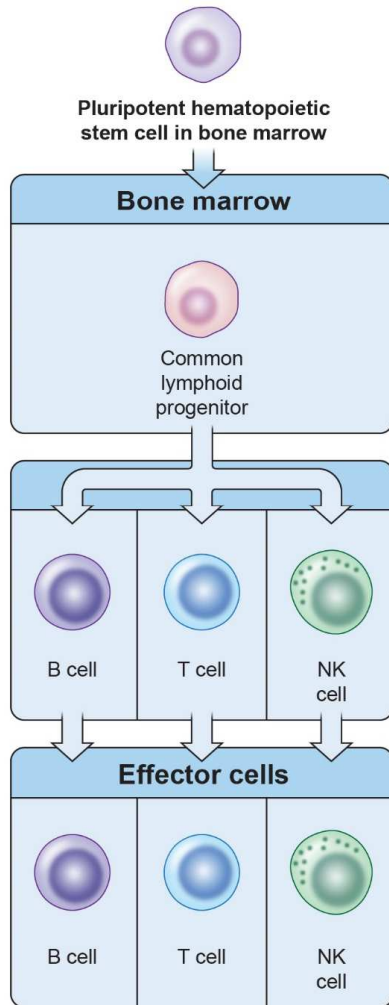
Reside in tissues



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



B cells

- Produce antibodies (Ab) that bind proteins

T cells

- Change antigens to peptides

Natural Killer (NK) cells

- Kill tumor and virus-infected cells
- Kill antibody-coated cells
- Play dominant role in mediating ADCC in vivo

Adaptive

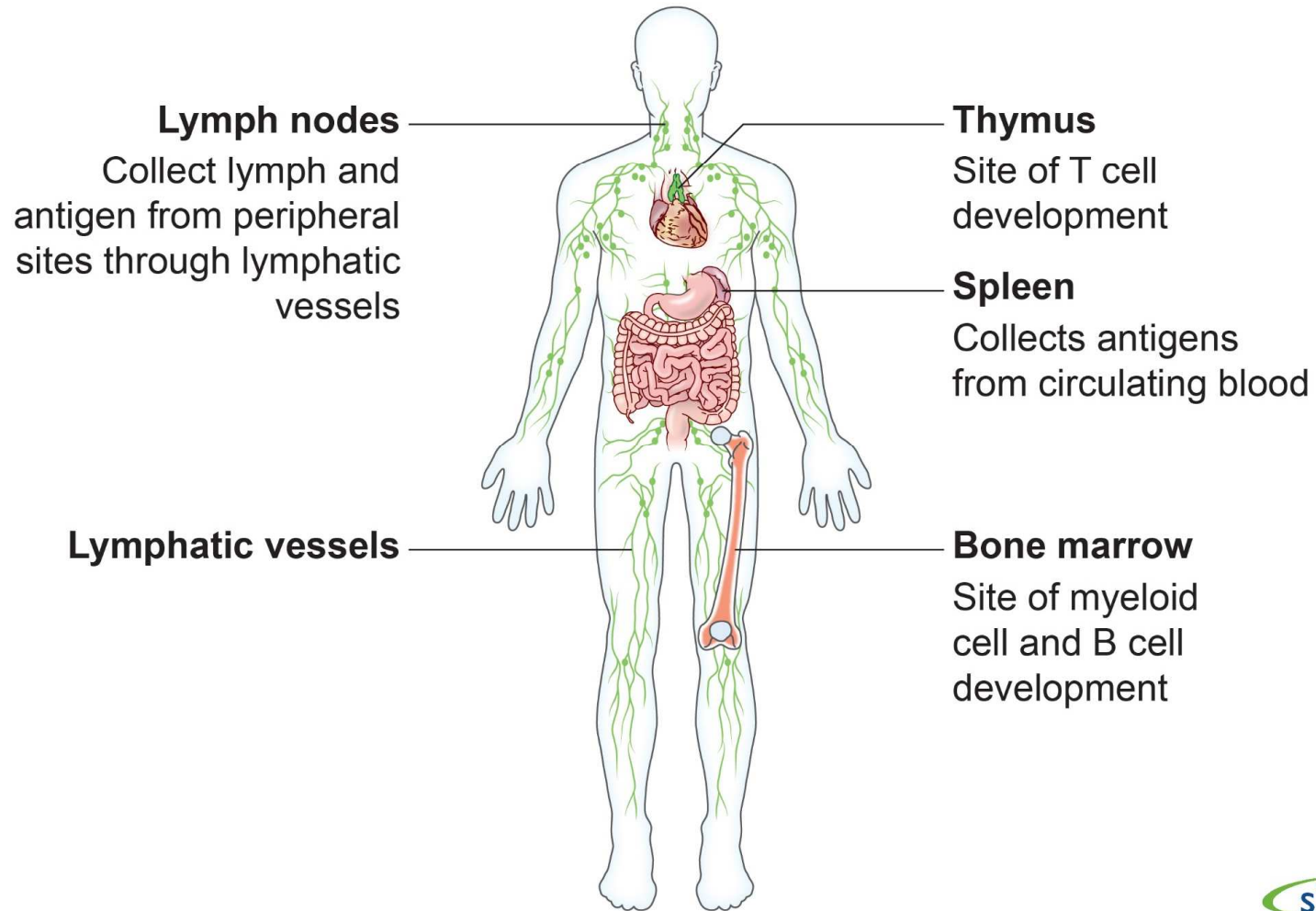
(recognize very specific antigens)

Innate

(recognize general features)



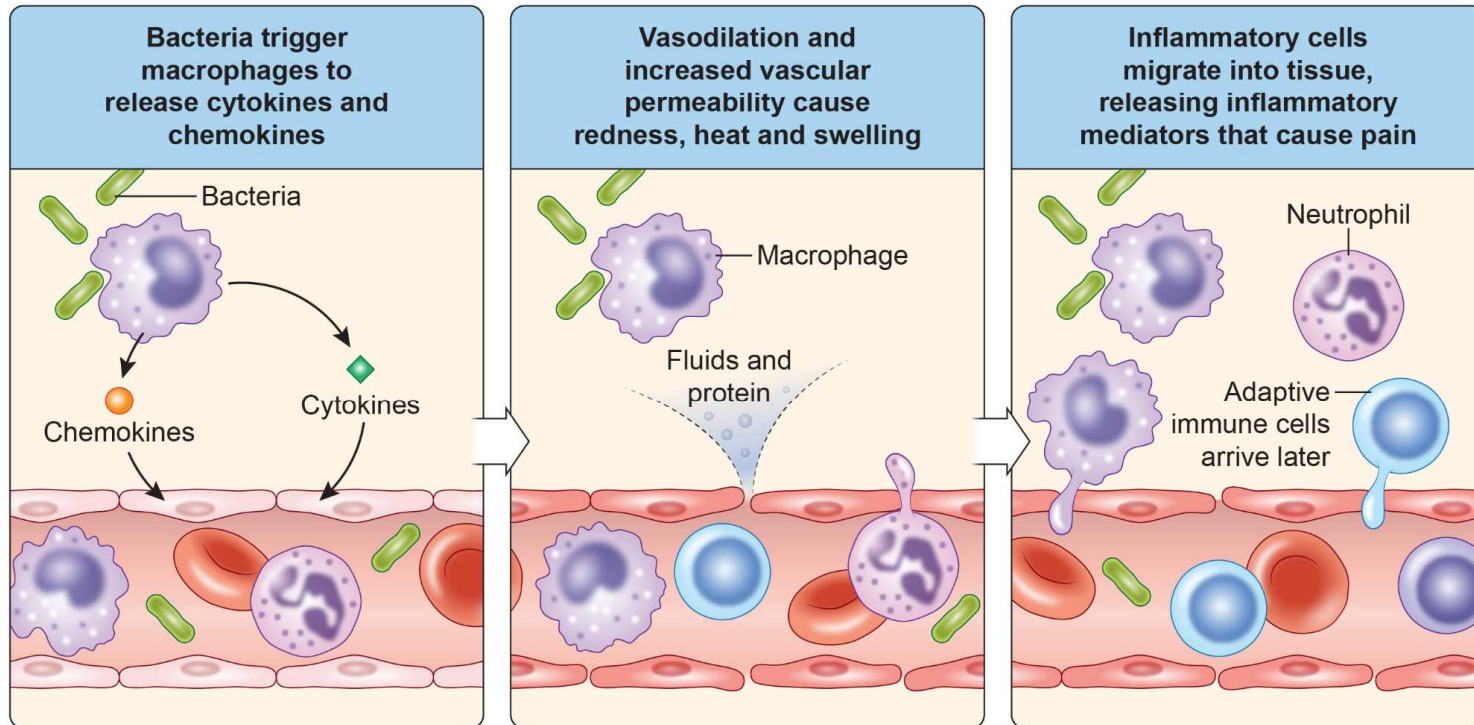
Lymphoid organs



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



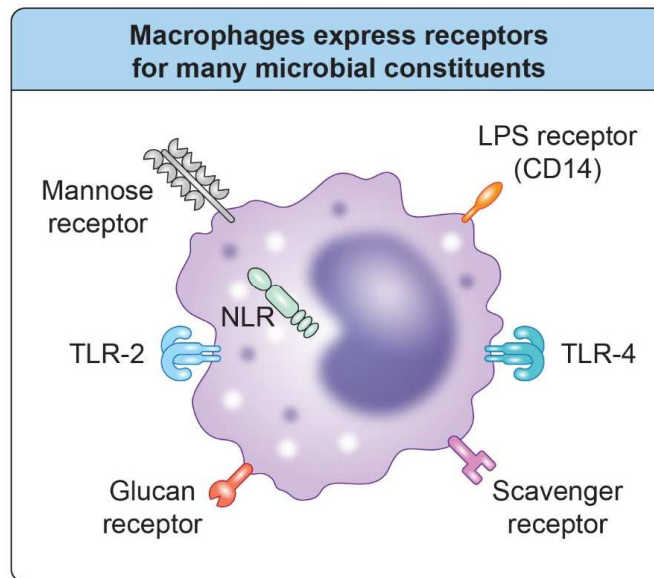
Infectious agents first activate innate immune cells resulting in an inflammatory response



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

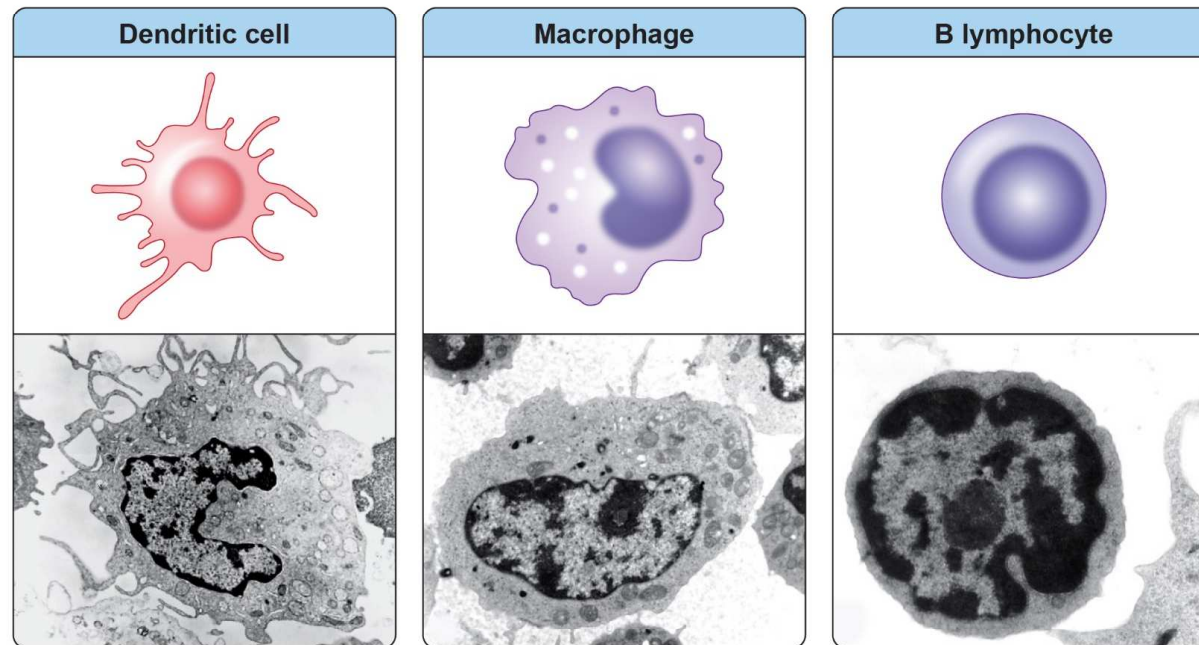
Types of PRRs

- 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)

Antigen processing and presentation

Professional APCs present Ag to naïve T cells and induce activation

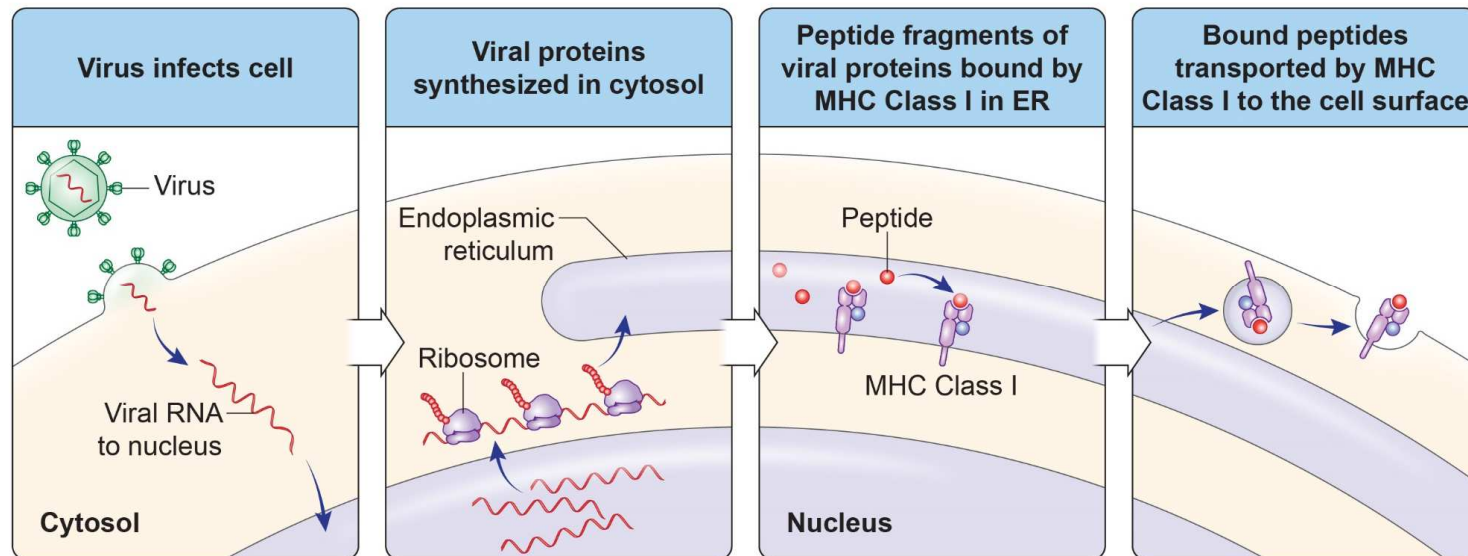


Immature DCs very
efficient at Ag processing
(in tissues)



Mature DCs very
efficient at Ag presentation
(in LNs)

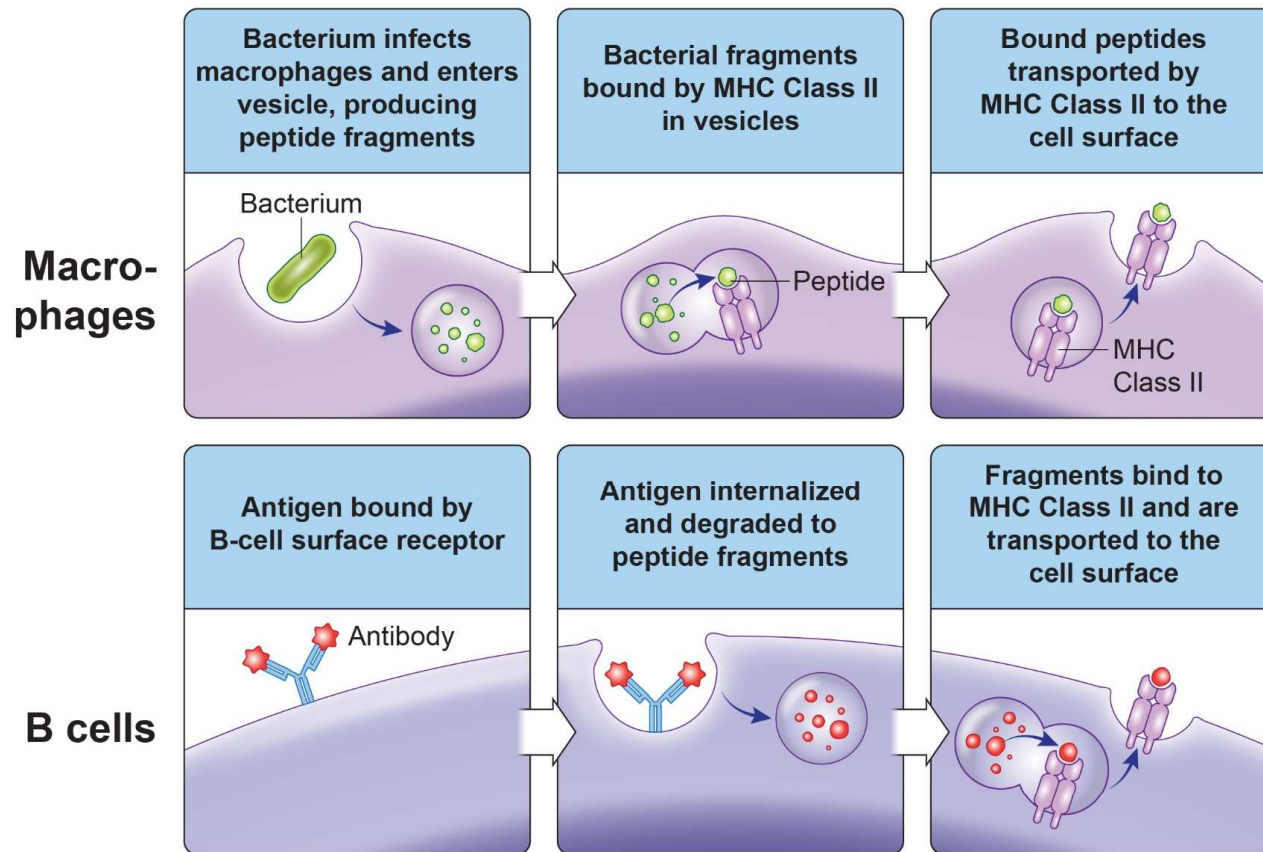
MHC Class I presents peptide antigens to CD8 T cells



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

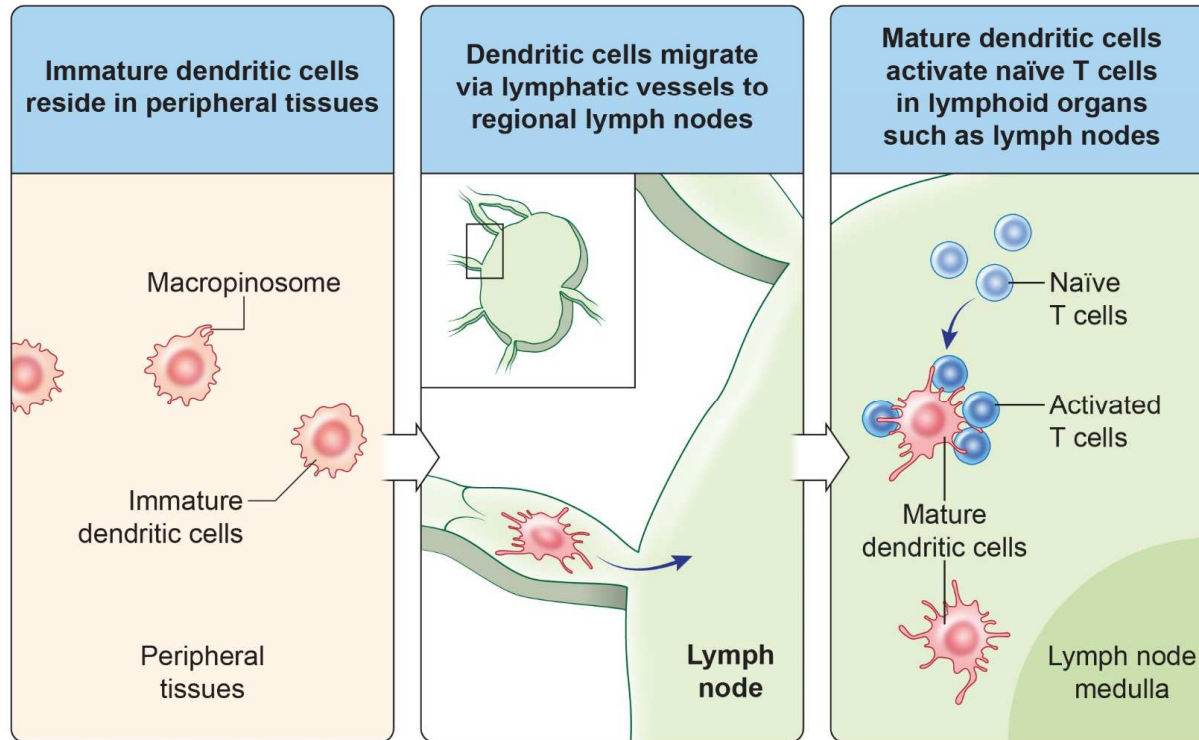
MHC Class II presents antigens to CD4 T cells



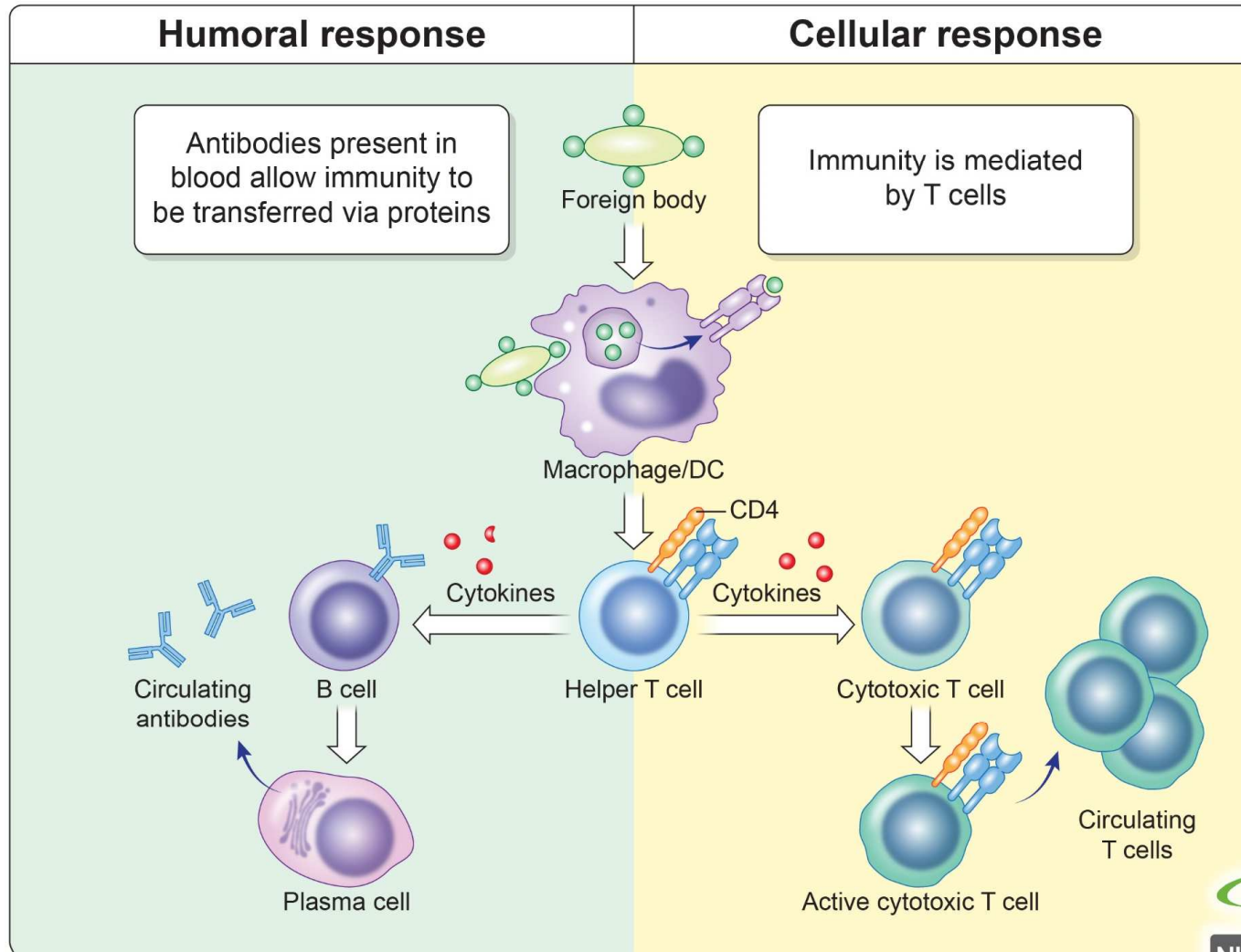
Major Histocompatibility Complex (MHC) Class II

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

DCs are important for initiating adaptive immune responses

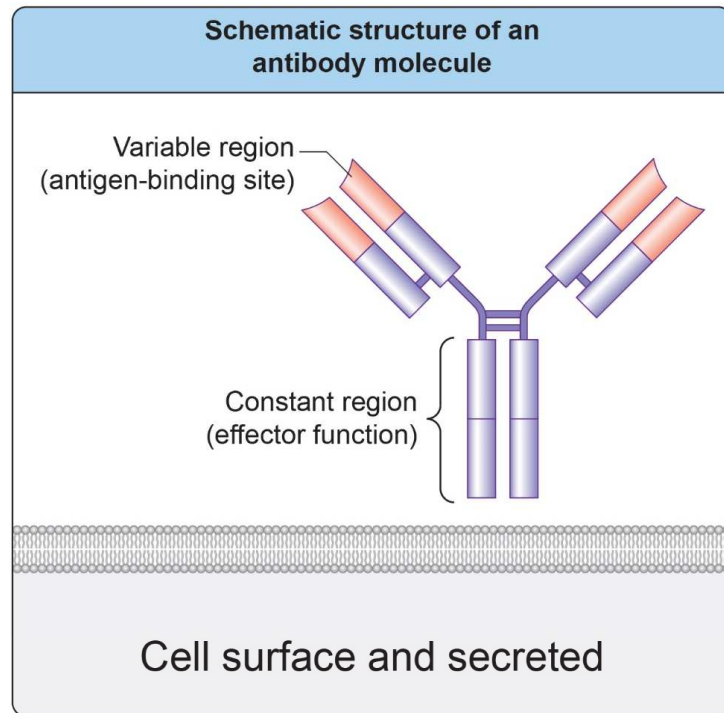


Adaptive immune responses

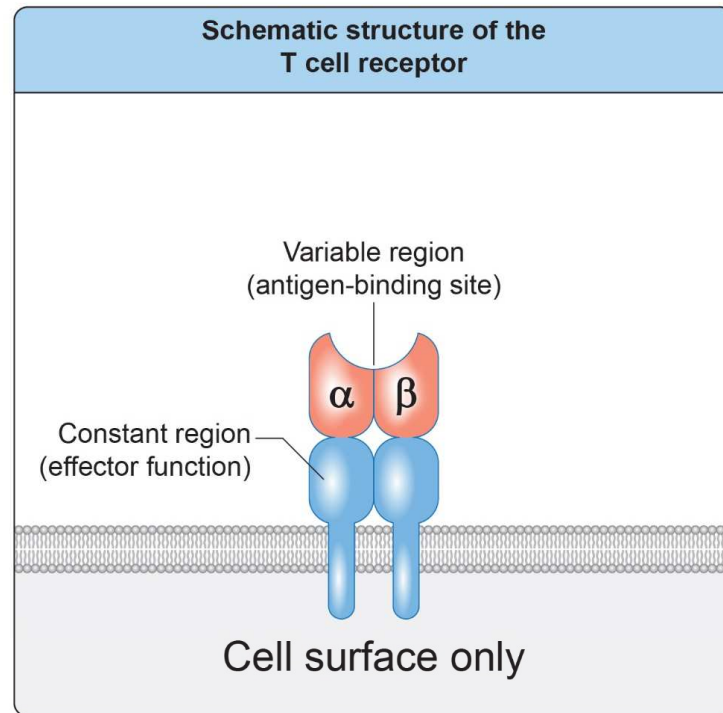


Antigen receptors

Antibody (Ab)

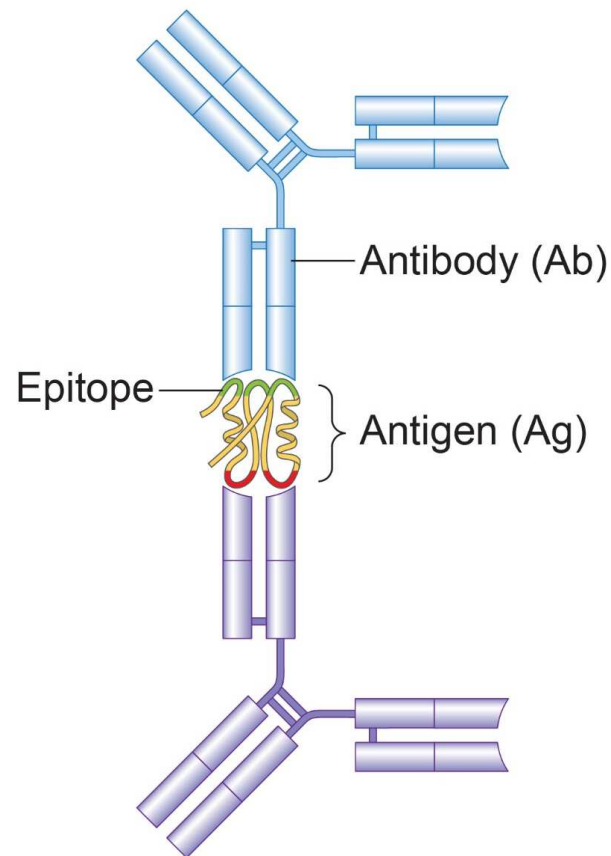


T cell receptor (TCR)

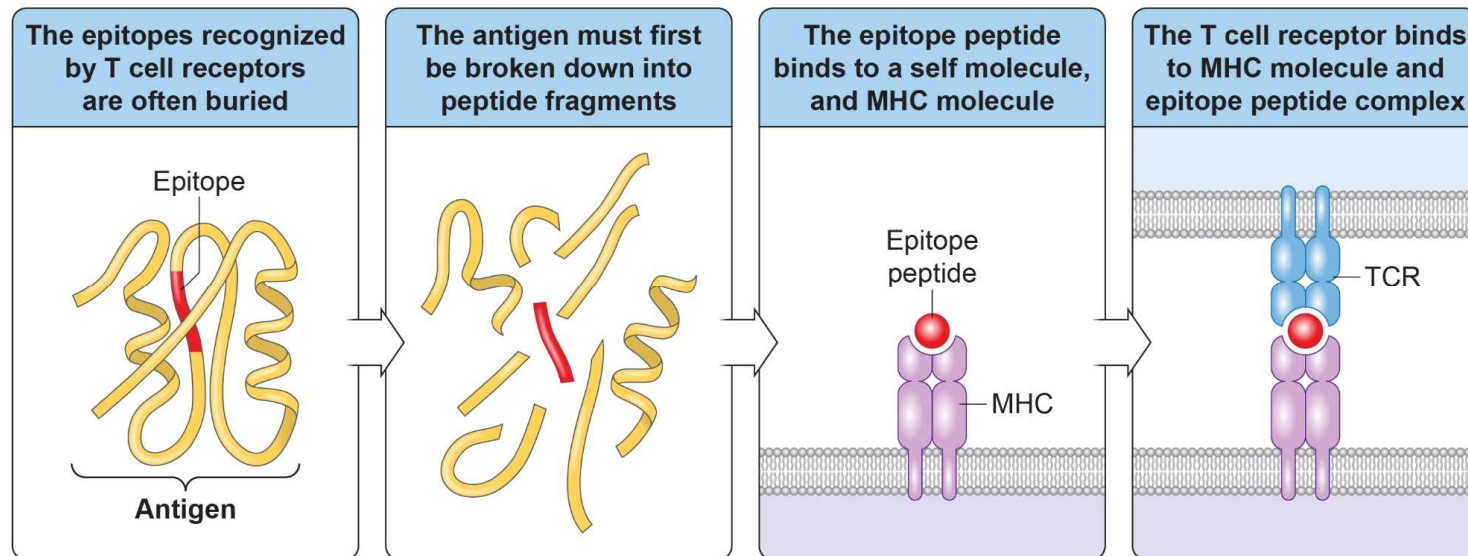


Antigen recognition by antibodies

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

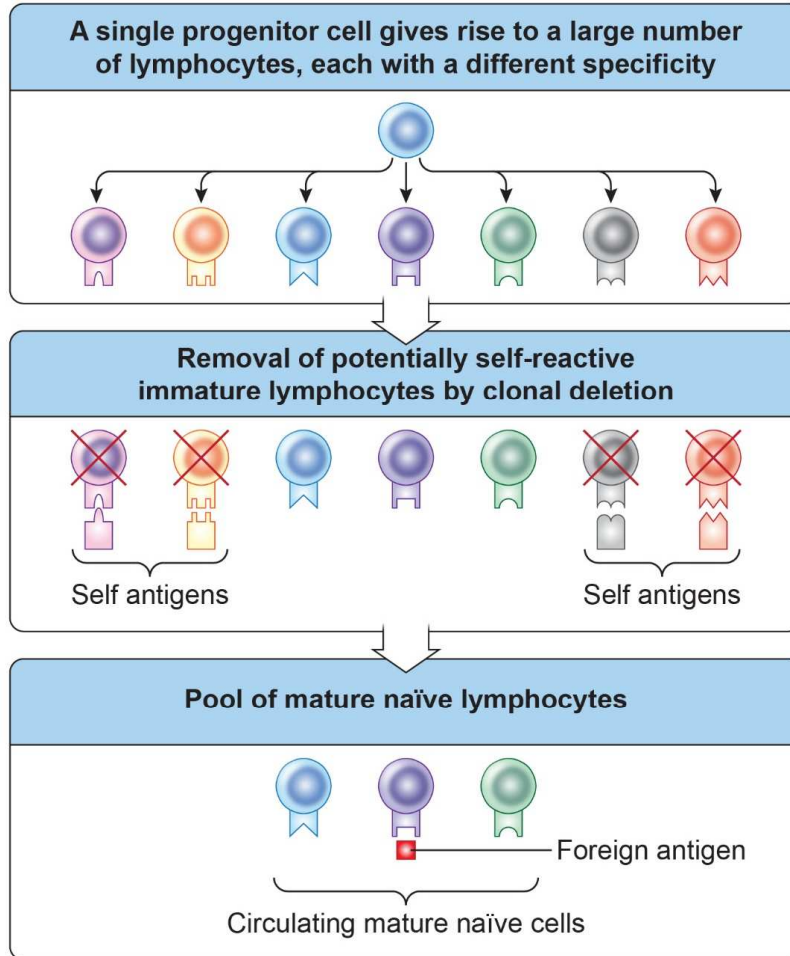


T cell receptors (TCRs) recognize processed proteins presented by MHC



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

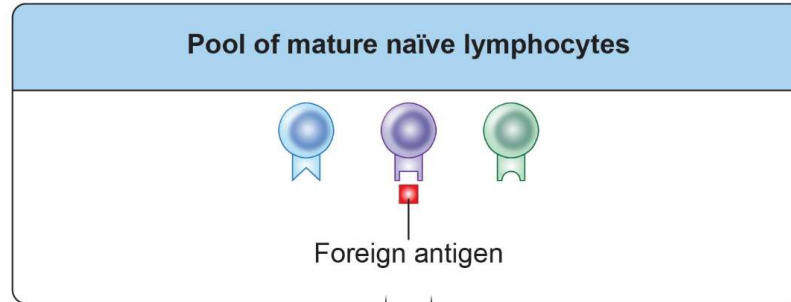
Mechanism of central tolerance

- Circulating mature naïve cells



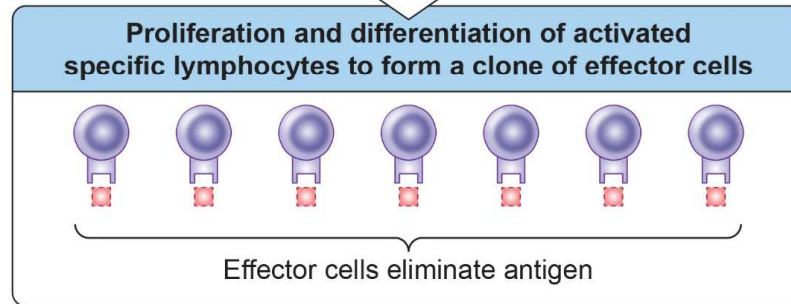
Lymphocyte activation

Naïve



Cells that recognize specific Ag are very rare

Activated or effectors



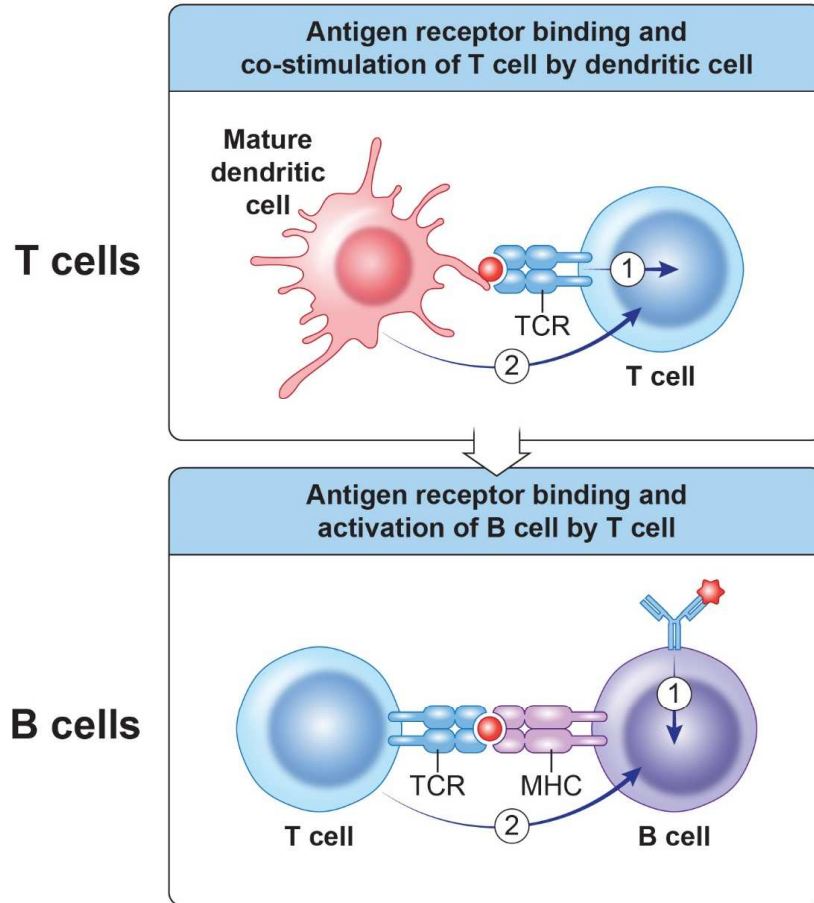
Results in:
• Expansion
• Acquisition of effector functions

What happens to T cells and B cells after immune response?

Differentiate into long-lived memory lymphocytes



Lymphocyte activation



Activation of T and B cells requires stimulation via:

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

Absence of co-stimulation leads to unresponsiveness

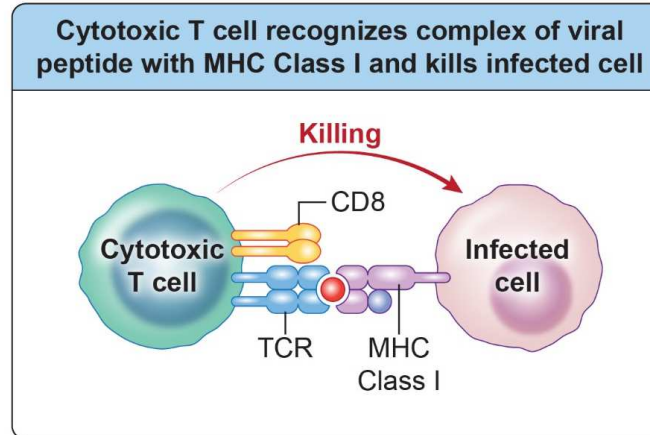
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Peripheral tolerance



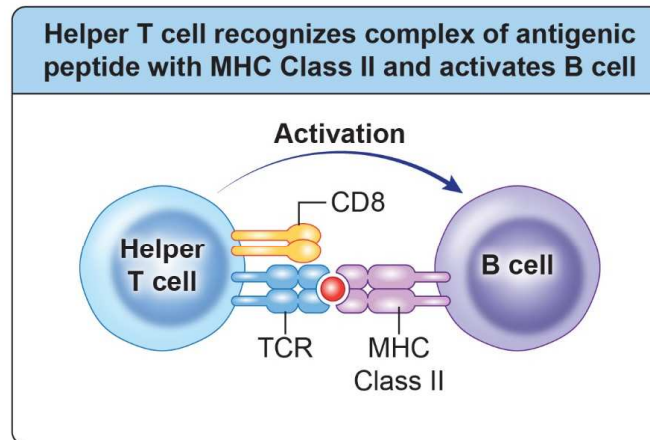
Effector mechanisms of adaptive immunity

CD8+ T cells
(Cytotoxic T cells)



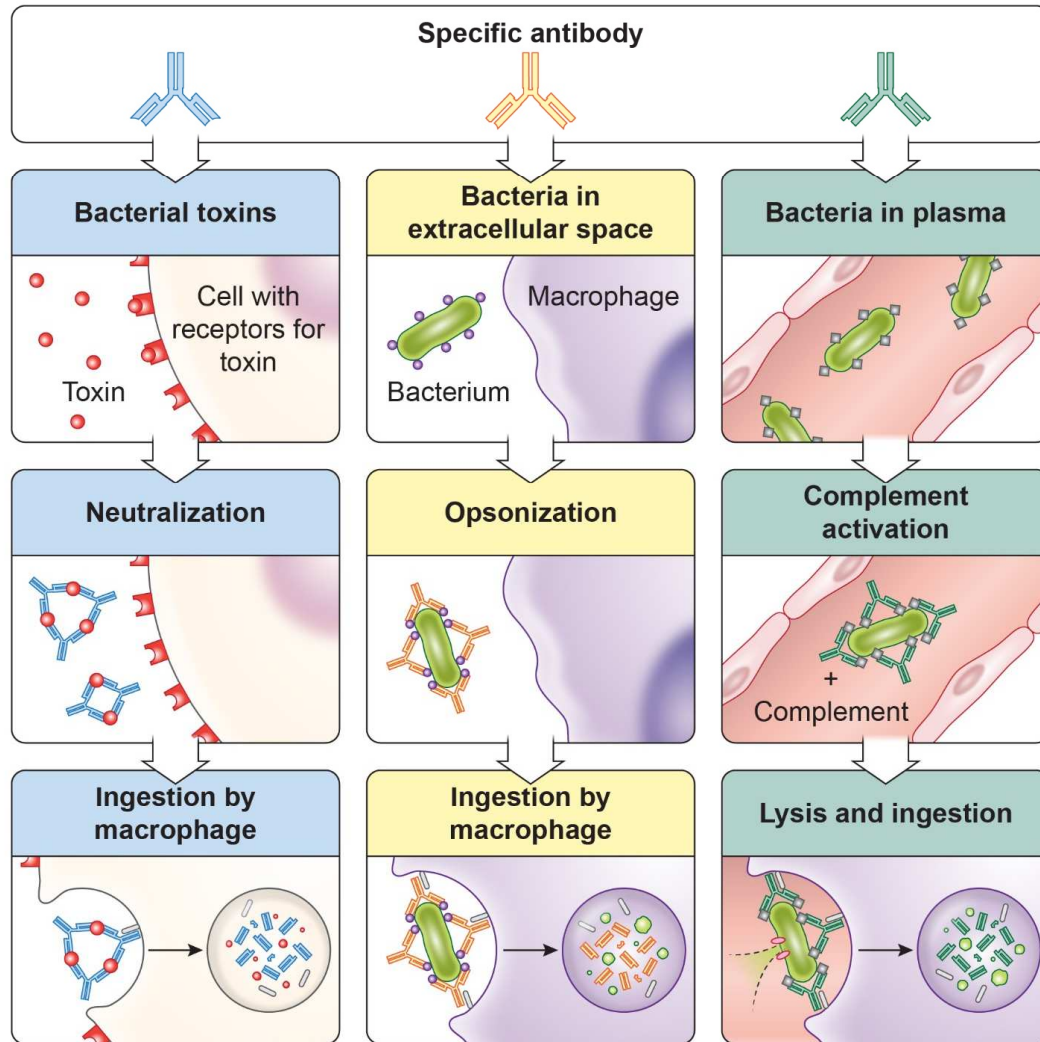
Produce proteins that lyse cells

CD4+ T cells
(Helper T cells)



Different subtypes:
Th1, Th2, Th17, Tregs

Effector mechanisms of adaptive immunity



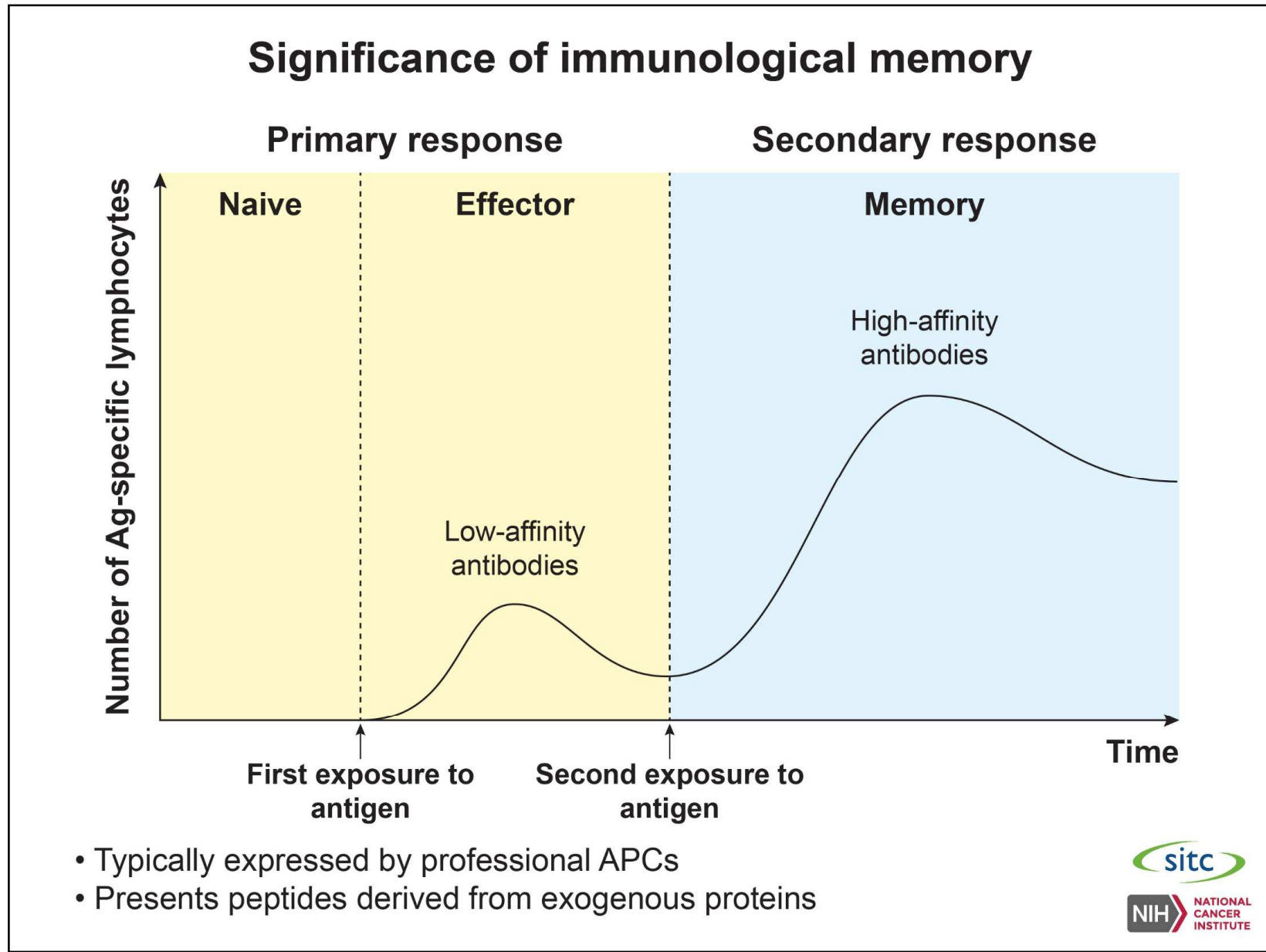
B Cells

Ab function:

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

Different classes (isotypes) of Ab

- IgM
- IgG
- IgE
- IgA



Immune responses can be beneficial or harmful

Antigen	Effect of response to antigen	
	Normal response	Deficient response
Infectious agent	Protective immunity	Recurrent infection
Innocuous substance	Allergy	No response
Grafted organ	Rejection	Acceptance
Self organ	Autoimmunity	Self tolerance
Tumor	Tumor immunity	Cancer

Effectiveness of mechanisms mediating immune tolerance and regulation

