

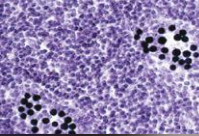
The Immune System: An Overview



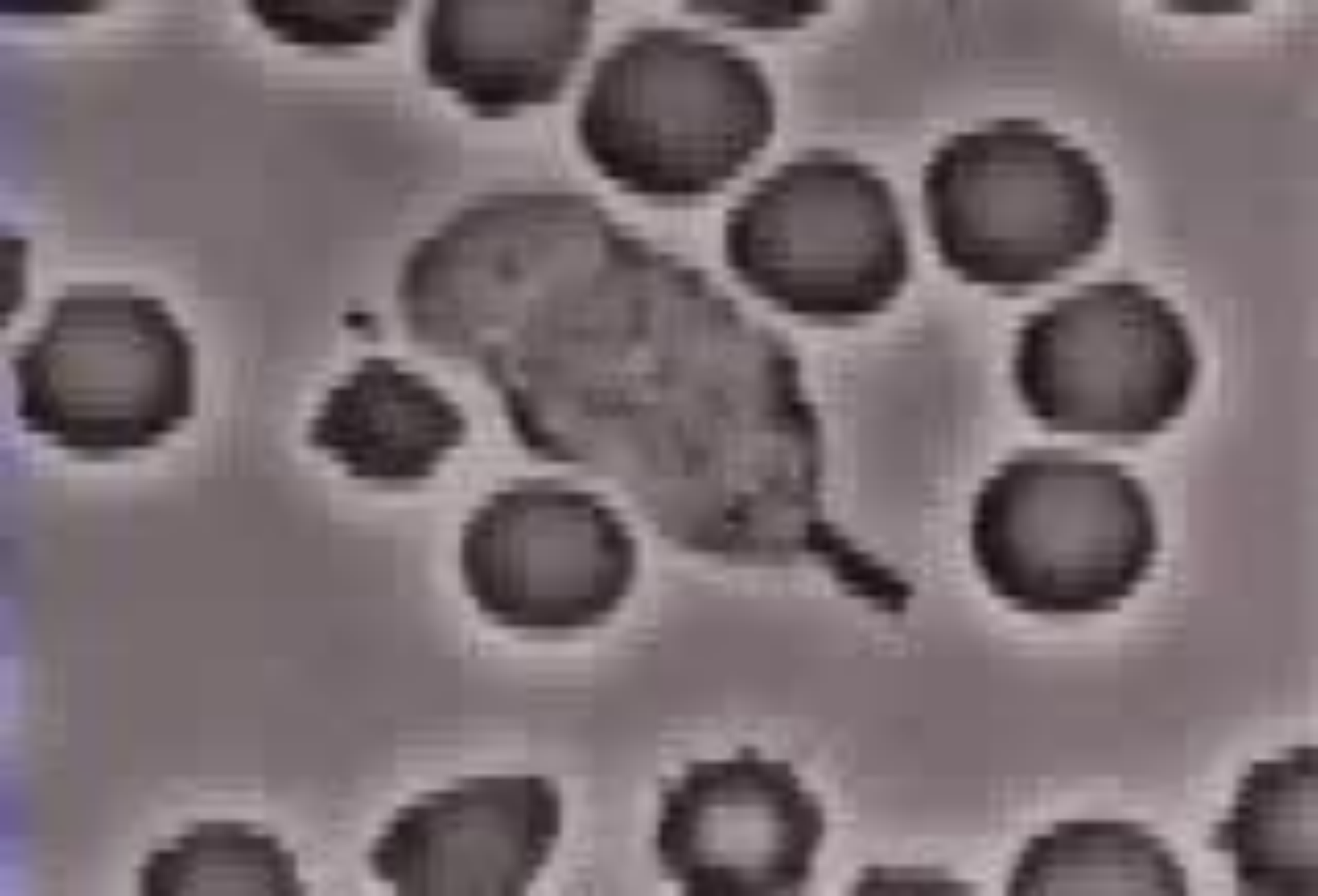
Shiv Pillai MD, PhD

Ragon Institute, Massachusetts General Hospital

Harvard Medical School



Magic for a melancholic mind



Innate vs Adaptive Immunity

Innate Immunity

(Immediate, not specific)

Adaptive Immunity

(Takes days, very specific, HUGE repertoire)

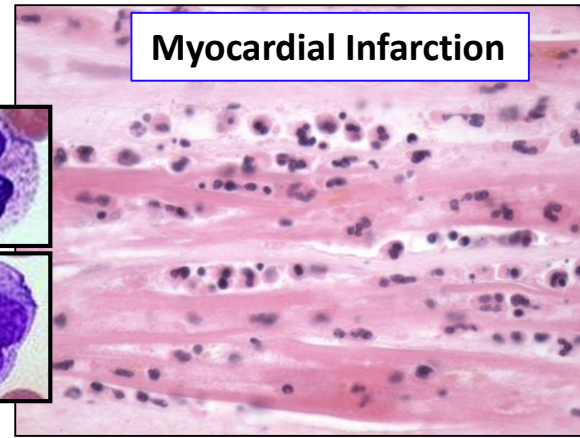
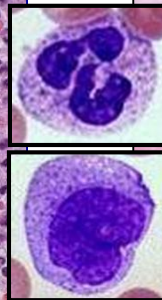
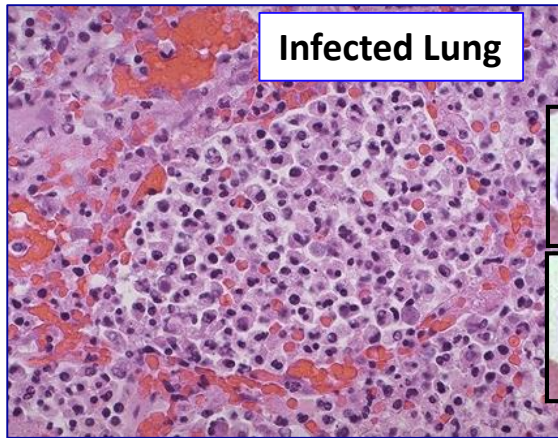
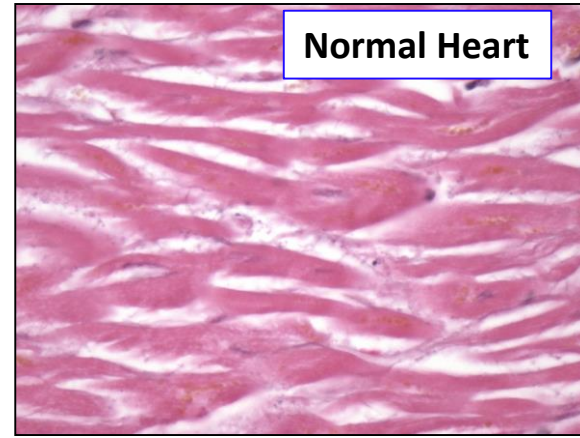
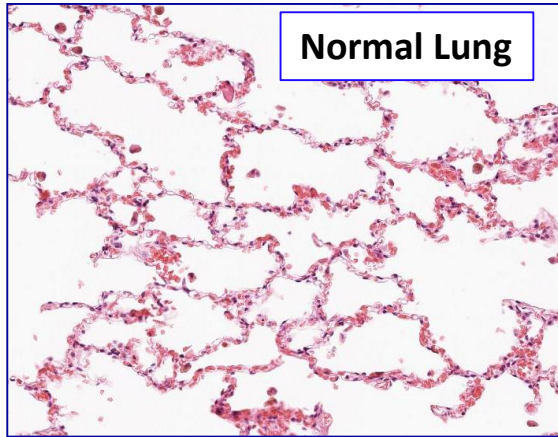
Innate Immunity

Inflammation

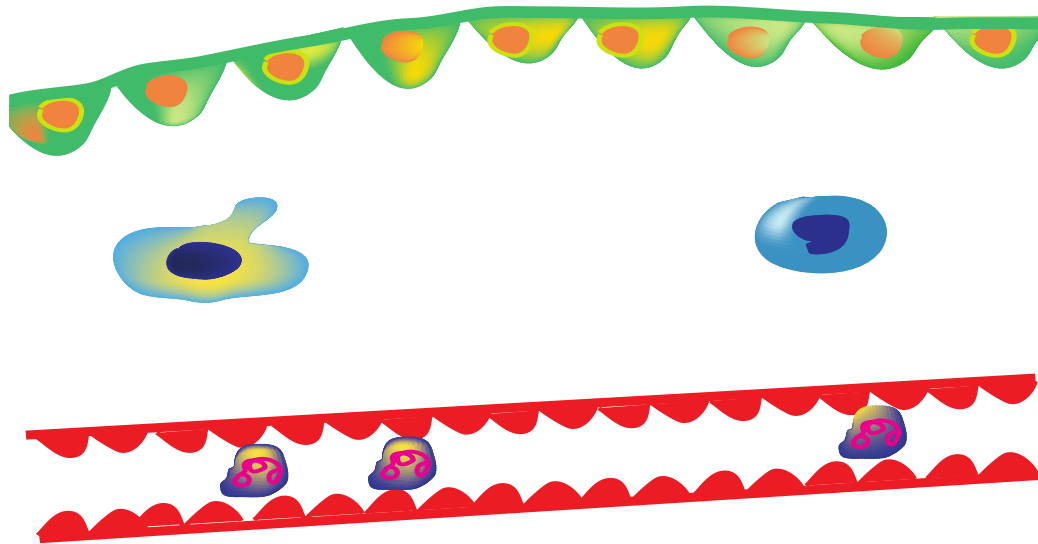
The anti-viral state

Acute Inflammation:

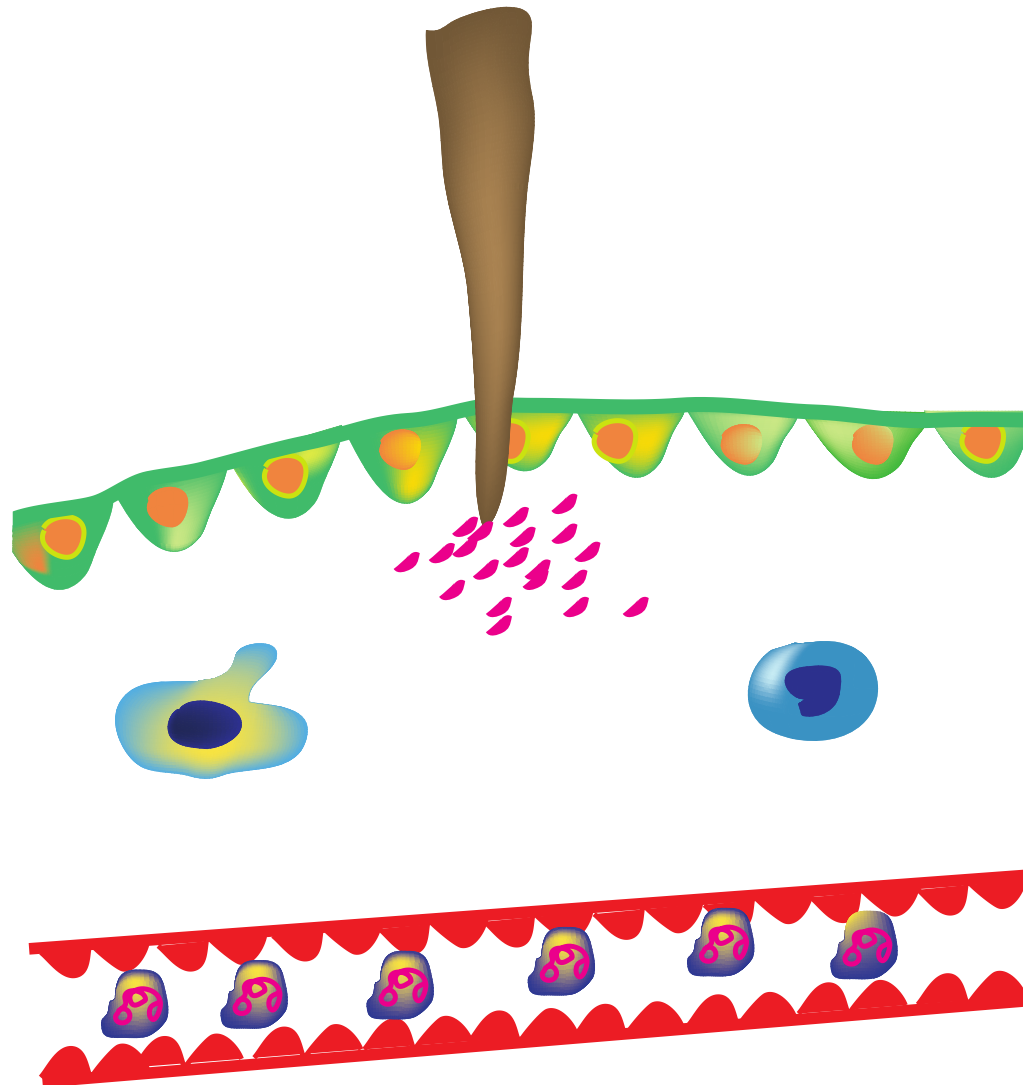
An Innate Immune Response to Infection or Sterile Injury



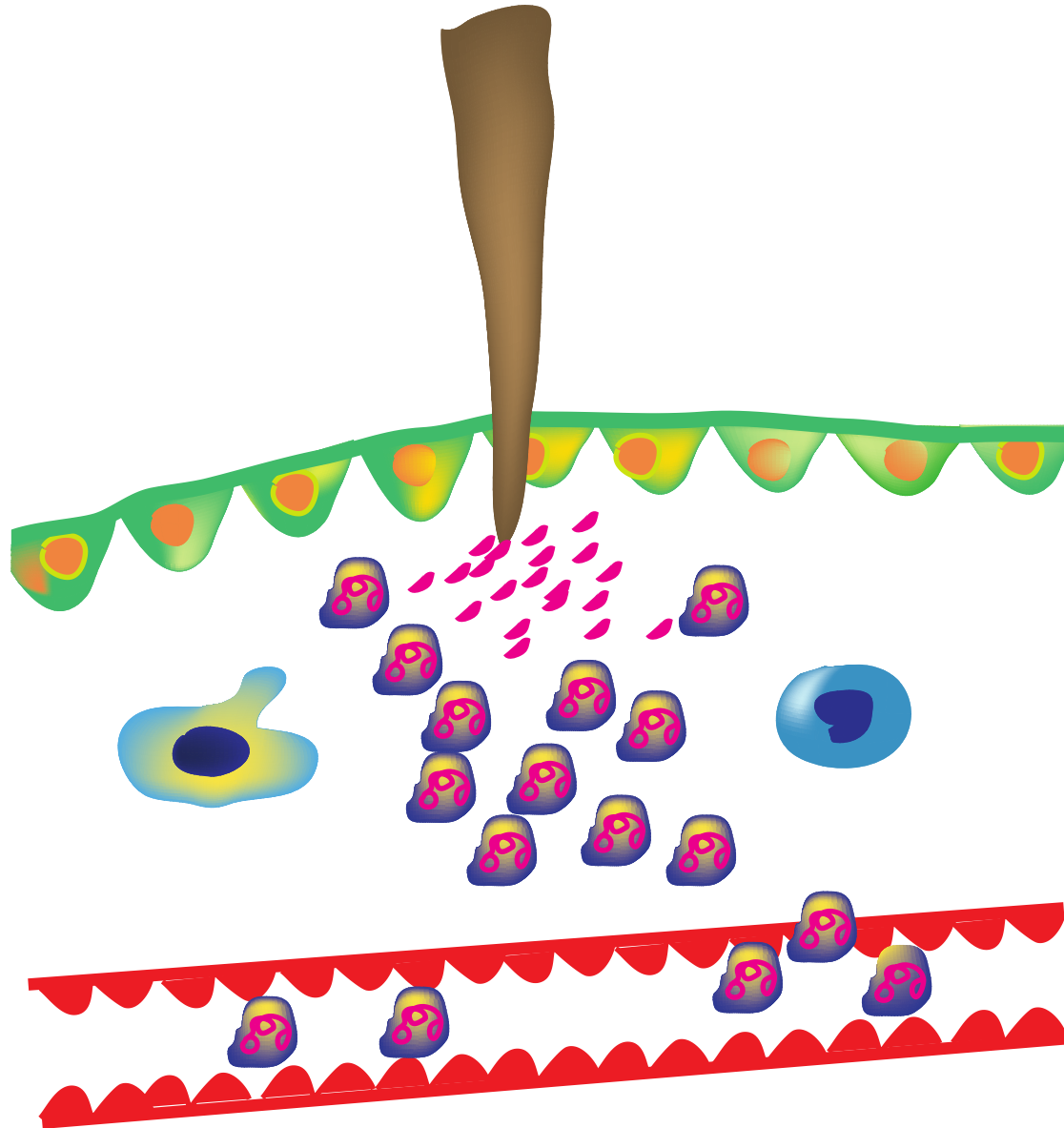
Tissue Sentinels: Macrophages and Mast Cells



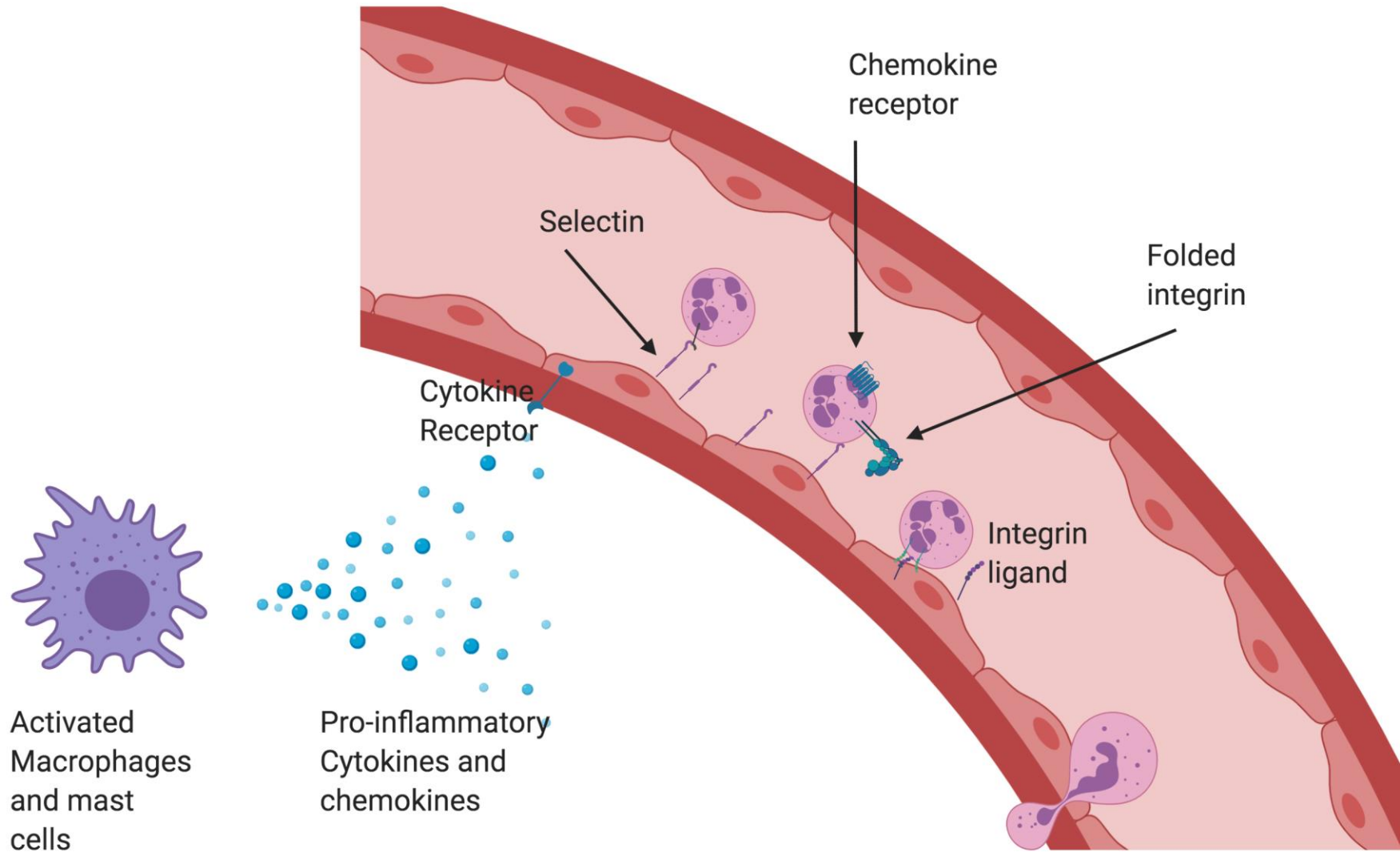
BARRIER DISRUPTION AND PENETRATION BY PATHOGENS



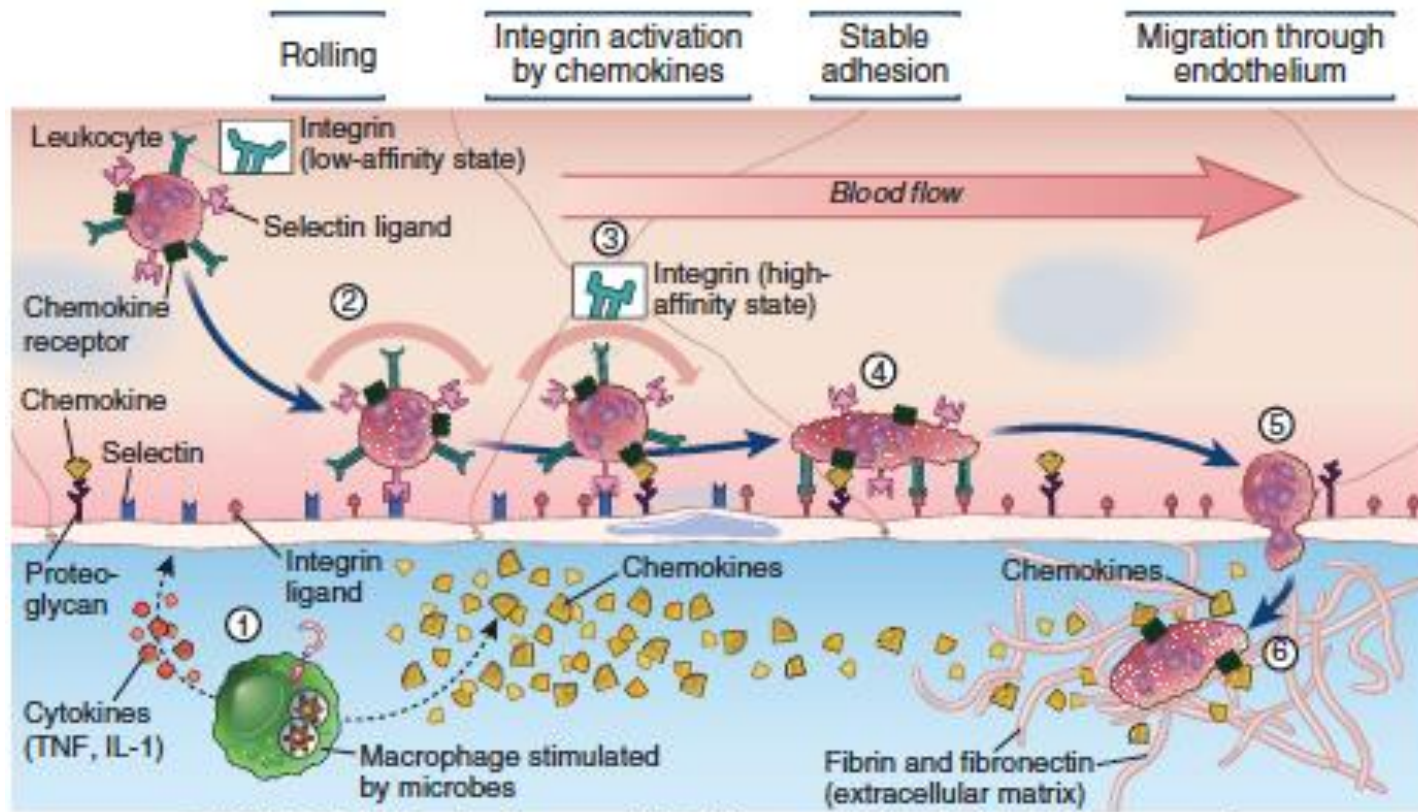
Neutrophil Recruitment and Inflammation



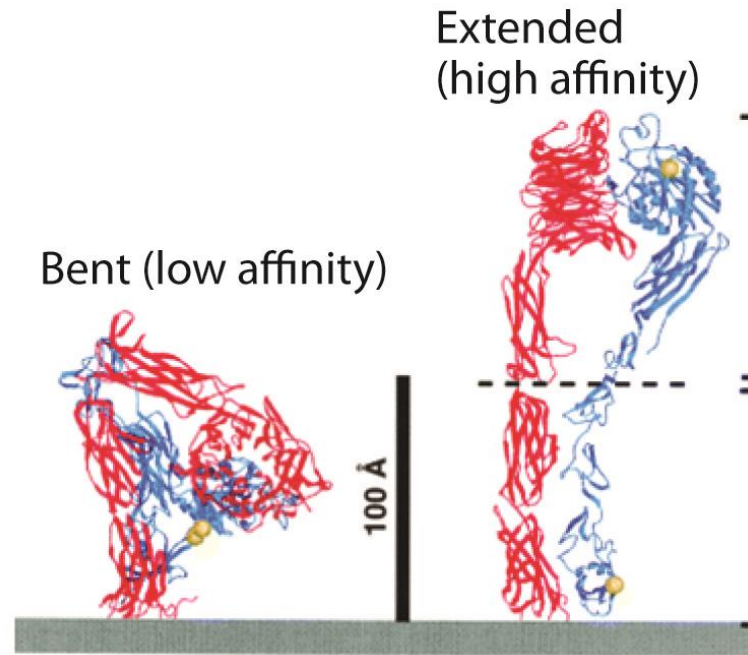
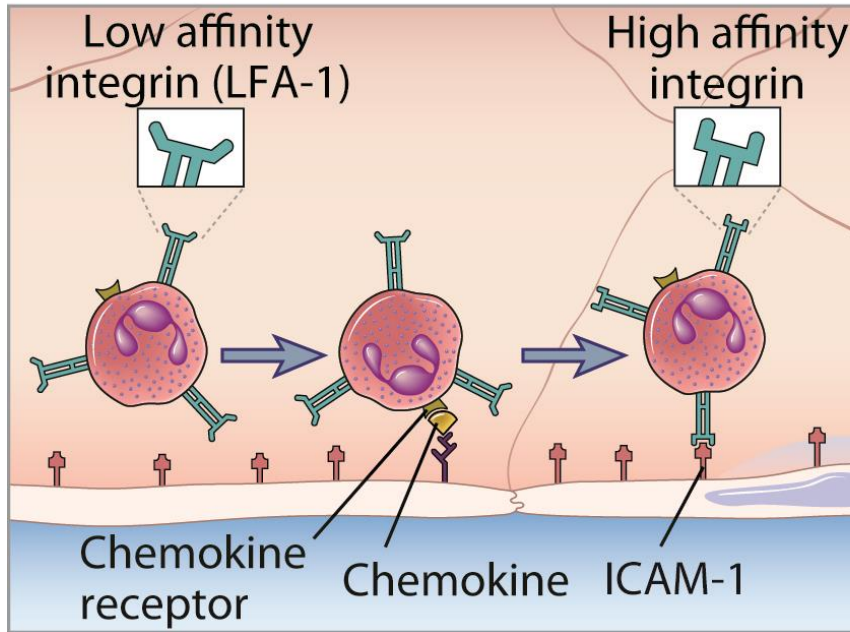
Three step model for leukocyte migration



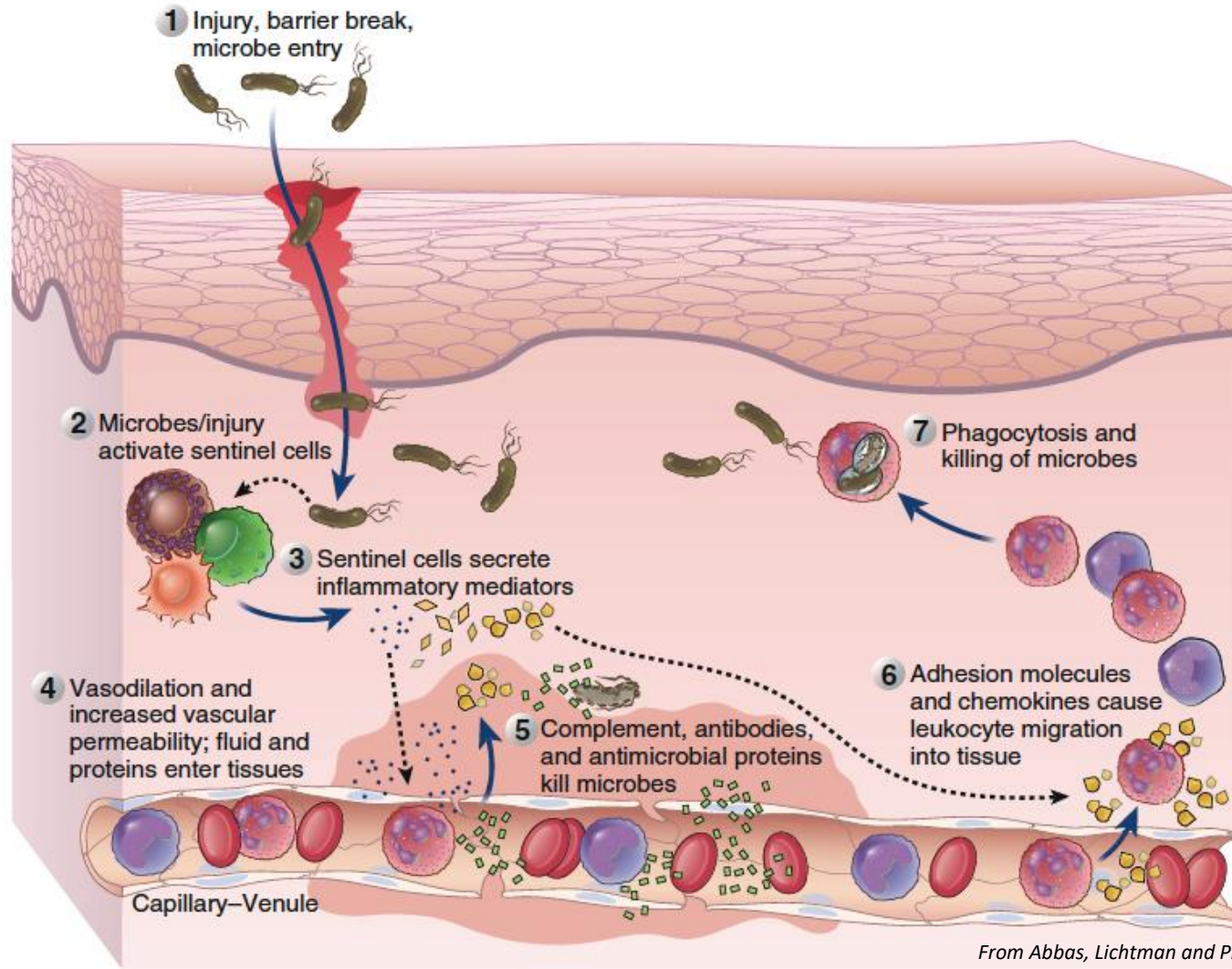
3-Step Model



Integrin Activation by Chemokines




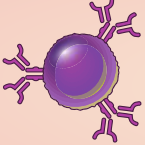

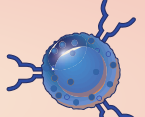
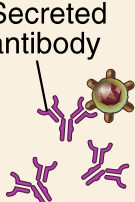
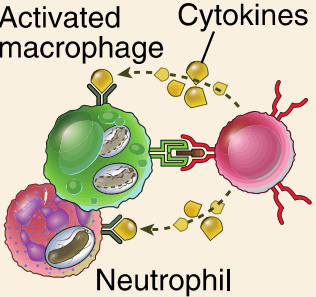
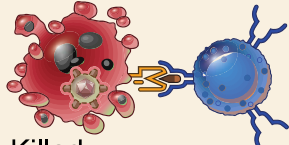


An overview of Inflammation



Pus and Glory.....

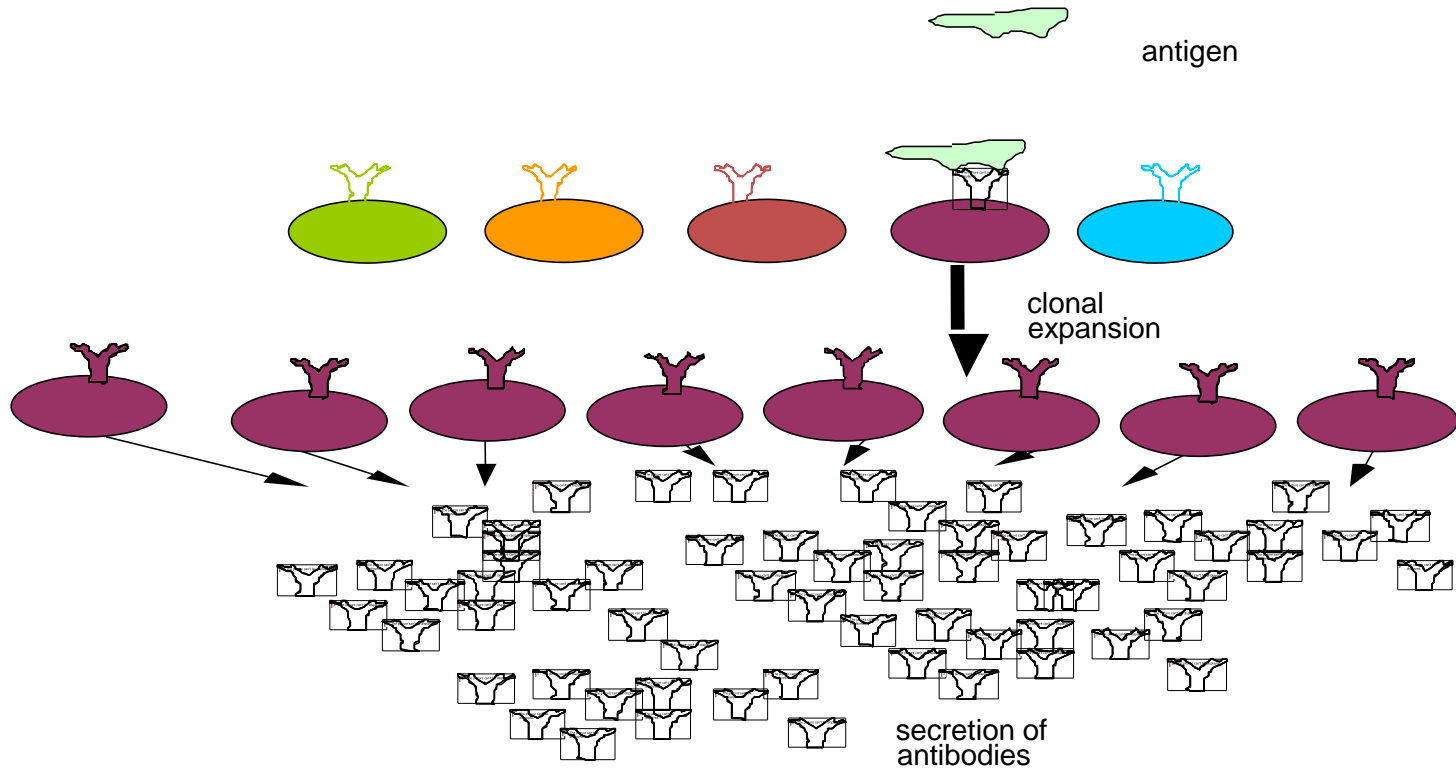
HUMORAL AND CELL-MEDIATED IMMUNITY

	Humoral immunity	Cell-mediated immunity	
Microbe	 Extracellular microbes	Extracellular microbes  Phagocytosed microbes that can live within macrophages	 Intracellular microbes (e.g., viruses) replicating within infected cell
Responding lymphocytes	 B lymphocyte	 Helper T lymphocyte	 Cytotoxic T lymphocyte
Effector mechanism	 Secreted antibody	 Activated macrophage Cytokines Neutrophil	 Killed infected cell
Functions	Antibodies prevent infections and eliminate extracellular microbes	Cytokine-activated phagocytes kill microbes	CTLs kill infected cells and eliminate reservoirs of infection

The central questions of Immunology

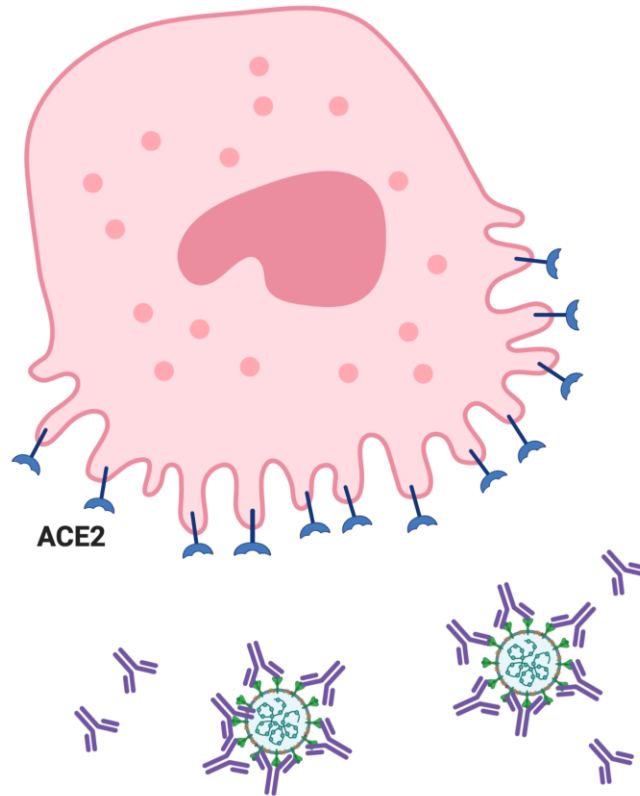
GOD

Self-Non-self Recognition



NEUTRALIZING ANTIBODIES BLOCK ENTRY OR NEGATE FUNCTION

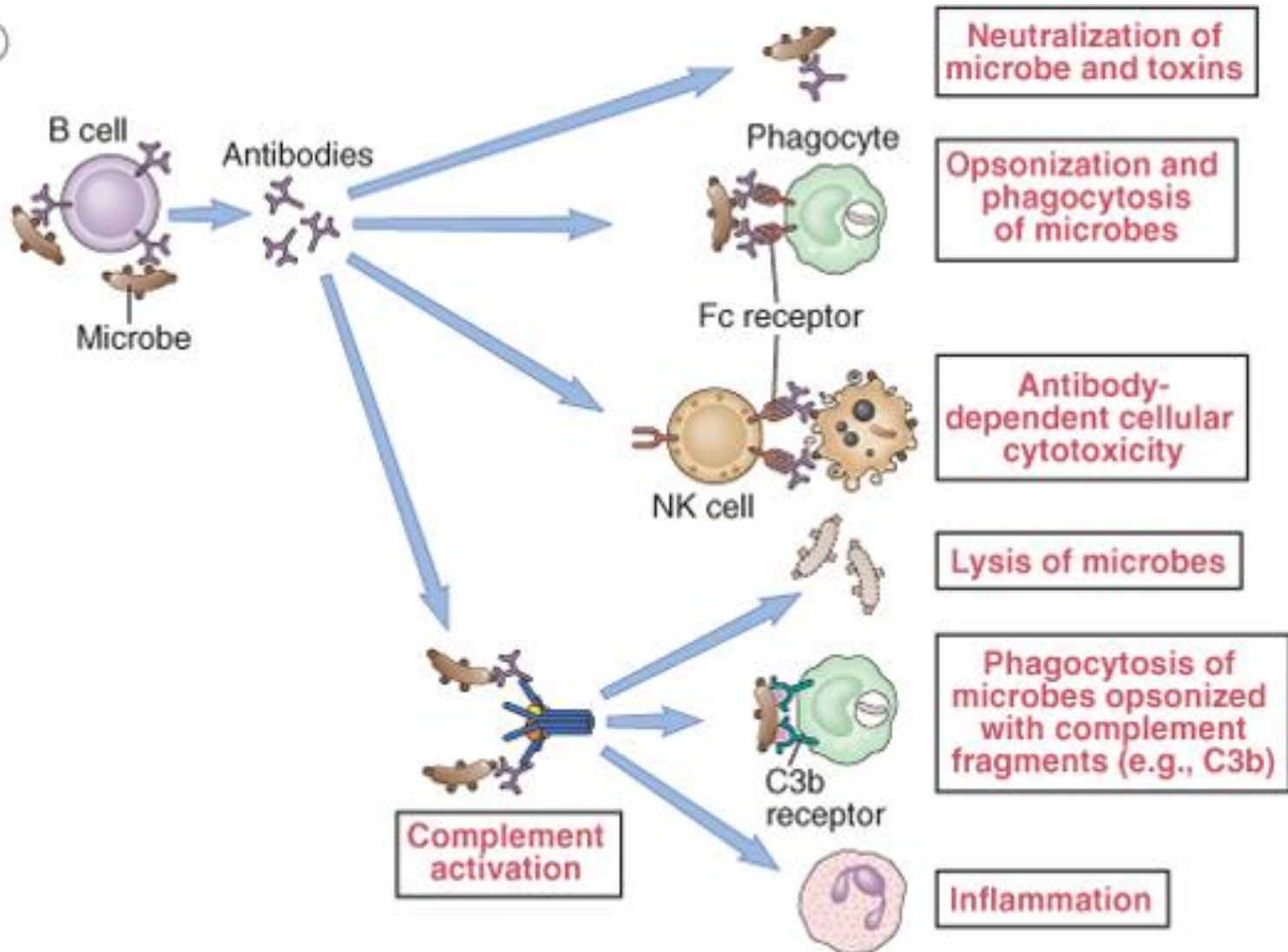
Antibodies preventing viral entry into cells



coronavirus neutralized by antibody

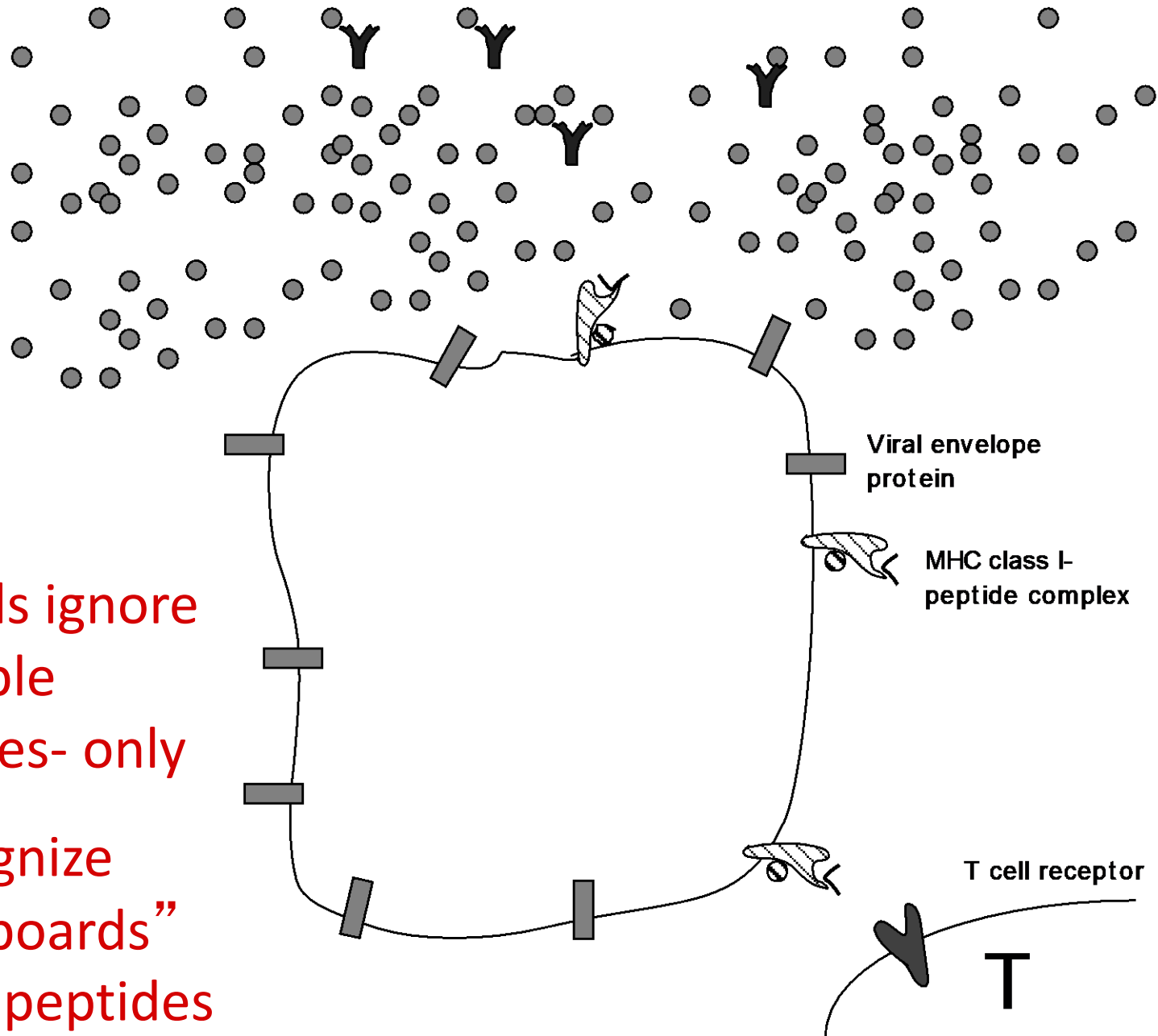
The effector functions of antibodies

(A)



Why do we need T cells?

T cells ignore
soluble
shapes- only
recognize
“billboards”
with peptides



The “rules” of adaptive immunity

Developing lymphocytes mature and are tolerized in central lymphoid organs (VDJ recombination and Central Tolerance)



Naïve lymphocytes home to secondary lymphoid organs (SLOs - mainly lymph nodes) in search of antigens



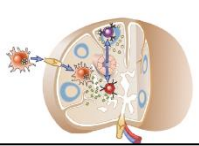
Lymphocytes require two signals for activation (occurs in SLOs) and develop into effector and memory cells



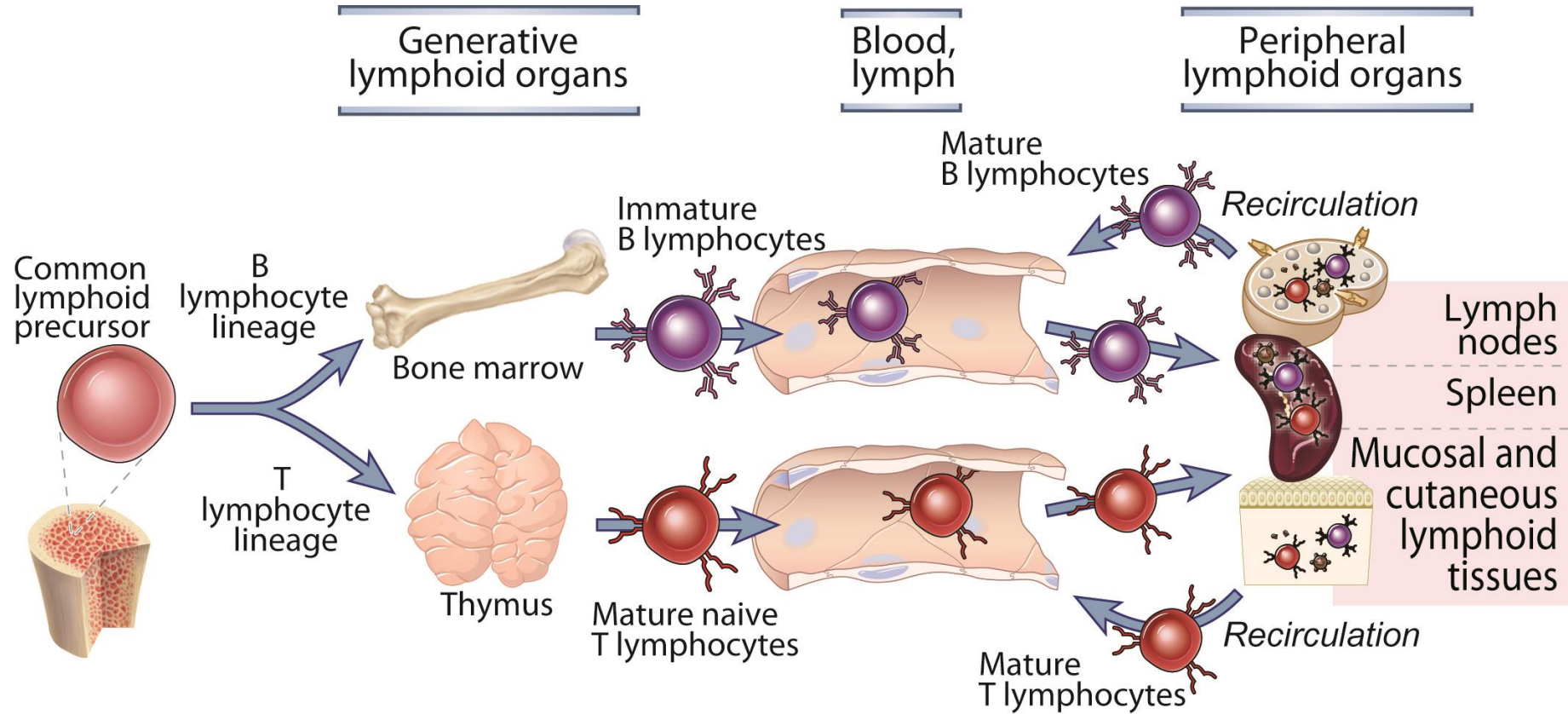
Effector lymphocytes migrate out of SLOs to sites of infection

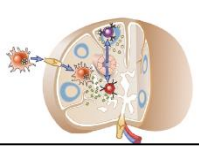


Eradication of infection, Contraction of Effectors and Memory

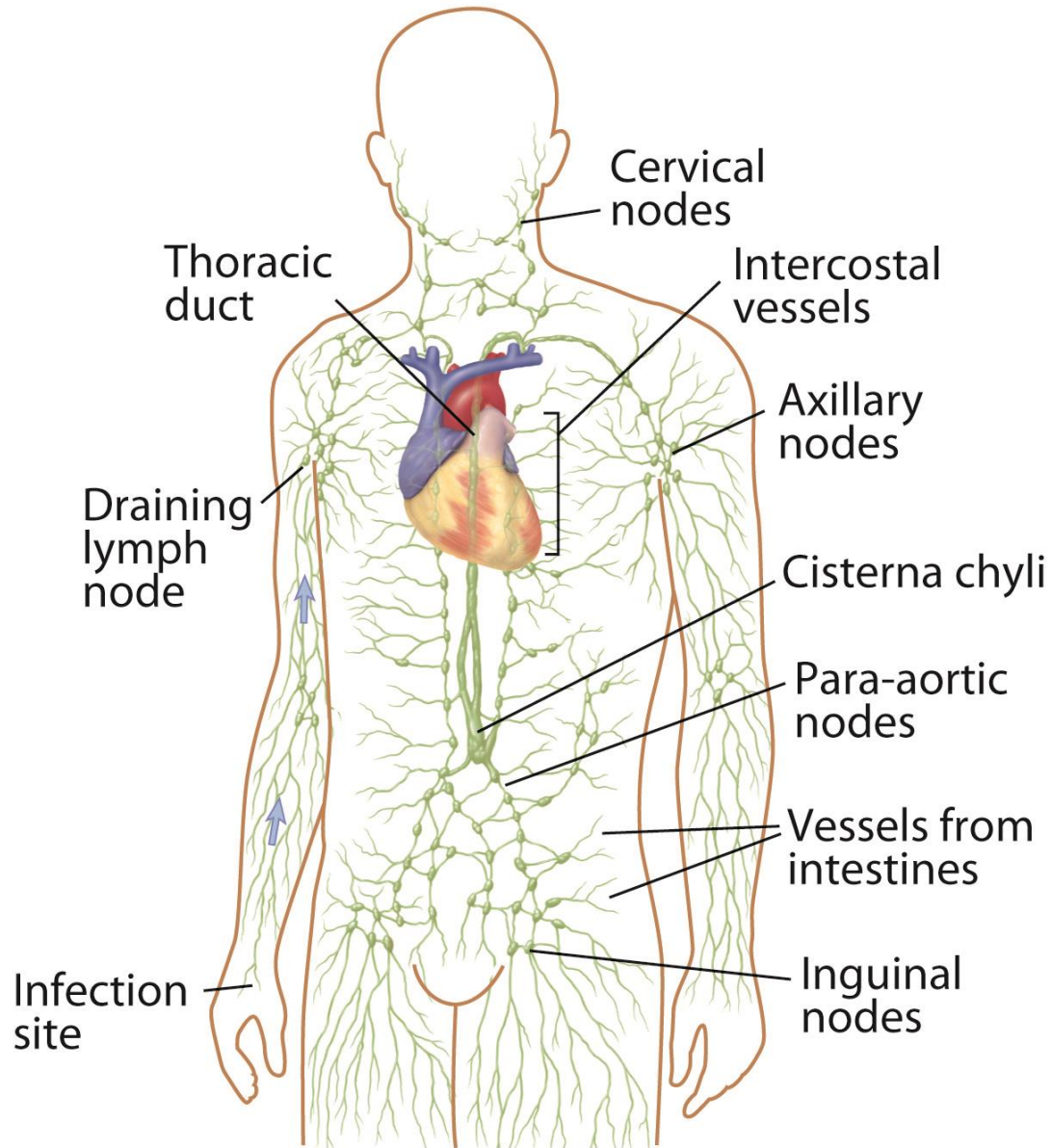


Maturation of Lymphocytes

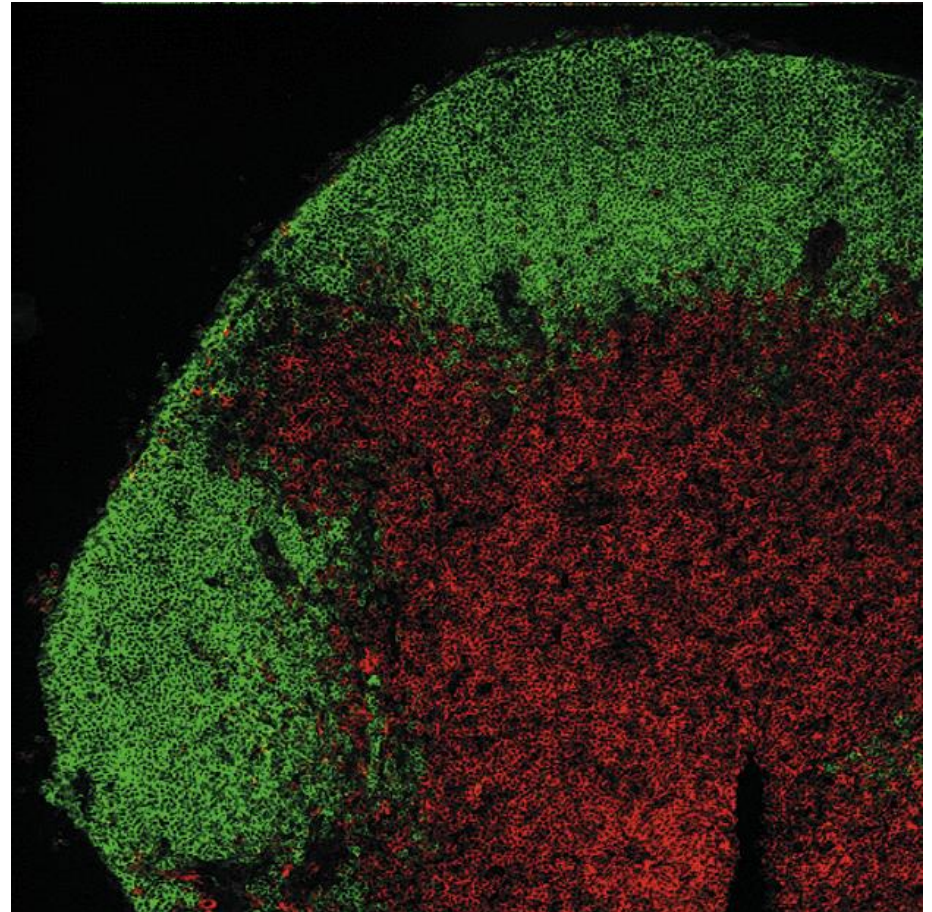
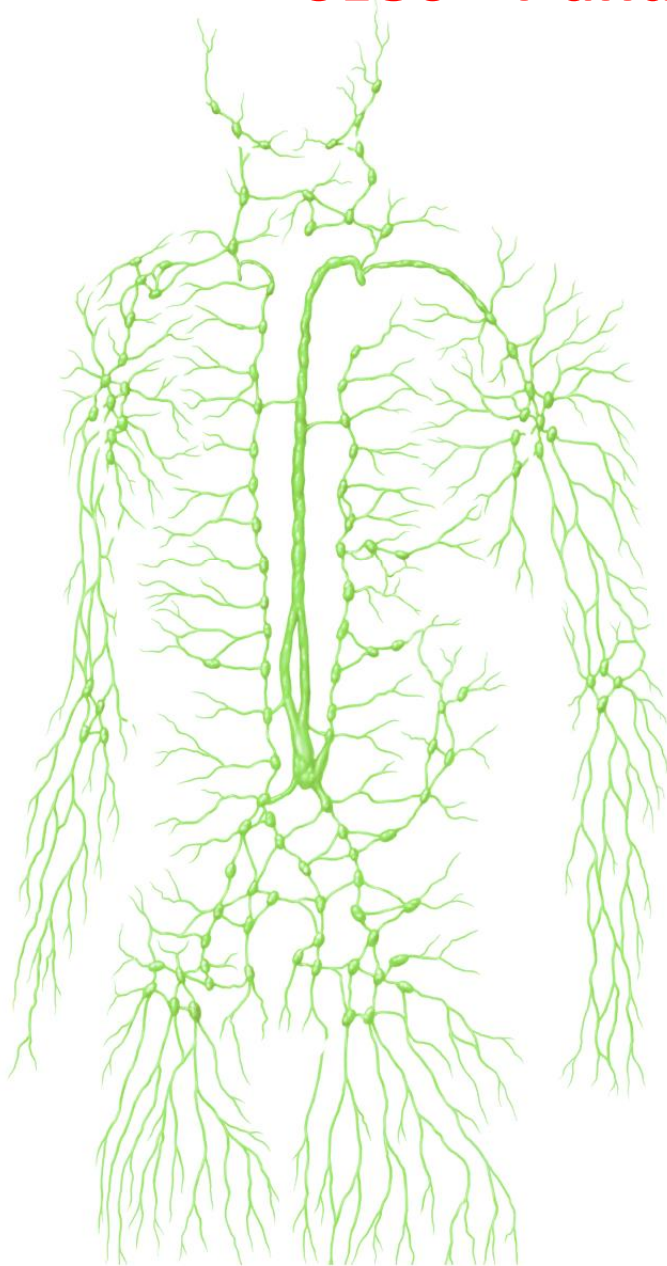


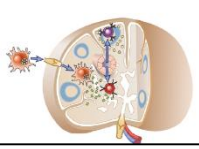


The Lymphatic System

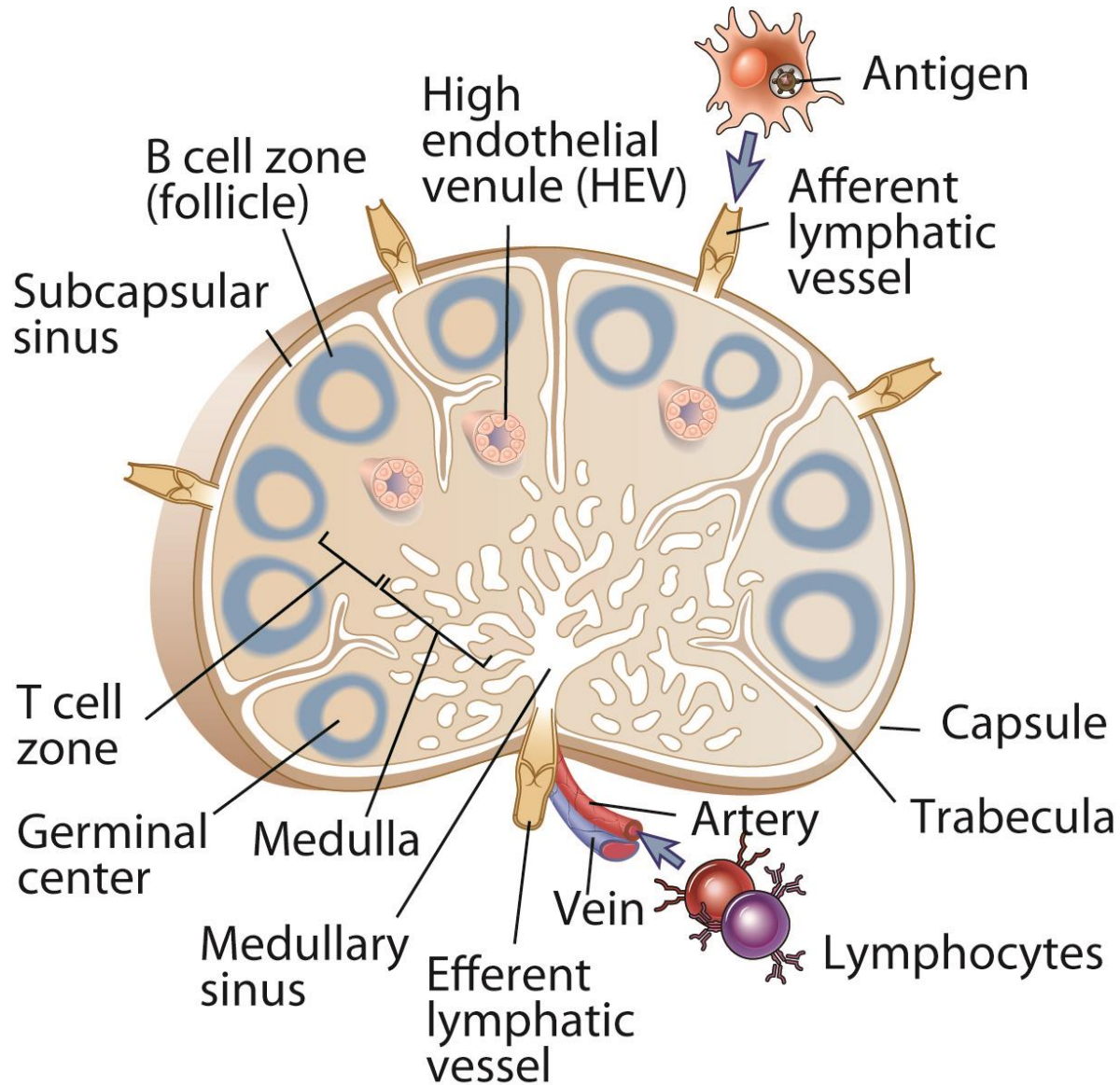


SLOs - T and B cell zones

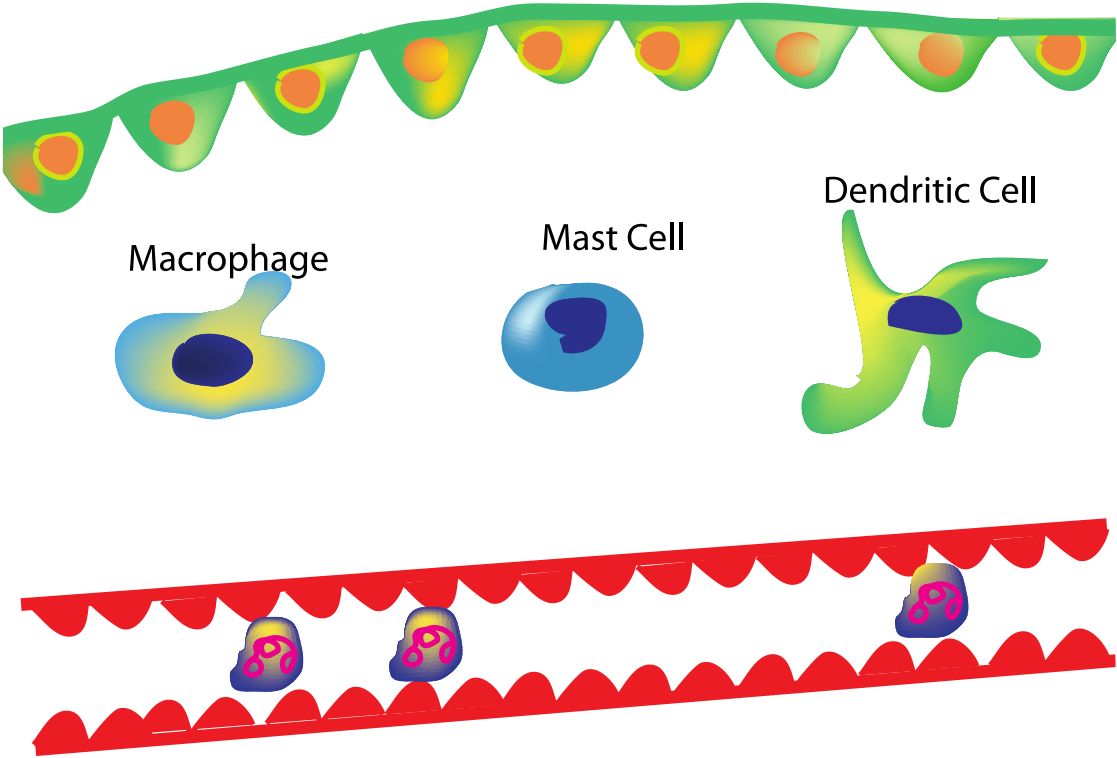


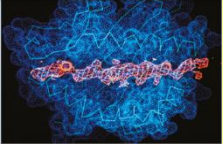


Lymph Node Morphology

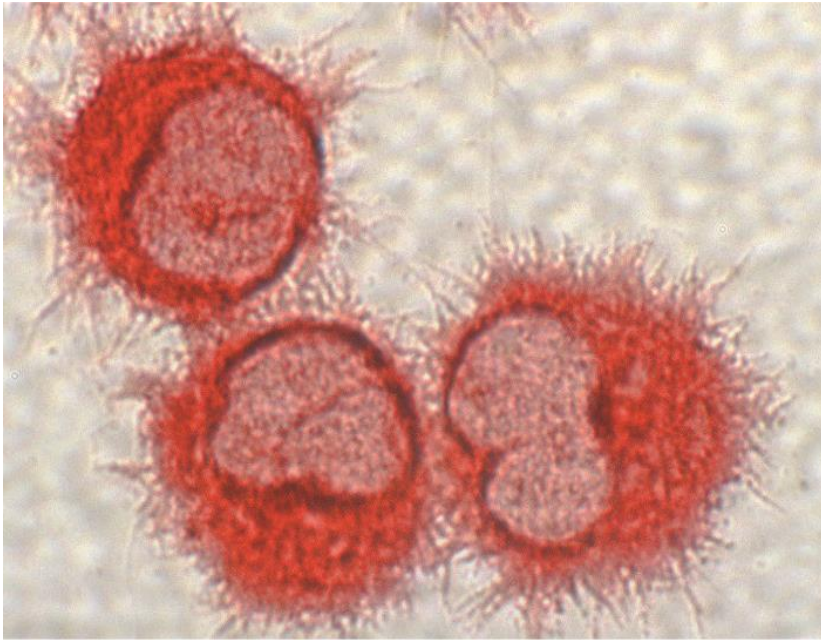


A Third Type of Sentinel Cell Initiates Adaptive Immunity

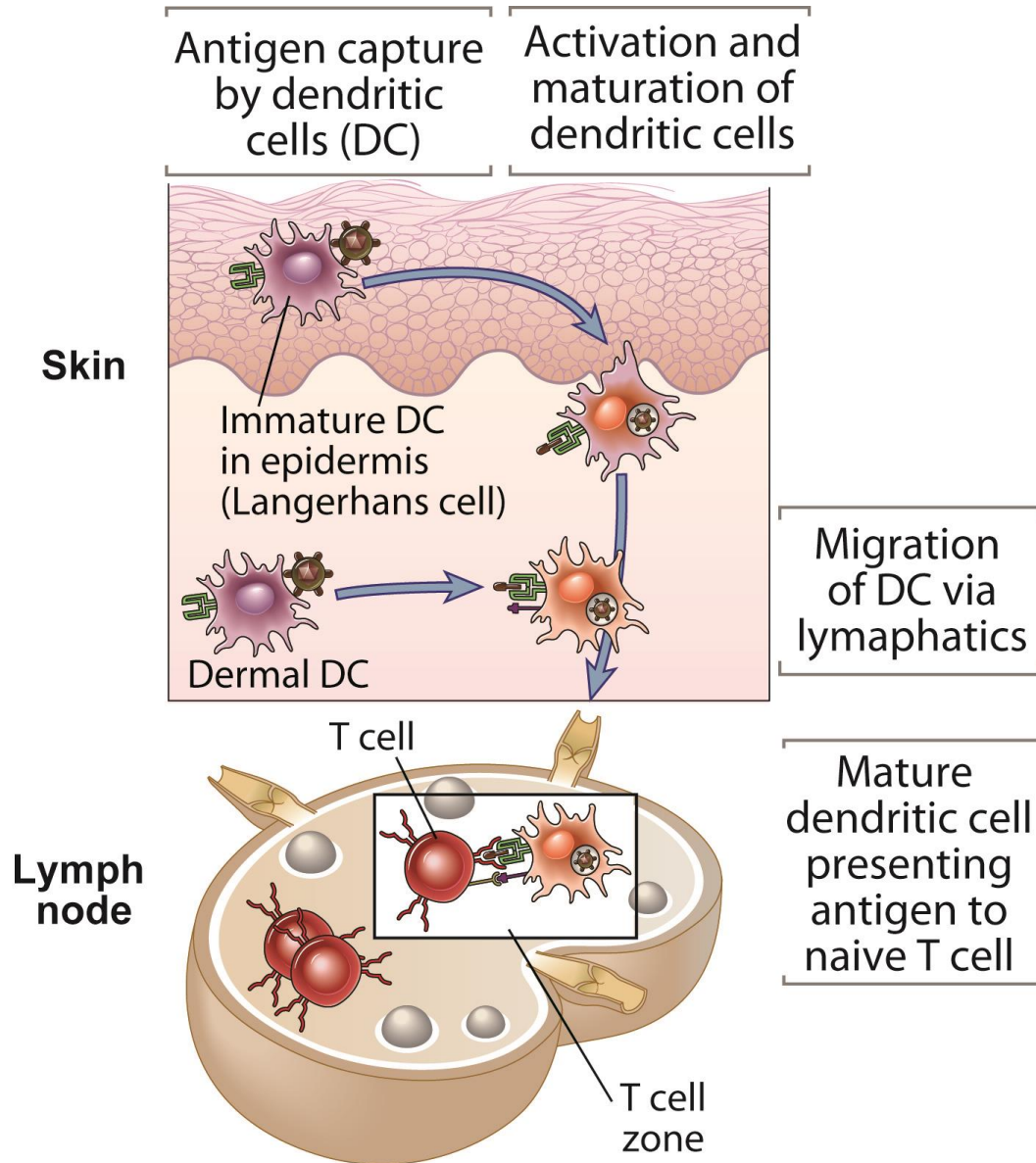




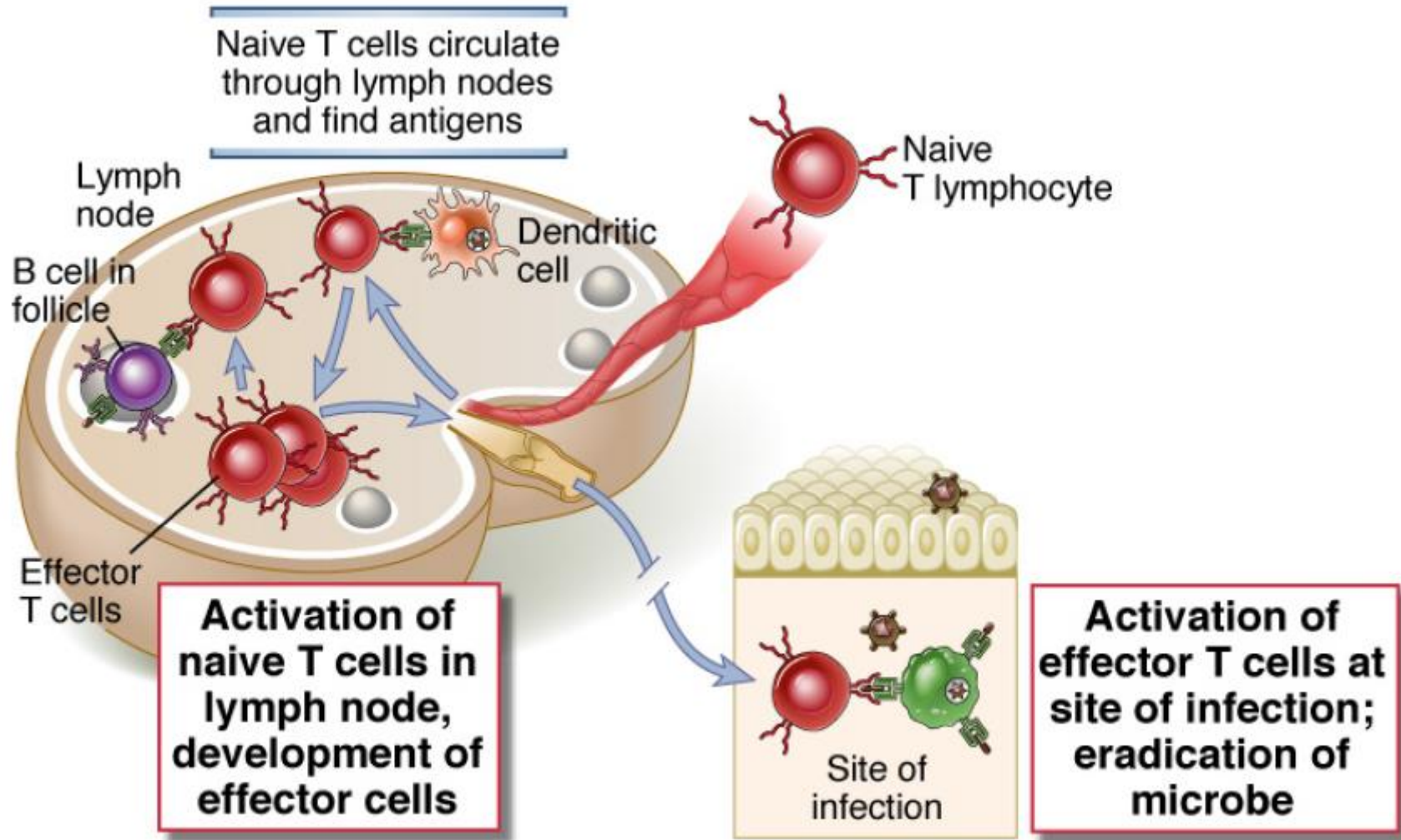
Dendritic Cells Initiate naive T cell activation



DC Antigen Capture and Presentation



DCs and antigen find specific Naïve T cells in SLOs in the T cell zone: activated Effector T cells return to the site of infection



Immunological Diseases

- Autoimmunity
 - Chronic inflammation
 - Infections
 - Allergies
 - Transplantation
 - Immunodeficiencies
 - Cancer
 - Virtually everything – even Type II diabetes, atherosclerosis and trauma
- New knowledge
 - =
 - New rational Therapies

THE ERA OF RATIONAL THERAPY HAS BEGUN

INHIBITING IMMUNITY

Autoimmunity,
Transplantation, Allergies

Biologicals: Many -
Rituxan, Tysabri etc

Small molecules: CsA,
FK506, rapamycin,
Inhibitors of Btk, Syk,
JAKs etc etc.

ENHANCING IMMUNITY

Cancer, HIV

Biologicals: Inhibitory
receptor blockade (Ab to
PD-1, CTLA-4)

Small molecules: coming

The center cannot hold.....