1 Innate Immunity

The point of the immune system is to defend against pathogens

A primary role of innate immunity is to activate acute inflammation

$\implies$ to understand immunity, you need to appreciate something about many different pathogens

1.1 Size Matters

Pathogens range in size

1. Virus: 0.01μm
2. Bacteria: $1 - 10\mu$m
3. Protozoa (Ex: Sleeping Sickness): $10 - 100\mu$m
4. Worms: $1 - 3$cm

$\implies$ Immune system doesn't work well on worms

1.2 White Blood Cells

White blood cells circulate through blood vessels and the lymph system

Ex: Spleen

All white blood cells are immune cells (Surveil for signs of infection)

Initiation of immune responses often begin in lymph nodes nearest to site of infection

Many lining intestines and none below knees

1.3 Innate Immune Cells

Ex: Macrophage, Neutrophil, Dendritic Cell

Key Aspects

1. All phagocytic and can kill bacteria and virus by engulfing them
2. Release mediators which directly kill pathogens
3. Make cytokines that can trigger more inflammation and attract other cells
4. Macrophage and Dentritic Cells activate active immunity

Differentiation

1. Macrophage

Found is virtually every tissue

Can engulf and kill bacteria

- Granules
- Generally come later than neutrophils
  - Sense and clean old (Phagocytose senescent) / infected / dead (Apoptotic) cells
- Orchestrate inflammation
  - Cytokines, proteases, and nucleases

2. Neutrophil (Polymorphonuclear Cells (PMNs) or Granulocytes)
   - Granules
     - Contain enzymes that kill bacteria
     - Contain reactive oxygen species (ROS) that kill bacteria
     - Can also cause tissue damage $\implies$ dangerous to release
   - Odd shaped nucleus
     - More nuclear membrane $\rightarrow$ more activation proteins
   - Consume and then commit suicide
     - Usually short-lived (1-3 days once activated)
     - Replenished from bone marrow

Phagocytosis

1. The engulfment of particulate material within a membrane-bound intracellular compartment called a phagosome
2. Material is degraded by enzymes found in lysosomes
3. Mechanism of endocytosis is critical for "killing" bacteria and viruses
   - Lysis: Killing by dissolving cell membrane
   - Lysosomes at a lower PH (used as a killing method)

1.4 Inflammation

Classic example: Wooden splinter (Breaks skin and invites pathogens)

Effects of Acute Inflammation

1. Brings innate immune cells to an infection site to phagocytize (kill) pathogens
2. Brings fluid to "cleanse" site
3. Brings immune molecules such as antibodies
4. Can increase "signals" to activate adaptive immune system
5. Unfortunately also damages uninfected cells

Symptoms of Inflammation

1. Redness
2. Pain
3. Swelling
4. Heat

Excessive acute inflammation can lead to severe disease such as pneumonia

Chronic inflammation is part of many diseases (autoimmunity, cancer, heart disease, Alzheimer's)

1.5 How do Innate Immune Cells Recognize Pathogens?

1. Pathogen-associated molecular patterns (PAMPs)

   Cells have Toll-like receptors (TLR) that bind to PAMPs and send signals that start immune responses

   Distinct surface structures have become PAMPs

   Bacteria (prokaryotes) are structurally distinct from eukaryotes

2. Ex: Lipopolysaccharide (LPS): Part of the outer membrane of gram-negative bacteria
3. TLRs release cytokines that act as 'alert signals' to activate inflammation

   Tumor necrosis factor (TNF) is an example of a cytokine

1.6 PAMPs

The best PAMPs are those not found in our cells

PAMPs on pathogens cause activavtion of TLRs

→ Produces cytokines/chemokines that activate inflammation and act as signals to activate adaptive immunity

→ Amount of inflammation is dependent on the amount of bacteria

Successful immune response involves balanced cytokine response

Too many cytokines $\implies$ 'shock' or death

Too few cytokines $\implies$ failure to contain infection

Viral DNA and RNA can be PAMPs

Why don't we recognize our host cell's DNA/RNA?

→ Usually found in a place or form different from normal

Ex:

1. Viral DNA in the cytosol is a PAMP. Host cell DNA is normally only in the nucleus

2. Double-stranded viral RNA is a PAMP. Host cell self RNA is normally single stranded