SAND2012-8396P

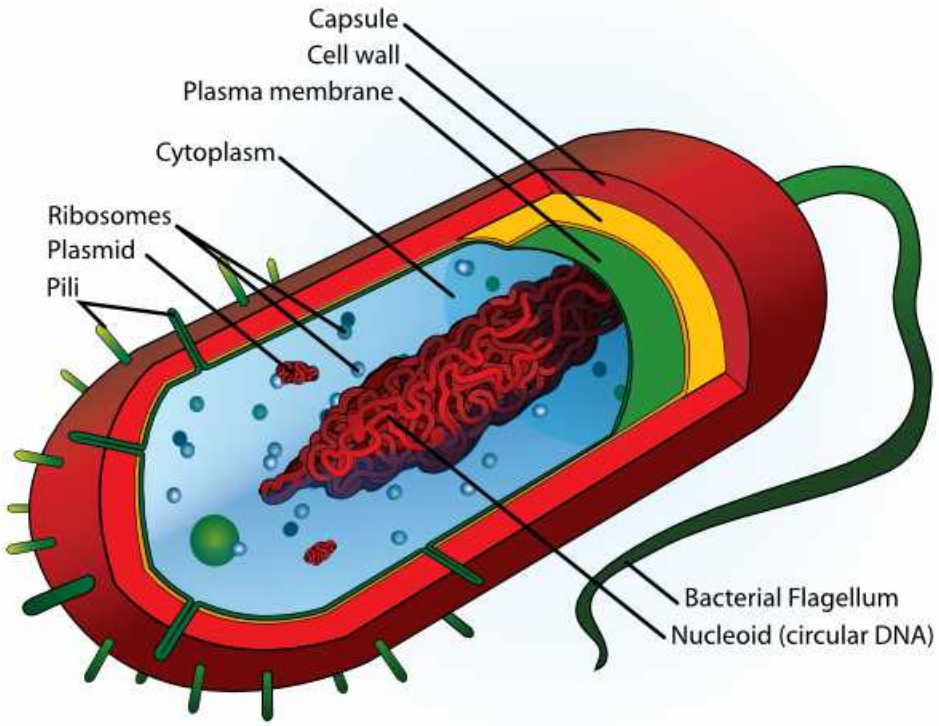
# RESPONSE TO BACTERIA

# Immunity to Bacteria and Fungi

- **Bacteria are ubiquitous and part of normal physiological processes**
  - Commensals in skin, gastrointestinal tract, and on mucous membranes
  - Many pathogenic bacteria reside in the gastrointestinal tract and on skin but do not cause disease
- **The development of disease is related to many factors**
  - Response of host
  - Damaged tissue
  - Location of the bacteria within the body
  - Virulence of the bacteria
- **Adaptation of bacteria to a host**
  - Factors that enable the bacteria to grow and survive in the host
    - **Virulence factors**
    - **Permit bacteria to adapt to a specific environment**
    - **Use virulence factors penetrate host barriers and evade the immune system**

# Bacterial Antigens

- **Bacterial antigens are on cell surfaces**
  - Cell wall
  - Capsule
  - Pili
  - Flagella



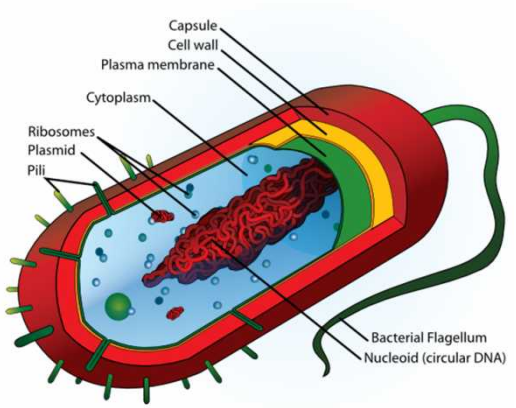
# Bacterial Antigens: Capsules

- **Capsules protect bacteria from being phagocytosis by macrophages**
  - Made of polysaccharides and proteins
  - Strongly bond by antibody
  - Antibody protection-antitoxic immunity
- ***B. anthracis* has both capsule and exotoxin**
  - Virulence factors are on the genes pOX1 and pOX2
  - pOX1 encodes for virulence factors and pOX2 encodes for the capsule
  - Vaccine is Sterne strain
    - **Lacks the virulence factor that produces a capsule**
      - Without a capsule it is easily recognized and destroyed by the immune system
    - **Not toxic – without one virulence factor the others cannot be produced**
  - Phagocytosis of unencapsulated bacteria

# Bacterial antigens: Pili and Flagella

- **Fimbriae or short projections that cover the surface of some Gram negative bacteria**
  - Especially important for characterizing and classification of *E.coli*
  - Sometimes used to attached to cells of body surfaces
  - Classified as F or K antigens
  - Antibodies to these pili prevent bacteria from attaching to cell surfaces reducing pathogenicity
    - **Potential target for vaccines**

- **Flagella are usually a weak, unstable antigen**
  - H antigens

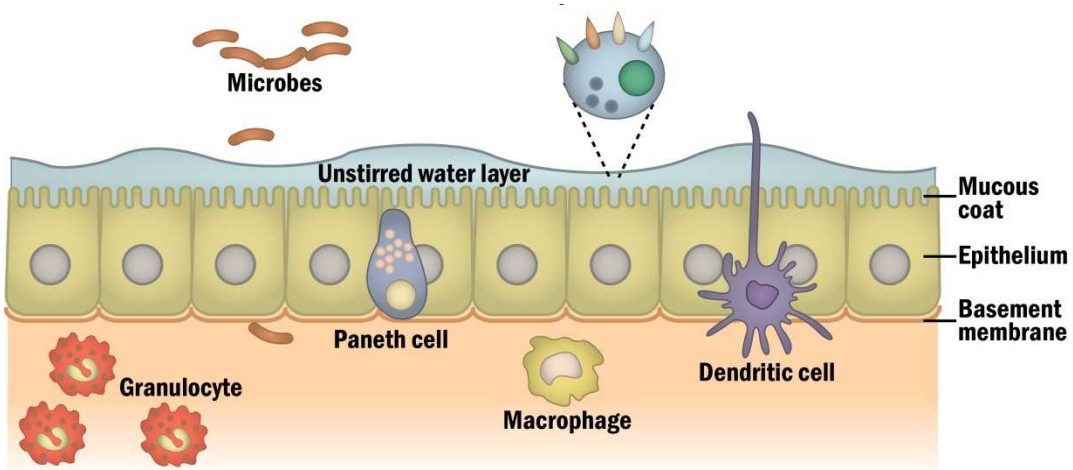


# Bacterial Antigens: Proteins and Toxins

- **Highly antigenic bacterial components**
  - Porins are bacterial proteins that form pores on the surface of gram negative bacteria
  - Heat-shock proteins are produced by stressed bacteria
  - Exotoxins are toxins secreted by bacteria or released when they die
- **Antibodies to toxins called antitoxins**
  - Toxoid- vaccines made from weakened exotoxins

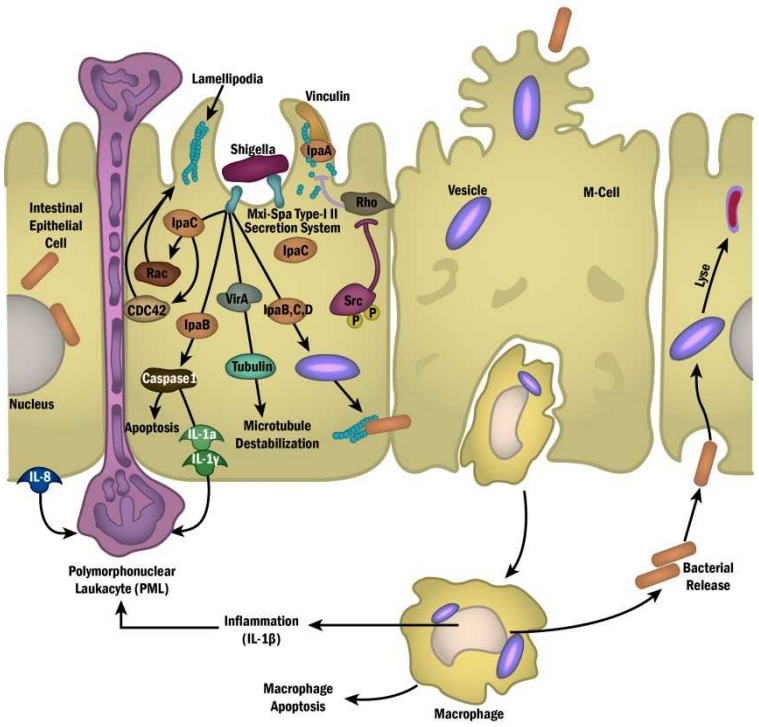
# Immune Response to Bacteria: Innate Immunity

- A combination of innate and acquired immunity
- Recognition of invading bacterial antigens induces inflammation, cytokine release, and complement activation
- Neutrophils, macrophages, and natural killer cells are important components of the immune system
- If the innate response is ineffective then the acquired response is activated



# Immune Response to Bacteria: Acquired Immunity

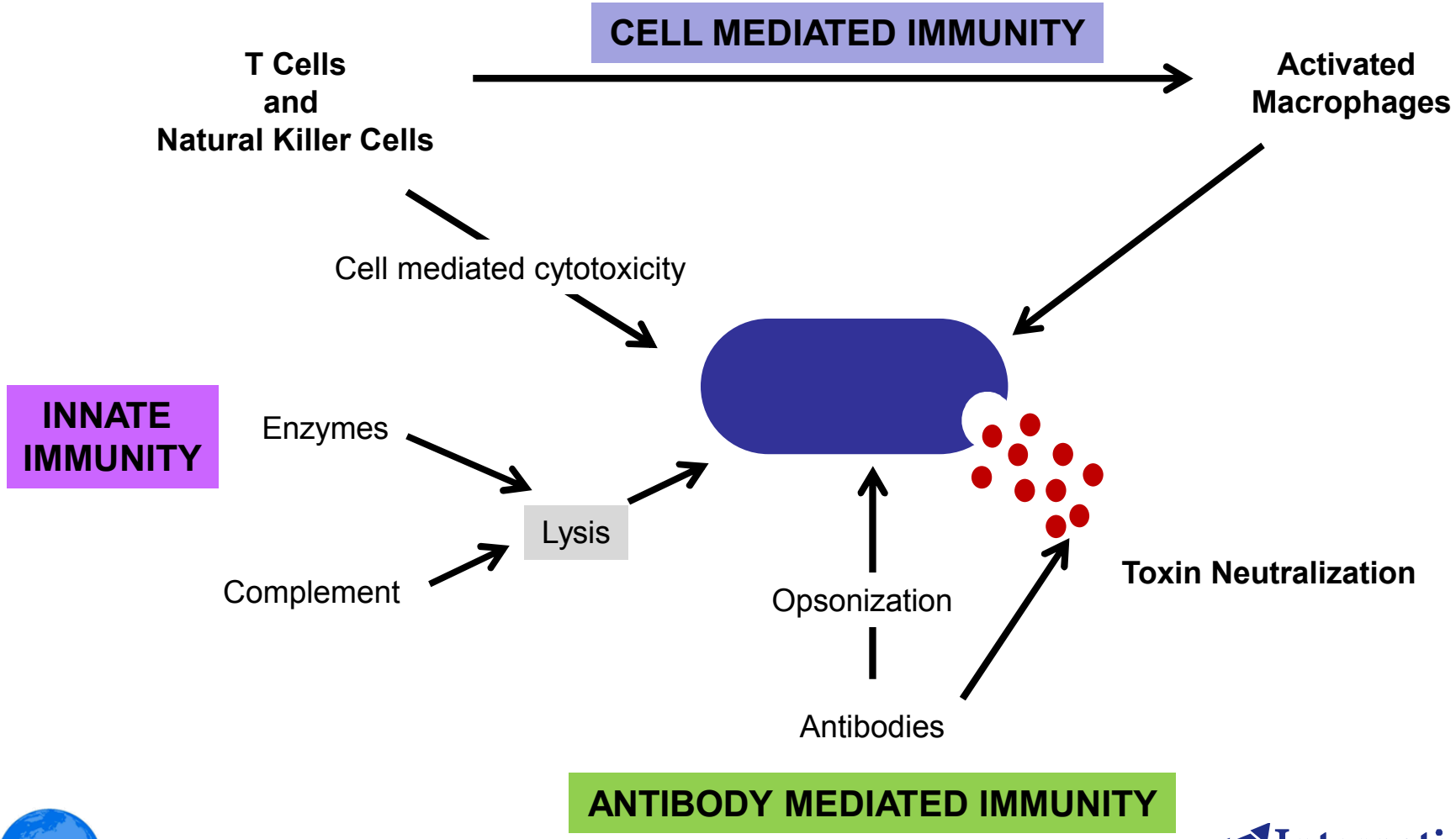
- **Five methods of eliminating bacterial infections**
  - Neutralization of toxins or enzymes by antibody
  - Killing through the classical complement pathway
  - Opsonization by antibodies and complement inducing phagocytosis and destruction by macrophages, T cells, and neutrophils
  - Destruction of intracellular bacteria by activated macrophages
  - Direct killing by cytotoxic and natural killer cells



# Elimination Process

- **Toxigenic Bacteria**
  - Must eliminate bacteria and neutralize toxin
- **Invasive Bacteria**
  - Mediated by antibodies against surface antigens
    - **Capsular proteins, O antigens, and/or pili**
  - Bacteria opsonized and then engulfed by phagocytic cells
- **Intracellular bacteria**
  - *Brucella abortus, Mycobacterium tuberculosis, Campylobacter jejuni, Rhodococcus equi, Listeria monocytogenes, Coxeilla burnetii* and some strains of Salmonella sp. can grow in macrophages
  - Macrophages undergo autophagy where they self-digest
  - Unvaccinated animals are unable to do this quickly
    - **Response in unvaccinated animal takes about ten days to develop**
  - ***Only live vaccines are effective against intracellular pathogens***

# Elimination of Bacteria



# Bacterial Evasion: Innate Immune System

- **Interference with receptors that activate T cells**
  - *Leptospira* and *Campylobacter* have antigens that are not recognized by T cell receptors
- **Interference with internal signaling pathways of T cells**
  - *Brucella, Pseudomonas, Shigella, Yersinia*
- **Resist antibacterial proteins**
  - *Staphylococcus aureus*
- **Block phagocytosis**
  - *Staphylococcus aureus, Salmonella*
- **Kill phagocytic cells**
  - *Mannheimia hemolytica (Pasteurella)* and *Fusobacterium* secrete leukotoxin
  - *Mycoplasma mycoides* kills bovine T cells
  - *Bacillus anthracis, Shigella, Staphylococcus aureus* activate lymphocyte death (apoptosis)

# Bacterial Evasion: Acquired Immunity

- **Change surface coat**
  - *Campylobacter*
  - *Anaplasma marginale*
- **Secrete enzymes that destroy antibodies and cytokines**
  - *Haemophilus influenzae, Streptococcus pneumoniae, Mannheimia hemolytica*
- **Stimulate production of anti-inflammatory mediators**
  - *Brucella*
- **Survival in macrophages**
  - *Mycobacteria avium paratuberculosis, Mycobacterium tuberculosis*
- **Inhibit cytokine production**
  - *Brucella, Salmonella, Yersinia*