SAND2012-8398P

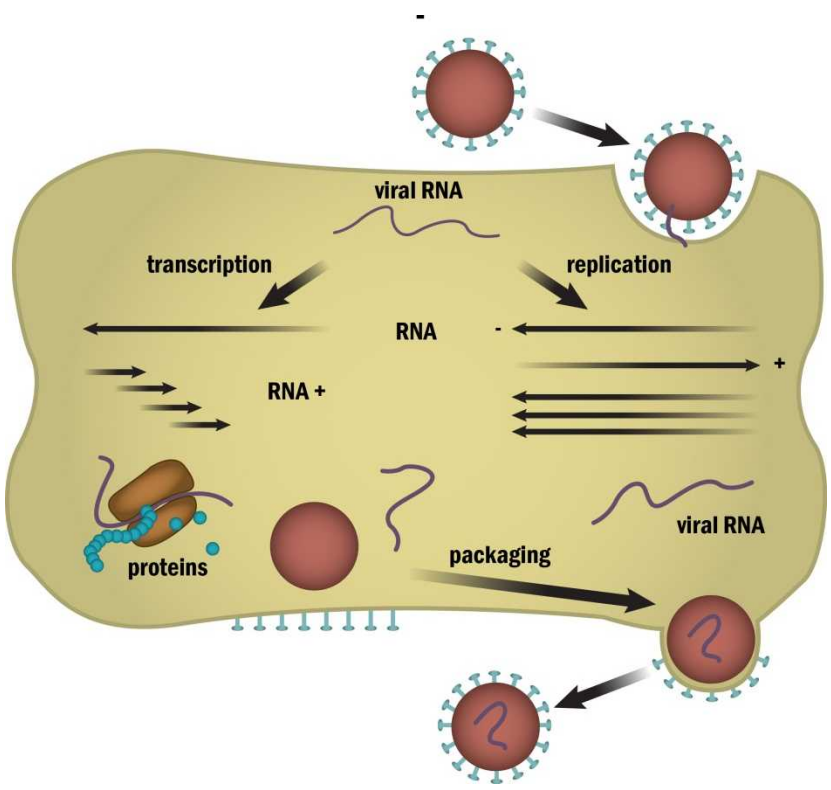
RESPONSE TO VIRUSES

Viruses

- **Viruses rely on the host for survival and replication**
  - Survival threatened by death of host or destruction of the immune system
- **Viruses are selected to evade the host immune system**
- **Viruses that are eliminated before replication can not spread**
- **Hosts eliminated by viruses can not support replication**
- **Rabies is an example of poor virus-host adaptation**
  - Rabies kills unnatural hosts
    - **Not an efficient host**
  - In natural hosts it can survive for an extended period of time and shed virus
- **Some host adapted viruses can cause significant disease but remain in the host – multiple strains exists to cause additional infection**
  - Foot and mouth disease and influenza
- **Persistent infections**
  - Lentivirus infections
    - **Equine infectious anemia**

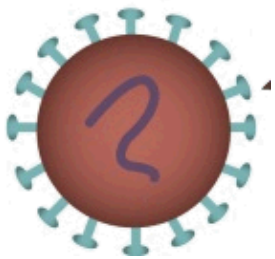
Immunity to Viruses

- Intracellular parasites; nucleic acid core enclosed by protein layers called a capsid
- Capsid proteins are good antigens
- Some viruses have envelopes made of lipoproteins and glycoproteins
- Produce proteins that provoke an immune response on cell surface of infected cells



Immune Response to Virus: Innate Immunity

- **Rapid innate responses eliminate viruses**
- **Cytokines like interferon are important in the elimination process**
  - Destroy envelope
  - Block replication
  - Block interaction with host cell
- **Because viruses invade host cells and antigens are not easily detected, the immune system has evolved to recognize viral genetic material (DNA and RNA)**

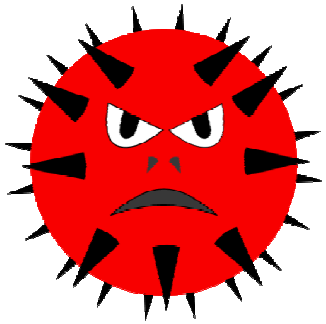


Response to Virus: Innate Immunity

- **Interferon**
  - Cytokines that protect other cells from virus, bacteria, and protozoa
  - Produced by virus infected cells within a few hours after invasion
    - **Peaks in two days and declines so that it is not detectable after seven days**
  - Several methods for viral inhibition
    - **Inhibition of viral replication**
    - **Block viral assembly with capsid**
    - **Direct destruction**

Elimination of Virus: Acquired Immunity - Antibodies

- **Viral capsid and envelope proteins are antigenic and targeted by the immune system**
- **Antibodies can prevent viral invasion by:**
  - Blocking the adsorption of virions to target cells
  - Stimulating phagocytosis of viruses
  - Triggering complement-mediated lysis of the virus
  - Induction of viral clumping to reduce the numbers available for cell invasion
- **Antibodies are also directed against viral proteins expressed on host cells**
  - Infected cells are targeted for destruction
- **Virus neutralizing antibodies include:**
  - Immunoglobulins G, M, and A



Elimination of Virus: Acquired Immunity – Cell Mediated

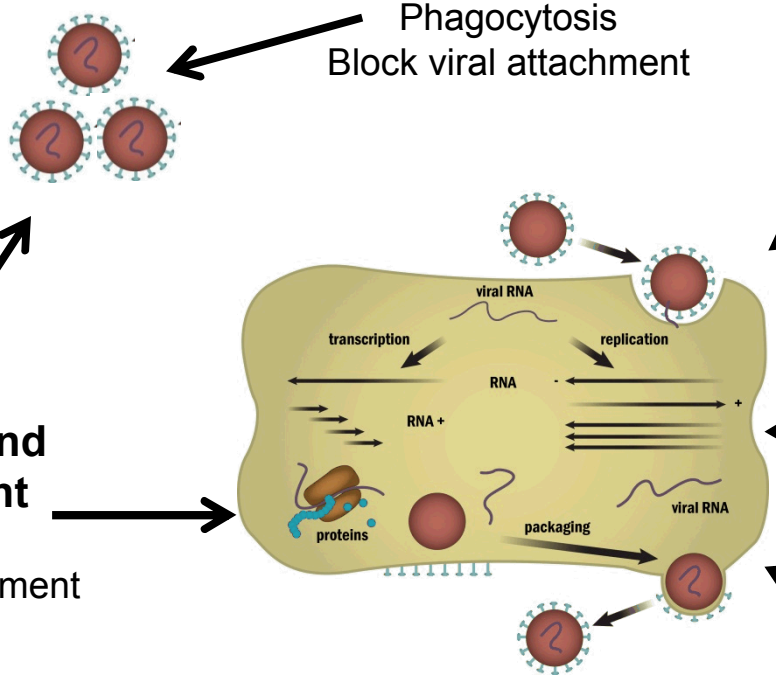
- **Cell mediated immunity is more important than antibodies in controlling viral diseases**
- **T cell derived mechanisms of elimination of viruses:**
  - Viral antigens are expressed on the surface of host cells and the host cell eliminated
    - **T cells recognize antigen presented with major histocompatibility antigens**
    - **May prevent replication in host cell if done quickly**
  - Cytotoxic T cells can kill viruses without killing the host cell by producing interferon and tumor necrosis factor
  - Macrophages can eliminate viruses after activation
    - **Viruses are readily engulfed by macrophages and destroyed**

Elimination of Viruses: Review

Complement
Lyse virus

Antibodies
Phagocytosis
Block viral attachment

Antibodies and Complement
Cell lysis



Antibodies and Complement
Viral lysis
Block viral attachment

Natural Killer Cells
Cell death

Cytotoxic T Cells
Cell death

Activated Macrophages
Phagocytosis
Cell death

Evasion of the Acquired Immune System

- **Viruses have evolved to support existence**
  - RNA viruses primarily rely on changing antigens to evade the immune system because of their small genome
  - DNA viruses have a larger genome and thus have many mechanisms to evade the host immune system
- **Mechanisms include:**
  - Inhibition of interferon
  - Disrupt antigen presentation
  - Mutation of the virus to prevent antibody binding
    - **Influenza**
  - Virus remains infectious even after antibody binding
  - Destroy antibodies
  - Latency – invade and then do not express antigen
  - Inhibit cell killing