Lecture 2: Virology

I. Background

A. Properties
1. Simple biological systems
   a. Aggregates of nucleic acids and protein
2. Non-living
   a. Cannot reproduce or carry out metabolic activities outside of a host cell
3. Require other cells for their reproduction
   a. “Perfect” reproductive machines
4. Viruses are not cells
   a. Infectious particles consisting of nucleic acid encased in a protein coat
   b. May have a membranous envelope
   c. Often very small

B. Structure

   Figure 19.3

1. Genome
   a. Depends on the type of virus
2. DNA virus
   a. Double-stranded DNA, single-stranded DNA
3. RNA virus
   a. Double-stranded RNA, single-stranded RNA
4. Viral genome is usually organized as a single linear or circular molecule of nucleic acid
5. Number of genes vary
   a. Smallest with four genes
   b. Largest have several hundred to a thousand
6. Capsid
   a. Protein shell enclosing the viral genome
b. Capsomeres
   i. Protein subunits
   ii. A limited number of different kinds of proteins making up the capsid

C. Viral shapes
1. Rod-shaped capsid
   a. More than 1,000 copies of a single protein arranged in a helix
   b. Rod-shaped viruses are commonly called helical viruses
2. Adenoviruses have 252 identical proteins arranged into a polyhedral capsid with 20 triangular facets—an icosahedron
   a. Commonly called icosahedral viruses

D. Accessory structures used during the infective process
1. Viral envelop
   a. Surrounds the capsids of some viruses
   b. Derived from the membrane of the host cell
   c. Contain host cell phospholipids and membrane proteins as well as proteins and glycoproteins of viral origin

E. Some viruses carry a few viral enzyme molecules within their capsids
1. Bacteriophages (T2, T4, T6)
   a. Viruses that infect E. coli
   b. Elongated icosahedral capsid heads that enclose their DNA and a protein tail piece that attaches the phage to the host and injects the phage DNA inside

Figure 19.3d

(d) Bacteriophage T4
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II. Viral Reproduction

A. Viruses reproduce only in host cells
1. Intracellular parasites
   a. Lack metabolic enzymes, ribosomes, and other equipment for making proteins
2. Isolated virus have no functions
   a. Unable to reproduce or perform any activity
3. Isolated virus is merely a packaged set of genes
   a. Viral particle merely transport genes one host cell to another

B. Limited number of potential hosts
1. Host range
   a. Each type of virus can infect and parasitize only a limited range of host cells
2. Specificity depends on the evolution of recognition systems by the virus
3. Viruses recognize host cells by a “lock and key” fit between proteins on the outside of the virus and specific receptor molecules on the host’s surface
   a. Some viruses have a broad enough host range to infect several species
   b. Most infect only a single species
4. Most viruses of eukaryotes attack specific tissues
   a. Human cold viruses infect only the cells lining the upper respiratory tract
   b. AIDS virus binds to only certain white blood cells

C. General characteristics of viral reproductive cycle

1. Viral infection begins when the genome of the virus enters the host cell
   a. Mechanism varies with the type of virus and host cell
      i. Inject DNA into a bacterium
      ii. Endocytosis
      iii. Fusion of the viral envelope with the plasma membrane of the host
2. Once inside, the viral genome utilize host cell machinery to copy viral nucleic acid and manufacture proteins from the viral genome
   a. Host provides nucleotides, ribosomes, tRNAs, amino acids, ATP, and other components for making the viral components dictated by the viral genes
   b. Most DNA viruses use the DNA polymerases of the host cell to synthesize new genomes along the templates provided by the viral DNA
   c. RNA viruses use special virus-encoded polymerases that can use RNA as a template
3. Nucleic acid molecules and capsomeres then self-assemble into viral particles
4. Completed virus exits the infected cell
   a. Simplest viruses exit by lysis
   b. Loss of function caused by the cellular damage are the symptoms associated with viral infection
   c. Usually causes the death of the host cell
5. Newly formed particles infect other cells

III. Lytic Cycle

A. Phage reproductive cycle culminates in the death of the host
   1. Process only produces new phages
      a. Lyse the cell membrane
      b. Produce virulent phages
      c. Restriction enzymes
         i. Cellular defense mechanisms
IV. Lysogenic Cycle

A. Viral genome is replicated without destroying the host
1. Viral DNA molecule is incorporated by genetic recombination into a specific site in the host genome
   a. Viral proteins break both circular DNA molecules and join them together
   b. Prophage stage
      i. One of the viral genes codes for a protein that represses most other prophage genes
      ii. Phage genome is largely silent
2. Every time the host divides, it copies the phage DNA and passes the copies to daughter cells
3. A single infected cell can quickly give rise to a large population of bacteria carrying the virus in prophage form
   a. Prophages are capable of giving rise to active phages that lyse their host cells
   b. Genome exits the bacterial chromosome and initiates a lytic cycle
4. Switch from the lysogenic to lytic mode may be triggered by an environmental signal such as certain chemicals or high-energy radiation

V. Viral Envelops

A. Membranous envelope derived from the host cell membrane
1. Most animal viruses with RNA genomes have an envelope
2. Use the envelope to enter the host cell
3. Glycoproteins on the envelope bind to specific receptors on the host’s membrane
4. Envelope fuses with the host’s membrane, transporting the capsid and the viral genome inside

B. Reproductive cycle of an enveloped virus with an RNA genome

1. Viral glycoproteins for new envelopes are made by ribosomes bound to the ER of the host cell
2. Viral glycoproteins are then glycosylated by cellular enzymes in the ER and Golgi apparatus
3. Glycoproteins are transported to the cell surface, where they wrap themselves in membrane as they bud from the cell
4. Viral envelope is thus derived from the host’s plasma membrane
   a. Viral genes specify some of the molecules in the membrane
5. Some viruses have envelopes that are not derived from plasma membrane
   a. Double-stranded DNA viruses reproduce within the cell nucleus using viral and cellular enzymes to replicate and transcribe their DNA

VI. RNA Viruses

A. Viruses with single-stranded RNA (class IV)
   1. Genome acts as mRNA and is translated into viral protein immediately after infection

B. RNA (class V) serves as a template for complementary RNA strands
   1. Function both as mRNA and as templates for the synthesis of additional copies of genome RNA

C. Retroviruses (class VI) have the most complicated life cycles
   1. Retroviruses carry an enzyme called reverse transcriptase that transcribes DNA from an RNA template
      a. Retroviruses are enveloped viruses that contain two identical molecules of single-stranded RNA and two molecules of reverse transcriptase
      b. HIV enters the host cell, reverse transcriptase molecules are released into the cytoplasm and catalyze the synthesis of viral DNA
      c. Viral DNA enters the cell’s nucleus and is inserted as a permanent provirus into a chromosome
      d. Host’s RNA polymerase transcribes the proviral DNA into RNA molecules that can function both as mRNA for the synthesis of viral proteins and as genomes for new virus particles released from the cell

VII. Viral Pathogenesis

A. Symptoms of disease result from infective process
   1. Some viruses damage or kill cells by triggering the release of hydrolytic enzymes from lysosomes
   2. Some viruses cause the infected cell to produce toxins that lead to disease symptoms
   3. Some have molecular components, such as envelope proteins, that are toxic
   4. In some cases, viral damage is easily repaired (respiratory epithelium after a cold)
   5. In others, infection causes permanent damage (nerve cells after polio)
   6. Many of the temporary symptoms associated with a viral infection result from the body’s own efforts at defending itself against infection
      a. Immune system is a complex and critical part of the body’s natural defense mechanism against viral and other infections

B. Medical interventions
   1. Vaccination
      a. Variants or derivatives of pathogenic microbes that stimulate the immune system to mount defenses against the actual pathogen
   2. Medical technology can do little to cure viral diseases once they occur
      a. Antibiotics are ineffective
      b. Prevent viral replication and permit immune clearance
i. HIV drugs

C. Emergence of these new viral diseases
1. Three processes
   a. Mutation
   b. Dissemination of a viral disease from a small, isolated population
   c. Spread of existing viruses from one species to another
2. RNA viruses tend to have high mutation rates because replication of their nucleic acid lacks proofreading
   a. Some mutations create new viral strains with sufficient genetic differences from earlier strains that they can infect individuals who had acquired immunity to these earlier strains
3. Viral disease can spread from a small, isolated population to become a widespread epidemic
   a. AIDS went unnamed and virtually unnoticed for decades before spreading around the world
      i. Technological and social factors, including affordable international travel, blood transfusion technology, sexual promiscuity, and the abuse of intravenous drugs, allowed a previously rare disease to become a global scourge
4. Spread of existing viruses from one host species to another
   a. Animals infected with multiple strains of flu virus, the different strains underwent genetic recombination
   b. Creates a virus capable of infecting human cells