Chapter 13
Viral Genetics

Influenza: 1918 Epidemic
30-40 million deaths world-wide

Emerging Viruses
- Viruses that “jump” host
  - switch species
  - Ebola, SARS, bird flu, hantavirus
  - The Coming Plague by Laurie Garrett

Smallpox
- Eradicated in 1976
  - vaccinations ceased in 1980
  - at risk population?

A Sense of Size
- Comparing size
  - eukaryotic cell
  - bacterium
  - virus
What is a virus? Is it alive?
- DNA or RNA enclosed in a protein coat
- Viruses are not cells
- Extremely tiny
  - need an electron microscope to see
  - smaller than ribosomes
  - ~20–50 nm

1st discovered in plants (1800s)
- tobacco mosaic virus
- couldn’t filter out
- couldn’t reproduce on media like bacteria

Variation in Viruses
- A package of genes in transit from one host cell to another

"A piece of bad news wrapped in protein"
- Peter Medawar

Variation in Viruses
- Parasites
  - lack enzymes for metabolism
  - lack ribosomes for protein synthesis
  - need host “machinery”

Viral Genomes
- Viral nucleic acids
  - DNA
    - double-stranded
    - single-stranded
  - RNA
    - double-stranded
    - single-stranded
  - Linear or circular
    - smallest viruses have only 4 genes, while largest have several hundred

Viral Protein Coat
- Capsid
  - crystal-like protein shell
  - 1-2 types of proteins
  - many copies of same protein

Viral Envelope
- Lipid bilayer membranes cloaking viral capsid
  - envelopes are derived from host cell membrane
  - glycoproteins on surface

Table 18.1 Classes of Animal Viruses, Grouped by Type of Nucleic Acid

Viral Envelope
- Lipid bilayer membranes cloaking viral capsid
  - envelopes are derived from host cell membrane
  - glycoproteins on surface
Generalized Viral Lifecycle

- **Entry**
  - Virus DNA/RNA enters host cell
- **Assimilation**
  - Viral DNA/RNA takes over host
  - Reprograms host cell to copy viral nucleic acid & build viral proteins
- **Self assembly**
  - Nucleic acid molecules & capsomeres then self-assemble into viral particles
  - Exit cell

Symptoms of Viral Infection

- Link between infection & symptoms varies
  - Kills cells by lysis
  - Cause infected cell to produce toxins
    - Fever, aches, bleeding...
  - Viral components may be toxic
    - Envelope proteins
- Damage?
  - Depends...
    - Lung epithelium after the flu is repaired
    - Nerve cell damage from polio is permanent

Viral Hosts

- **Host range**
  - Most types of virus can infect & parasitize only a limited range of host cells
    - Identify host cells via “lock & key” fit between proteins on viral coat & receptors on host cell surface
  - Broad host range
    - Rabies = can infect all mammals
  - Narrow host range
    - Human cold virus = only cells lining upper respiratory tract of humans
    - HIV = binds only to specific white blood cells

Bacteriophages

- **Viruses that infect bacteria**
  - Ex. Phages that infect *E. coli*
  - Lambda phage
  - 20-sided capsid head encloses DNA
  - Protein tail attaches phage to host & injects phage DNA inside

Bacteriophage Lifecycles

- **Lytic**
  - Reproduce virus in bacteria
  - Release virus by rupturing bacterial host
- **Lysogenic**
  - Integrate viral DNA into bacterial DNA
  - Reproduce with bacteria

Lytic Lifecycle of Phages
### Lysogenic Lifecycle of Phages

- The phage injects its DNA into the bacterial chromosome to become a prophage.
- Bacterial cell continues to divide and synthesize new phage DNA and proteins.
- When cell divides, prophage DNA replicates and is transmitted to daughter cells.
- Occasionally, a prophage is extricated, following a lytic cycle.
- New phage DNA and proteins are synthesized and assembled into phages.
- The cell lyses, releasing phages.

### Defense Against Viruses

- Bacteria have defenses against phages:
  - bacterial mutants with receptors that are no longer recognized by a phage
  - natural selection favors these mutants
  - bacteria produce **restriction enzymes**
    - recognize & cut up foreign DNA

- It’s an escalating war!
  - natural selection favors phage mutants resistant to bacterial defenses

### RNA Viruses

- **Retroviruses**
  - have to copy viral RNA into host DNA
    - enzyme = **reverse transcriptase**
    - RNA $\rightarrow$ DNA $\rightarrow$ mRNA
  - host’s RNA polymerase now transcribes viral DNA into viral mRNA
  - mRNA codes for viral components
  - host’s ribosomes produce new viral proteins

- **HIV**
  - **Human ImmunoDeficiency Virus**
  - causes AIDS
    - **Acquired ImmunoDeficiency Syndrome**
    - opportunistic diseases
  - envelope with glycoproteins for binding to specific WBC
  - capsid containing 2 RNA strands & 2 copies of reverse transcriptase

### HIV Infection

- HIV enters host cell
  - macrophage & CD4 WBCs
  - cell-surface receptor
  - **reverse transcriptase** synthesizes double stranded DNA from viral RNA
  - high mutation rate
  - Transcription produces more copies of viral RNA
  - translated into viral proteins
  - proteins & vRNA self-assemble into virus particles
  - released from cell by “budding” or by lysis

### HIV Treatments

- inhibit vRNA replication
  - AZT
    - thymine mimic
  - protease inhibitors
    - stops cleavage of polyprotein into capsid & enzyme proteins

- **Combination Therapy**
  - Replication (AZT) HIV RNA
  - Protease inhibitors
  - Envelope proteins
  - Critical protein
  - Vaccine or Drug Therapy
  - Vaccine incorporating defective nef protein
Potential HIV treatments
- Block receptors
  - chemokines
  - bind to & block cell-surface receptors
    - 11% of Caucasians have mutant receptor allele
- Block vRNA replication
  - CAF replication factor

Cancer Viruses
- Viruses appear to cause certain human cancers
  - hepatitis B virus
    - linked to liver cancer
  - Epstein-Barr virus = infectious mono
    - linked to lymphoma
  - papilloma viruses
    - linked with cervical cancers
  - HTLV-1 retrovirus
    - linked to adult leukemia

Cancer Viruses
- Transform cells into cancer cells after integration of viral DNA into host DNA
  - carry oncogenes that trigger cancerous characteristics in cells
  - version of human gene that normally controls cell cycle or cell growth
- Most tumor viruses probably cause cancer only in combination with other mutagenic events

Prions
- Misfolded proteins
  - infectious
  - make plaques (clumps) & holes in brain as neurons die

Protein as Information Molecule?!
- Prions challenge Central Dogma
  - transmit information to other proteins

Stanley Prusiner
UC School of Medicine
1982 | 1997