

The Zombies of the Scientific Community

Viruses

Viruses on the Biological Spectrum

- Viruses can infect every type of cell:
 - Bacteria
 - Algae
 - Fungi
 - Protozoa
 - Plants
 - Animals

What are viruses and what do they look like?

- Viruses do not satisfy all of the characteristics of life.
- Often, viruses are called obligate intracellular parasites because they need a host cell in order to continue on.
- Viruses cannot reproduce on their own!
- Remember, viruses are not out to get you!
- They replicate within the cell and as a consequence of their living, you get sick... or worse.

Viruses

- Viruses are small (about 17 nanometers in diameter).
- Some viruses are as large as 1000 nanometers, which is barely visible under light microscopy.
- Viruses occur in all organisms
- In every case, the basic structure is the same.
- They are segments of DNA or RNA wrapped in a protein coat called the capsid.

Viral Size Range

- Ultramicroscopic size
- Smaller than the average bacterium
- Electron microscopes are required to detect them
 - Parvoviruses: 0.02 μm in diameter
 - Mimiviruses: 450 nm in length—larger than some small bacteria
 - Cylindrical viruses: 0.8 μm long, but 0.015 μm in diameter

Viral Components

- Capsid
 - Shell surrounds the nucleic acid
 - Nucleocapsid: capsid and nucleic acid together
- Envelope
 - Not found in all viruses
 - Usually a modified piece of the host cell membrane
- Naked viruses
 - Consist only of a nucleocapsid

- Spikes
 - Found on both naked and enveloped viruses
 - Project from either the nucleocapsid or envelope
 - Allow viruses to dock with their host cells
- Virion
 - Fully formed virus able to establish infection in a host

The Viral Capsid: The Protective Outer Shell

- Capsomeres
 - Identical protein subunits that spontaneously self assemble to form the capsid
- Helical capsid
 - Rod-shaped capsomeres that form a continuous helix around the nucleic acid
- Icosahedral capsid
 - Three-dimensional, 20-sided figure with 12 evenly spaced corners

The Viral Capsid

- Complex capsids
 - Found in bacteriophage, the viruses that infect bacteria
 - Have multiple types of proteins
 - Take shapes that are not symmetrical

The Viral Envelope

- Composed of the membrane system of the host
 - Cell membrane or nuclear membrane
 - Regular membrane proteins are replaced with viral proteins
 - Spikes: protruding glycoproteins essential for attachment to the host cell

Nucleic Acids: At the Core of a Virus

- Genome: the full complement of DNA and RNA carried by a cell
- Viruses contain either DNA or RNA **but not both**
- The number of viral genes is small compared to that of a cell
- Possess only the genes necessary to invade host cells and redirect their activity

Nucleic Acids

- Positive-sense RNA
 - Single-stranded RNA genomes ready for immediate translation into proteins
- Negative-sense RNA
 - RNA genomes that need to be converted into the proper form to be made into proteins

Other Substances in the Virus Particle

- Enzymes for specific operations within the host cell
 - Polymerases: synthesize DNA and RNA
 - Replicases: copy RNA
 - Reverse transcriptase: synthesizes DNA from RNA

- Substances from the host cell
 - Arenaviruses pack along host ribosomes
 - Retroviruses “borrow” the host’s tRNA molecules

Classification of Viruses

- Informal classification system:
 - Animal, plant, or bacterial viruses
 - DNA or RNA viruses
 - Helical or icosahedral
- Criteria of a formal classification system:
 - Structure
 - Chemical composition
 - Similarities in genetic makeup
- Virus families:
 - Suffix *–viridae*
- Virus genera:
 - Suffix *–virus*

Multiplication Cycles in Animal Viruses

- General phases in the life cycle of animal viruses:
 - Adsorption
 - Penetration
 - Uncoating
 - Synthesis
 - Assembly
 - Release from the host cell

Adsorption

- Invasion begins when the virus encounters a susceptible host and **adsorbs** specifically to receptor sites on the cell membrane
 - Adsorb: to attach (like a virus)
 - Absorb: to soak in (like a paper towel)

Host Range

- A virus can invade its host cell only through making an exact fit with a specific host molecule
- Restricted host range: hepatitis B only infects liver cells of humans
- Moderately restrictive host range: poliovirus infects intestinal and nerve cells of primates
- Broad host range: rabies virus infects various cells of all mammals

Penetration and Uncoating of Animal Viruses

- Endocytosis: entire virus is engulfed by the cell and enclosed in a vacuole or vesicle
- Uncoating: enzymes in the vacuole dissolve the envelope and capsid, releasing the virus into the cytoplasm

Synthesis: Replication and Protein Production

- Viral nucleic acid takes control over the host's synthetic and metabolic machinery
 - Mechanism varies depending on whether the virus is a DNA or RNA virus
 - RNA viruses replicate in the cytoplasm
 - DNA viruses replicate in the nucleus

Release of Mature Viruses

- Enveloped viruses are liberated by budding or exocytosis
 - Nucleocapsid binds to the membrane
 - A small pouch is formed
 - Pinching off of the pouch releases the virus with its envelope
 - Viruses are shed gradually without destruction of the cell

Damage to the Host Cell

- Cytopathic Effects (CPEs)
 - Virus-induced damage to the cell that alters its microscopic appearance
 - Cells can become disoriented, undergo major changes in shape or size, or develop intracellular damage
- Inclusion bodies
 - compacted masses of viruses or damaged cell organelles in the nucleus or cytoplasm
- Syncytia (singular, syncytium)
 - fusion of multiple host cells into single large cells containing multiple nuclei

Persistent Infections

- A carrier relationship that develops in some cells
 - Cell harbors the virus and is not immediately lysed
 - Provirus: viral DNA incorporated into the DNA of the host
 - Chronic latent state: periodic activation after a period of viral inactivity

Viruses and Cancer

- Oncogenic viruses
 - Experts estimate that up to 13% of human cancers are caused by viruses
- Transformation
 - Virus carries genes that directly cause cancer
 - Virus produces proteins that induce a loss of growth regulation in the cell

Viruses That Infect Bacteria

- Bacteriophage
 - Discovered in 1915 by Frederick Twort and Felix d'Herelle
 - Parasitize every known bacterial species
 - Often make the bacteria they infect more pathogenic for humans

Bacteriophage

- "T-even" bacteriophage infect *Escherichia coli*
 - T-2 and T-4
 - Most widely studied bacteriophage
 - Go through similar stages as animal viruses

Bacteriophage Life Cycle

- **Lytic phase or lytic cycle**
 - life cycle of bacteriophage that ends in destruction of the bacterial cell
- **Lysogenic cycle**
 - bacteriophage becomes incorporated into the host cell DNA

Lysogeny: The Silent Virus Infection

- **Temperate phages**
 - Have the ability to undergo adsorption and penetration but do not immediately undergo replication or release
- **Prophage**
 - an inactive state in which phage DNA is inserted into the host chromosome
- **Induction**
 - activation of a prophage in a lysogenic cell to progress directly into viral replication and the lytic cycle

The Danger of Lysogeny in Human Diseases

- Occasionally, phage genes in the bacterial chromosome cause the production of toxins or enzymes that cause pathology in the human
- **Lysogenic conversion**
 - The acquisition of a new trait from a temperate phage
 - Responsible for the diphtheria toxin, cholera toxin, and botulism toxin

Virus Identification

- Cytopathic effects
- Serological tests
 - Detect antibodies against viruses in a patient.
 - Use antibodies to identify viruses in neutralization tests, viral hemagglutination, and Western blot.
- Nucleic acids
 - RFLPs
 - PCR

Techniques in Cultivating and Identifying Animal Viruses

- *In vivo* methods: viral cultivation in lab animals or embryonic bird tissues
- *In vitro* methods: viral cultivation in cell or tissue culture
- Primary Purposes of Viral Cultivation:
 - Isolate and identify viruses in clinical specimens
 - Prepare viruses for vaccines
 - Do detailed research on viral structure, multiplication cycles, genetics, and effects on host cells

Using Live Animal Inoculation

- Specially bred strains of animals used for animal cultivation of viruses:
 - White mice

- Rats
- Hamsters
- Guinea pigs
- Rabbits
- Injection sites for viral exposure:
 - Brain
 - Blood
 - Muscle
 - Body cavity
 - Skin
 - Footpads

Using Bird Embryos

- Benefits of using bird embryos:
 - Embryonic development occurs in a protective shell
 - Intact and self-supporting unit with its own sterile environment and nourishment
 - Furnishes several embryonic tissues that support viral multiplication

Using Cell (Tissue) Culture Techniques

- **Cell culture** or **tissue culture**: *in vitro* virus cultivation systems
 - A simple and effective way to grow populations of isolated animal cells in culture dishes
 - Most viruses are propagated through cell culture
 - Much of a virologist's work involves developing and maintaining cultures

Primary Cell Cultures

- Freshly isolated animal tissue is placed in a growth medium
- Cells undergo mitotic division, producing a monolayer on the surface
- Retain the characteristics of the original tissue from which they were derived

Continuous Cell Cultures

- Have altered chromosome numbers
- Grow rapidly
- Show changes in morphology
- Can be continuously subcultured if they are given fresh nutrient media

Detecting Viral Growth in Culture

- Degeneration and lysis of infected cells
- Plaques
 - Clear, well-defined patches in the cell sheet
 - Macroscopic manifestations of cytopathic effects
 - Develops when viruses released from an infected cell radiate out to surrounding cells and infect them
 - Infection spreads gradually and symmetrically from the original point of infection

Other Noncellular Infectious Agents

- Spongiform encephalopathies
 - Implicated in chronic, persistent disease in humans and animals
 - Brain tissue removed from affected animals resembles a sponge
- Prions
 - Common feature of spongiform encephalopathies
 - Distinct protein fibrils deposited in brain tissue of affected animals
- Creutzfeldt-Jakob Disease (CJD)
 - Afflicts the central nervous system of humans
 - Causes gradual degeneration and death
 - Transmissible by an unknown mechanism
 - Several animals are victims of similar diseases:
 - Scrapie: sheep, mink elk
 - Bovine spongiform encephalopathy: cows
- Prion infection
 - Exact mode of infection is unknown
 - Protein composition of prions has revolutionized ideas of what can constitute an infectious agent
 - Questions about how prions replicate given that they have no nucleic acid
- Satellite viruses
 - Dependent on other viruses for replication
 - Adeno-associated virus (AAV)
 - Originally thought that it could only replicate in cells infected with the adenovirus
 - Now found to infect cells infected with other viruses or that have had their DNA disrupted through other means
- Viroids
 - Virus-like agent that parasitizes plants
 - About one-tenth the size of an average virus
 - Composed only of naked strands of RNA—lack a capsid or other type of coating
 - Significant pathogens in economically important plants: tomatoes, potatoes, cucumbers, citrus trees, and chrysanthemums

Viruses and Human Health

- Impossible to measure the number of viral infections worldwide
- Most common cause of acute infections that do not result in hospitalization:
 - Colds, chickenpox, influenza, herpes, warts
- Viral infections that only occur in certain regions:
 - Dengue fever, Rift Valley fever, Yellow fever
- Some have high mortality rates:

- Rabies
 - Ebola
- Other viral infections lead to long-term disability
 - Polio
 - Neonatal rubella
- Viruses mutate at a rapid rate
- Difficult to design therapies against viruses
- Scientists focus on developing vaccines against viruses since so few antiviral drugs are available and antibiotics are ineffective
- Interferon (IFN)
 - Naturally occurring human cell product
 - Used with some success in preventing and treating viral infections