

VIRUSES

A. What are viruses?

- **Virion:** a complete virus particle that consist of DNA or RNA molecule enclosed in a coat of protein.

- Viruses can exist in **two phases:**

- **Extra Cellular**

- Virions: posses few enzymes if any and cannot reproduce independently of living cells.

- **Intra Cellular**

- Viruses exist primarily as replicating nucleic acids that induce host metabolism to synthesise virions, complete virus particles.

1. Problems

a. Viruses are too small to be seen under the light microscope (~65 nm).

b. Viruses can't be grown in the absence of the host cell: **obligate intracellular parasites.**

- Animal, plant, insect, and bacterial (bacteriophage) viruses

2. Solutions

a. development of the electron microscope

b. development of cell culture techniques to grow viruses

c. **Bacteriophage assay**

(1) Mix virus and bacterial cells in a test tube that contains 0.7% agar (“soft agar”).

(2) Pour contents of tube onto the surface of a nutrient agar plate and let solidify.

- (3) *Incubate for 24 hours.*
- (4) *Result in **Plaques**:*
a “lawn” of bacteria pockmarked by clear spots of viral growth.
 - *Each plaque is assumed to arise from a single infectious virus particle.*

3. *Tissue culture techniques for animal viruses were developed in the 1950’s.*

Virus morphology

- *10-300 nm in size (recall that limit of resolution of the best light microscopes is about 200 nm).*

Shape

- (1) *filamentous (tubular); e.g., tobacco mosaic virus*
- (2) *polyhedral (roughly spherical); e.g., adenovirus (causes respiratory infections, different than rhinovirus which causes colds)*
- (3) *combined (polyhedral head attached to a filamentous tail); e.g., *E. coli* bacteriophage T4*

Enveloped *viruses are surrounded by a lipid membrane.*

Envelope is common in animal viruses that “bud” out of the host cell.

Chemical composition

- *All virions are constructed around a **nucleocapsid core** which is composed of a*
 - *Nucleic acid (DNA or RNA) held within a protein coat called the capsid.*
 - **Capsid:**
 - *Head consists of a hollow protein shell that encloses the viral nucleic acid.*
 - *Protects the viral genetic material and aids in the transfer between host cells.*

- (1) All **cells** contain dsDNA as their genetic material.
- (2) In different viruses, the genetic material may be dsDNA, ssDNA, dsRNA, or ssRNA.
 - **Tail** (if present) is composed of **protein**.

Outside of the host cell, the virus particle (virion) is completely inert: no metabolism or other biological activities.

How do viruses grow?

Growth of bacteriophages:

- a. **Lytic growth** (ex: bacteriophage T4, animal and plant viruses infect through a similar set of steps)
 - **Lytic Cycle:** Life cycle that culminates with the host cell bursting and releasing virions.
- (1) **Adsorption:** binding to a specific component of the host cell surface (receptor).
- (2) **Penetration:** injection of viral nucleic acid into the host cell cytoplasm by passage through the hollow tail tube (due to syringe action of the contractile sheath).
- (3) **Reproduction** of viral components: protein synthesis and nucleic acid replication using mostly host cell machinery.
- (4) **Assembly** of viral components into intact viral particles.
- (5) **Release** through lysis of the host cell (an alternative used by some viruses is extrusion through the host cell membrane, doesn't necessarily kill the cell).
- (6) During lytic growth, a single bacteriophage particle infecting a bacterial cell can typically produce 50-200 progeny in 30-40 minutes.

- b. **Lysogenic growth** (ex: *E. coli* bacteriophage λ)
- (1) adsorption
 - (2) penetration
 - (3) Integration of the viral DNA into the bacterial chromosome, where it is carried as a “silent” genetic element (prophage).
 - (4) However, the potential for lytic growth remains.
 - (5) Environmental stress (UV light, exposure to DNA-damaging chemicals, etc.) triggers excision of the viral DNA from the bacterial chromosome and the resumption of lytic growth.
 - (6) Only some, not all, phages are capable of lysogenic growth.
- c. Lytic growth can be thought of as a “hit and run” strategy for viral reproduction and lysogenic growth as a “playing the waiting game” strategy.

Growth of animal viruses

- a. Virus multiplication is similar to bacteriophage lytic growth (uncoating during phagocytosis versus injection, some lytic and others bud out from the cell (enveloped) => persistent infection (may not kill cell, but cell not function normally, other effects like surface enzymes that lyse red blood cells and immune system reacts to cell).
 - b. latent infection - delay between first infection and appearance of symptoms.
3. **Retroviruses** (ex: HIV causative agent of AIDS)
- a. Growth of retroviruses
 - (1) Virus particles contain ssRNA.
 - (2) In the host cell, the viral enzyme reverse transcriptase synthesizes dsDNA using viral RNA as the template.

- (3) *Viral DNA then integrates into host cell chromosomes where it directs viral reproduction.*
- (- can be a latent infection, can remain dormant, incorporated in genome of host)*
- b. *Some retrovirus infections can transform the host cell (from normal into malignant).*
- (1) *The genetic material of some retroviruses contains an oncogene (cancer-causing gene or tumor suppressor gene) which is responsible for the transformation.*
- (2) *About 20 different oncogenes have been identified so far.*
- c. *Potential oncogenes (proto-oncogenes) have been found in normal, uninfected cells. Proto-oncogenes encode proteins that stimulate the proliferation of cells.*
- d. *Retroviral oncogenes are slightly altered versions of cellular proto-oncogenes.*
- e. *Hypothesis: retrovirus incorporates cellular proto-oncogenes from the host cell DNA in a mutated form (activated to function as oncogenes).*
- f. *Every cell in the body contains proto-oncogenes that could turn the cell malignant under the appropriate conditions. What factors influence this process?*
- (1) *environmental effects*
- (2) *genetic effects*
- g. *It is estimated that up to 20% of all human cancers are caused (at least in part) by chronic viral infections.*
- h. *Viruses that are implicated in human cancers (weaken immune system (ex-AIDS) or deliver oncogenes):*

- (1) **Retroviruses:**
- *Human T-cell Leukemia virus (HTLV-1) and*
 - *Human Immunodeficiency Virus (HIV)=Kaposi's lymphoma (cancer of the lining of the blood vessels).*
- (2) **DNA viruses:**
- **Human Papilloma Virus**
cervical cancer, may be due to coinfection with cancer causing herpes virus
 - **Epstein-Barr Virus**
Nasopharyngeal cancer and Burkitt's lymphoma: a cancer of the lymph glands
 - **Hepatitis B Virus - liver cancer**

Other viral diseases of animals: herpes, smallpox, rabies