Virus

How do viruses differ?

1) genetic material within a virus
   a. DNA or RNA but never both
   b. Several different configuration of nucleic acids
      1) (ds)DNA, (ss)DNA, (ds)RNA, (ss(+))RNA, (ss(-))RNA, RNA retro
   c. viral genomes are much smaller than genomes of host

2) the cells they attack
   a. viruses infect only particular host’s cells
   b. affinity of viral surface proteins or glycoproteins for surface of host cell
      1) HIV attacks only lymphocytic T4 helper and not muscle cells
      2) Generalist: Rabies virus infects mammals

3) the composition of their capsid coats
   a. composed of a single or several proteins
      1) subunits called capsomeres

4) their shape
   a. shapes used to classify virus
      1) Helical
      2) Polyhedral
         a) icosahedron with 20 sides
      3) Complex
         a) many different shapes not readily fitting into either of the two categories
            1) small pox virus with several covering layers including a lipid layer

5) the presence or absence of an envelope
   a. Non-enveloped virus: naked virus
   b. viral envelope may be similar in composition to a cytoplasmic membrane derived from host
      1) envelopes’s protein and glycoproteins play a role in the recognition of host cell

How are viruses classified?

1) Viruses are classified by:
   a. Nucleic acid
   b. presence of an envelope,
   c. shape
   d. size

2) Relationships between virus not well understood
   a. Only three orders established
      1) Virus classified according to Family relationships: *viridae*
How are viruses classified

ICTV classification

The International Committee on Taxonomy of Viruses (ICTV) developed the current classification system and put in place guidelines that put a greater weighting on certain virus properties in order to maintain family uniformity. A universal system for classifying viruses, and a unified taxonomy, has been established since 1966. In determining order, taxonomists should consider the type of nucleic acid present, whether the nucleic acid is single- or double-stranded, and the presence or absence of an envelope. After these three main properties, other characteristics can be considered: the type of host, the capsid shape, immunological properties and the type of disease it causes. The system makes use of a series of ranked taxons. The general structure is as follows:

Order (-virales)

Family (-viridae)

Subfamily (-virinae)

Genus (-virus)

Species (-virus)

The recognition of orders is very recent; to date, only 3 have been named, most families remain unplaced. The committee does not formally distinguish between subspecies, strains, and isolates. In total there are 3 orders, 56 families, 9 subfamilies, 233 genera. ICTV recognizes about 1,550 virus species but about 30,000 virus strains and isolates are being tracked by virologists.[25]
In addition to this classification system, the Nobel Prize-winning biologist David Baltimore devised the Baltimore classification system.[26][27] The ICTV classification system is used in conjunction with the Baltimore classification system in modern virus classification.[28][29][30]

Baltimore Classification

The Baltimore Classification of viruses is based on the method of viral mRNA synthesis.

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Baltimore classification Group Contains

<table>
<thead>
<tr>
<th>Group</th>
<th>Contains</th>
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<tbody>
<tr>
<td>I</td>
<td>dsDNA viruses</td>
</tr>
<tr>
<td>II</td>
<td>ssDNA viruses</td>
</tr>
<tr>
<td>III</td>
<td>dsRNA viruses</td>
</tr>
<tr>
<td>IV</td>
<td>(+) ssRNA viruses</td>
</tr>
<tr>
<td>V</td>
<td>(-) ssRNA viruses</td>
</tr>
<tr>
<td>VI</td>
<td>ssRNA-RT viruses</td>
</tr>
<tr>
<td>VII</td>
<td>dsDNA-RT viruses</td>
</tr>
</tbody>
</table>

ss: single-stranded, ds: double stranded
RT: reverse transcribing

The Baltimore classification of viruses is based on the mechanism of mRNA production. All viruses must generate positive strand mRNAs from their genomes, in order to produce proteins and replicate themselves, but different mechanisms are used to achieve this in each virus family. This classification places viruses into seven groups:

- **I**: Double-stranded DNA (e.g. Adenoviruses, Herpesviruses, Poxviruses)
- **II**: Single-stranded (+)sense DNA (e.g. Parvoviruses)
- **III**: Double-stranded RNA (e.g. Reoviruses)
- **IV**: Single-stranded (+)sense RNA (e.g. Picornaviruses, Togaviruses)
- **V**: Single-stranded (-)sense RNA (e.g. Orthomyxoviruses, Rhabdoviruses)
- **VI**: Single-stranded (+)sense RNA with DNA intermediate in life-cycle (e.g. Retroviruses)
- **VII**: Double-stranded DNA with RNA intermediate (e.g. Hepadnaviruses)

As an example of viral classification, the chicken pox virus, Varicella zoster (VZV), belongs to family Herpesviridae, subfamily Alphaherpesvirinae and genus Varicellovirus. It remains unranked in terms of order. VZV is in Group I of the Baltimore Classification because it is a dsDNA virus that does not use reverse transcriptase.
A) Positive single-stranded RNA viruses (picornaviruses)

\[ +RNA \rightarrow \text{Proteins (after processing by host and virus-coded proteinase)} \]

\[ \text{Viral replicases} \rightarrow +RNA \rightarrow -RNA \rightarrow +RNA \text{ (virion)} \]

B) Double-stranded RNA viruses (reoviruses)

\[ \pm RNA \rightarrow +RNA \rightarrow \text{Protein} \]

\[ \text{Replicase} \rightarrow -RNA \text{ (virion)} \]

C) Negative single-stranded RNA viruses (paramyxoviruses - mumps and measles orthomyxoviruses — influenza)

\[ -RNA \rightarrow +RNA \rightarrow \text{Proteins} \]

\[ \text{viral replicase} \rightarrow +RNA \rightarrow -RNA \text{ (virion)} \]

D) Retroviruses (Rous sarcoma virus, HIV)

\[ +RNA \rightarrow +RNA/-DNA \rightarrow -DNA \rightarrow \pm DNA \rightarrow +mRNA \rightarrow \text{Protein} \]

**RNA Reproductive Strategies**

Do different virus attack different tissues/organs systems within the human body?

<table>
<thead>
<tr>
<th>Localized Infections:</th>
<th></th>
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<tbody>
<tr>
<td><strong>Virus</strong></td>
<td><strong>Primary Replication:</strong></td>
</tr>
<tr>
<td>Rhinoviruses</td>
<td>Upper respiratory tract</td>
</tr>
<tr>
<td>Rotaviruses</td>
<td>Intestinal epithelium</td>
</tr>
<tr>
<td>Papillomaviruses</td>
<td>Epidermis</td>
</tr>
</tbody>
</table>

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<tr>
<th>Systemic Infections:</th>
<th></th>
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<tbody>
<tr>
<td><strong>Virus</strong></td>
<td><strong>Primary Replication</strong></td>
</tr>
<tr>
<td>Enterovirus (poliovirus)</td>
<td>Intestinal epithelium</td>
</tr>
<tr>
<td>Herpesvirus (HSV type 1 and 2)</td>
<td>Oropharynx or urogenital tract</td>
</tr>
<tr>
<td>Rabies virus</td>
<td>Muscle cells and connective tissue</td>
</tr>
</tbody>
</table>

**RNA Reproductive Strategies**

What is a Bacteriophage, what is their mode of action (MOA) upon bacteria and how do they differ from animal virus?

Bacteriophages

A. Fine structure
   1. Capsid (head), {sheath, tail fiber, baseplate, pin} = Tail

B. Detection and quantification (see lab 15)

C. Life cycle of a lytic phage
   1. Molecular events during 5 distinct stages:
      a. 1 - attachment; 2 - penetration; 3 - biosynthesis 4 - maturation 5 - release
   2. Eclipse period
      a. The period of time is when viral multiplication is complete, yet, infective virions are not present.
   3. Burst time
      a. averages 20 - 40 minutes
      b. the number of phage particles released from a single cell is referred to burst size
         Ranging from 50 to 200 particles

D. Life cycle of a lysogenic phage

Lysogeny is a state of cell chromosome where a bacteriophage genome has been inserted into the bacterial chromosome by nonreciprocal recombination occurring between the phage chromosome and the bacterial chromosome. This insertion occurs at specific locations in each of chromosomes where there in homology of sequences in the two chromosomes.

Lysogenic conversion is the state of a cell that shows new properties like ability to form cytotoxins. The tox gene, coding for a toxic protein affecting eukaryotic cells, is on the phage genome that is expressed in the bacterium without causing lysis of the bacterial cell and production of more phage. The tox gene that is located in a corynephage chromosome codes for diphtheria toxin that kills susceptible human cells. When this phage chromosome becomes inserted into chromosome of the bacterium Corynebacterium diphtheriae, human infection with this microbe leads to formation and release of diphtheria toxin in the human host producing symptoms of diphtheria.

1. Molecular events during replication
   a. Lysogenic phages are also called temperate phages
      (1) may also induce lytic cycle,
      (2) are also capable of incorporating into the host DNA (inserted phage DNA is called a prophage)
   b. In lysogeny, the phage remains latent or inactive.
      (1) Host cells are known as lysogenic cells.

2. Formation of prophage
   a. 1 - Penetration;
2 - Original linear phage DNA forms a circle;
3 - circular DNA becomes part of the circular bacterial DNA (the lysogenic cycle);
4 - Prophage genes are repressed by two repressor proteins products of the prophage virus

3. Relationship to specialized (restricted) transduction
   a. When host cell replicates ---- prophage DNA is replicated but prophage remains silent
   b. Spontaneous event or UV light or certain chemicals causes phage to pop out of host DNA
      becoming active
      (1) Lytic cycle initiated

4. Important results of lysogeny
   **First**, the lysogenic cell is immune to reinfection by the same phage virus but the cell
      is not immune to other virion attacks.

   **Second**, Phage conversion: The host cell may exhibit new properties.

      Example: Corynebacterium diphtheriae (causes diphtheria) The organism can produce toxin
      only when it carries a temperate phage, prophage carries the gene coding for the toxin

   **Third, Specialized transduction**: Transfer of bacterial DNA from previous to new
      host. Bacterial DNA is packaged along with prophage DNA in the same capsid.
      (1) Bacteriophage λ picks up the gal gene for galactose carrying it to galactose negative cell

**How does lysogenic conversion affect a bacteria?**

The important out comes of lysogenic conversion of a bacteria by a bacteriophage are:

1) Bacteria become immune to further attack by similar phage virus

2) The temperate phage become incorporated into the new host structure along with a
   viral gene that codes for a protein that
   suppresses phage expression. This
   incorporated phage is now called a prophage

3) The lysogenic temperate phage may be carrying a gene from a previous host cell that
   provides a new phenotype expression for the infected host.
How do Animal Viruses Differ from Bacterial type viruses?

A. Replication of animal viruses
   1. Multiplication of animal virus follow the basic patter that of bacteriophage with several differences
      a. mechanism of cellular penetration
      b. Synthesis and assembly of new viral components differs
         (1) Animal viruses have different enzymes not found in phages

B. Cultivation
   1. Attachment to receptor site on cell membrane
      a. Animal virus do not contain appendages like tail fibers
      b. Attachment sites of virus may include spikes: *Influenza viurs*
      c. Gene variation between animals results in variability of susceptibility of animal host
   2. Penetration 3 methods of viral penetration into eukaryotic host cell
      a. **endocytosis:** folding of the cell membrane inward engulfing enveloped virus
         1) Enveloped virus uncoats within cytoplasm of host release nucleic acid
      b. **Fusion:** Envelope of Enveloped viruses fuse with host plasma membrane
         (1) releasing capsid into cell’s cytoplasm HIV works in this manner
      c. **Direct penetration** of nucleic acid into cytoplasm through membrane of host without capsid entering the cytoplasm
   3. Uncoating
      a. Viral nucleic acid separates from its protein coat.
      b. Enzymes degrade the proteins of the viral capsid releasing the virus nucleic acid
         Poliovirus works in this manner

C. Replication & Maturation

   **Biosynthesis of Nucleic Acid**
   Virus uses the host system to make new nucleic acid
   Proteins and capsid are synthesized in cytoplasm.
   Proteins migrate into nucleus and are assembled into active virus.
   Released from host cell

DNA viruses

   Transcription and translation using host enzymes

   Exception is Poxviruses - All component synthesized in cytoplasm. Poxviruses use their own transcriptase enzyme
D. Importance: Interactions with host cells

1. **Active infections** caused by DNA viruses include hepatitis, infectious mononucleosis, Burkitt’s lymphoma, chicken pox, and small pox.

2. **Latent infections** caused by DNA viruses include genital herpes and pharyngitis caused by adenoviruses.

3. **Oncogenic** (cancer-causing) and potentially oncogenic DNA viruses are common; such viruses cause cancer of the liver and genitourinary tract, as well as lymphoma and papilloma.

4. **Prions**: infectious protein particles:
   a. the gene of PrP$^\text{c}$ is located on chromosome 20 in the humans. PrP$^\text{c}$ produced by cells is secreted to the cell surface. This type of disease runs in the family line.
   b. PrP$^\text{c}$ is reacts with PrP$^\text{c}$ on the cell surface converting the PrP$^\text{c}$ to PrP$^\text{sc}$
   c. PrP$^\text{sc}$ is taken in by endocytosis and accumulates in the lysome.
Animal virus

http://textbookofbacteriology.net/themicrobialworld/AnimalViruses.html

HIV

http://www.youtube.com/watch?v=RO8MP3wMvqg

PBS NOVA Now: Flu (Avian)

http://www.pbs.org/wgbh/nova/sciencenow/3318/02.html

PBS NOVA Now: Flu (Avian) (part 2)

http://www.pbs.org/wgbh/nova/sciencenow/3302/04.html

Lysogenic cycle

http://www.youtube.com/watch?v=_J9-xKitsd0

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Influenza A Virus Replication