

## Chapter 18 - The Viruses of Eucaryotes

### Animal Viruses

- ◆ Classical methods to categorize animals viruses were based upon host preferences, which eventually proved to be unsatisfactory
- ◆ Modern schemes for the classification of animal viruses is based upon:
  - \* Morphology
  - \* Physical and chemical composition
  - \* Genetic relatedness

### Animal Virus Reproduction

- ◆ Similar in many respects to that exhibited by phage
- ◆ Consists of several stages:
  - \* Absorption
  - \* Penetration and uncoating
  - \* Replication of nucleic acids
  - \* Synthesis and assembly of capsids
  - \* Release of mature viruses
- ◆ Absorption
  - \* Attachment to host through random collisions of the virion and a receptor site on the cell's plasma membrane
  - \* Receptor site
    - Protein or glycoprotein
      - ❖ Bind hormones or other molecules important in cellular function
      - ❖ Immunoglobulins (antibodies)
      - ❖ Other types of molecules
    - Distribution is often tissue specific, e.g.,
      - ❖ polio virus - gut, nasopharynx, spinal cord cells
      - ❖ measles virus - body-wide receptors
  - \* Entry is often by endocytosis (passive uptake)
  - \* Virus molecules involved in absorption:
    - One or more capsid structural proteins
    - Envelope glycoproteins, e.g., influenza spike proteins hemagglutinin and neuraminidase

## ◆ Penetration and uncoating

- \* During or following penetration, the capsid is removed and the viral nucleic acid is released
- \* From absorption to final uncoating may take minutes or hours, depending upon the virus
- \* Viruses typically use one of two different mechanisms for penetration/uncoating
  - Enveloped viruses enter the cell by a process involving the fusion of membranes
    - ❖ Viral envelope proteins bind to plasma membrane receptors to form a fusion pore
    - ❖ Virus enters cytoplasm and capsid uncoats
    - ❖ Usually a virus polymerase begins transcription inside the nucleocapsid just prior to entry
  - Some enveloped viruses as well as non-enveloped viruses enter the host cell by endocytosis
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    - ❖ Enveloped viruses are enclosed in a coated vesicle which may or may not fuse with a lysosome
      - Capsid may uncoat inside endosome, or
      - Virus envelope fuses with endosome membrane to be released into the cytoplasm
    - ❖ Non-enveloped (“naked”) viruses are enclosed in a vesicle which becomes acidified upon lysosomal fusion
      - Acid-induced conformational change causes capsid to uncoat
      - Nucleic acid is released via a membrane pore or rupture of the vesicle

## ◆ Replication and transcription

## \* DNA viruses

- Early genes take over host cell machinery and begin synthesis of viral DNA and RNA
- Site of DNA replication:
  - ❖ Most viruses - host cell nucleus
  - ❖ Poxviruses - cytoplasm
- mRNA synthesis:
  - ❖ Most viruses - use host cell polymerase
  - ❖ Poxviruses - uses viral-encoded polymerase

- Examples of viral replication models
  - ❖ Parvovirus - simplest of the DNA viruses (ssDNA)
    - Genome encodes on three capsid proteins
    - Relies on host cell enzymes to synthesize all viral molecules
    - DNA is replicated only during host cell DNA replication (S phase of cell cycle)
  - ❖ Herpesviruses - dsDNA virus
    - Genome contains 50-100 genes
    - DNA is transcribed by host RNA polymerase to form other RNAs that direct the synthesis of viral molecules, including DNA replicated using a virus-encoded polymerase
  - ❖ Poxvirus - (e.g., vaccinia virus), largest viruses known and morphologically complex (dsDNA)
    - Genome contains over 200 genes
    - Enters cell via receptor-mediated endocytosis
    - Core, which contains the DNA and a DNA-dependent RNA polymerase, escapes into cytoplasm to synthesize early mRNAs
    - About 1.5 hours after infection, DNA replication occurs and late mRNA synthesis takes place
    - Reproductive cycle is complete in 24 hours
  - ❖ Hepadnaviruses (e.g., hepatitis B virus) - contain circular dsDNA that is replicated using reverse transcriptase
    - Upon infection, DNA is transcribed in the nucleus using host RNA polymerase
    - One of the RNAs formed is termed the **pregenome RNA**
    - Viral proteins are produced in cytoplasm
    - Pregenome RNA is incorporated into an immature core particle where reverse transcriptase forms a -DNA copy of it
    - -DNA is converted to dsDNA by DNA polymerase

- \* RNA viruses
  - RNA viruses are very diverse in their replication/reproduction schemes
  - Basic principles
    - ❖ ssRNA viruses replicate in the host cell cytoplasm using a viral **replicase** enzyme (except retroviruses) to form a dsRNA termed a replicative form
    - ❖ Retroviruses (ssRNA) uses a separate enzyme, **reverse transcriptase**, to make dsDNA (**proviral DNA**) which then directs viral reproduction
    - ❖ dsRNA viruses make positive-stranded RNA molecules that act as mRNA and direct viral reproduction
- ◆ Synthesis and assembly of virus capsids
  - \* Late genes direct the synthesis of capsid proteins
  - \* Capsid molecules self assembly to form empty capsids
  - \* Nucleic acid is incorporated into the capsid by an unknown mechanism
  - \* Often, paracrystalline clusters of complete viruses or procapsids are formed
- ◆ Virion release
  - \* Naked viruses are released by cell lysis
  - \* Enveloped viruses
    - Viral encoded proteins incorporated into the plasma membrane
    - Nucleocapsid buds through this region
    - Some viruses use other as sources for their envelope
      - ❖ Herpesvirus - nuclear membrane
      - ❖ Hepadnavirus - endoplasmic reticulum
      - ❖ Coronavirus - Golgi and endoplasmic reticulum
  - \* Actin filaments may help in viral release

### Cytocidal Infections

- ◆ Virus infections that result in cell death are termed cytocidal infections
- ◆ Viruses can also cause a variety of **cytopathic effects**, of which more than one may occur in any single infection
  - \* Inhibition of normal cellular metabolism
  - \* Lysosomal damage which leads to cellular destruction
  - \* Altered plasma membrane by insertion of virus-specific proteins which subsequently leads to attack by the immune system
  - \* Toxic effects of high viral protein levels

- \* Formation of inclusion bodies within the host cell which disrupts cell structure
- \* Chromosomal disruptions/damage
- \* Transformation of host cell into a malignant cell

### Other Types of Infections

- ◆ Most virus infections are **acute** - rapid onset, but last for a relatively short time
- ◆ Viruses can also cause other types of infections
  - \* **Persistent (chronic)**
    - Last many years
    - Virus is detectable and clinical symptoms are mild or absent for long periods of time;
    - Examples - hepatitis B, HIV
  - \* **Latent**
    - Virus stops reproducing and remains dormant for a period of time before becoming active again
    - No symptoms or detectable viruses during latent period
    - Examples - herpes simplex, varicella-zoster (shingles), cytomegalovirus, Epstein-Barr
- ◆ Mechanisms of persistence and latency are unclear, but may be due to several reasons
  - \* Virus may integrate into the host genome
  - \* Virus may become less antigenic, thus less susceptible to immune system attack
  - \* Virus may mutate to be less virulent or slower reproducing, e.g., formation of defective interfering particles
- ◆ **Slow viral infections**
  - \* Symptoms take years to emerge, e.g., measles and subacute sclerosing panencephalitis
  - \* Some may not be viruses at all, but rather a group of nonviral agents termed **prions**, e.g., scrapie, kuru, Creutzfeldt-Jakob disease

### Viruses and Cancer

- ◆ The formation of cancer cells (carcinogenesis) is a complex multistep process in normal cellular growth and differentiation are dramatically altered
- ◆ **Oncogenes** are cancer-causing genes that under the usual circumstances help regulate normal cell growth and differentiation

- ◆ Certain viruses may play a role in initiating carcinogenesis
  - \* May carry oncogenes that when incorporated into the host cell genome promote uncontrolled cell growth
  - \* May carry promoters that if incorporated next to a host oncogene may cause it to function at higher, less regulated levels which will alter normal cell growth patterns

### Other Viral/Viral-Like Agents

- ◆ Viruses are also known to attack other types of eucaryotes
  - \* Plant viruses - almost all are ssRNA or ds RNA viruses (a few exceptions)
  - \* Fungal viruses are mainly dsRNA and sometimes dsDNA
  - \* Algal viruses appear to have dsDNA genomes
  - \* Protozoan viruses are both dsRNA and dsDNA in origin
- ◆ Viroids are exceedingly small, simple plant viruses composed of very short ssRNA circular molecules transmitted by mechanical means or by pollen
- ◆ Prions
  - \* Infectious protein particle
  - \* Cause of scrapie and perhaps other similar diseases (e.g., “mad cow disease”)
  - \* Causes other proteins to misfold when contacted, thereby altering function