Lecture 18: Viruses - Viral multiplication strategies

The genome of a virus encodes relatively few proteins
- Among these, of course, are the proteins that make up the virion capsid
- The genome also encodes a number of viral enzymes, that are not usually part of the virion
  = Most of these are concerned with replication and processing of the viral genome
  = Some viral enzymes also play a role in assembly of the virion
- Even with its own enzymes, a virus is entirely dependent on the host cell for protein synthesis

The best understood viral life cycles are those of the T-even bacteriophages; these serve as good examples for the events of viral multiplication in bacteriophages, plant viruses and animal viruses (Tortora et al., Figure 13.10)
- The capsids of T-even bacteriophages are complex, and the genome has enough DNA for over 100 genes (this is a large number of genes for a virus)
- The multiplication cycle of a T-even phage begins with attachment or adsorption of the phage virion to an Escherichia coli host cell; weak bonds (e.g., hydrogen bonds) are formed between virion proteins and receptor sites on the surface of the E. coli cell
- Following successful attachment, penetration of the viral genome occurs
  = A lysozyme (cell-wall lytic enzyme) in the phage "tail" catalyzes hydrolysis of a portion of the cell's peptidoglycan
  = This creates a hole through the "core" of the tail is driven through the cell wall by contraction of the tail "sheath"
  = The DNA genome passes through the tail, and across the plasmid membrane into the E. coli cytoplasm
  = The virion capsid remains outside of the cell; only the genome enters the cytoplasm
- Once the genome is inside of the cell, several of its genes are expressed that lead to organized expression of additional genes and biosynthesis of viral components
  = First the genome itself is replicated, which provides multiple copies of phage genes
  = Then, phage genes are expressed, leading to synthesis of capsid proteins and viral enzymes
- The period of time from penetration until complete virions are assembled is known as the eclipse period; during this time, infectious virions cannot be recovered from cells
- After the genome is replicated and capsid proteins are synthesized, complete virions are assembled during the maturation phase
  = Maturation is an orderly process and, in T-even phages, involves activities of phage-encoded enzymes and "scaffolding proteins"
  = An essential part of maturation is packaging of the phage genome into the partially assembled capsids
- Once the virions have been fully assembled, they are released by lysis of the host cell, catalyzed by a phage-encoded lysozyme
- Note that expression of viral genes must be temporally regulated; that is, particular genes must be expressed at the proper time in the multiplication process
  = Genes for enzymes involved in genome replication must be early genes, as they are required early in the infection
  = Genes for enzymes involved in maturation and release are late genes
The stages involved in multiplication of T-even phages can be demonstrated experimentally in a *one-step growth experiment* (Tortora et al., Figure 13.11).

Some bacteriophages, called *temperate phages*, can "choose" between two alternate strategies for multiplication; the classic example of a temperate phage is the *E. coli* phage *lambda* (Tortora et al., Figure 13.12).

- In one strategy, the *lytic cycle*, multiplication of the phage occurs as in T-even phages.
- In the other strategy, the *lysogenic cycle*, penetration of the phage genome (which becomes circulized when it enters the cytoplasm) is followed by its recombinant integration into the host cell's chromosome.

  - The integrated phage genome, known as a *prophage*, is replicated along with the chromosome; in a sense, the phage is multiplying by this mechanism!
  - At some future time, the prophage can become *excised* from the genome, at which time it can direct the lytic production of virions.
- The prophage state, or *lysogeny*, is maintained by the action of phage-encoded *repressors* (similar to the *lac* repressor) that prevent transcription of genes involved with the lytic cycle; excision is linked to inactivation of these repressors.
- The presence of the prophage in a the chromosome of a *lysogenic cell* can have some interesting effects:
  - The lysogenic cell is "immune" to infection with another phage of the same type, since the prophage repressor proteins will immediately bind to the "incoming" genome, preventing expression of its genes.
  - Some toxins associated with infectious diseases are encoded by prophages, including those leading to diphtheria, scarlet fever and botulism.
- If excision of a prophage is aberrant, and host genes are excised along with the phage genome, the virions released from the subsequent lytic cycle can cause *specialized transduction* of the host genes to other cells (Tortora et al. Figure 13.13).
  - Specialized transduction differs from generalized transduction in that only those genes adjacent to where the prophage integrated can be transferred.
  - Specialized transducing phages are often "defective" since, in the process of picking up host genes, they may leave behind some of their own!

The multiplication of animal viruses follows the basic pattern of bacteriophage multiplication, with some important differences (Tortora et al. Table 13.3)

- Penetration usually occurs by *endocytosis*, in which the the plasma membrane folds inward and surrounds the virion (Tortora et al. Figure 13.14).
  - In the process of attachment, the virion basically "tricks" the host cell into treating it as something that should be brought into the cytoplasm.
  - The result is that the virion enters the cell enclosed in a *vesicle* formed from the plasma membrane.
- Some enveloped viruses may enter by *fusion* of the virion envelope with the plasma membrane, which drops the virion directly into the cytoplasm.
- Entry of the virion into the cytoplasm is followed by *uncoating* of the viral genome through enzyme-catalyzed digestion of the capsid proteins.
- Subsequent events - biosynthesis of viral components, maturation, and release - vary greatly among different groups of animal viruses (Tortora et al. Table 13.4).
For DNA viruses, the genome must migrate into the nucleus before the genes can be expressed (Tortora et al., Figure 13.15)

For RNA viruses, gene expression can occur in the cytoplasm (Tortora et al., Figure 13.17)

- If the virion genome is *plus strand RNA*, it can serve directly as a messenger RNA and be translated into viral proteins by the host cell's ribosome
- If the virion genome is *minus strand RNA*, it must be transcribed by a viral RNA-dependent RNA polymerase (which must be brought in with the genome)

In one group of RNA viruses, the *retroviruses* (of which *HIV-1* and *HIV-2* are the best known), the nucleotide sequence of the viral genome is copied as DNA by a viral *reverse transcriptase* (Tortora et al., Figure 13.19)

- The reverse-transcribed DNA is then integrated into a host chromosome as a *provirus*
- The provirus genes can then be transcribed to provide viral mRNAs and virion genomes
- Alternatively, the provirus can remain latent the way the a prophage does
- Sometimes, integration of the provirus can cause malignant transformation of the host cell

Different RNA viruses employ a variety of (often very complicated) multiplication strategies

- In contrast to phage release, release of animal virus virions does not always kill the host cell (although the cell usually dies anyway due to damage accumulated during the multiplication cycle)

Many enveloped viruses are released by *budding* (Tortora et al., Figure 13.20)

Naked viruses are more likely to be released by lysis of the host cell