Tikrit University/ Science College/ Biology Department

Forth class/ Microbiology / Virology

Lecture 4

Types of Viral Infections

●Lytic and Lysogenic Infections:

Most bacteriophages are either virulent or temperate. A **virulent phage** is one that has only one option: to begin multiplying immediately upon entering its bacterial host, followed by release from the host by lysis. T4 is an example of a virulent phage. **Temperate phages** have two options: upon entry into the host, they can multiply like virulent phages and lyse the host cell, or they can remain within the host without destroying it. Bacteriophage lambda is an example of this type of phage.

The relationship between a temperate phage and its host is called **lysogeny**. The form of the virus that remains within its host is called a **prophage**. A prophage is simply the viral nucleic acid either integrated into the bacterial chromosome or free in the cytoplasm. The infected bacteria are called **lysogens** or **lysogenic bacteria**. Lysogenic bacteria reproduce and in most other ways appear to be perfectly normal. However, they have two distinct characteristics. The first is that they cannot be reinfected by the same virus; that is, they have immunity to superinfection. The second is that as they reproduce, the prophage is replicated and inherited by progeny cells. This can continue for many generations until conditions arise that cause the prophage to initiate synthesis of phage proteins and to assemble new virions, a process called **induction**. Induction is commonly caused by changes in

growth conditions or ultraviolet irradiation of the host cell. As a result of induction, the lysogenic cycle ends and the lytic cycle commences; the host cell lyses and progeny phage particles are released.

Another important outcome of lysogeny is **lysogenic conversion**. This occurs when a temperate phage changes the phenotype of its host. Lysogenic conversion often involves alteration in surface characteristics of the host. For example, when a member of the genus Salmonella is infected by epsilon phage, the phage changes the activities of several enzymes involved in construction of the carbohydrate component of the bacterium's lipopolysaccharide. This eliminates the receptor for epsilon phage, so the bacterium becomes immune to infection by another epsilon phage. Other lysogenic conversions give the host pathogenic properties. This is the case when *Corynebacterium diphtheriae*, the cause of diphtheria, is infected with phage. The phage genome encodes diphtheria toxin, which is responsible for the disease. Thus, only those strains of *C. diphtheriae* that are infected by the phage (i.e., lysogens) cause disease.

Clearly the infection of a bacterium by a temperate phage has significant impact on the host, but why would viruses evolve this alternate cycle? Two advantages of lysogeny have been recognized. The first is that lysogeny allows the viral nucleic acid to be maintained within a dormant host. Bacteria often become dormant due to nutrient deprivation, and while in this state, they do not synthesize nucleic acids or proteins. In such situations, a prophage would survive but most virulent bacteriophages would not be replicated, as they require active cellular biosynthetic machinery. Furthermore, their genome would be degraded as the host cell entered dormancy. The second advantage arises when there are many more phages

in an environment than there are host cells, a situation virologists refer to as a high multiplicity of infection (MOI). In these conditions, lysogeny enables the survival of infected host cells within a population that has few uninfected cells. When MOI is high, a virulent phage would rapidly destroy the available host cells in its environment. However, a prophage will be replicated as the host cell reproduces.

Archaeal viruses can also be virulent or temperate. In addition, many archaeal viruses establish chronic infections. Unfortunately, little is known about the mechanisms they use to regulate their replicative cycles.

●Infections of Eukaryotic Cells:

Viruses can harm their eukaryotic host cells in many ways. An infection that results in cell death is a cytocidal infection. As with bacterial and archaeal viruses, this can occur by lysis of the host. Infection does not always result in lysis of host cells. Some viruses (e.g., herpesviruses) can establish persistent infections lasting many years. Eukaryotic viruses can cause microscopic or macroscopic degenerative changes or abnormalities in host cells and in tissues that are distinct from lysis. These are called **cytopathic effects (CPEs)**. Viruses use a variety of mechanisms to cause cytopathic and cytocidal effects. One mechanism of particular note is that some viruses cause the host cell to be transformed into a malignant cell.

●Viruses and Cancer:

Cancer is one of the most serious medical problems in developed nations, and it is the focus of an immense amount of research. A tumor is a growth or lump of tissue resulting from **neoplasia**—unregulated abnormal new cell growth and reproduction. Tumor cells have aberrant shapes and

altered plasma membranes that may contain distinctive molecules (tumor antigens). These changes result from the tumor cells becoming less differentiated. Their unregulated proliferation and loss of differentiation result in invasive growth that forms unorganized cell masses. This reversion to a more primitive or less differentiated state is called **anaplasia**.

Some viruses have been shown to cause cancer in animals, including humans; it is estimated that about 10 to 20% of human cancers have a viral etiology.

Considerable research into the causes of cancer has focused on the mutations that allow cancerous cells to grow uncontrollably. Those studies show that there are two types of genes that must be mutated: proto-oncogenes and tumor suppressor genes. Their names suggest that these genes are somehow abnormal. But this is not the case. Proto-oncogenes and tumor suppressor genes are normal cellular genes. **Proto-oncogenes** must be expressed if cell division is to occur. However, they normally are expressed only if the cell receives an appropriate signal, such as the binding of a growth factor to a receptor on the cell surface. When such a signal is received, the cell initiates the cell cycle, but it cannot continue past a checkpoint controlled by the activity of proteins encoded by **tumor suppressor genes**.

These proteins are called **tumor suppressor proteins**. When tumor suppressor proteins are active, they prevent progression through the cell cycle. Thus, for cell division to occur, protooncogene proteins (sometimes called oncoproteins) must be active, and tumor suppressor proteins must be inactive.

We now turn out attention to viruses and their role in causing cancer. These viruses are called **oncoviruses**. Most human oncoviruses have dsDNA genomes, and most of these viruses cause cancer in a similar way—by interacting with and inactivating either Rb or p53. Oncoviruses that are retroviruses (e.g., HTLV-1) exert their oncogenic powers in a different manner. Some carry genes called **oncogenes** that stimulate the activity of cellular proto-oncogenes. For example, HTLV-1 infects immune system cells called T cells. During the infection HTLV-1 produces a regulatory protein that activates expression of numerous cellular proto-oncogenes. Other retroviruses transform cells into cancerous cells when the viral genome integrates into the host chromosome such that strong, viral regulatory elements are near a cellular proto-oncogene. These elements cause the nearby proto-oncogene to be transcribed at a high level, causing the cellular gene to be considered an oncogene.

Definition statement:

- **Induction**: an event in the life cycle of some viruses(e,g., temperate bacteriophages) that results in the provirus initiating synthesis of mature virions and entering the lytic cycle.

- **Lysogen**: a bacterium or archaeal cell that is infected with a temperate virus.

- **Lysogeny**: the state in which a viral remains within a bacterial or archaeal cell after infection and reproduces along with it, rather than taking control of the host cell and producing new virions.

- **Lytic cycle**: the infection of a host cell by a virus that induces cell death through lysis and release of progency viruses.

●**Provirus(prophage)**: the latent form of a virus that remains within a host cell, usually integrated into the host chromosome; in archaeal and bacterial hosts, this occurs during the lysogenic cycle; when the virus is a bacteriophage, the provirus is called a prophage.

●**Temperate phage**: a bacteriophage that infects bacteria and establishes a lysogenic relationship with it is host rather than causing immediate lysis.

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