MOLECULAR VIROLOGY

BIO 554 - 3 units

Advanced course suitable for senior undergraduate students as well as graduate students. All aspects of virology will be covered with emphasis on human viruses and molecular mechanisms of virus replication.

Instructor: Dr. J. Perrault
M/W, 11:00 - 12:15, NLS 134
Prerequisite*: Bio 366
Concurrent registration in Bio 467 or Bio 549 recommended

* prerequisite enforced

BIOLOGY 554 - MOLECULAR VIROLOGY

Fall semester 2004

Instructor: Dr. Jacques Perrault, NLS401, 594-5150, jperrault@sunstroke.sdsu.edu
Office hours: Tu/Th, 12:30 PM to 1:30 PM

Course Intent: This course is designed for advanced undergraduate and graduate students. All aspects of virology will be covered including types of viruses, replication and expression mechanisms, pathogenesis, epidemiology, and host defenses. Emphasis will be on molecular mechanisms used by eukaryotic viruses and their relationship to those used by host cells.

Prerequisites: Successful completion of Bio 366 (Biochemistry, Cell, and Molecular Biology) or the equivalent is mandatory before taking this course. You will be asked to provide evidence of this. Successful completion of or concurrent registration in Bio 467 is also recommended but not mandatory.
Exams and Grading: The course grade will be based on two written exams (50% each). The first exam will cover the first half of the lecture material and the second exam will cover the second half of the lectures as well as the material from student oral presentations. The latter will take place during the final two weeks of the course and will be based on recent primary virology literature. A maximum of eight students will have the option of giving an oral Powerpoint presentation that will earn them a maximum of 10 extra points towards their final grade (10% of grade).


Recommended reference texts: S.J. Flint et al., "Principles of Virology: Molecular Biology, Pathogenesis, and Control", ASM Press, 2000. All attempts will be made to have this text on reserve for your use at the library. Your required text also lists other useful reference texts. One of these (Field’s Virology) will be put on reserve for you at the library as well.
Internet resources: Animations and other materials that accompany your text can be found at http://www.blackwellpublishing.com/Wagner/default.asp. Your text also lists several useful web sites that deal with virology. We will explore some of these during class time but you are strongly encouraged to do so on your own.

Class notes: You will have access to all lecture material on the SDSU Blackboard site as PDF files. I will try as best I can to post lecture and reading material ahead of class time.

PLEASE MAKE SURE TO CONSULT THIS BLACKBOARD SITE ON A REGULAR BASIS FOR LECTURE NOTES, UPDATES, CORRECTIONS, SAMPLE EXAMS, AND ANNOUNCEMENTS

SEQUENCE OF LECTURE MATERIAL

INTRODUCTION TO VIRUSES
Chapter 1. Introduction- The impact of viruses on our view of life (read on your own)
Chapter 2. An outline of virus replication and viral pathogenesis
Chapter 5. Virus structure and classification

REVIEW OF MOLECULAR AND CELL BIOLOGY
Chapter 13. Viruses use cellular processes to express their genetic information

GENERAL ASPECTS OF VIROLOGY
Chapter 6. The beginning and the end of the virus multiplication cycle
Chapter 9. Visualization and enumeration of virus particles (read on your own)
Chapter 10. Replicating and measuring biological activity of viruses
Chapter 11. Physical and chemical manipulation of virus structural components
Chapter 12. Characterization of viral products expressed in the infected cell (read on your own)
Chapter 14. Molecular genetics of viruses

MIDTERM EXAM?
SEQUENCE OF LECTURE MATERIAL (CONT’D)

DISCUSSION OF INDIVIDUAL VIRUS GROUPS

Chapter 15. Replication of positive-sense RNA viruses
Chapter 16. Replication strategies of RNA viruses requiring RNA-directed
mRNA transcription as the first step in viral gene expression
Chapter 20. Retroviruses: converting RNA to DNA
Chapter 21. Hepadnaviruses: variations on the retrovirus theme
Chapter 17. Replication strategies of small and medium-sized DNA viruses
Chapter 18. Replication of some nuclear-replicating eukaryotic DNA viruses
with large genomes

DEFENCE AGAINST VIRUSES AND BENEFICIAL USES

Chapter 8. Strategies to protect against and combat viral infection
Chapter 22. Viruses and the future - promises and problems

SOME IMPORTANT TERMS AND CONCEPTS

Note - Please make sure you understand the concepts covered in Chapter 1 from Wagner and Hewlett

• pathogenesis = mechanism causing disease
• virulence = severity of disease-causing potential
• virus infections can often be inapparent and not cause disease
• host response (immune status) is key in outcome of infection
• origin of viruses still debated (likely depends on which virus)
• prions (subviral agents) behave like viruses but apparently lack a nucleic acid genome
CHAPTER 2

AN OUTLINE OF VIRUS MULTIPLICATION
AND VIRAL PATHOGENESIS

CELLS VERSUS VIRUSES

Animal cell

E. coli length is ~ 5 µm

Plant cell

Average eucaryotic cell diameter is ~ 50 µm

Viruses generally range in size from 75 to 200 nm (0.075-0.200 µm)
BASIC PATTERN OF VIRUS REPLICATION IN CELLS

1. Virus *entry* into cells (via host cell receptors)
2. Virus *genes expressed* using viral and/or host-encoded functions
3. Viral proteins *modify host cell functions* to ensure viral replication
4. Viral proteins *assemble into capsids* that protect viral genomes
5. Virus is *released* and infects new cells

Ch. 2

VIRUS SOURCE AND TRANSMISSION

1. Source of virus is called *reservoir* (e.g., infected animal)
2. Agent or means by which an infection is spread or transmitted from one individual to another is called a *vector* (e.g., aerosol)

*Note- sometimes the reservoir is the same as the vector as in the case of some insect-transmitted viruses*

Ch. 2
PATHOGENESIS OF VIRUS INFECTION IN ORGANISMS

- early stages = incubation period
- spread in host most often involves circulatory or nervous system

Fig. 2.2

SITES OF VIRUS ENTRY INTO ORGANISMS

not all viruses use the same entry

spread in circulatory system causes viremia

some examples:
- poliovirus and HIV enter lymphatic system directly via gut-associated lymphatic tissue
- some neurotropic viruses enter CNS via peripheral nerves (e.g. rabies, herpes)

Fig. 2.3
VIRUS SPREAD IN CIRCULATORY SYSTEM

- this **commonly occurs** with many but not all viruses

- in some cases this involves **free virus** or virus adsorbed to the surface of cells that are not infected (**passive spread**)  

- in other cases, the virus **replicates** in cells of the **lymphatic system** (**B cells, T cells, macrophages, etc.**)
HIGH LEVEL VIRUS MULTIPLICATION IN ORGANISMS GENERALLY CAUSES DISEASE SYMPTOMS

1. Disease symptoms are due to replication in specific target tissues

2. Tissue tropism is determined by both viral and host factors (receptor distribution, intracellular interactions, inflammation, host innate immunity, etc.)

3. Presence of virus receptors plays crucial role in disease symptoms:
   - polio receptors found only in intestinal mucosa and lymphatic tissue
   - HIV recognizes CD4+ receptor on T lymphocytes
   - rabies likely uses acetylcholine receptor at nerve cell synapses
   - vaccinia (smallpox related) uses epidermal growth factor receptor

HOST IMMUNE RESPONSE TO VIRAL INFECTION

1. Immune response has both an innate component (acting early) and an adaptive component (based on specific recognition of foreign antigens).

2. Innate responses include tissue inflammation, macrophage destruction of infected cells, fever, and interferon production which limits spread of virus to uninfected cells.

3. Infection often results in an effective and long-lived adaptive host immune response (unless lethal!).

4. Adaptive response requires maturation of both B and T lymphocytes (short-lived effector T cells kill cells expressing foreign antigens on their surfaces; helper T cells drive maturation of B cells into antibody-secreting cells).

5. Generation of long-lived memory lymphocytes appears crucial for future protection.
**LATER STAGES OF VIRAL INFECTION: SPREAD TO OTHER INDIVIDUALS AND FATE OF HOST**

1. *Where* the virus accumulates (disease symptom) often *plays a role in spread* to other individuals (e.g. mosquito-borne encephalitis; chicken pox vesicles; colds and sneezing; sexual practices; herpesvirus in saliva)

2. Many acute infections involve complete *recovery* of host and *clearance* of virus; others sometimes lead to lifelong *latent infections* where no virus is produced (e.g. herpes, hepatitis)

3. Some *chronic diseases* are suspected to involve long term *persistent virus* infections (diabetes, multiple sclerosis, rheumatoid arthritis, and others).

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**CHAPTER 5**

**VIRUS STRUCTURE AND CLASSIFICATION**
VIRUS STRUCTURE: DIMENSIONS

VIRUS CLASSIFICATION

1. Virus genome
   - DNA or RNA
   - single-stranded (ss) or double-stranded (ds)

2. Virion structure
   - icosahedral or helical capsid
   - enveloped or non-enveloped (naked capsid)

3. Baltimore scheme
   - based on how virus produces mRNAs
   - mostly used to distinguish different types of RNA viruses (plus sense, minus sense, ds)
STRUCTURE OF YELLOW MOTTLE VIRUS

Fig. 5.3

Ch. 5

STRUCTURE AND RELATIVE SIZES OF VIRUSES

DNA VIRUSES

Fig. 5.2

Ch. 5
**TABLE 5.1 A Classification Scheme for Viruses**

**DNA-containing viruses**

<table>
<thead>
<tr>
<th>Type of Virus</th>
<th>Classification</th>
<th>Example</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-strand DNA viruses</td>
<td>Positive sense (virus RNA-like cellular mRNA)</td>
<td>Norovirus, enteroviruses, adenoassociated viruses</td>
<td>-</td>
</tr>
<tr>
<td></td>
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<td>Retroviruses, adenoviruses</td>
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</tr>
<tr>
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<td></td>
<td>Bacteriophage</td>
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<td></td>
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**RNA-containing viruses**

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<tr>
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**NOTE:**

- **TEXTBOOK ERROR:** (-) NOT (+)
- **STUDY TIP:** (b) Some helical RNA viruses

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**Ch. 5**

**STRUCTURE AND RELATIVE SIZES OF VIRUSES (cont’d)**

**Fig. 5.2**

**TABLE 5.1**

* A Classification Scheme for Viruses

* based on so-called “Baltimore” scheme

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**Ch. 5**
### TABLE 5.1 A Classification Scheme for Viruses (continued)

#### II. Double-stranded RNA viruses
   A. Nonenveloped
      1. Icosahedral—reovirus, "rotavirus"

#### III. Single-stranded DNA viruses
   A. Nonenveloped
      1. Icosahedral
         a. Paroviruses (Canine distemper, adenine-associated virus)
         b. Bacteriophage \( \Phi X 174 \)

   feline

#### IV. Double-stranded DNA viruses
   A. Nuclear replication
      1. Nonenveloped
         a. Icosahedral
            i. Small circular DNA genome (paroviruses—SV40, "polioviruses, " papovaviruses")
            ii. "Medium"-sized, complex morphology, linear DNA (adenoviruses)
      2. Enveloped—nucleic replicating
         a. Icosahedral
            i. Herpesviruses (linear DNA)
            ii. Hepadnaviruses (virus encapsulates RNA that is converted to DNA by reverse transcriptase)
   B. Cyttoplasmic replication
      1. Icosahedral
      2. Complex symmetry
         a. Poxviruses
   C. Bacterial viruses
      1. Icosahedral with tail
         a. T-series bacteriophages
         b. Bacteriophage \( \lambda \)

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Hepatitis B

**smallpox**
BRIEF REVIEW OF MOLECULAR BIOLOGY OF CELLS

CHAPTER 13

FLOW OF CELLULAR GENETIC INFORMATION

DNA → RNA → PROTEIN

DNA replication

transcription

reverse transcription

Note: control of the above processes relies on cis-acting and trans-acting signals
CELLULAR DNA REPLICATION

Key concepts:

1. 5’ to 3’ synthesis and antiparallel strands
2. Base-pairing rules and chemistry
3. Replication fork
4. Discontinuous synthesis and Okazaki fragments
5. Leading versus lagging strand
6. RNA priming
7. Initiation versus elongation
8. Enzymes (DNA polymerases, topoisomerases, helicases, ssDNA-binding proteins, DNA ligase)
9. DNA repair synthesis
10. Process is similar in prokaryotes and eukaryotes

Fig. 13.1
CELLULAR VERSUS VIRUS DNA REPLICATION

- DNA virus genome replication follows same basic rules with some variation

- in some cases, the virus uses the cellular enzymes for the most part (e.g., SV40)

- in other cases, most required enzymes are supplied by the virus (e.g., herpes shown here)

Fig. 13.2

CELLULAR TRANSCRIPTION IN EUKARYOTES

Key concepts:

1. **Nuclear** location
2. Roles of Pol I, II, and III (rRNA, mRNA, and small RNAs)
3. **Start** site (cap site)
4. mRNAs are almost always **monocistronic** (encode one gene)
5. **Promoter** sequences (proximal TATA box, upstream sequences)
6. **Enhancer** sequences
7. General and specific **transcription factors**
8. **Capping**, **methylation**, and **polyadenylation**
9. **Intron** versus **exon**, snRNAs, and **splicing**
10. Nuclear **transport**
TRANSCRIPTION INITIATION IN EUKARYOTES IS A MULTISTEP PROCESS

ACTIVATION OF EUKARYOTIC TRANSCRIPTION BY UPSTREAM ACTIVATORS
POSTTRANSCRIPTIONAL MODIFICATION AND MATURATION OF EUKARYOTIC mRNA

Fig. 13.5

HYPOTHETICAL EXAMPLE OF EUKARYOTIC mRNA PROCESSING

Fig. 13.6
CELLULAR VERSUS VIRUS TRANSCRIPTION

1. **RNA viruses** (other than retroviruses) use a **bewildering array of transcription mechanisms** that differ considerably from that of their hosts (many shut down host cell DNA transcription).

2. Transcription mechanisms in **DNA viruses** vary depending on the agent but **share** many **similarities with host** cells (sometimes using cellular enzymes).

3. **Temporal regulation** is common (especially DNA viruses) with early transcripts encoding regulatory functions.

4. Large DNA viruses often **encode enzymes required** for their own transcription (e.g., smallpox, insect baculoviruses, T-even bacteriophages).

5. Viruses often encode functions that **alter posttranscriptional** splicing and/or transport of mRNAs, or **edit** their own transcript.

---

**mRNA SPliciNG PATTerns IN SOME VIRUSES**

**retrovirus**

1. Splicing to reveal a cryptic translational reading frame downstream of another. (Common in retroviral replication)

2. Splicing to change a translation terminator and to fuse two translational reading frames. (Common in retroviral replication)

**papovavirus**

3. Removal of a long "leader" sequence to generate "normal" sized mRNA. (Papovaviruses and adenoviruses use the same processing to generate different mRNAs).

4. Generation of mRNA "libraries" encoding related proteins by using alternate splice sites. (Common in adenoviruses and papovaviruses replication)

**adenovirus, EBV**

5. Splicing to reveal an in-frame reading frame that is translated.

**adenovirus, papovavirus**

6. Splicing to reveal an in-frame reading frame that is translated.

---

Fig. 13.7A
CELLULAR TRANSCRIPTION IN PROKARYOTES

Key concepts:

1. mRNAs are most often *polycistronic* (encode several genes).
2. Single transcripts regulated by an upstream operator sequence that binds a repressor are called *operons*.
3. **Transcription** and **translation** are **coupled** (no nucleus).
4. Relies on a **single RNA polymerase** (α, β, β’, and σ subunits).
5. **Promoter sequences** at -10 and -35 positions.
6. Transcription is often **inducible** (inducer binding to repressor)
7. Transcription rate is regulated by **catabolite repression**
8. Transcription **termination** is either ρ-dependent or ρ-independent.

*Note - some bacteriophage depend mostly on the host transcription machinery (e.g., MS2) while others encode some transcription components (e.g., T-odd and T-even bacteriophages)*
EXAMPLE OF PROKARYOTIC OPERON

Fig. 13.8

COMPOSITION OF BACTERIAL RNA POLYMERASE

Fig. 13.9
**RHO-DEPENDENT TRANSCRIPTION TERMINATION IN BACTERIA**

\[ \rho \text{ recognizes specific sequences in the nascent transcript and its helicase activity causes dissociation of RNA/DNA hybrid in the transcription active site} \]

Fig. 13.10

---

**RHO-INDEPENDENT TRANSCRIPTION TERMINATION IN BACTERIA**

Fig. 13.11
EUKARYOTIC TRANSLATION

Key concepts:

1. Small **40S ribosomal subunit** binds to met-tRNA to form an **initiation complex** (requires eIF-2, eIF-3, eIF-4C, and GTP).
2. Initiation complex **binds to methylated cap** at 5’ end of mRNA (requires eIF-4A, eIF-4B, and eIF-4F)
3. Initiation complex **scans 5’ to 3’** along mRNA until it reaches an AUG start site in the proper context (**Kozak sequence**)
4. **60S ribosome subunit joins** initiation complex and **initiation factors are released** (requires eIF-5, eIF-6 and GTP hydrolysis)
5. **80S complex elongates** chain until reaching a **stop codon** (UAA, UGA, or UAG)
6. **Polypeptide chain is released** with the help of release factors

**NOTE** - internal initiation of translation does not take place for mRNAs that contain cap structures (majority)

INITIATION OF EUKARYOTIC TRANSLATION

- **many viruses alter or inhibit host translation** through various mechanisms (e.g., eIF-2 inhibition)
- **some viruses partially suppress termination** at specific stop codons in their own mRNAs to produce longer proteins with different properties (e.g., retroviruses)
TRANSLATION OF
MULTIPLE OPEN READING FRAMES

- up to three open reading frames (ORFs) are possible in mRNAs
- generally only one is read by the ribosomes (the one in frame with the first AUG start codon from the 5’ end)
- in some cases (more common in viruses), ribosomes can start using alternate AUGs producing different proteins from the same sequence

\[
\text{frame 1 } 5’…\textbf{AUG} \text{ GGC UAU GGA UGG CCA AAG}…3’ \\
\text{frame 2 } 5’…\text{AUG GGC UAU GGA UGG CCA AAG}…3’ \\
\text{frame 3 } 5’…\text{AUG GGC UAU GGA \textbf{UGG} CCA AAG}…3’
\]

Note - mRNA splicing sometimes also uncovers “cryptic” ORFs that become functional because an upstream AUG start is removed

PROKARYOTIC TRANSLATION

Key concepts:

1. mRNA 5’ end has no cap structure.
2. Many mRNAs are polycistronic and each gene is translated separately (internal initiation).
3. AUG start is defined by upstream Shine-Delgarno sequence (short polypyrimidine tract that base pairs with end of 16S rRNA)
4. Formation of initiation complex (N-formylmethionine-tRNA and 30S subunit) requires IF-1, IF-2, IF-3, and GTP.
5. Initiation complex binds directly to AUG start followed by 50S subunit joining and release of factors.
6. Elongation and release at stop codons is very similar to eukaryotes.
INITIATION OF PROKARYOTIC TRANSLATION

Fig. 13.13

CHAPTER 6

THE BEGINNING AND END OF THE VIRUS REPLICATION CYCLE
EARLY STAGES OF VIRUS REPLICATION CYCLE: CELLULAR RECEPTORS FOR VIRUSES

- virus receptors are generally **cellular transmembrane glycoproteins** that perform normal cellular functions

- receptors generally project some distance from the cell surface and the interaction with viruses is **highly specific**

![Diagram](image)

**Fig. 6.1**

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**TABLE 6.1** Some Cellular Receptors for Selected Animal Viruses

<table>
<thead>
<tr>
<th>Name</th>
<th>Cellular Function</th>
<th>Virus Receptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAG</td>
<td>Nucleate assembly</td>
<td>Adenovirus</td>
</tr>
<tr>
<td>CD4</td>
<td>T lymphocyte activation</td>
<td>HIV</td>
</tr>
<tr>
<td>TLR1</td>
<td>Antigen recognition</td>
<td>Togaviruses, SINV</td>
</tr>
<tr>
<td>MHC</td>
<td>Ag presentation, stimulation of B cell differentiation</td>
<td>Yersinia, Bacillus</td>
</tr>
<tr>
<td>Boyr</td>
<td>T and B</td>
<td>Interferon (tumour)</td>
</tr>
<tr>
<td>Leukocyte adhesion</td>
<td>Junction and transport</td>
<td>Marek's herpesvirus (lymphoma)</td>
</tr>
<tr>
<td>IGF receptor</td>
<td>Insulin-like signaling receptor</td>
<td>Vesnavirus A virus (leukemia)</td>
</tr>
<tr>
<td>Hemoglobin receptor</td>
<td>Normal tropism:-alpha</td>
<td>Adenovirus</td>
</tr>
<tr>
<td>FGF</td>
<td>Growth factor</td>
<td>Tumour viruses</td>
</tr>
<tr>
<td>CDG/CD4</td>
<td>Complement receptor</td>
<td>Feline-leukemia viruses</td>
</tr>
<tr>
<td>INH</td>
<td>Tumor necrosis factor receptor family</td>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>Sialic acid</td>
<td>Ubiquitous component of eucaryote glycosylated proteins</td>
<td>Influenza virus, neuraminidase</td>
</tr>
</tbody>
</table>

Ch. 6
CO-RECEPTORS AND ALTERNATE RECEPTORS

1. Some viruses require additional cell surface proteins or co-receptors for entry (e.g., HIV requires CCR5 on macrophages and CXCR4 on T lymphocytes, each utilized by different virus variants).

2. If the major receptor is absent, an alternate receptor is sometimes used, often with lower efficiency (e.g. SV40, a simian virus, infecting murine and hamster cells in culture).

3. measles virus vaccine utilizes CD46 as a receptor but wild-type measles use SLAM (CDw150) which is expressed in B and T cells.

4. Some viruses after gaining entry into cells can bypass receptor and infect adjacent cells by cell to cell fusion (syncytia formation).

MECHANISMS OF VIRUS ENTRY THROUGH RECEPTORS: NON-ENVELOPED VIRUSES

- receptor-mediated endocytosis is generally employed by non-enveloped viruses (poliovirus example is illustrated here).

- acidification of endocytotic vesicle usually plays a crucial role in triggering virus genome release.

Fig. 6.2
MECHANISMS OF VIRUS ENTRY THROUGH RECEPTORS: ENVELOPED VIRUSES

Note - which of the above two mechanisms is used depends on the virus

Fig. 6.3

EXAMPLE OF ENTRY BY PLASMA MEMBRANE FUSION: PSEUDORABIES VIRUS

Note - pseudorabies is a herpesvirus family virus and is not related to rabies virus

Fig. 6.3
BACTERIOPHAGE ENTRY MECHANISMS

**Table 6.2** Some E. coli Bacteriophage Receptors

<table>
<thead>
<tr>
<th>Virus</th>
<th>Structure</th>
<th>Normal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>OmpF</td>
<td>Porin protein</td>
</tr>
<tr>
<td></td>
<td>Lipopolysaccharide</td>
<td>Outer membrane structure</td>
</tr>
<tr>
<td>T4</td>
<td>OmpC</td>
<td>Porin protein</td>
</tr>
<tr>
<td></td>
<td>Lipopolysaccharide</td>
<td>Outer membrane structure</td>
</tr>
<tr>
<td>T6</td>
<td>Tsx</td>
<td>Nucleoside transport protein</td>
</tr>
<tr>
<td>T11 and T15</td>
<td>Tad</td>
<td>Formineme transport protein</td>
</tr>
<tr>
<td>λ</td>
<td>Lamb</td>
<td>Maltose transport protein</td>
</tr>
<tr>
<td>MS2</td>
<td>4 plus</td>
<td>Conjugation</td>
</tr>
</tbody>
</table>

Ch. 6

BACTERIOPHAGE ENTRY MECHANISMS: T4 PHAGE EXAMPLE

**T4 phage entry is a multi-step process**

1st step: weak interaction between *tail fiber protein* and cell surface receptor (OmpC lipopolysaccharide)

2nd step: strong interaction between *tail pins* and outer membrane which triggers compression of tail sheath and tail tube penetration through cell wall

3rd step: viral *pilot protein* enables DNA translocation through inner membrane

Fig. 6.4
BYPASSING VIRUS RECEPTORS BY EXPERIMENTAL TRANSFECTION

e.g., VZV (varicella-zoster virus)
DNA transfected into susceptible cells

expression of virus glycoprotein gene measured by fluorescent antibody

VZV is in the herpes virus family and causes chickenpox and shingles

LATE STAGES OF VIRUS REPLICATION CYCLE:
HELICAL CAPSID ASSEMBLY

illustrated here is the assembly of the helical nucleocapsid of TMV (tobacco mosaic virus)

specific contacts between viral RNA and proteins govern assembly process

Fig. 6.6
LATE STAGES OF VIRUS REPLICATION CYCLE: ICOSAHEDRAL NUCLEOCAPSID ASSEMBLY

- assembly of most icosahedral virus capsids involves **maturational proteases** that trigger conformational changes in procapsids

- **genome** is **inserted** into empty procapsid for some viruses (e.g., phage P22) or **capsid assembles around genome** for others (e.g., poliovirus)

FORMATION OF VIRUS ENVELOPE

- synthesis of virus **surface glycoproteins** follows a path similar to cellular counterparts (sorting through Golgi)

- **lipids** are derived entirely from cellular membranes while virus proteins displace host proteins at sites of budding
BUDDING OF ENVELOPED VIRUSES

Note - some viruses bud from both **nuclear** and **plasma** membranes (e.g., herpes viruses); others bud only from the plasma membrane (e.g., most RNA viruses)

CMV (human cytomegalovirus, a type of herpesvirus) budding from the nucleus

Pseudorabies virus egress from cytoplasm

- empty capsids and “dense bodies” of aggregated matrix proteins are sometimes formed

virus matrix (tegument) proteins serve as adapters (“glue”) to bring viral capsids to membrane areas modified by insertion of virus glycoproteins

Fig. 6.9