VIROLOGIA 2005/2006

APRESENTAÇÃO 10

(Vírus com genoma de DNA)

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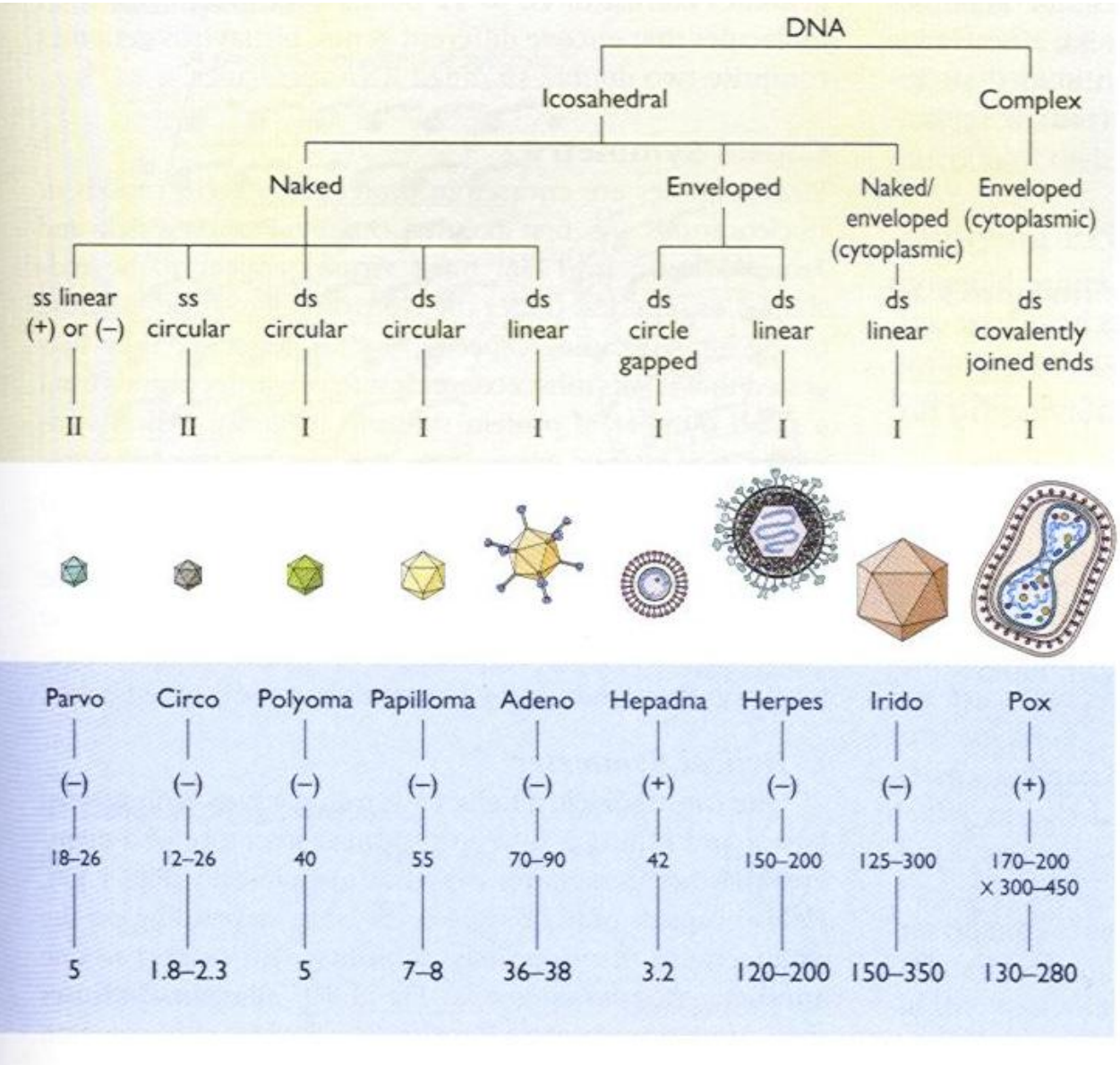
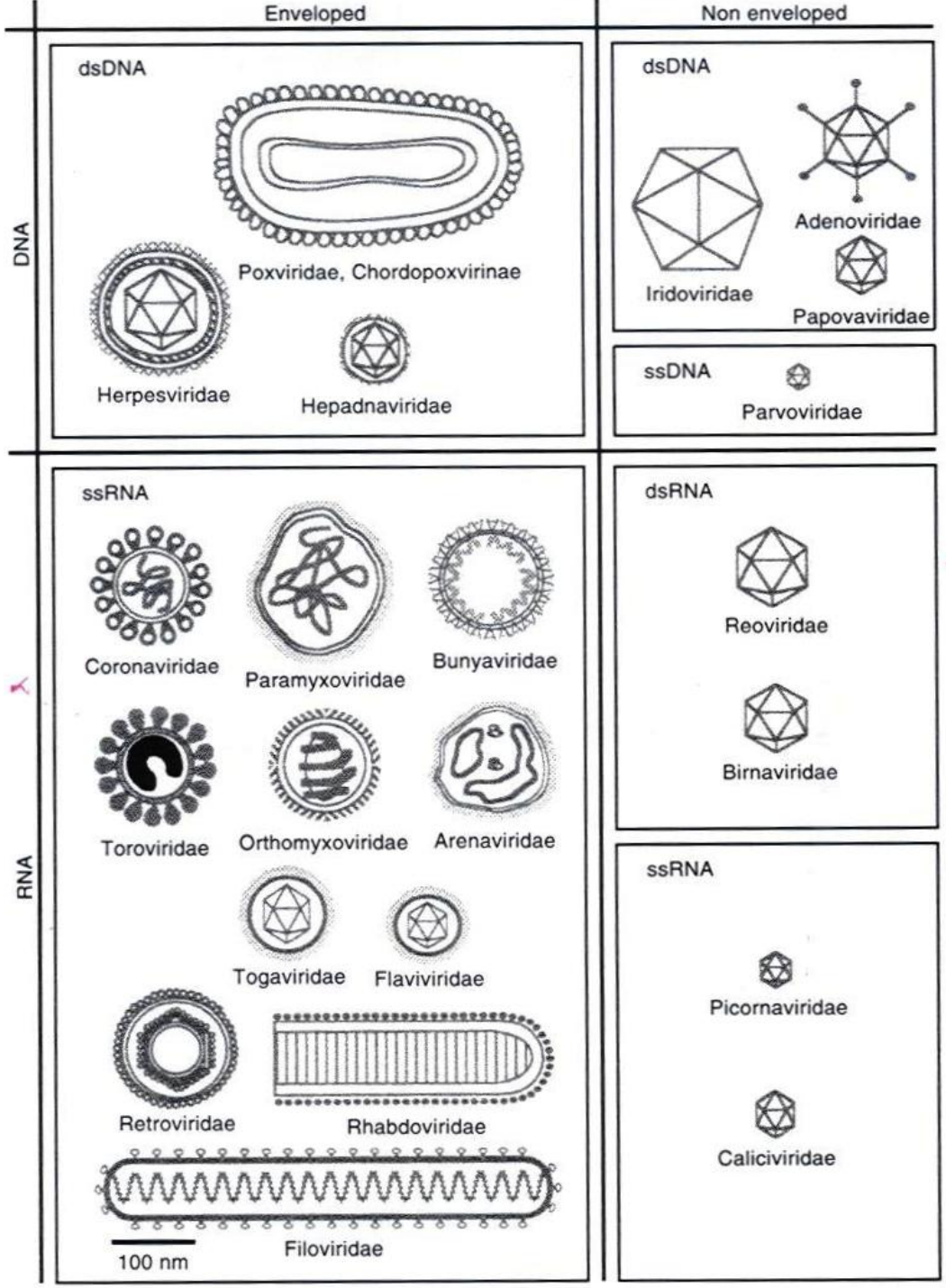
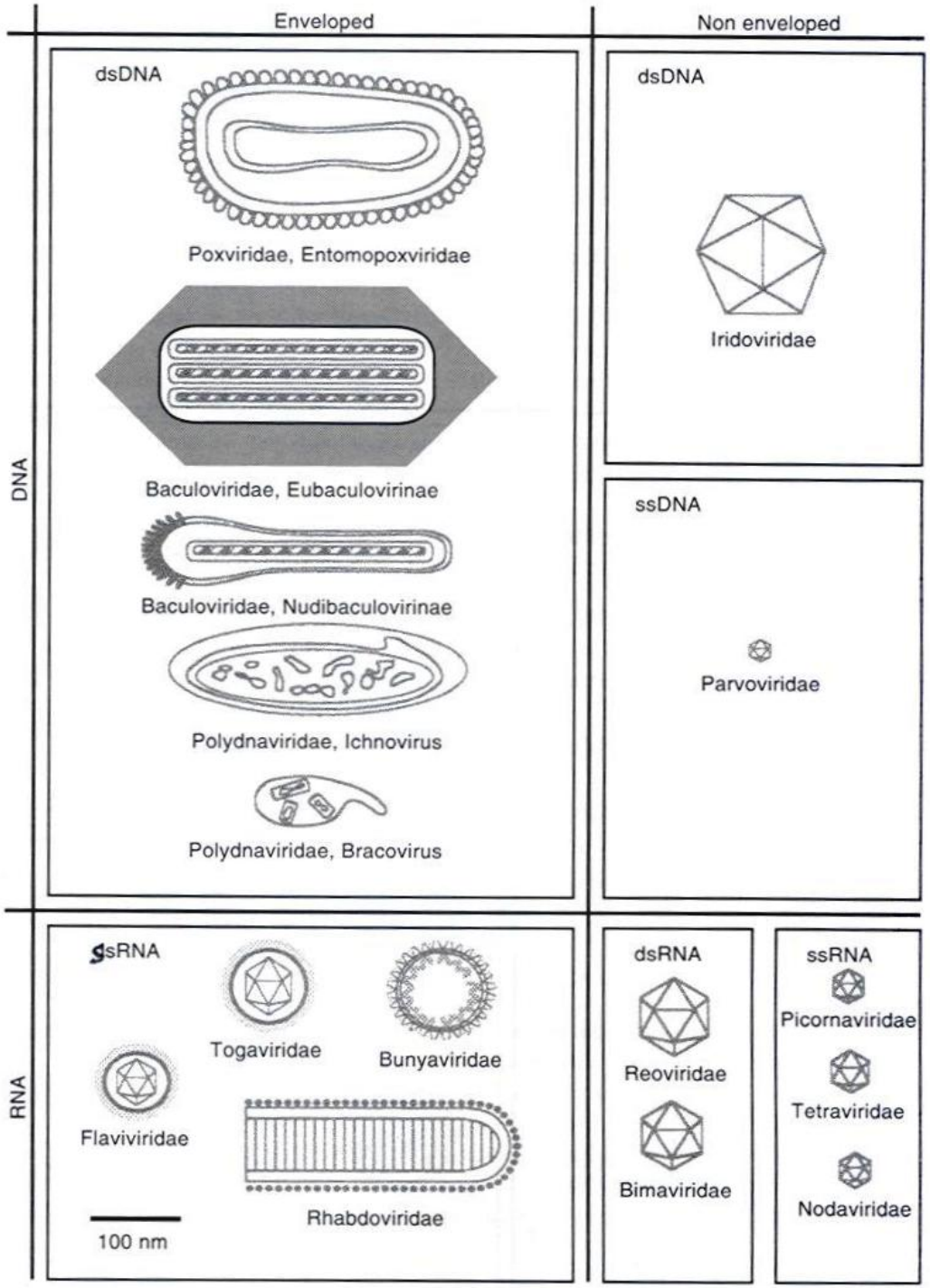


Figure 1.10 Classification schemes for animal viruses. Summary of the major characteristics of 23 representative families of viruses that infect vertebrates. Not all virus families are shown in the figure. Adapted from M. H. V. van Regenmortel et al. (ed.), *Virus Taxonomy: Classification and Nomenclature of Viruses. Seventh Report of the International Committee on Taxonomy of Viruses* (Academic Press, Inc., San Diego, Calif., 2000).



Famílias de Vìrus que infectam Vertebrados

Levy, J. A., Fraenkel-Conrat, H. and Owens, R. A. (1994). "Virology". 3rd edition. Prentice-Hall, Inc.



Famílias de Vírus que infectam Invertebrados

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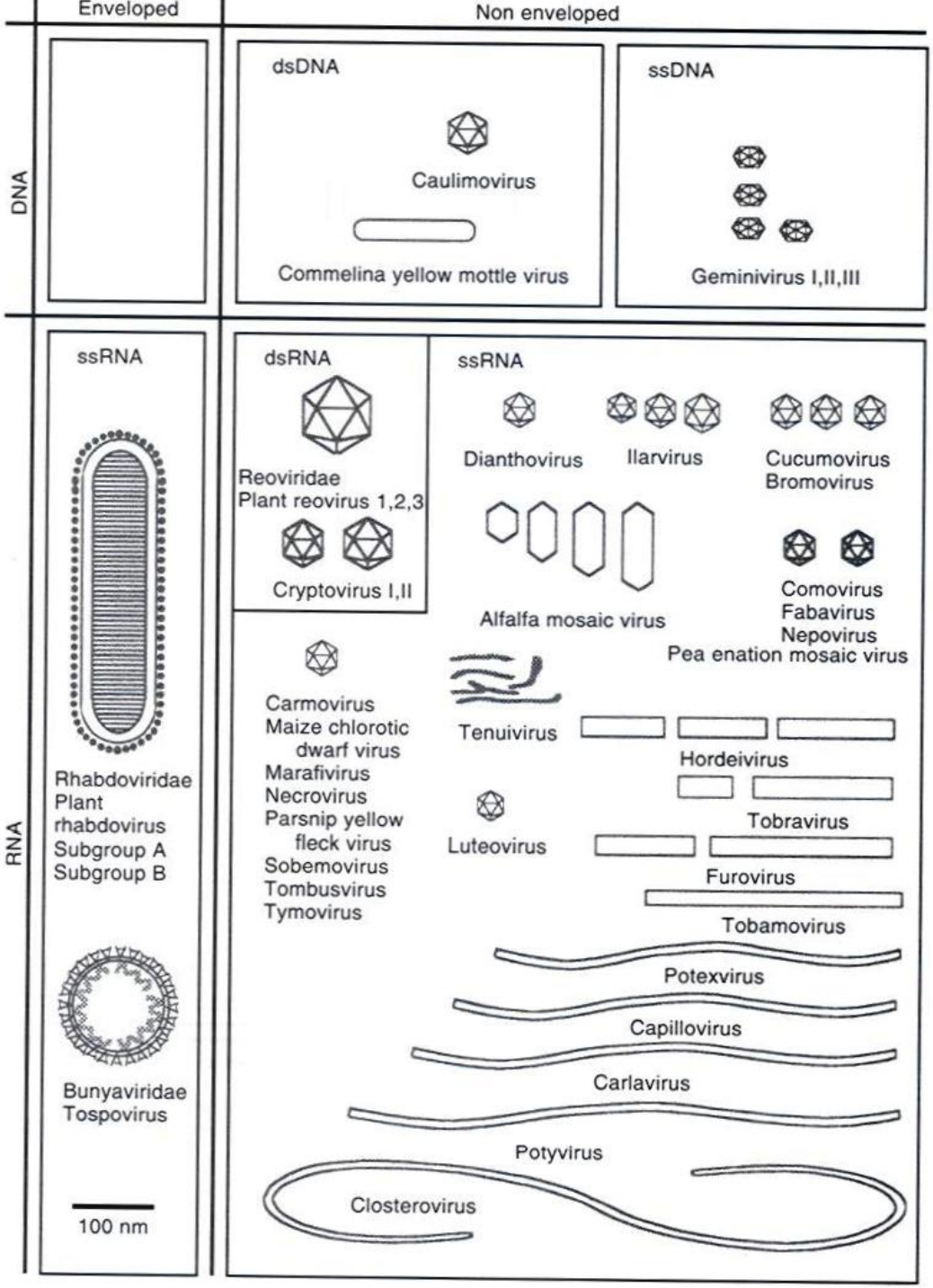


Grupos de Vírus que infectam Plantas

Levy, J. A., Fraenkel-Conrat, H. and Owens, R. A. (1994). "Virology". 3rd edition. Prentice-Hall, Inc.

1. Parvoviruses

(a) Autonomous

5′ ABBA XYYX 3′

(b) Adeno-associated virus

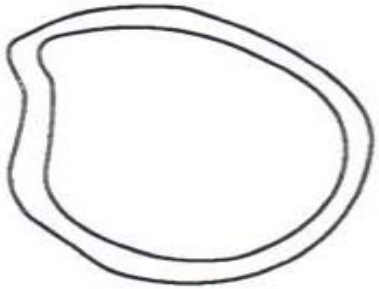
5′ ABC C′B′A′ 3′

(+) or (−) polarity

Approximate molecular weigh

1.7 X 10^6

2. Papovavirus



3.6 X 10^6

3. Adenovirus

ABC

abc

cba

CBA

22 X 10^6

4. Herpesvirus

AB

ab

baac

Ca

BAAC

cA

90 X 10^6

5. Poxvirus

ABC

abc

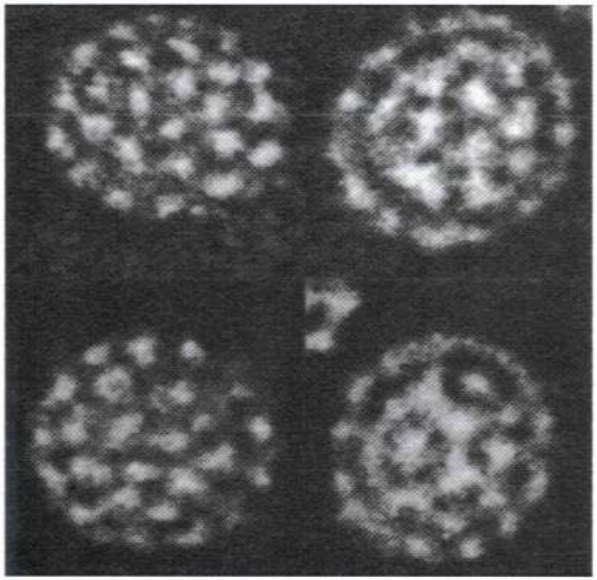
cba

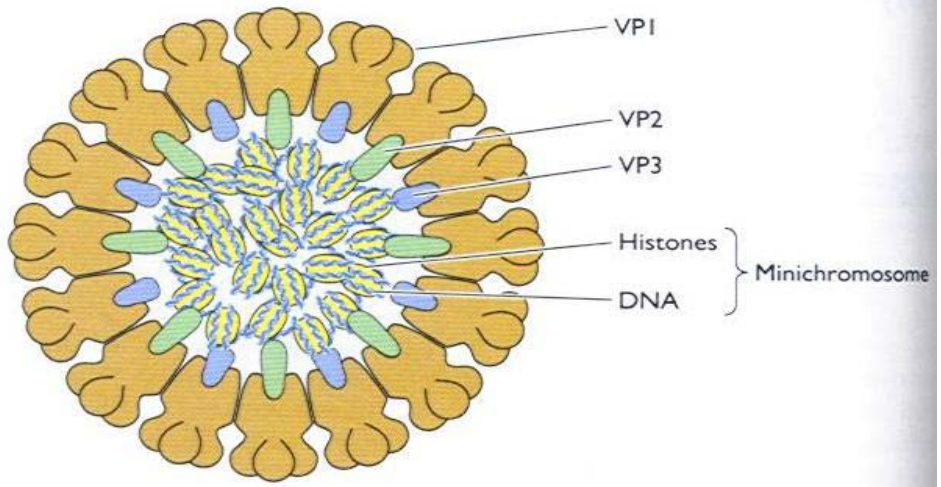
CBA

122 X 10^6

Vírus	Hospedeiro	Tumor ou doença (hosp.)
Papiloma de Shope	Coelho	Papilomas, carcinomas (coelho)
Papiloma bovino	Gado	Papilomas (gado), linfomas (hamsteres)
Papilomas humanos	Homem	Verrugas, papilomas laríngeos e cervicais, carcinomas (Homem)
Polioma	Murganho	Tumores vários (roedores)
Vírus símio 40 (SV40)	Macaco	Linfomas, sarcomas (hamster, rato)
Vírus linfotrópicos	Macaco	Sarcomas (hamster)
Vírus JC	Homem	Leucoencefalopatia multifocal progressiva (Homem), tumores (roedores, primatas)
Vírus BK	Homem	Lesões do tracto urinário após imunossupresão (Homem) tumores (roedores)
Vírus vacuolizante renal	Coelho	–
Vírus K	Murganho	–

A





B

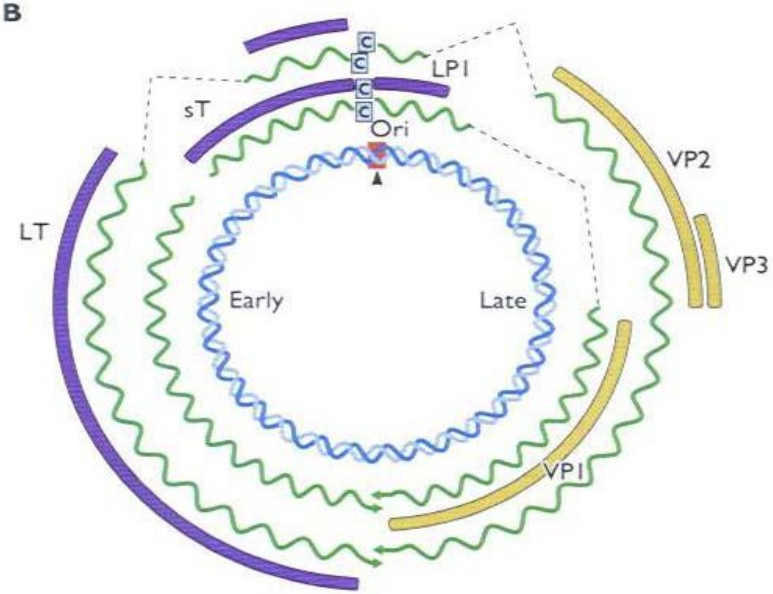


Figure 15 Structure and genome organization

Polyomaviruses

Family: *Polyomaviridae*

Genus	Type species
Polyomavirus	Simian virus 40

The family *Polyomaviridae* includes mouse polyomaviruses and two human viruses, JC and BK viruses, which were isolated from a patient with progressive multifocal leukencephalopathy and an immunosuppressed recipient of a kidney transplant, respectively. Under some conditions, mouse polyomavirus infection of the natural host results in formation of a wide variety of tumors (hence the name). A characteristic property of the members of this family is an ability to transform cultured cells or to induce tumors in animals. Investigation of such transforming activity has provided much information about mechanisms of oncogenesis, including the discovery of the cellular tumor suppressor protein p53. These viruses, particularly simian virus 40, have also been important in elucidation of cellular mechanisms of transcription and its regulation. For example, the simian virus 40 enhancer was the first member of this class of regulatory sequences to be identified.

Figure 15 Structure and genome organization. (A) The virion. (Left) Electron micrograph of negatively stained simian virus 40 virions. From F. A. Andered et al., *Virology* **32**:511–523, 1967, with permission. (Right) Diagram of the virion, showing the names and locations of virion proteins and the organization of the 5,243-bp circular, double-stranded DNA genome into approximately 25 nucleosomes by the cellular histones H2A, H2B, H3, and H4 (the core histones). One molecule of either VP2 or VP3, which possess a common C-terminal sequence, is associated with each VP1 pentamer. **(B) Genome organization.** Locations of the origin of viral DNA synthesis (Ori) and of the early and late mRNA sequences encoding the large and small T antigens (LT and sT) and the virion structural proteins VP1, VP2, and VP3 are indicated. The late mRNA species generally contain additional open reading frames in their 5′-terminal exons, such as that encoding leader protein 1 (LP1).

Figure 16 Single-cell reproductive cycle of simian virus 40. The virion attaches to permissive monkey cells upon binding of VP1 to a major histocompatibility complex (MHC) class I molecule on the surface of the cell. The virion is then endocytosed in caveolae **(1** and **2)**, is transported to the endoplasmic reticulum, and enters that organelle **(3)**. It is then transported to the nucleus and uncoated by unknown mechanisms **(4)**. The viral genome packaged by cellular nucleosomes is found within the nucleus **(5)**. The early transcription unit is transcribed by host cell RNA polymerase II **(6)**. After alternative splicing and export to the cytoplasm **(7)**, the early mRNAs are translated by cytoplasmic ribosomes to produce the early proteins LT and sT **(8)**. The former is imported into the nucleus **(9)**, where it binds to the simian virus 40 origin of replication to initiate DNA synthesis **(10)**. Apart from LT, all components needed for viral DNA replication are provided by the host cell. As they are synthesized, daughter viral DNA molecules associate with cellular nucleosomes to form the viral nucleoproteins often called minichromosomes. LT also stimulates transcription of the late gene from replicated viral DNA templates **(11)**. Processed late mRNAs are exported to the cytoplasm **(12)**, and translated to produce the virion structural proteins VP1, VP2, and VP3 **(13)**. These structural proteins are imported into the nucleus **(14)** and assemble around viral minichromosomes to form progeny virions **(15)**. Virions are released by an unknown mechanism **(16)**.

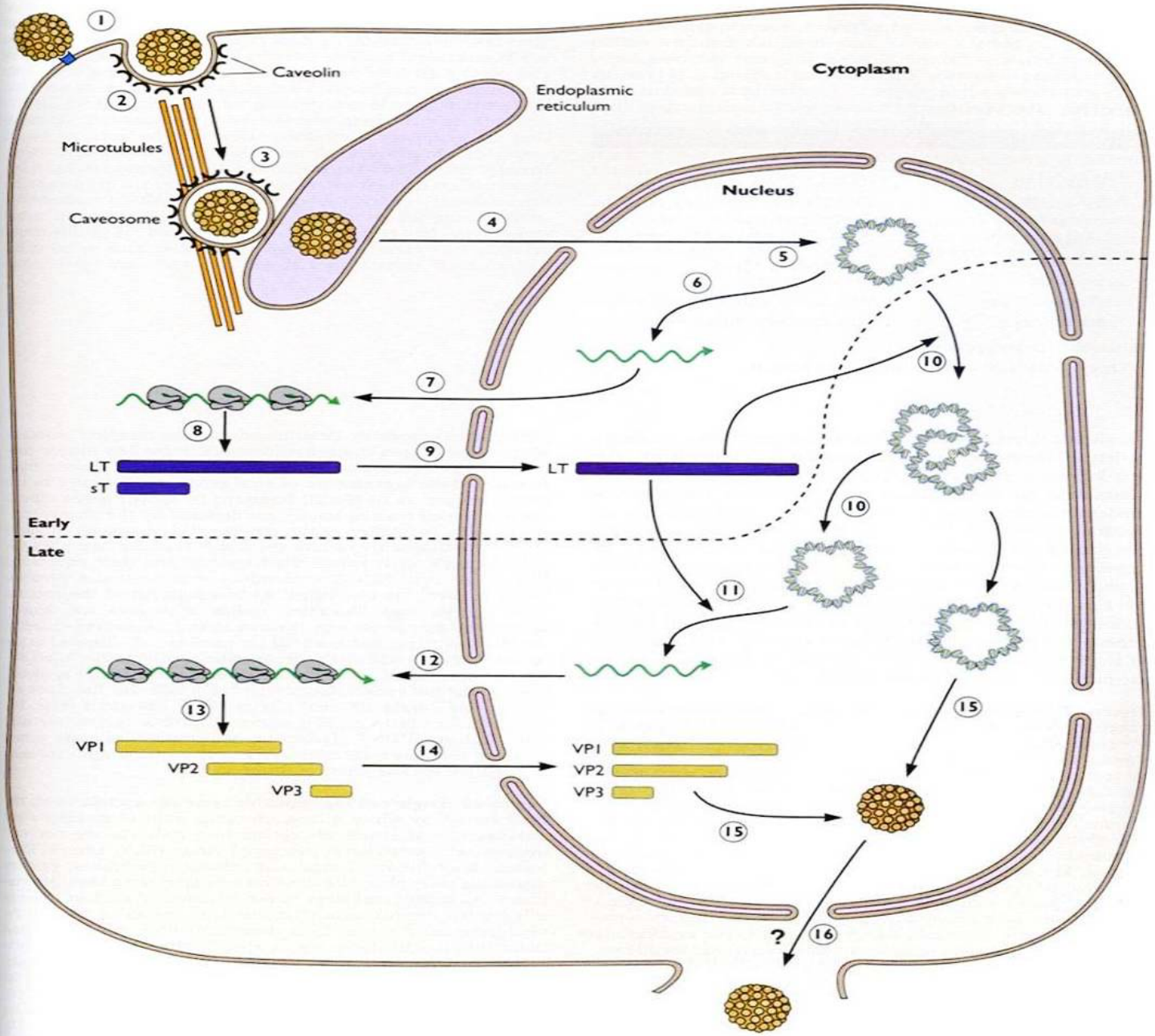


Figure 16 Single-cell reproductive cycle of simian virus 40

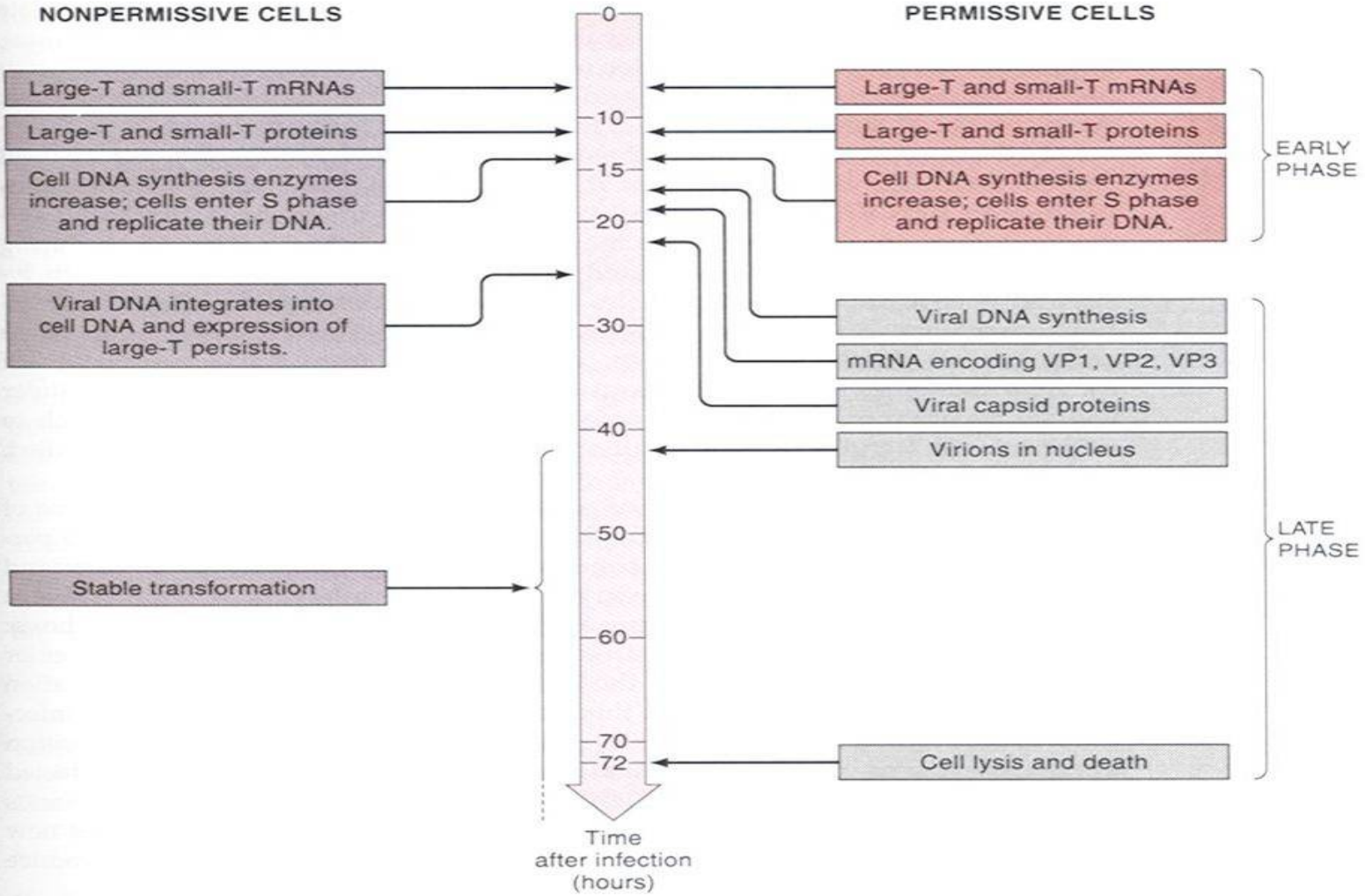
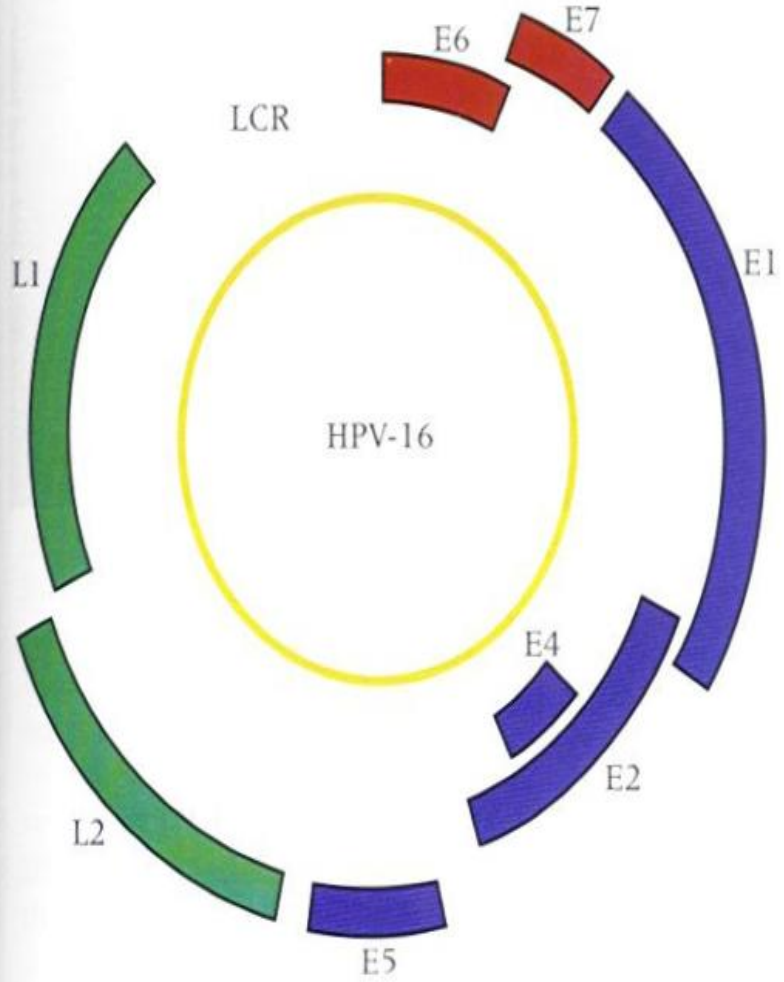


Figure 1.7
Course of SV40 infection of permissive and nonpermissive cells. The vertical arrow indicates the time (hr) following infection (0 hr) at which various events occur. Until about 14 hours (the early phase), both permissive and nonpermissive cells respond similarly to the infection. However, the ensuing events—viral DNA synthesis, late mRNA, viral capsid protein synthesis, the formation of virions and death of the cell—occur only in permissive cells. In nonpermissive cells, viral DNA integrates into the cellular DNA; transformation occurs if large-T expression persists.

Associações de papilomavírus humanos com lesões

Tipos	Lesão
1	Verrugas cutâneas
5, 8, 47	Tumores cutâneos EV
2, 57	Tumores cutâneos/mucosos
6, 11, 13, 42	Tumores mucosos, baixo risco
16, 18, 31, 33, 35, 39, 51, 58	Tumores mucosos, alto risco



A map of the chromosome of HPV-16, showing the positions of six of the eight early viral genes (E1 through E8) and the two major late viral genes (L1 and L2). The E6 and E7 viral gene products are the tumor antigens expressed in human carcinomas.

Adenoviruses

Family: *Adenoviridae*

Genus	Type species
Mastadenovirus	Human adenovirus C
Aviadenovirus	Fowl adenovirus A

Human serotypes are widespread in the population. Infection by these viruses is often asymptomatic, but can result in respiratory disease in children (members of subgenera B and C), conjunctivitis (members of subgroup B and D) and gastroenteritis (subgroup F serotypes 40 and 41). Human adenoviruses 40 and 41 are the second leading cause (after rotaviruses) of infantile viral diarrhea. These viruses share capsid morphology and linear double-stranded DNA genomes, but the members of the two genera differ in size, organization, and coding sequences. The *Mastadenovirinae* comprise some 50 human adenoviruses and adenoviruses of other mammals, including mice, sheep, and dogs, and some are oncogenic in rodents. Study of human adenovirus transformation has provided fundamental information about mechanisms that control progression of cells through the cell cycle and oncogenesis. Characteristic features of replication of these viruses include precise temporal control of viral gene expression and an unusual mechanism of initiation of viral DNA synthesis (protein priming). Mastadenoviral genomes also include genes transcribed by cellular RNA polymerase III.

Figure 1 Structure and genome organization of human adenovirus type 5. (A) The virion. (Left) Electron micrograph of a negatively stained human adenovirus type 5 particle showing the triangular faces of the icosahedral capsid and the fibers. Bar = 50 nm. Courtesy of M. Bisher, Princeton University. (Right) Diagram of the virion illustrating the major structural units of the capsid, hexons and pentons, additional proteins (e.g., VI and IX) that stabilize the capsid, and the viral core proteins. The latter are associated with the linear double-stranded DNA genome of nearly 36 kb, which carries covalently linked terminal protein at its 5′ ends. **(B) Genome organization.** The origins of replication (Ori) at each end of the genome, the terminal protein (TP) covalently attached to each end of the genome, and the eight RNA polymerase II (green arrows) and three RNA polymerase III (tan arrows) transcription units are shown. Arrows indicate the direction of transcription. The three small major late (ML) exons designated l-1, l-2, and l-3 are spliced to form the 202-nucleotide tripartite leader common to all messenger RNA (mRNA) species processed from major late primary transcripts. These mRNAs, which form the five families (L1, L2, L3, L4, and L5) defined by their common 3′ polyadenylation sites, encode all but one (polypeptide IX) of the virion structural proteins, as shown for several of the capsid proteins.

Figure 2 Single-cell reproductive cycle of human adenovirus type 2. The virus attaches to a permissive human cell via interaction between the fiber and the coxsackie-adenovirus receptor on the cell surface. The virus enters the cell via endocytosis **(1** and **2)**, a step that depends on the interaction of a second virion protein, penton base, with a cellular integrin protein. Partial disassembly takes place prior to entry of particles into the cytoplasm **(3)**. Further uncoating takes place and the viral genome associated with core protein VII is imported into the nucleus **(4)**. The host cell RNA polymerase II transcription system transcribes the immediate-early E1A gene **(5)**. Following alternative splicing and export of E1A mRNAs to the cytoplasm **(6)**, E1A proteins are synthesized by the cellular translation machinery **(7)**. These proteins, which are extensively modified by phosphorylation, are imported into the nucleus **(8)**, where they regulate transcription of both cellular and viral genes and the proliferation state of the host cell. The larger E1A protein stimulates transcription of the viral early genes by cellular RNA polymerase II **(9a)**. Transcription of the VA genes by host cell RNA polymerase III also begins during the early phase of infection **(9b)**. The early pre-mRNA species are processed, exported to the cytoplasm **(10)**, and translated **(11)**. These early proteins include the viral replication proteins, which are imported into the nucleus **(12)** and cooperate with a limited number of cellular proteins in viral DNA synthesis **(13)**. Replicated viral DNA molecules can serve as templates for further rounds of replication **(14)** or for transcription of late genes **(15)**. Some late promoters are activated simply by viral DNA replication, but maximally efficient transcription of the major late transcription unit requires the late IVa2 protein and a second, unidentified, infected-cell-specific protein. Processed late mRNA species are selectively exported from the nucleus as a result of the action of early E1B 55kDa and E4 Orf6 proteins **(16)**. Their efficient translation in the cytoplasm **(17)** requires the major VA RNA, VA RNA-I, which counteracts a cellular defense mechanism, and the late L4 100kDa protein. The latter protein also serves as a chaperone for assembly of trimeric hexons as they and the other structural proteins are imported into the nucleus **(18)**. Within the nucleus, capsids are assembled from these proteins and progeny viral genomes to form noninfectious immature virions **(19)**. Assembly requires a packaging signal located near the left end of the genome, as well as the IVa2 and L4 33kDa proteins. Immature virions contain the precursors of the mature forms of several proteins. Mature infectious virions are formed **(20)** when these precursor proteins are cleaved by the viral protease, encoded within the L3 region, and assembled into the virion core. Progeny virions are released **(21)**, usually upon destruction of the host cell via mechanisms that are not well understood.

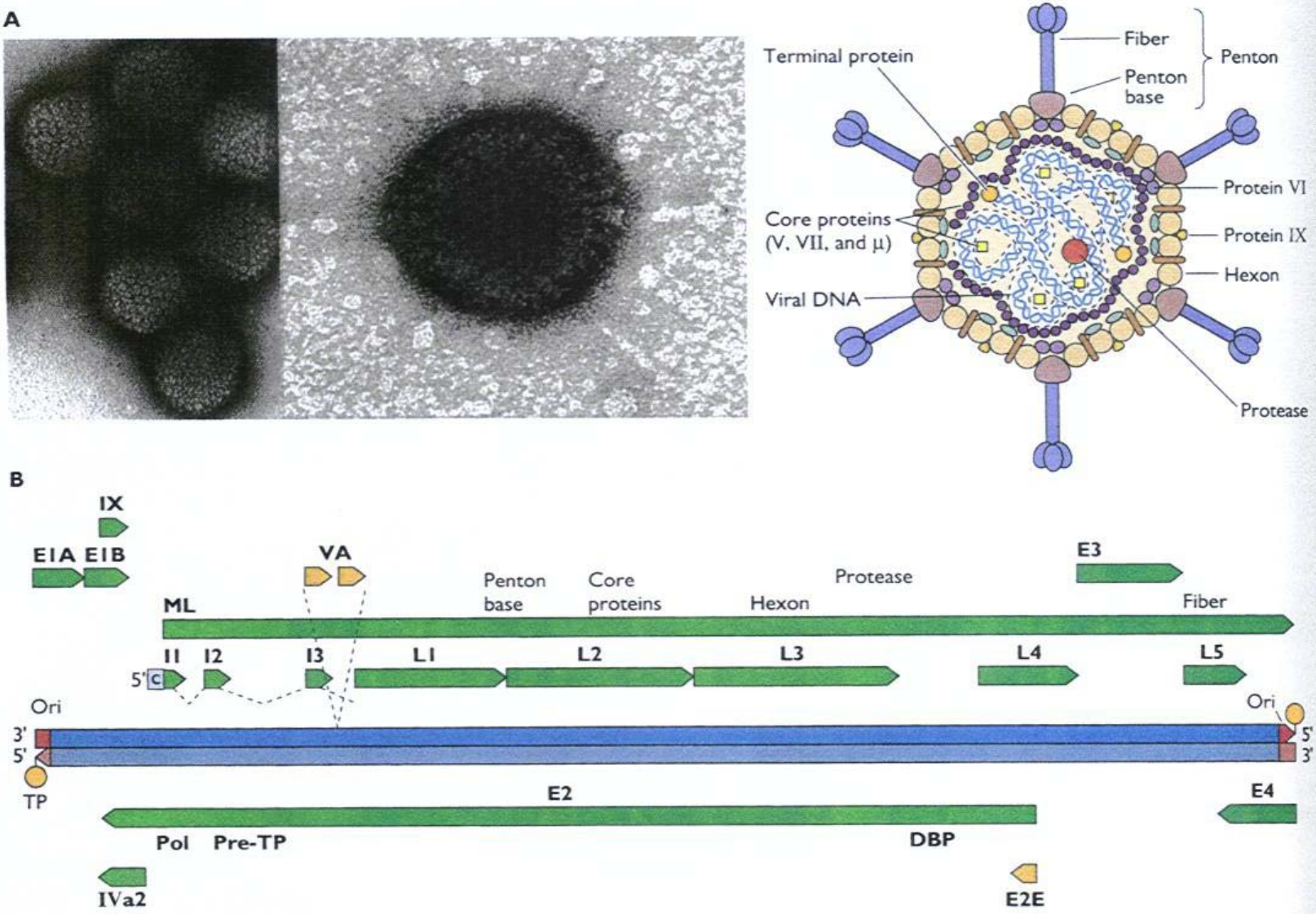
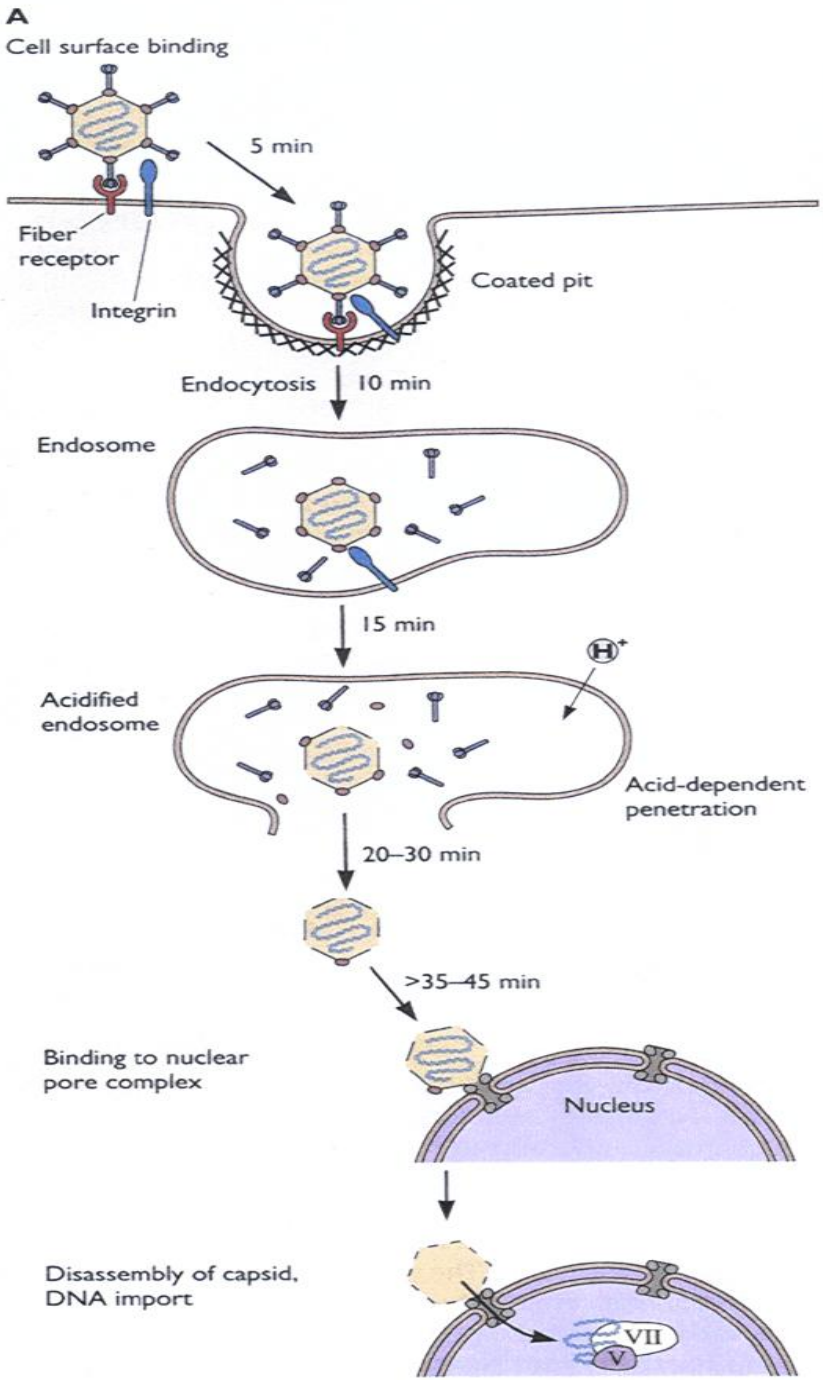
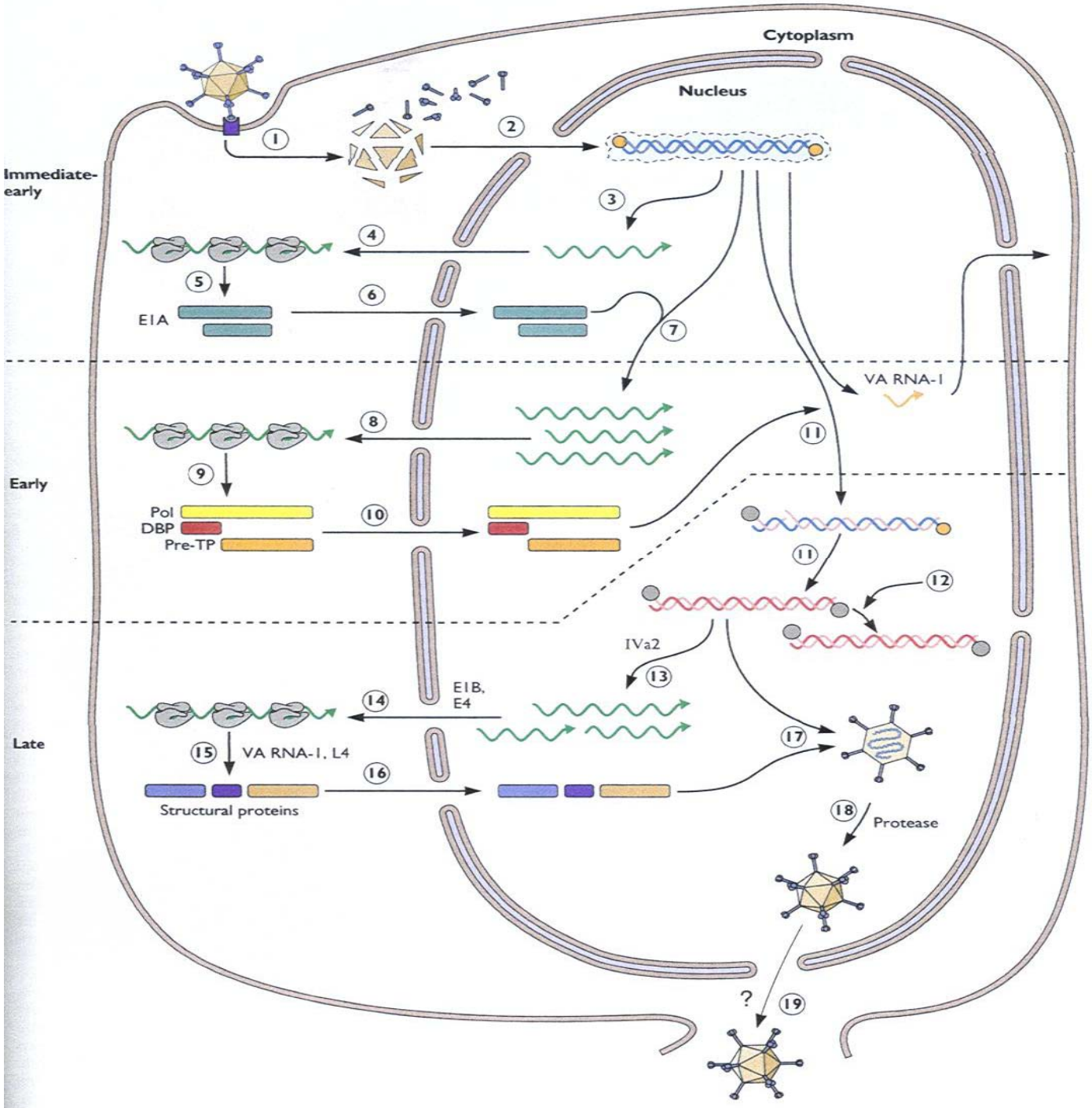


Figure 15 Structure and genome organization of the adenovirus human adenovirus type 2.


A
Cell surface binding
5 min
Fiber receptor
Integrin
Coated pit
Endocytosis
10 min
Endosome
15 min
H+
Acidified endosome
Acid-dependent penetration
20–30 min
>35–45 min
Binding to nuclear pore complex
Nucleus
Disassembly of capsid, DNA import
VII
V


Cytoplasm
Nucleus
Immediate-early
Early
Late
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2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
E1A
Pol
DBP
Pre-TP
VA RNA-1
IVa2
E1B,
E4
VA RNA-1, L4
Structural proteins
Protease
?