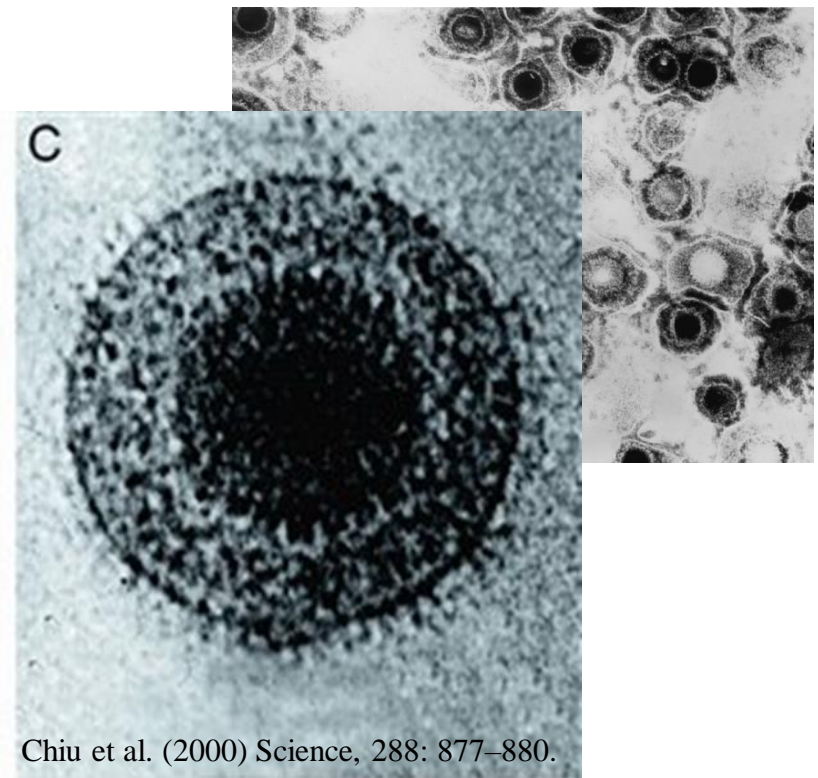
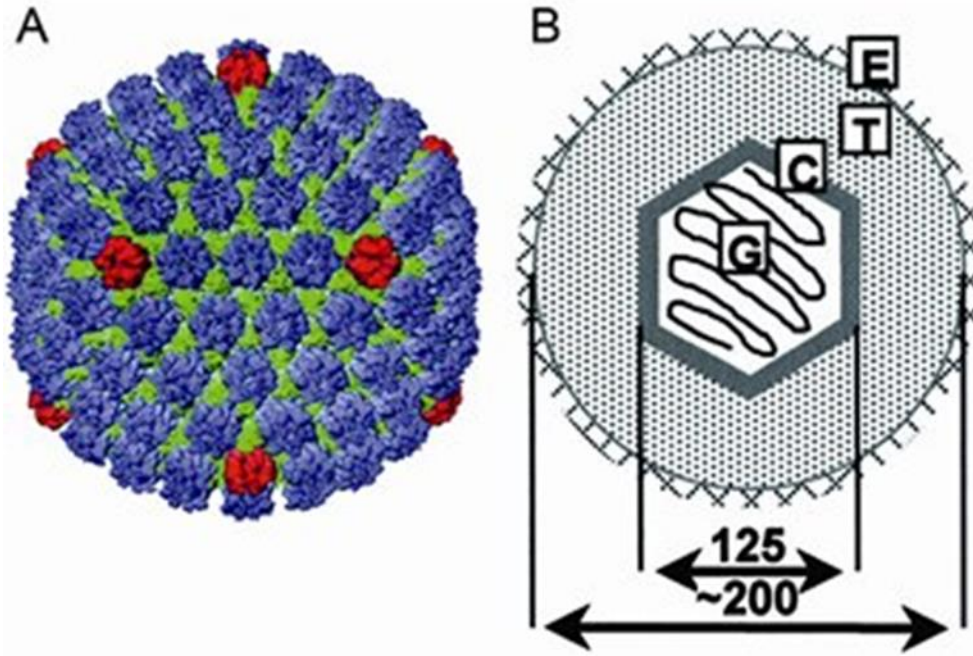


Viruses with dsDNA genomes (2):



Order *Herpesvirales*

More than 100 viruses of mammals, birds, fishes, reptiles, amphibians and shellfish.

Commonalities: genome type and size, virion type, dual viral cycle (infection types)

Herpesviridae - mammals, birds, reptiles

Family Herpesviridae - in mammals, birds and reptiles

Subfamilies: α -, β -, γ -herpesvirinae, 8 human viruses in all three subfamilies.

Alphaherpesvirinae

HHV-1 (HSV-1)

HHV-2 (HSV-2)

HHV-3 (VZV)

Betaherpesvirinae

HHV-5
(HCMV)

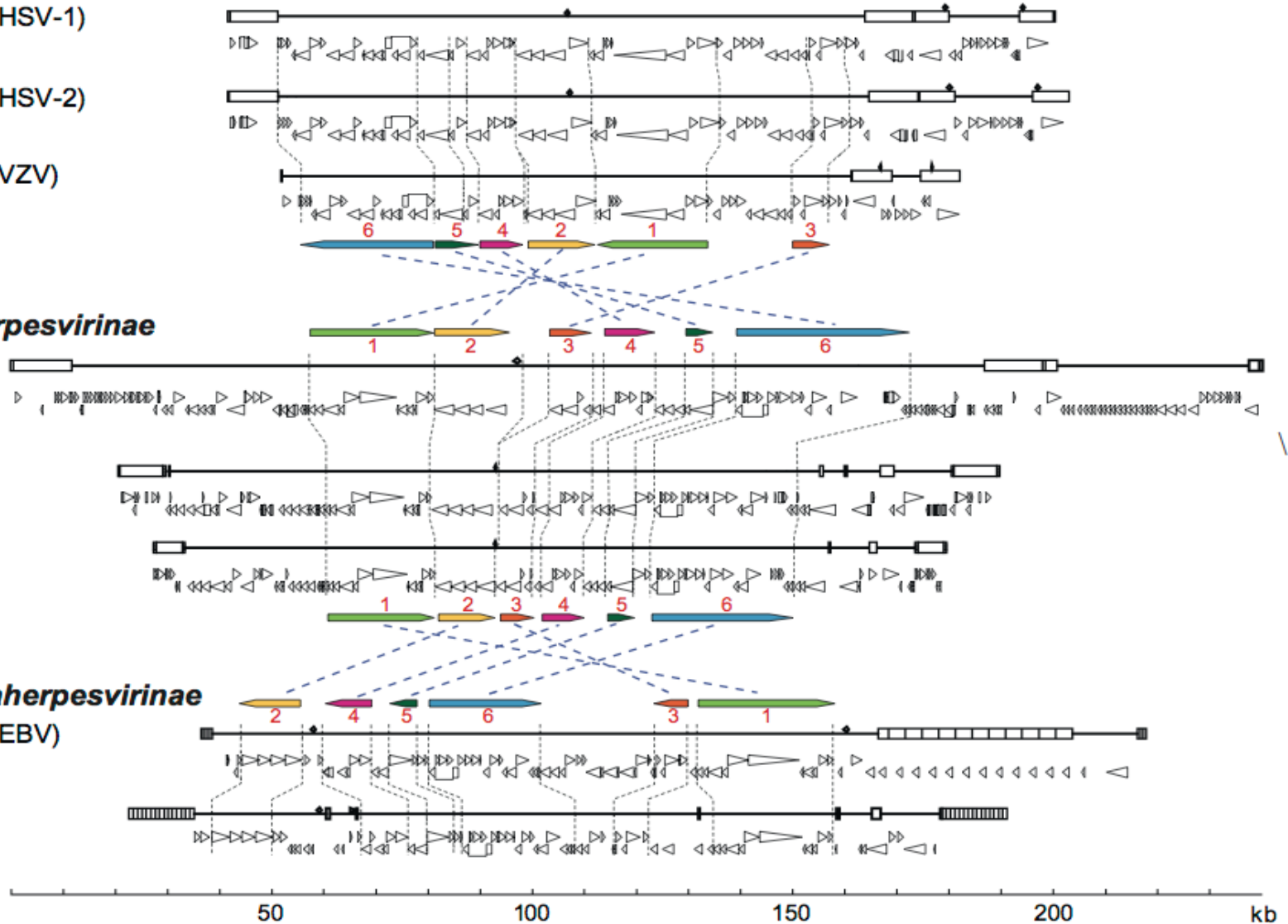
HHV-6

HHV-7

Gammapherpesvirinae

HHV-4 (EBV)

HHV-8



***α-herpesvirinae*: short lytic cycle, latency in sensory neurons, painful skin symptoms**

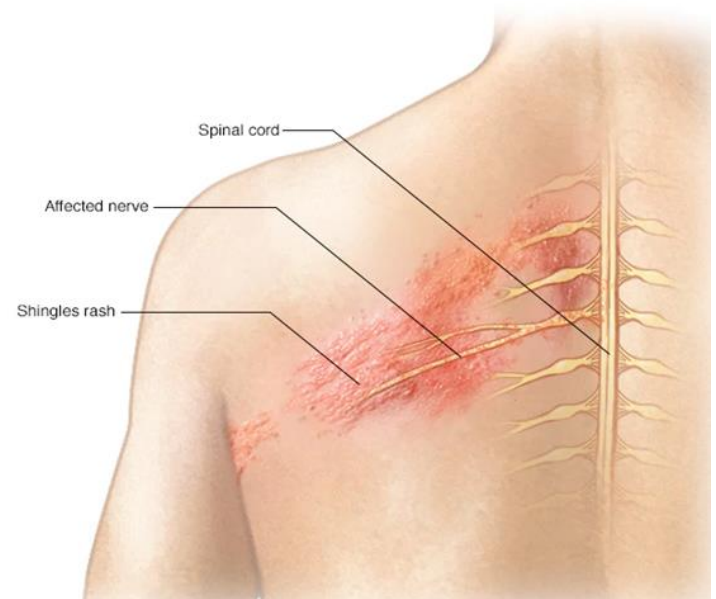
- HHV-1 (*Human herpesvirus 1*) = HSV-1 (herpes simplex virus), contact transmission, mucosa, skin, cornea infections (epithelial cells), transport to the neuron nuclei.

Persistent , latent infection, symptoms during productive (acute) infection.

HHV-2 = HSV-2, genital herpes, sexually transmitted, epithelial cells, infant mortality is 54%!

Herpesviruses are neurothropic!

HHV-3 = VZV (varicella-zoster), chickenpox and shingles, aerosol (droplet) transmission usually in childhood, latent in neurons (and T-cells) of head and torso.

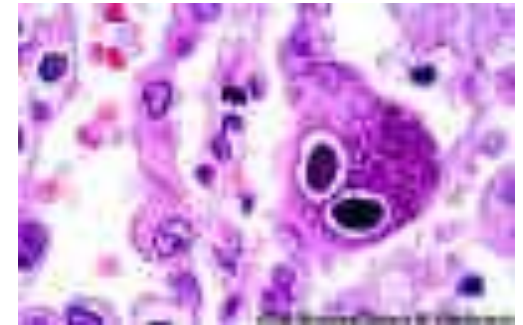


β-herpesvirinae: long cycle, latency in different cell types (mostly white blood cells), enlarged cells

HHV-5 = (h)CMV (human cytomegalovirus) – mild symptoms or asymptomatic infections (10% infectious mononucleosis cases), ubiquitous (90%). Contact transmission and bodily fluids (saliva, urogenital excreta, blood, milk, sperm), fomites, transplantation, transfusion).

Replication in lymphocytes, latency in bone marrow (myeloid progenitor cells to be differentiated to monocyte).

Congenital hCMV) in fetuses and newborns (brain, liver, spleen damage, mental impairment, deafness, death), immunocompromised patients: transplanted (the most important virus tested) and AIDS (retinitis, colitis).



<http://pathmicro.med.sc.edu/virol/herpes.htm>

HHV-7 (from CD4+ T-cell culture of a healthy person), transmission by saliva, urogenital excreta.

β-herpesvirinae: long cycle, latency in different cell types (mostly white blood cells), enlarged cells

HHV-6, (HHV6A i 6B) children – *exanthem subitum*, (*roseola infantum*, 6th disease),

All children usually infected 6 m.-2 y., mild respiratory disease, high fever (40°C) 3-4 days, rash on torso afterwards.

Latency in CNS, macrophages, monocytes, probably in T-cells, reactivation (short fever).

Saliva and contact transmission, episome is integrated in telomeres.

Chronic fatigue syndrome?



***γ-herpesvirinae*: latency in lymphocytes, oncogenic**

HHV-4 = EBV (Epstein-Barr virus) – mononucleosis (90%, a kissing disease), transmission from saliva to epithelial cells and mostly B-cells (latency), some to T-cells, tonsils and on to lymphatic tissue.

Primary acute infection 4-8 weeks, various symptoms, mostly not severe.

Burkitt's lymphoma (endemic, sporadic, AIDS), nasopharynx carcinoma, sometimes Hodgkin lymphoma, non-Hodgkin lymphoma in AIDS, post-transplant lymphoproliferative disease.

HHV-8 (Kaposi sarcoma – KSHV, isolated in 1994 from tumor tissue), lymphocytes and other host cells.



EBV and multiple sclerosis (MS) link! Seminar?

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HOME > SCIENCE > VOL. 375, NO. 6578 > LONGITUDINAL ANALYSIS REVEALS HIGH PREVALENCE OF EPSTEIN-BARR VIRUS ASSOCIATED WITH MULTIPLE...

 REPORT | MULTIPLE SCLEROSIS



Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

[KJETIL BJORNEVIK](#)  [MARIANNA CORTESE](#)  [BRIAN C. HEALY](#)  [JENS KUHLKE](#) [MICHAEL J. MINA](#)  [YUMEI LENG](#)  [STEPHEN J. ELLEDGE](#)  [DAVID W. NIEBUHR](#)

[ANN I. SCHER](#)  [ALBERTO ASCHERIO](#)  [+2 authors](#) [Authors Info & Affiliations](#)

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TWiV 869: Epstein-Barr virus and MS, a perfect storm
<https://youtu.be/zqtI36oNWtI>

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Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GialCAM

Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GialCAM

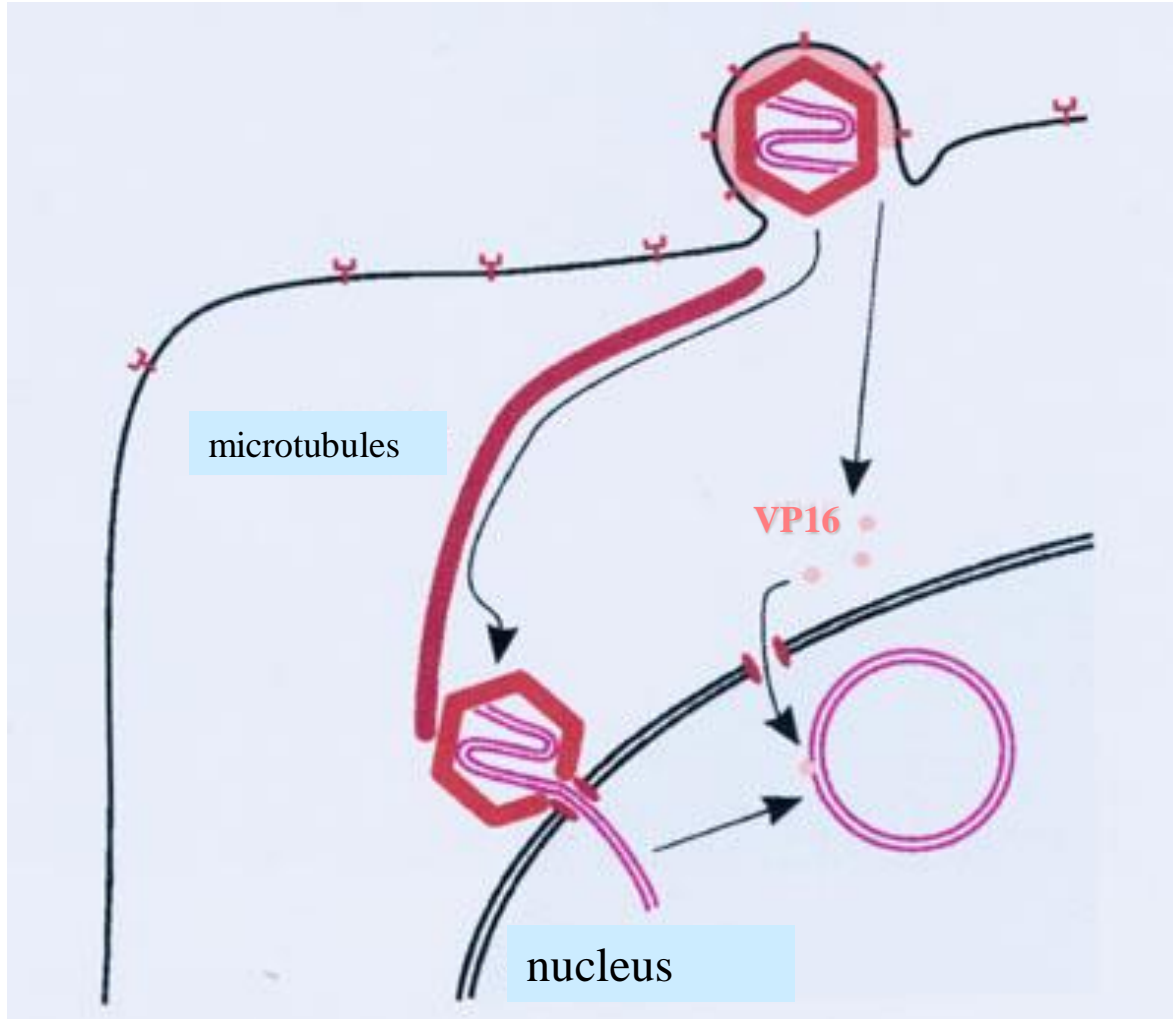
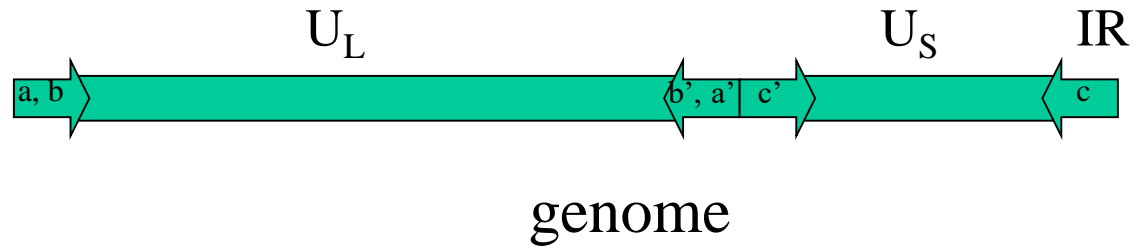
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Abstract

Multiple sclerosis (MS) is a heterogenous autoimmune disease in which autoreactive lymphocytes attack the myelin sheath of the central nervous system. B lymphocytes in the cerebrospinal fluid (CSF) of patients with MS contribute to inflammation and secrete oligoclonal immunoglobulins^{1,2}. Epstein-Barr virus (EBV) infection has been epidemiologically linked to MS, but its pathological role remains unclear³. Here we demonstrate high-affinity molecular mimicry between the EBV transcription factor EBV nuclear antigen 1 (EBNA1) and the central nervous system protein glial cell adhesion molecule (GialCAM) and provide structural and in vivo functional evidence for its relevance. A cross-reactive CSF-derived antibody was initially identified by single-cell sequencing of the paired-chain B cell repertoire of MS blood and CSF, followed by protein microarray-based testing of recombinantly expressed CSF-derived antibodies against MS-associated viruses. Sequence analysis, affinity measurements and the crystal structure of the EBNA1-peptide epitope in complex with the autoreactive Fab fragment enabled tracking of the development of the naive EBNA1-restricted antibody to a mature EBNA1-GialCAM cross-reactive antibody. Molecular mimicry is facilitated by a post-translational modification of GialCAM. EBNA1 immunization exacerbates disease in a mouse model of MS, and anti-EBNA1 and anti-GialCAM antibodies are prevalent in patients with MS. Our results provide a mechanistic link for the association between MS and EBV and could guide the development of new MS therapies.



HHV-1
virion

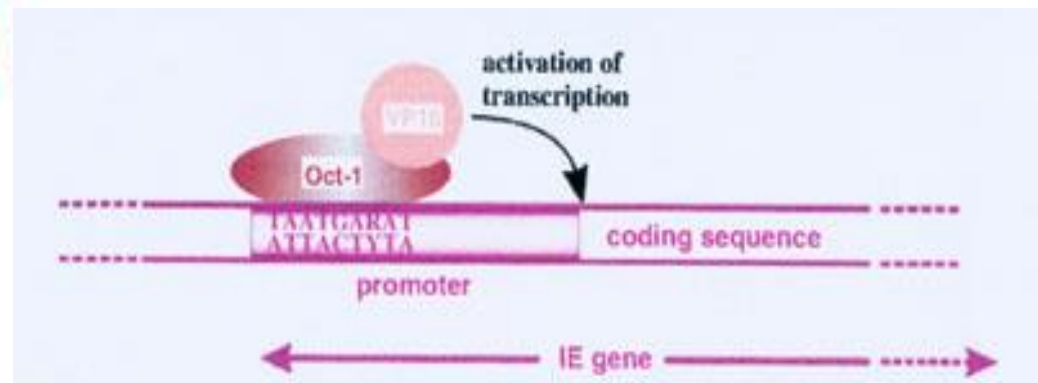
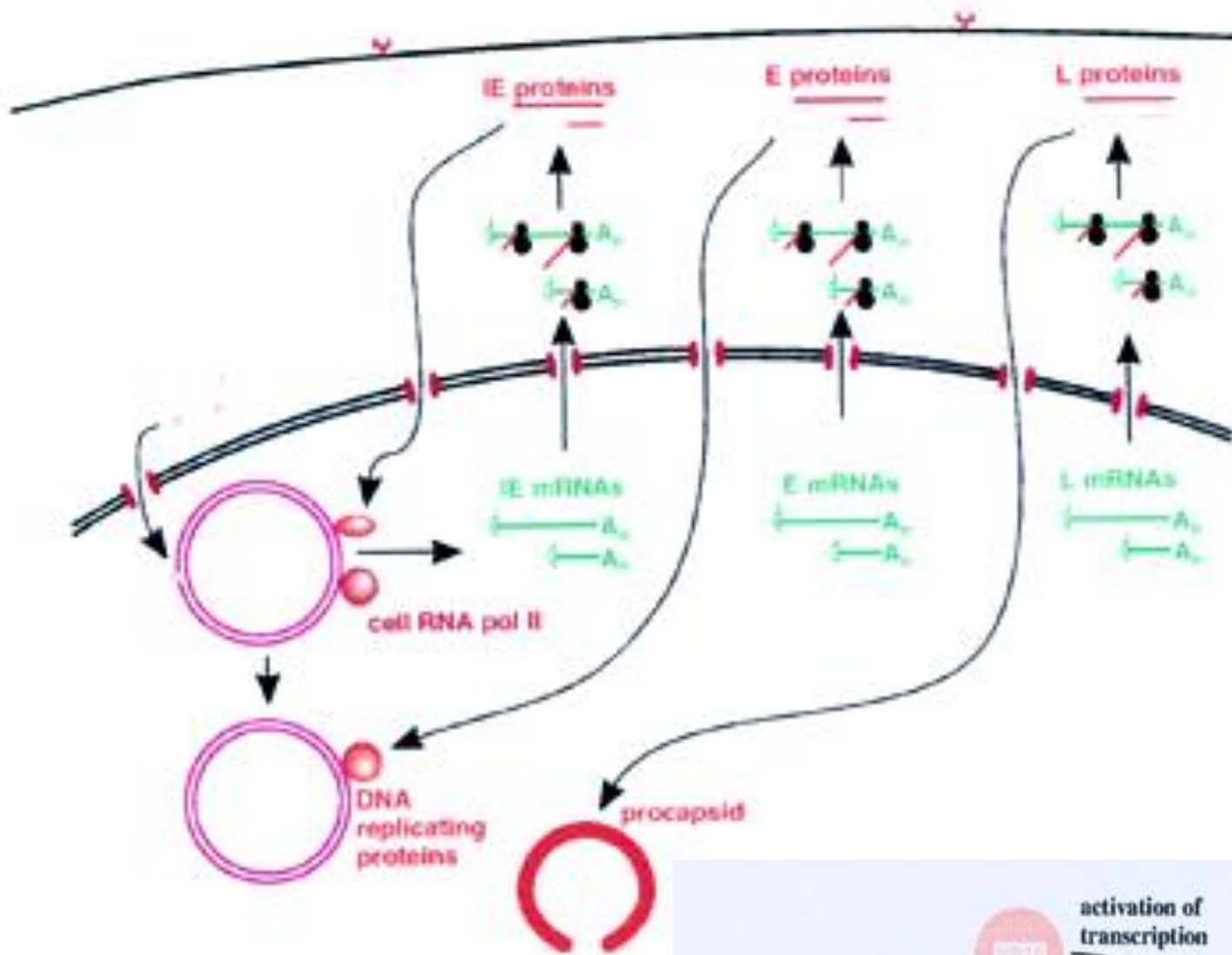


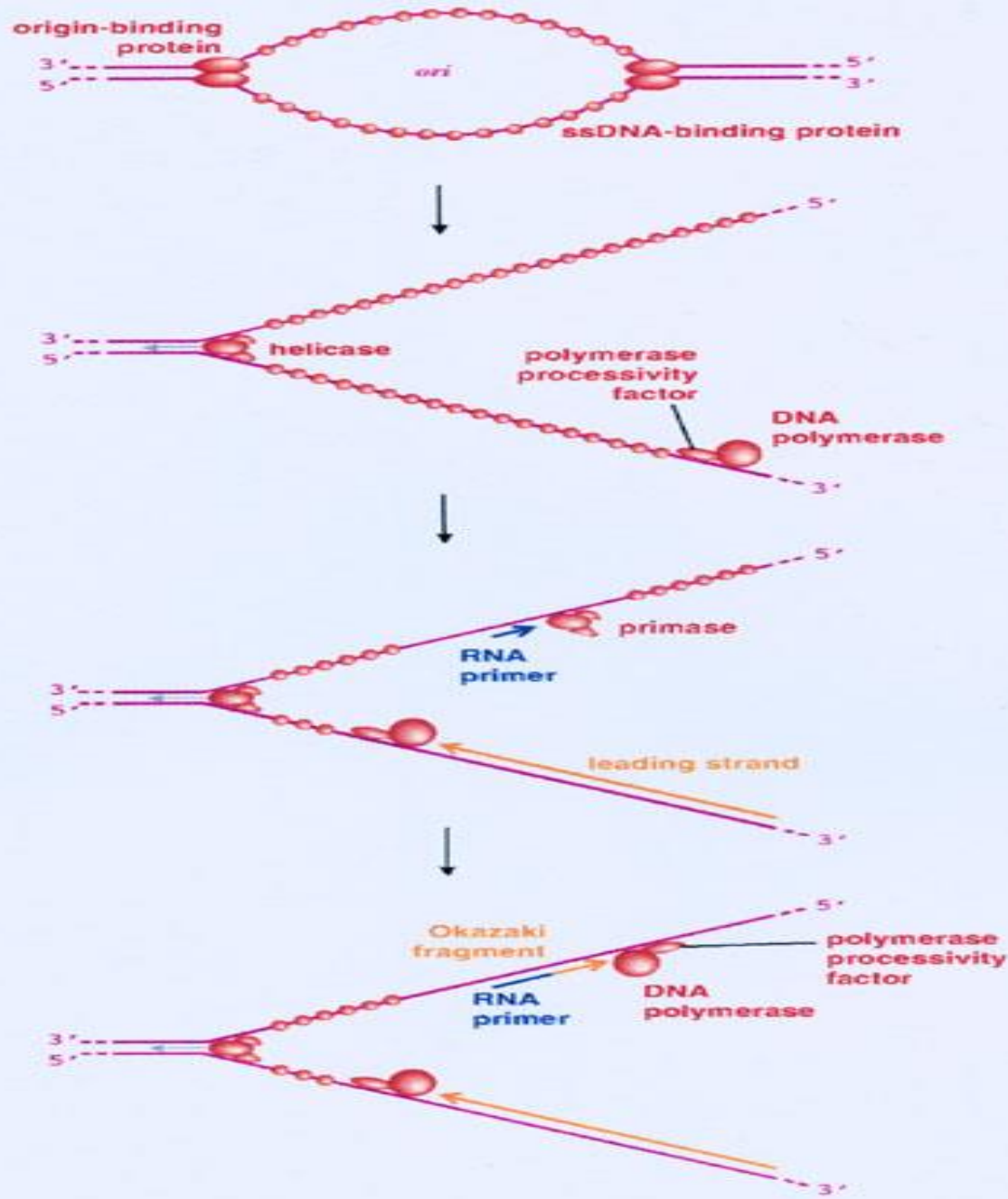
Linear genome
circularizes!

Encodes about 70 proteins.

Virion proteins:

- tegument – min. 15 proteins (VP16) + viral mRNAs
- (nucleo)capsid - VP5
- envelope with at least 12 glycoproteins (gB, gC, gD)





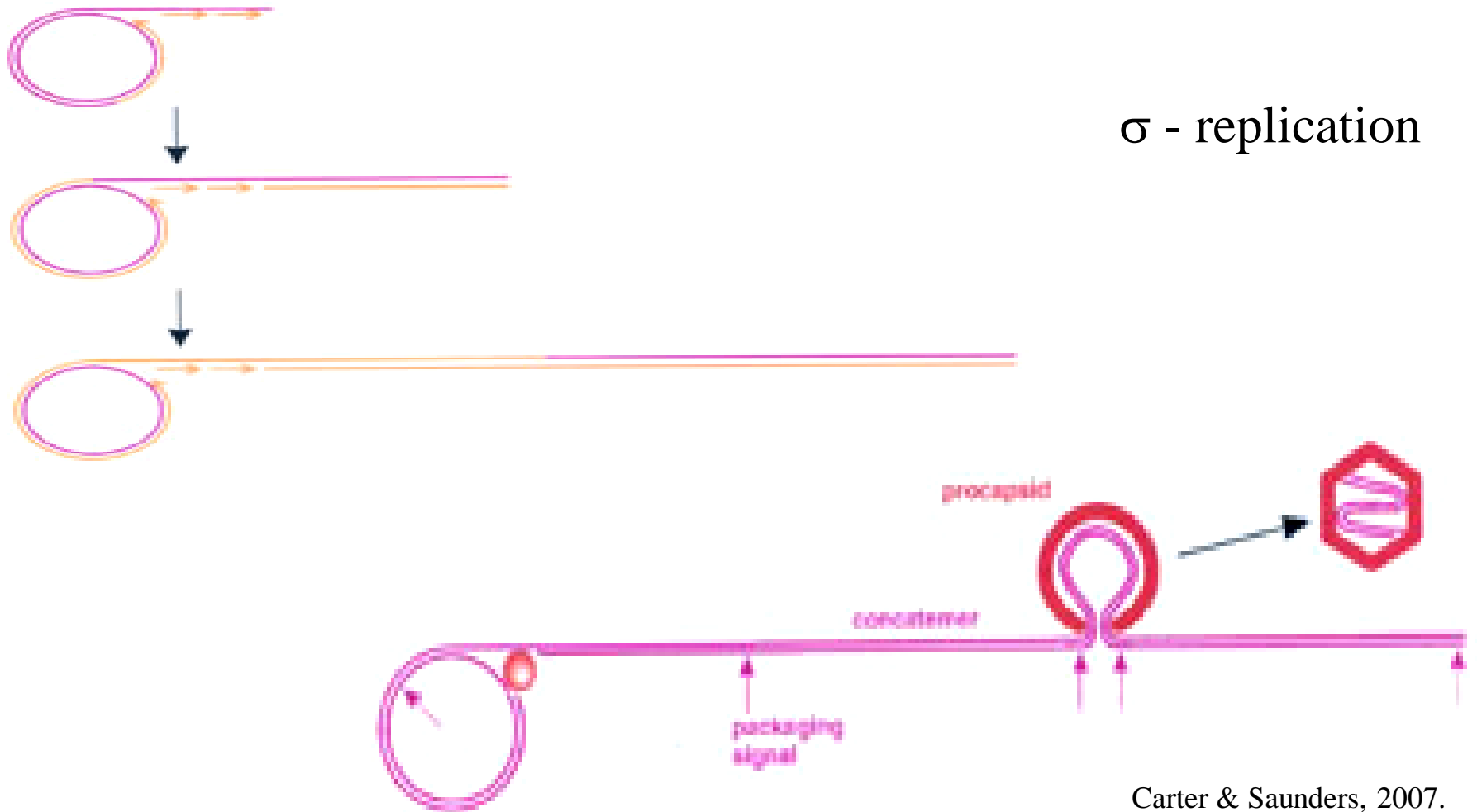
θ – replication

- proteins bind to 1/3 origins of replication.

-seven E proteins essential

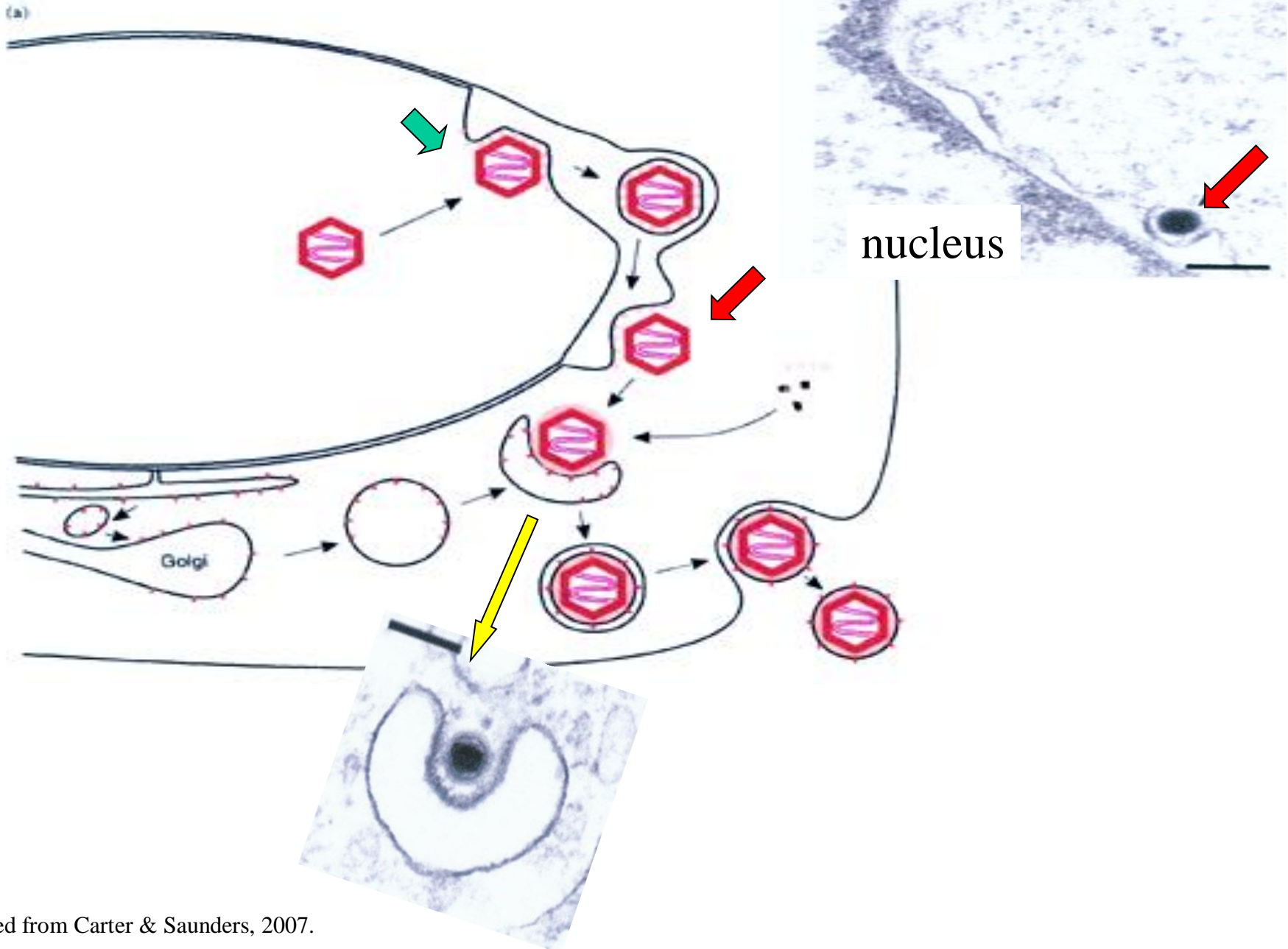


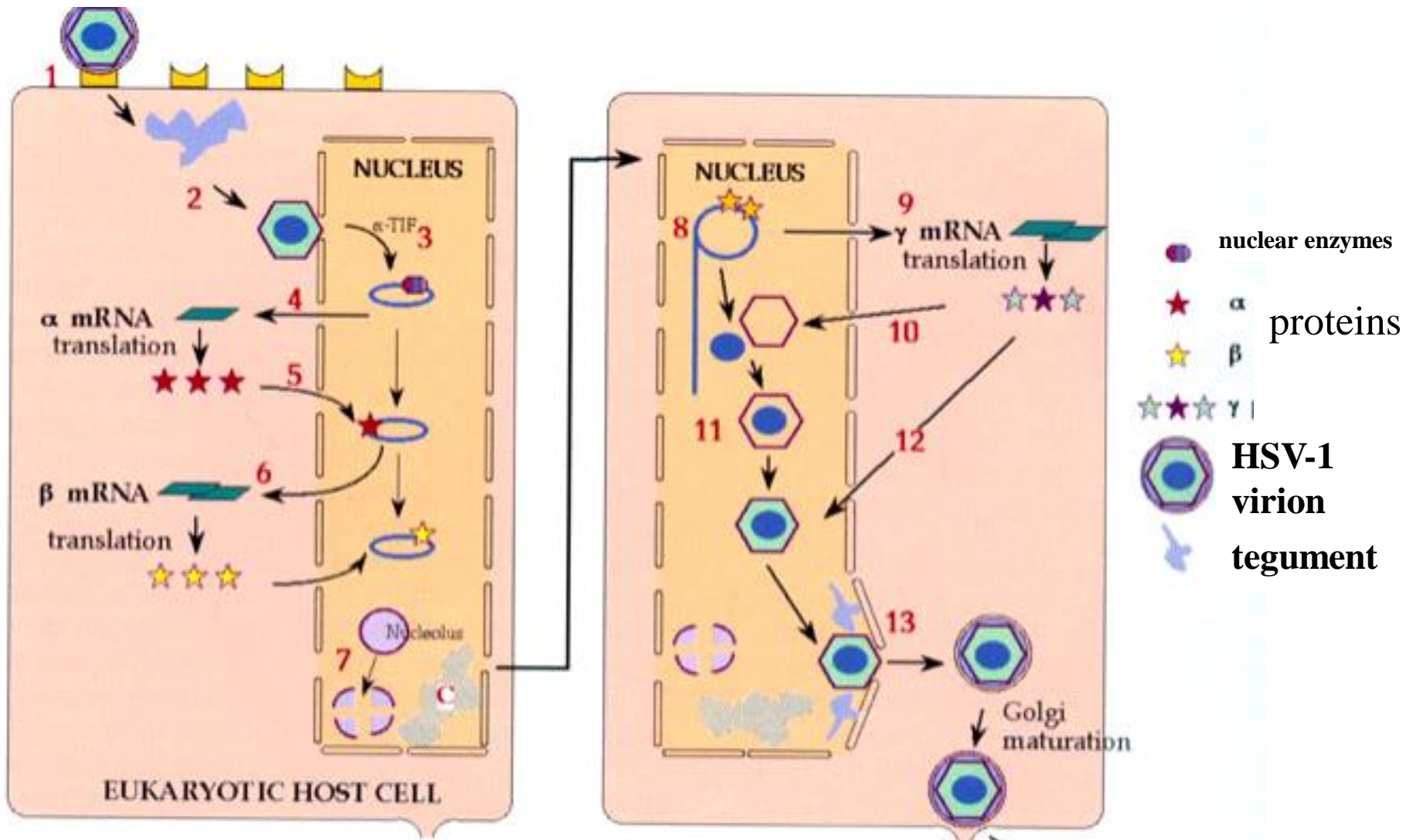
Strauss & Strauss, 2002.



Carter & Saunders, 2007.

HHV-1 exit





- HHV-1 replication cycle (transcriptome regulation)
- vegetative (“lytic”) and latent infection

<https://www.bing.com/videos/riverview/relatedvideo?&q=HSV+Latency+Cycle+Animation&&mid=C5885FA91304ADADB362C5885FA91304ADADB362&&FORM=VRDGAR>

How does a herpesvirus maintains latency?

HHV LATs – Latency Associated Transcripts

DNA HHV-1 genome region called Latency Associated Transcript Region is in the terminal repeats.

A set of micro RNAs (miRNAs) important for latency is also transcribed from the same locus.

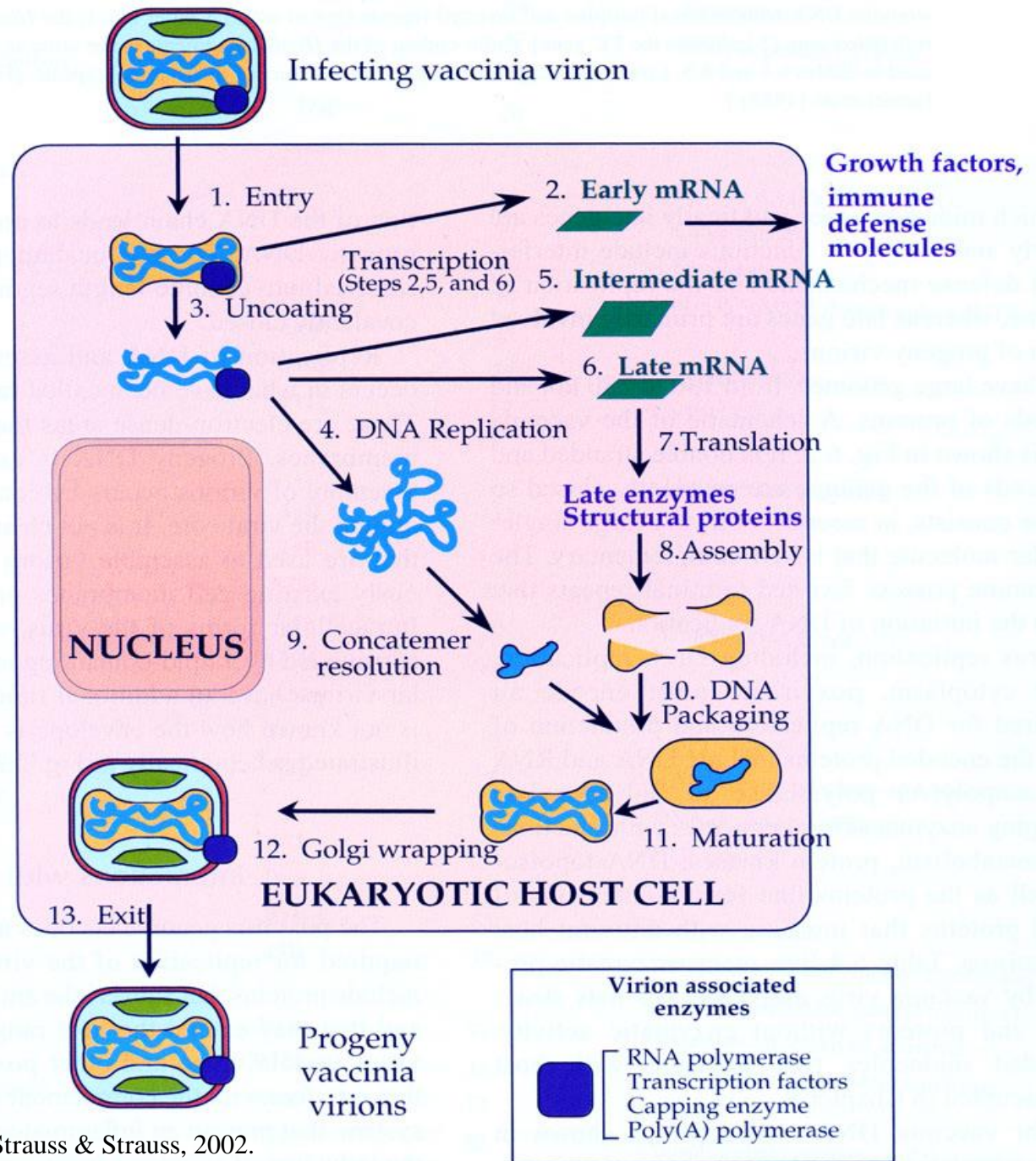
Farrell et al. 1991. Herpes simplex virus latency-associated transcript is a stable intron. *Proceedings of the National Academy of Science (USA)* 88: 790–794.

Phelan D, Barrozo ER, Bloom DC. 2017. HSV1 latent transcription and non-coding RNA: a critical retrospective. *J Neuroimmunol* 308:65–101. <https://doi.org/10.1016/j.jneuroim.2017.03.002>.

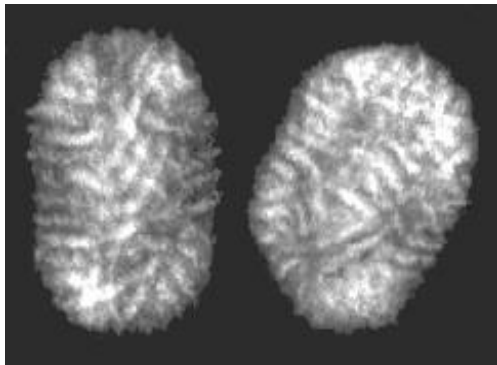
Singh N, Tschärke DC. 2020. Herpes simplex virus latency is noisier the closer we look. *J Virol* 94:e01701-19. <https://doi.org/10.1128/JVI.01701-19>.

Family	Subfamily	Genus	Species (virus)
<i>Poxviridae</i>			
	<i>Chordopoxvirinae</i>	<i>Avipoxvirus</i>	fowlpox
		<i>Capripoxvirus</i>	sheeppox
		<i>Leporipoxvirus</i>	myxoma
		<i>Molluscipoxvirus</i>	<i>Molluscum contagiosum</i>
		<i>Orthopoxvirus</i>	vaccinia
			variola (major, minor)
		<i>Parapoxvirus</i>	orf,
			pseudocowpox (pseudovaccinia)
		<i>Suipoxvirus</i>	swinepox
		<i>Yatapoxvirus</i>	Yaba monkey tumorvirus
			Tanapox monkey virus
	<i>Entomopoxvirinae</i>	<i>Entomopoxvirus A</i>	<i>Melolontha melolontha</i> entomopoxvirus
		<i>Entomopoxvirus B</i>	<i>Amsacta moorei</i> entomopoxvirus
		<i>Entomopoxvirus C</i>	<i>Chironomus luridus</i> entomopoxvirus

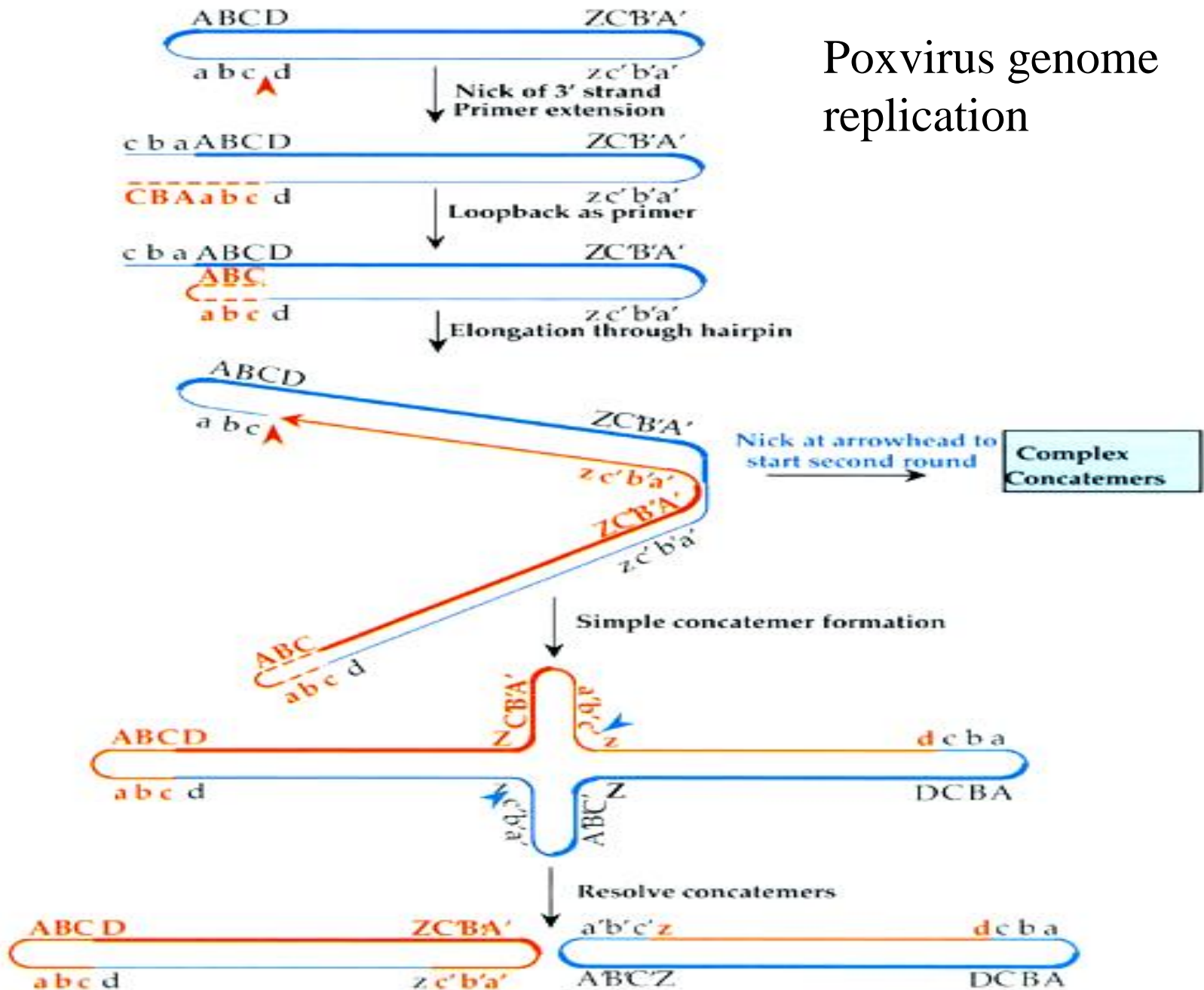
Linear dsDNA-genome with covalently closed ends, 130-300 kbp. More than 200 genes, about 100 proteins, complex structure, complete cycle in the cytoplasm.



Strauss & Strauss, 2002.



Poxvirus genome replication



Baculoviridae – 90-160 kbp genome, big but not in the NCLDV group in literature, may be a seminar topic.

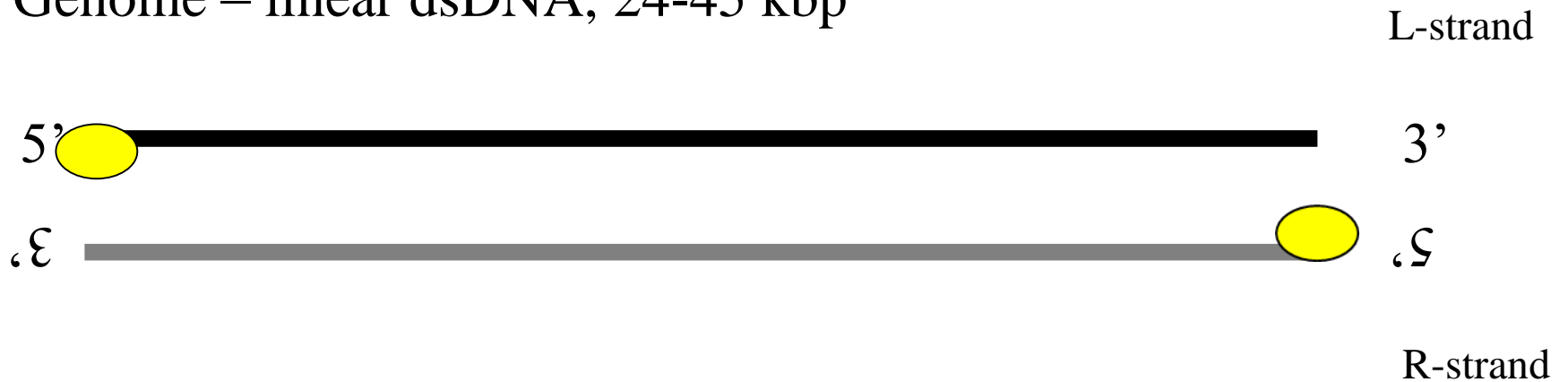
Main features for viruses with big dsDNA genomes :

- complex,
- genes in both DNA strands,
- linear genomes or linear that can circularize (**Herpes** and **Pox**)
- not found in plant hosts,
- may cause tumors,
- important cloning vectors,
- important in gene therapy.

Adenoviridae

70-100 nm, preterminal protein -  primer for DNA synthesis .

Genome – linear dsDNA, 24-45 kbp

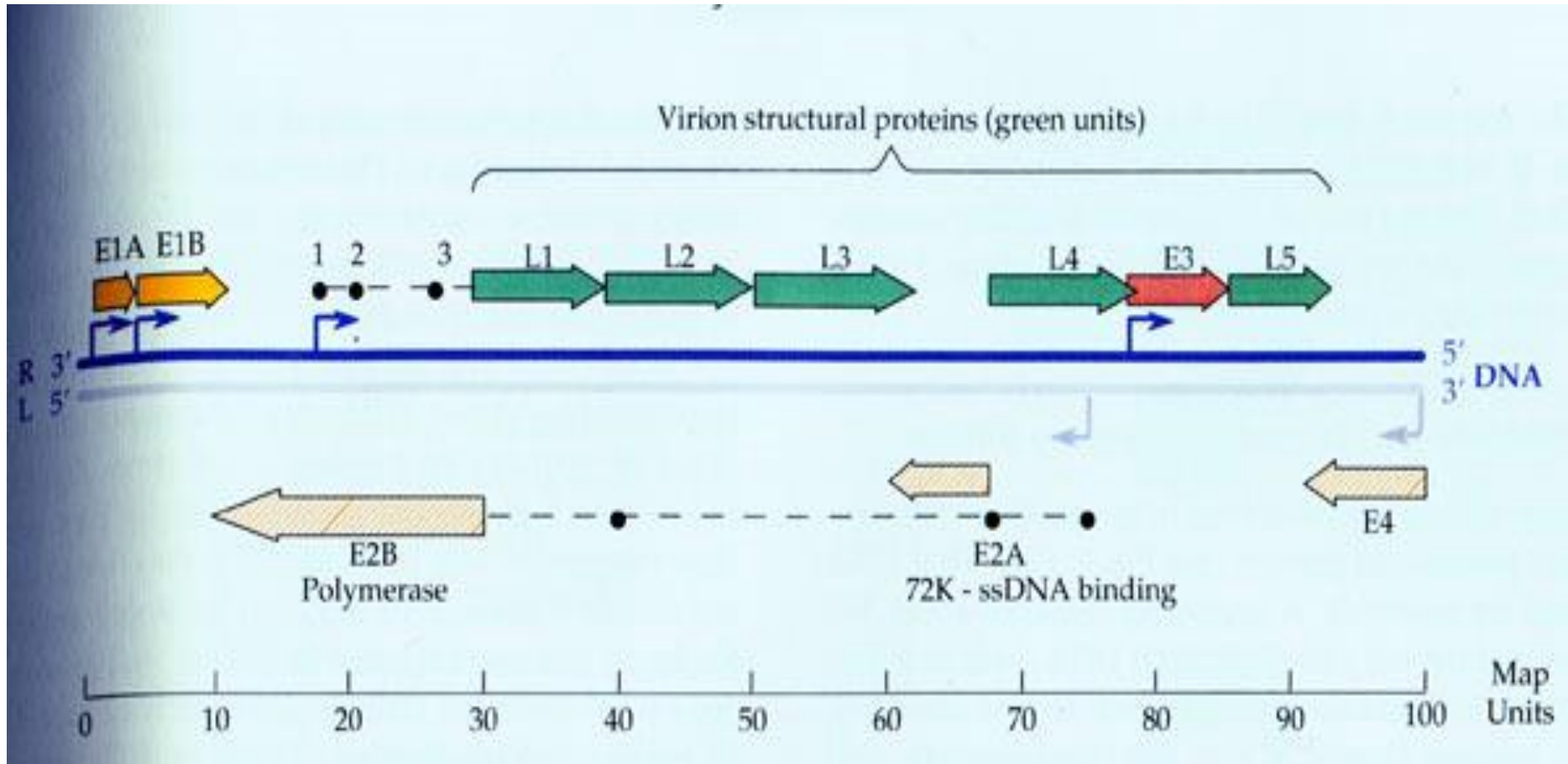


C) Adenovirus DNA Replication by Displacement Synthesis



Human adenovirus type 2 – genome organization and transcription

(36 kbp)



Adenoviral oncogenic proteins (E1A, E1B) interact with cellular proteins

