

Genetiikan perusteiden toisen jakson kaavailua

Tiedämme *kaiken* siitä, miten geenit siirtyvät sukupolvelta seuraavalle solun ja yksilön tasolla

Toisen jakson sisältö:

Mitä geenit ovat?

Miten geenit toimivat?

Mikä tai kuka uskaltaa vainota ja käyttää hyväksi geenitoiminnasta syntynyttä kovin pätevää yksilöä?

Patogeenit

CELL kappale 24

Pedot

Leijonat, karhut, sudet jne., ja tietenkin toiset ihmiset

Loiset

Monisoluiset eukaryootit: madot, punkit, hyönteiset

Sienet: hiivat, silsat, sienet (kts [lepakon valkonenäsyndrooma](#))

Protistat (= yksisoluiset eukaryootit), esimerkiksi malaria, bilhartsia, toksoplasma, unitauti

Bakteerit miljoonaisina laumoina

Virukset

Prionit (BSE)

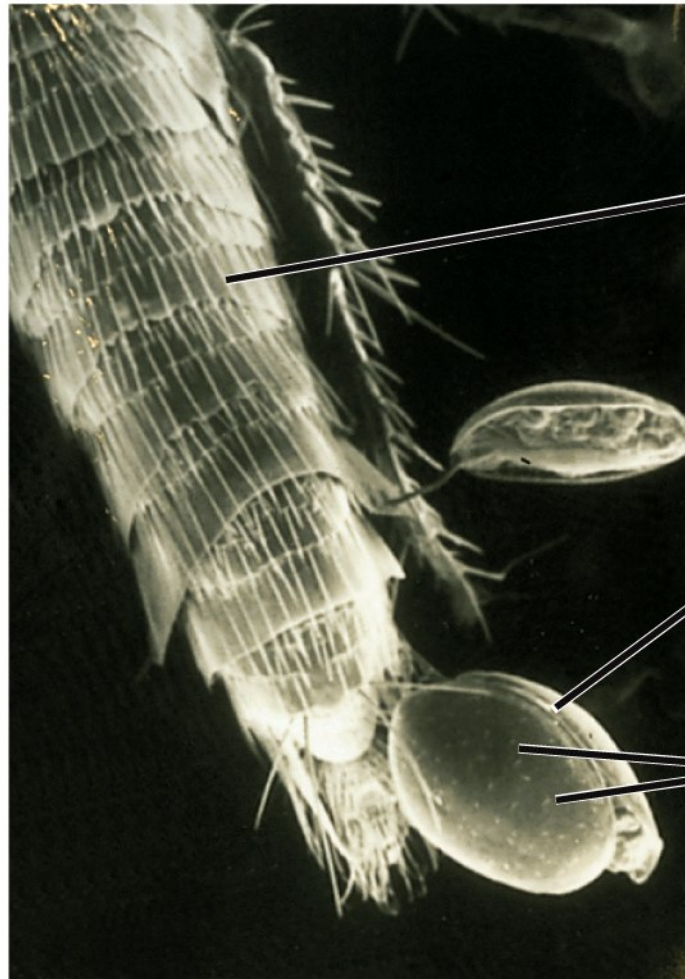
Ihmisen luonnollisten kuolinsyiden edustaja





(A)

0.2 mm



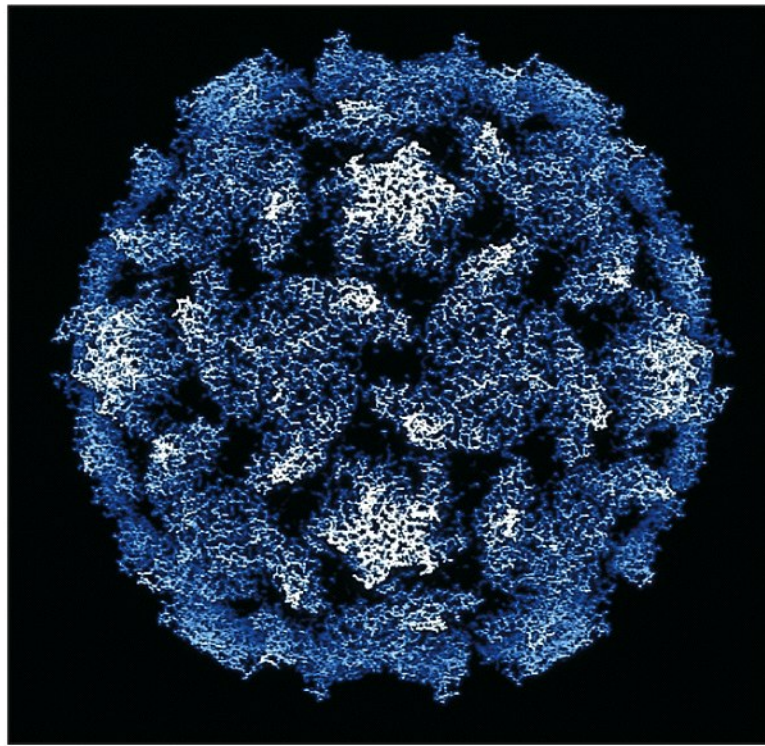
(B)

Figure 24-1 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Niveljalkaisvektorit kuljettavat lukemattomia patogeeneja

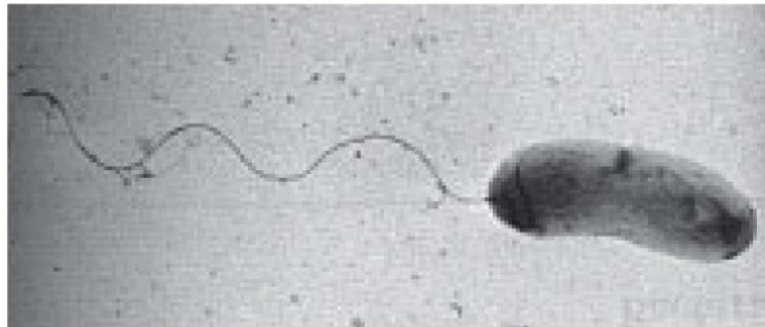


Niveljalkaisvektorit kuljettavat lukemattomia patogeeneja



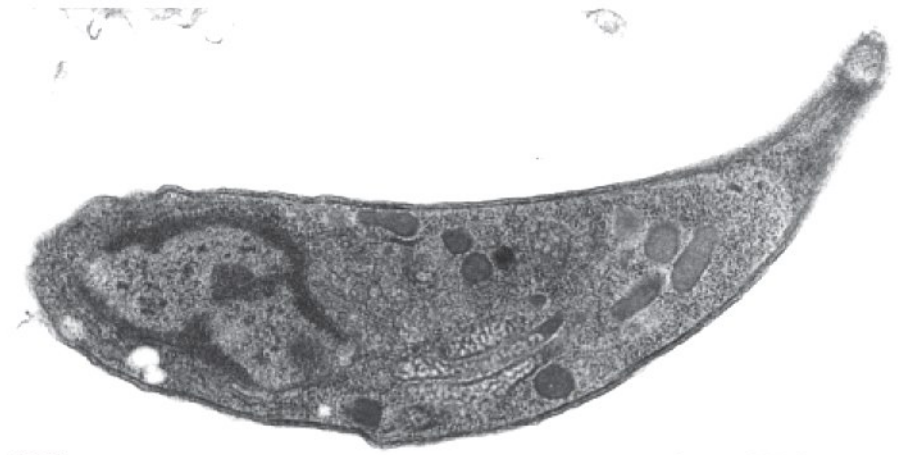
(A)

10 nm



(B)

1 μ m



(C)

1 μ m



(D)



Coccus



Coccobacillus



Vibrio



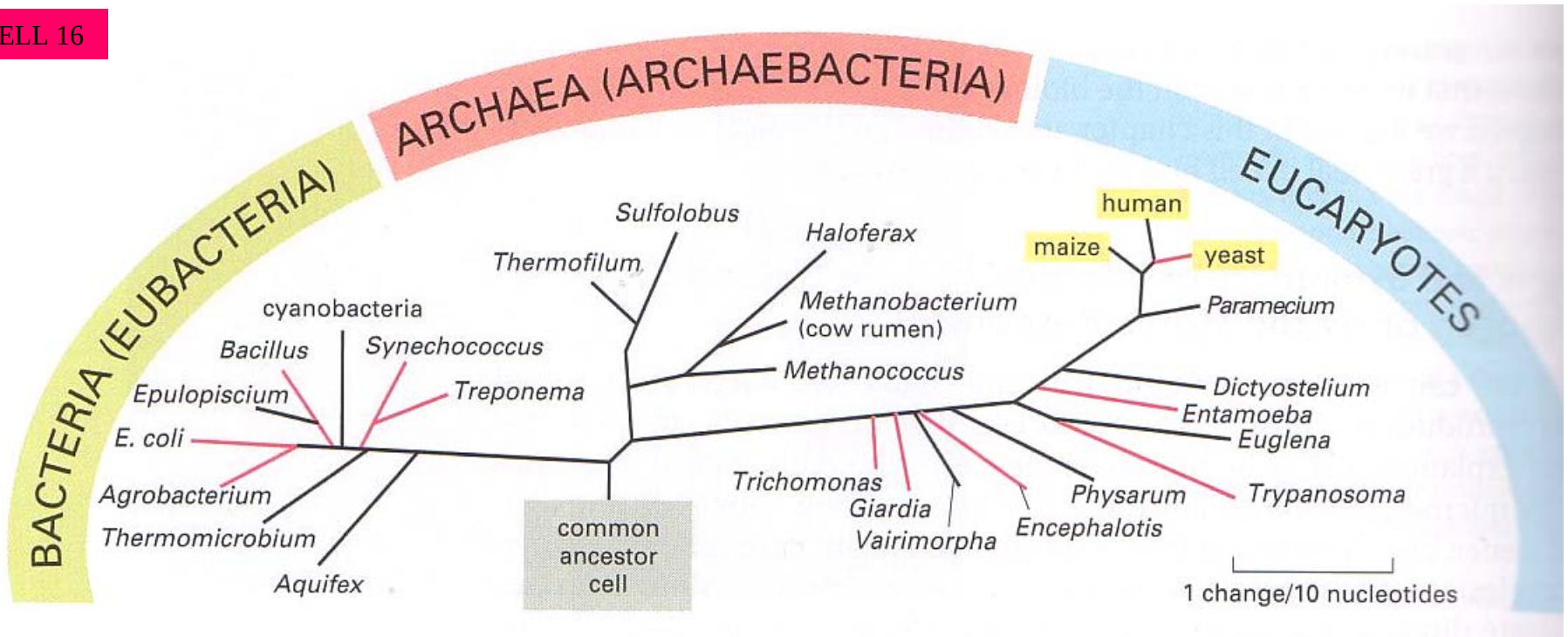
Bacillus



Spirillum



Spirochete



Patogeenien fylogeneettinen diversiteetti (punaiset haarat)

Arkit ovat aivan viattomia?

Tästä kuvasta puuttuvat vielä virukset, joita ei voida sijoittaa fylogenieioihin. Ne lienevät jostakin karanneita geenejä, mutta niin spesialisoituneita, ettei lähtökohtia osata hahmottaa

Patogeeni sairautta aiheuttava

- obligaat
- fakultatiivinen
- opportunistinen

Virulenssi sairastuttamis- tai tarttumiskyky

Toksiini myrkky

Malaria 2 milj/vuosi

Plasmodium falciparum

Anopheles gambiae

Sekä loisio että vektori sekvensoitiin kokonaan vuonna 2002, siinä toivossa että asialle voitaisiin tehdä jotakin

Loisio on entinen levä: sen tietty plasmidi on monikalvoinen sekundaarinen kloroplasti

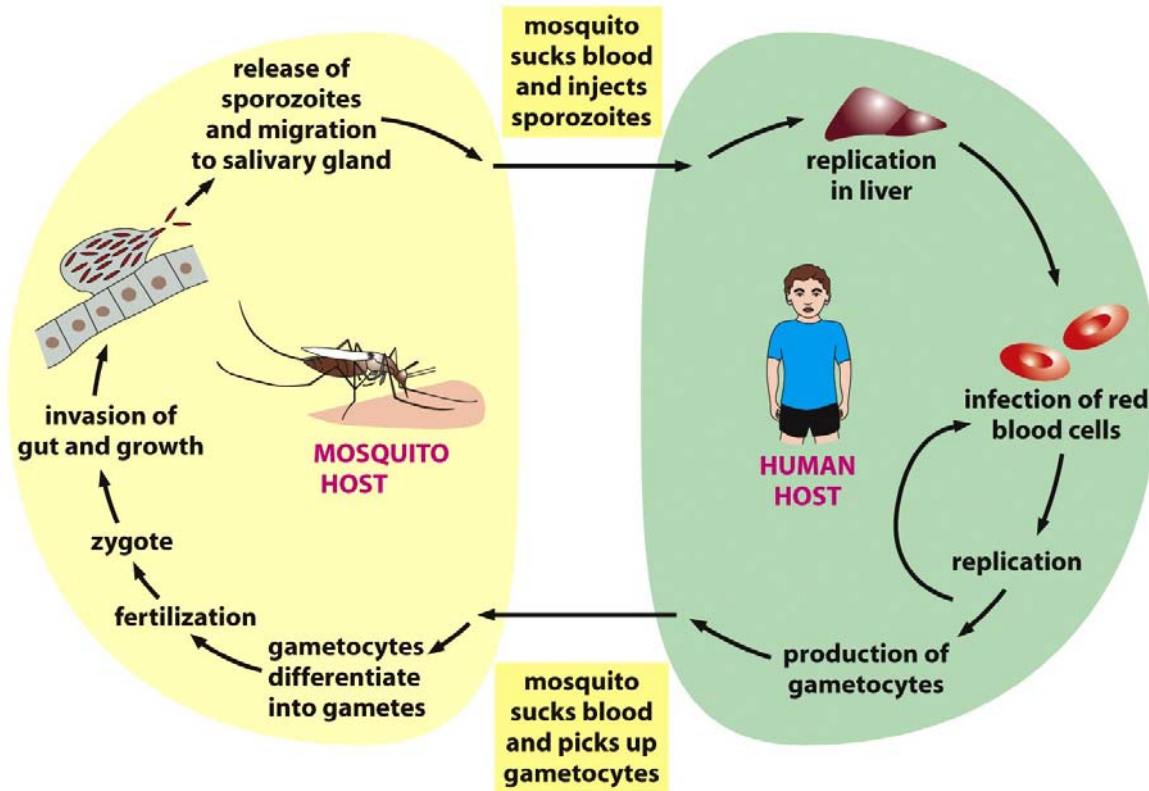


Figure 24-10a Molecular Biology of the Cell 5/e (© Garland Science 2008)

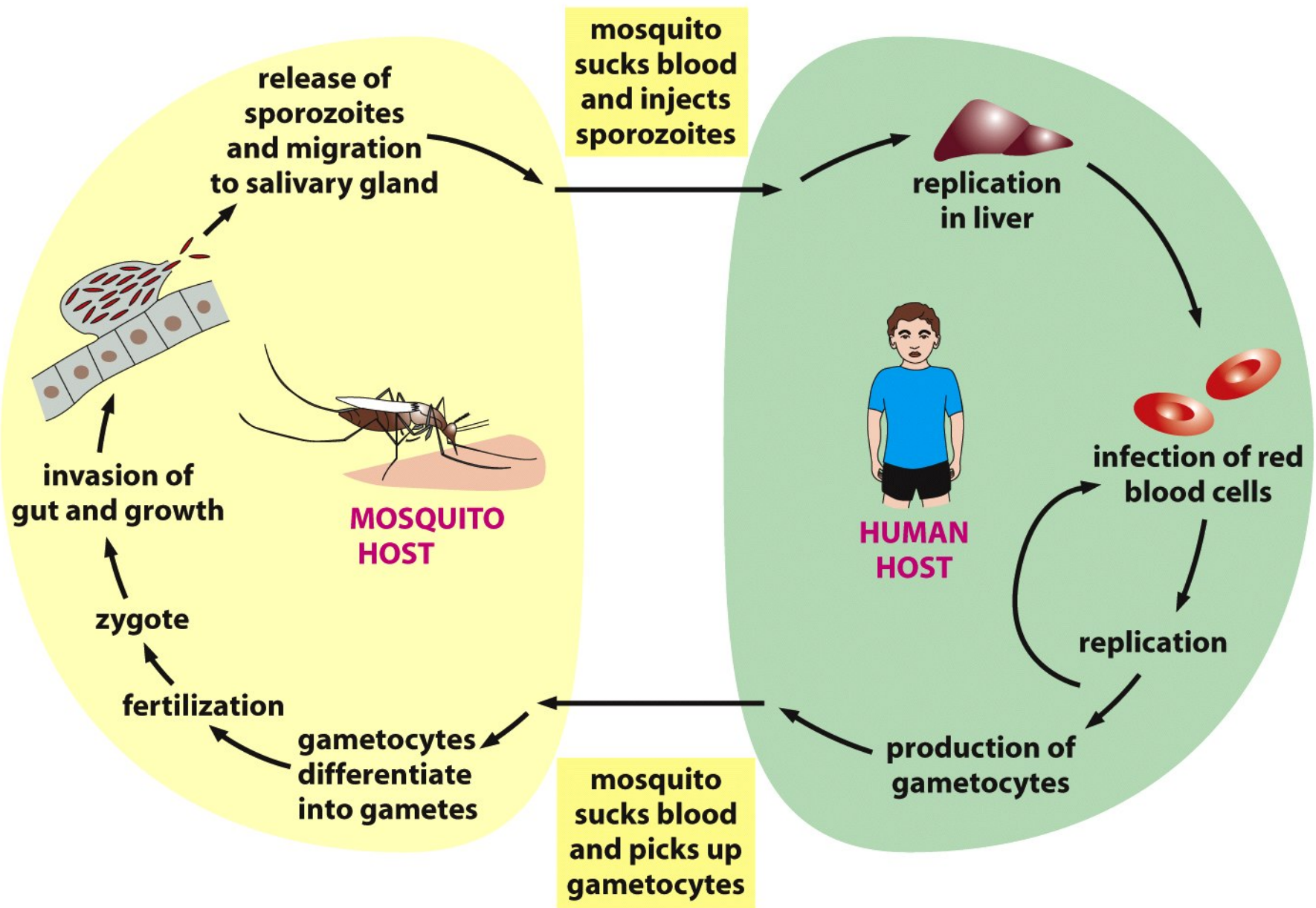
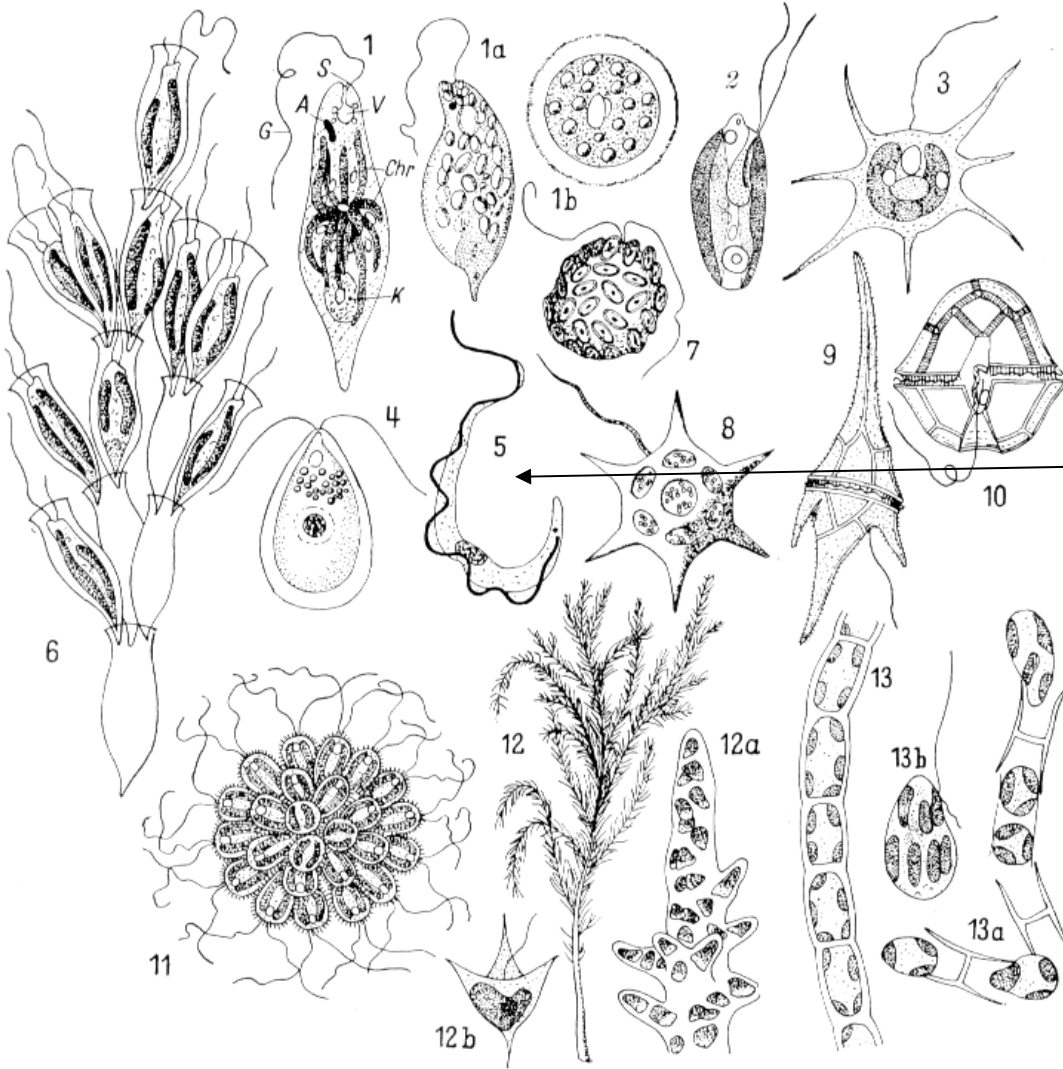
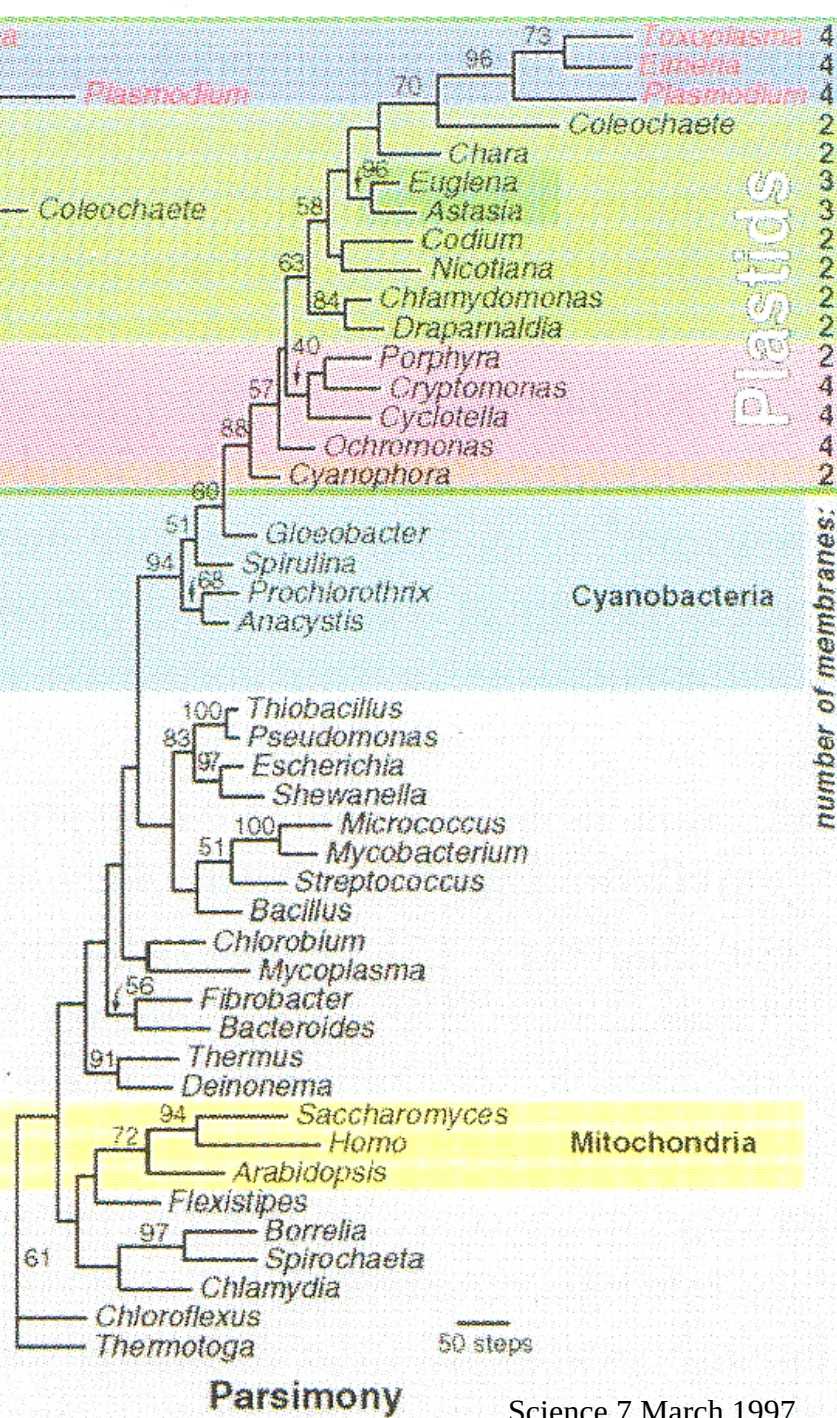


Figure 24-10a Molecular Biology of the Cell 5/e (© Garland Science 2008)



Trypanosoma

Abb. 107. Verschiedene Flagellatentypen: 1 *Euglena* (K Kern, Chr grüne Chromatophoren, A Augenfleck, V pulsierende Vakuole, S Schlundspalte, G Geißel), 1a dieselbe mit Paramykonkörnern, 1b dieselbe im Palmella-Zustand; 2 *Cryptomonas*, zweigeißliger Flagellat mit olivgrünen (braungrünen) Chromatophoren; 3 *Chrysamoeba* mit amöboiden Kriechbewegungen; 4 *Polythoma*, farbloser Flagellat mit Zellwand; 5 *Trypanosoma*, parasitäre, farblose Form mit undulierender Membran; 6 *Dinobryon*, Zellen in Gehäusen zu Kolonien vereinigt; 7 *Calyptrosphaera* (Coccolithinae) mit Kalkausscheidungen; 8 *Distephanus* (Silicoflagellatae) mit Kieselskelett, 9 *Ceratium* und 10 *Peridinium* mit Panzer aus Zelluloseplatten (Peridineae); 11 *Synura*, einfache Kolonie; 12 *Hydrurus*, Kolonie aus verzweigten Gallertfäden, 12a das Ende eines Fadens stärker vergrößert, 12b bewegliches Schwärmerstadium; 13 *Conferva* (= *Tribonema*), eine Fadenalge, 13a der Faden in H-förmige Zellwandstücke zerfallend und Schwärmer bildend, 13b einzelner Schwärmer mit ungleichen Geißeln (Heterocontae).

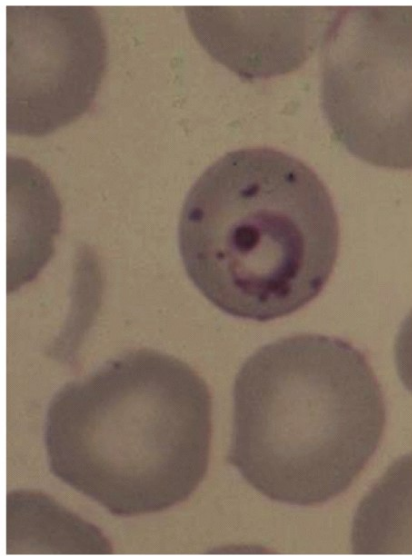


Toxoplasma, *Eimeria*, *Plasmodium*

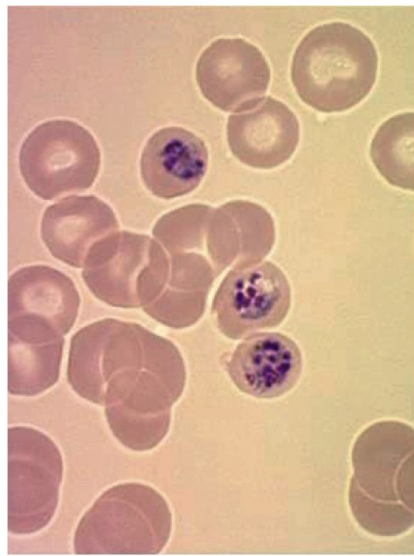
Loiselämään sopeutuneet muodot ovat menettäneet kloroplastin vihreyden kokonaan.

Rakenne kalvoineen on vielä jäljellä ja varmaan tekeekin jotakin

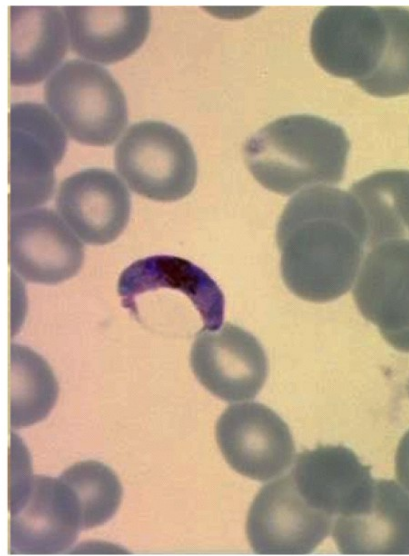
Plastidin neljä kalvoa todistavat sekundaarisesta endosymbioosista



(B) 5 μm



(C) 10 μm



(D) 10 μm

Figure 24-10bcd Molecular Biology of the Cell 5/e (© Garland Science 2008)

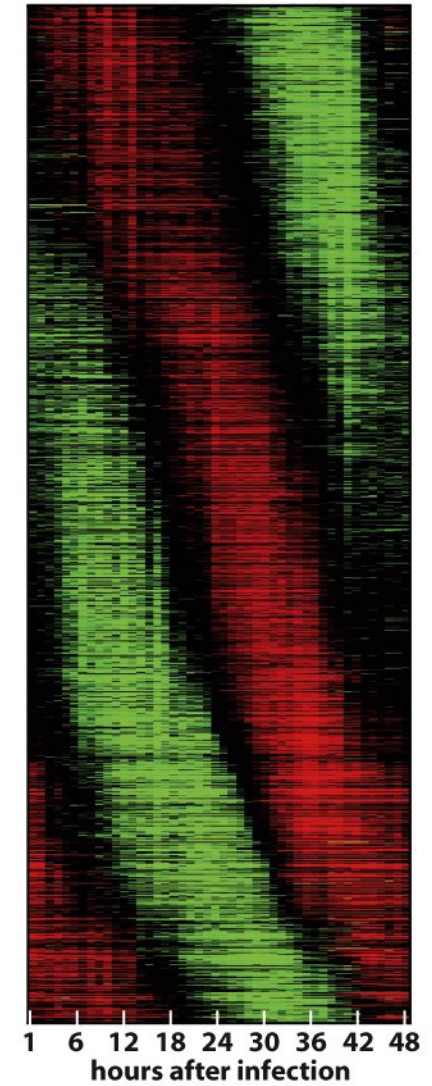


Figure 24-11 Molecular Biology of the Cell 5/e

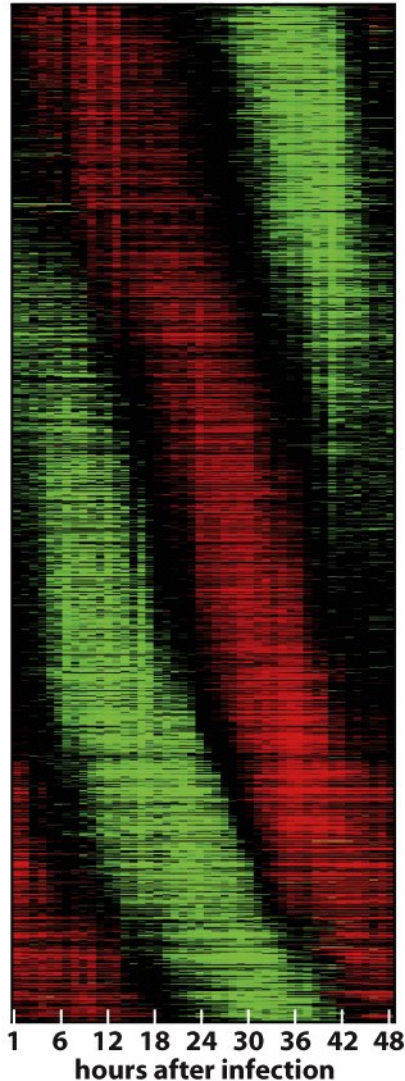
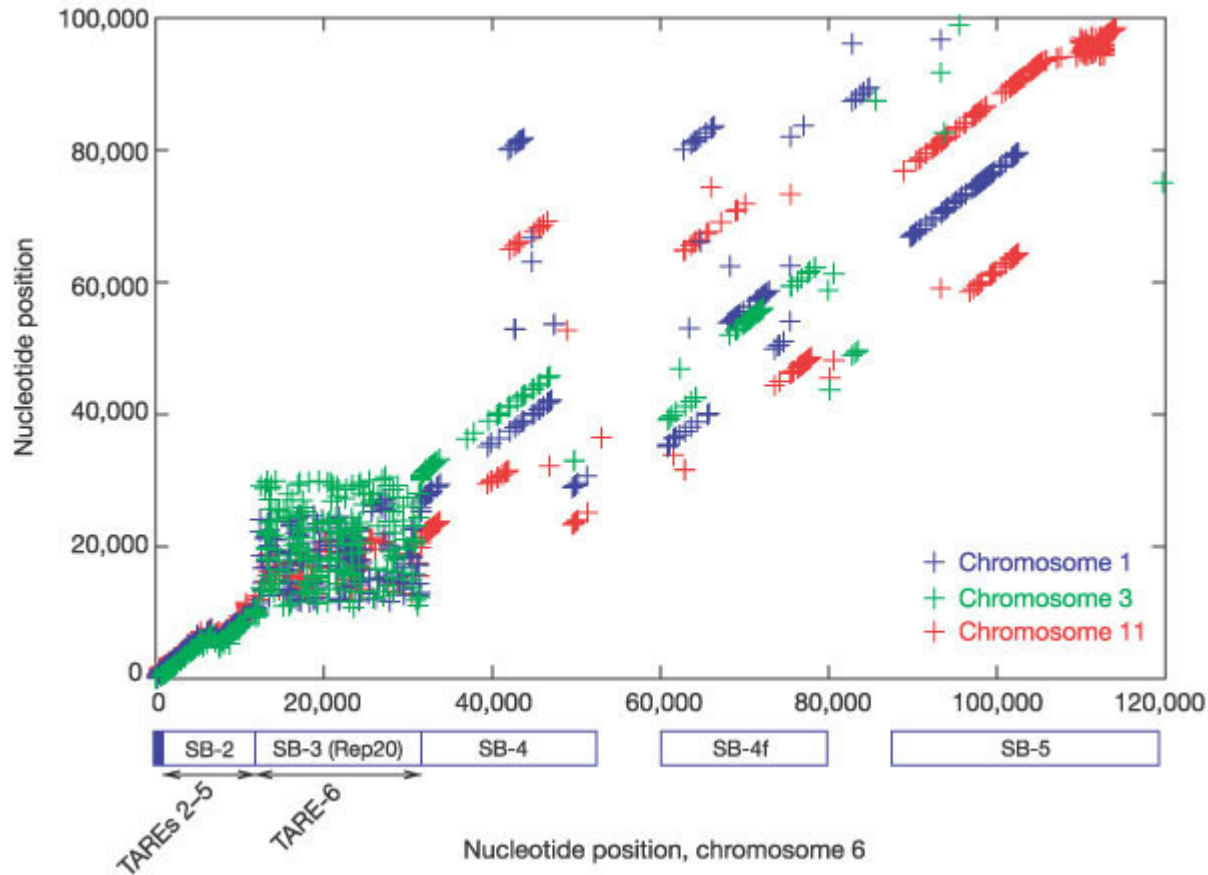


Figure 24-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Plasmodium väistää
immuunijärjestelmää
muuttumalla koko ajan. Se
tekee uuden pinnankin
jatkuvasti ja piileskelee
punasoluissa

Rokotetta ei ole

Genomi sekvensoitu,
samoin päävektorin
(*Anopheles gambiae*)



Jotain analyysia *Plasmodiumin* kromosomeista

Nature **419**, 498-511 (3
October 2002)

[LINKKI](#)

Science

4 October 2002

Vol. 298 No. 5591
Pages 1-310 \$10

THE MOSQUITO GENOME
Anopheles gambiae

[Linkki](#)



AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

*Plasmodium
falciparum*

tärkein vektori on

Anopheles gambiae

Muita moskiittojen
levittämiä:

Dengue-kuume

Filariasis

Keltakuume

Jap. aivokalvontulehdus

Dissertationes Forestales 73



Helsingin yliopisto
2008

The decline of northern malaria and population dynamics
of *Plasmodium vivax*

Lena Huldén

Pohjoisen malarian perikato
kuvattiin tässä väitöskirjassa

[LINKKI](#)

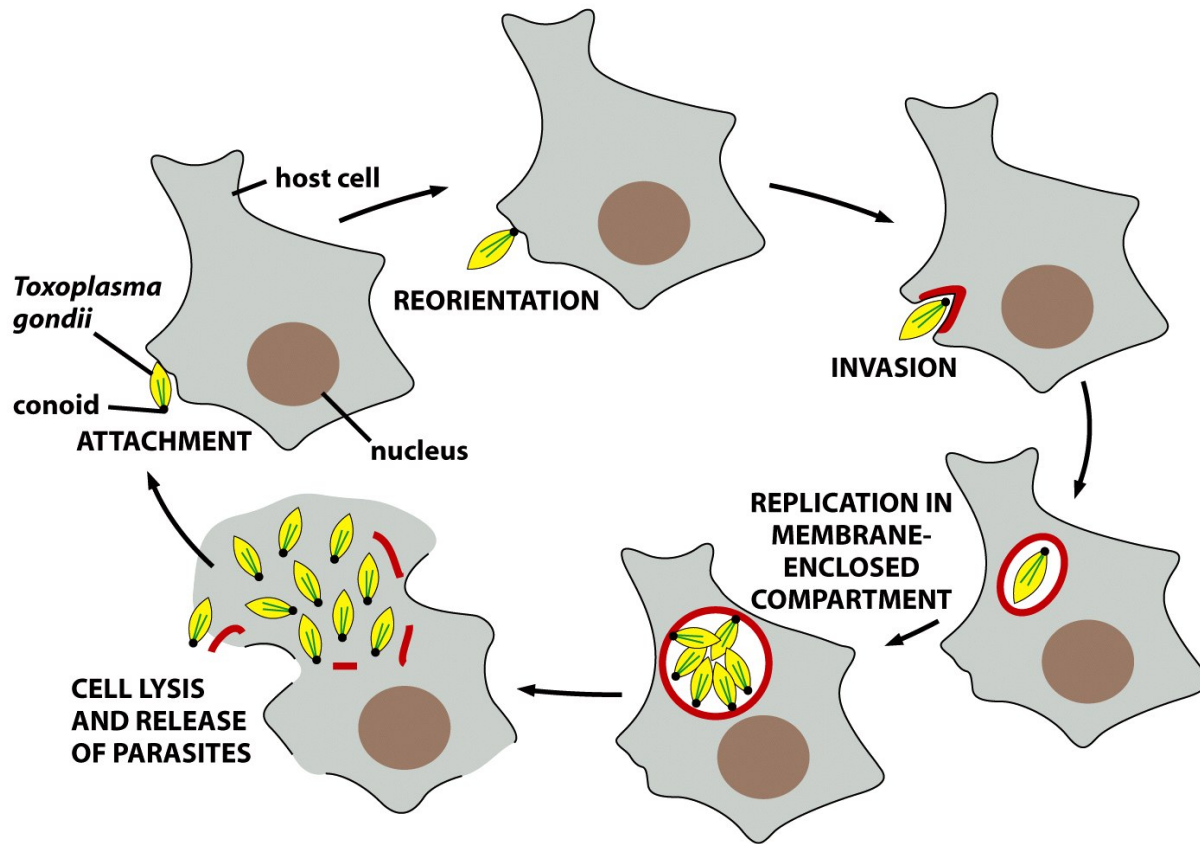


Figure 24-27a Molecular Biology of the Cell 5/e (© Garland Science 2008)

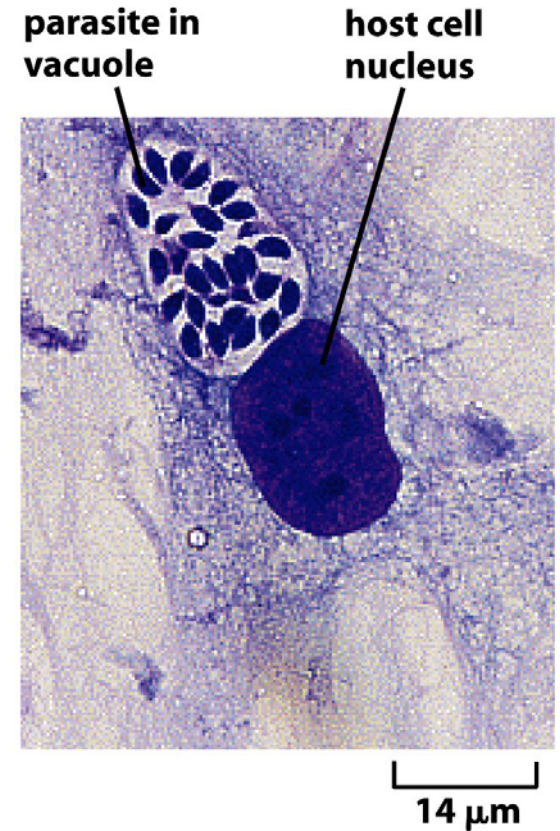


Figure 24-27b Molecular Biology of the Cell 5/e (© Garland Science 2008)

Toxoplasma gondii

CELL 1510

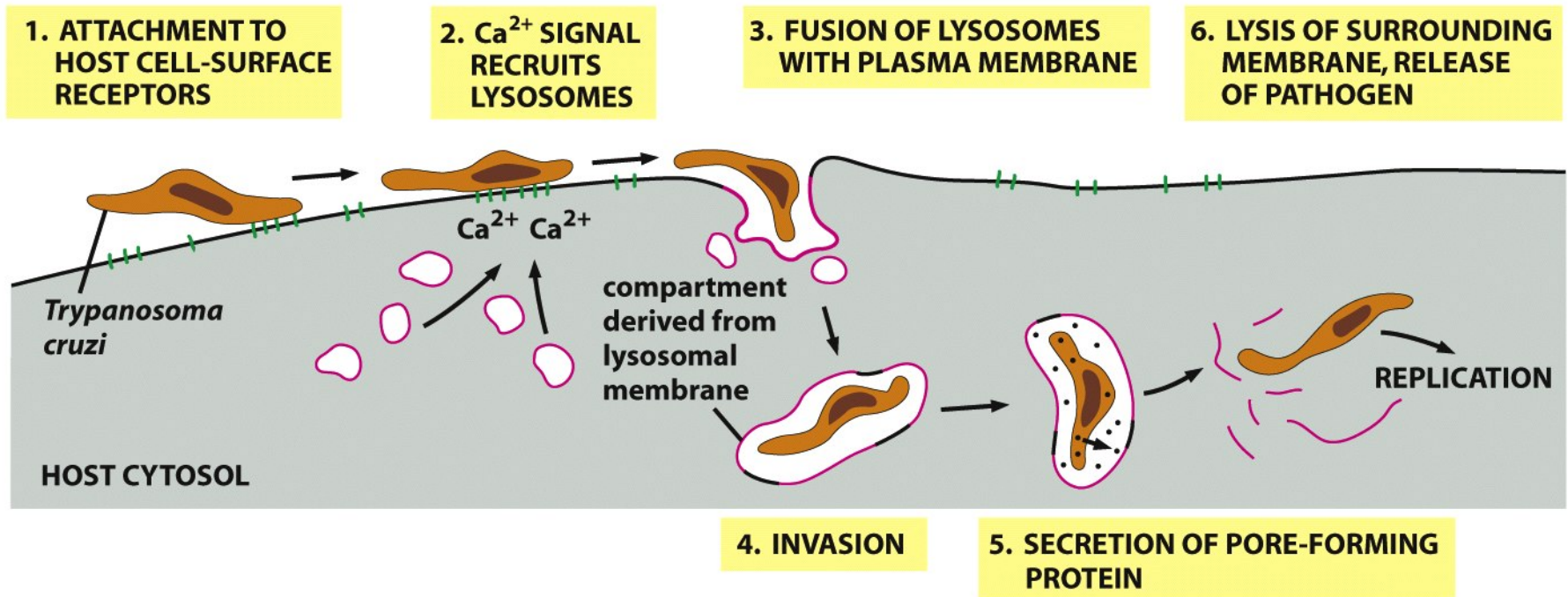


Figure 24-28 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Trypanosoma brucei

CELL 1510

Microsporidium

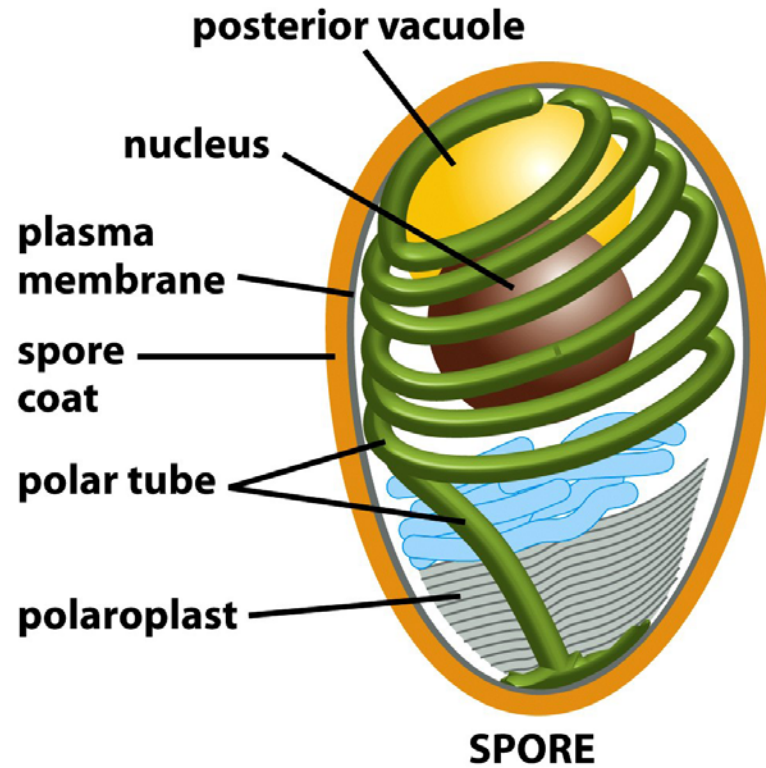


Figure 24-29a Molecular Biology of the Cell 5/e (© Garland Science 2008)

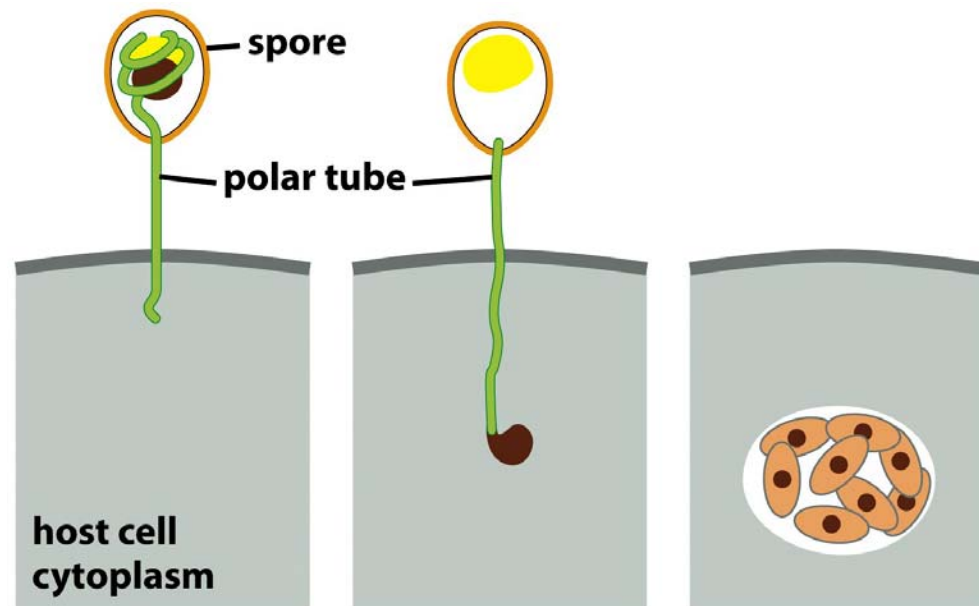


Figure 24-29b Molecular Biology of the Cell 5/e (© Garland Science 2008)

CELL 1511



Valkonenätauti

Fig. 1. (A) A little brown bat, found in Howes Cave on 6 January 2008, exhibits white fungal growth on its muzzle, ears, and wings. (B) Fungal invasion of bat skin (periodic

Virukset

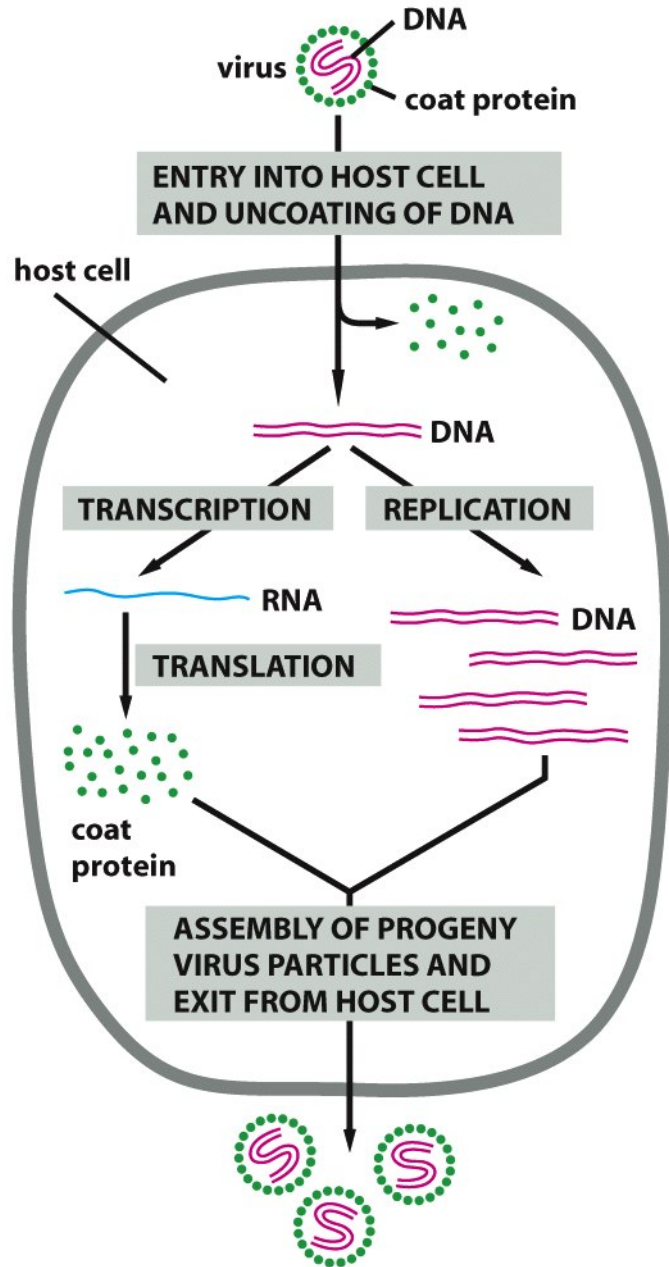


Figure 24-12 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Simppelin viruksen elämänsykli

Virukset käyttävät isäntäsolujen geneettistä koneistoa omien monistumistarpeidensa tyydyttämiseen

Myös rekombinaatiossa isännän pitää auttaa

Lisäksi isäntä joutuu jelpsimään viruksen uusiin isäntiin, sen se usein tekee mielellään

Viruksella ei ole syytä tappaa!
Sairaus on ihan *collateraalidamagea*

single-stranded RNA

tobacco mosaic virus
bacteriophage R17
poliovirus



single-stranded DNA

parvovirus



**double-stranded
circular DNA**

SV40
papilloma viruses



double-stranded RNA

reovirus



**single-stranded
circular DNA**

M13
 ϕ 174 bacteriophages
circovirus



double-stranded DNA

T4 bacteriophage
herpes viruses



**double-stranded DNA with
each end covalently sealed**

poxvirus



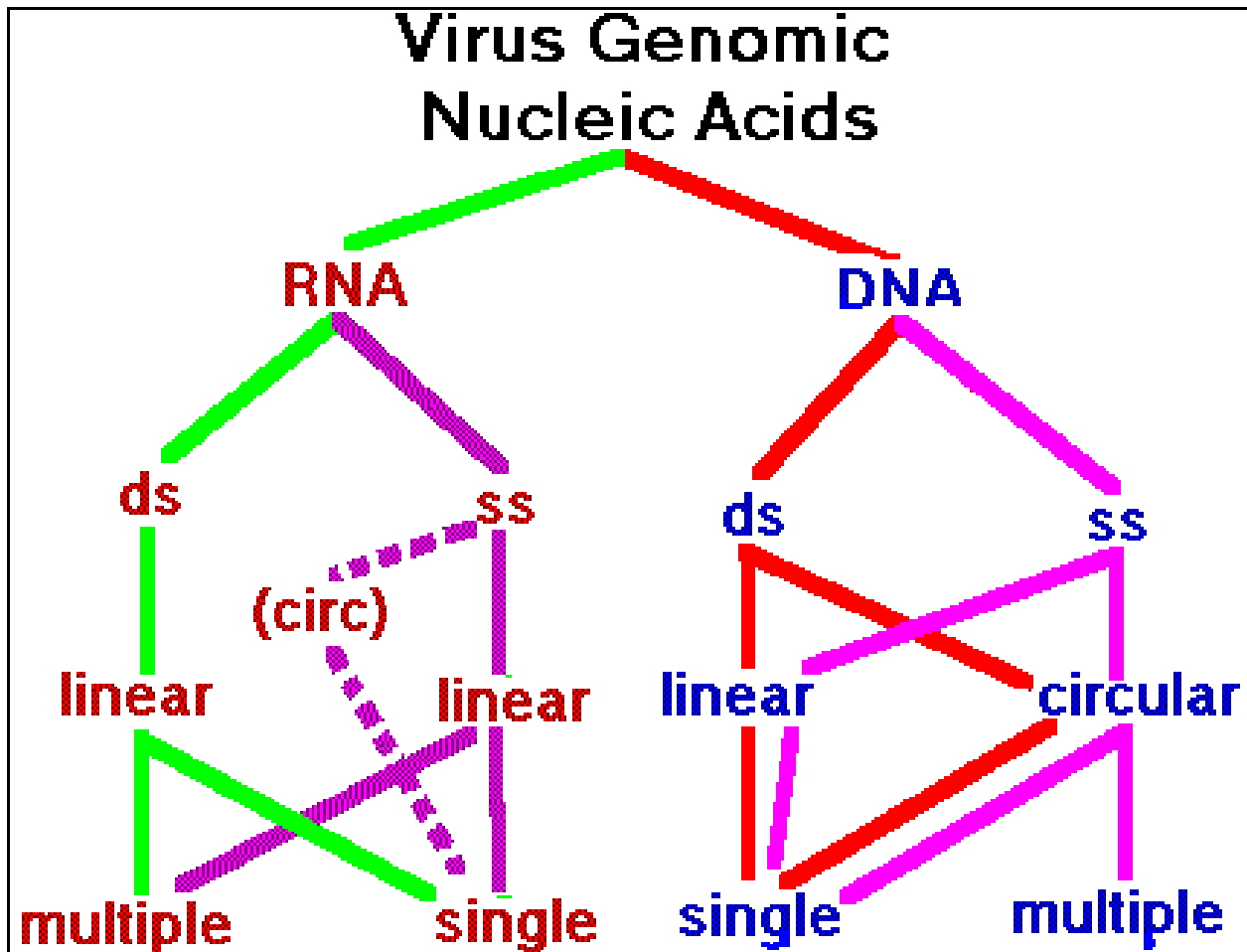
**double-stranded DNA
with covalently linked
terminal protein**

adenovirus

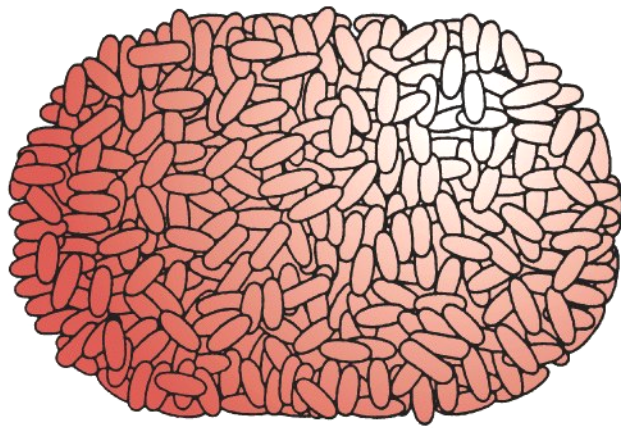


Figure 24-14 Molecular Biology of the Cell 5/e (© Garland Science 2008)

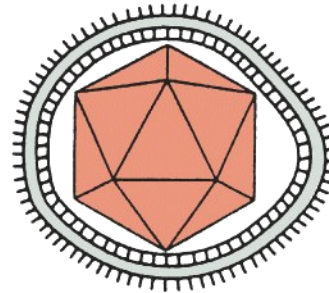
Virukset voivat pakata geeninsä lukuisiin eri nukleiinihappomuotoihin, mutta geenin tai muutamia niillä on.



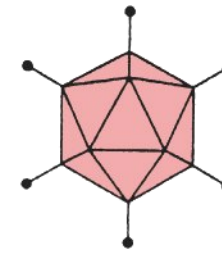
Virusten geneettinen materiaali voi olla monissa eri muodoissa



poxvirus



herpesvirus



adenovirus



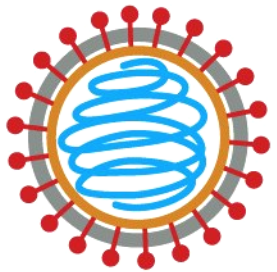
papilloma virus



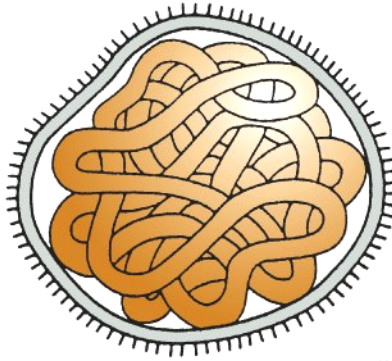
parvovirus

100 nm

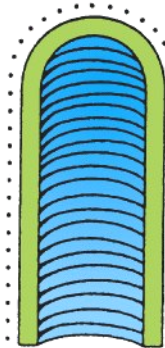
DNA VIRUSES



influenza virus



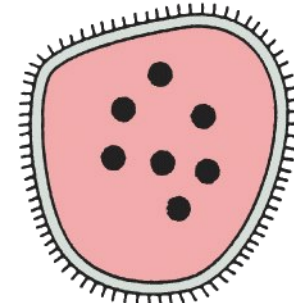
mumps virus



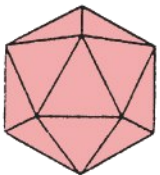
rabies virus



**HIV
(AIDS virus)**



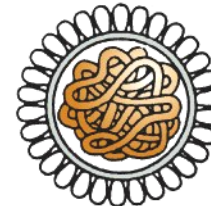
LCM virus



rotavirus



**eastern equine
encephalitis virus**



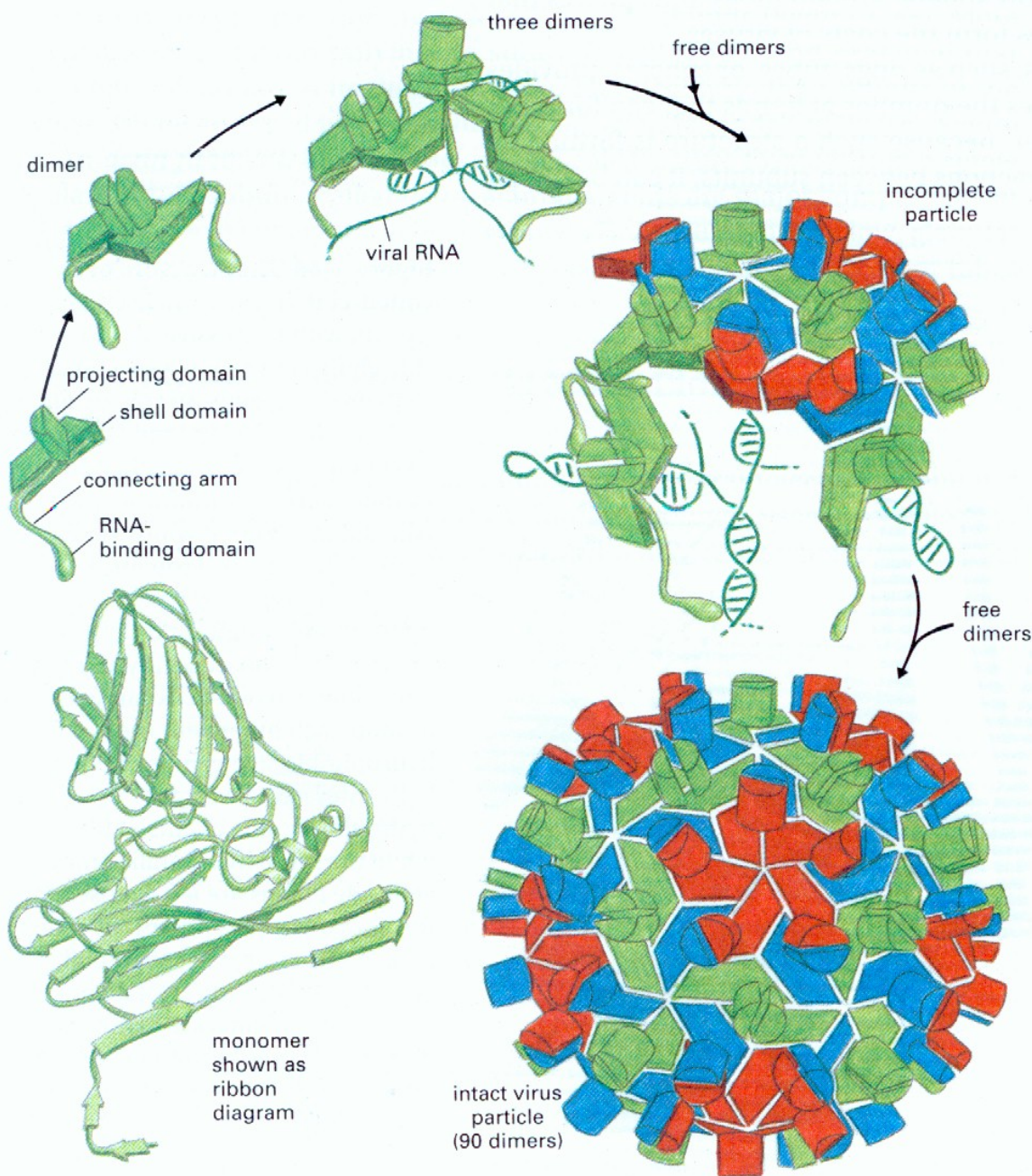
**corona virus
(common cold)**



poliovirus

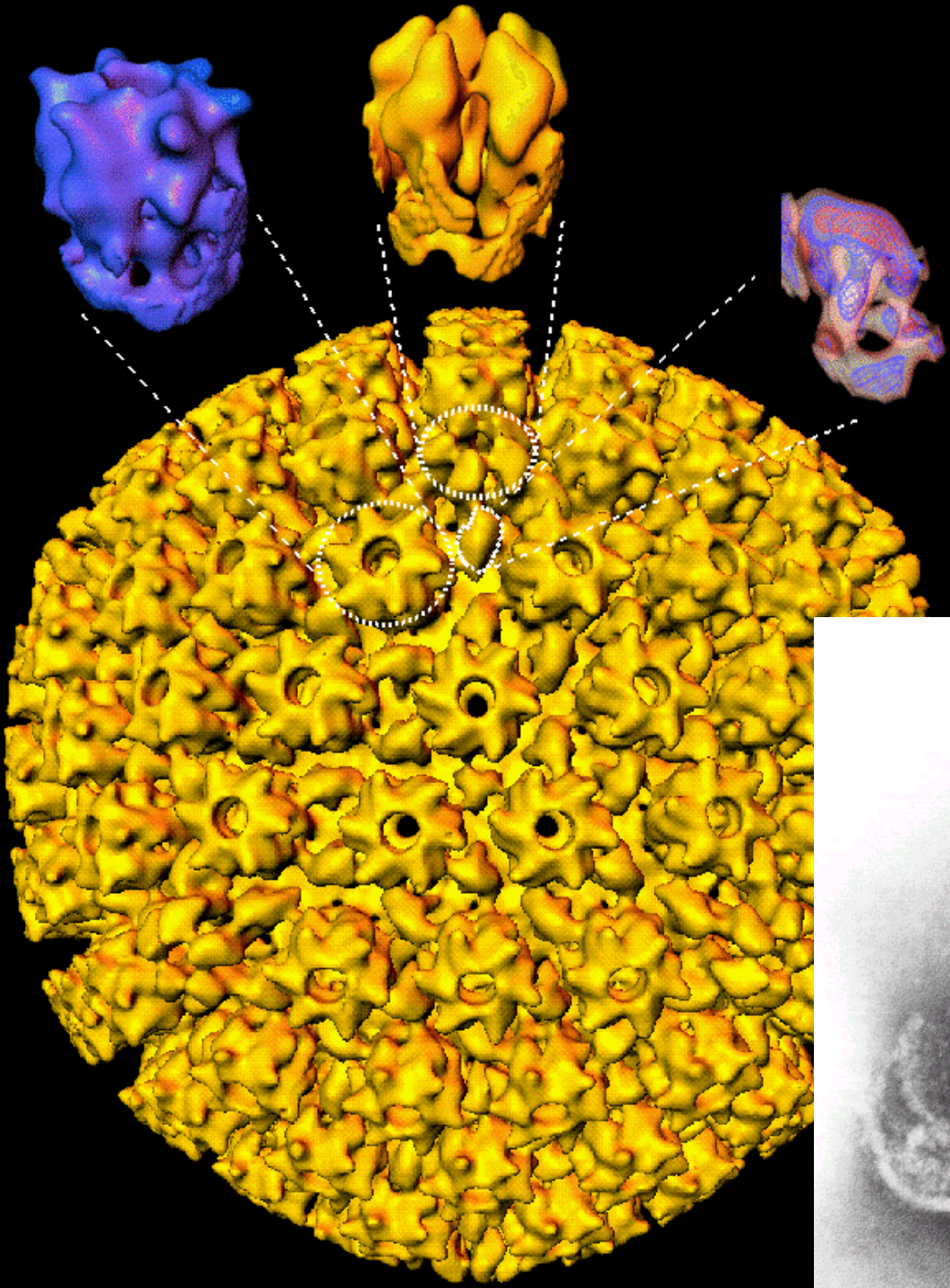
RNA VIRUSES

Figure 24-13 Molecular Biology of the Cell 5/e (© Garland Science 2008)



Virukset rakentavat kuorensa yksinkertaisista toistuvista osista

Kuoressa säästetään geenejä toistamalla samaa motiivia

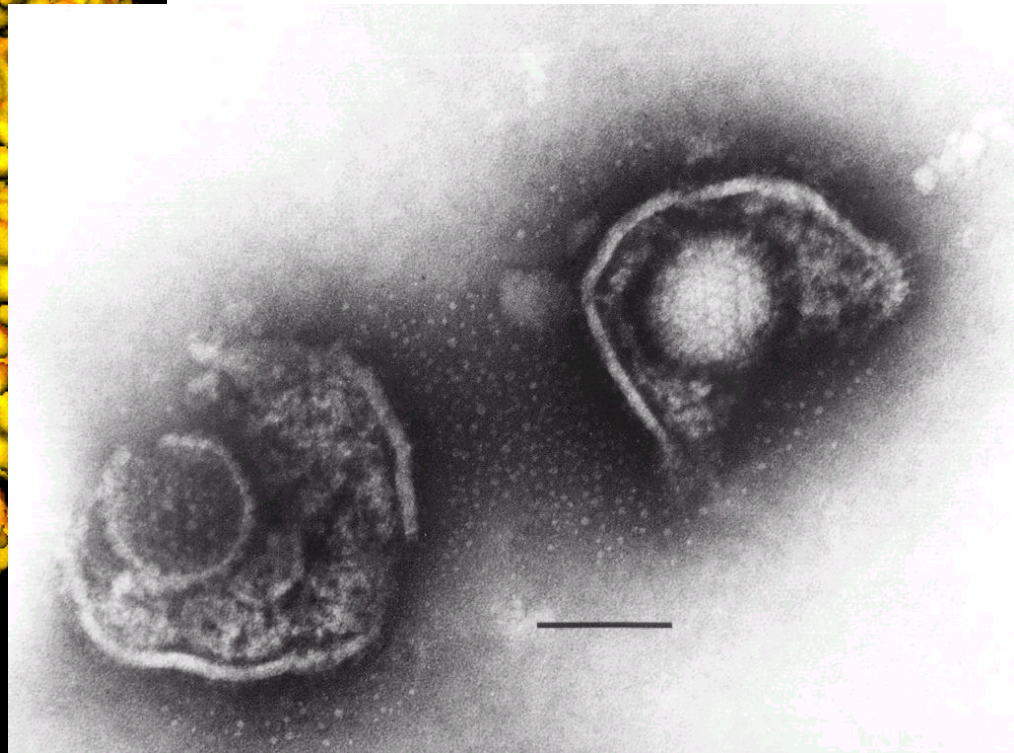


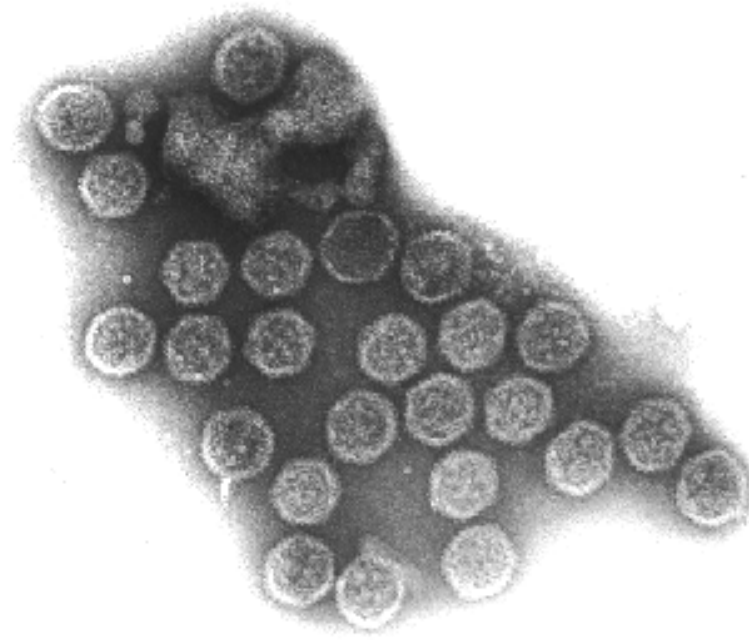
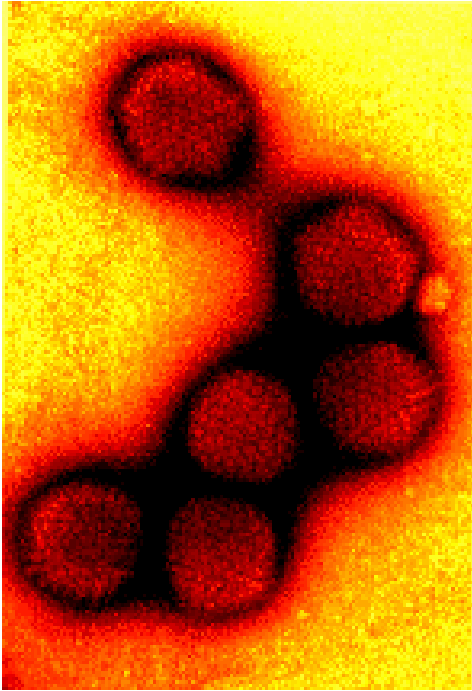
DNA-virus *Herpes simplex*

lineaarinen 2-juosteinen DNA

120 kb- 220 kb

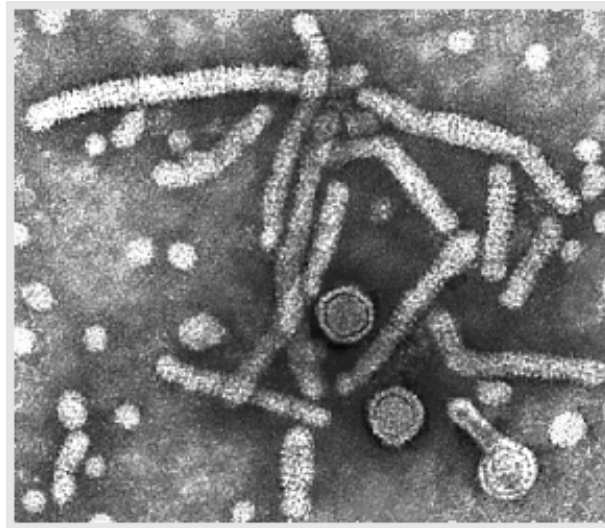
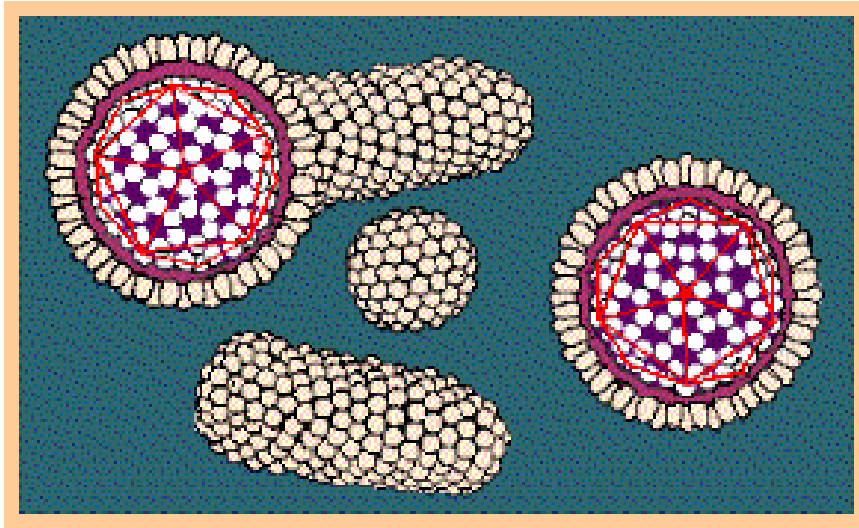
enveloped





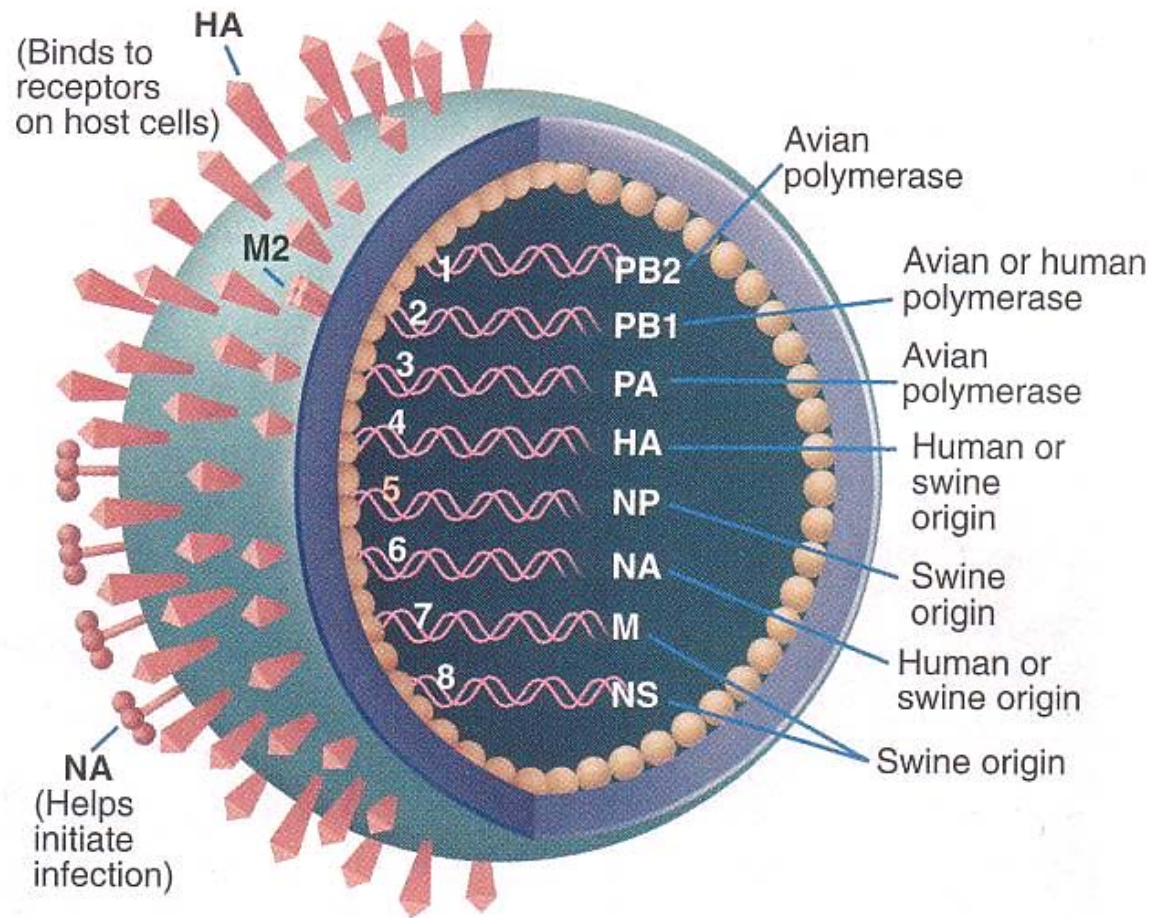
Adenovirus

DNA ds non-enveloped



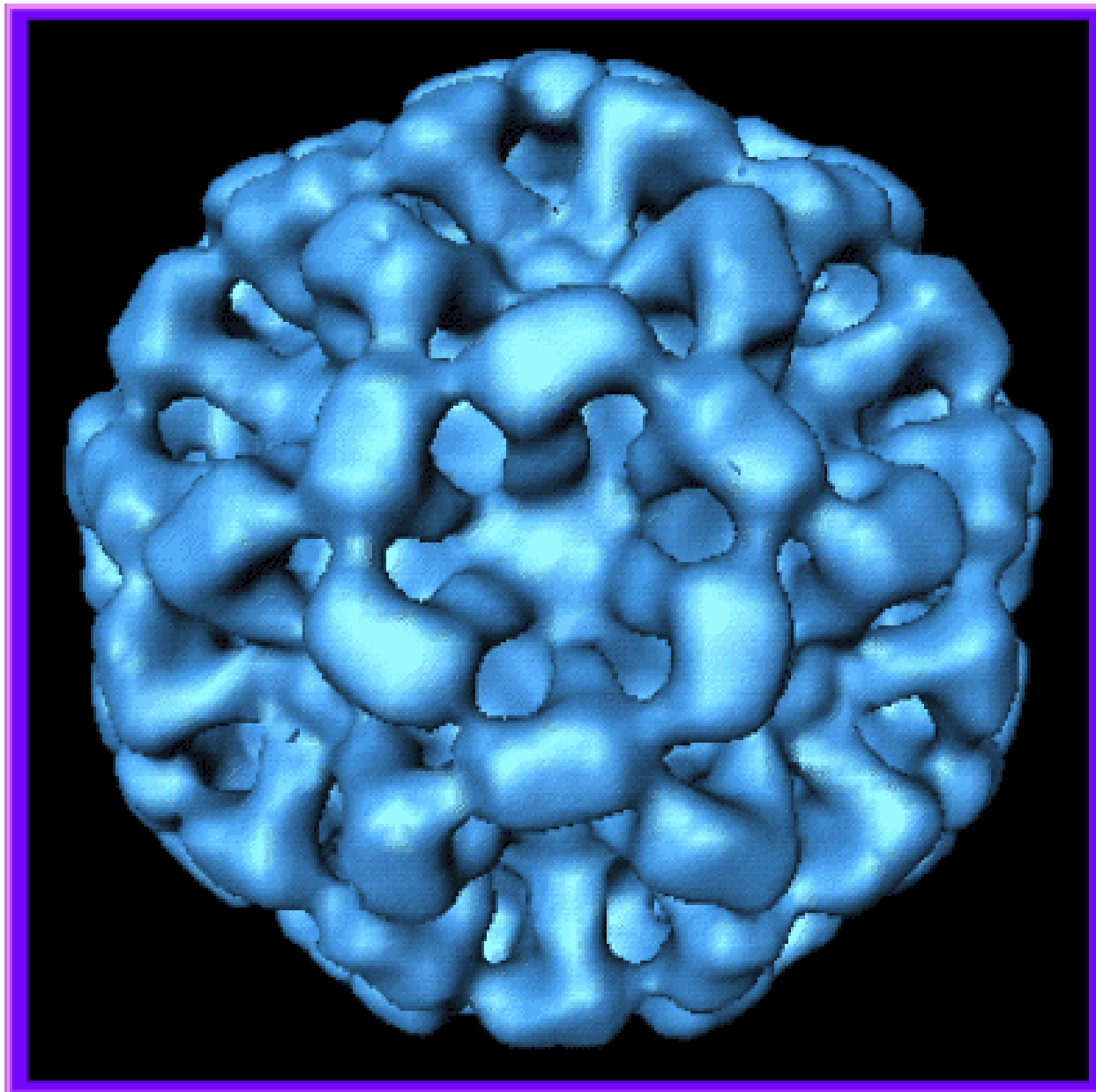
Hepatitis B

Hepadnavirus, DNA ds/ss, enveloped

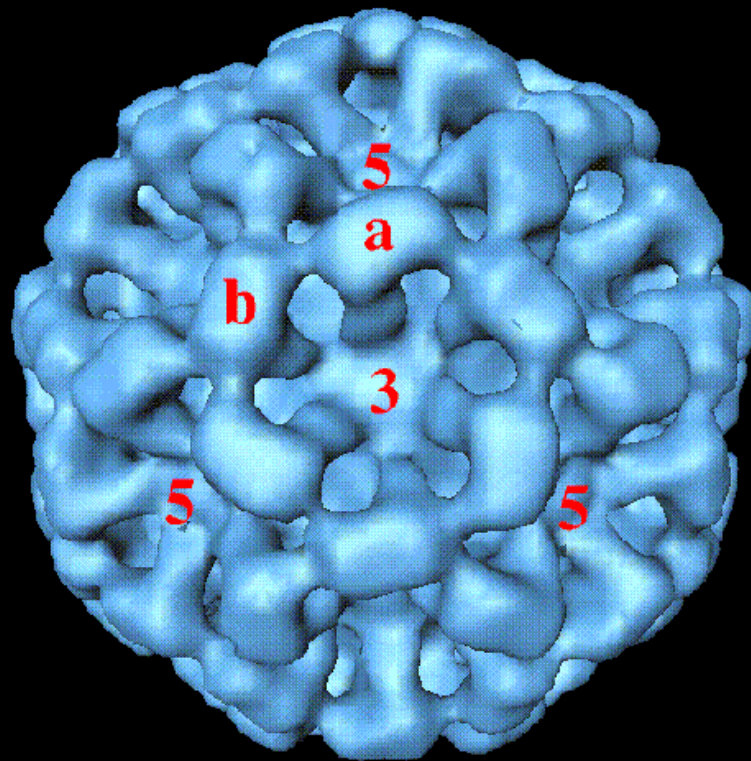


New flus. The influenza viruses now found in North American pigs have genes from both human and bird viruses.

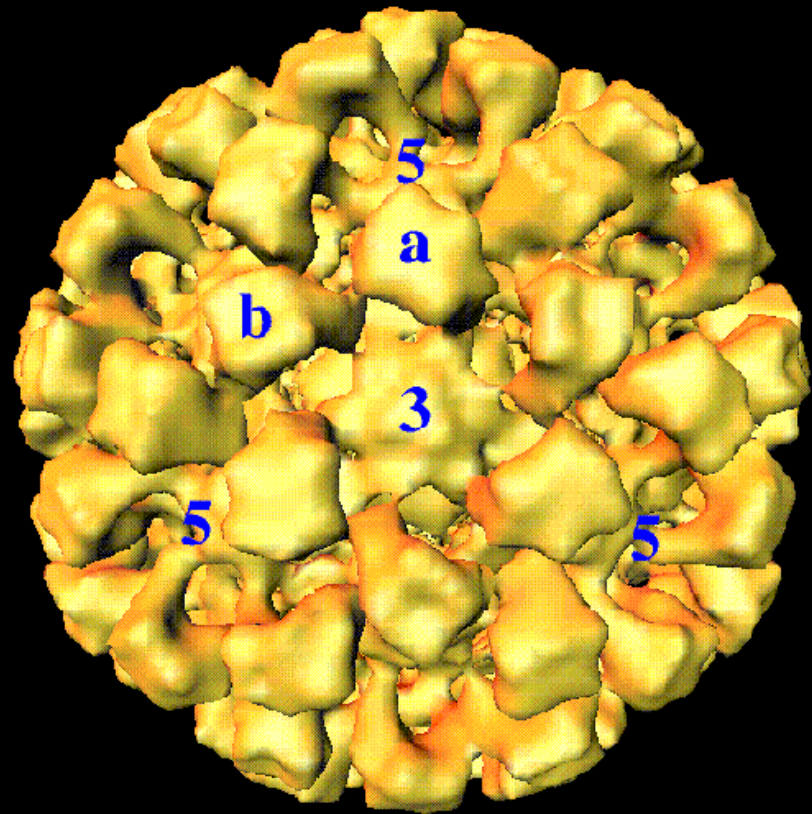
Uusi sikaflunssa USA:ssa: Science 7 March 2003



Kalikiviruksen kaunis kuori

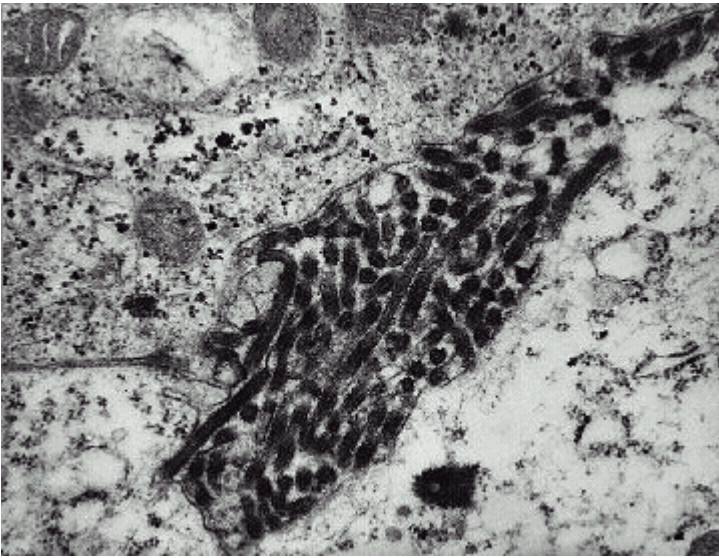


rNV Capsid

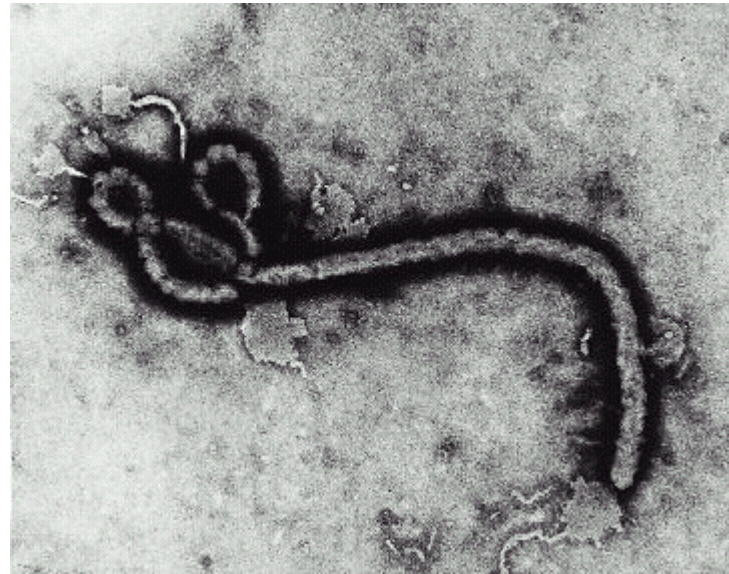


Primate Calicivirus

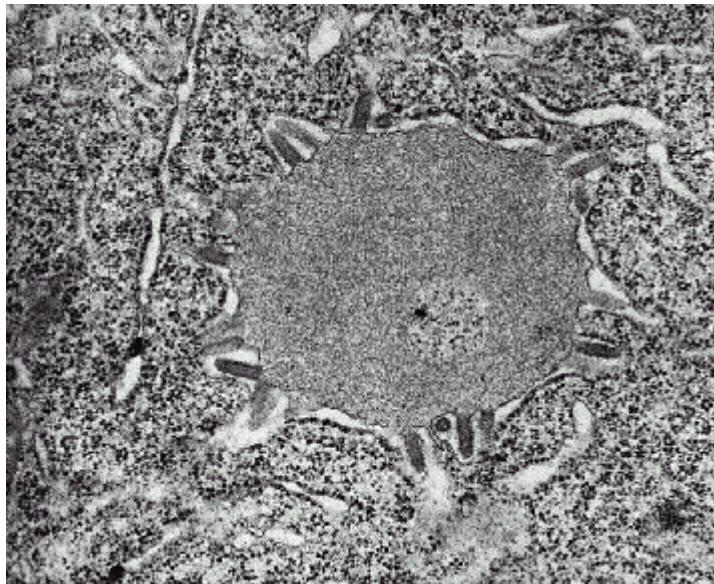
Three-dimensional structures of recombinant Norwalk capsid (rNV capsid) and primate calicivirus determined to 22 Å resolution using electron cryomicroscopy and computer image processing techniques.



Marburg-filovirus



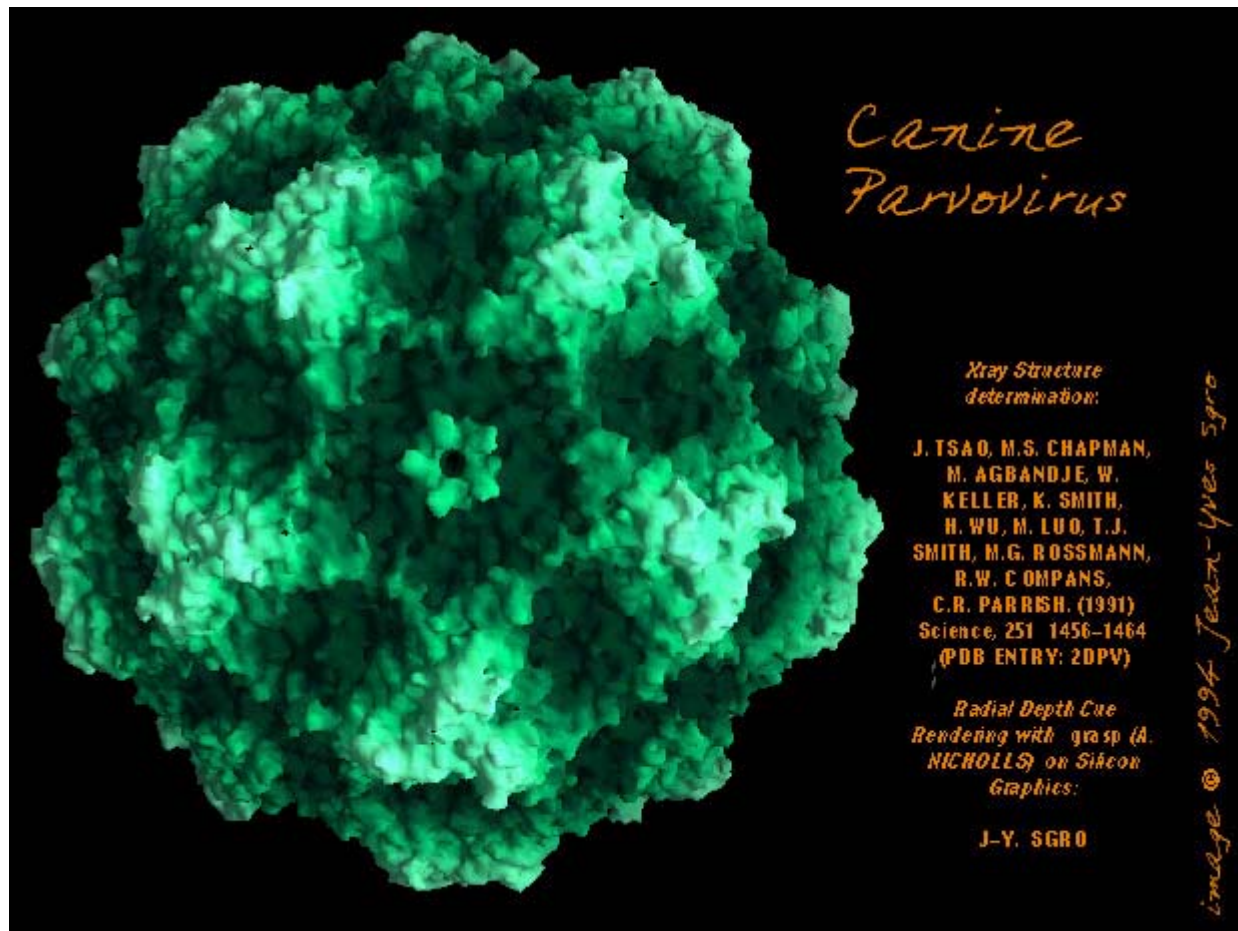
Ebola-filovirus



Rabies

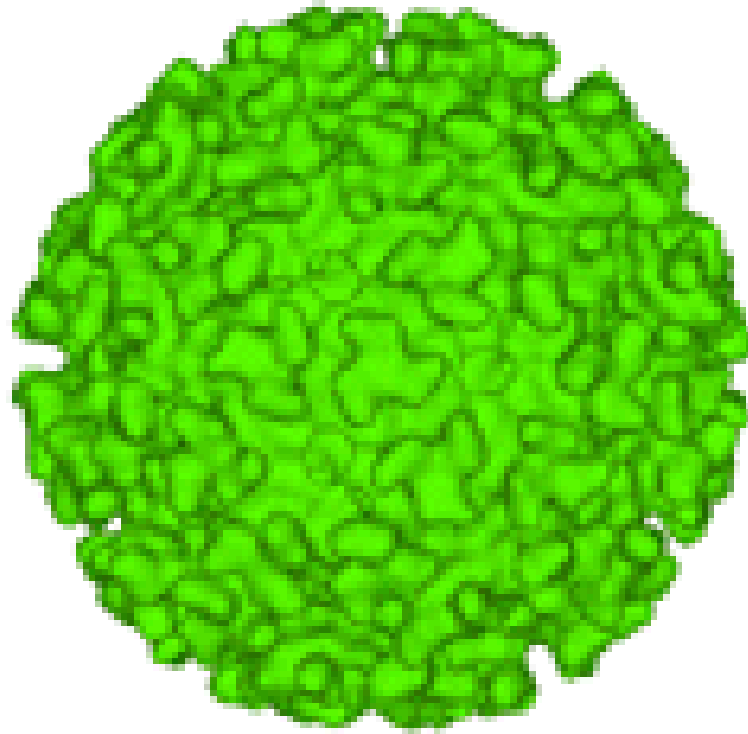
Ebola Zaire





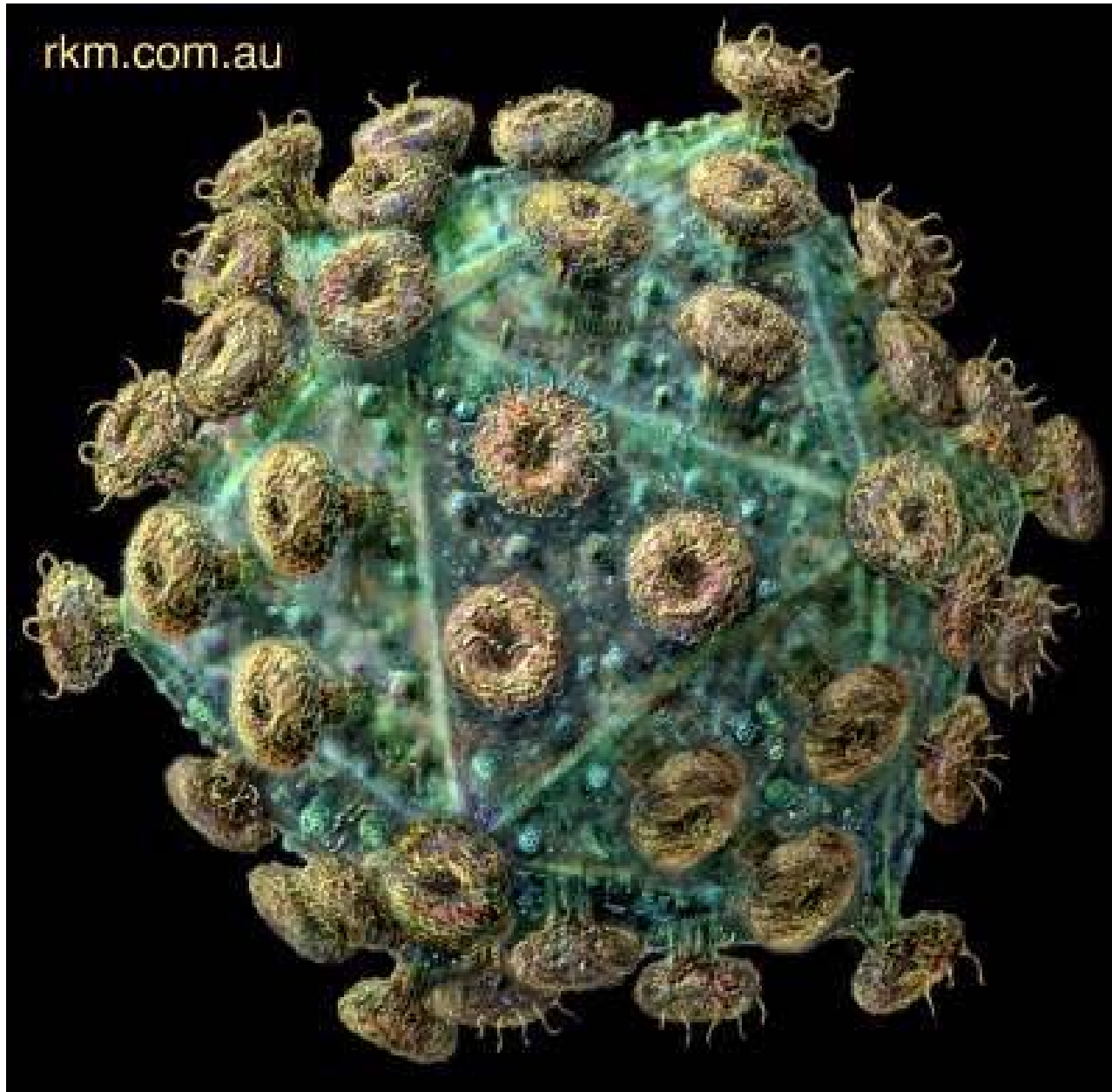
Koirain parvovirus

DNA single stranded, non-enveloped

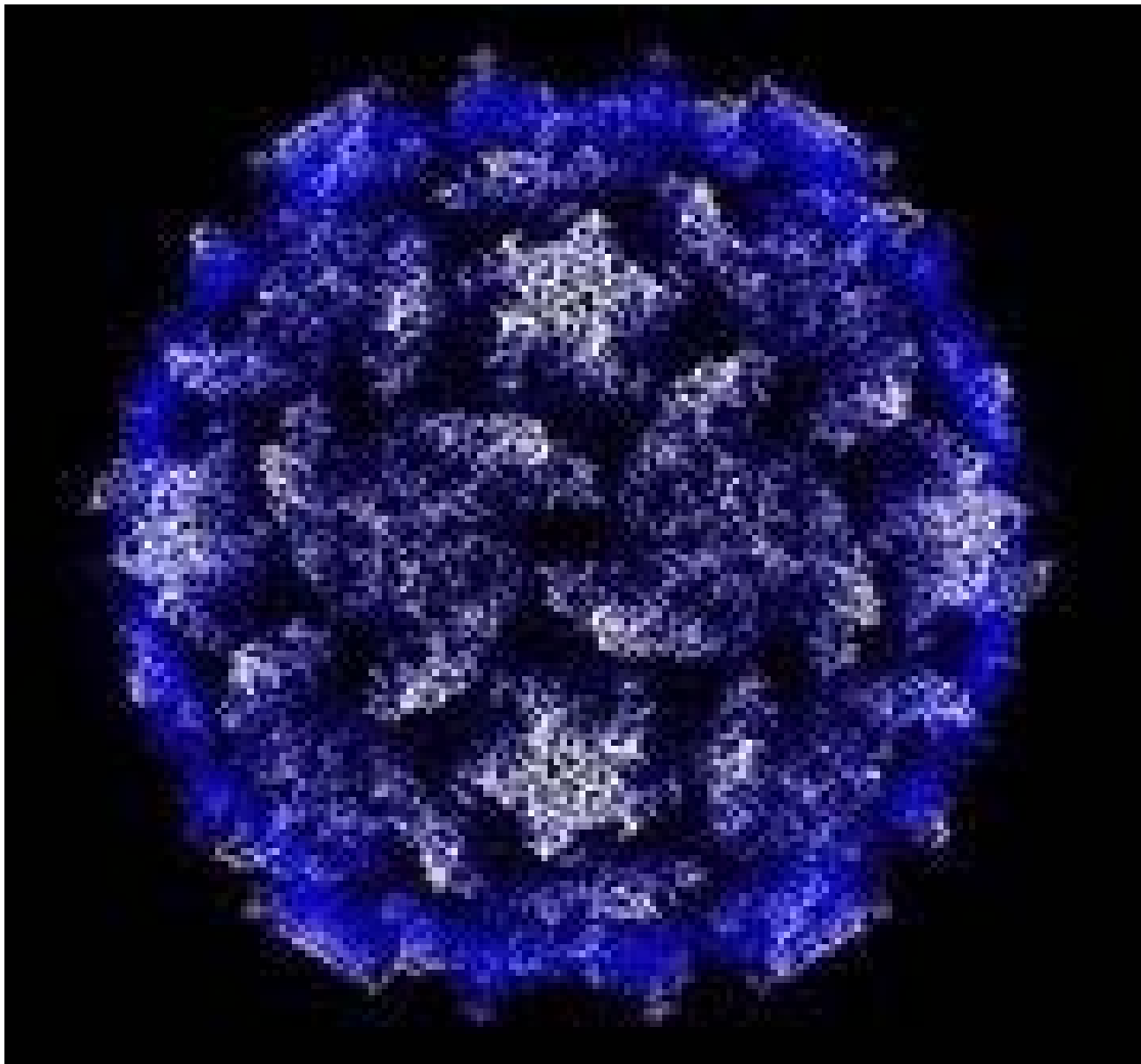


Semliki Forest virus
RNA, envelope

rkm.com.au



HIV



Ihmisen poliovirus Picornavirukset



The Big Picture Book of Viruses

BROUGHT TO YOU BY THE GARRY LAB

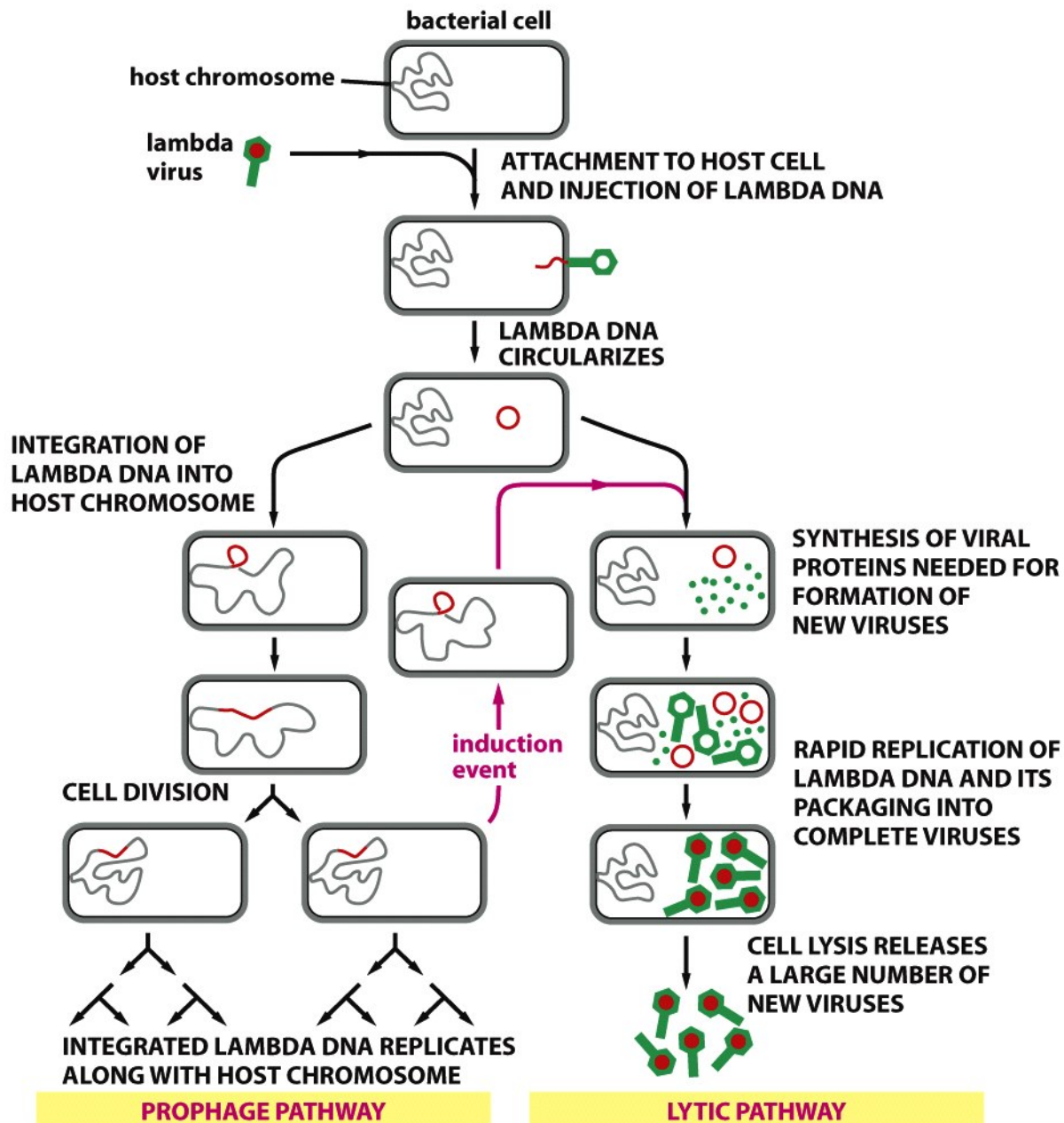
Genome & Physical Characteristics

Virus Family

Type	Nucleic Acid Description	Envelope	Name
DNA	ds	enveloped	Baculoviridae
			Herpesviridae
			Iridoviridae
			Poxviridae
			"African Swine Fever Viruses" (unnamed family)
	ss	nonenveloped	Adenoviridae
			Caulimoviridae
			Myoviridae
			Phycodnaviridae
			Tectiviridae
			Papovaviridae
			Circoviridae
			Parvoviridae
	ds/ss	enveloped	Hepadnaviridae

CLICK

SISÄÄN?

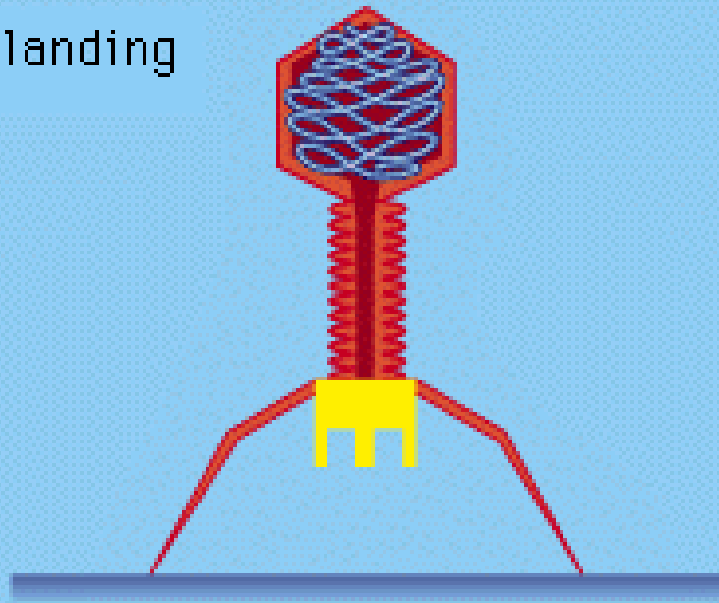


Bakteriofaagit ovat viruksia (luokitteluasia), mutta varsin monimutkaisia

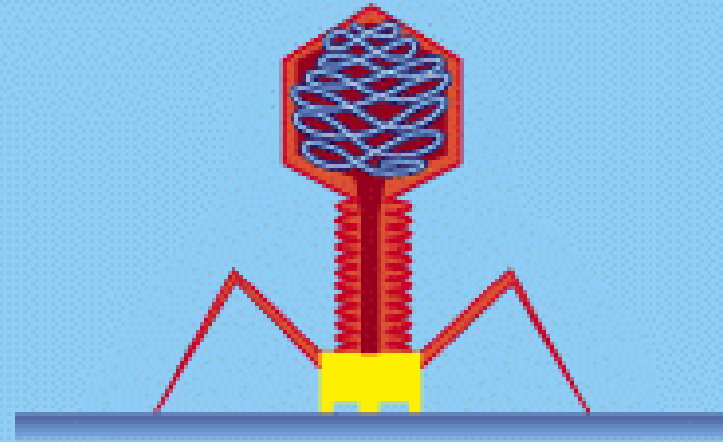
Niiden perimä on DNA-muodossa

Faagi lambda osaa elää kahdella tavalla, lyyttisesti ja lysogeenisesti profagina

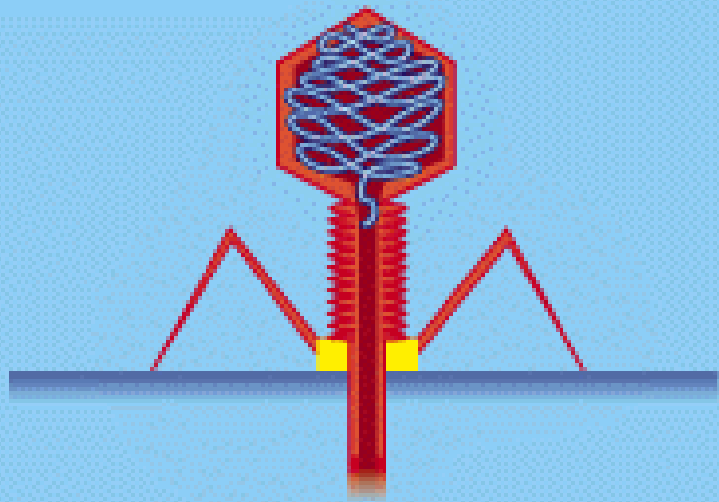
landing



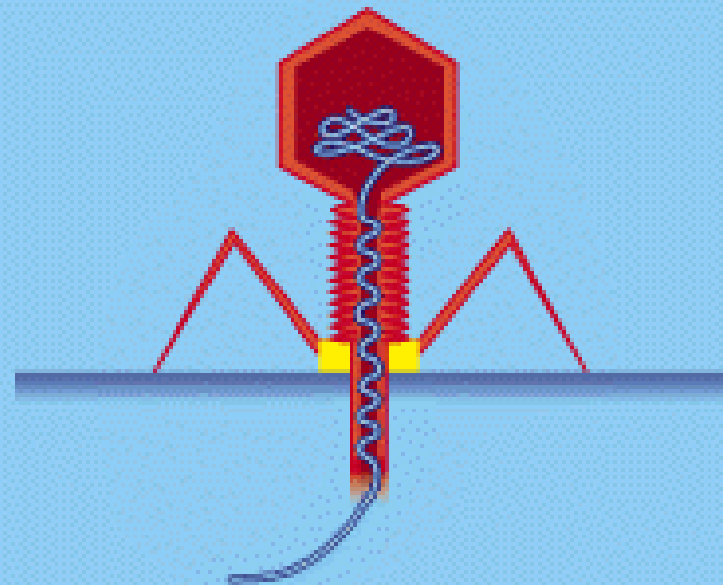
pinning



tail contraction
and penetration



DNA injection



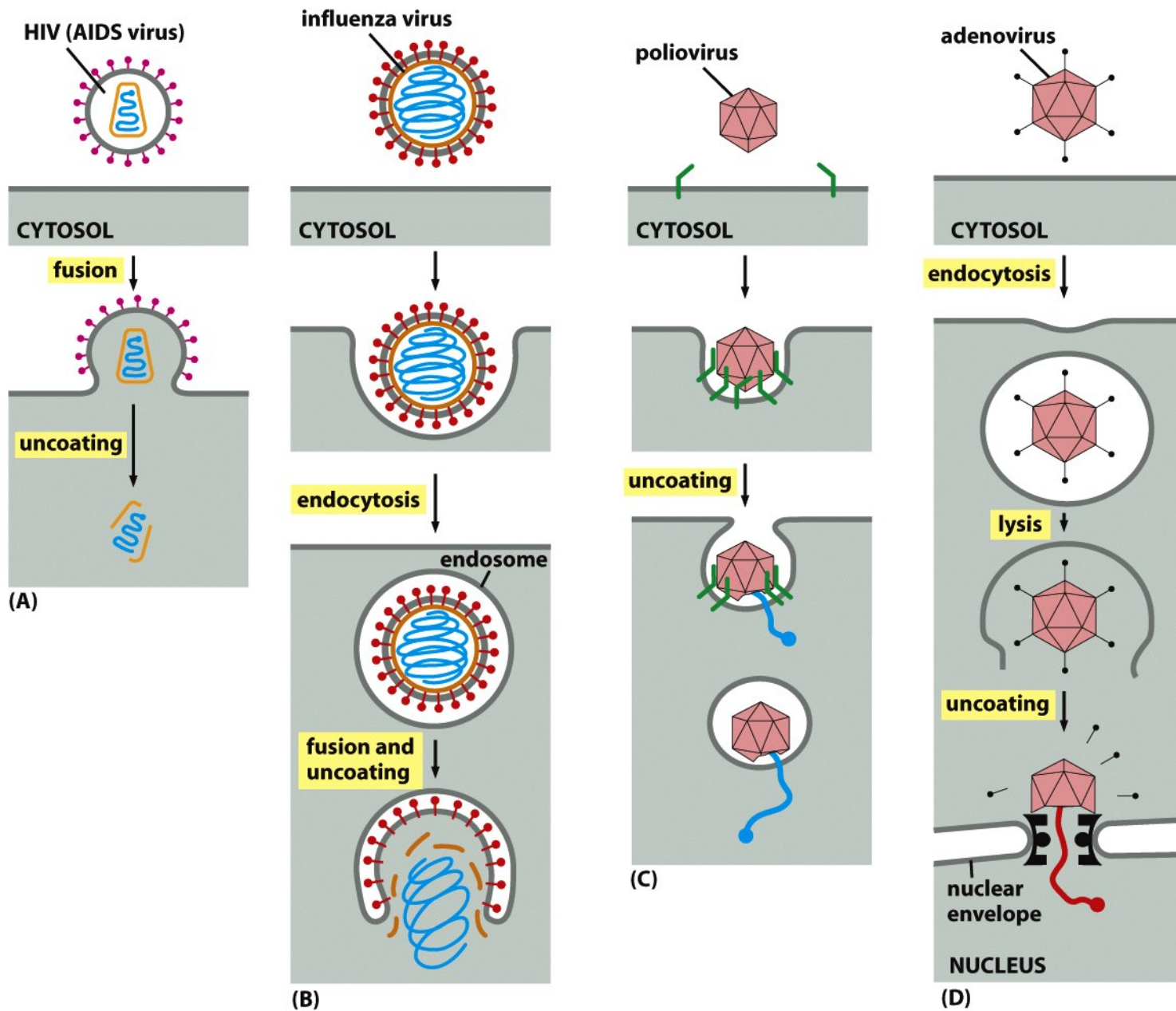
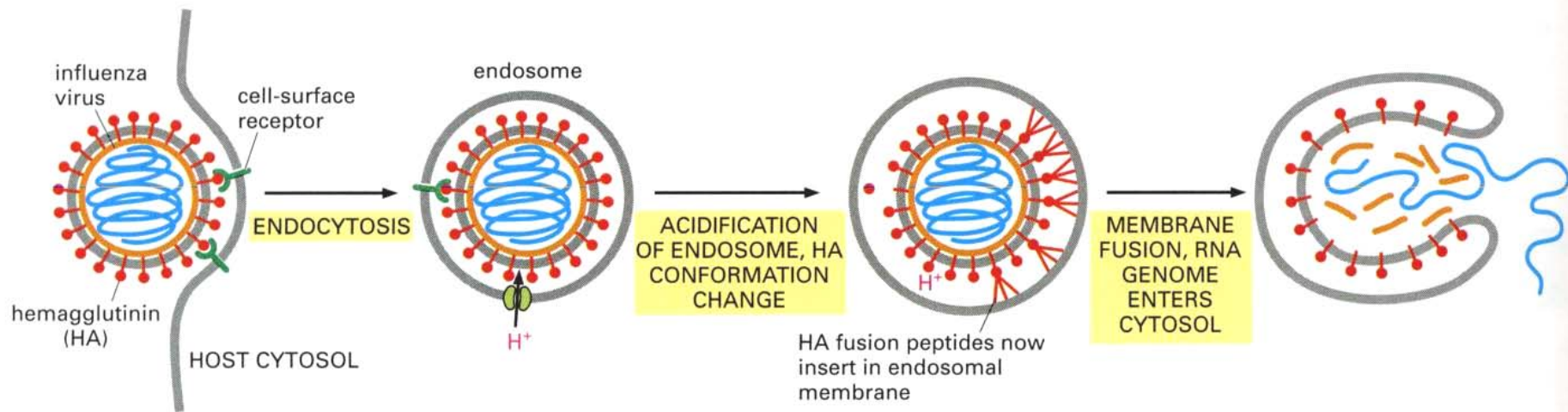


Figure 24-24 Molecular Biology of the Cell 5/e (© Garland Science 2008)



Influenssaviruksen sisäänmeno

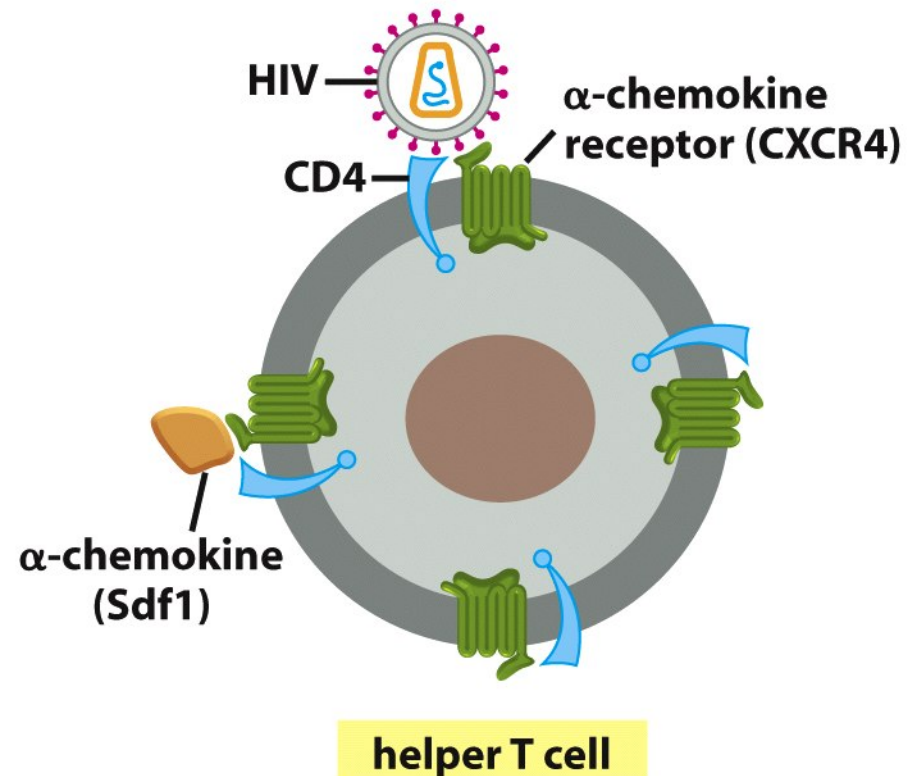
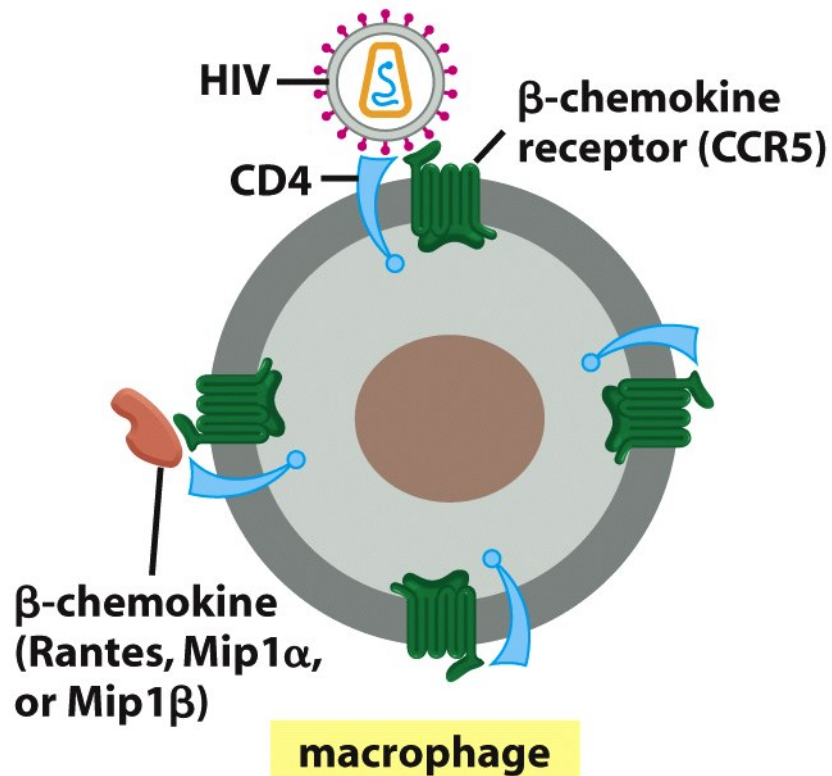
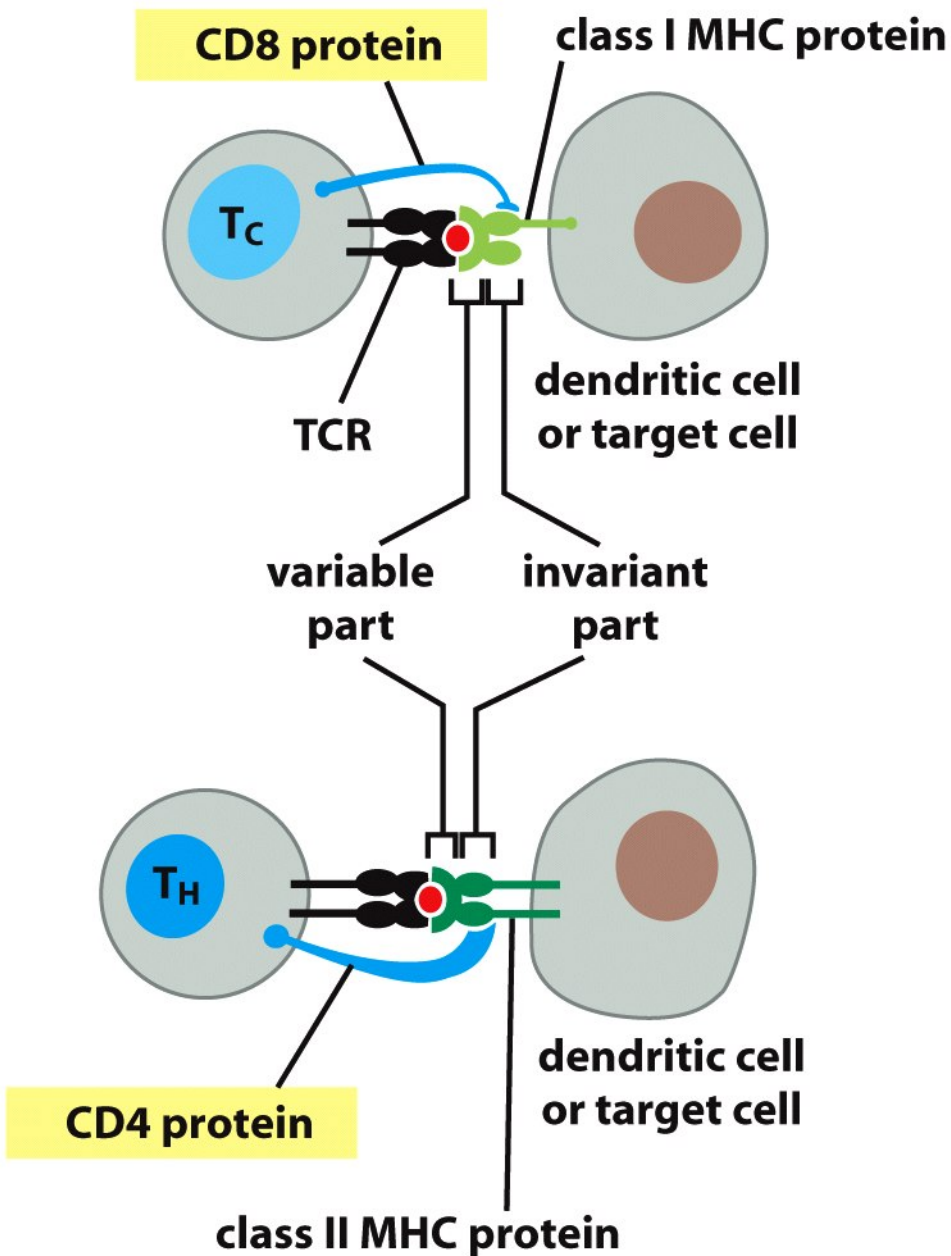


Figure 24-23 Molecular Biology of the Cell 5/e (© Garland Science 2008)

HIVin sisäänmeno immuunijärjestelmän soluihin



MHC-proteiini esittelee juuri löytämänsä polypeptidiä T-soluille

T-helper solu tunnistaa tilanteen **CD4**-proteiininsa avulla

Ikävä kyllä, HIV tunnistaa T-helper –solun **CD4**-proteiinin takia ja käyttää sitä sisäänpääsyyn!

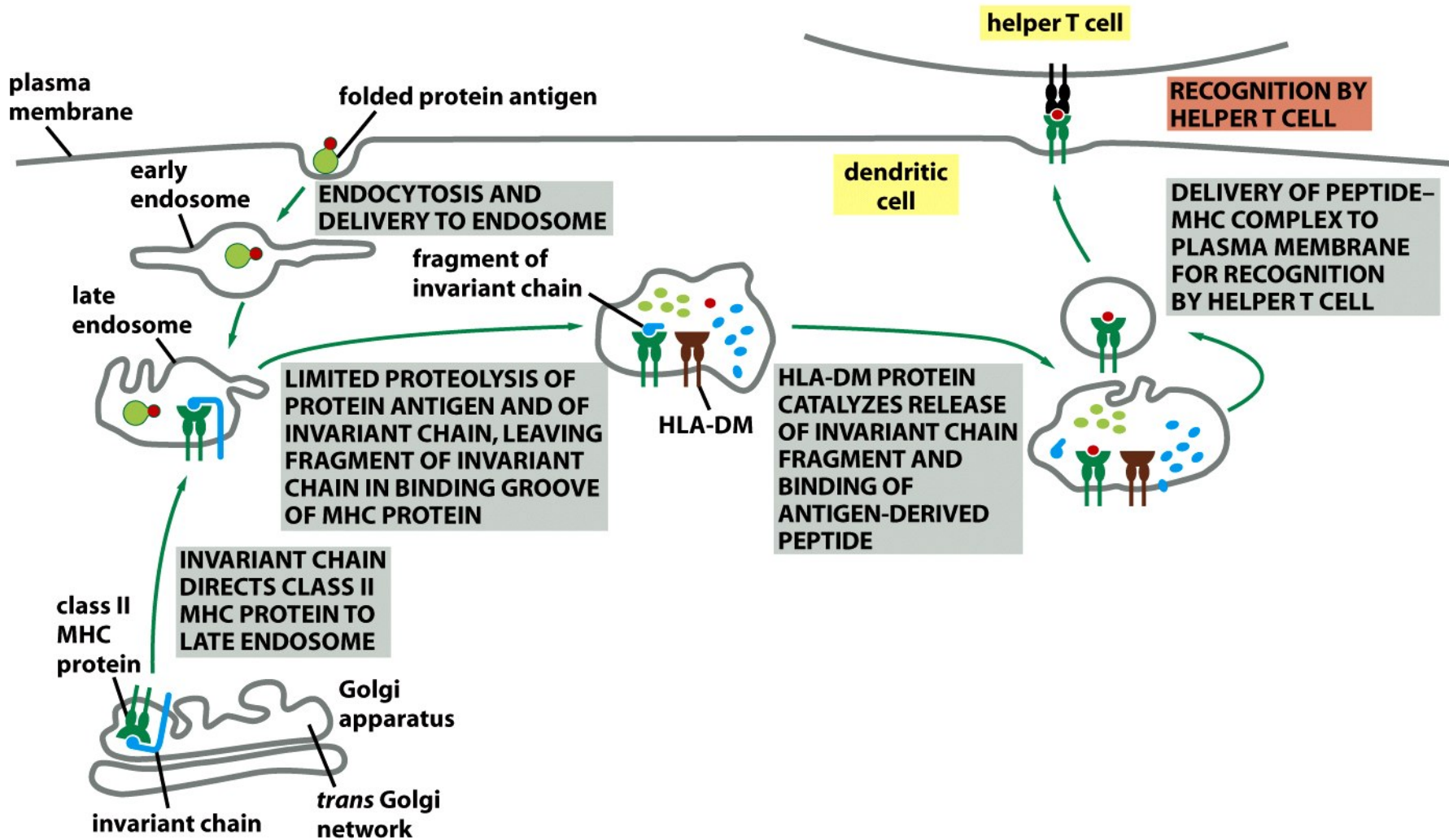
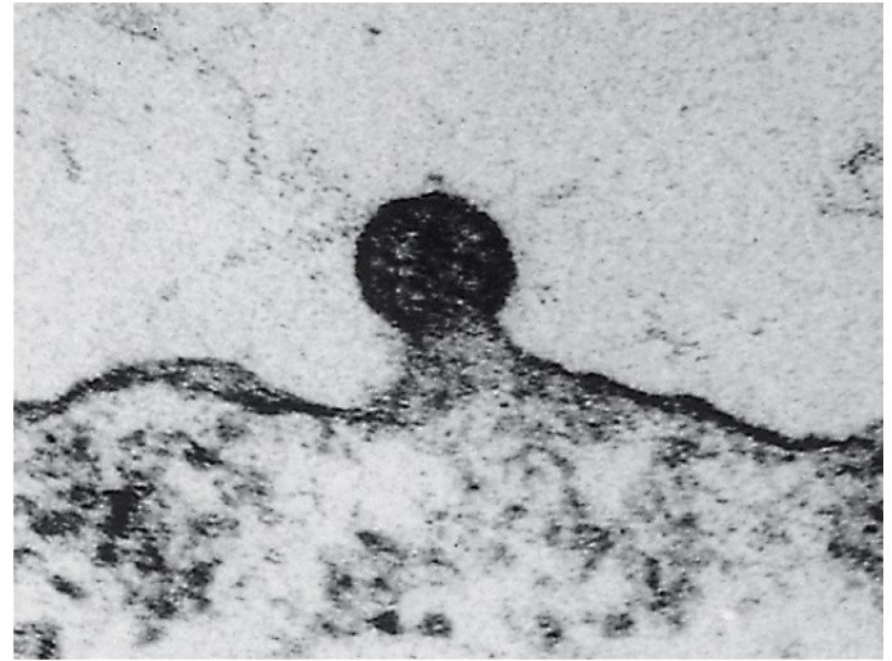
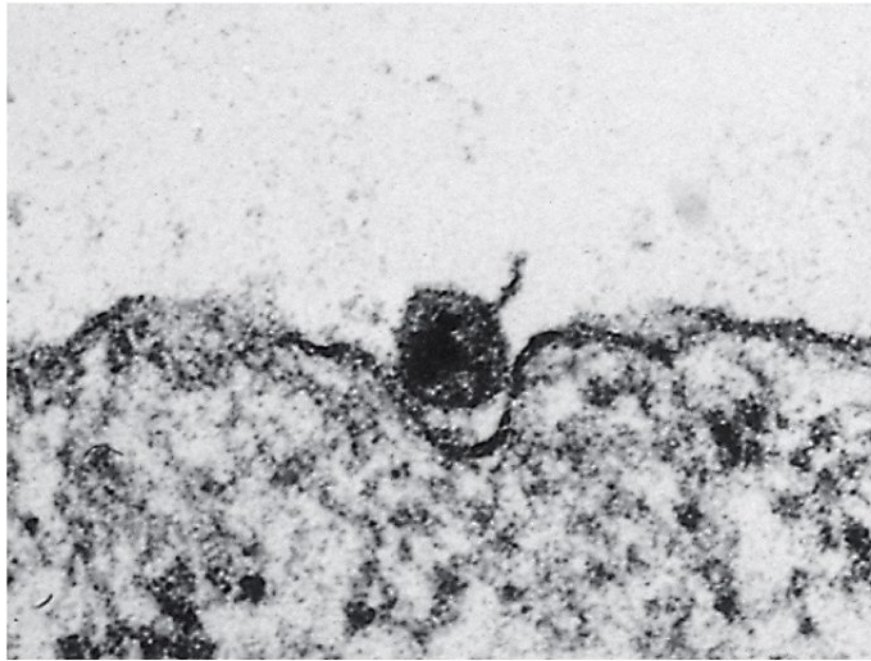


Figure 25-61 Molecular Biology of the Cell 5/e (© Garland Science 2008)



200 nm

Figure 13-19a Molecular Biology of the Cell 5/e (© Garland Science 2008)

HIV menossa soluun fuusioimalla membraaninsa solun kalvoon

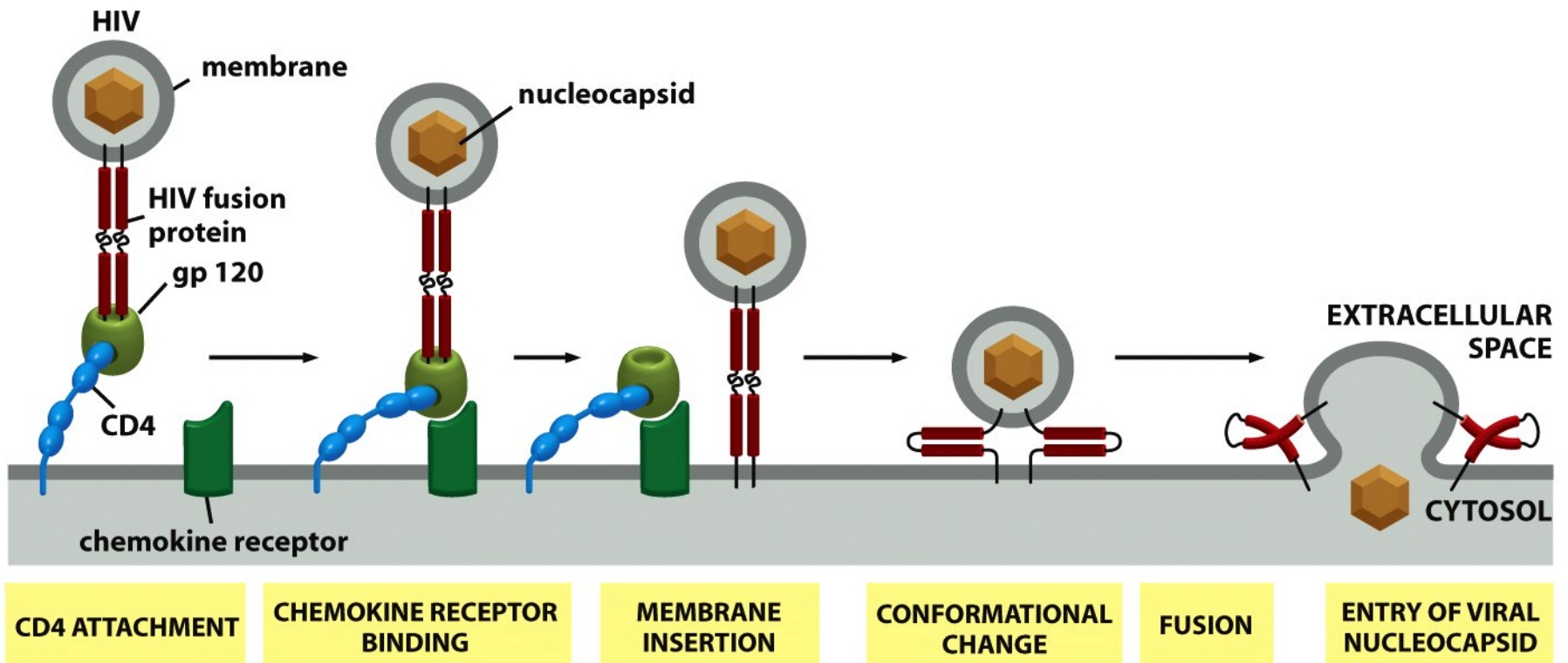


Figure 13-19b Molecular Biology of the Cell 5/e (© Garland Science 2008)

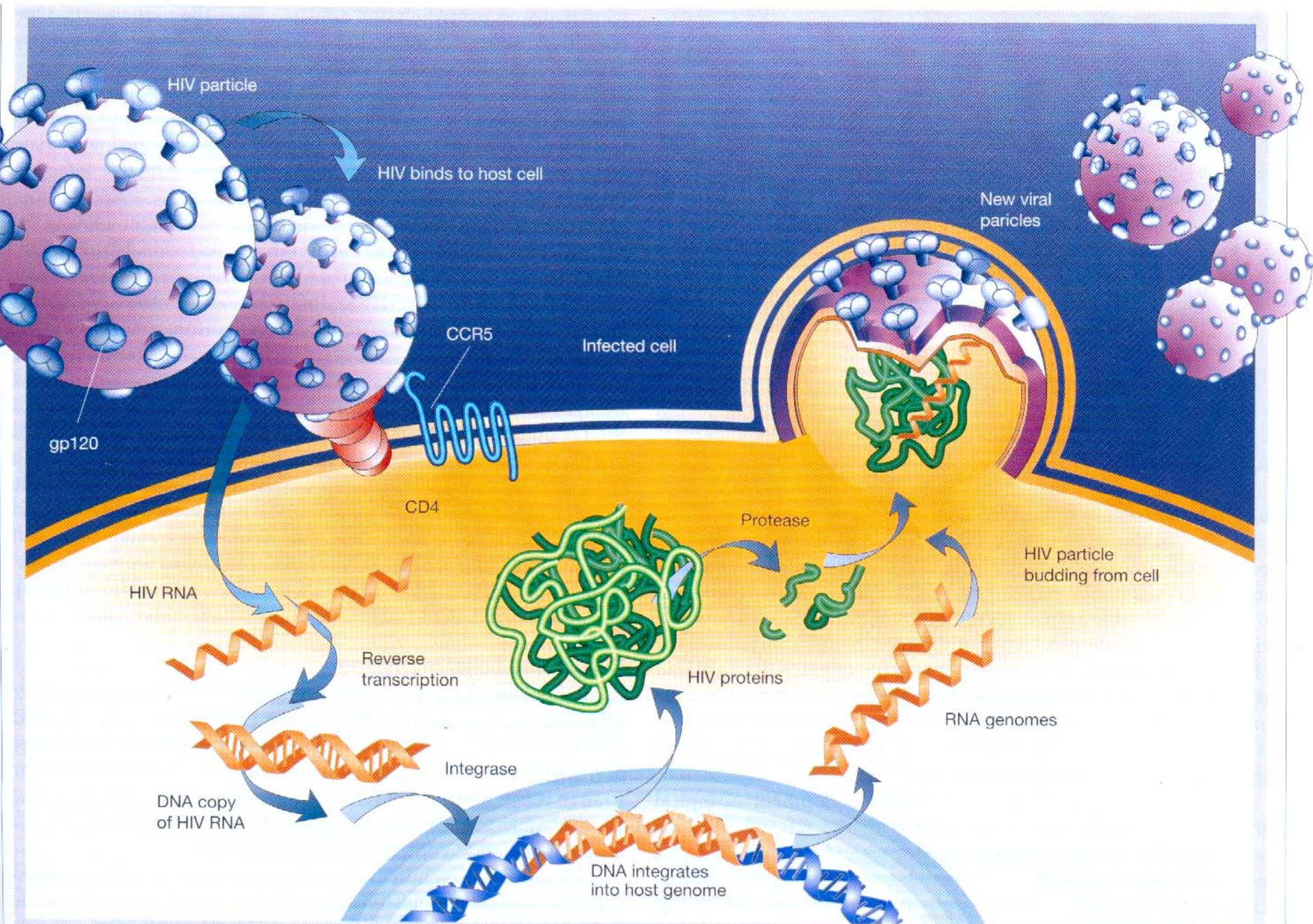


Figure 1 The human immunodeficiency virus. Replication cycle of HIV showing multiple steps available for attack by antiretroviral drugs.



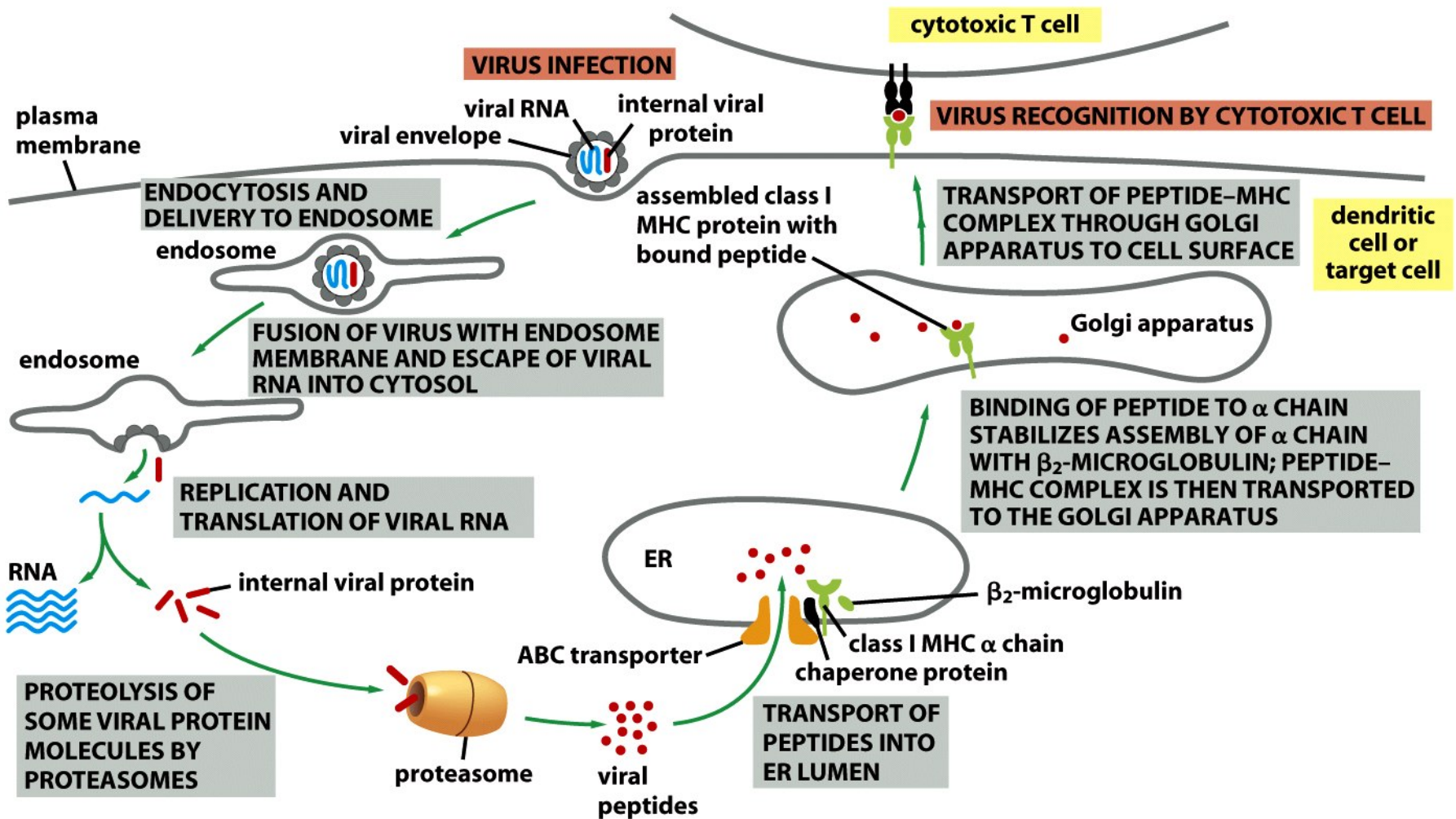


Figure 25-59 Molecular Biology of the Cell 5/e (© Garland Science 2008)

MHC: kuinka virus yms. havaitaan solussa ja kavalletaan sytotoksiselle T-solulle

Monistuminen

Rekombinaatio

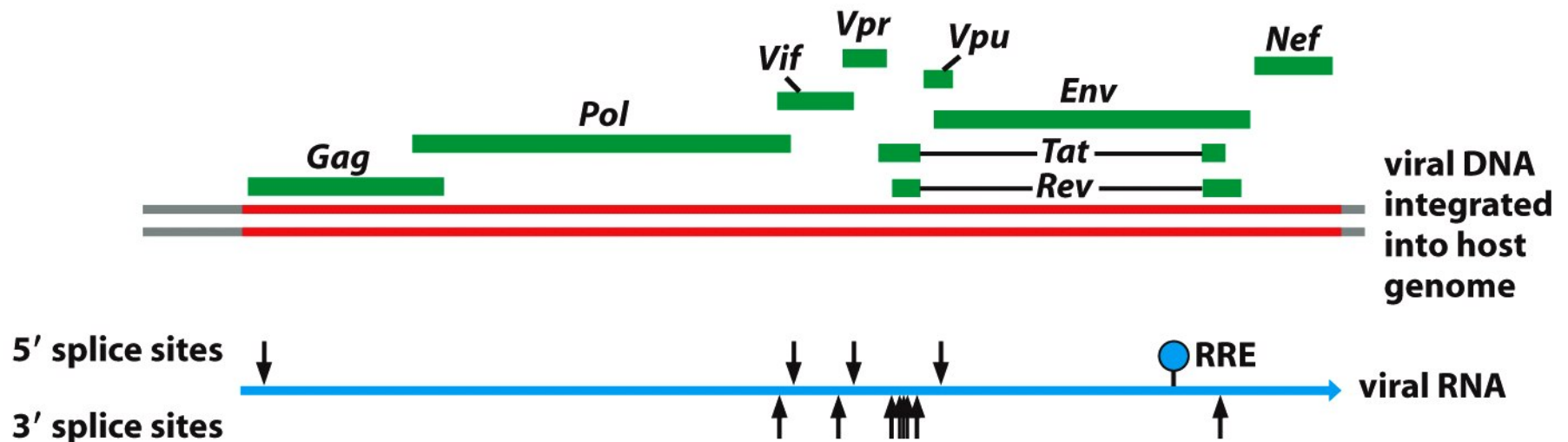


Figure 7-102 Molecular Biology of the Cell 5/e (© Garland Science 2008)

HIVin geenikartta

Gag, *Pol* ja *Env* ovat retrovirusten vakiogeenit

Gag proteiini pilkotaan kapsidiksi

Pol on käänteistranskriptaasi

Env = envelope

HIV-genomi: mRNA:n editointia

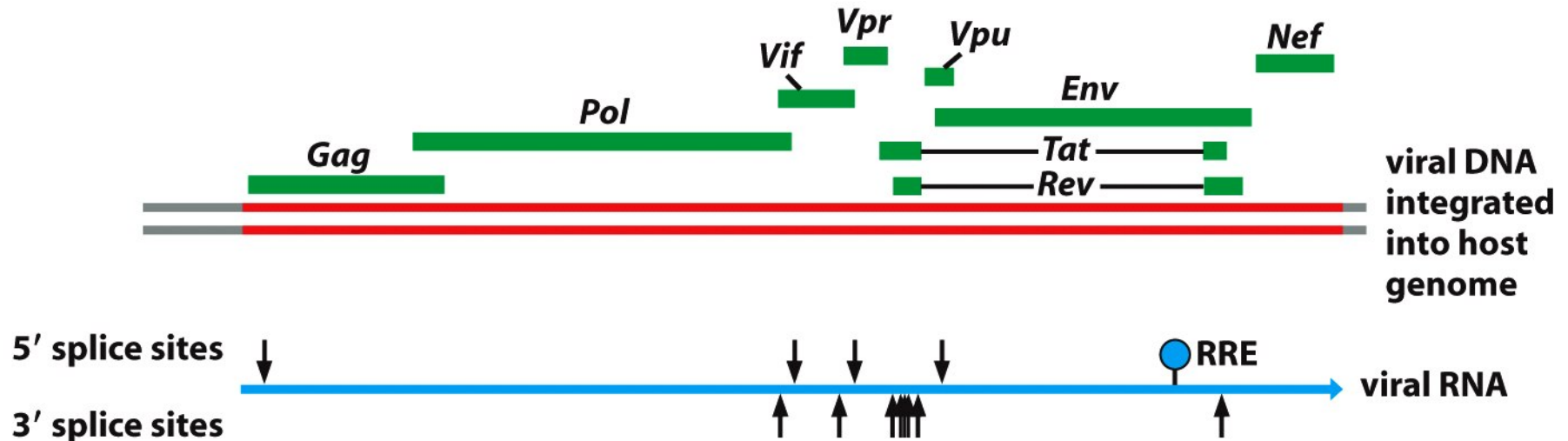
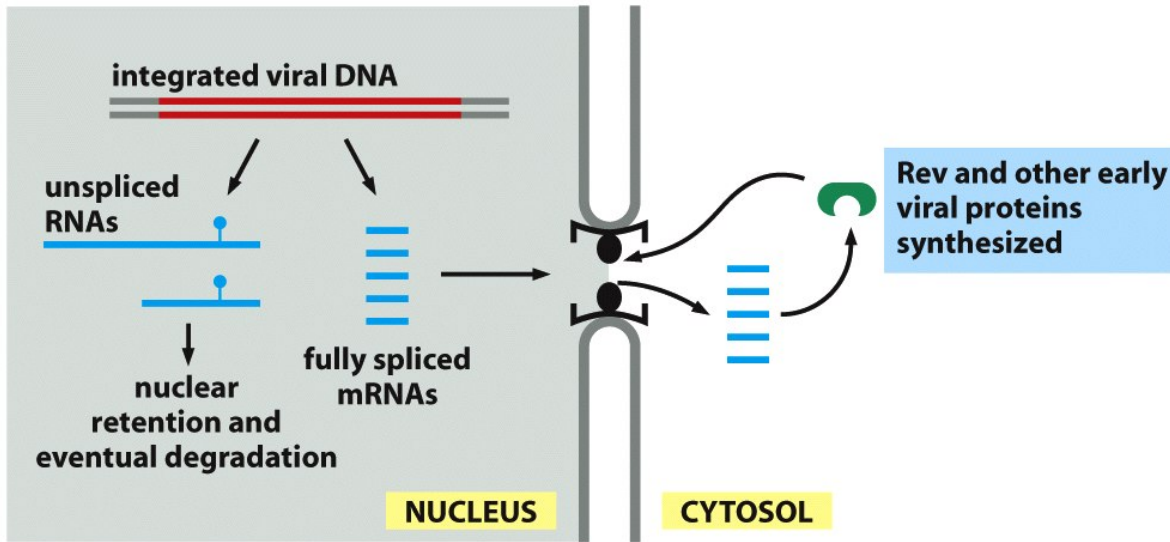


Figure 7-102 Molecular Biology of the Cell 5/e (© Garland Science 2008)

RNA:n editointi ja vaihtoehtoisesta splicing. Geenit ovat osittain päällekkäisiäkin. Esimerkiksi pol-proteiini tuotetaan niin, että mRNA luiskahtaa ribosomilla taaksepäin kun gag-proteiini on valmis. RRE on rev-proteiinin "kahva" eli mRNA:n sekundaaristrukturissa oleva hiuspinni

(A) early HIV synthesis

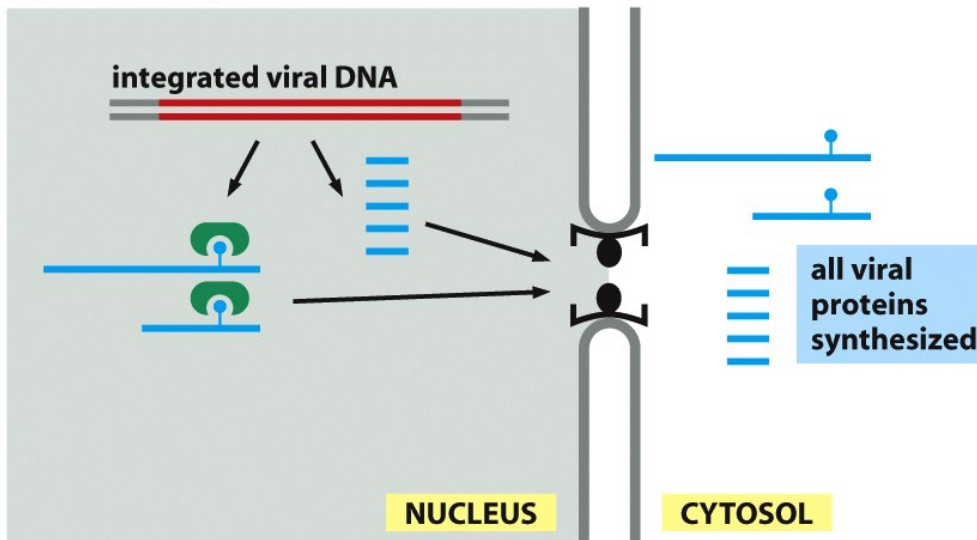


Virus säätelee toimintojensa ajoitusta.

Ensin toimivat *rev*, *tat* ja *nef*

Silputtamaton *env* ei pääse tumasta ulos

(B) late HIV synthesis



Rev-proteiini hoitaa huijauksen ja silputtamatonkin pääsee ulos tumasta

Virus pääsee latenssivaiheeseen piileskelemään?

Figure 7-103 Molecular Biology of the Cell 5/e (© Garland Science 2008)

early HIV synthesis

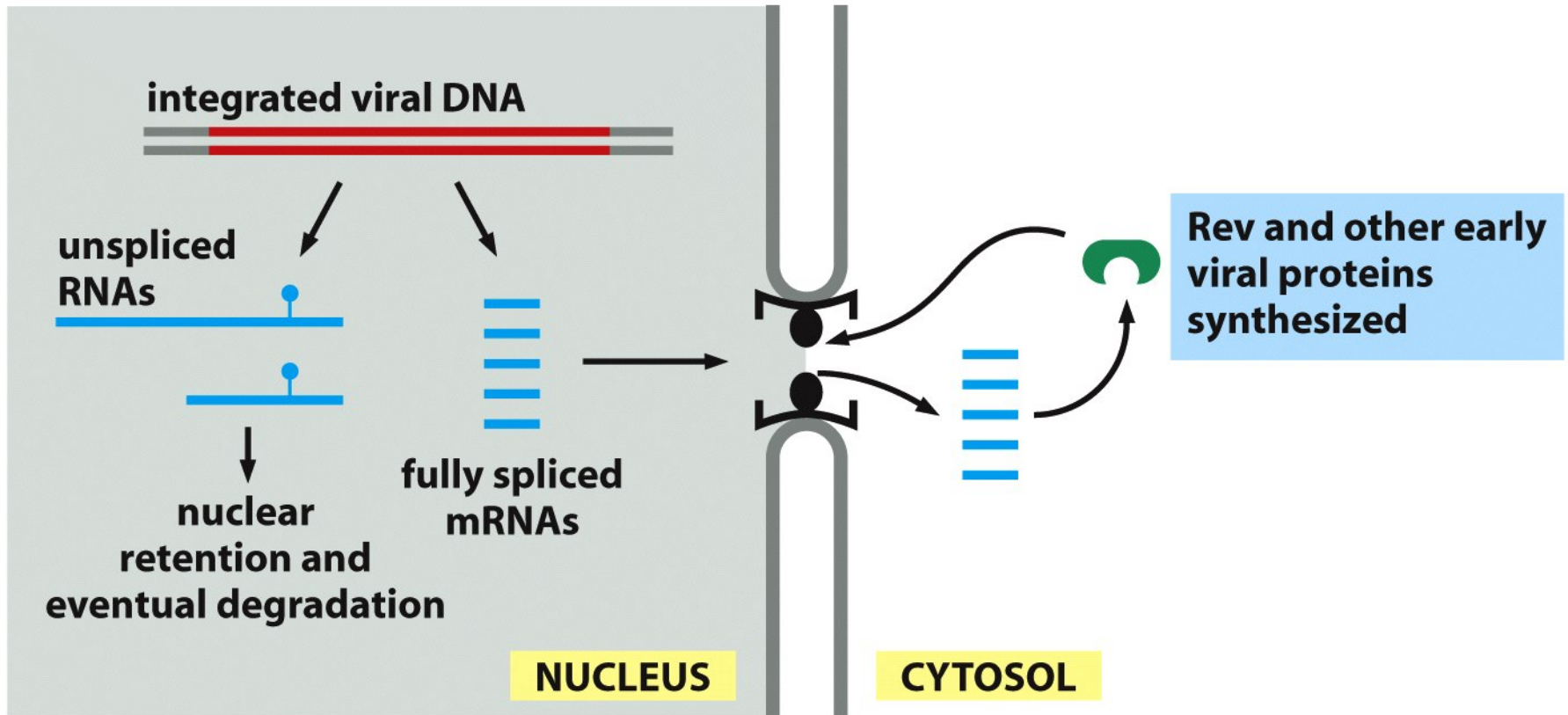


Figure 7-103a Molecular Biology of the Cell 5/e (© Garland Science 2008)

late HIV synthesis

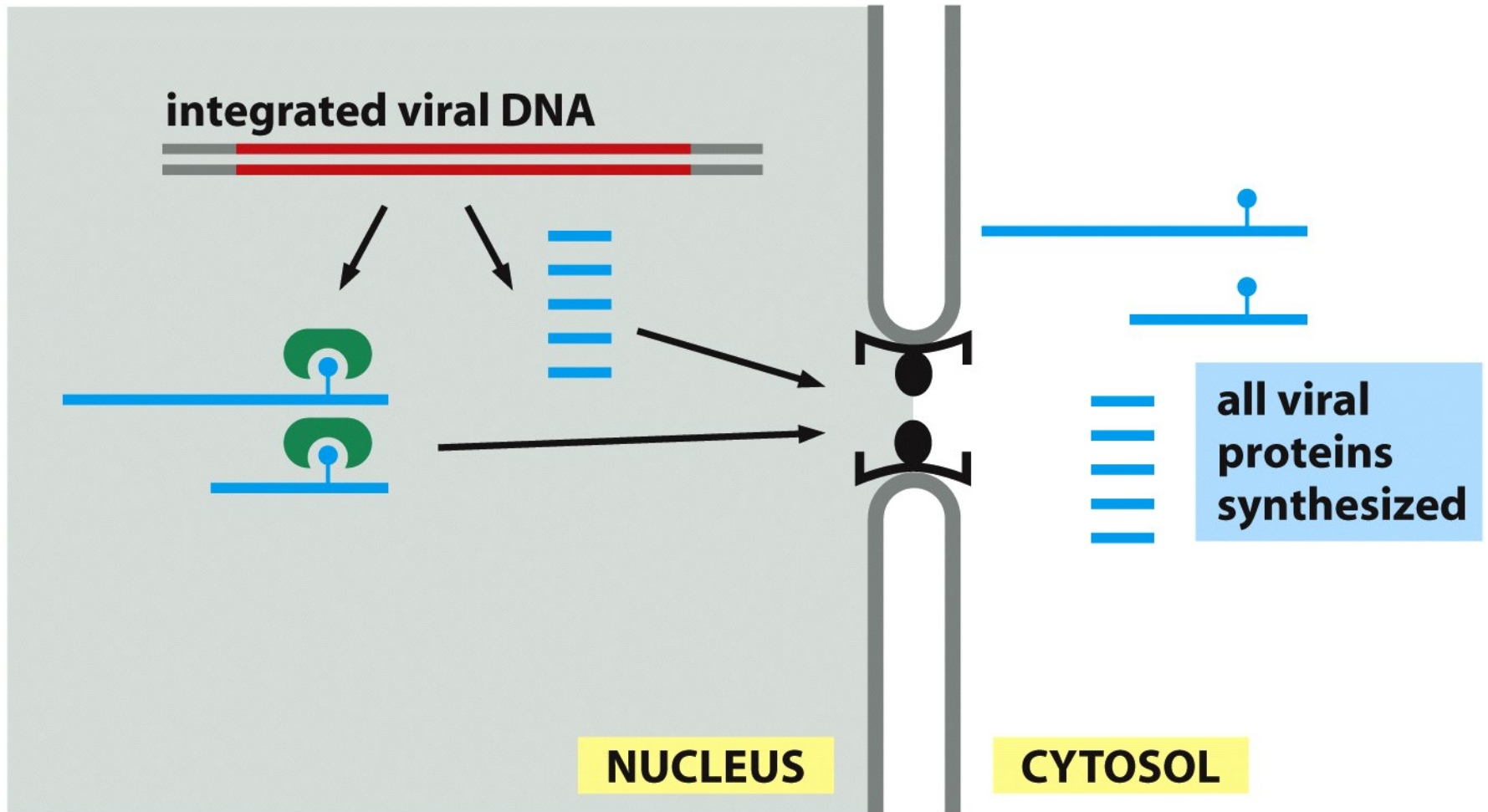


Figure 7-103b Molecular Biology of the Cell 5/e (© Garland Science 2008)

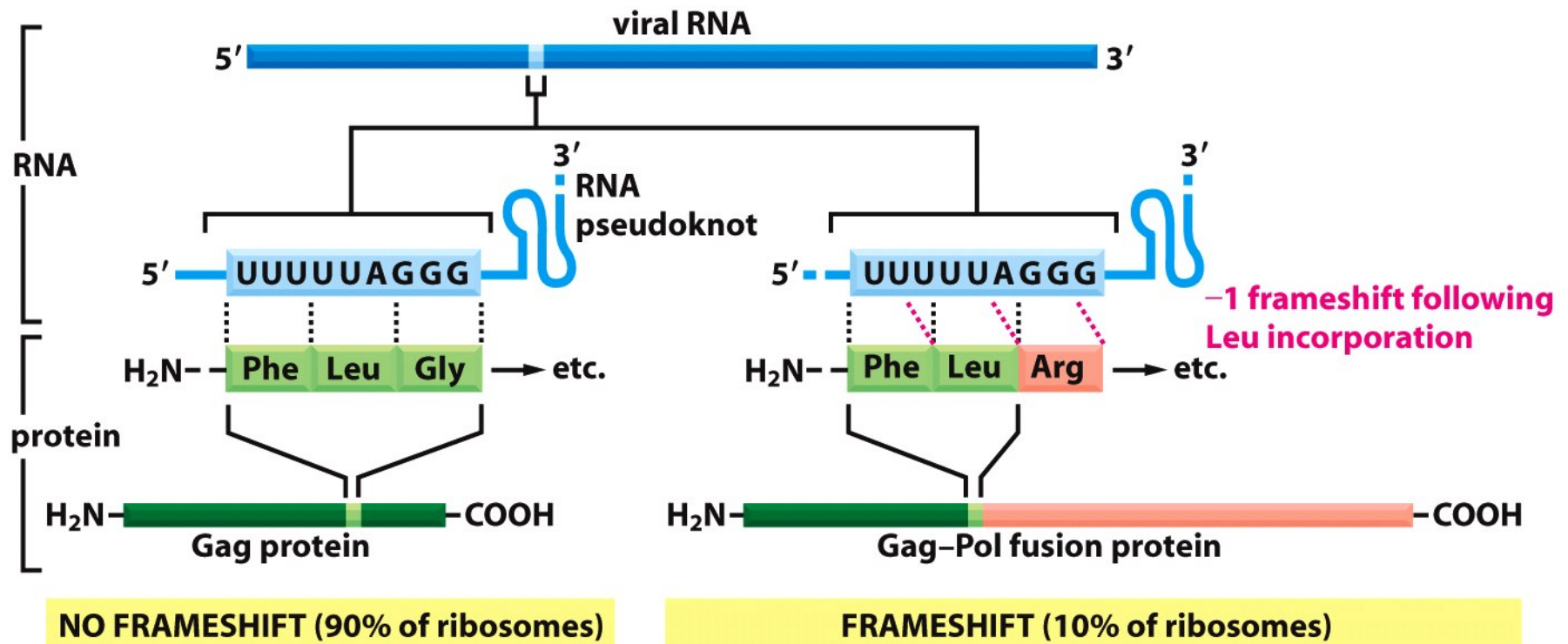
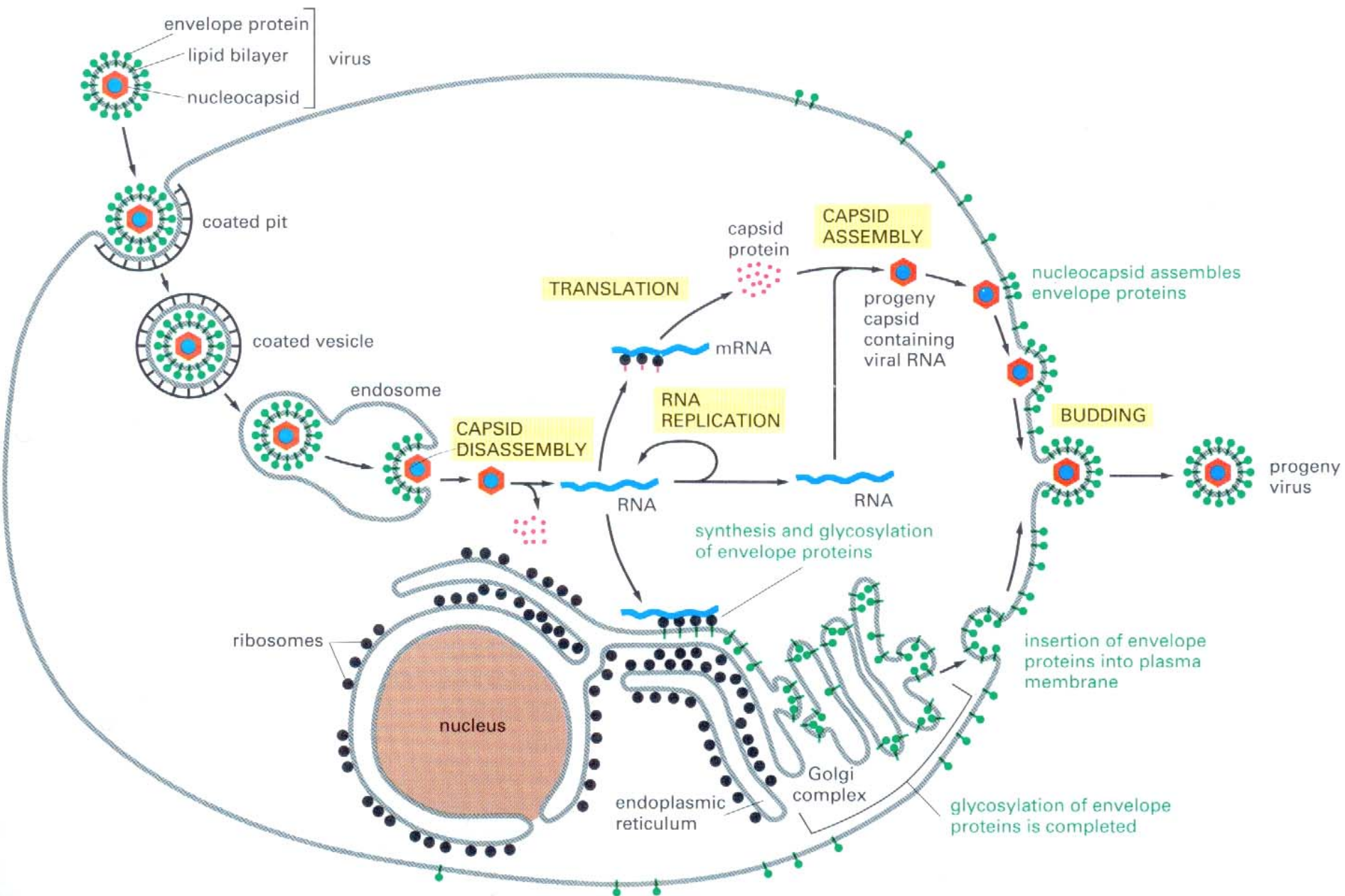


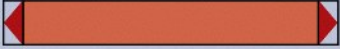
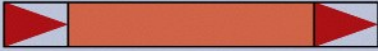
Figure 6-78 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Translational frameshifting



Semliki Forest -viruksen elinkierto

Table 5–3 Three Major Classes of Transposable Elements

CLASS DESCRIPTION AND STRUCTURE	SPECIALIZED ENZYMES REQUIRED FOR MOVEMENT	MODE OF MOVEMENT	EXAMPLES
DNA-only transposons			
 short inverted repeats at each end	transposase	moves as DNA, either by cut-and-paste or replicative pathways	P element (<i>Drosophila</i>) Ac-Ds (maize) Tn3 and Tn10 (<i>E. coli</i>) Tam3 (snapdragon)
Retroviral-like retrotransposons			
 directly repeated long terminal repeats (LTRs) at each end	reverse transcriptase and integrase	moves via an RNA intermediate produced by a promoter in the LTR	Copia (<i>Drosophila</i>) Ty1 (yeast) THE1 (human) Bs1 (maize)
Nonretroviral retrotransposons			
 Poly A at 3' end of RNA transcript; 5' end is often truncated	reverse transcriptase and endonuclease	moves via an RNA intermediate that is often produced from a neighboring promoter	F element (<i>Drosophila</i>) L1 (human) Cin4 (maize)

These elements range in length from 1000 to about 12,000 nucleotide pairs. Each family contains many members, only a few of which are listed here. In addition to transposable elements, some viruses can move in and out of host cell chromosomes by transpositional mechanisms. These viruses are related to the first two classes of transposons.

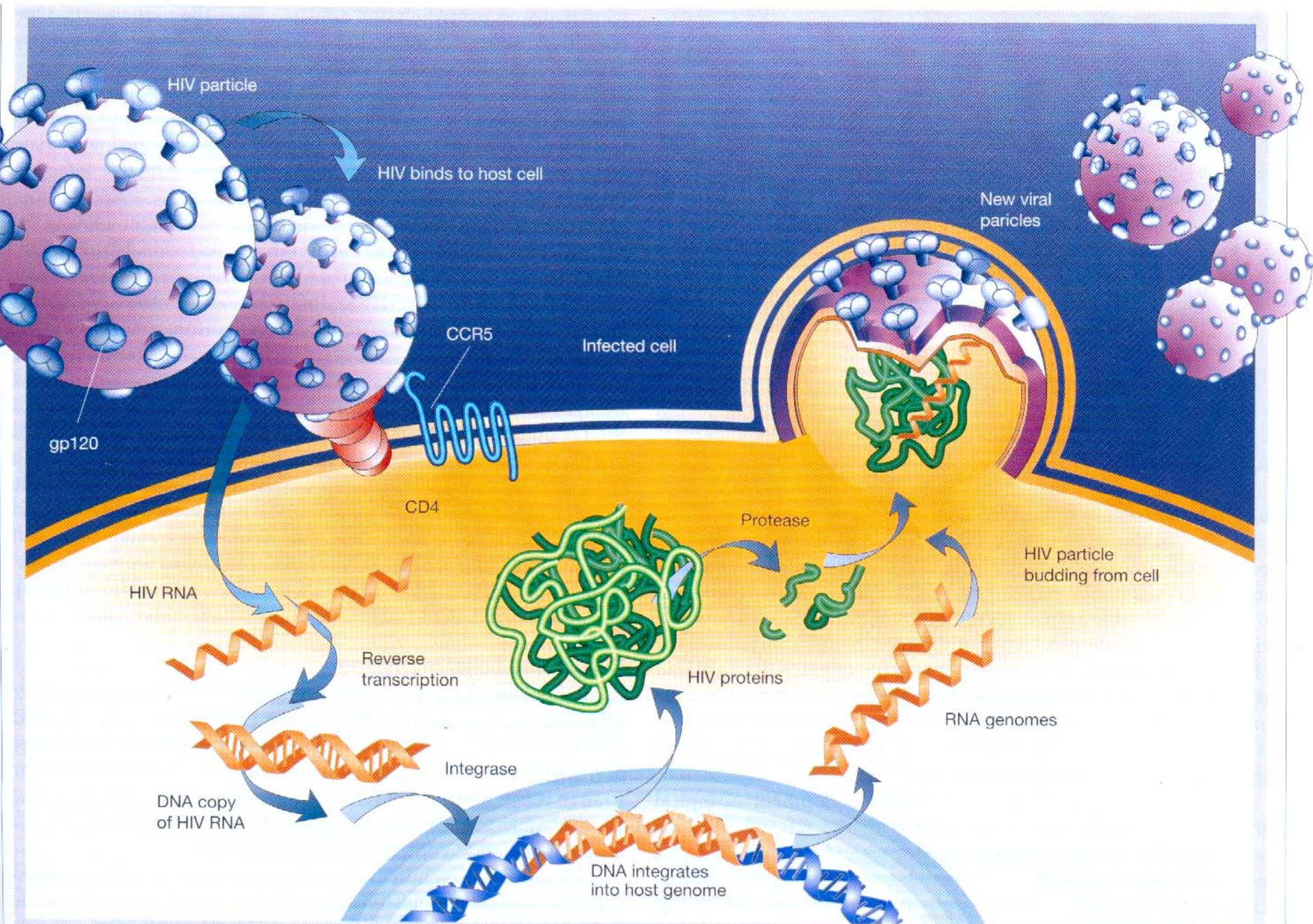
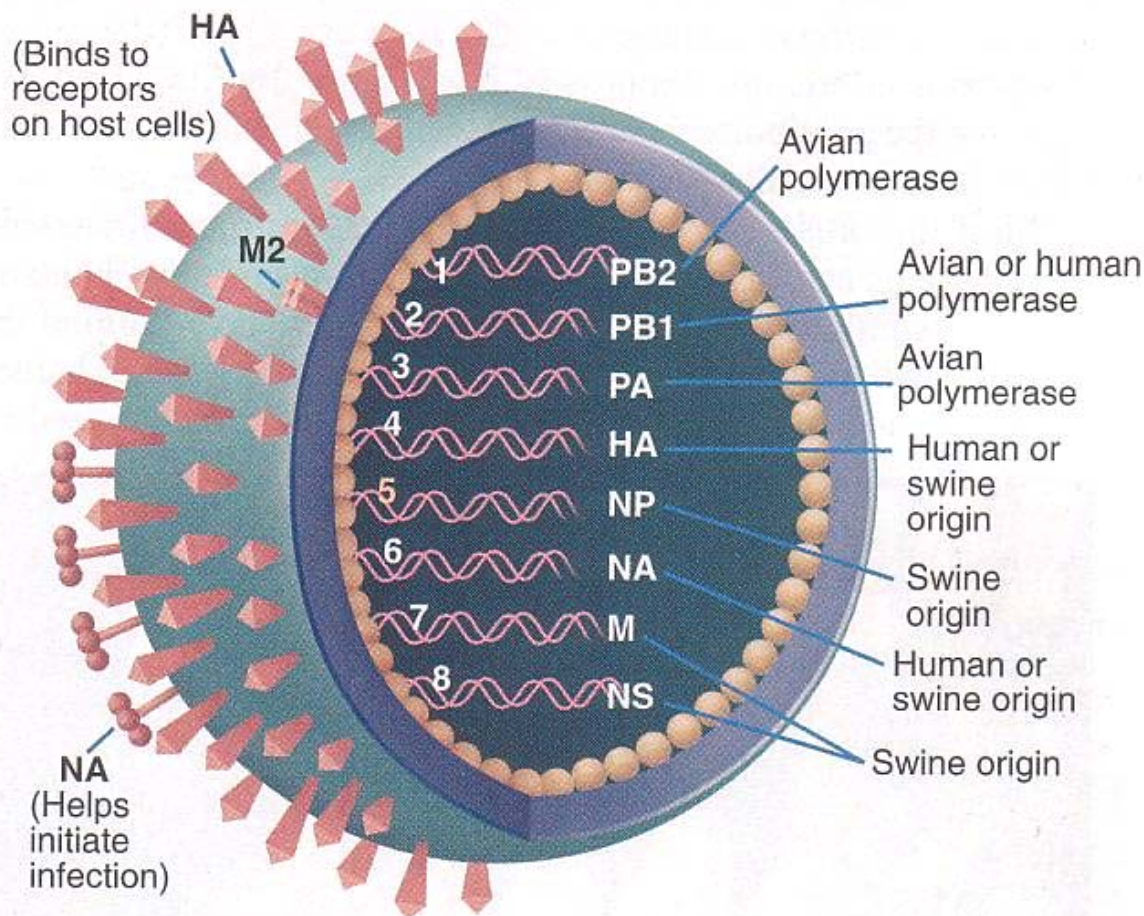


Figure 1 The human immunodeficiency virus. Replication cycle of HIV showing multiple steps available for attack by antiretroviral drugs.



New flus. The influenza viruses now found in North American pigs have genes from both human and bird viruses.

Kun/jos samaan
isäntään pääsee
useampia viruksia,
ne voivat koota
eteenpäin lähtemistä
varten uusia
kokeiluyhdistelmiä

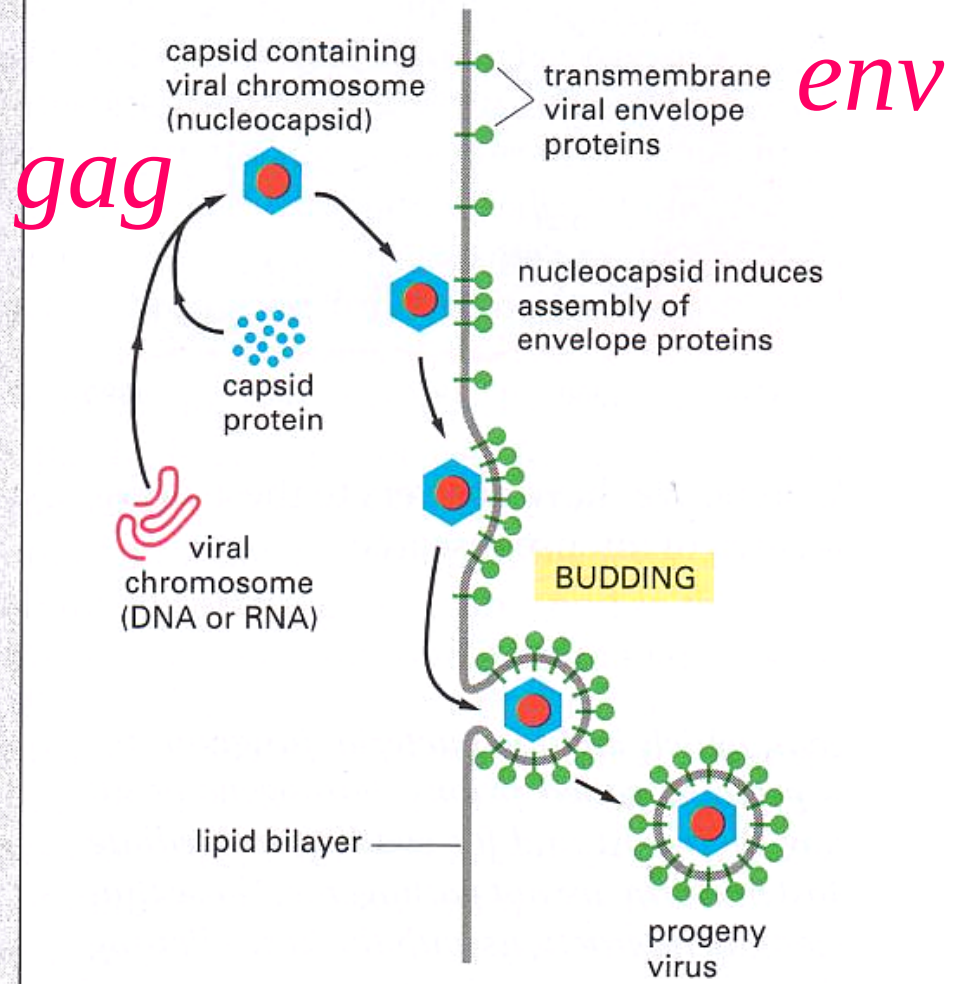
Joillakin viruksilla
kapseliin astuukin kaksi
geenisettiä, vähän niin
kuin Noan arkkiin

ULOS?



(A)

100 nm



(B)

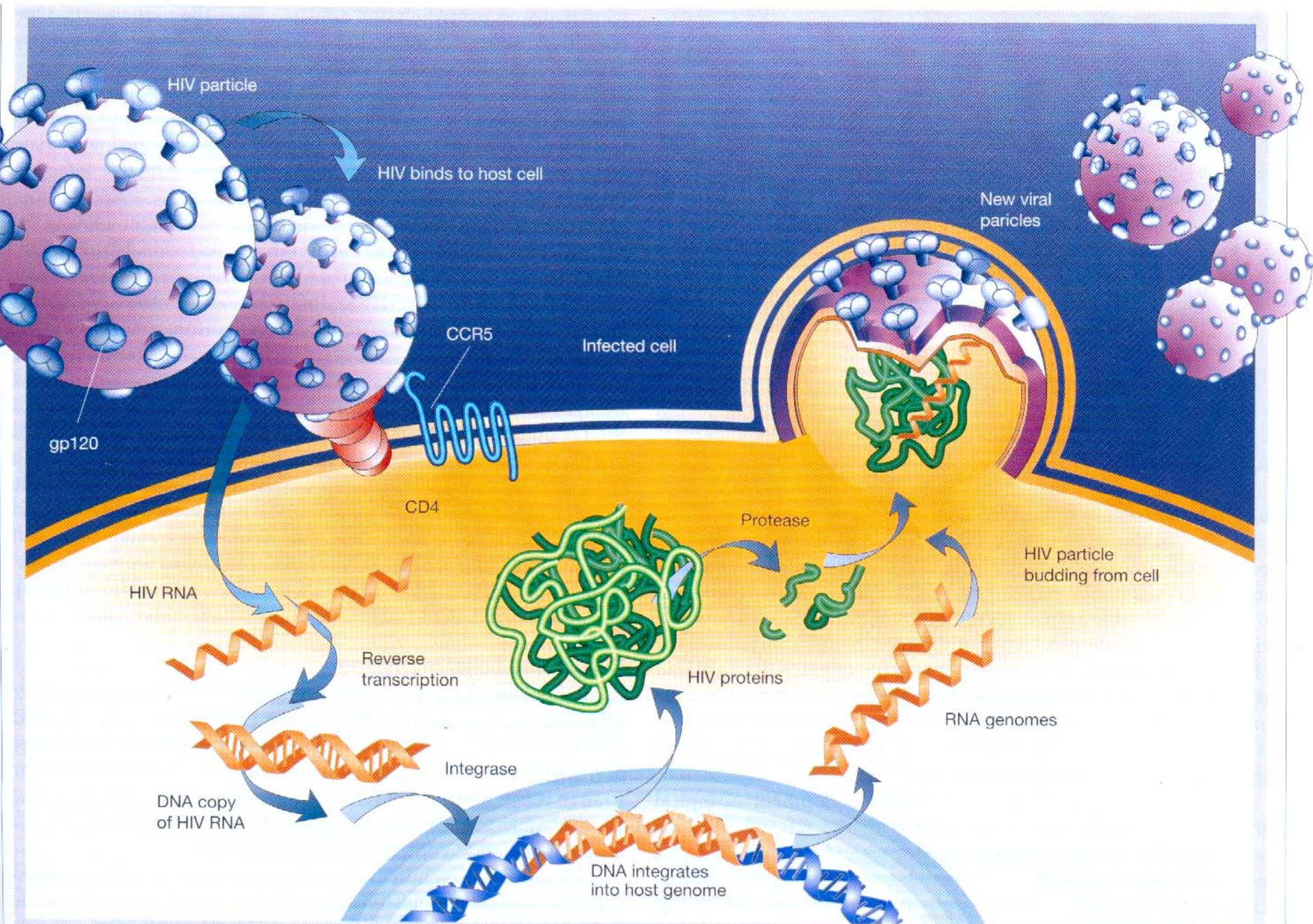
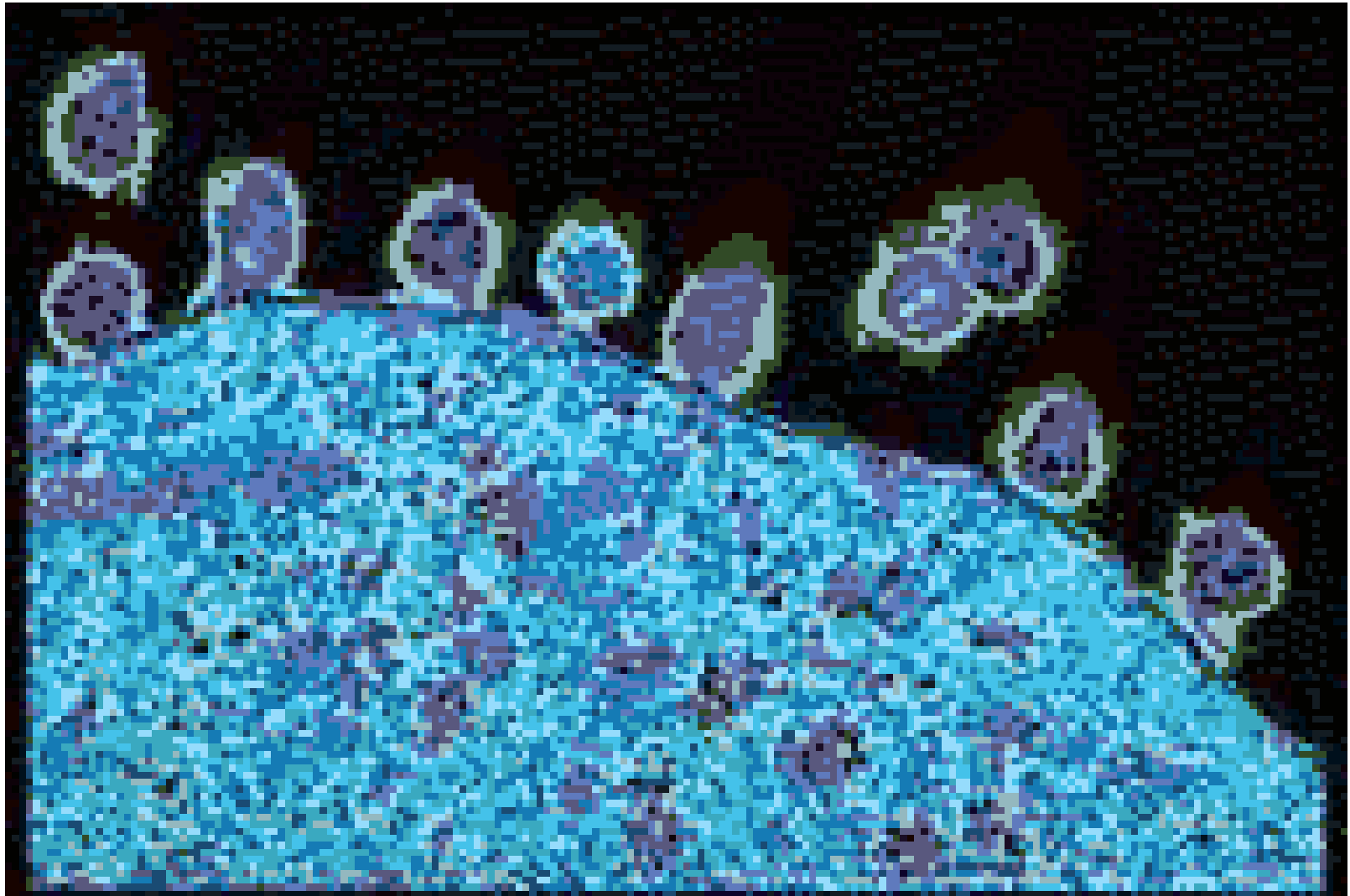
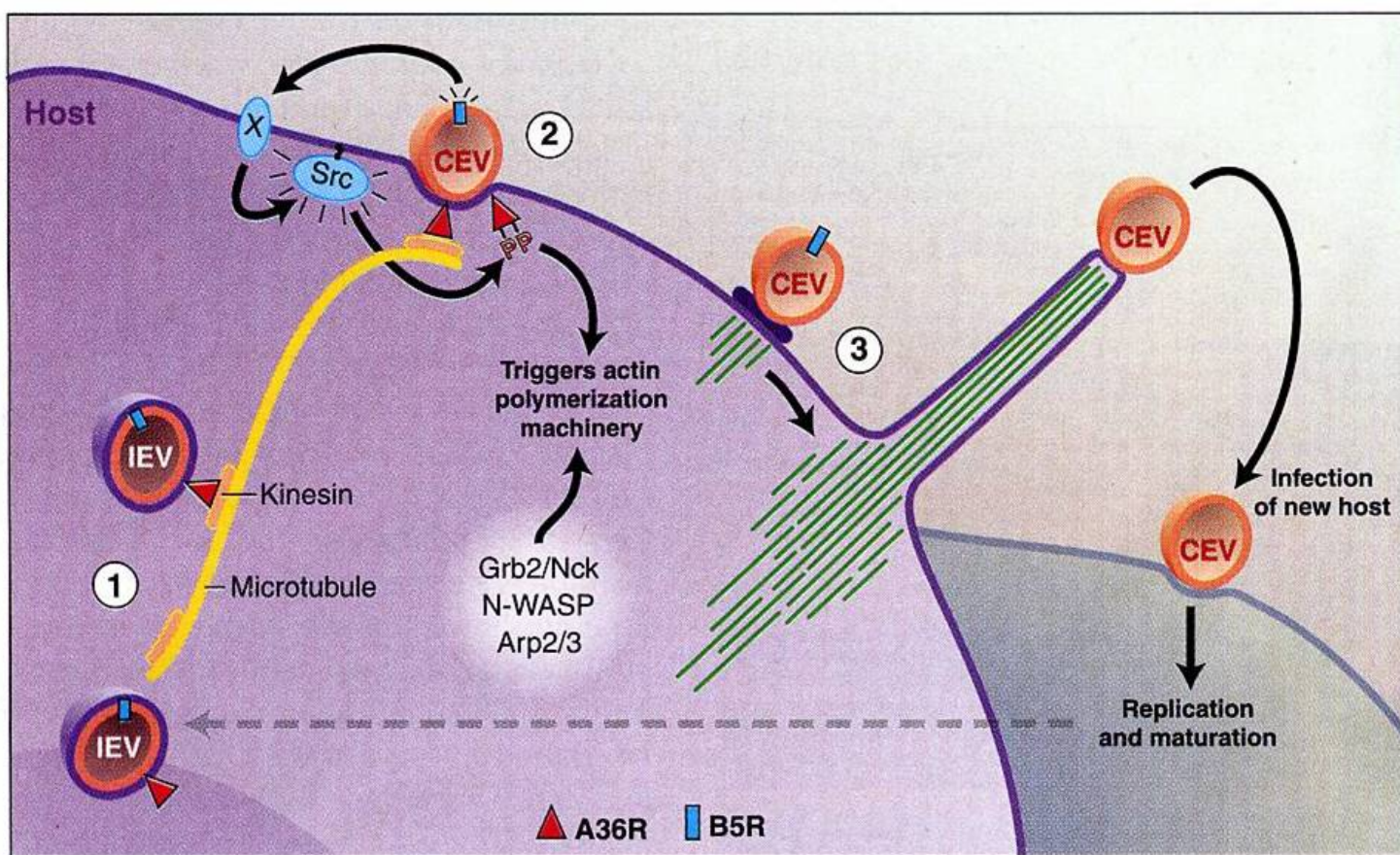


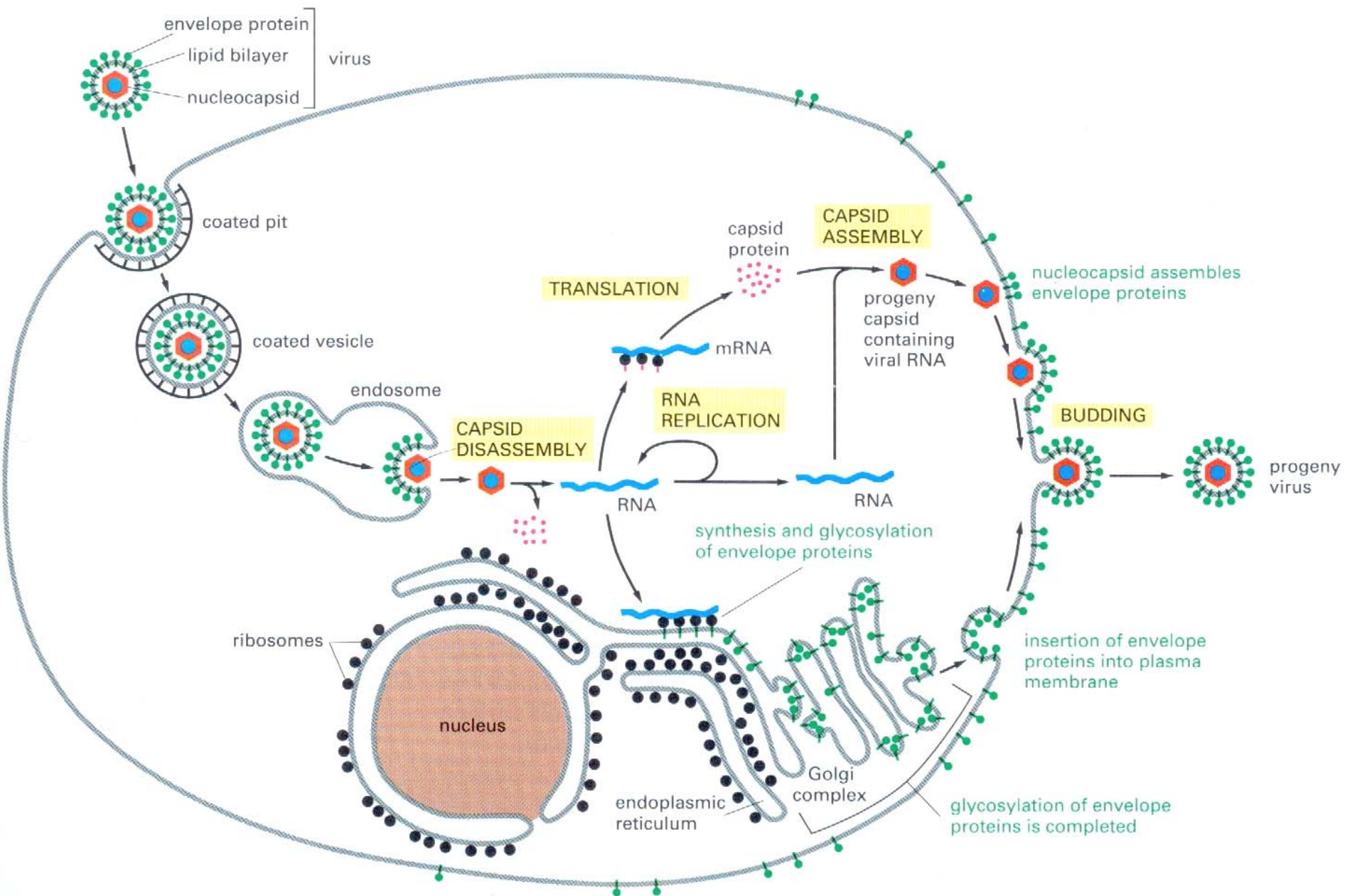
Figure 1 The human immunodeficiency virus. Replication cycle of HIV showing multiple steps available for attack by antiretroviral drugs.



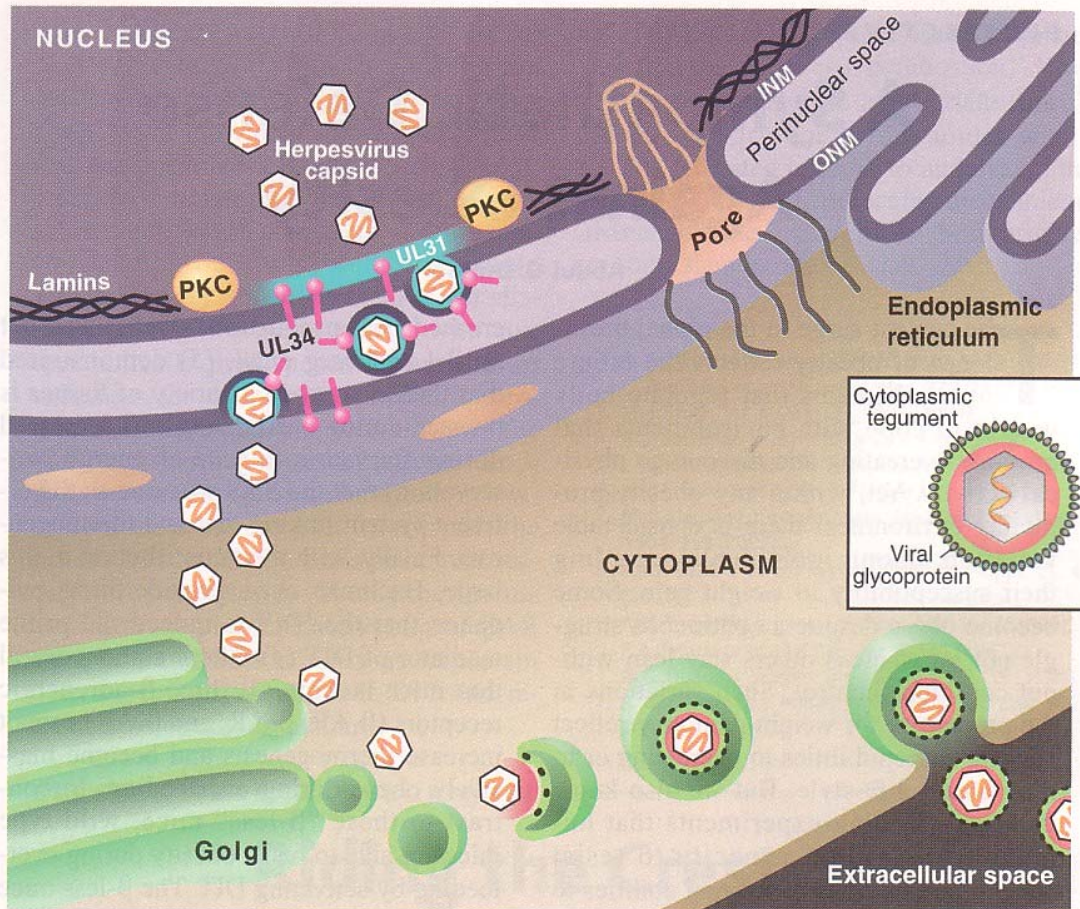
HIV silmikoi. Retrovirus



Switching modes of transport. Vaccinia virus uses Src, a host cell tyrosine kinase, to switch from microtubule-dependent intracellular transport to actin-dependent extracellular extrusion. Step 1: IEV particles, formed in the perinuclear region, interact with kinesin through the viral A36R protein, allowing microtubule-dependent transport (yellow line) to the cell periphery. Step 2: After fusion with the plasma membrane, an infectious CEV is released but remains associated with the extracellular surface of the host. A second viral protein, B5R, interacts with an unknown host cell surface protein (X) to activate the cellular tyrosine kinase Src. Src, in turn, phosphorylates A36R at two sites (PP), triggering its dissociation from kinesin. This leads to recruitment of the host cell's actin polymerization machinery, including two adapter proteins, Nck and Grb2, the scaffold protein N-WASP, and the Arp2/3 nucleation complex. Step 3: Polymerization of actin monomers into filaments (green) drives the formation of a fingerlike protrusion, which launches the CEV of vaccinia virus away from the host cell, facilitating cell-to-cell spread of viral progeny.



Semliki Forest -viruksen elinkierto



The great escape. Newly replicated herpesvirus DNA is inserted into preformed capsids in the nucleus of the host cell. To reach the inner nuclear membrane (INM) of the nuclear envelope, the subviral particles must transit through the physical barrier of the nuclear lamin meshwork. The viral protein UL34 (pink) of HSV-1 (the homolog of M50/p35 in murine CMV) is a type II transmembrane protein that is localized at the INM in infected cells via its interaction with UL31 (turquoise), a viral protein in the nucleus. UL34 and UL31 recruit protein kinase C (PKC) to the nuclear membrane, resulting in an increase in phosphorylation of the lamins. This causes partial disruption of the lamin network, thereby facilitating envelopment of subviral particles at the INM. The particles acquire some of their tegument proteins and a primary envelope by budding through the INM. They then lose their primary envelope as they bud through the outer nuclear membrane (ONM) of the nuclear envelope and are released into the cytoplasm. The DNA-containing capsids move to the Golgi complex, where they acquire additional tegument proteins and a mature envelope. Finally, they travel in Golgi-derived vesicles to the plasma membrane, where they are released from the host cell.

Ollaanko me aivan avuttomia?

Ei, kyllä taistelu on kovaa ja
voittojakin saavutetaan

Immuunisysteemi pääsee joskus
myös solujen sisään
ennättäneiden kimppuun

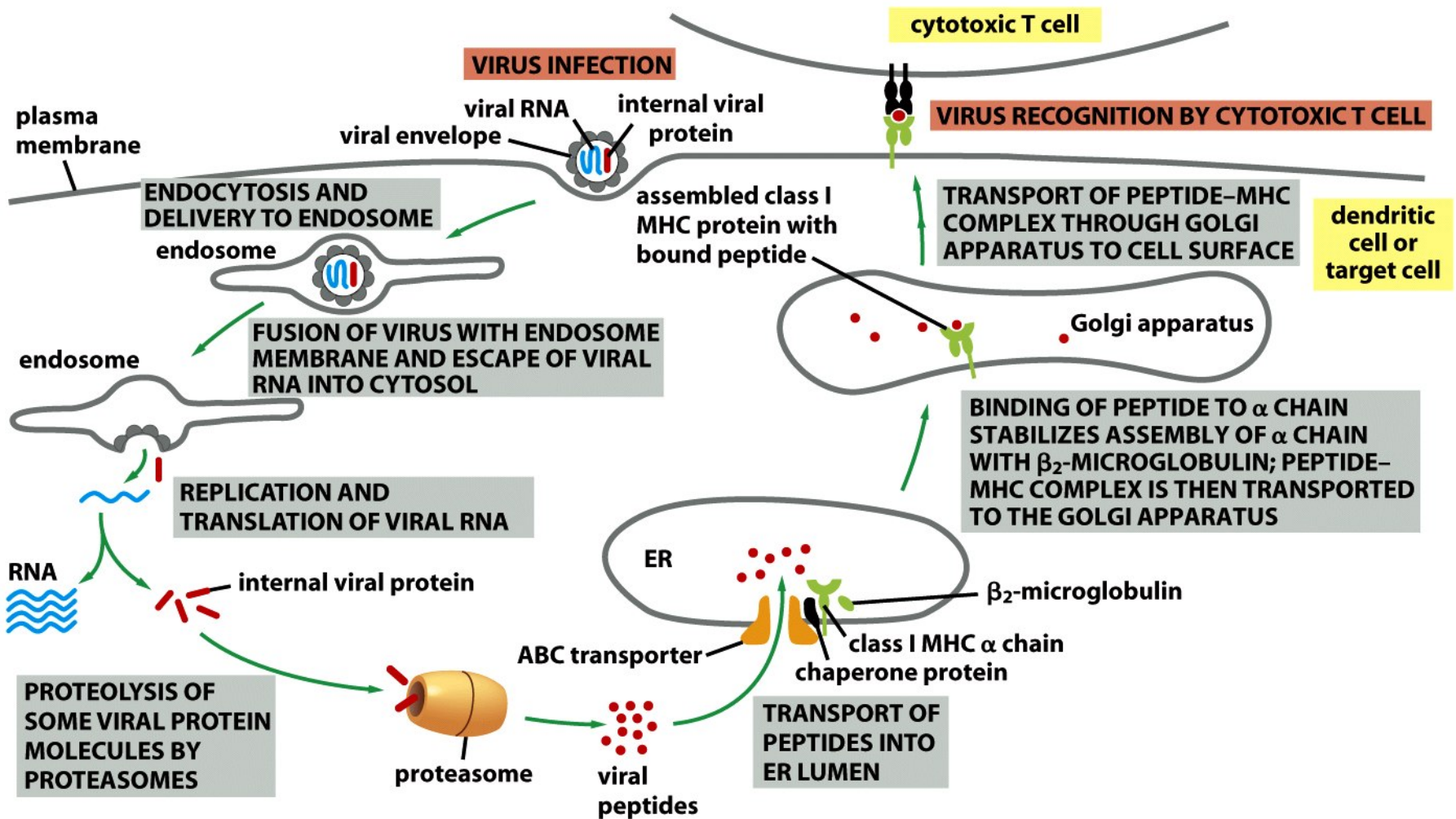


Figure 25-59 Molecular Biology of the Cell 5/e (© Garland Science 2008)

MHC: kuinka virus yms. havaitaan solussa ja kavalletaan sytotoksiselle T-solulle

Kirjassa on valtavasti uutta tietoa bakteeri-infektioiden molekyylibiologiasta, mutta sen hyppäämme yli tässä kurssissa. Nauttikaa niistä tiedoista yksityisesti.

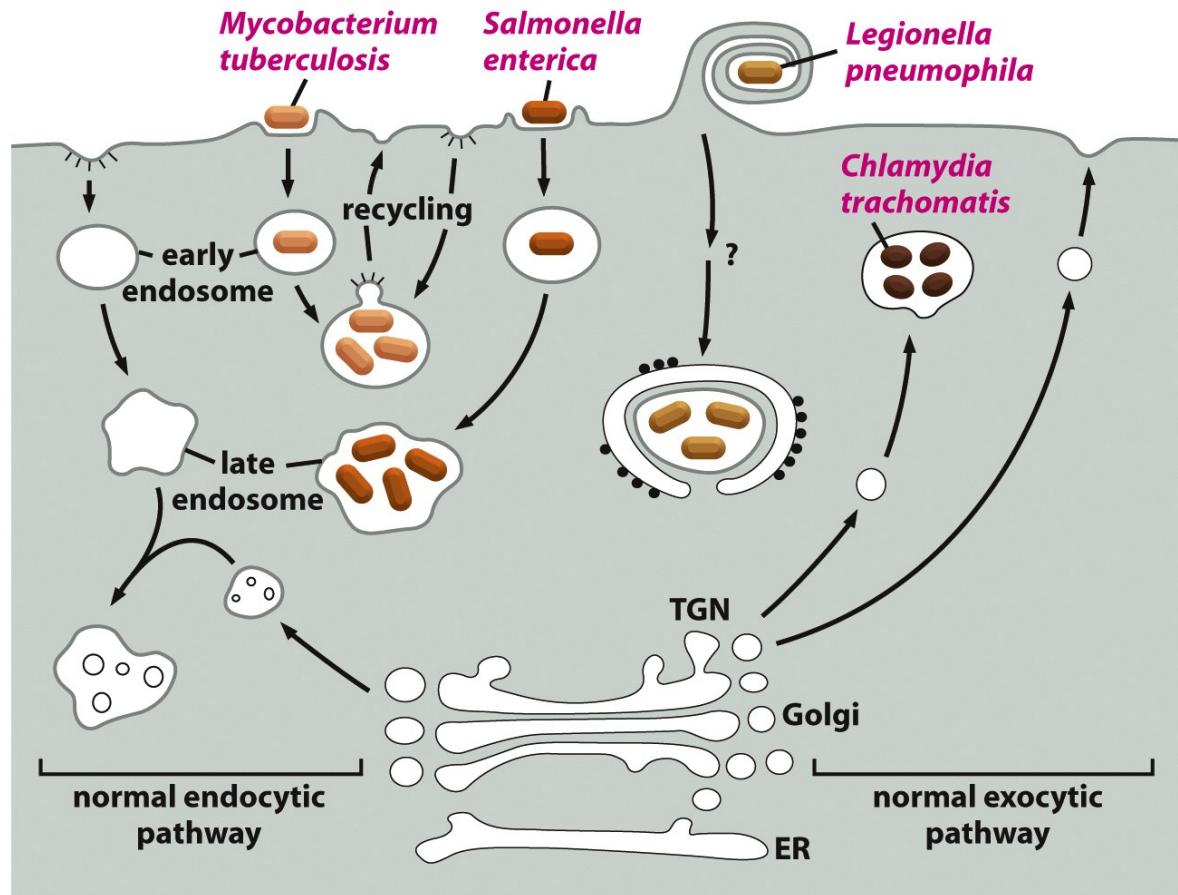


Figure 24-32 Molecular Biology of the Cell 5/e (© Garland Science 2008)