

Surface of Enveloped Viruses

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54237220

1. Introduction: Diversity of viruses and viral surfaces

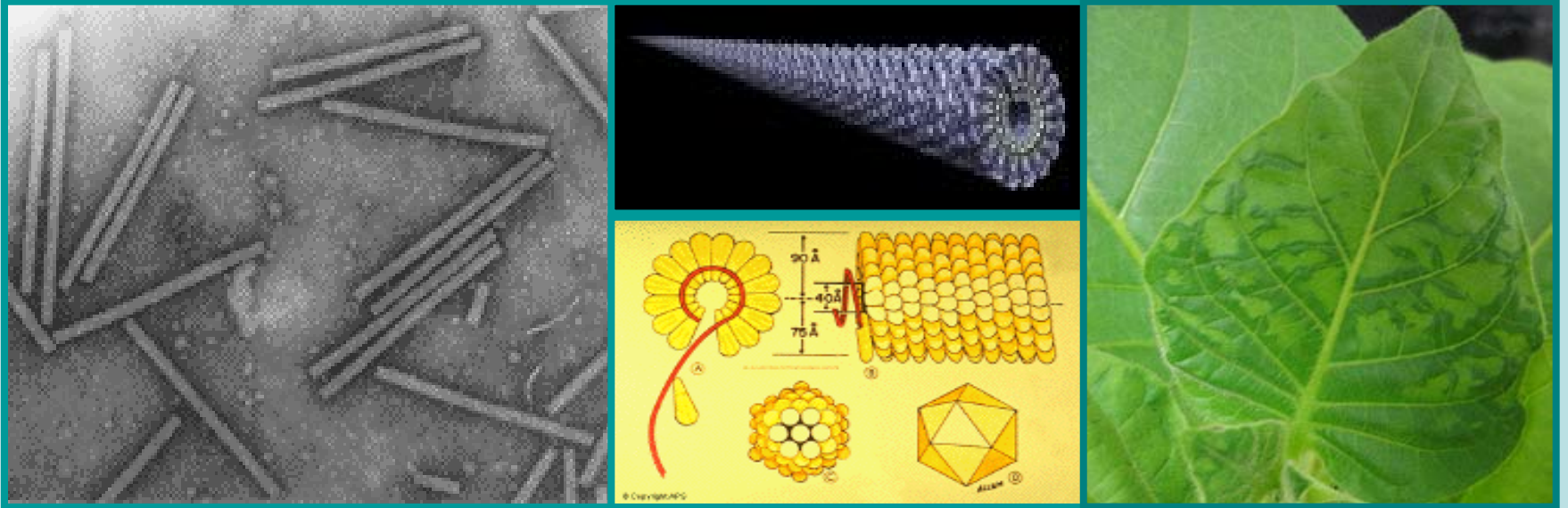
2. Membrane fusion: A critical step of viral entry into the cell

3. Membrane budding: A major mode for the assembly of viral envelopes

4. Host receptor: A determinant of viral transmission

烟草花叶病毒

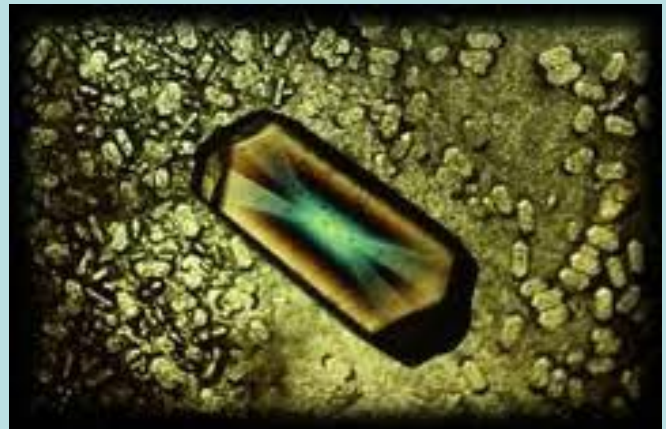
Tobacco Mosaic Virus



Stanley



1935年



Host and Genome of Viruses

General Host

Algae
Archaea
Bacteria
Fungi
Invertebrates
Plants
Protozoa
Vertebrates



Genome types

DNA viruses:

dsDNA viruses
ssDNA viruses

Reverse Transcriptase:

dsDNA-RT viruses
ssRNA-RT viruses

RNA Viruses:

dsRNA viruses
(-)ssRNA viruses
(+)ssRNA viruses



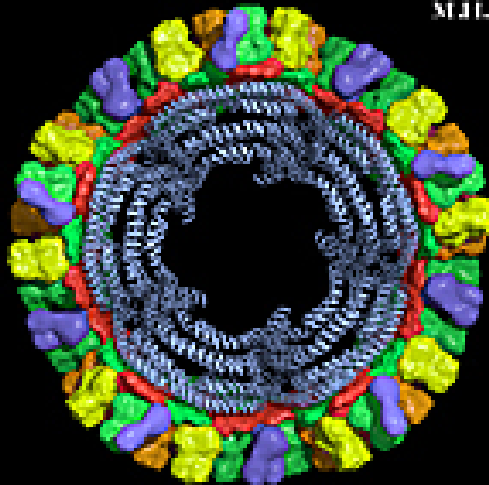
Reports of the International Committee on Taxonomy of Viruses

Virus Taxonomy

Seventh Report of the International Committee on Taxonomy of Viruses

Edited by

M.J.W. van Regenmortel
C.M. Fauquet
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J. Maniloff
M.A. Mayo
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C.H. Pringle
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Virology Division

International Union of Microbiological Societies

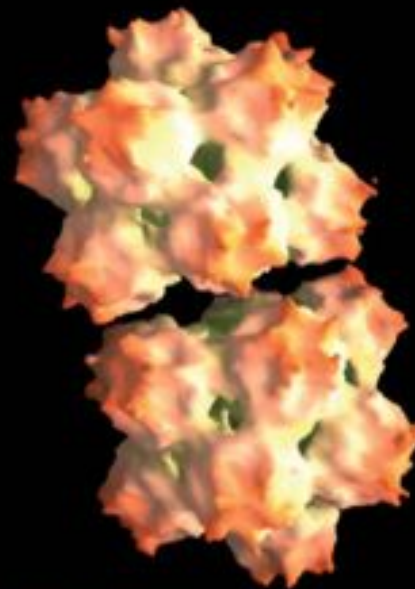


Virus Taxonomy

Eighth Report of the International Committee on Taxonomy of Viruses

Edited by

C. M. Fauquet
M. A. Mayo
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U. Desselberger
L. A. Ball



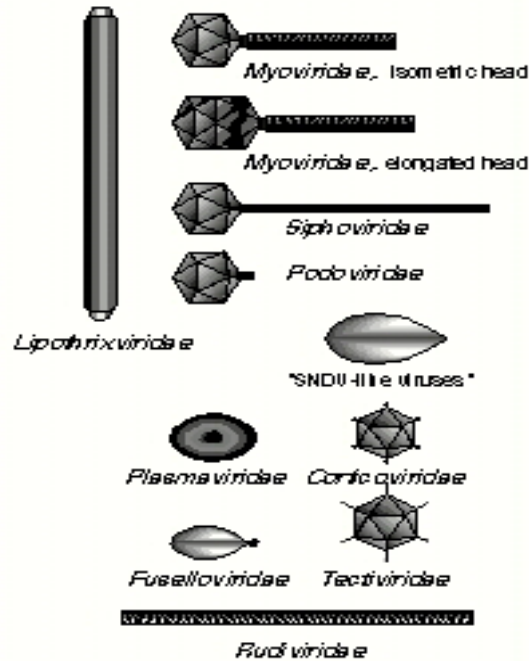
Virology Division International Union of Microbiological Societies

感染细菌的病毒

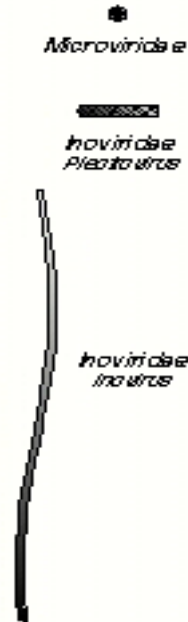
Families and Genera of Viruses Infecting Bacteria

DNA

dsDNA



ssDNA



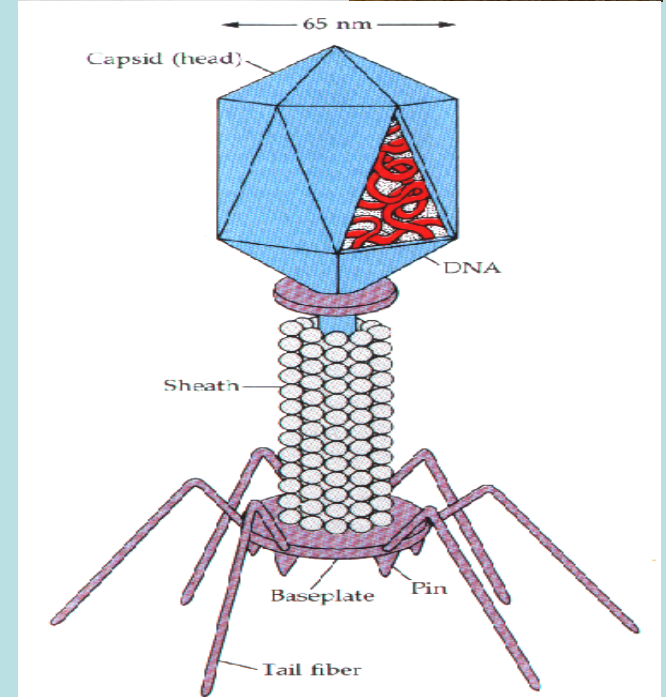
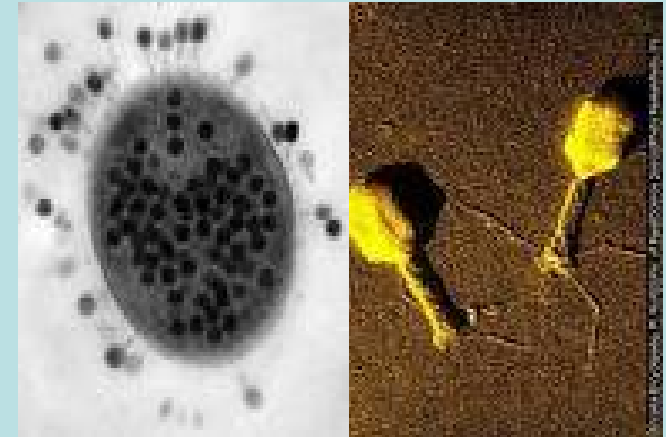
RNA

dsRNA



100 nm

ssRNA

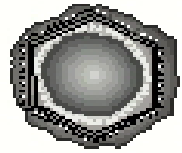


Families and Genera of Viruses Infecting Vertebrates

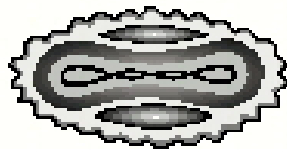
感染人类和动物的病毒

DNA

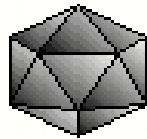
dsDNA



Adenoviridae



Poxviridae
Choriopoxvirinae



Iridoviridae
Banaviruses
Lymphocystivirus

ssDNA



Circoviridae

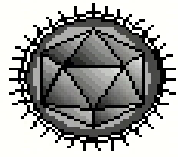


Parvoviridae
Parvovirinae

dsDNA (RT)



Hepadnaviridae



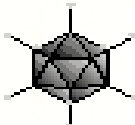
Herpesviridae



Polyomaviridae



Papillomaviridae



Adenoviridae

dsRNA



Reoviridae
Orbivirus
Rotavirus
Astrovirus

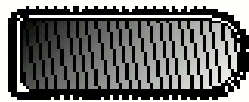


Birnaviridae
Arenaviridae
Arteriviridae

ssRNA (-)



Orthomyxoviridae



Rhabdoviridae
Lysseviruses
Vesiculovirus
Echovirus
Novirhabdovirus



Distemper



Paramyxoviridae



Bornaviridae

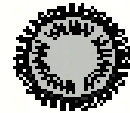


Arnaviridae

ssRNA (RT)



Retroviridae



Bunyaviridae
Sarbecovirus
Hantavirus
Nairovirus
Phlebotomus

ssRNA (+)



Caliciviridae



HEV-like



Nodaviridae
Sarbecovirus



Togaviridae



Picornaviridae



Flaviviridae



Coronaviridae



Arteriviridae

100 nm

RNA



Families and Genera of Viruses Infecting Plants

DNA

dsDNA (RT)
Caulimoviridae

Caulimovirus
CsVMV-III
PUCV-III
SbCMV-III

Beet virus
RTBV-III

ssDNA
Geminiviridae

Mastovirus
Curtovirus

Begomovirus

Nanovirus

RNA

dsRNA
Rhabdoviridae

Rhabdovirus
Phlyctovirus
Cryzovirus
Partitiviridae

Alphapartivirus
Betapartivirus
Yersinioviridae






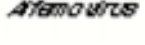















Yersiniovirus


ssRNA (-)
Rhabdoviridae

Rhabdovirus
Cytorhabdovirus
Nucleorhabdovirus
Bunyaviridae

Bunyavirus
Tospovirus

Tenuivirus
Carpovirus











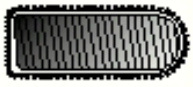








ssRNA (+)
Bromoviridae
Secoviridae
Secovirus
Tombusviridae
Tombusvirus
Luteoviridae
Marsivirus
Sabivirus
Tymovirus
Limovirus
Comoviridae
Comovirus
Alfamo virus









Tobamovirus

Tobamovirus

Tobamovirus

Hordeovirus

Rovirus

Pepovirus

Papovirus

Betovirus

Alfavirus, Calfavirus, Foveavirus, Potexvirus

Capillivirus, Trichovirus, Vitivirus

Potyvirus

Closteroviridae


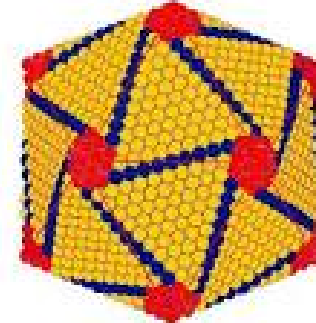
感染植物的病毒



感染昆虫的病毒

Families and Genera of Viruses Infecting Invertebrates

DNA	dsDNA		ssDNA			
	 <p><i>Poxviridae</i> <i>Entomopoxvirinae</i></p>  <p><i>Iridoviridae</i> <i>Iridovirus</i> <i>Chironomus virus</i></p>  <p><i>Baculoviridae</i></p>  <p><i>Polydnaviridae</i> <i>Ichnovirus</i></p>  <p><i>Polydnaviridae</i> <i>Braconovirus</i></p>  <p><i>Ascoviridae</i></p>	 <p><i>Circoviridae</i></p>  <p><i>Parvoviridae</i> <i>Densovirinae</i></p>				
RNA	dsRNA		ssRNA (-)		ssRNA (+)	
	 <p><i>Reoviridae</i> <i>Capripotus</i></p>  <p><i>Birnaviridae</i> <i>Entomobirnavirus</i></p>	 <p><i>Rhabdoviridae</i></p>  <p><i>Bunyaviridae</i></p> <p>100 nm</p>	 <p><i>Picornaviridae</i></p>  <p>CFLV-1</p>  <p><i>Togaviridae</i></p>  <p><i>Tetraviridae</i></p>  <p><i>Flaviviridae</i></p>  <p><i>Nodaviridae</i></p>	 <p><i>Metaviridae</i> <i>Erenovirus</i></p>		



Structural difference of animal and plant viruses

Families and Genera of Viruses Infecting Plants

DNA

dsDNA (RT)

Caulimoviridae

Caulimovirus
CsUMV-II like
PICV-II like
SbCMV-II like
Bacnavirus
RTBV-II like

ssDNA

Geminiviridae

Mestivirus
Curtovirus
Begomovirus
Nanovirus

Families and Genera of Viruses Infecting Plants

RNA

dsRNA

Reoviridae
Rift virus
Phytoreovirus
Oryza virus

Partitiviridae
Alpharhabdovirus
Beetarhabdovirus

Varicosavirus

100 nm

ssRNA (-)

Bunyaviridae
Tospovirus
Rhabdoviridae
Cytorhabdovirus
Nucleorhabdovirus
Tenuivirus
Ophiovirus

ssRNA (RT)

Pseudoviridae

Curtovirus

ssRNA (+)

Bromoviridae
Sequiviridae
Tombuviridae
Luteoviridae
Mastovirus
Sabumovirus
Tymovirus
Limnavirus
Ilarivirus
Alfavirus
Comoviridae
Tobamovirus
Tobamovirus
Tobamovirus
Hordeovirus
Purpurvirus
Pepivirus
Pomovirus
Serivirus
Alfavirus, *Carpovirus*, *Foveavirus*, *Potentivirus*
Capillivirus, *Trichovirus*, *Trichovirus*
Polyoviridae
Closteroviridae

Families and Genera of Viruses Infecting Vertebrates

DNA

dsDNA



Astarviridae



Poxviridae
Chordopoxvirineae



Iridoviridae
Renevivirus
Lymphocystivirus

ssDNA

Circoviridae

Parvoviridae
Parvovirineae

dsDNA (RT)

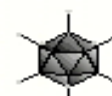
Hepadnaviridae



Herpesviridae

Polyomaviridae

Papillomaviridae



Adenoviridae

Families and Genera of Viruses Infecting Vertebrates

RNA

dsRNA

Reoviridae
Orthoreovirus
Oribivirus
Calivirus
Rotavirus
Aquareovirus

Bimaviridae
Apicostemovirus
Alfavirus

100 nm

ssRNA (-)



Orthomyxoviridae



Paramyxoviridae



Rhabdoviridae
Lyssavirus
Yersiniovirus
Ephemerovirus
Novirhabdovirus



Bomaviridae



Arenaviridae



Filoviridae

ssRNA (RT)



Retroviridae



Bunyavirus

Hantavirus
Nairovirus
Pireovirus

ssRNA (+)

Caliciviridae

Picornaviridae

Astroviridae

HEV-like

Flaviviridae

Flaviviridae

Nodavirus
Seterovirus

Coronaviridae

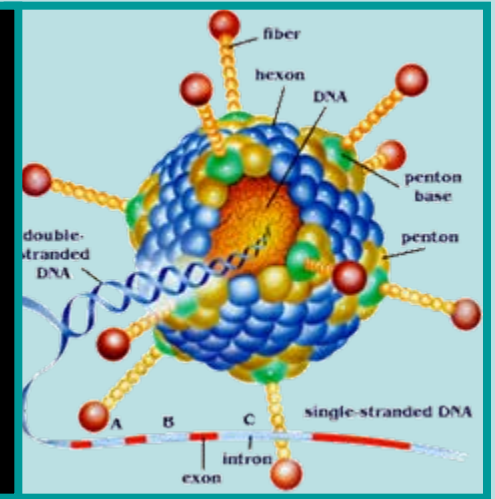
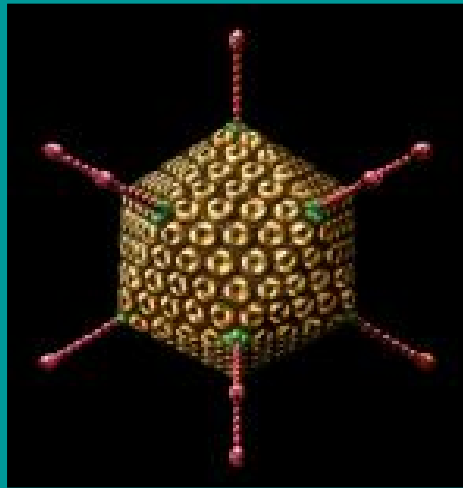
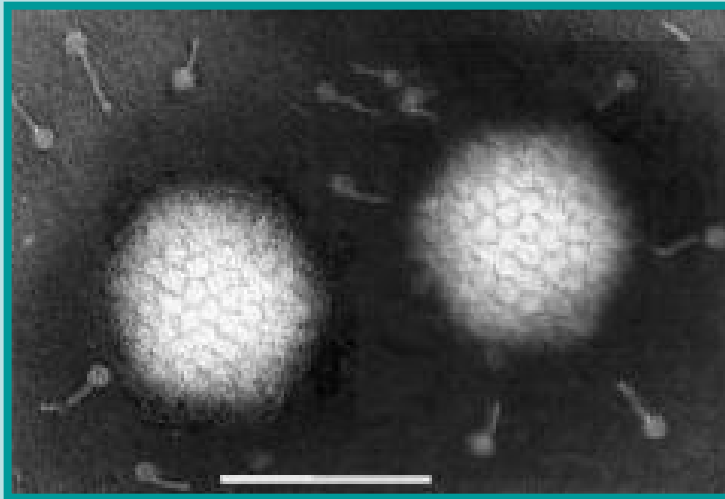
Coronaviridae

Togaviridae

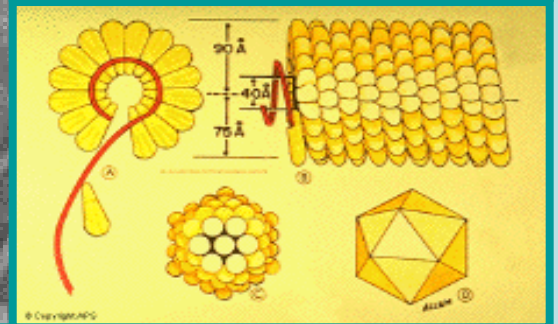
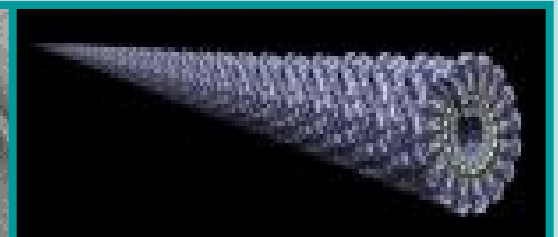
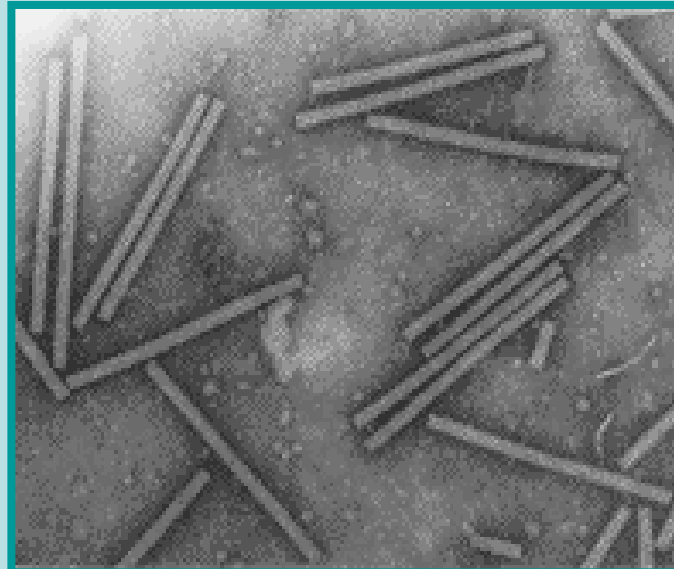
Arteriviridae

Arteriviridae

Naked Viruses

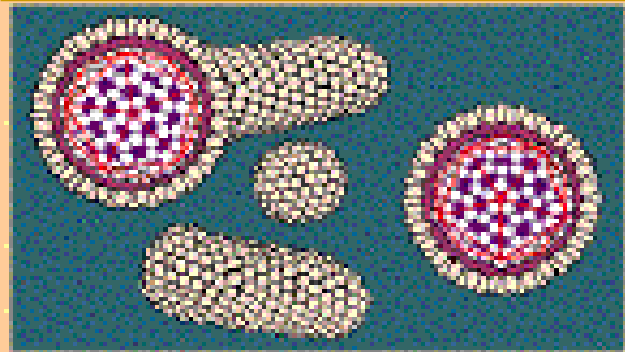
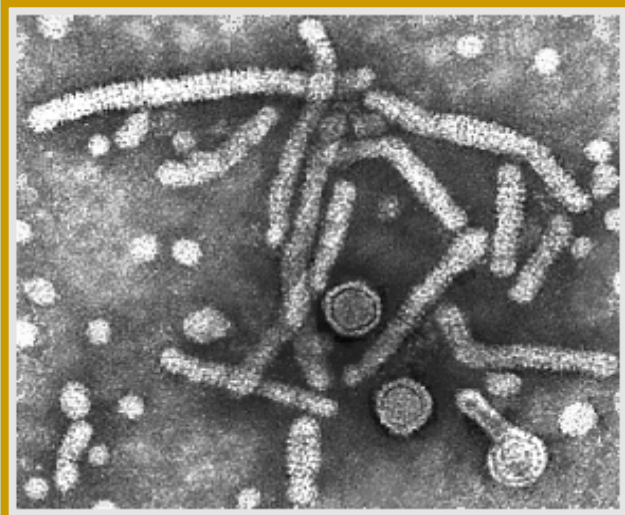


Adenovirus

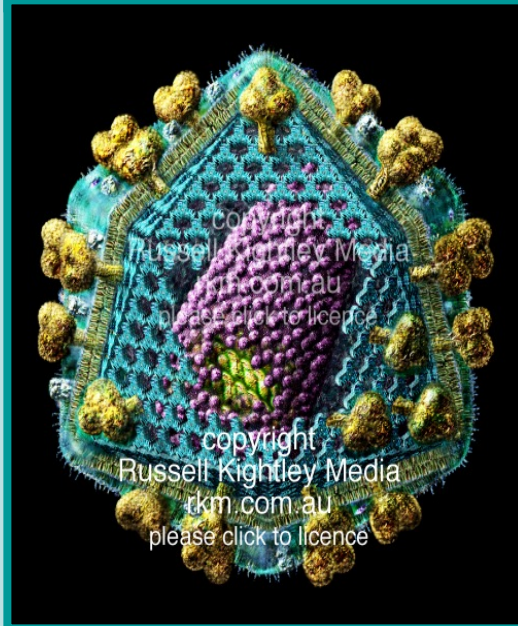
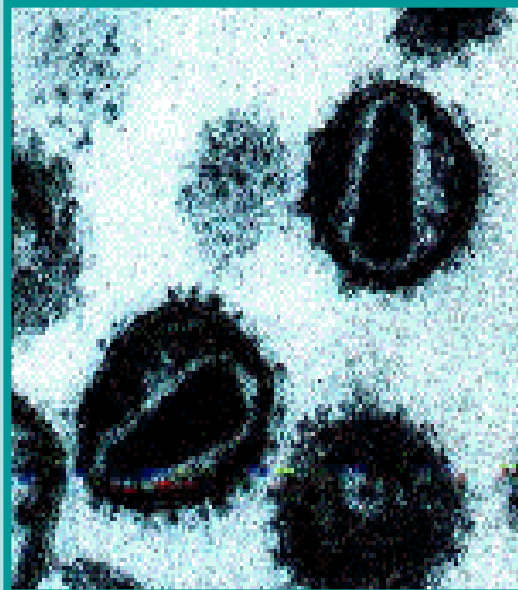


Tobacco Mosaic Virus

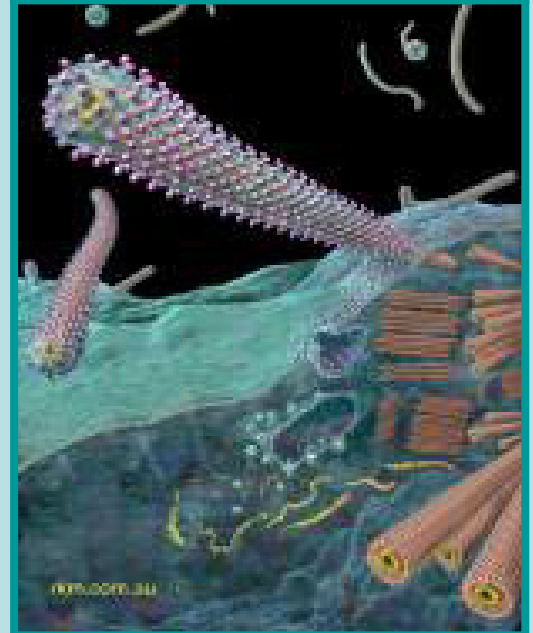
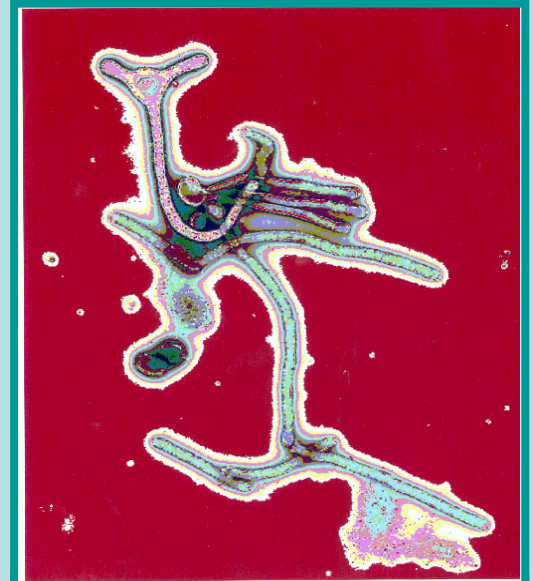
Enveloped viruses



HBV



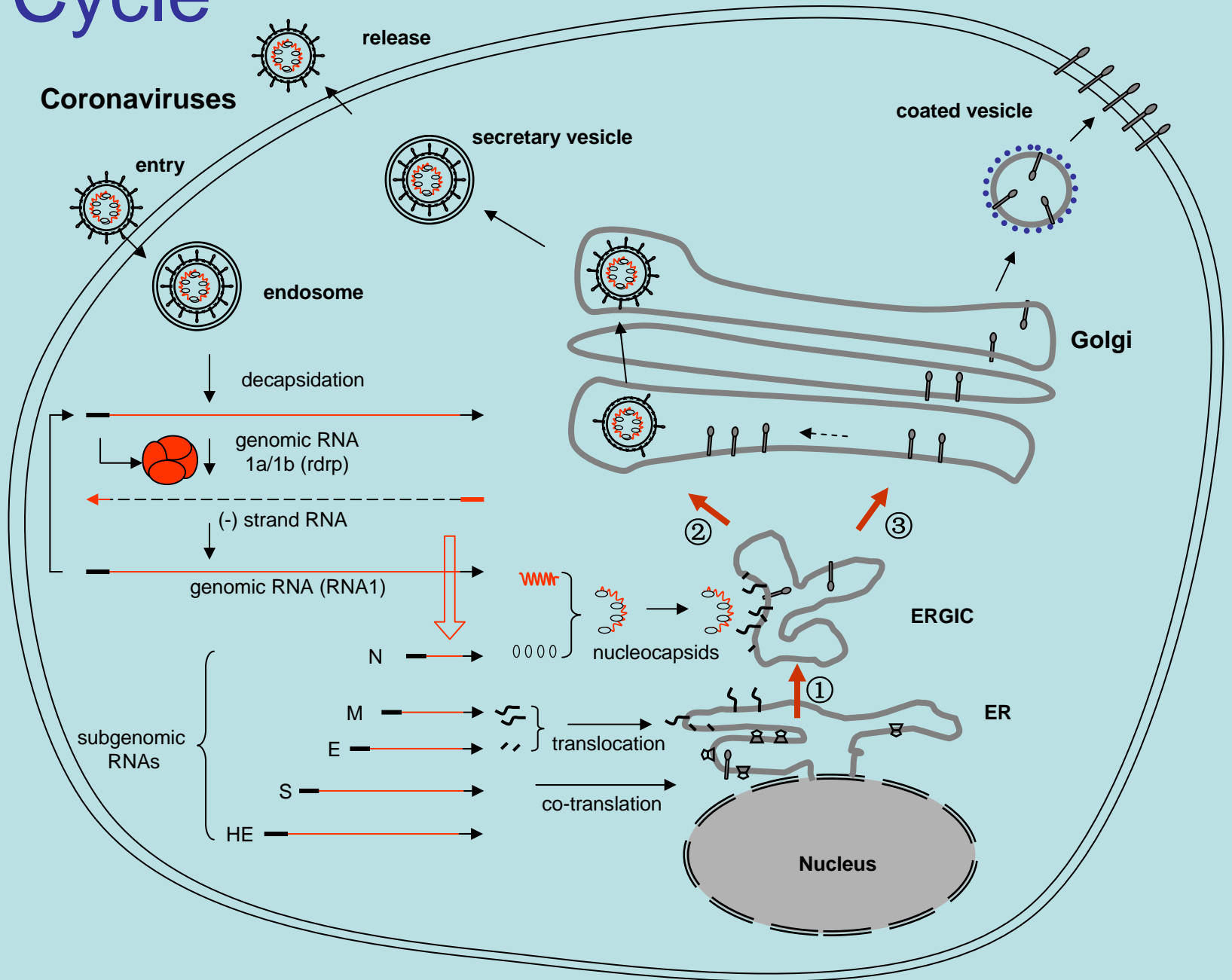
HIV



Ebola Virus

1. Introduction: Diversity of viruses and viral surfaces
2. Membrane fusion: A critical step of viral entry into the cell
3. Membrane budding: A major mode of the assembly of viral envelopes
4. Host receptor: A determinant of viral transmission

Life Cycle



Class I fusion proteins

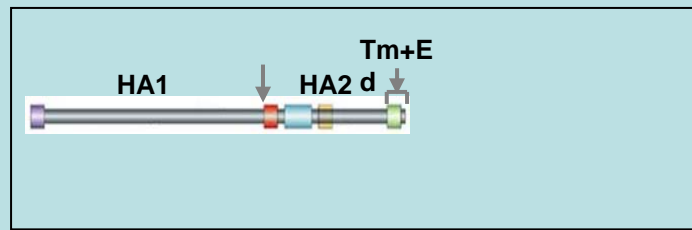
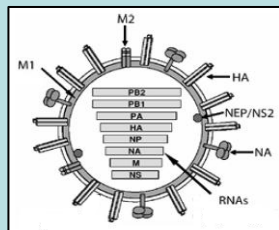
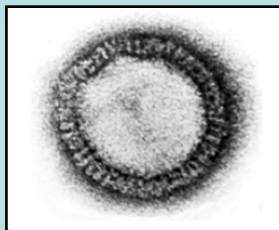
Orthomyxovirus: **HA0** → **HA1+HA2** (Influenza)

Paramyxovirus: **F0** → **F1+F2** (Measles, NDV, Sendai, RSV)

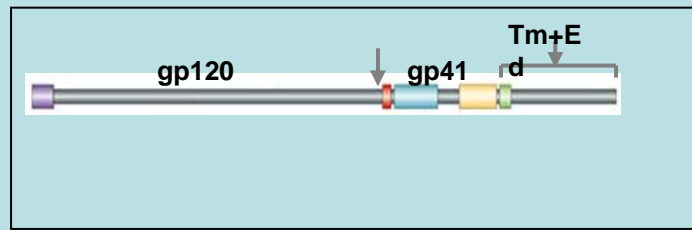
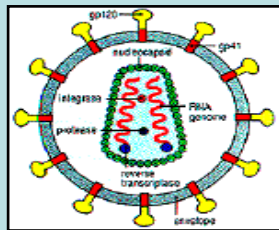
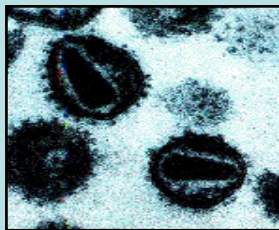
Retrovirus: **gp160** → **gp120+gp41** (HIV)

Coronavirus: **S** → **S1+S2** (MHV)

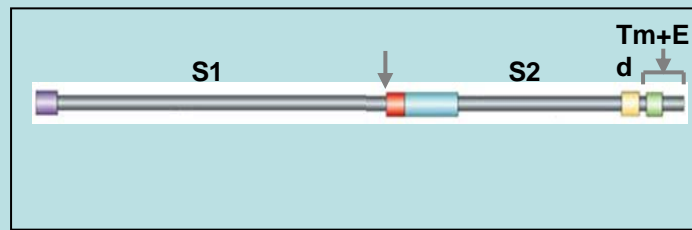
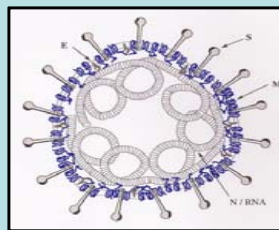
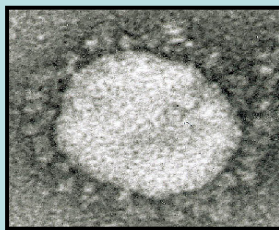
Filovirus: **GP** → **GP1+GP2** (Ebola)



正粘病毒

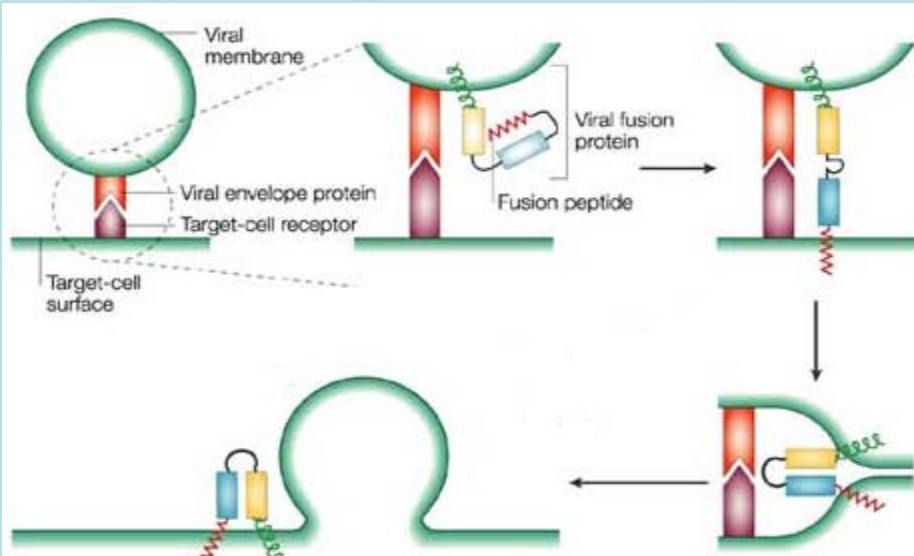


逆转录病毒

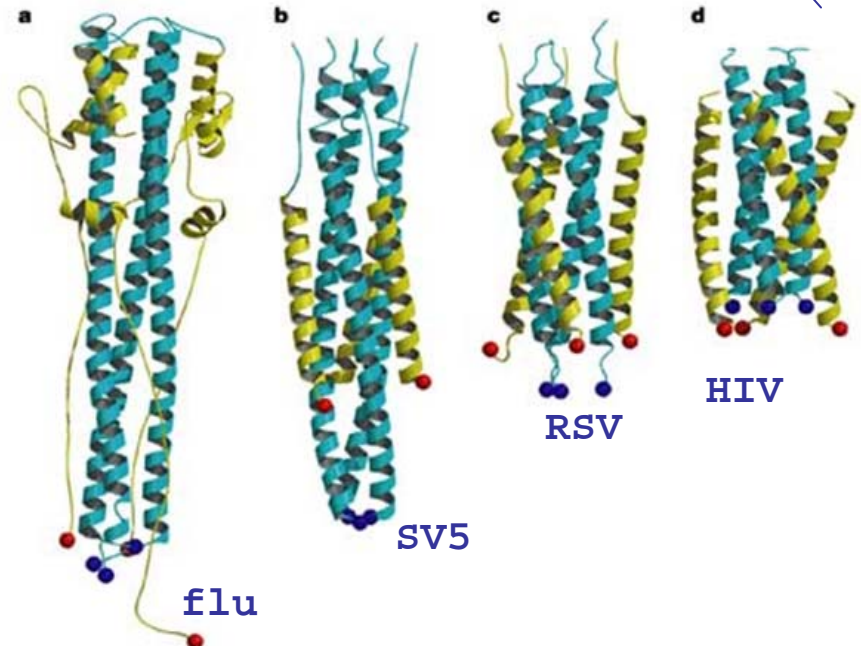
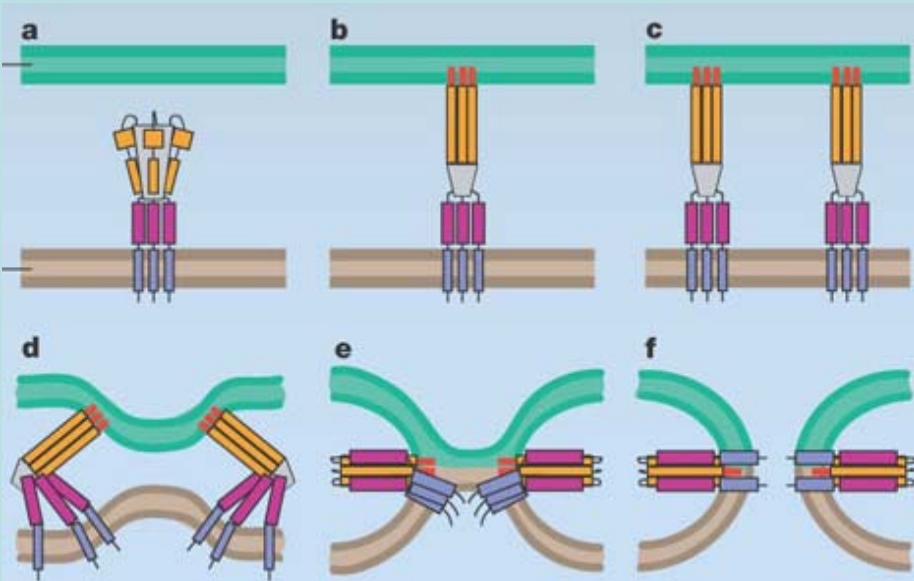


冠状病毒

Class I Membrane Fusion



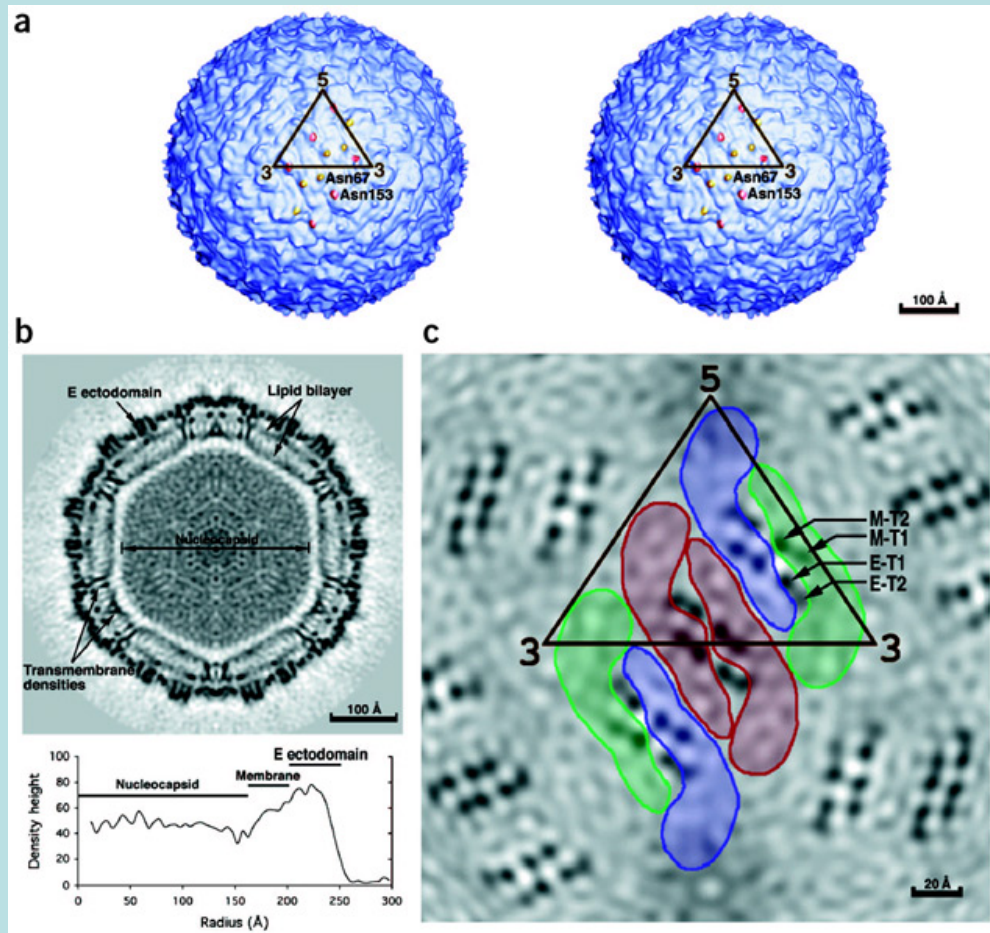
6-Helix Bundle



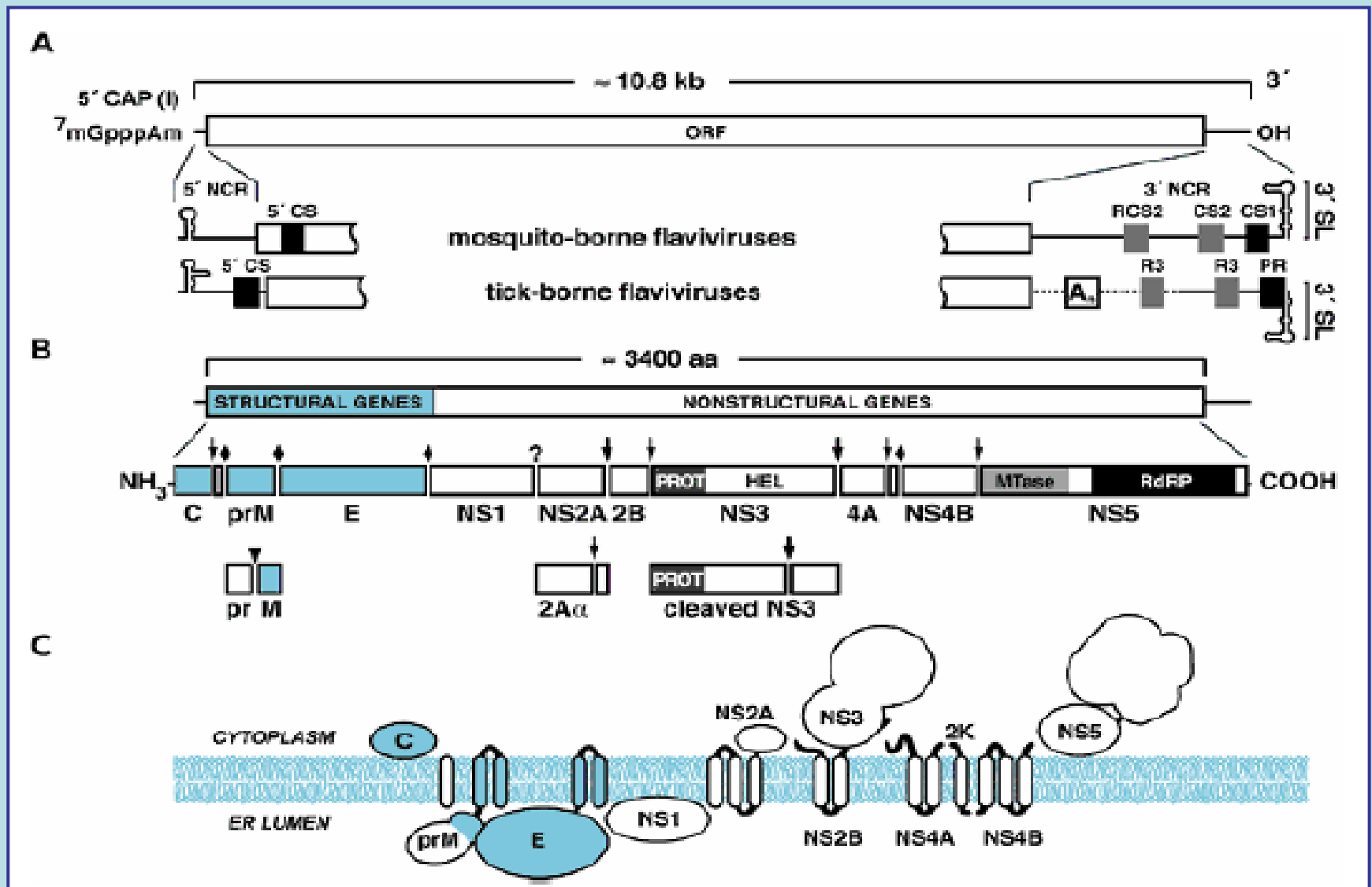
Class II fusion proteins

Flaviviruses: **E protein** (Dengue, YF, TBE, WN)

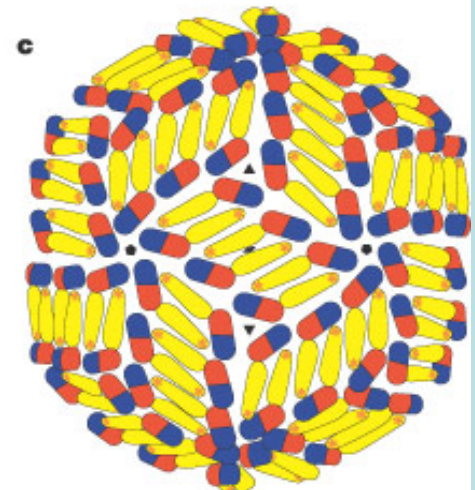
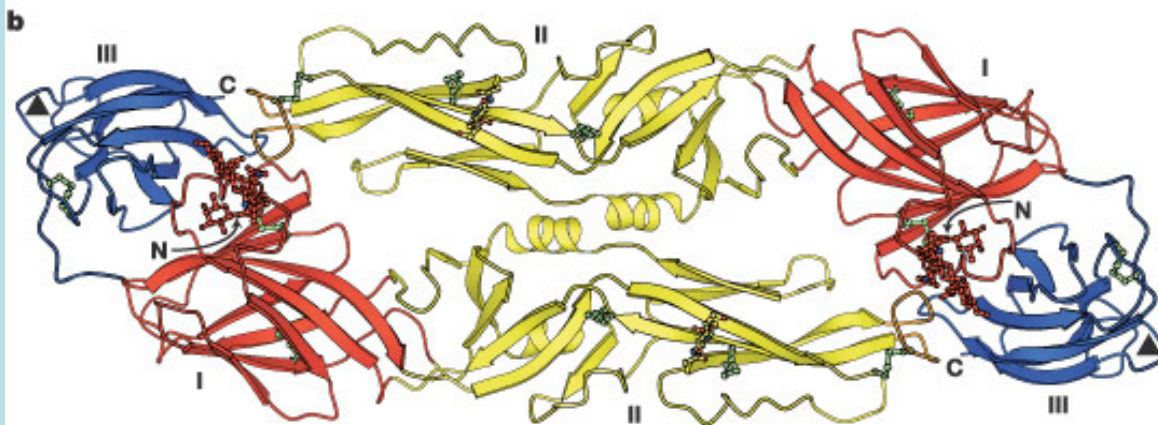
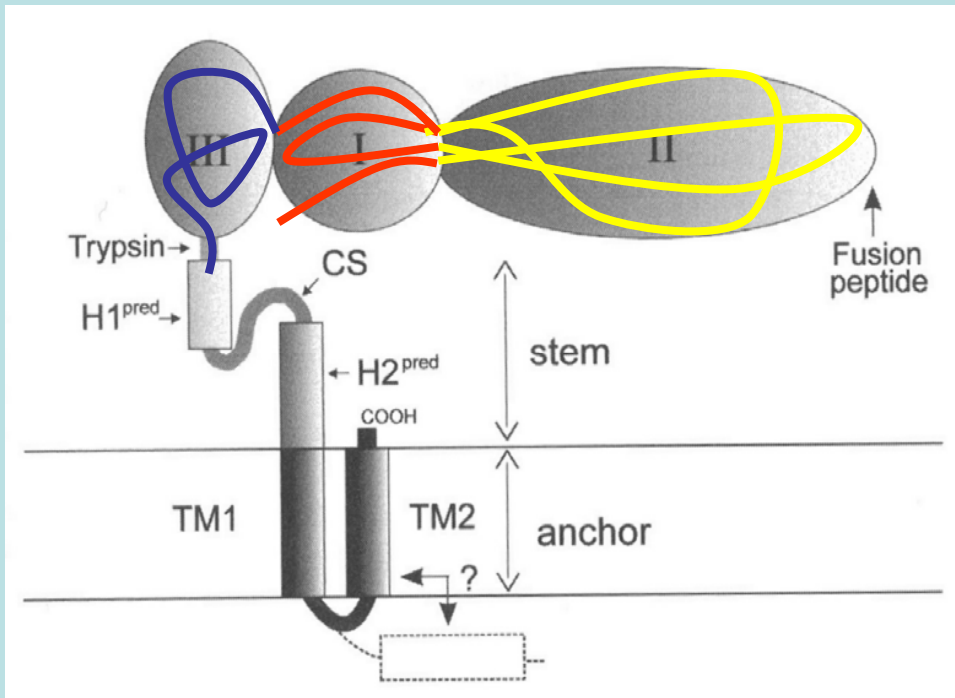
Alphaviruses: **E1 protein** (Sindbis, Semliki Forest)



Genes and proteins of Flavivirus

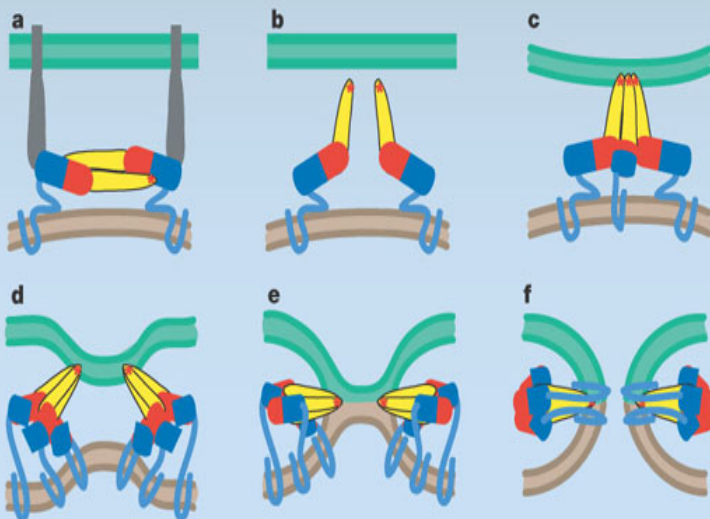
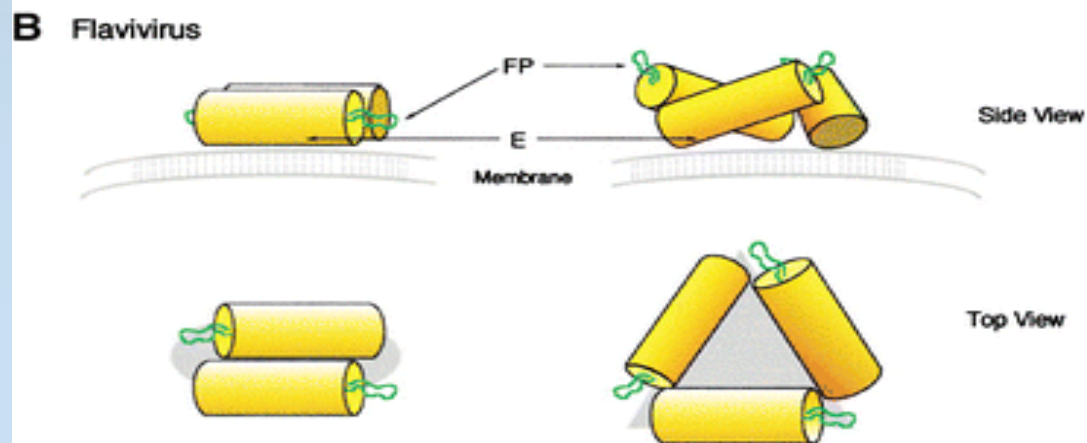
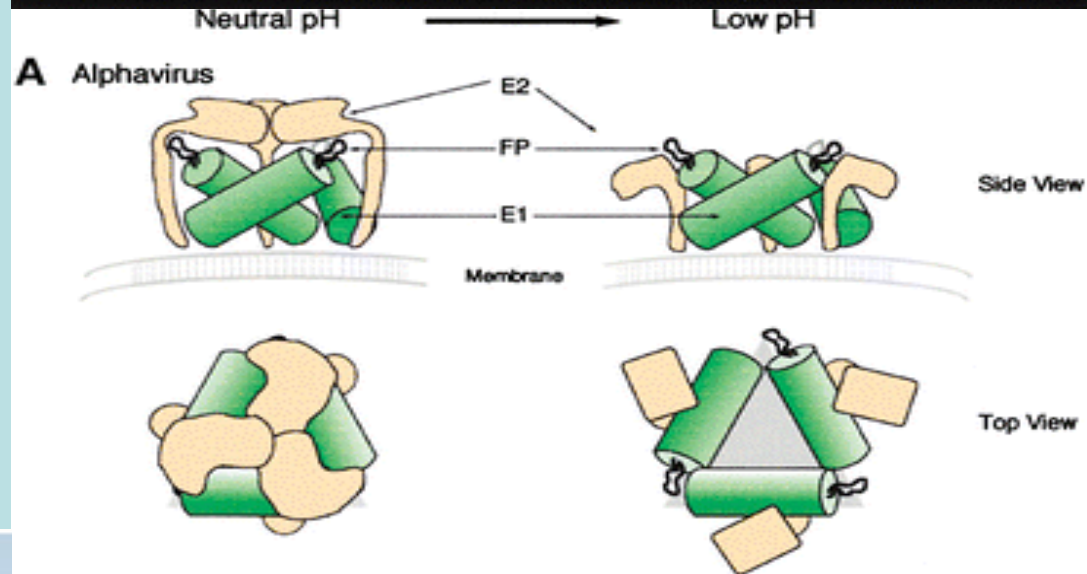
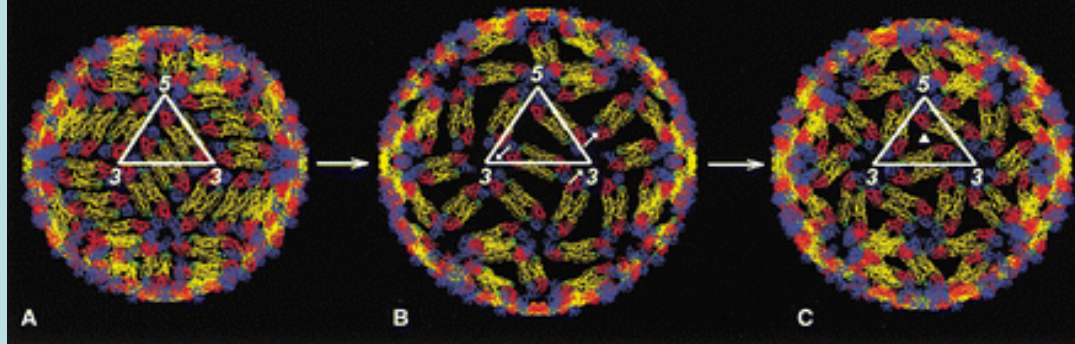


E protein of Flavivirus

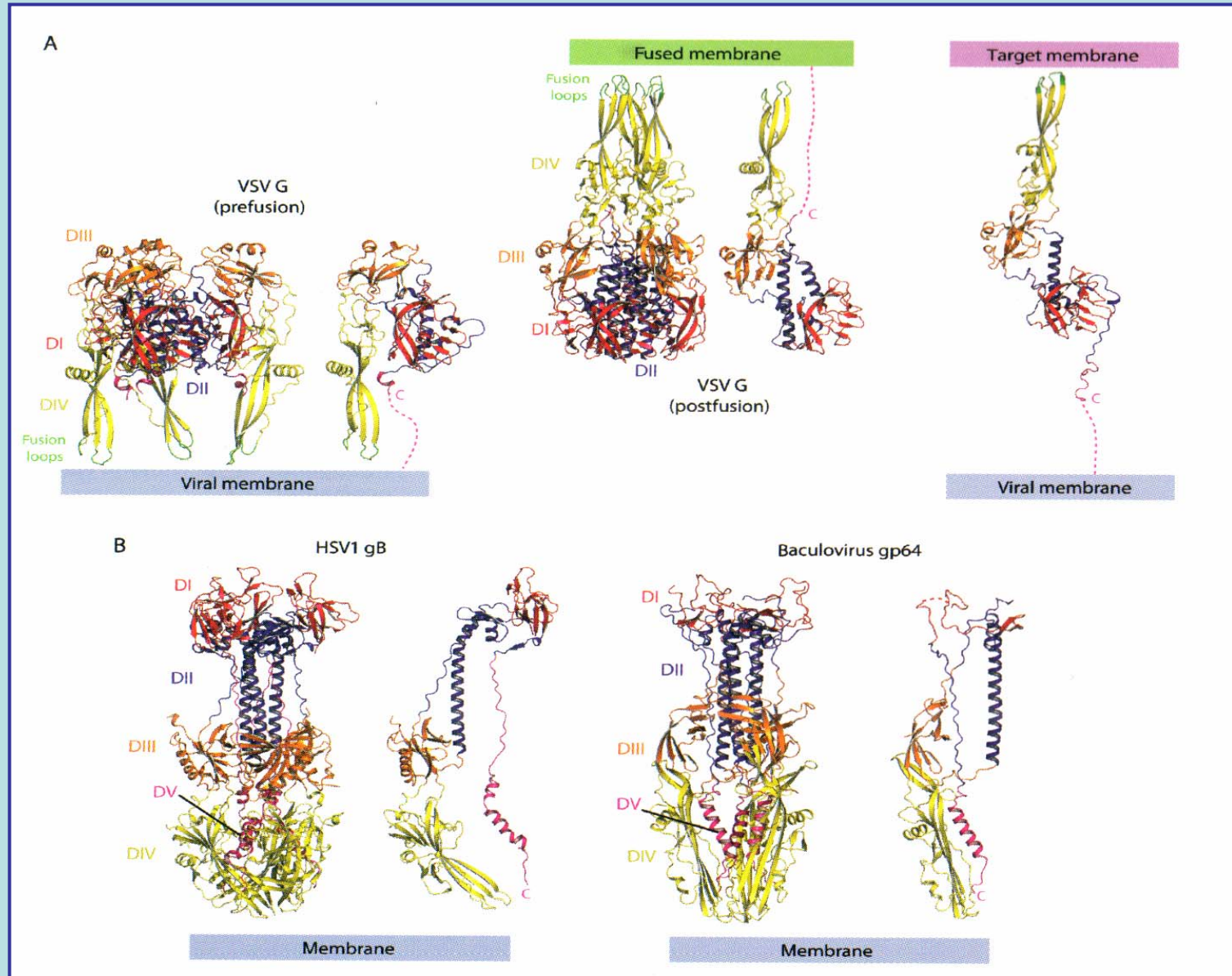


Transformation of E protein

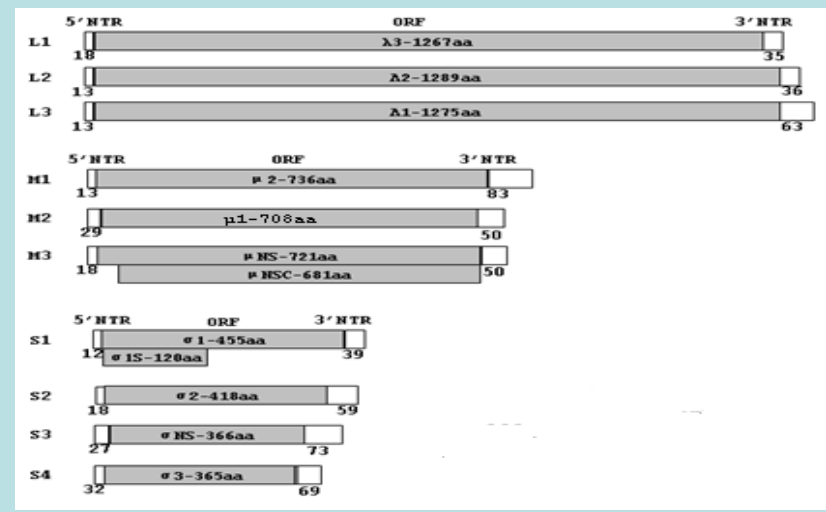
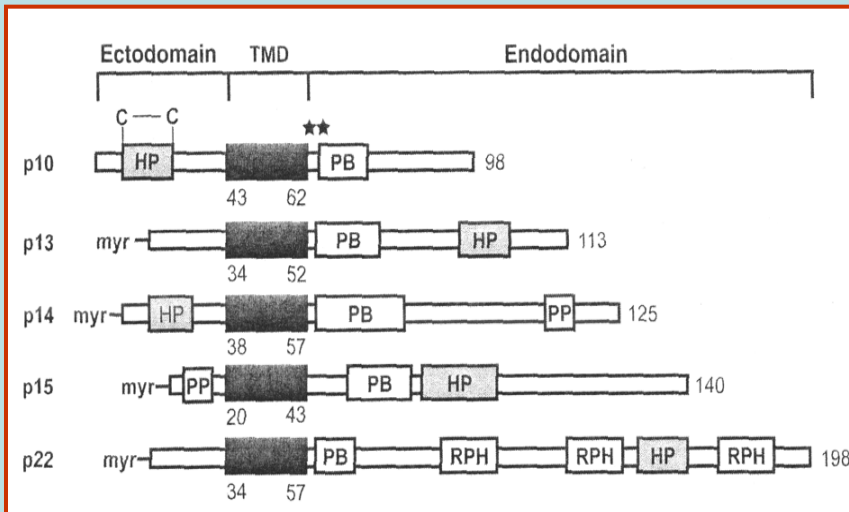
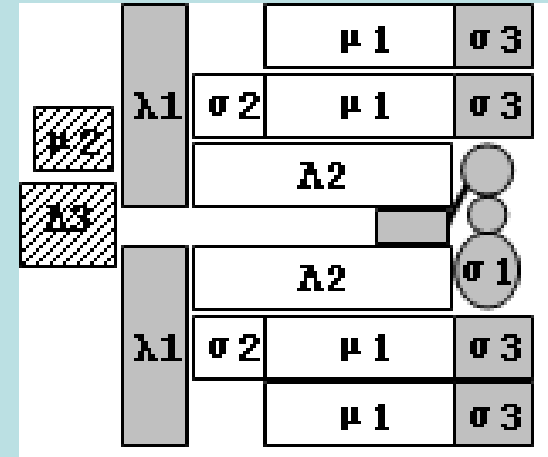
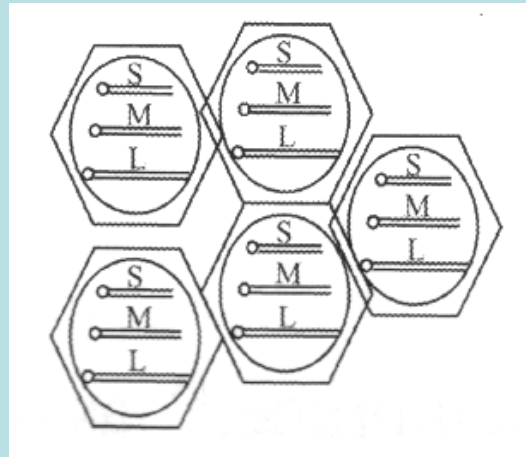
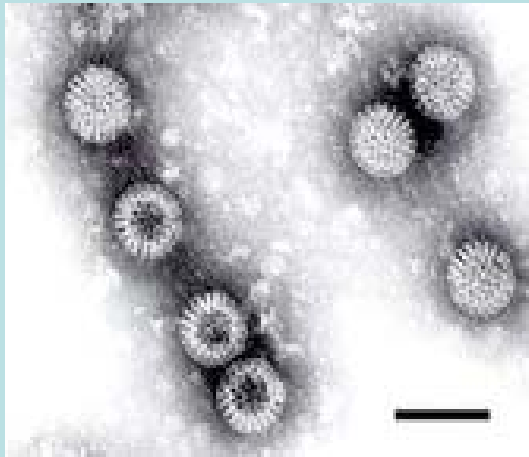
Dissociation of Dimer
 ↓ at low pH
 monomers
 (Exposure of FP)
 Lipid ↓
 Trimer



Class III fusion proteins

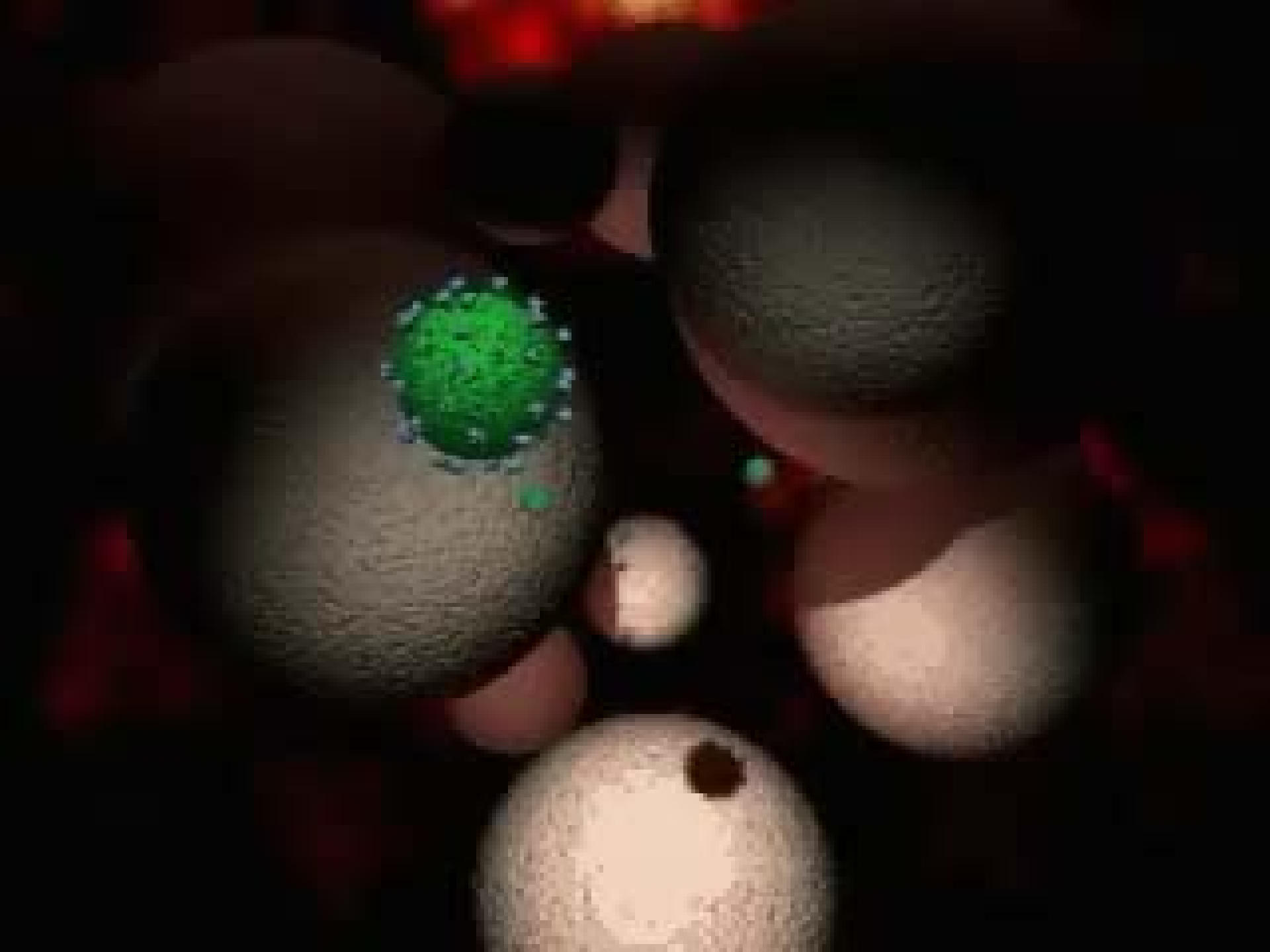


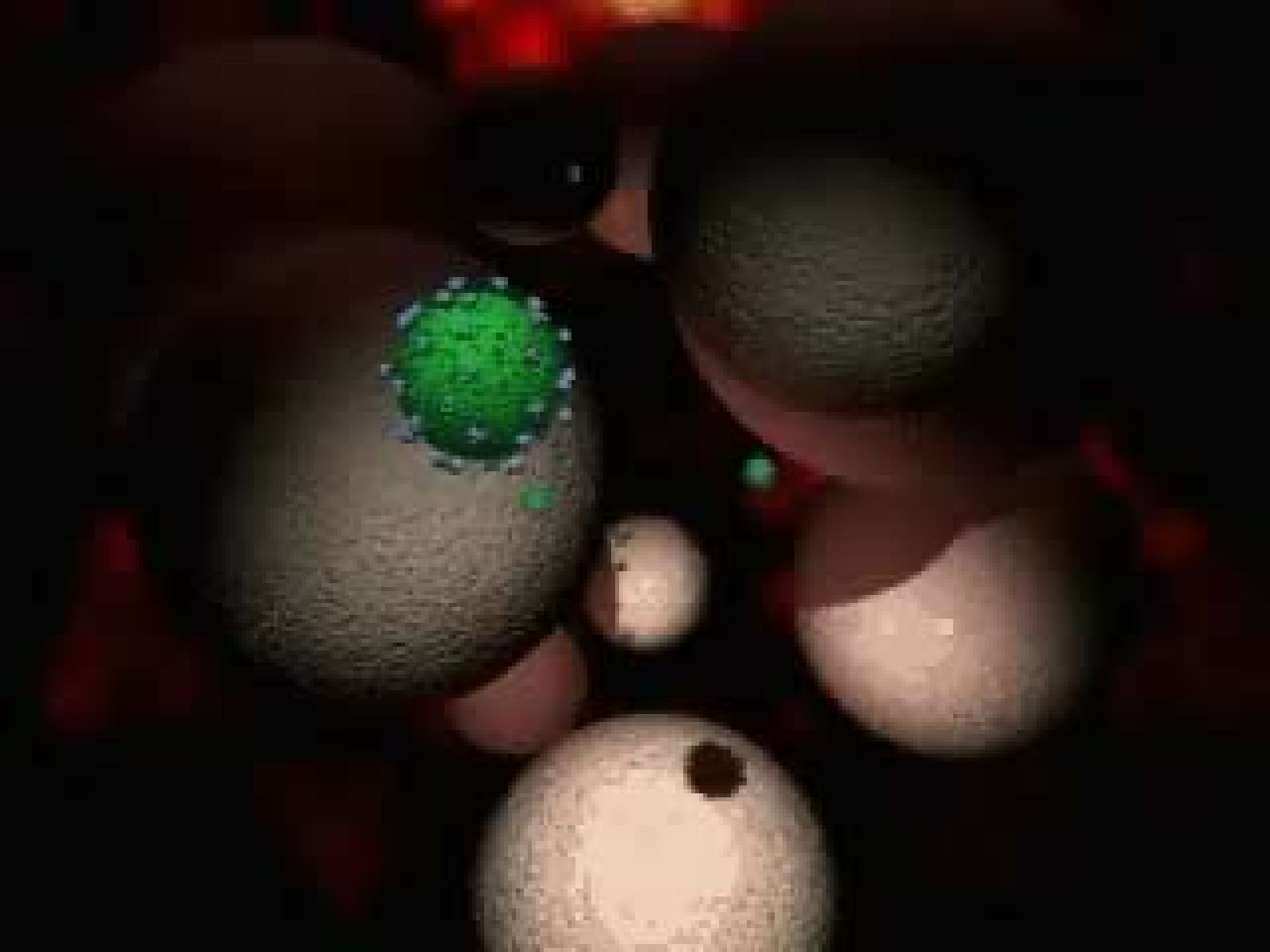
FAST Proteins of Reoviruses (Fusion-associated Small Transmembrane)



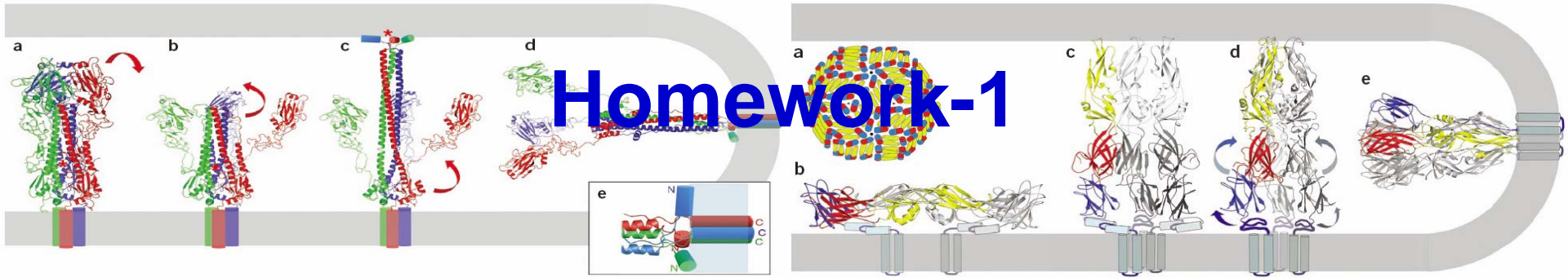
Cartoon show:

**Inhibition of membrane fusion :
A new target for antiviral therapy**



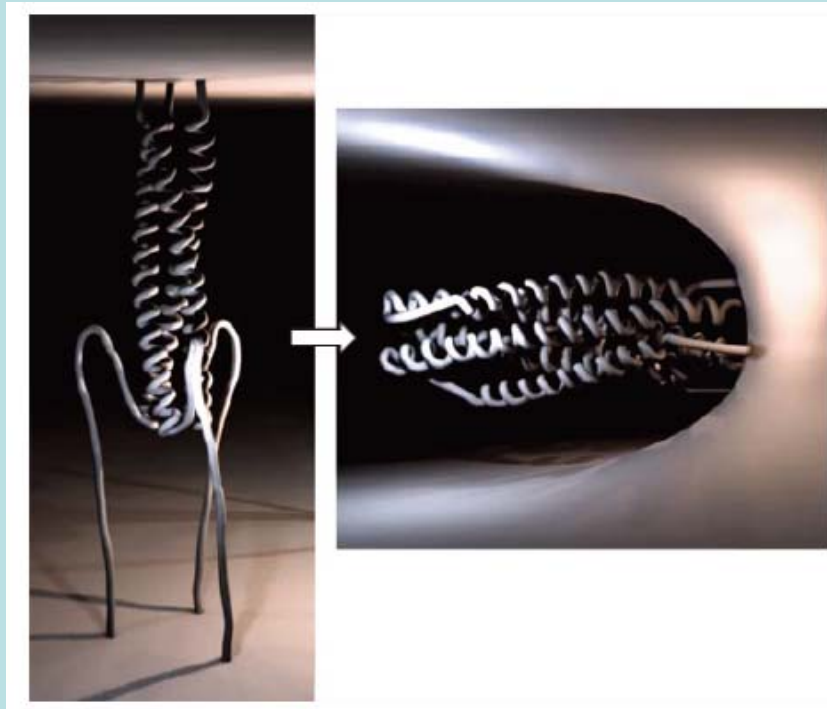


Homework-1



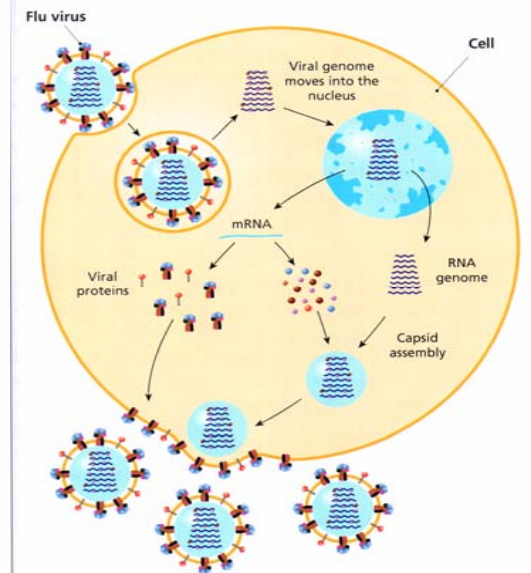
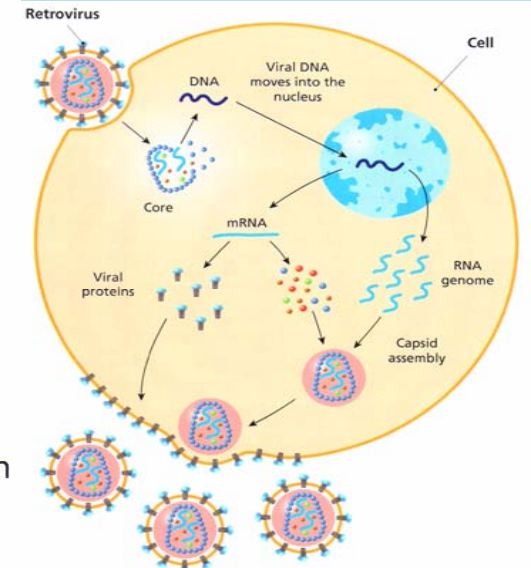
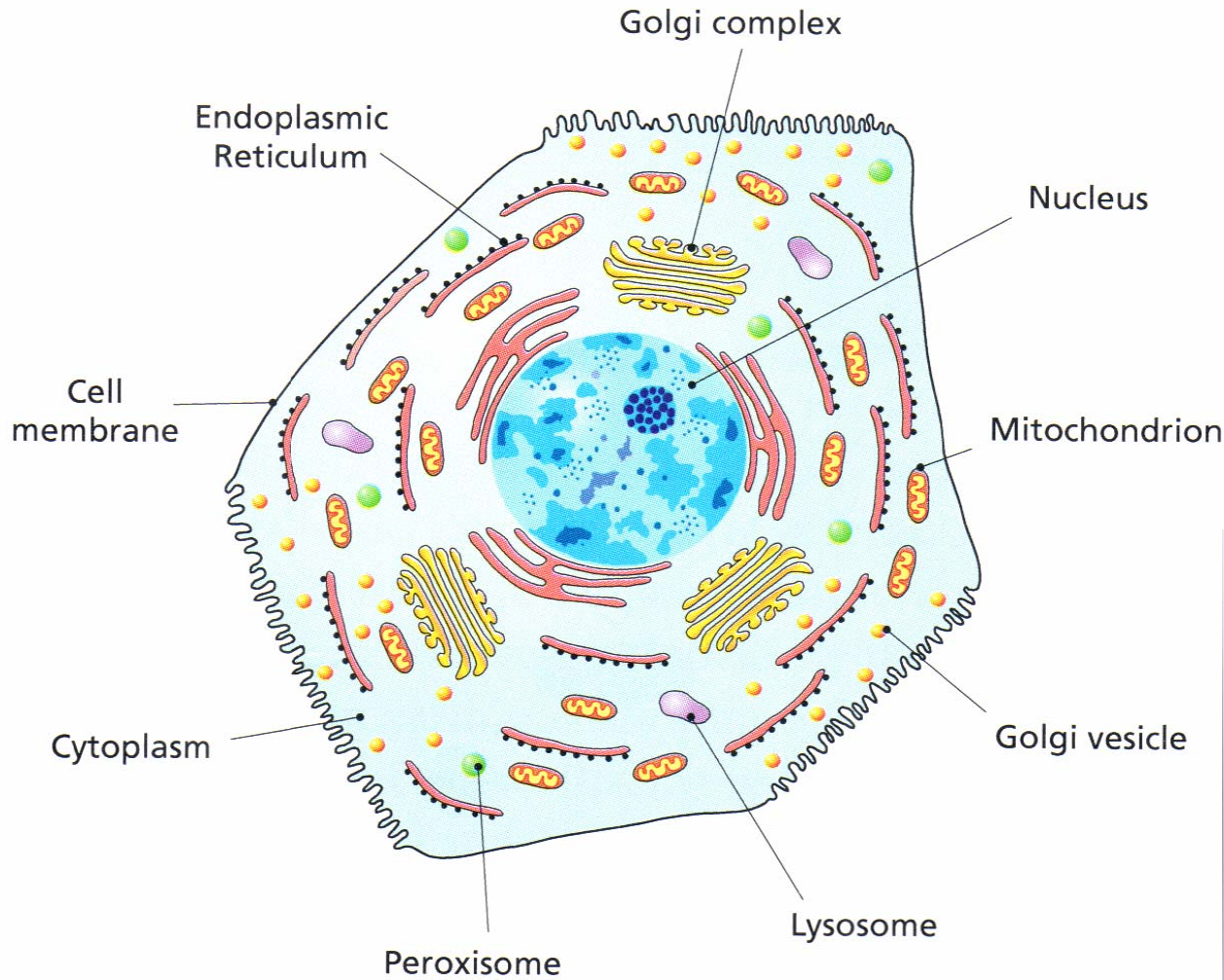
Stephen, C. Harrison (2008) : Viral membrane fusion.

Nat. Struct. & Mol. Biol. 15, 690-698

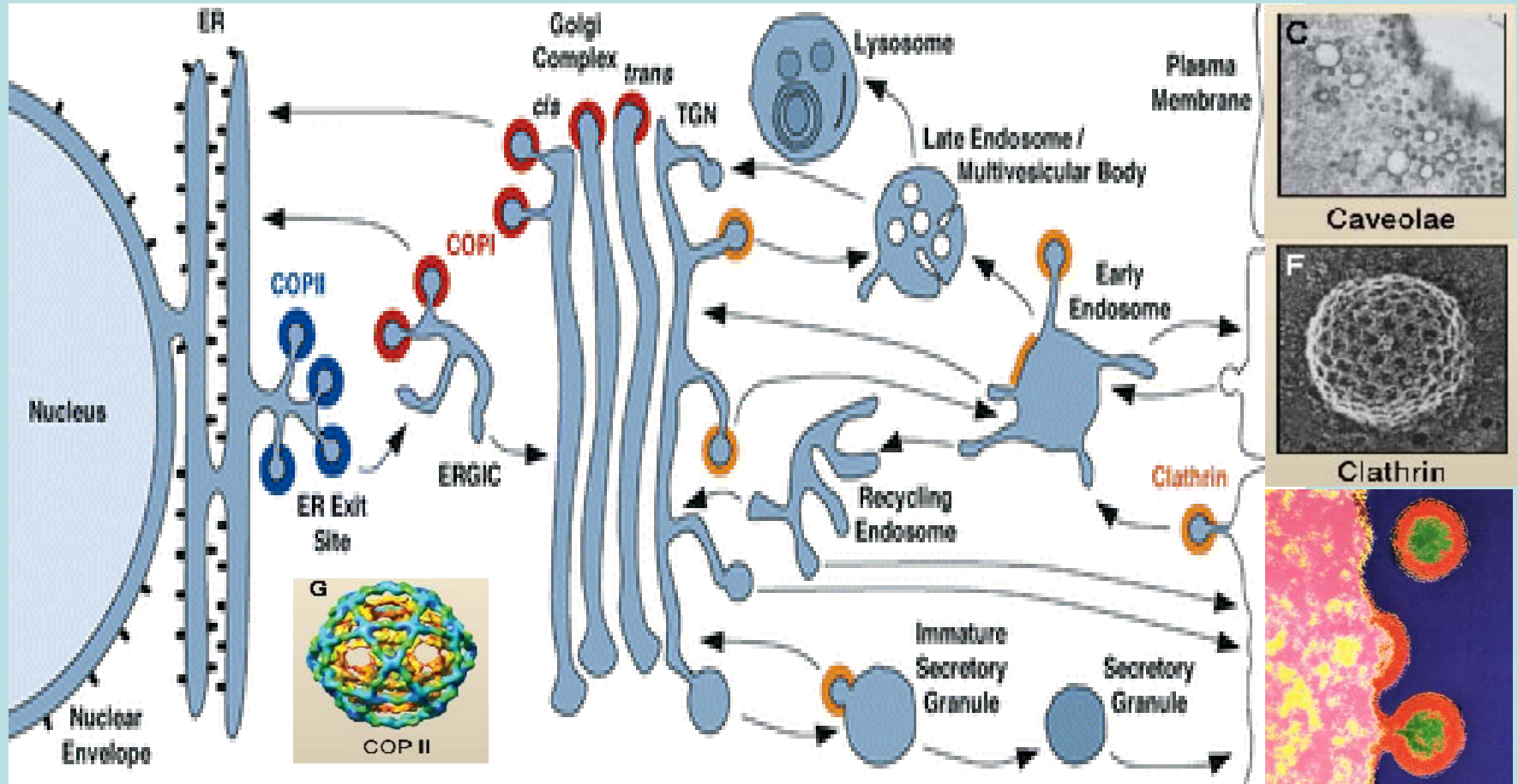


1. Introduction: Diversity of viruses and viral surfaces
2. Membrane fusion: A critical step of viral entry into the cell
3. Membrane budding: A major mode for the assembly of viral envelopes
4. Host receptor: A determinant of viral transmission

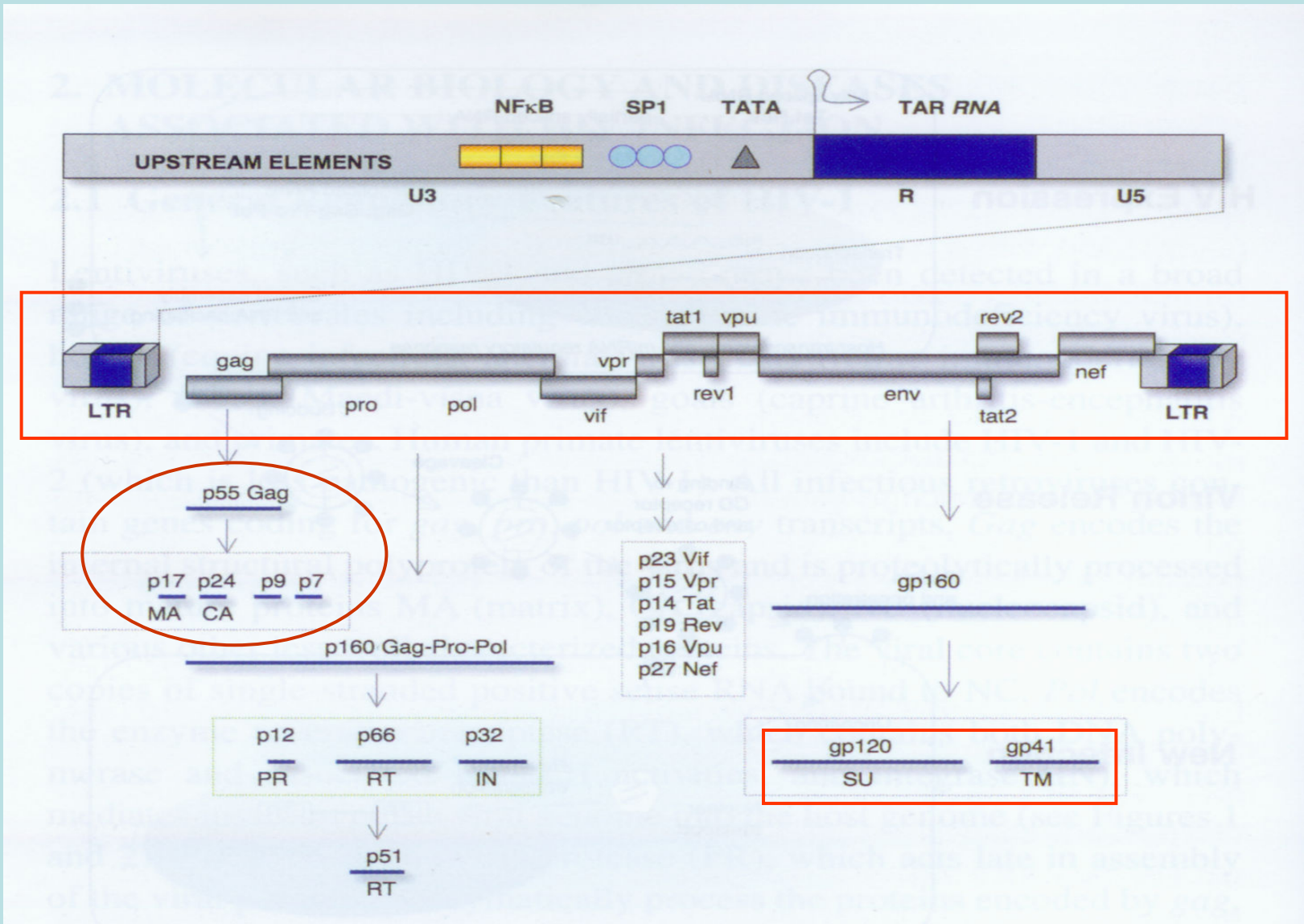
Cells and viral replication



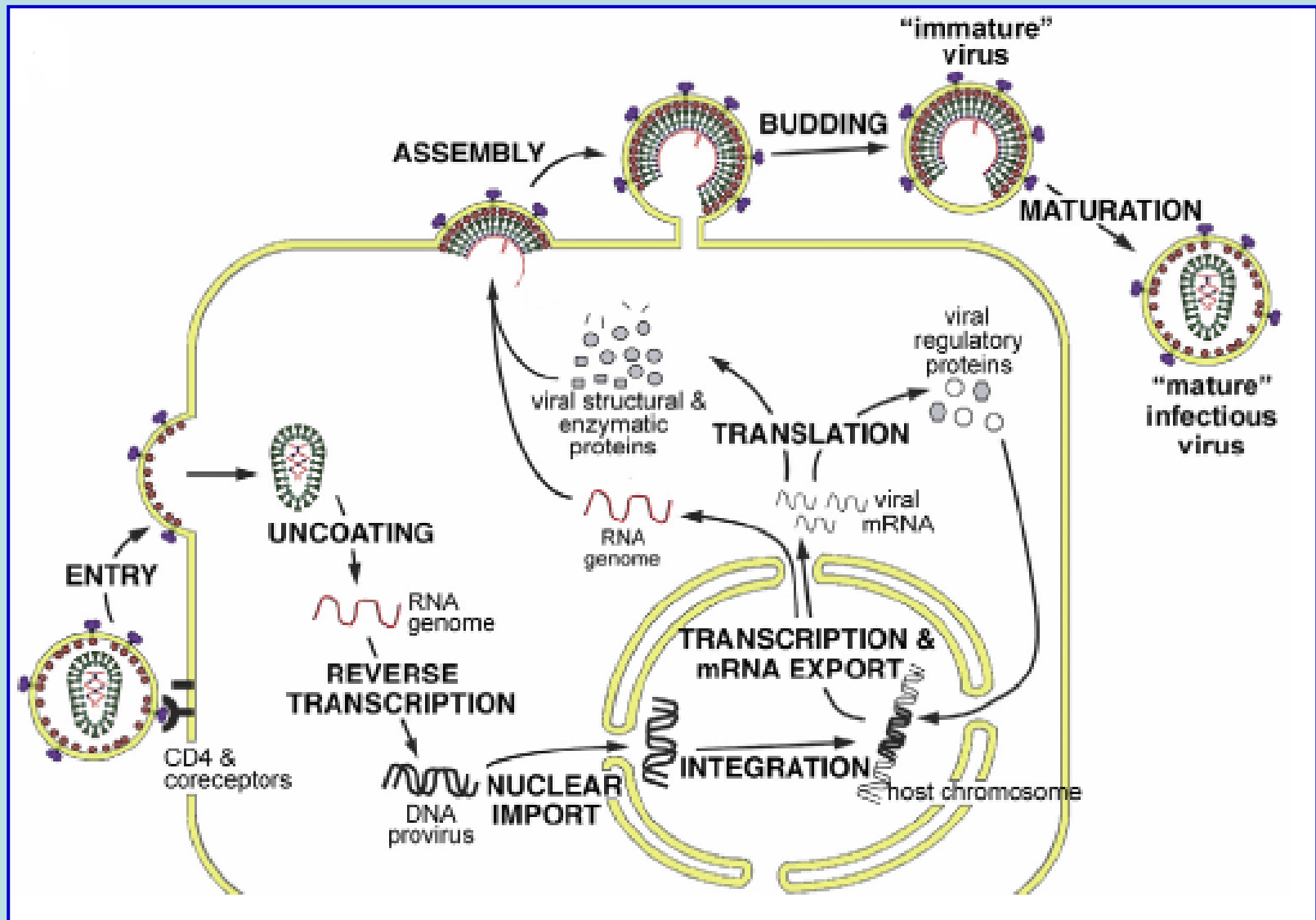
Trafficking of cellular and viral Proteins



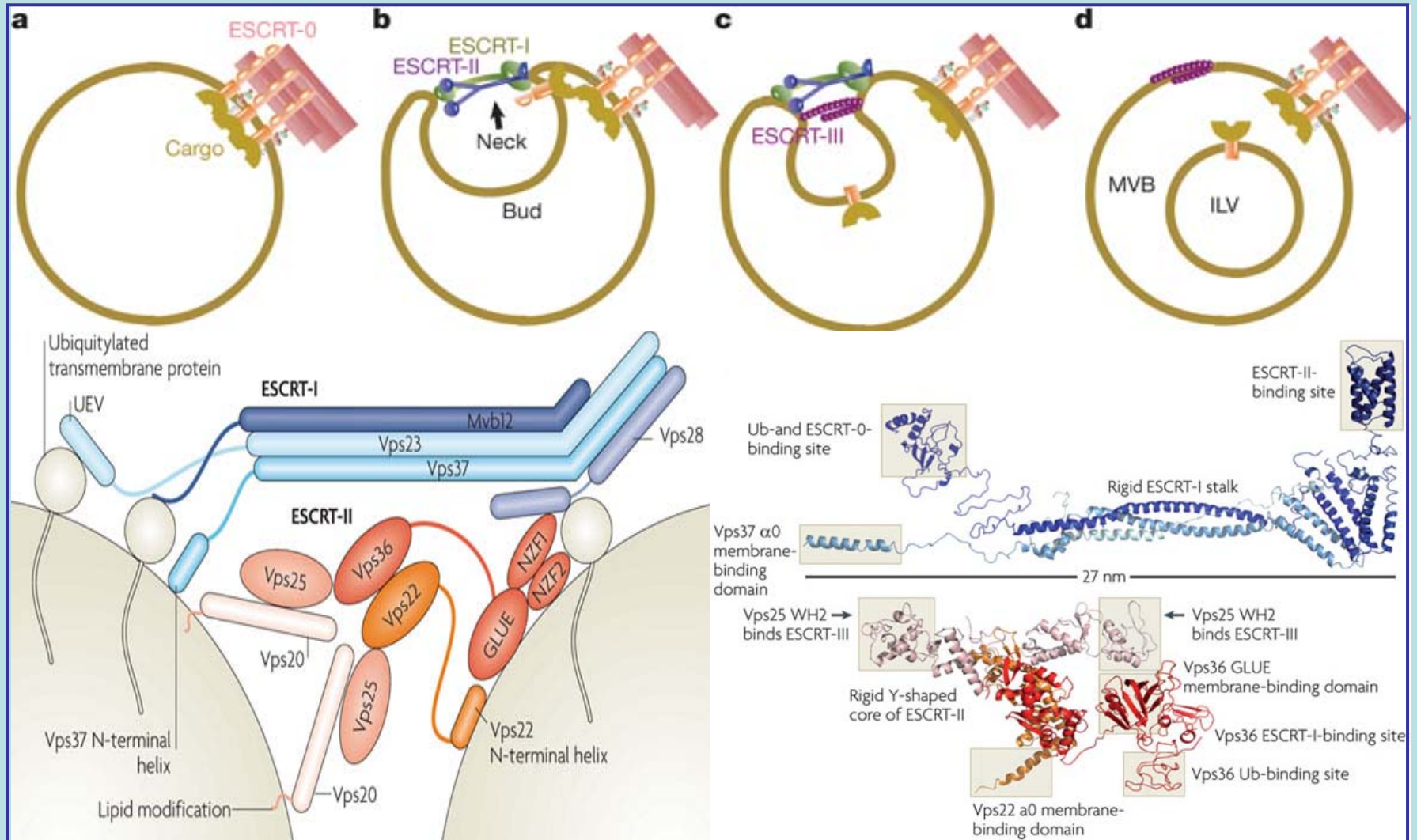
Genes and proteins of HIV



HIV Entry to and release from cells

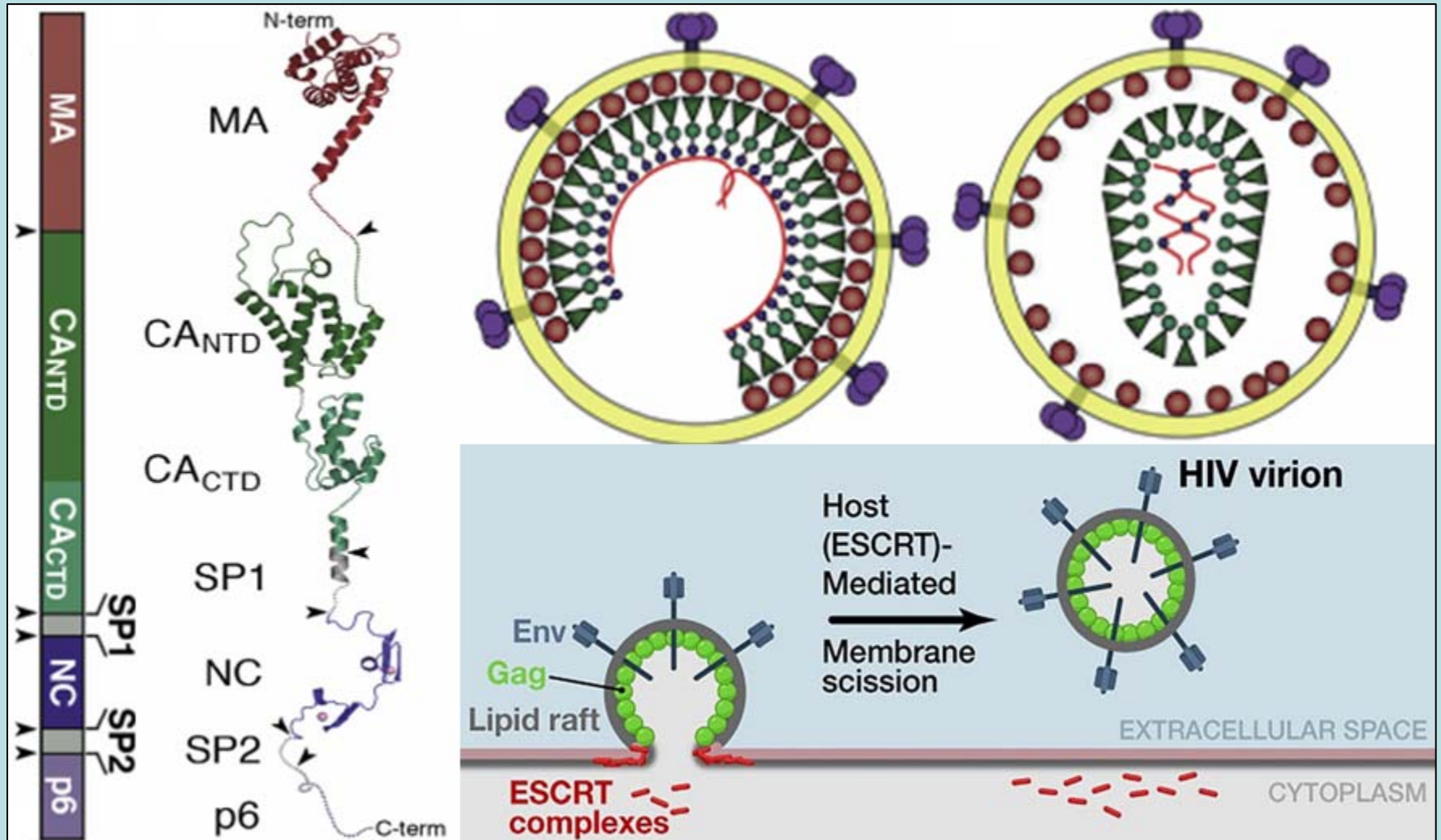


MVB and ESCRT

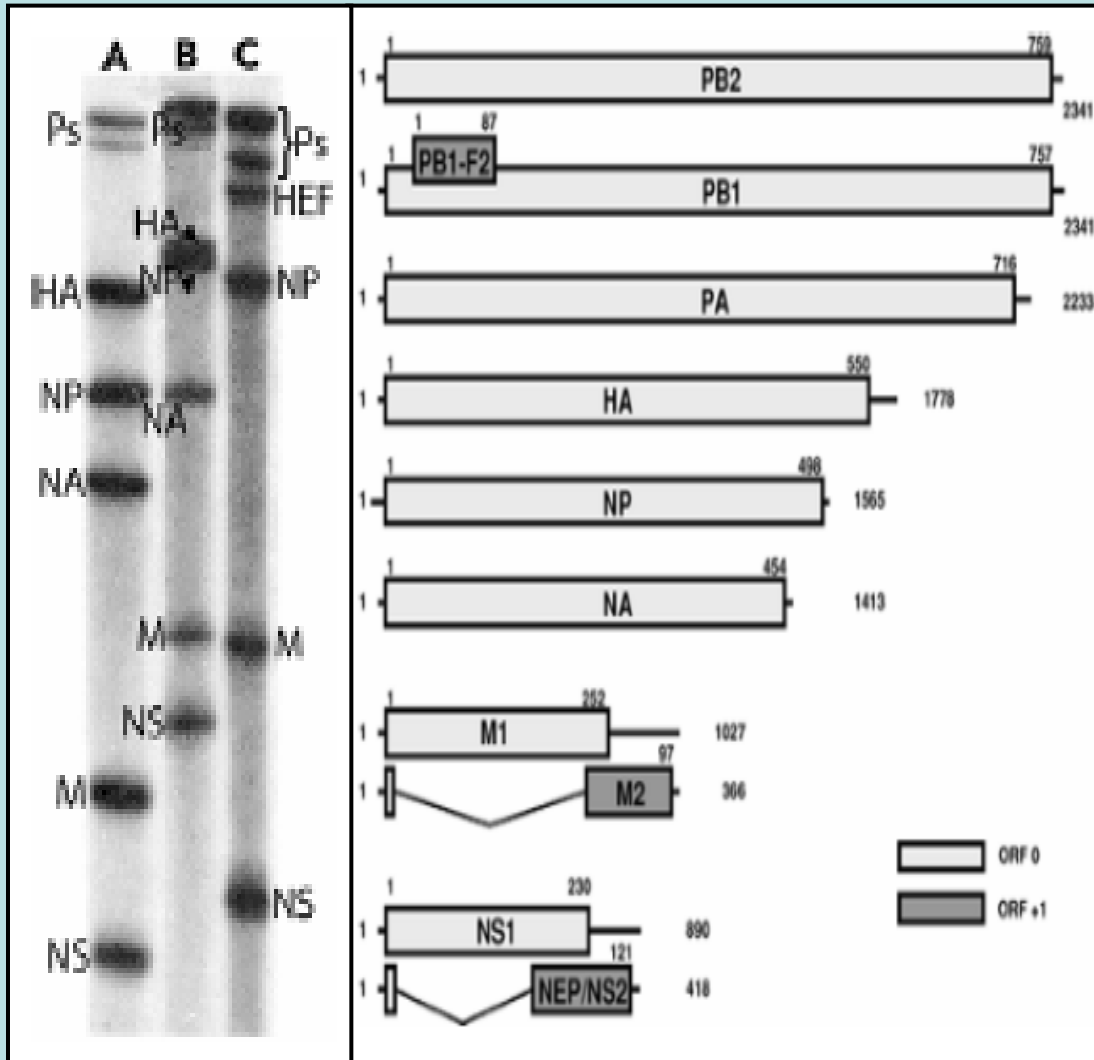


Multivesicular bodies (MVBs) and endosomal sorting complex required for transport (ESCRT)

Gag and HIV Assembly

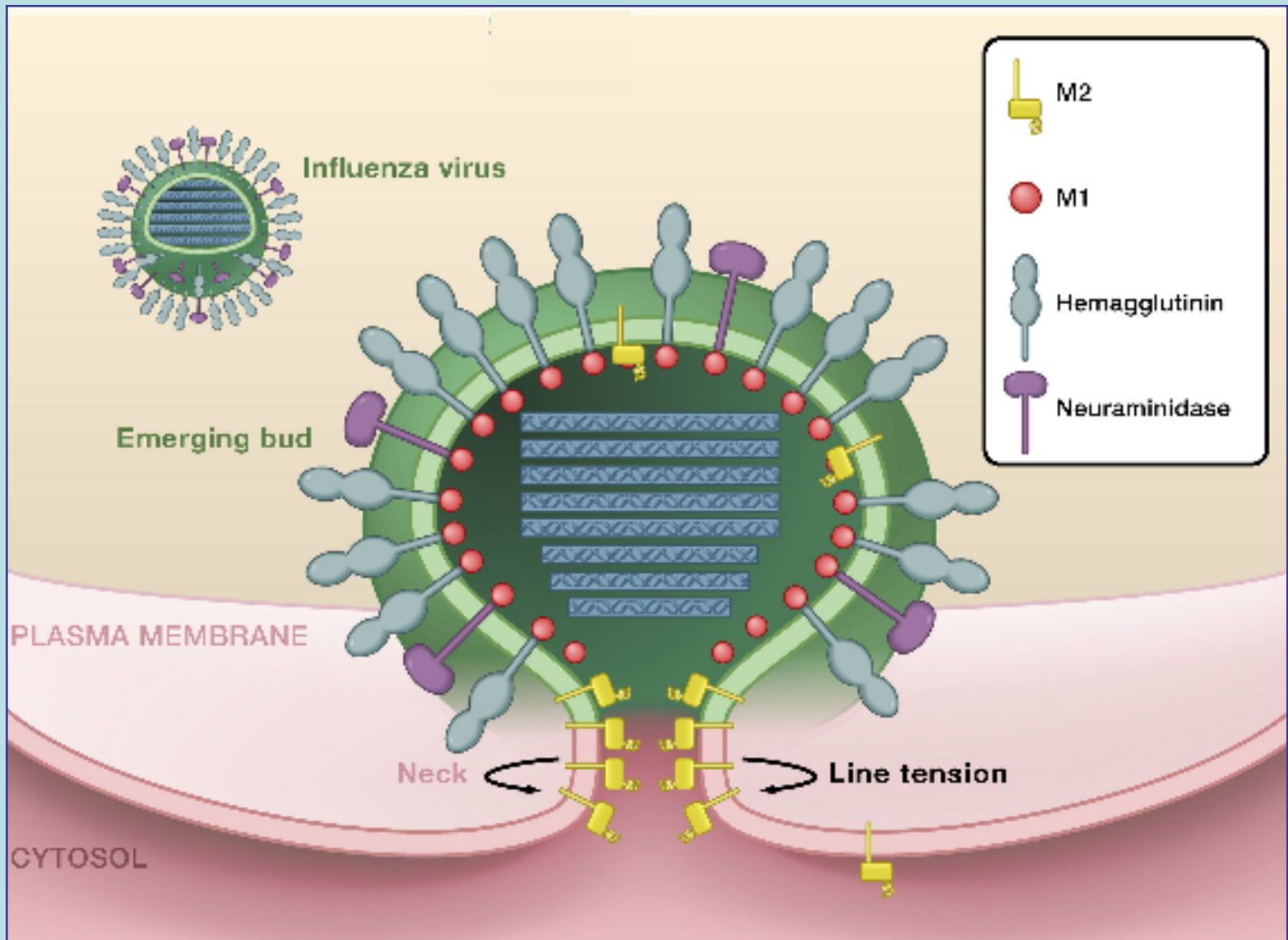


Genes and Proteins of Influenza Virus



- PB2** RNA聚合酶成分
- PB1** RNA聚合酶成分
- PA** RNA聚合酶成分
- HA** 与黏附, 融合等有关
- NP** 核衣壳蛋白
- NA** 分解唾液酸
- M1** 基质蛋白, 包膜和核蛋白
- M2** 膜蛋白, 离子通道蛋白
- NS1** 非结构蛋白, 抑制mRNA
- NS2** 非结构蛋白, 功能不清楚

Membrane Scission of Influenza Virus

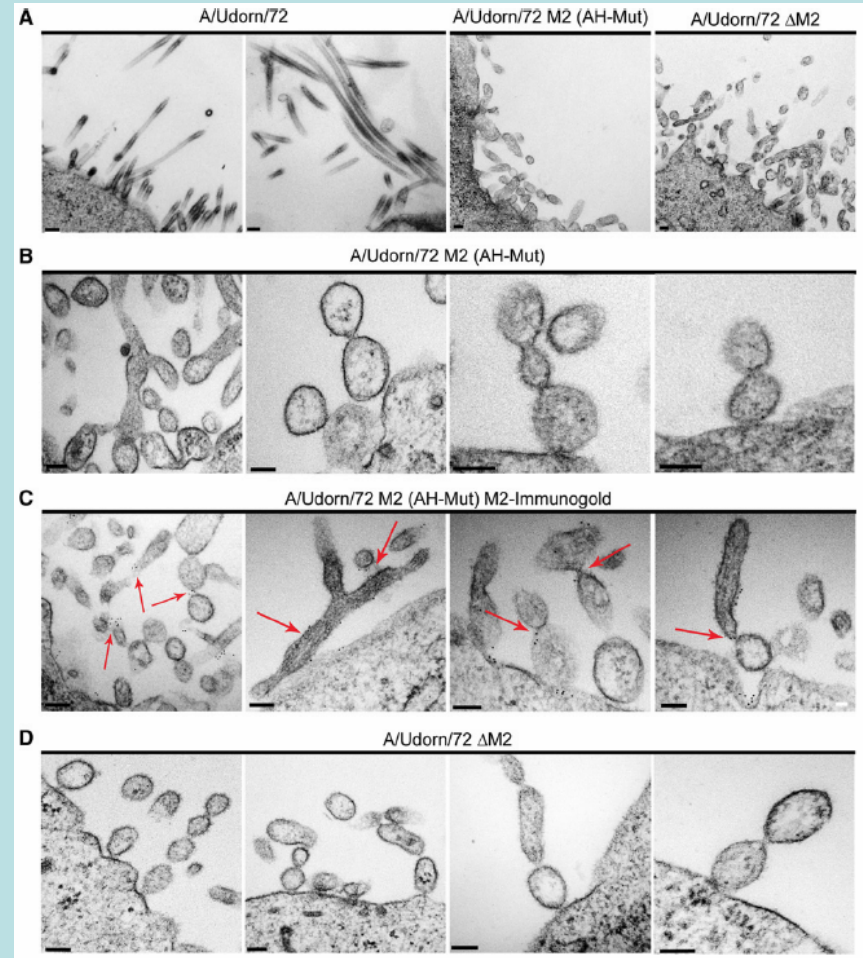


Homework-2

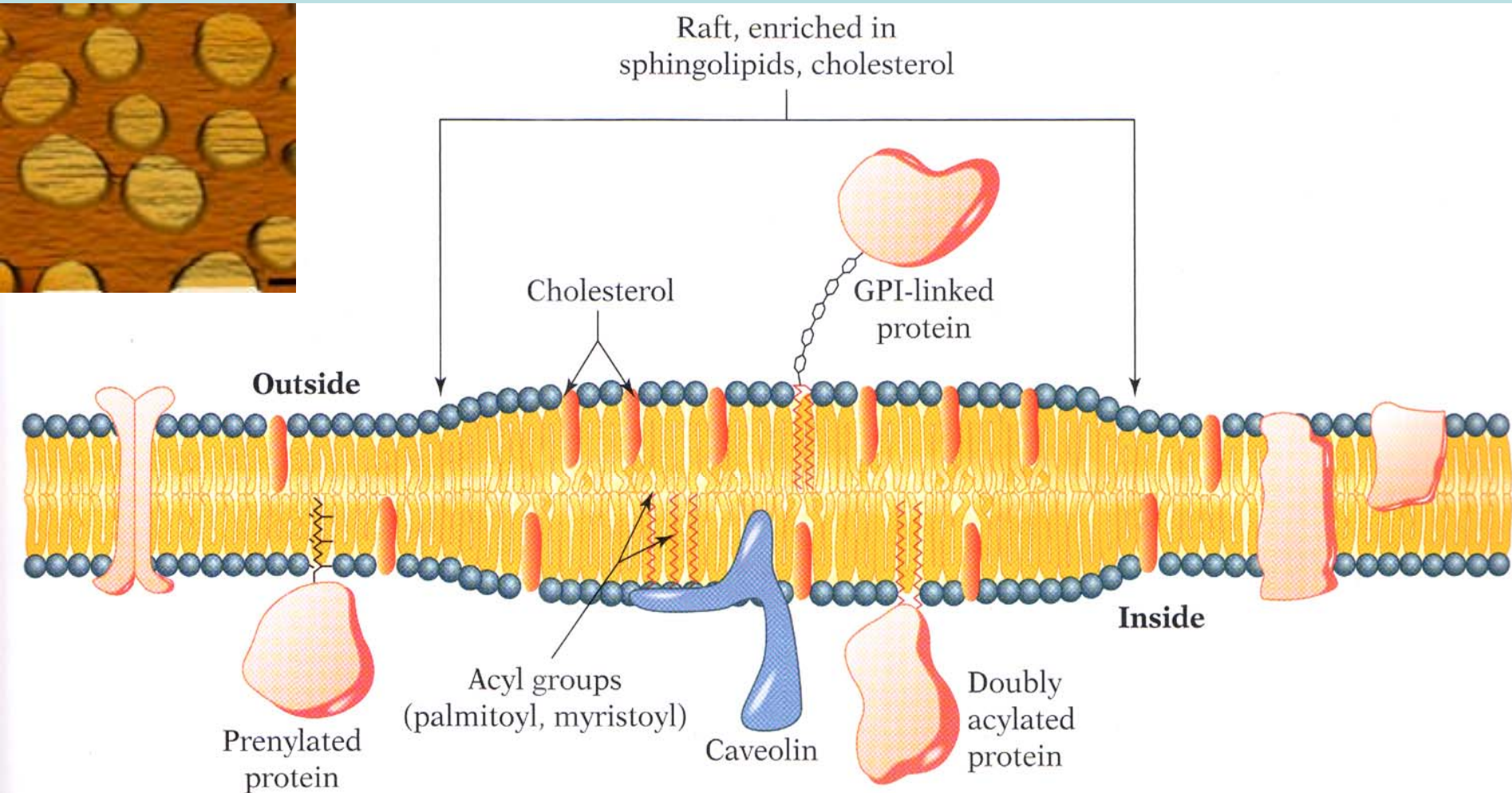
J.B. Rossman, X. Jing, G.P. Leser and
R.A. Lamb

Influenza Virus M2 Protein
Mediates ESCRT-Independent
Membrane Scission

CELL 142, 902–913, 2010

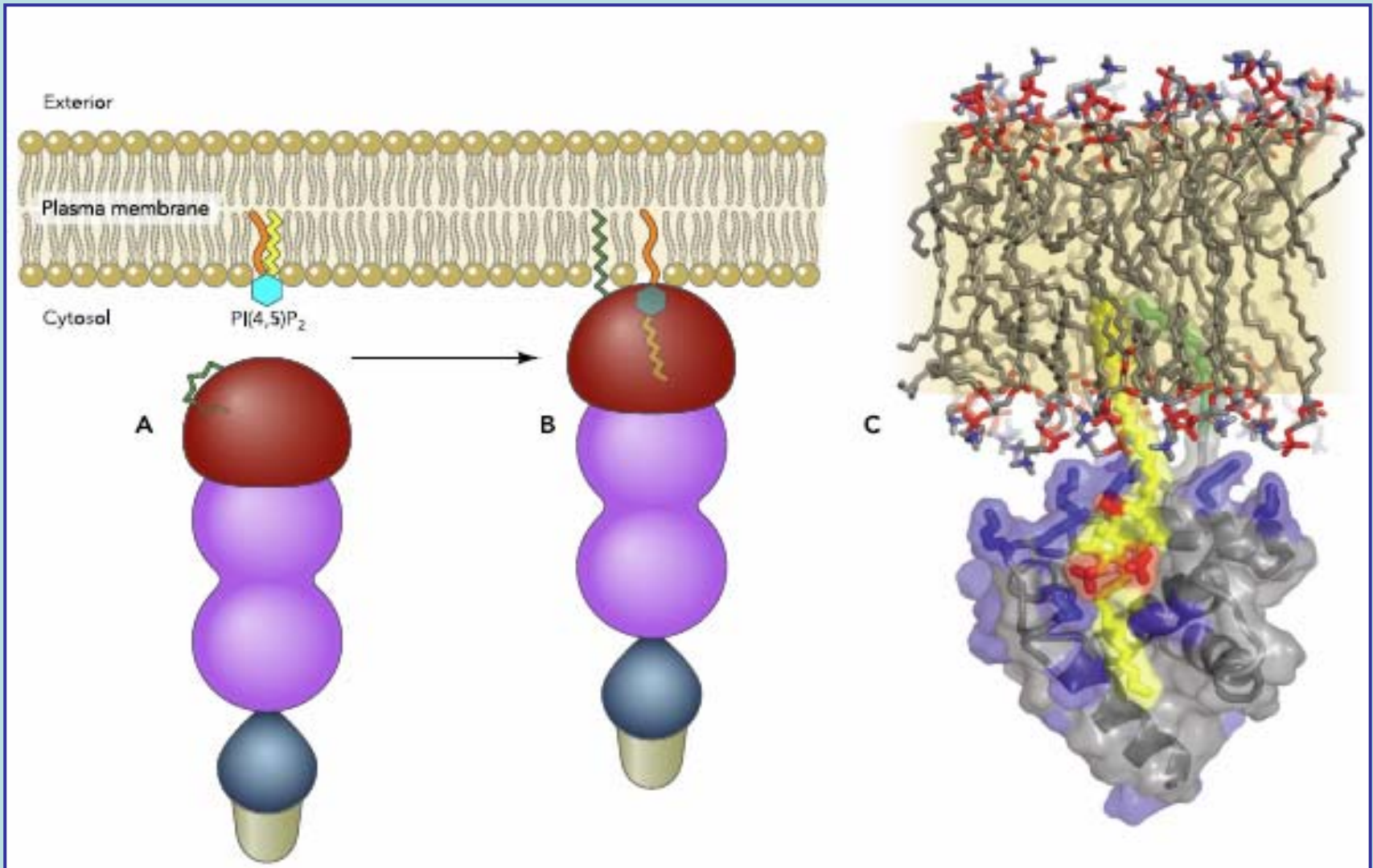


Lipid Rafts

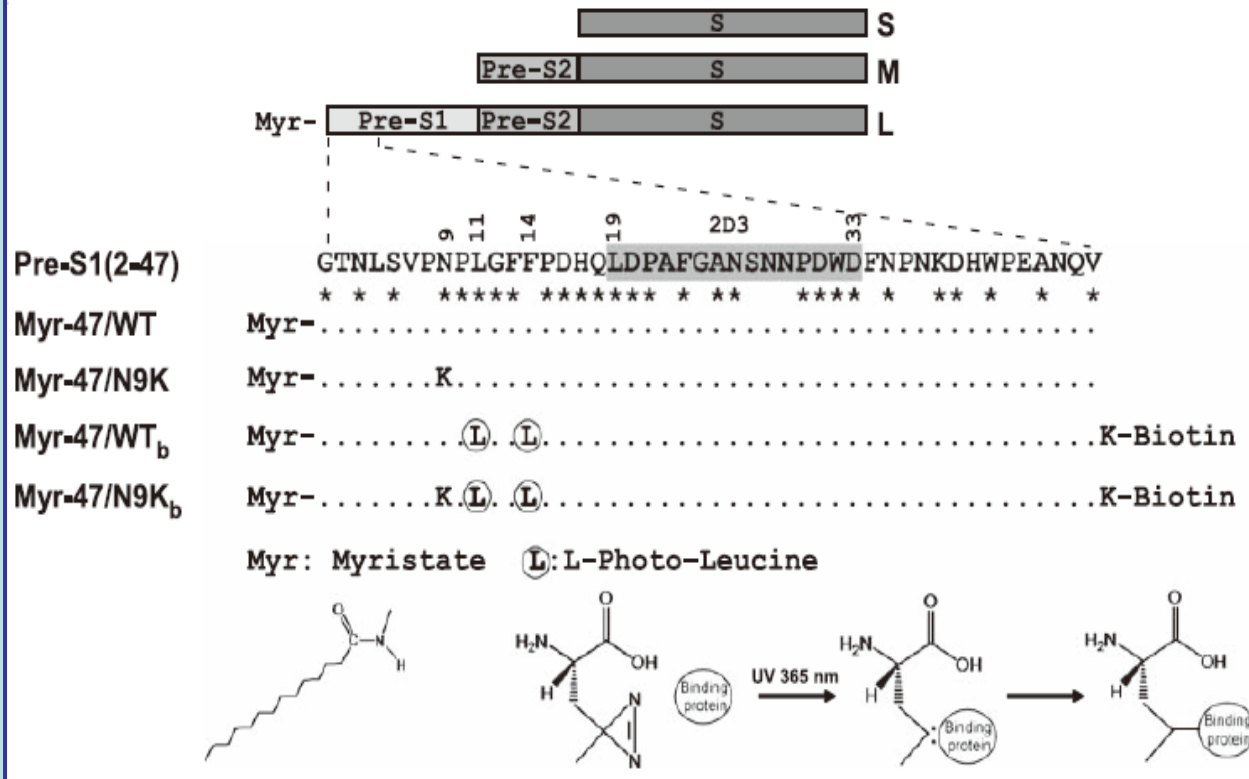
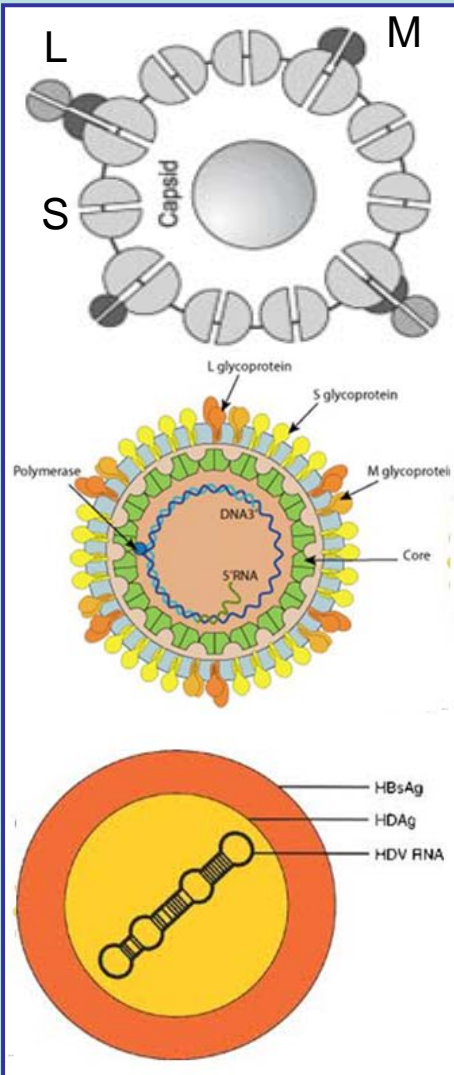


Lipid rafts. Membranes have stable but transient microdomains that are enriched in cholesterol and sphingolipids, along with glycosylphosphatidylinositol (GPI)-linked proteins and proteins anchored by acyl groups. From Nelson, D. L., and M. M. Cox (eds.), *Lehninger Principles of Biochemistry*, 4th ed., W. H. Freeman, 2005, p. 385. © 2005 by W. H. Freeman and Company.

MA protein interacts with lipids



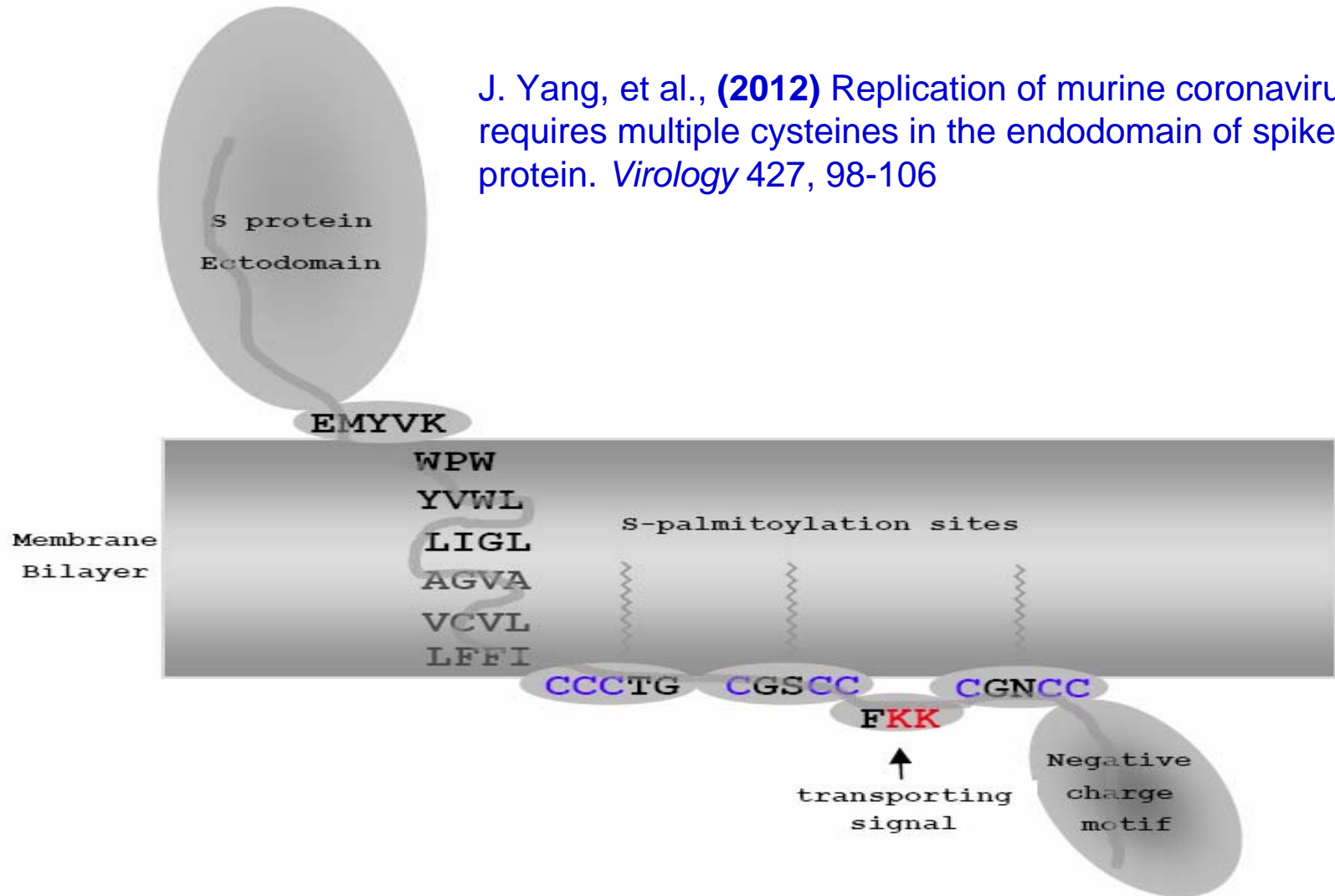
Myristoylation of HBV and HDV preS1



H. Yan, et al., (2012) Sodium taurocholate cotransporting polypeptide is a functional receptor for human hepatitis B and D virus. *eLife*,1:e00049

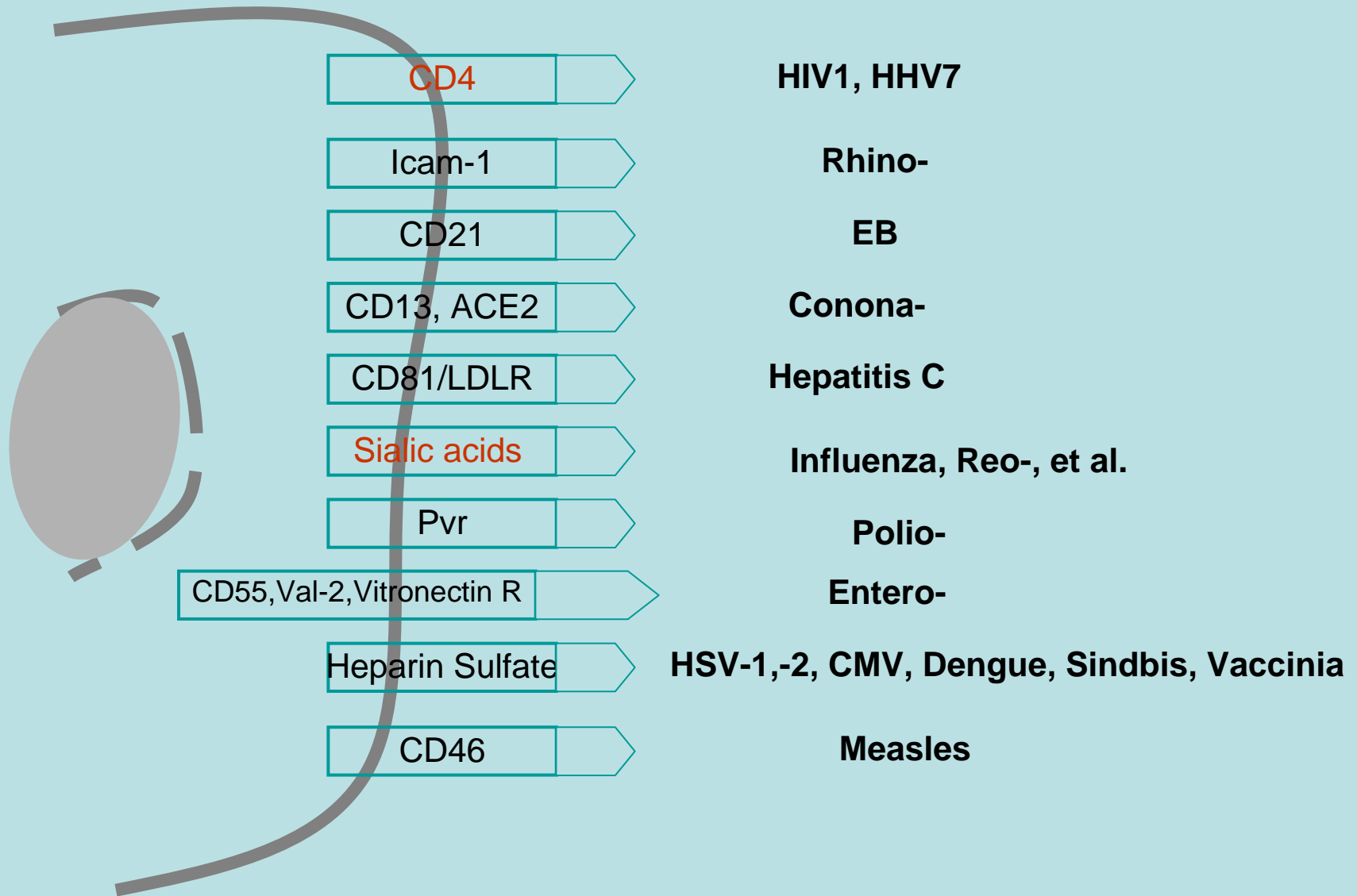
Palmitoylation of MHV S protein

J. Yang, et al., (2012) Replication of murine coronavirus requires multiple cysteines in the endodomain of spike protein. *Virology* 427, 98-106

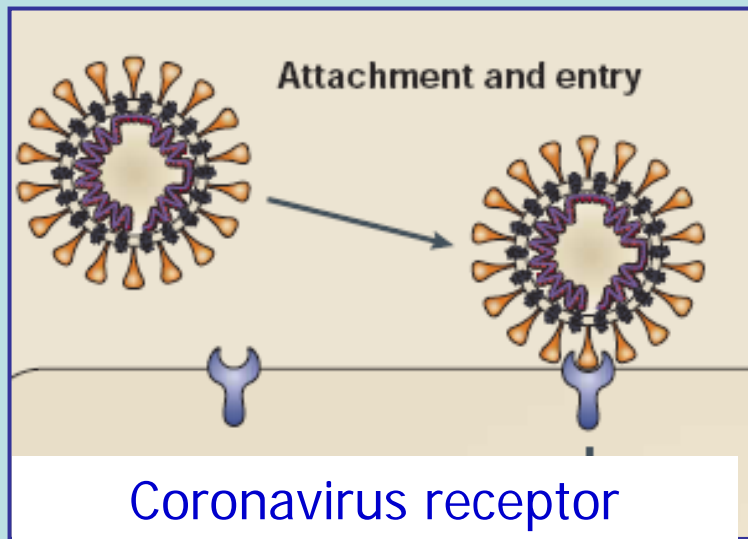


- 1. Introduction: Diversity of viruses and viral surfaces**
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- 4. Host receptor: A determinant of viral transmission**

Diversity of Viral Receptors



Specificity of Viral receptor



H 高特异性受体

CEACAMs (Carcinoembryonic antigen-related cell adhesion molecules): **MHV**

ACE2 (Angiotensin-converting enzyme 2): **SARS-CoV and HCoV-NL63**

DPP4 (dipeptidyl peptidase 4): **HCoV-EMC**

M 中等特异性受体

APN (Aminopeptidase N):

Human APN: **HCoV-229E**

Porcine APN: **TGEV**

Canine APN: **CCoV**

Feline APN: **FCoV**

Alpha-coronaviruses

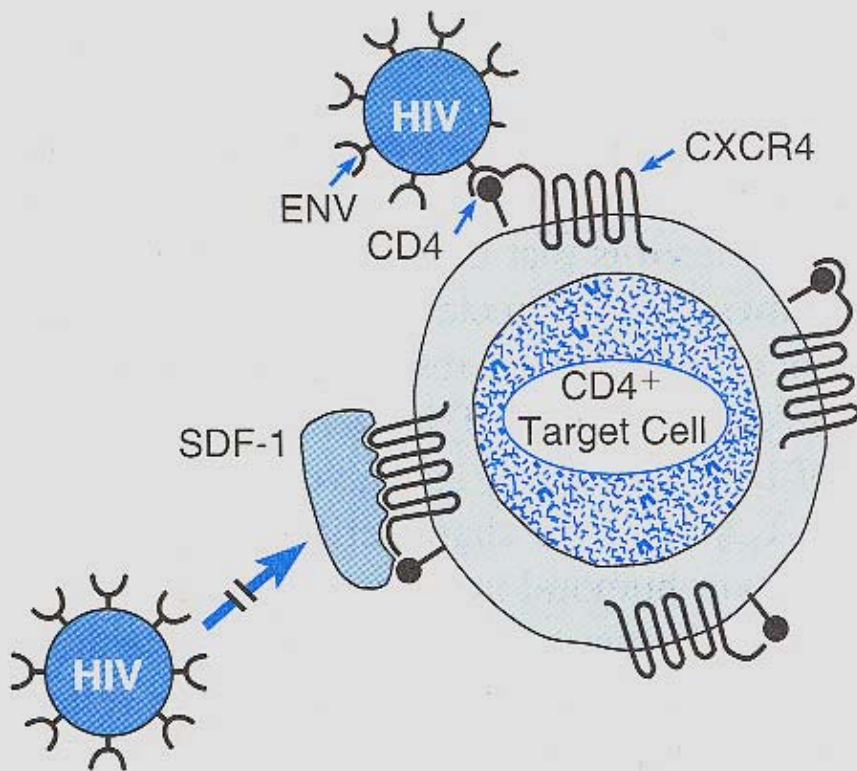
L 低特异性受体

DC-SIGN:

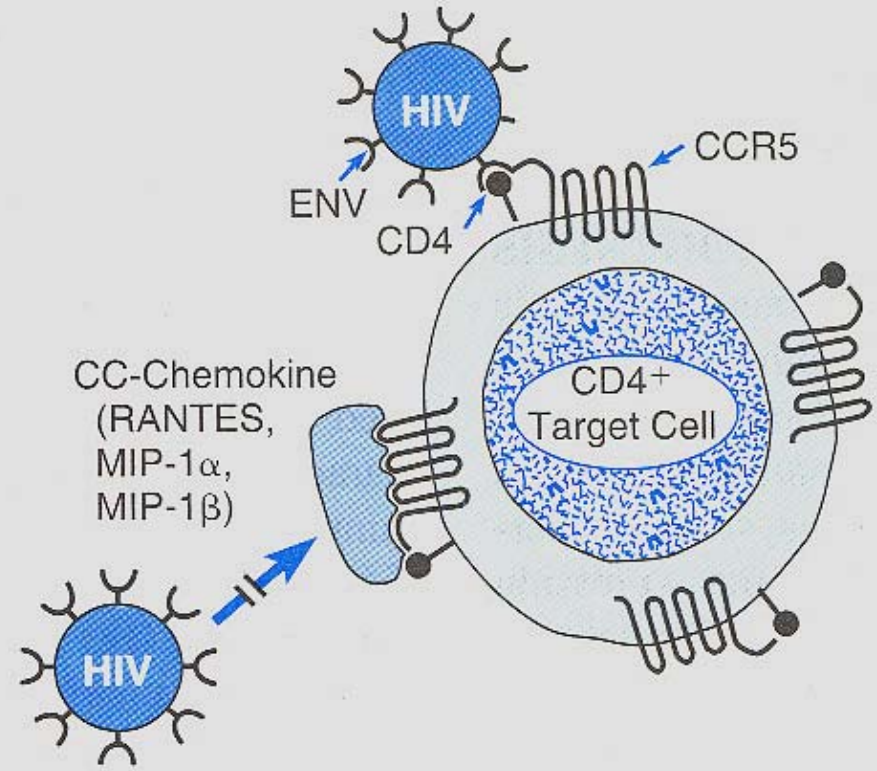
the calcium-dependent (C-type) lectin dendritic cell-specific intercellular adhesion molecule-3 grabbing non-integrin (CD209)

L-SIGN (DC-SIGNR): DC-SIGN related protein (CD299)

HIV Co-receptor: CXCR4 and CCR5



X4 (T-Tropic) Strain of HIV-1

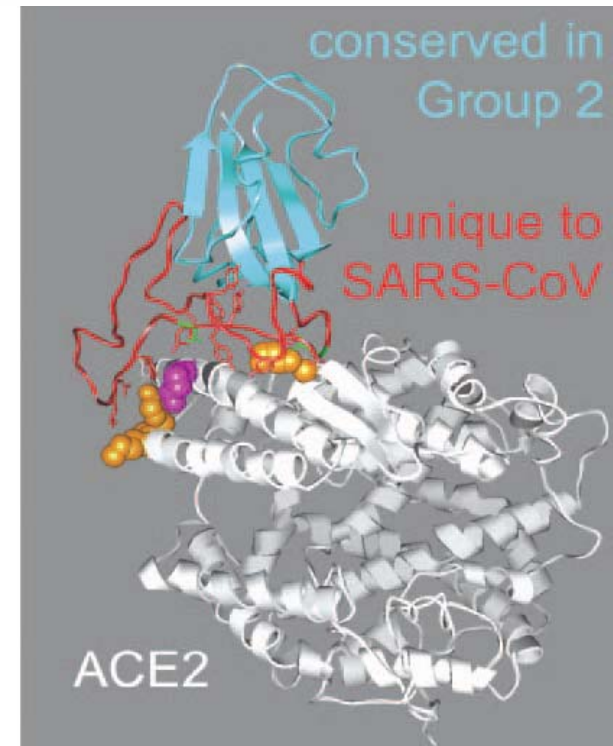
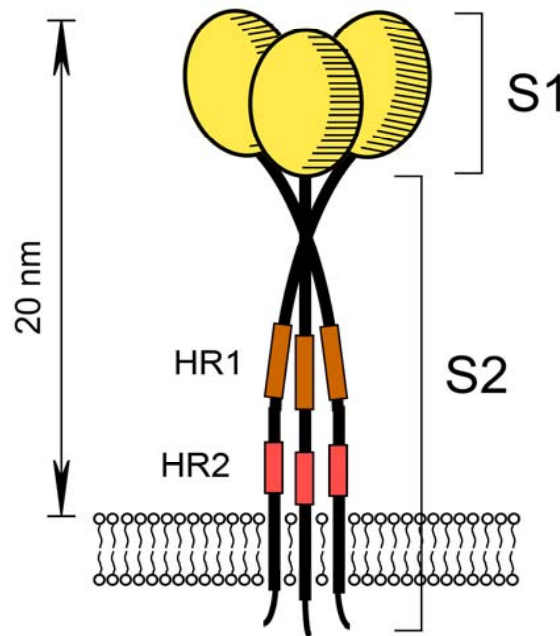
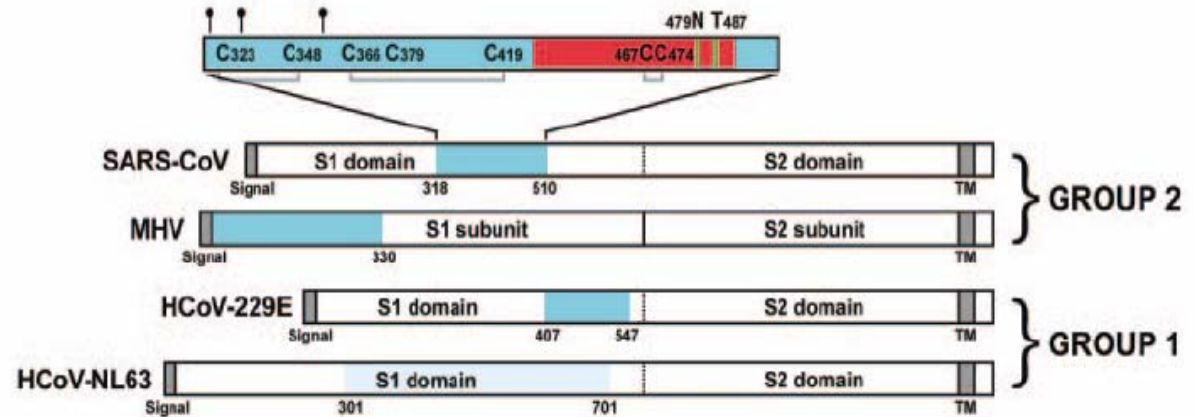
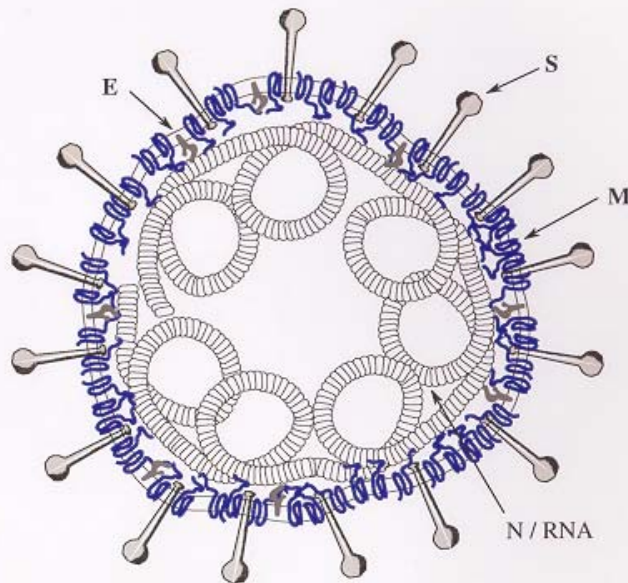
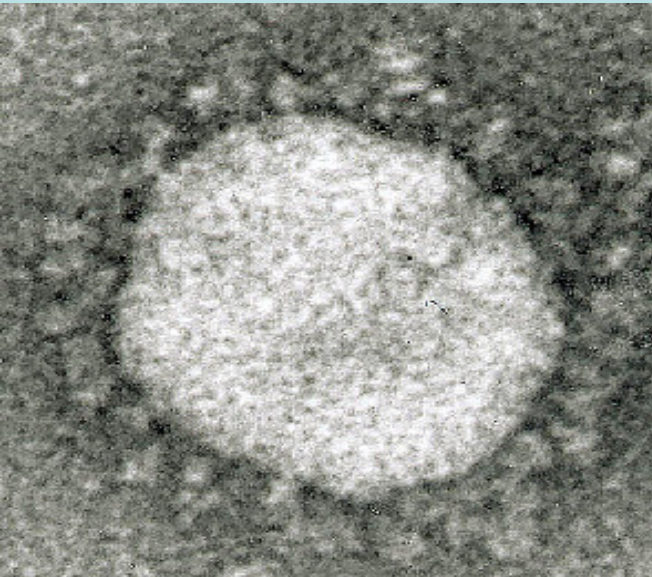


R5 (M-Tropic) Strain of HIV-1

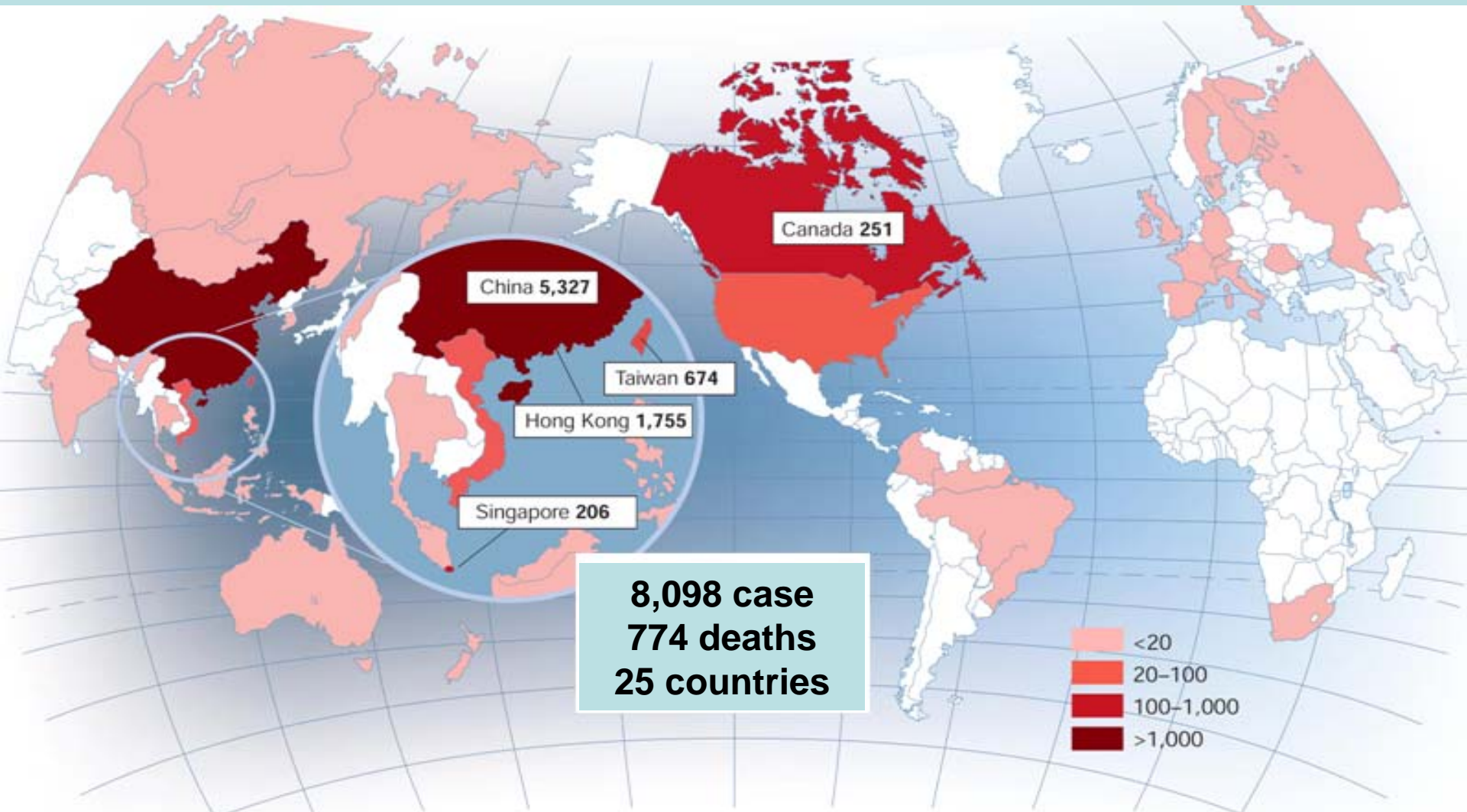
Viroceptor and Virokine

- **Virus-encoded homolog of cellular receptors of cytokines**
 - Vaccinia virus-**B8R/B18R**: receptor for IFN- γ / α
 - Cowpox virus-**crmB/D**: binding to TNF- α / β , LT- α
 - Variola virus-**vCKBP**: binding to virious chemokines
 - Human herpesvirus-6-**U12/U51**: binding to various chemokines
 - Epstein-Barr virus-**BARF1**: binding to M-CSF
 - Maxoma virus-**T2/T7**: binding to IFN- γ / β
 - Cytomegalovirus-**US28**: binding to various chemokines
- **Virus-encoded mimics of host cytokine**
 - **Small and powerful immune proteins**
 - **Possess immunosubversive activities**
 - **These viral genes are from host cells**
 - Vaccinia virus-**19 kDa protein**: EGF
 - Cowpox virus-**38K gene**: Inhibitor of IL1 β Convertase
 - KSHV: **Viral IL6/Viral MIP-1,2,3**
 - Epstein-Barr virus-**BCRF1**: viral IL10
 - Maxoma virus-**SERP1/2**:Inhibitor of IL1 β Convertase
 - Cytomegalovirus-**CMV IL10**
 - Orf virus-**14.7/16 kDa protein**: VEGF
 - HIV-**tat protein**: VEGF, integrin, chemokines

Coronavirus and S protein RBD

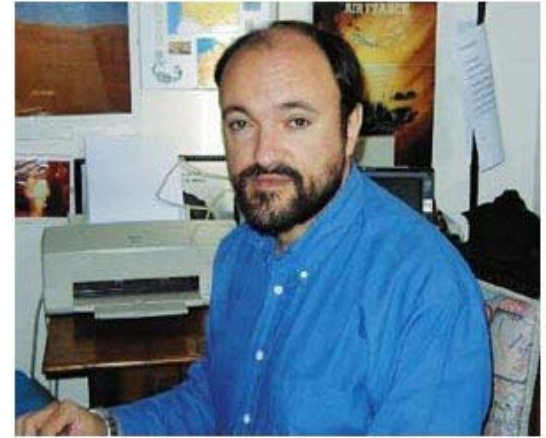


SARS: 2002-2003



<http://www.nature.com/nature/focus/sars/map.html>

WHO: Global Alert and Response



Dr. Carlo Urbani
February 2003

Hanoi, Vietnam

2012 (5, 73)

2002

2003

Nov. 16

Feb. 14

Feb. 28

Mar. 12

July

Atypical pneumonia
in China

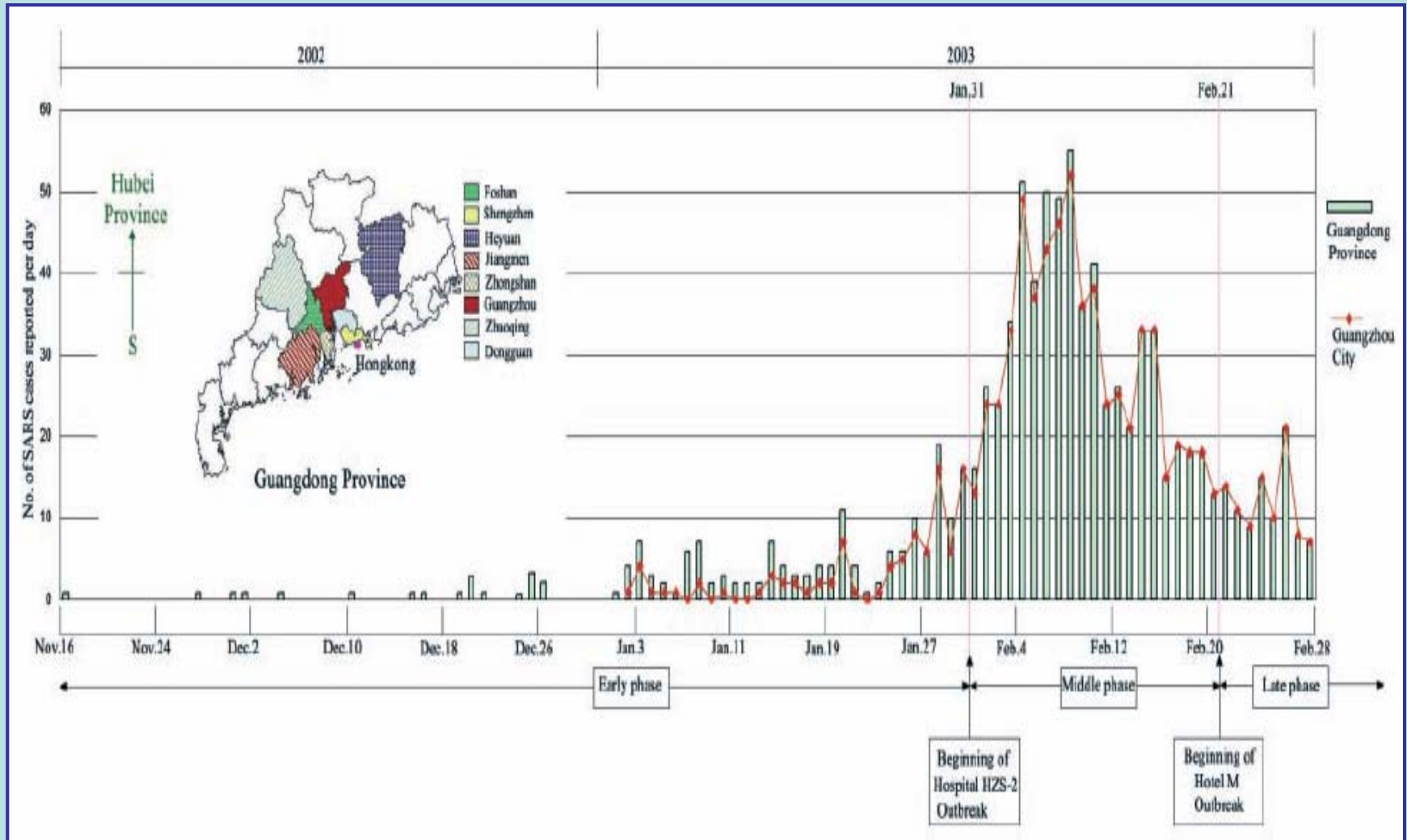
Hong
Kong
hotel

WHO
alerted

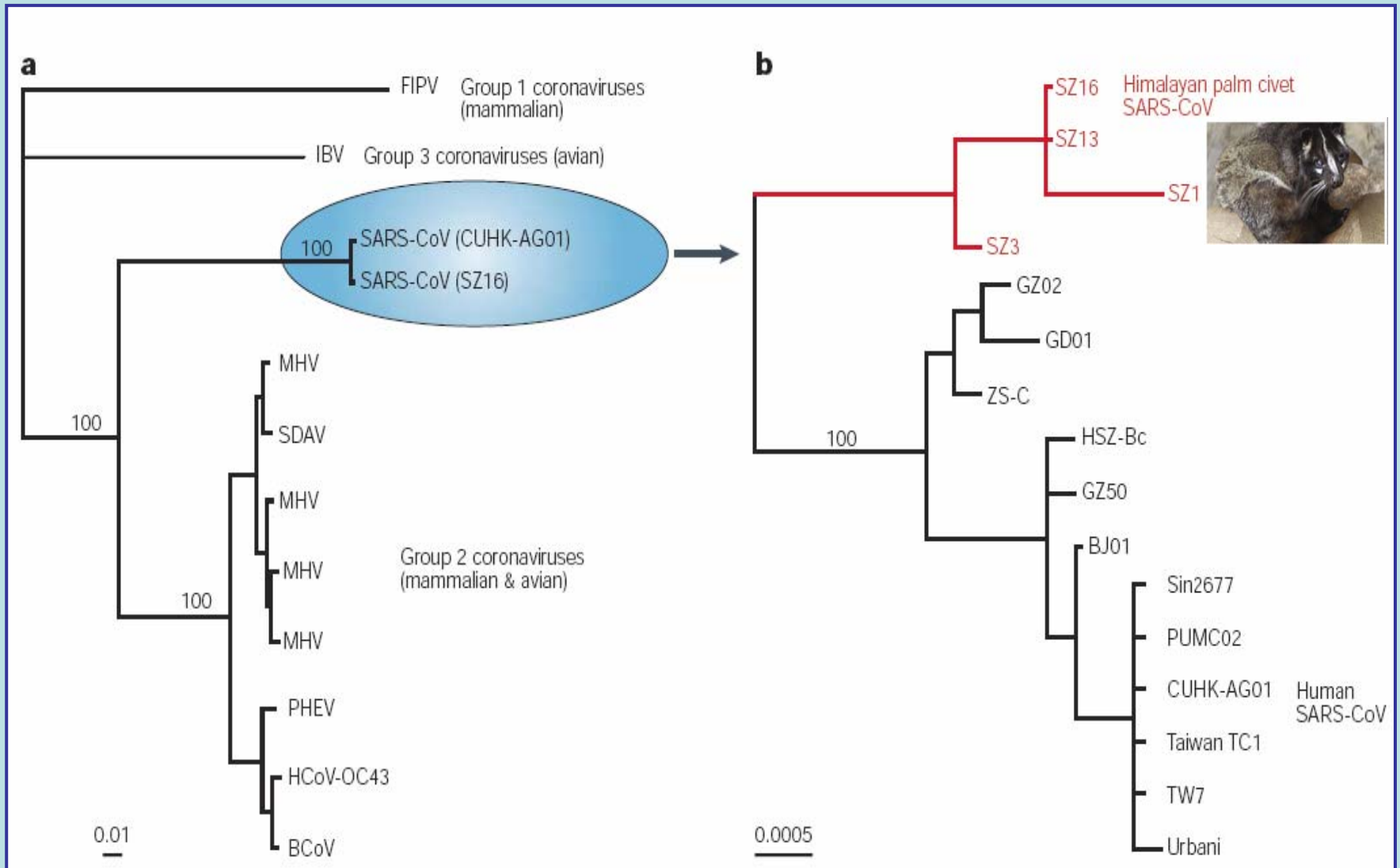
Global
alert

Human chain of
transmission broken

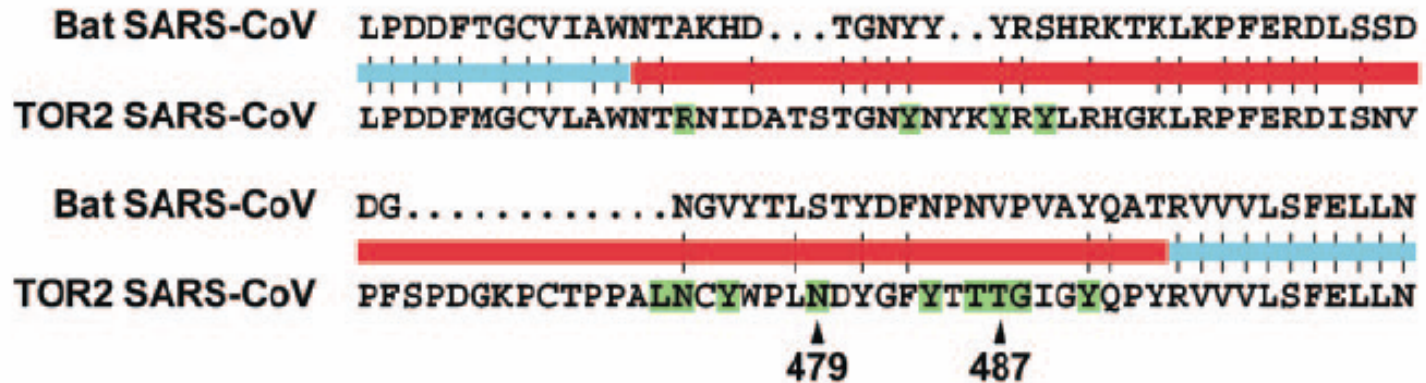
SARS Time-Course



Molecular evolution of SARS – CoV



Variation of S protein RBD



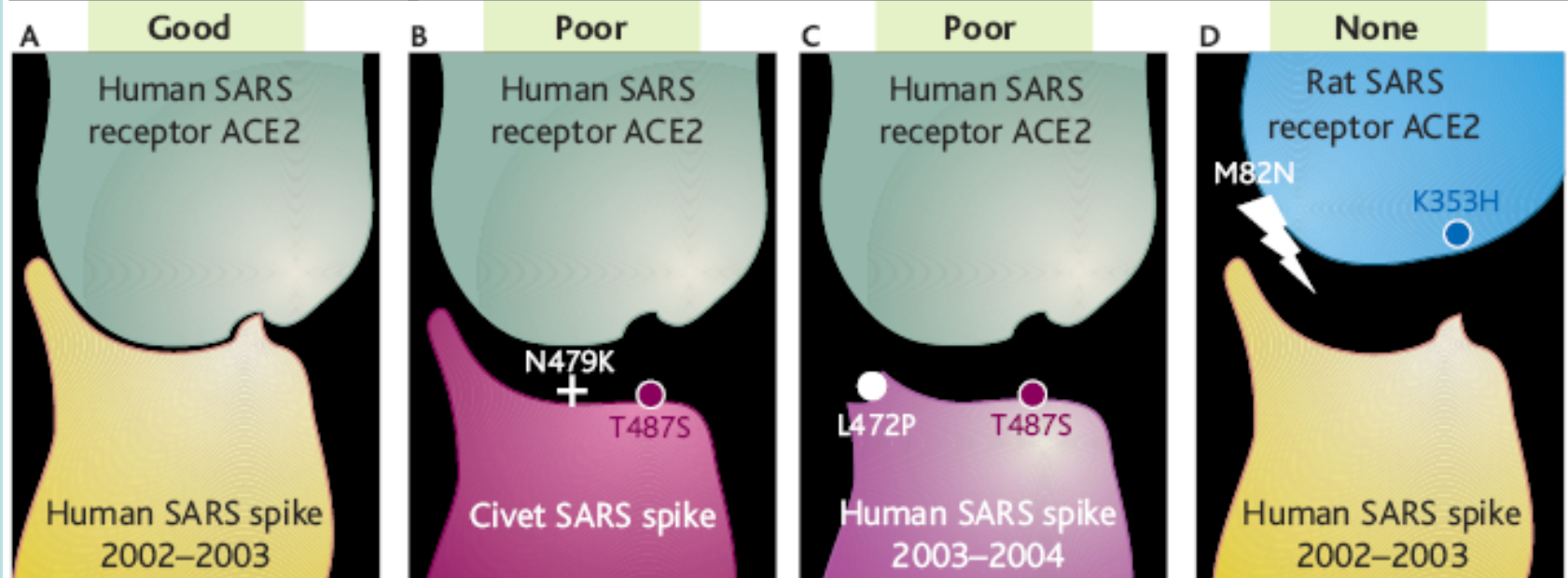
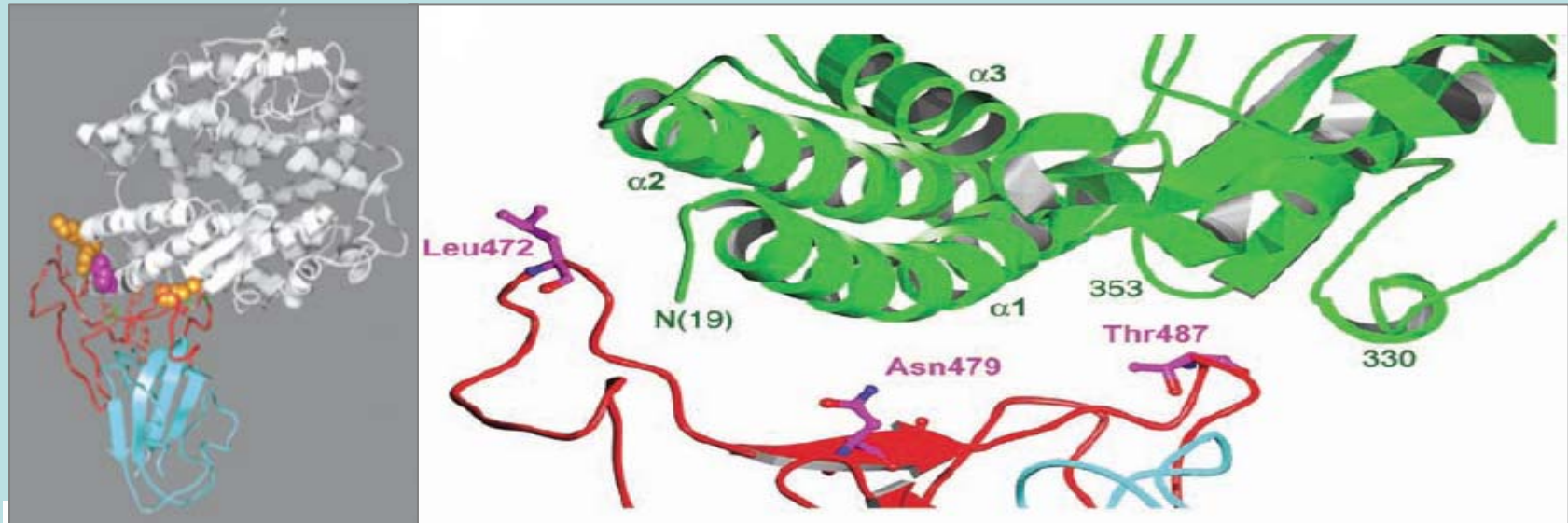
Predominant S-protein amino acids:

S-protein residue #	SARS-CoV from 2003-2004 (e.g. GD03)	SARS-CoV from palm civets (e.g. SZ3)	SARS-CoV from 2002-2003 (e.g. TOR2)
479	N	K	N
487	S	S	T

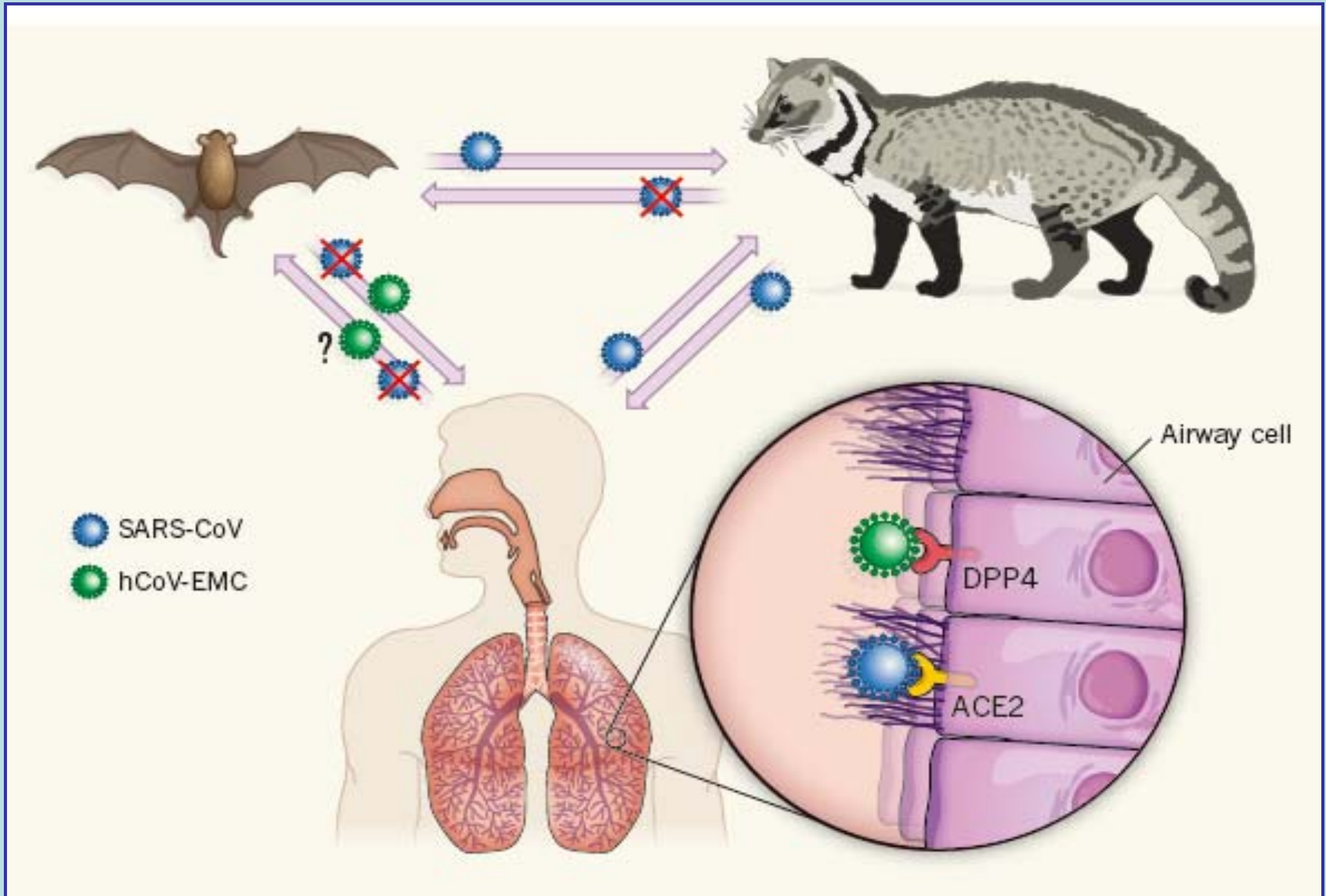
Most efficient ACE2 association:

S-protein residue #	Reservoir ACE2	Palm civet ACE2	Human ACE2
479	K?	K=N	N
487	S?	T	T

Adaptation of SARS Coronavirus to Humans



Transmission of Coronaviruses



总结

- 病毒表面结构呈现多样性，分为有包膜和无包膜病毒。病毒包膜主要由膜蛋白和脂质层构成，其结构与功能密切相关。
- 病毒表面包膜主要有三个主要功能：结合受体决定病毒的宿主特异性；通过构象变化实现膜融合；定位膜表面，启动病毒粒子装配与释放。
- 病毒表面膜蛋白采用类似于细胞固有的一些机制实现其功能，并具有进化适应的能力。

Thank you!