


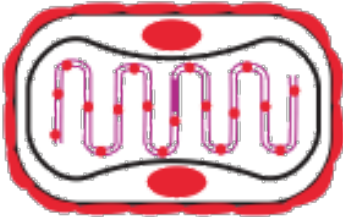
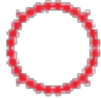



Structural Virology

Lecture 10

Pavel Plevka

Virus vaccines

Live attenuated virus		Polio (Sabin)
Inactivated virus		Polio (Salk)
Virion subunit		Influenza (haemagglutinin and neuraminidase)
Live recombinant virus		Rabies (for wildlife vaccination)
Virus-like particles		Hepatitis B
DNA		SARS coronavirus (experimental)

Naked Virion

Enveloped Virion

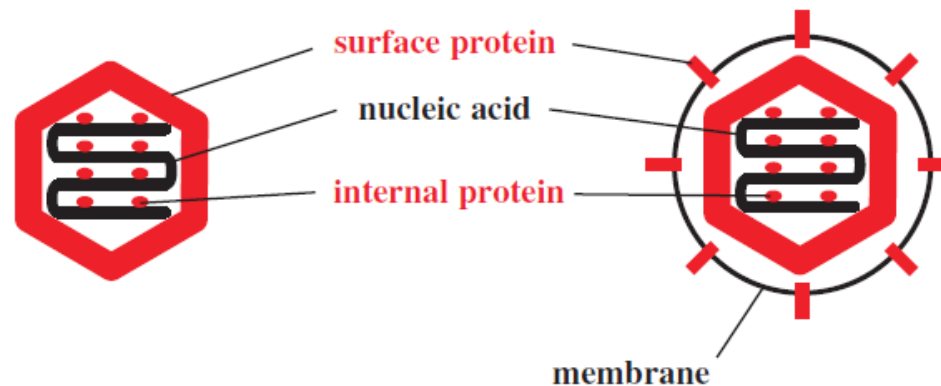
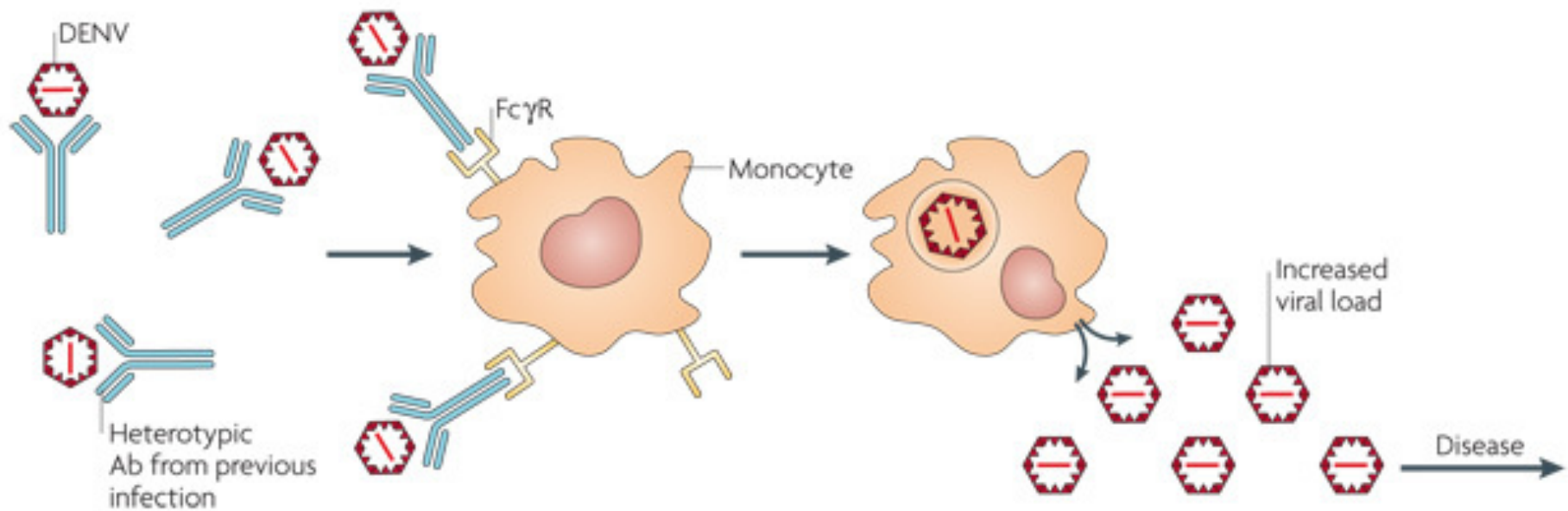


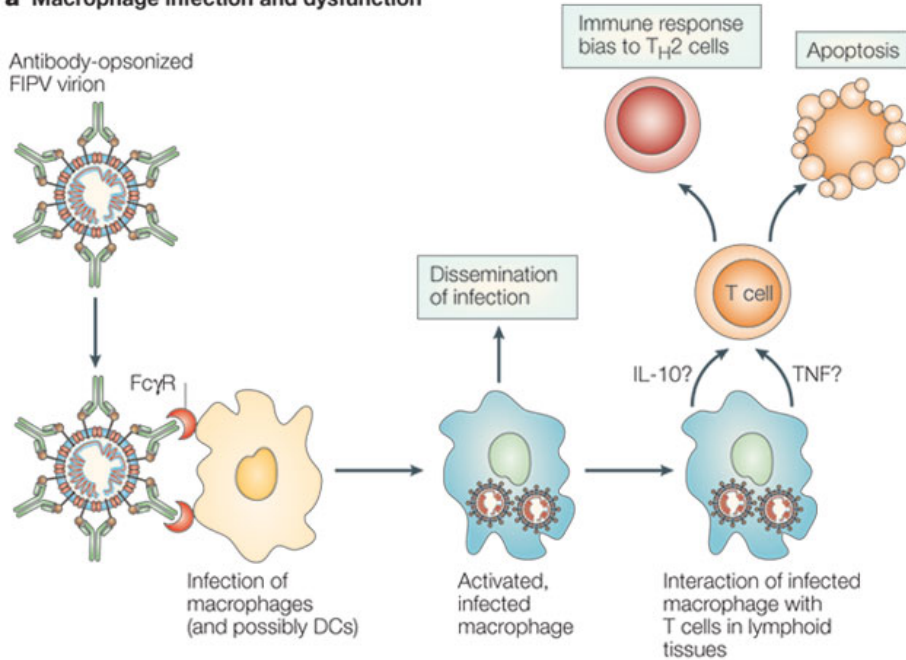
Figure 24.1 Inactivation targets in virions. Infectivity of a virion may be destroyed by damage to a nucleic acid, a protein, and/or a lipid membrane. Alteration of a surface protein might prevent a virion from attaching to its host cell and/or from entering the cell. Stripping the envelope from an enveloped virion removes the surface proteins and achieves the same outcome. Alteration of internal proteins can destroy properties, such as enzyme activities, essential for the replication of the virus.

Antibody dependent enhancement dengue

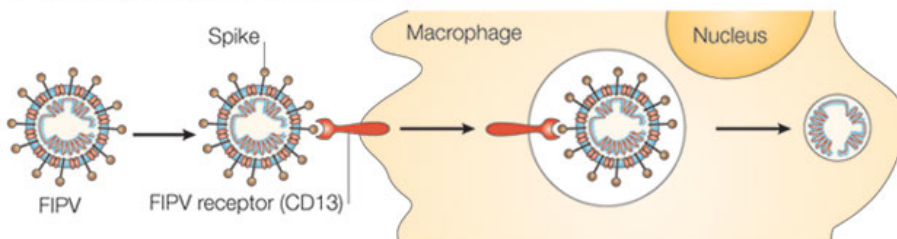


Antibody dependent enhancement - coronaviruses

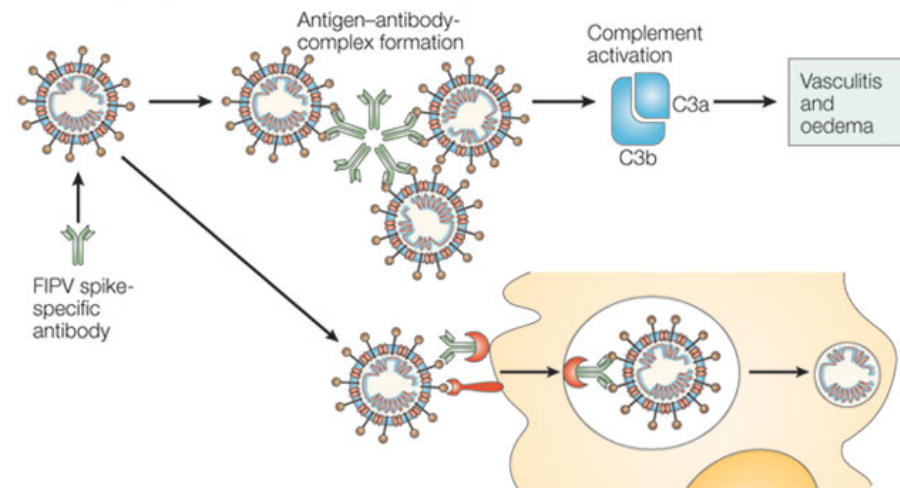
a Macrophage infection and dysfunction



b Coronavirus-receptor-mediated entry



c Antibody-dependent enhancement of entry



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Smallpox



- killed an estimated 400,000 Europeans annually during the 18th century.
- was responsible for a third of all blindness.
- of those infected, 20–60%—and over 80% of infected children—died
- responsible for an estimated 300–500 million deaths during the 20th century

Vaccine Types

- Attenuated viruses
- Inactivated viruses
- Virion subunits
- Recombinant viruses
- Virus-like particles
- Synthetic peptides
- DNA vaccines

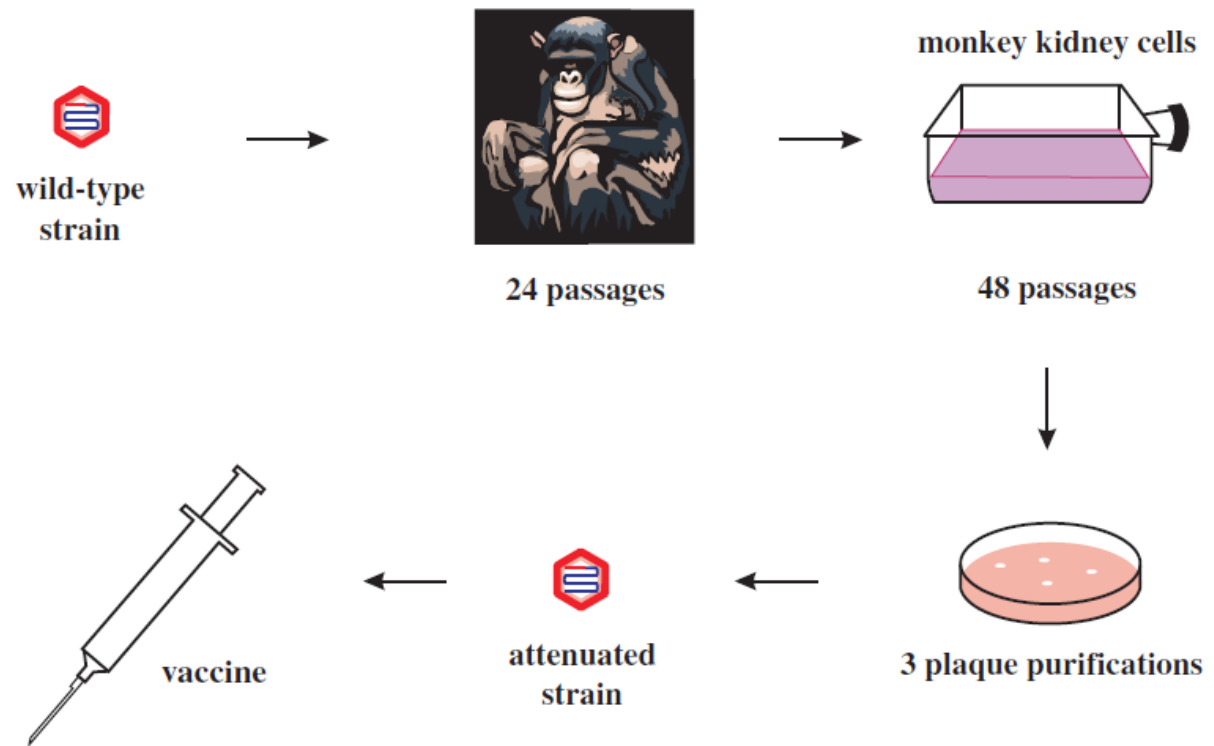


Figure 25.1 Derivation of attenuated poliovirus strain (Sabin type 1) from wild-type poliovirus strain (Mahoney 1).

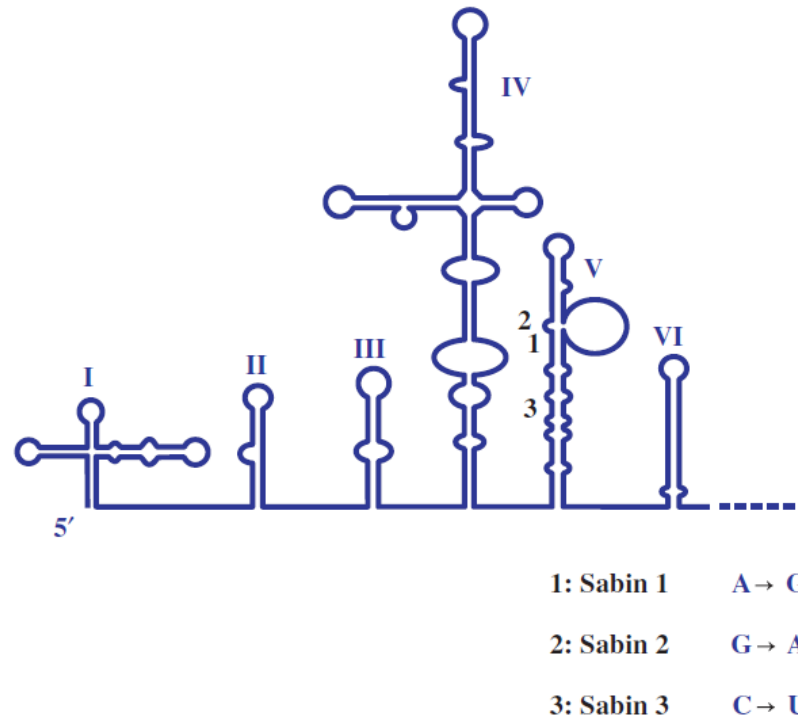


Figure 25.2 5' end of poliovirus RNA with expanded view of domain V. For each of the three Sabin strains a mutation in domain V that contributes to the attenuation of neurovirulence is indicated.

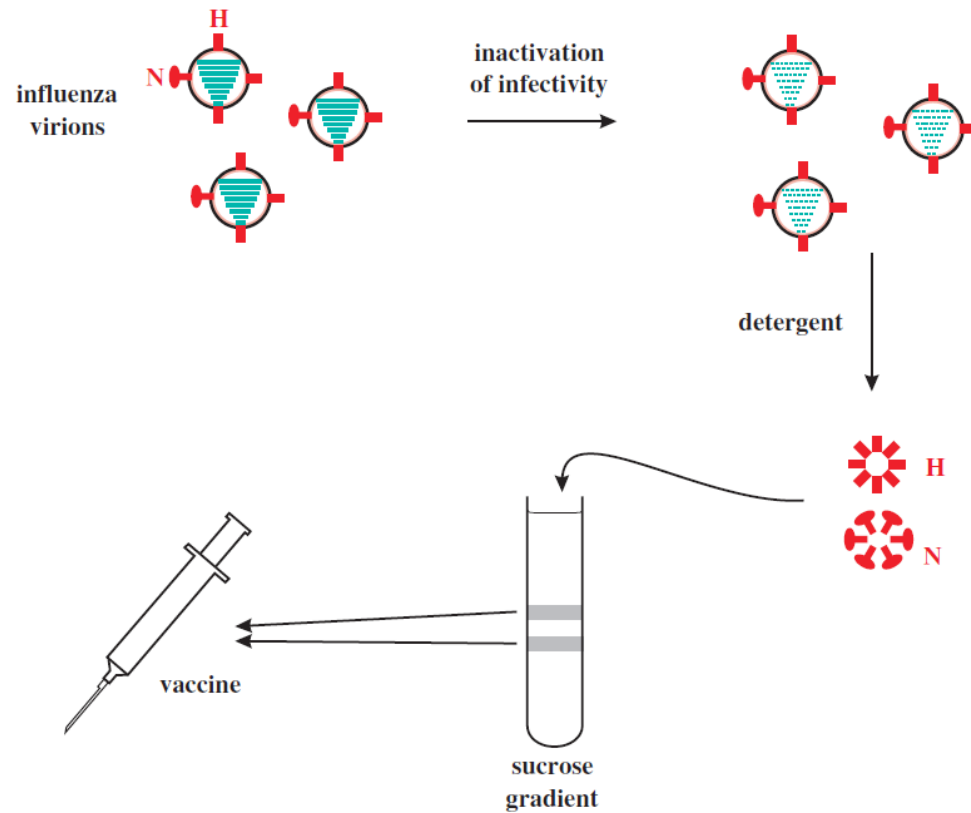


Figure 25.3 Outline of production method for influenza virus subunit vaccine. Hemagglutinin (H) and neuraminidase (N) are extracted from inactivated influenza virions and purified by sucrose gradient centrifugation. The bands from the gradient are harvested and incorporated into the vaccine.



Figure 25.4 Production of vaccine in chick embryos.
Source: Courtesy of the World Health Organization.

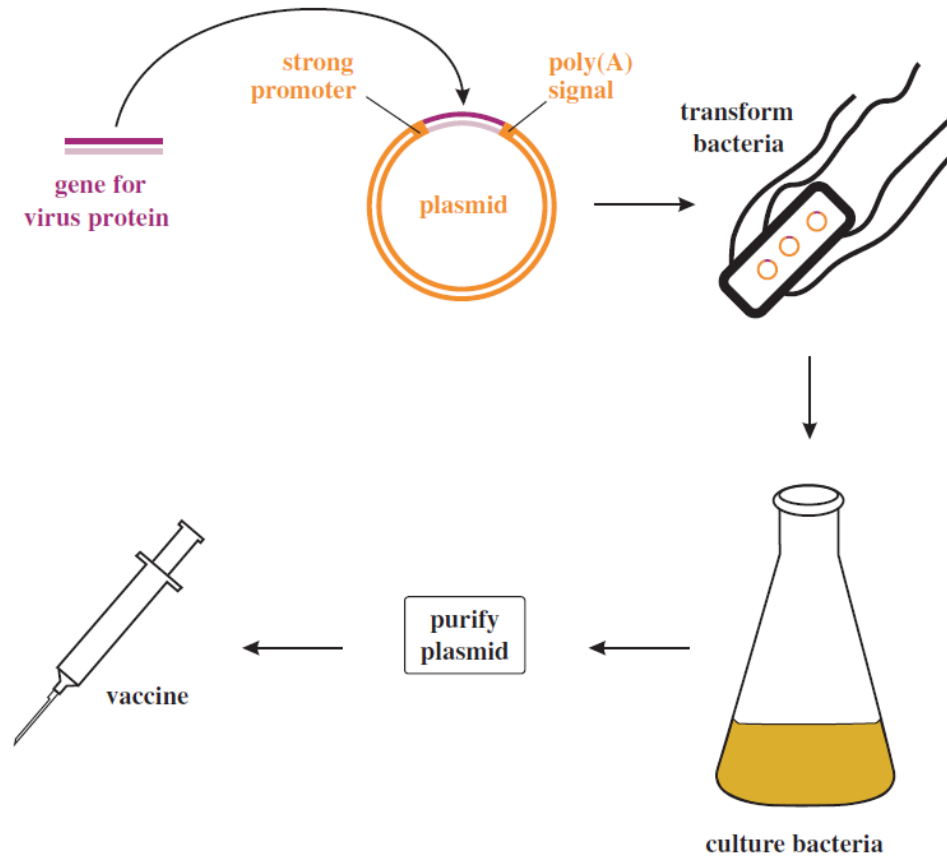
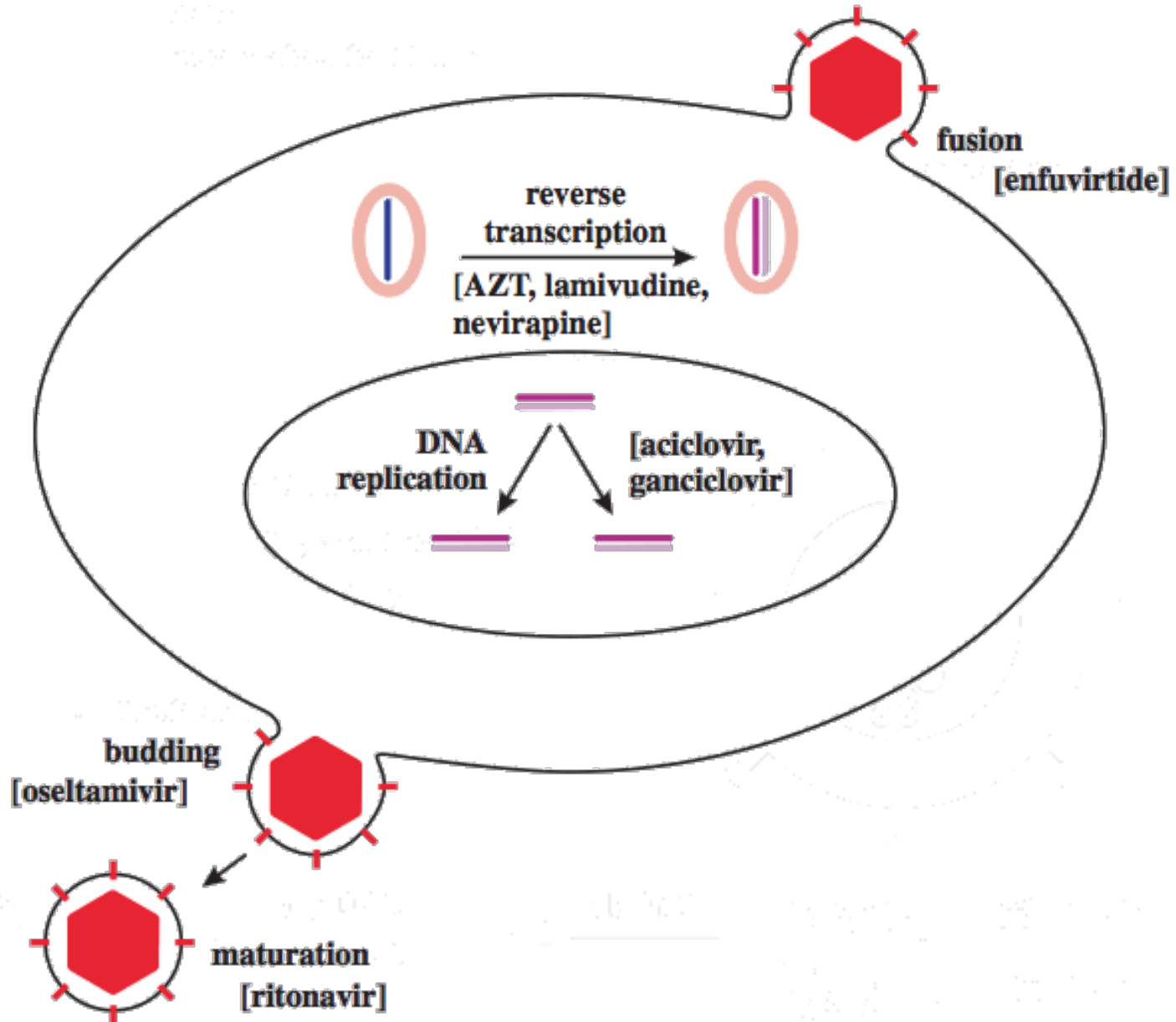


Figure 25.5 Production of a DNA vaccine. The virus protein gene is inserted into a plasmid, which is then cloned in bacteria. The plasmid is extracted from the bacterial cells, purified, and incorporated into a vaccine.

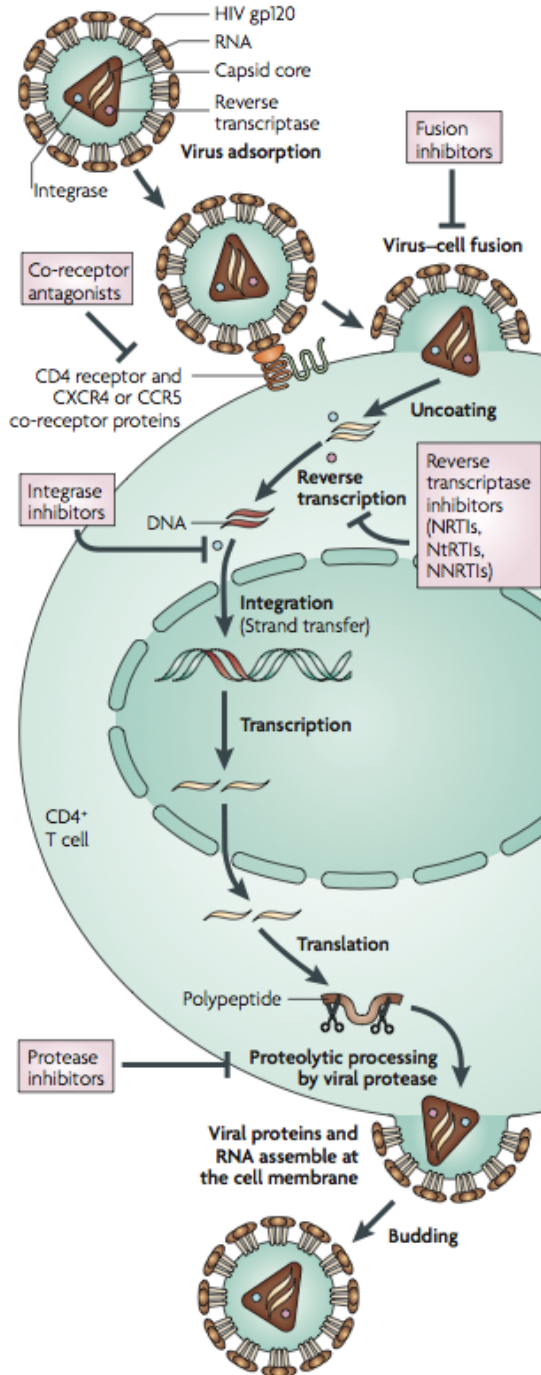
Learning outcomes

- explain how virus diseases are controlled with vaccines
- evaluate the types of virus vaccine in medical and veterinary use
- evaluate types of virus vaccine that are experimental
- describe methods used to manufacture virus vaccines
- evaluate procedures designed to ensure the safety of virus vaccines

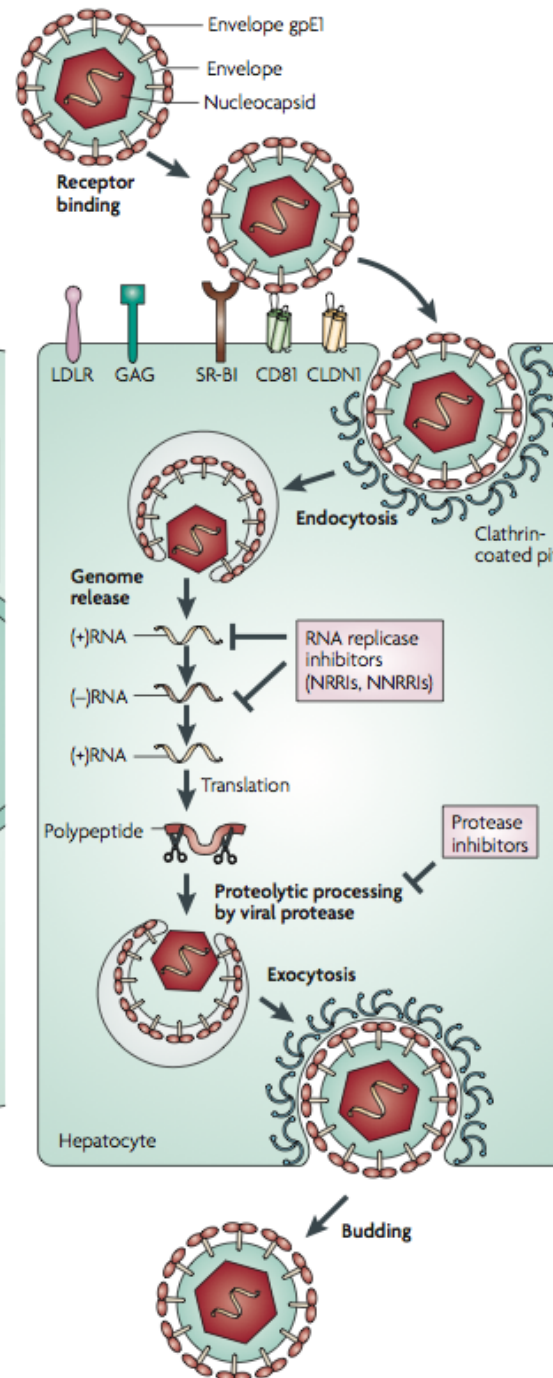
Antiviral compounds



HIV

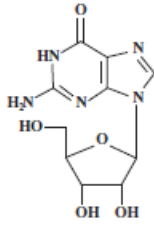


HCV

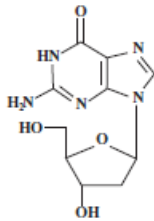


Nucleosides

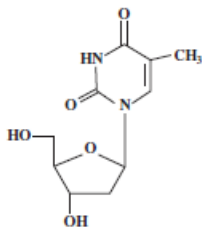
Guanosine



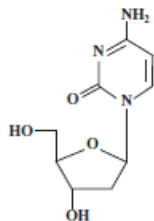
2'-deoxyguanosine



2'-deoxythymidine

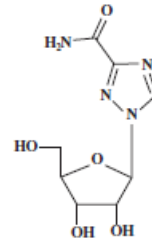


2'-deoxycytidine

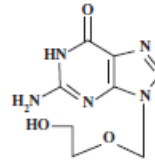


Nucleoside analogs

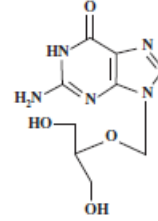
Ribavirin



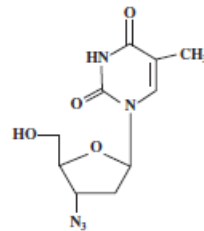
Aciclovir



Ganciclovir



Azidothymidine



Lamivudine

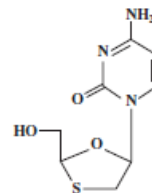
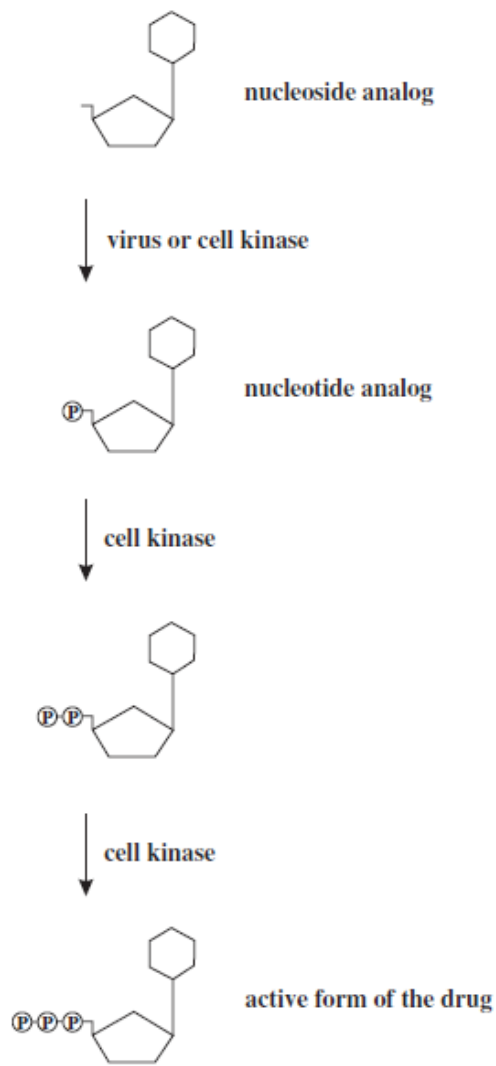




Figure 26.2 Nucleoside analogs used as anti-viral drugs. The analogs are derived from the nucleosides shown on the left.



Key:  phosphonate
 phosphate

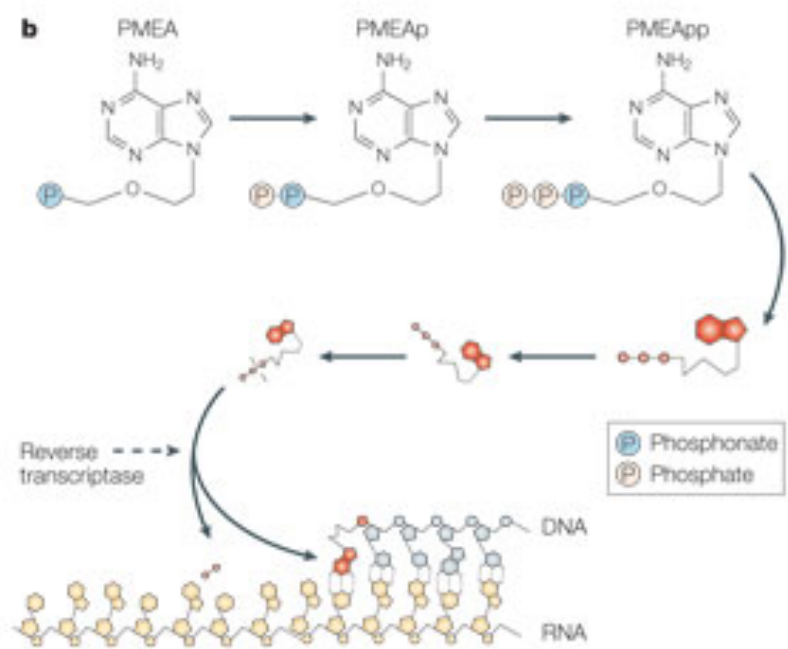
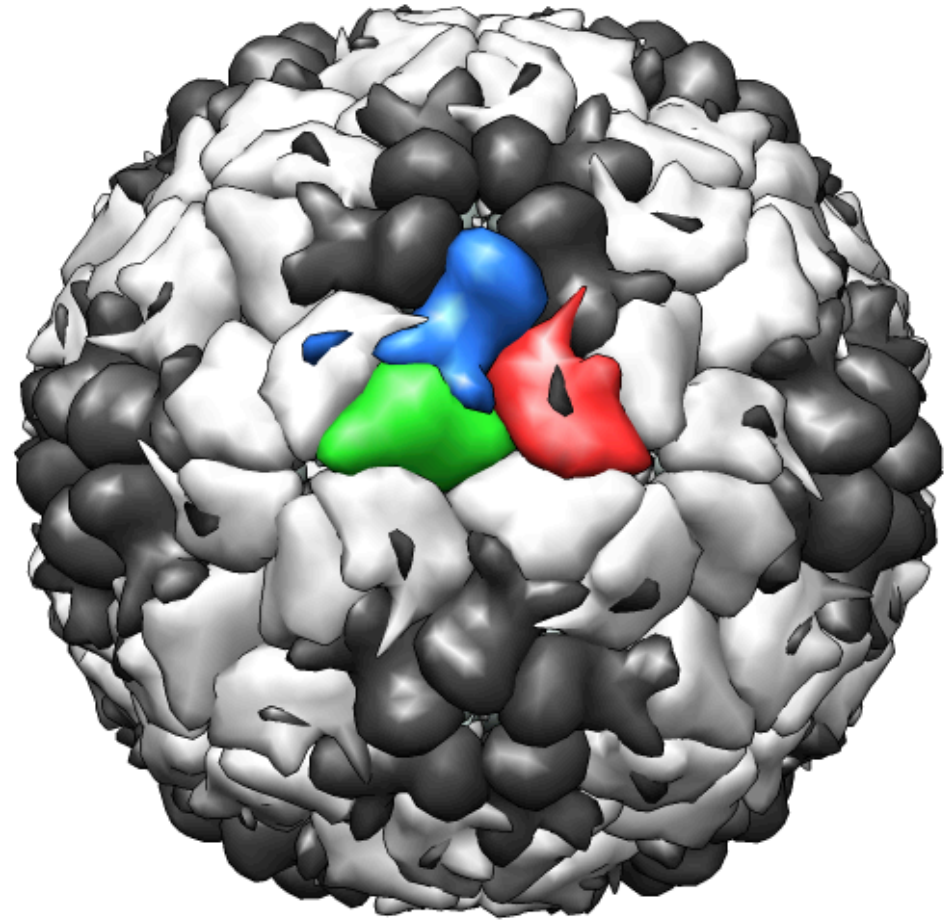
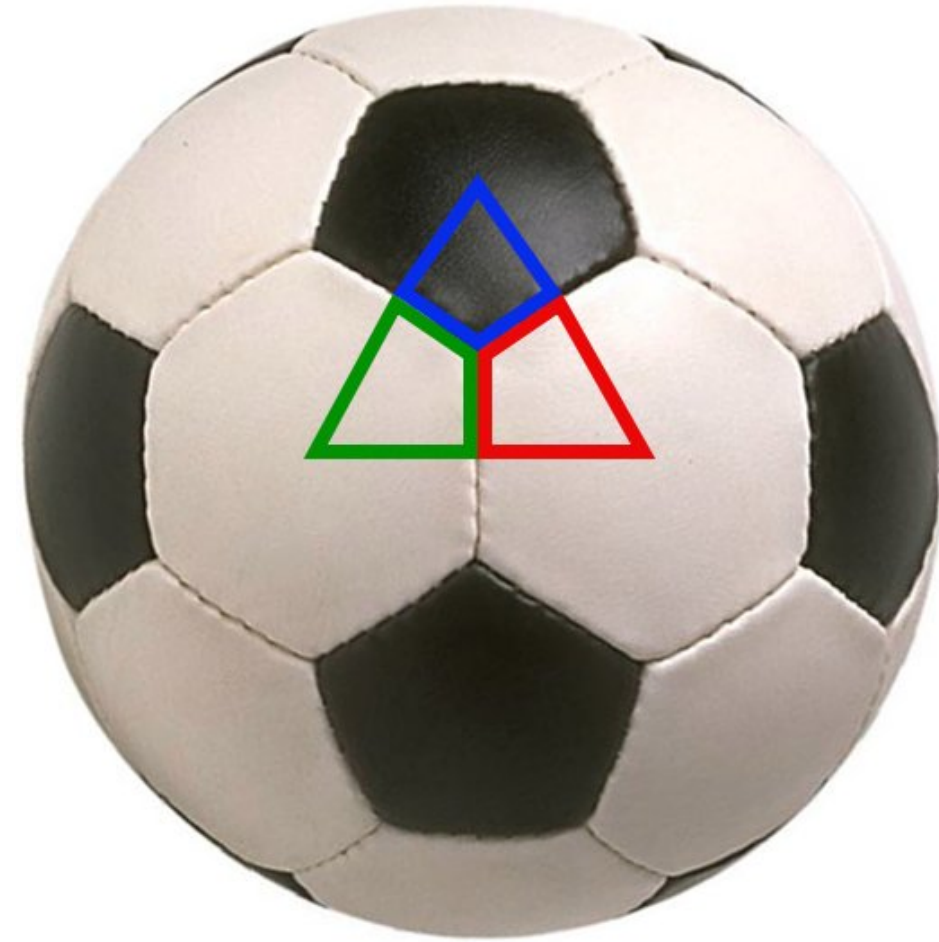
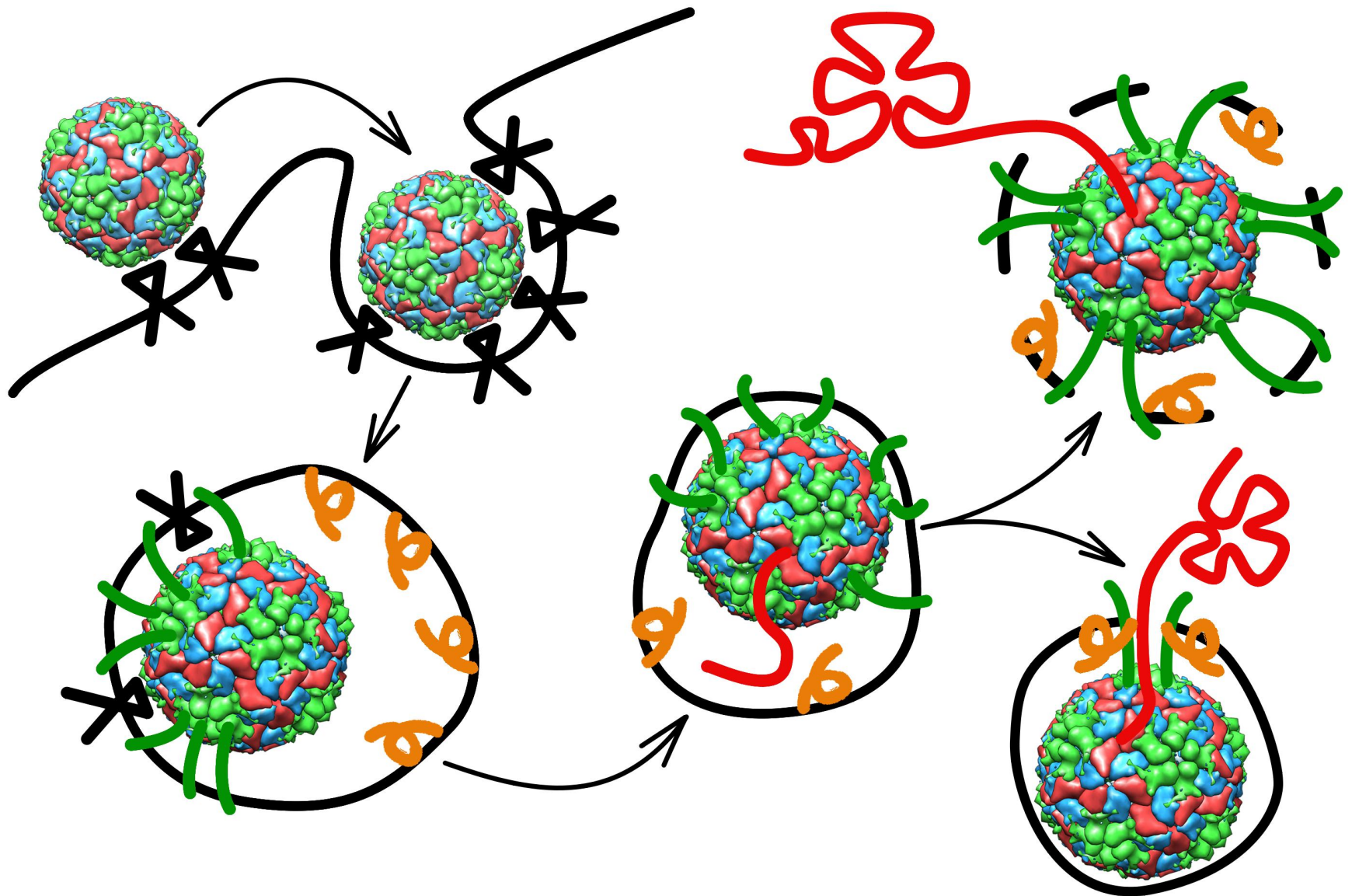


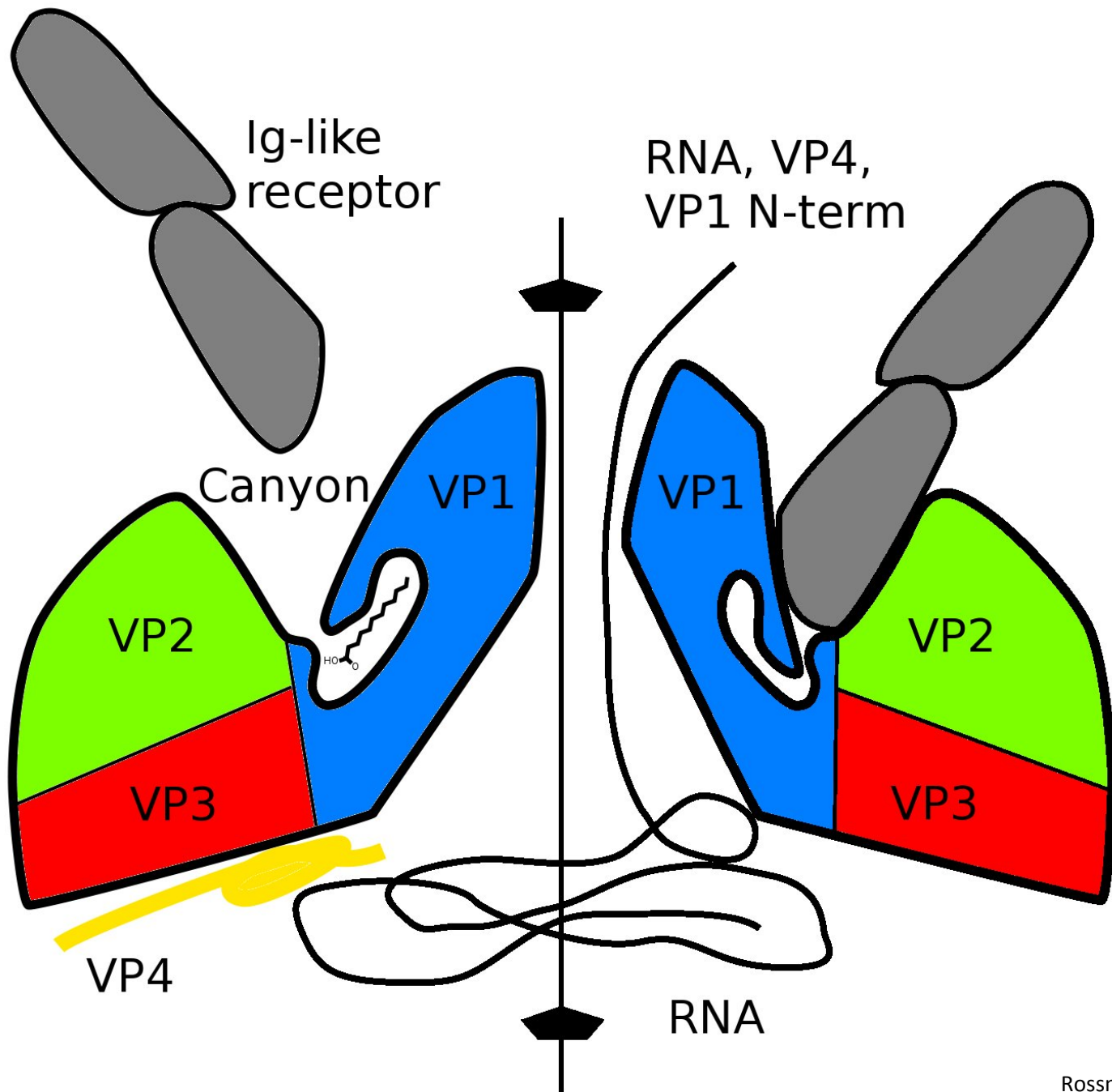
Figure 26.3 Phosphorylation of a nucleoside analog. The active form of the drug is the 5' triphosphate derivative of the nucleoside analog.

Picornavirus virion

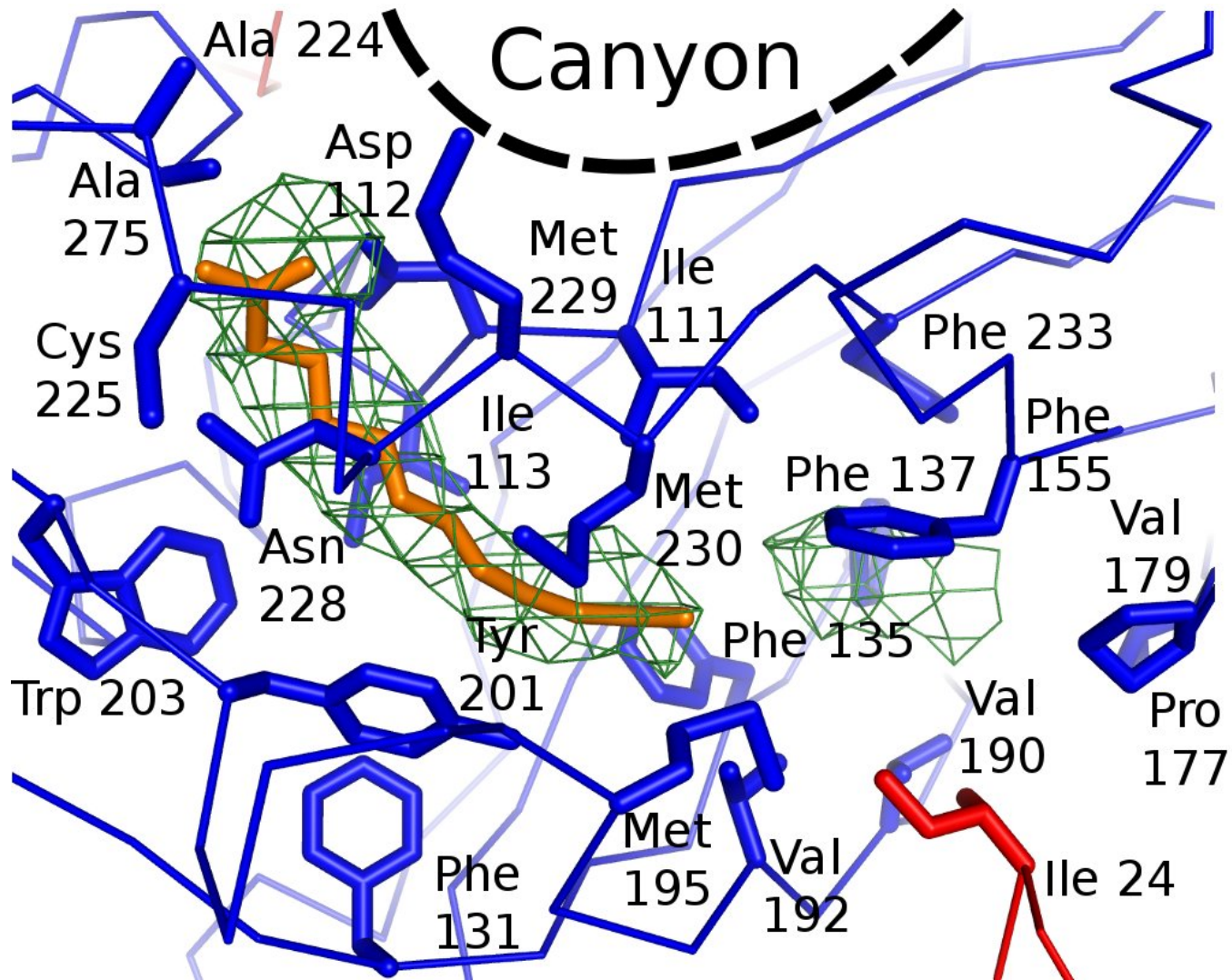


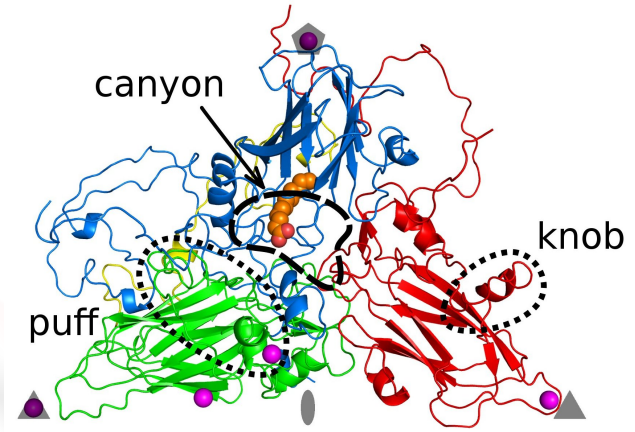
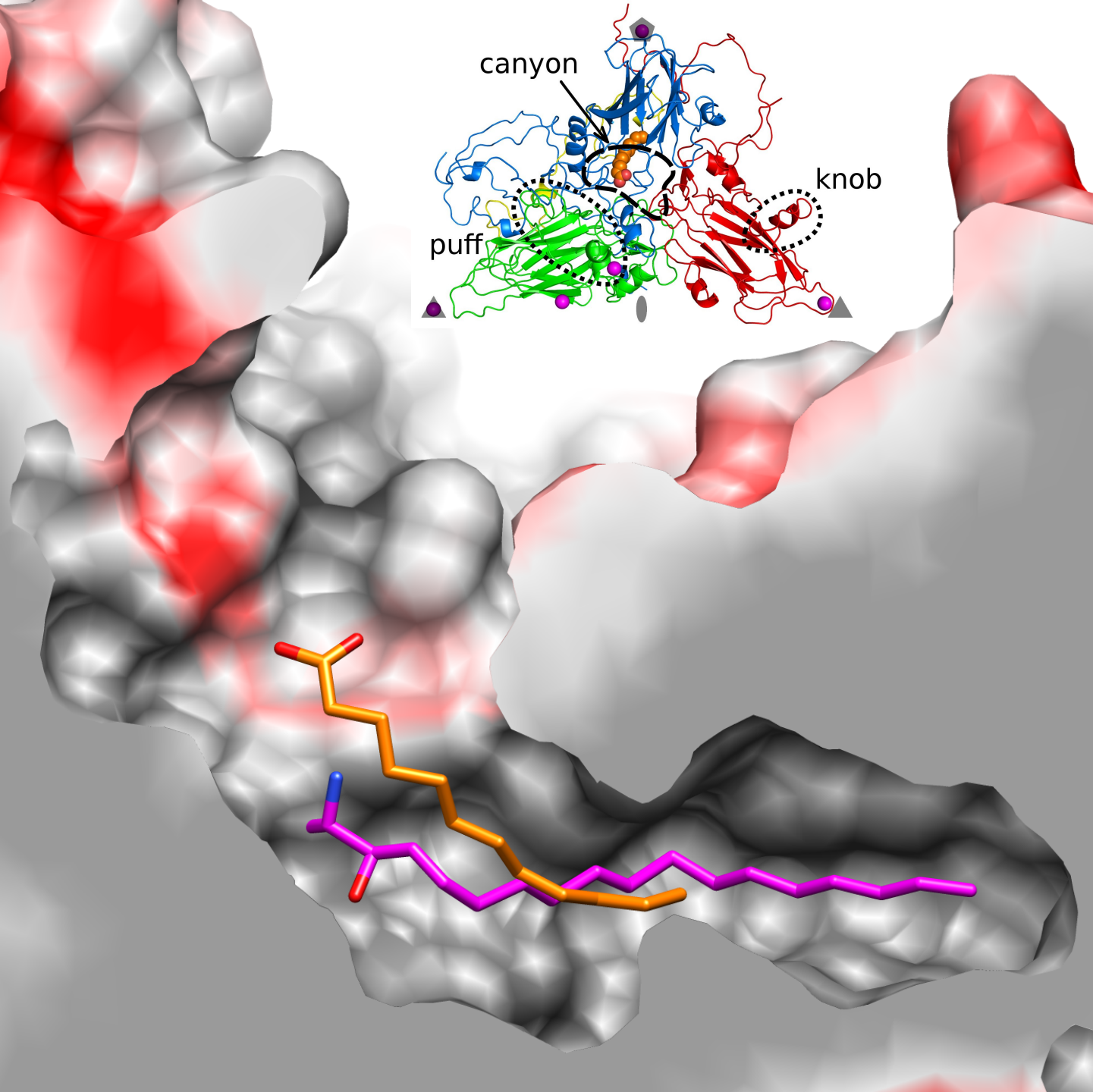
1. Genome delivery into cytoplasm

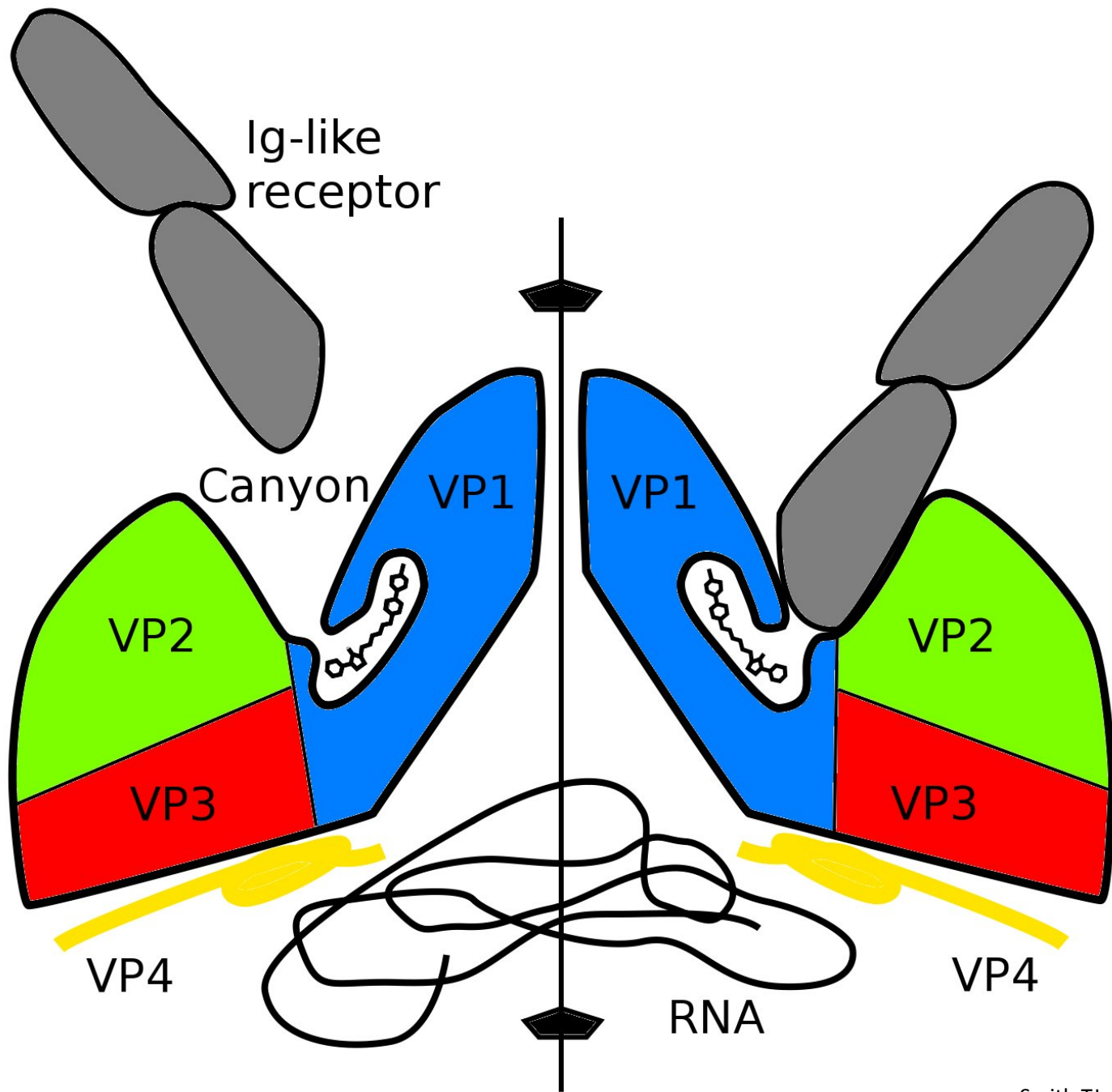




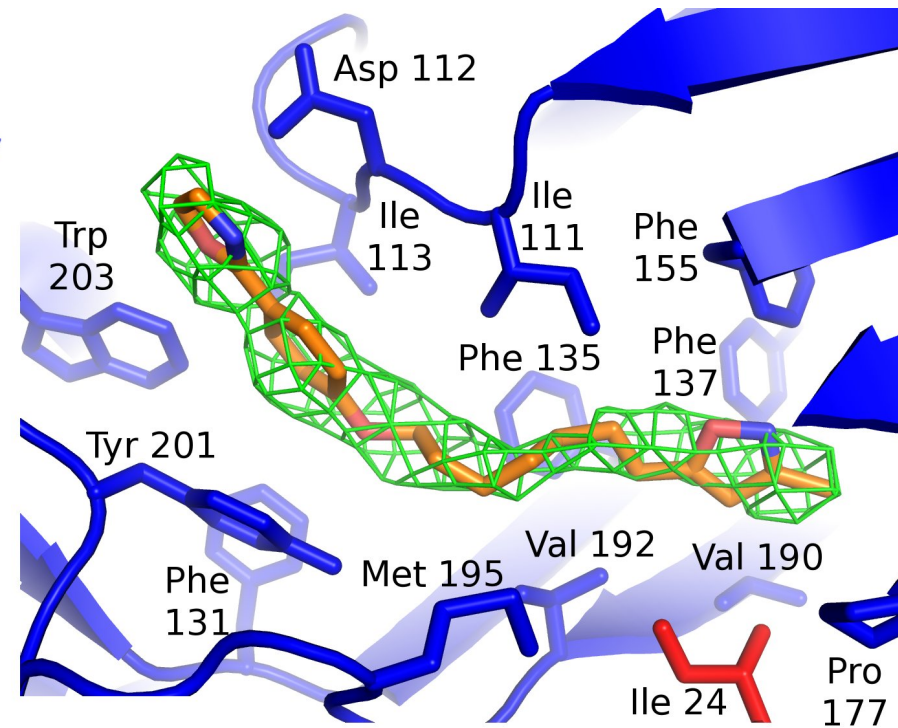
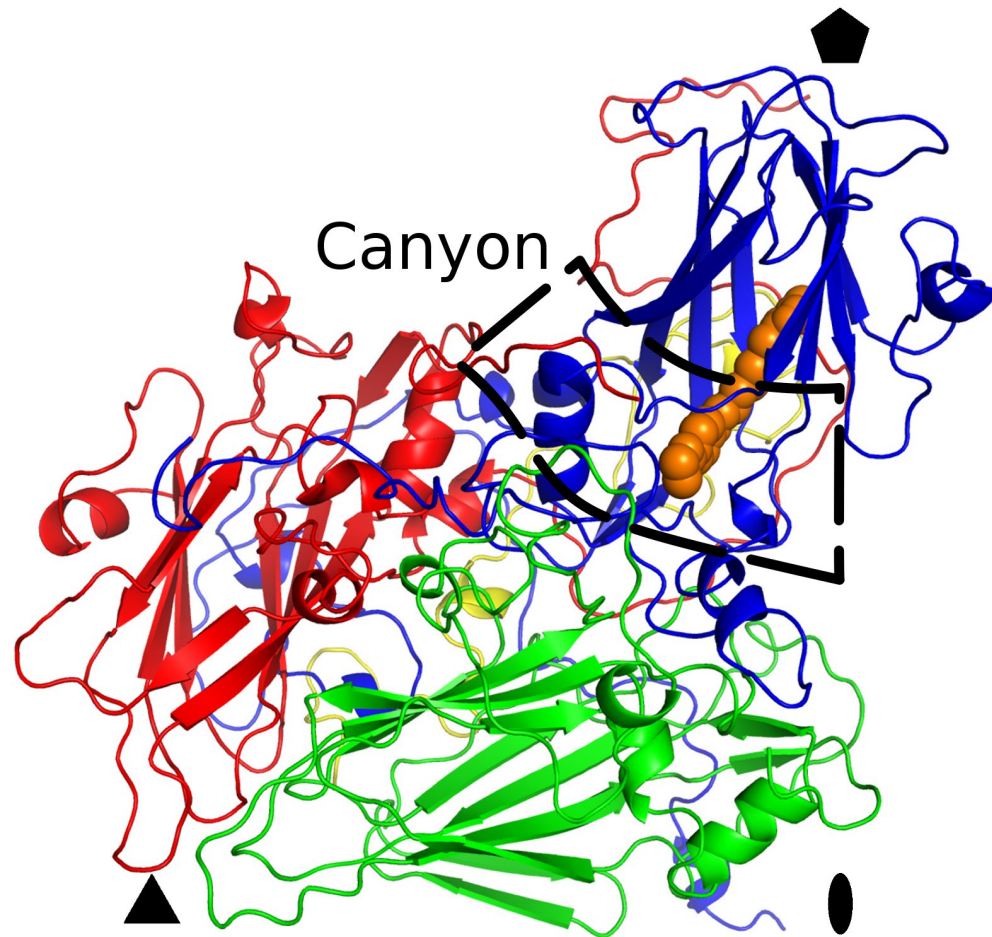
Pocket factor in EV71

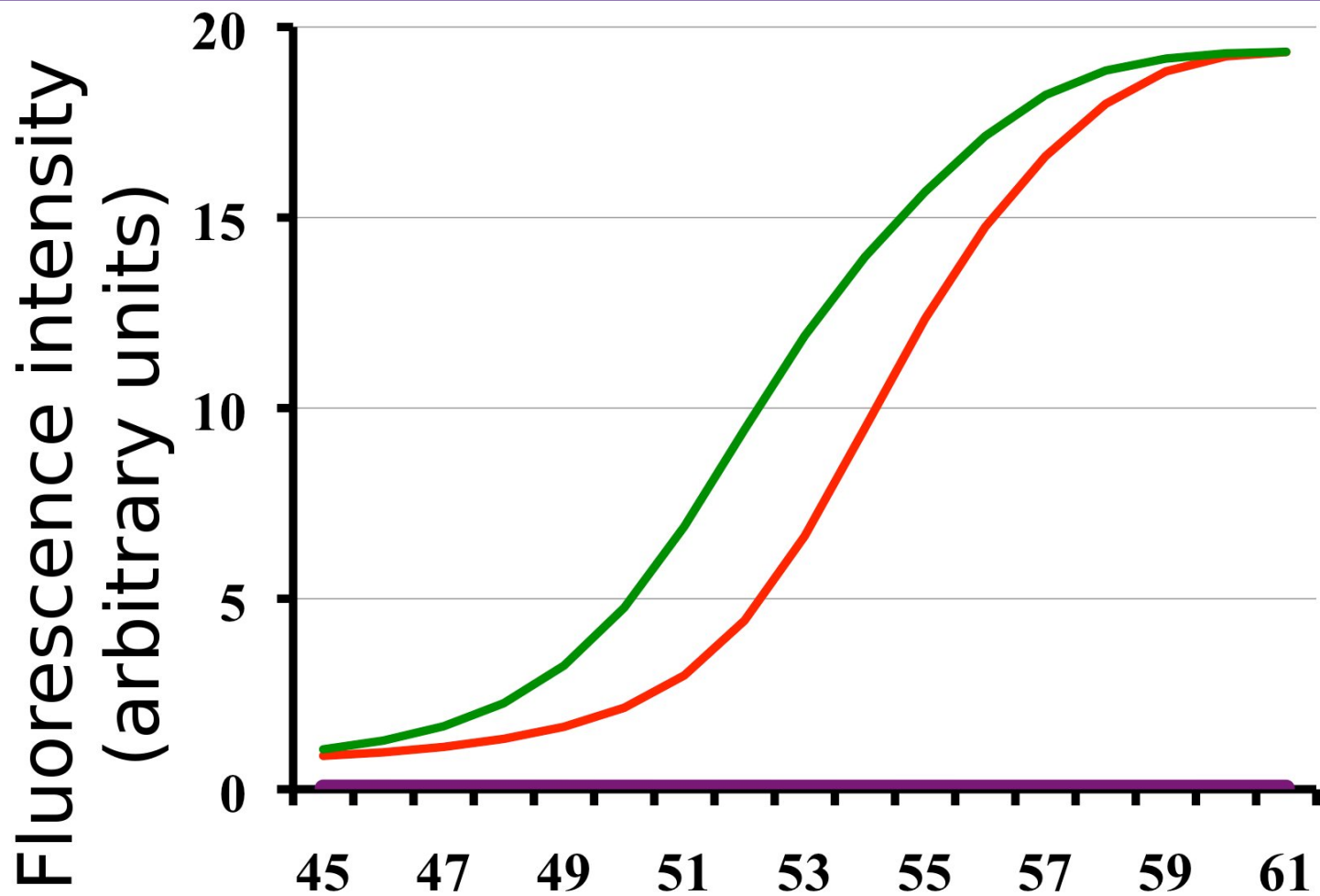




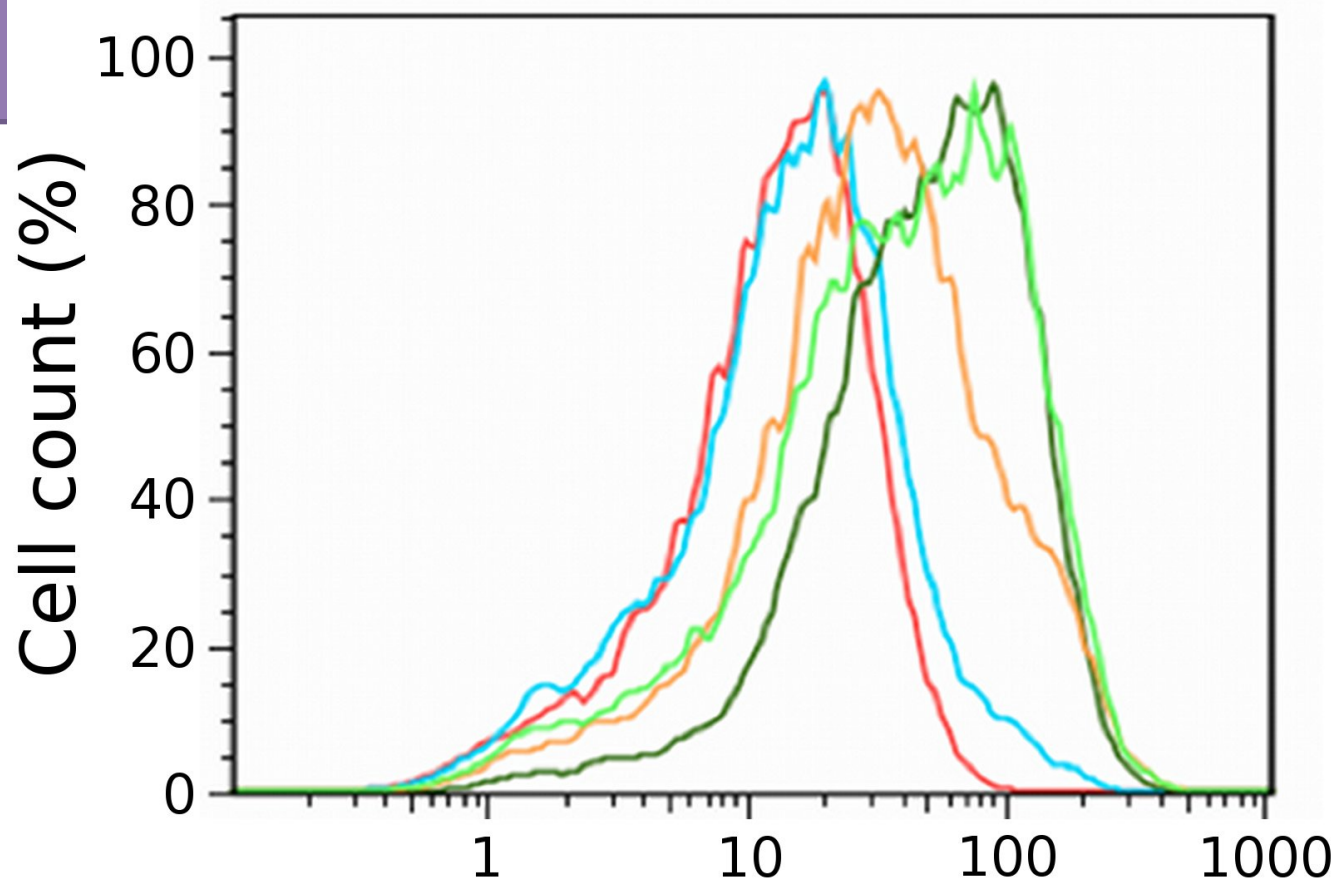


Inhibition of EV71 by WIN 51711





- no virus
- EV71
- EV71 + 300µM WIN 51711



Fluorescence intensity
(arbitrary units)

■ no virus

■ EV71

■ EV71 + 146 μM WIN 51711

■ EV71 + 291 μM WIN 51711

■ EV71 + 583 μM WIN 51711

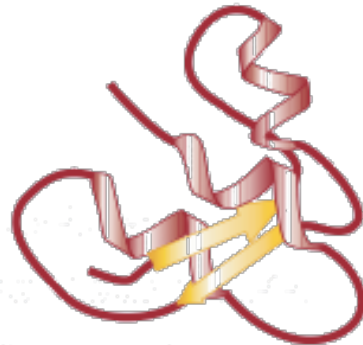
Learning outcomes

- evaluate procedures used to develop new anti-viral drugs
- describe the modes of action of selected anti-viral drugs
- discuss virus resistance to drugs

Prions

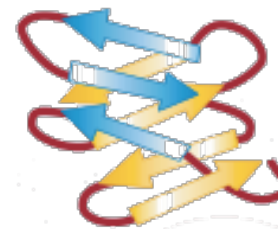
PRION (INfectious PROtein)

Normal protein



More α helix than β sheet

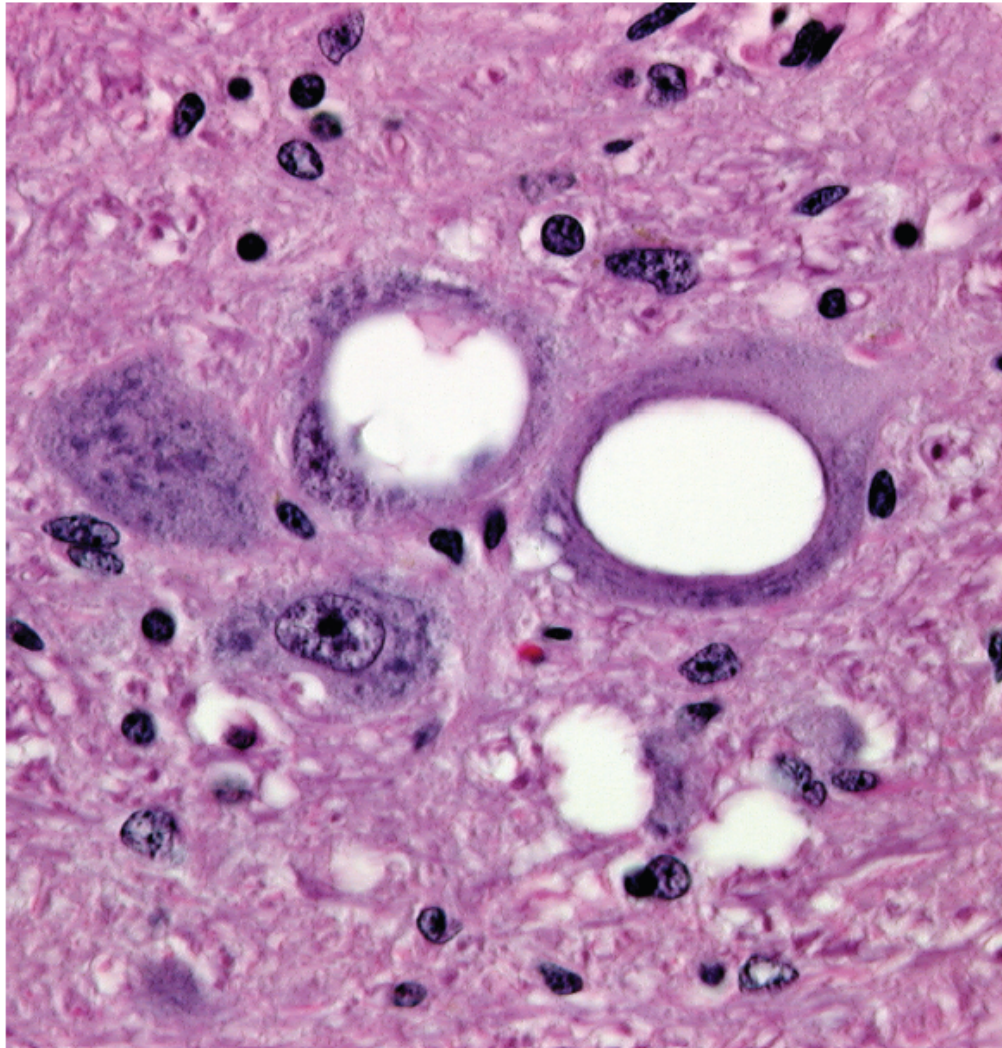
Misfolded protein



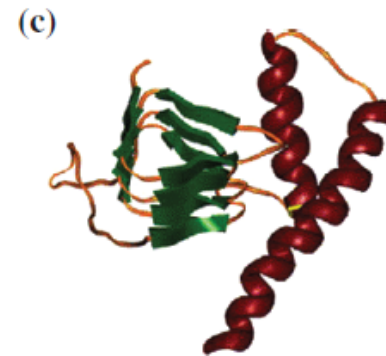
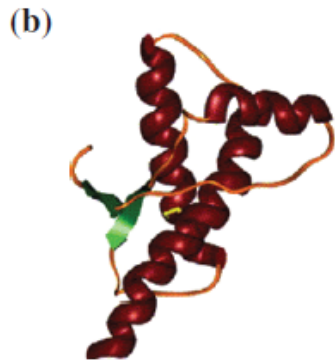
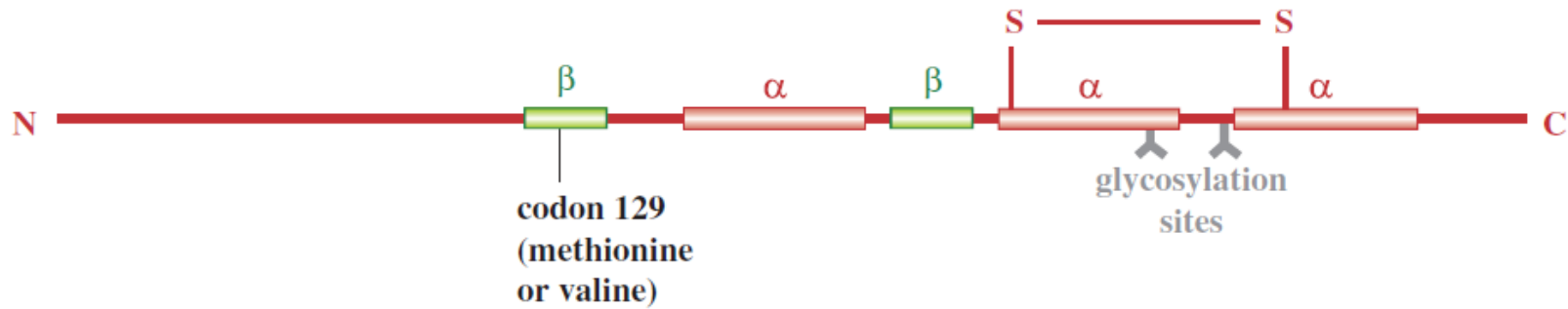
Mainly β sheet

- Prion diseases:**
- scrapie (sheep)
 - bovine spongiform encephalopathy
 - sporadic Creutzfeldt-Jakob disease (humans)
 - variant Creutzfeldt-Jakob disease (humans)

Brain with Scrapie



Normal and misfolded form of prion



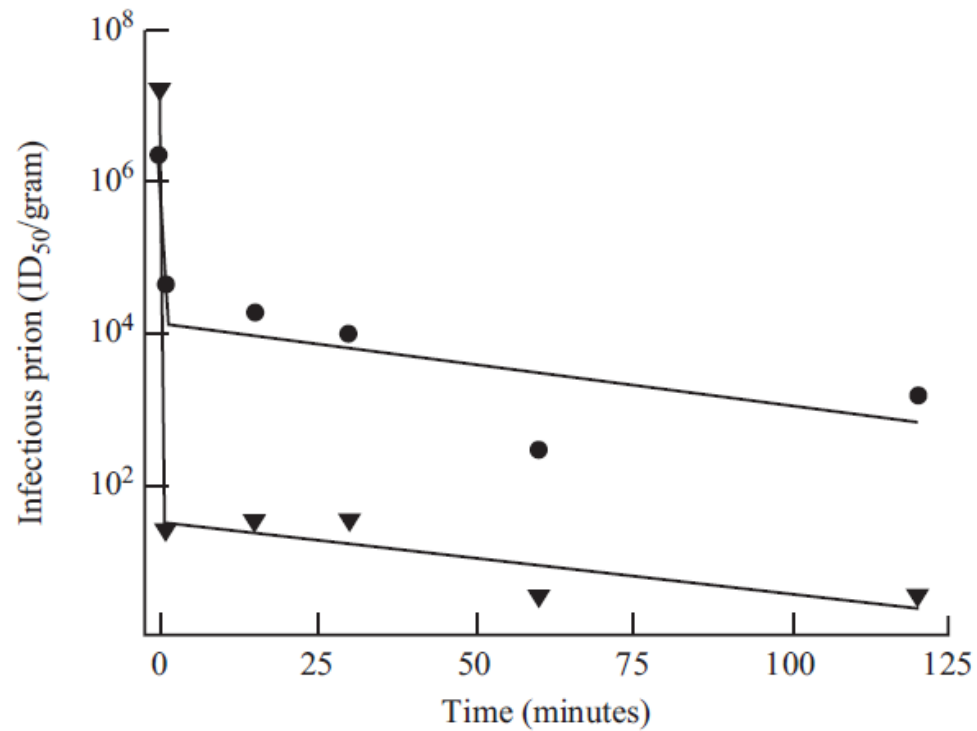


Figure 27.3 Inactivation of two strains of scrapie prion in an autoclave at 126 °C.

Source: Data from Somerville (2002) *Trends In Biochemical Sciences*, 27, 606. Reprinted by permission of Elsevier and the author.

Creutzfeldt-Jacob disease x BSE

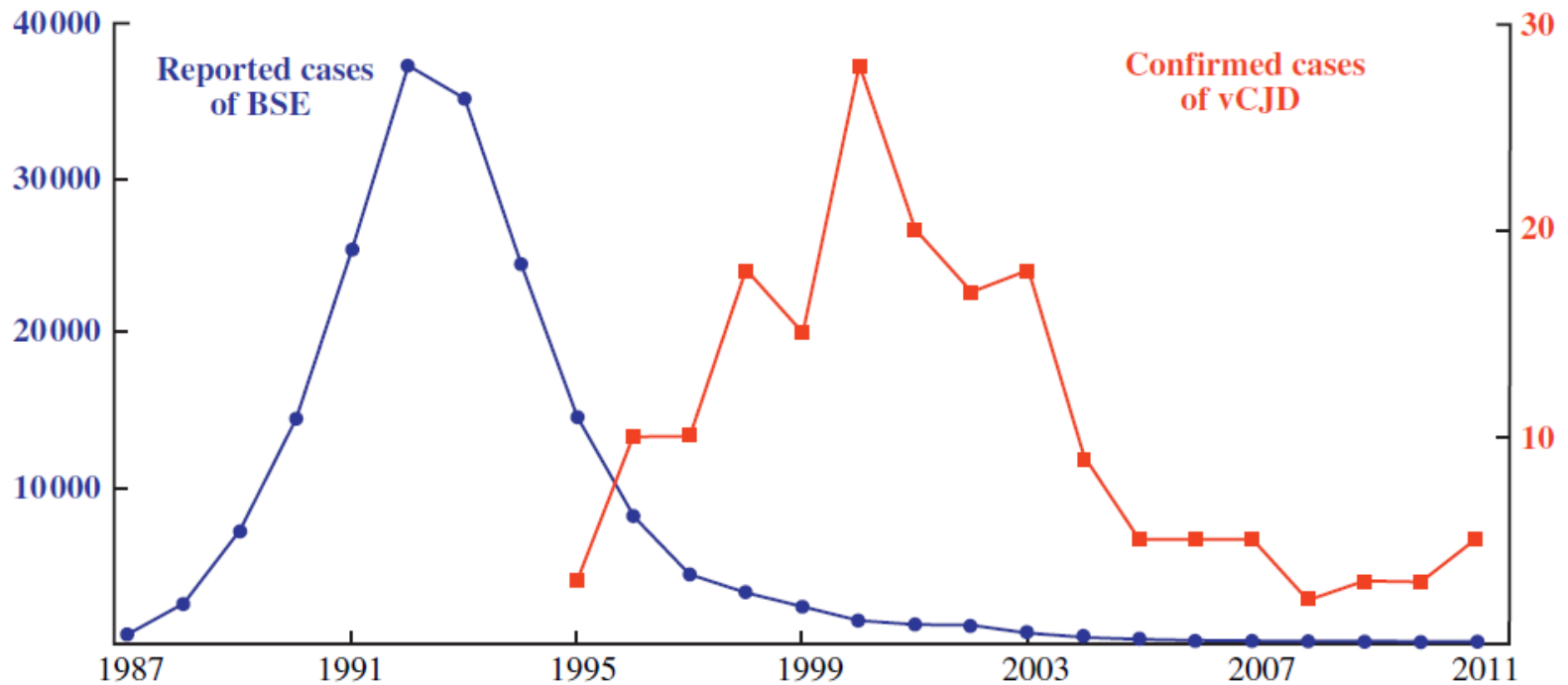


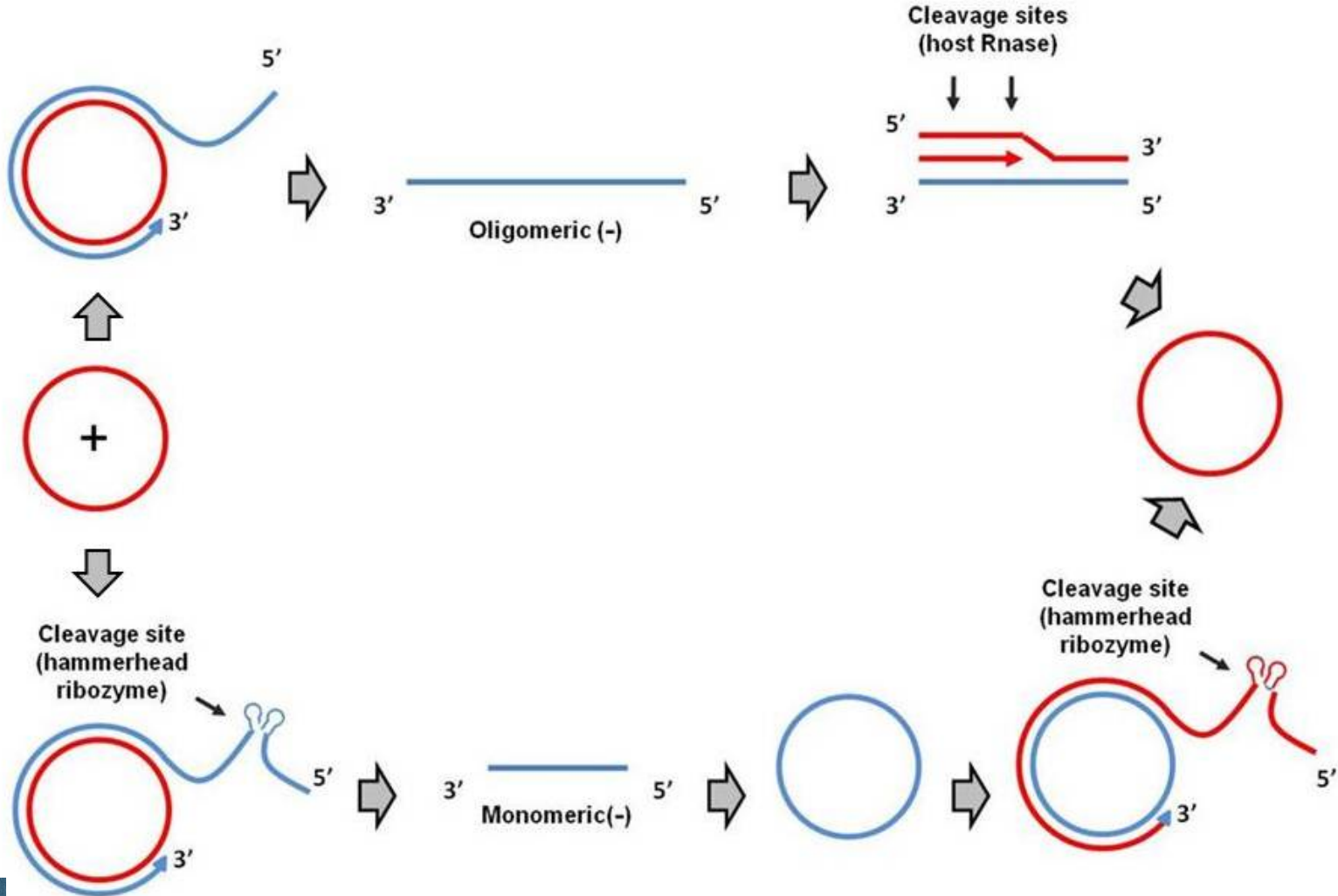
Figure 27.4 Numbers of cases of BSE and vCJD in the UK.

Source: BSE data from World Organization for Animal Health. vCJD data from UK National CJD Surveillance Unit.

Viroids

Pospiviroidae Family

Asymmetric
Pathway



Virophage - Sputnik

