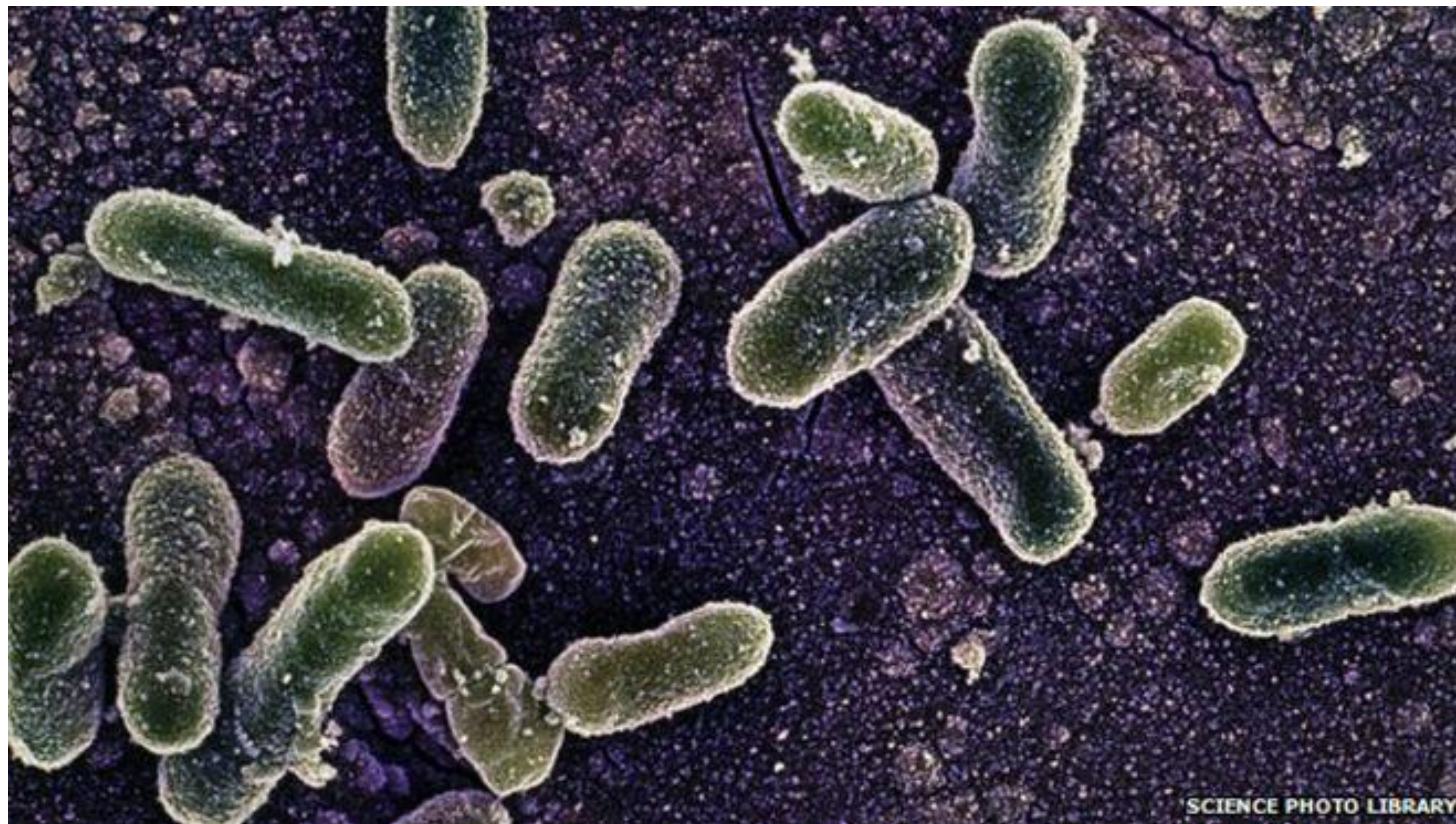
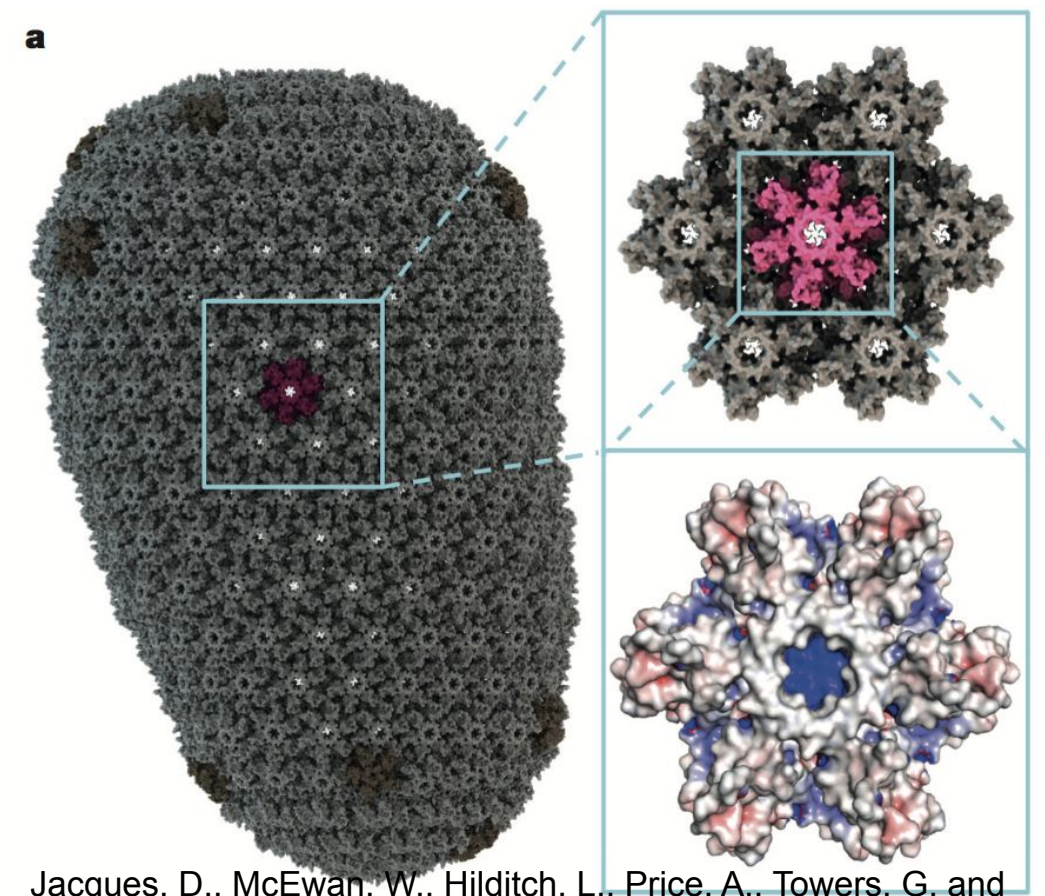


# Pathogenesis of bacteria and viruses



<http://www.bbc.com/news/health-28804267>



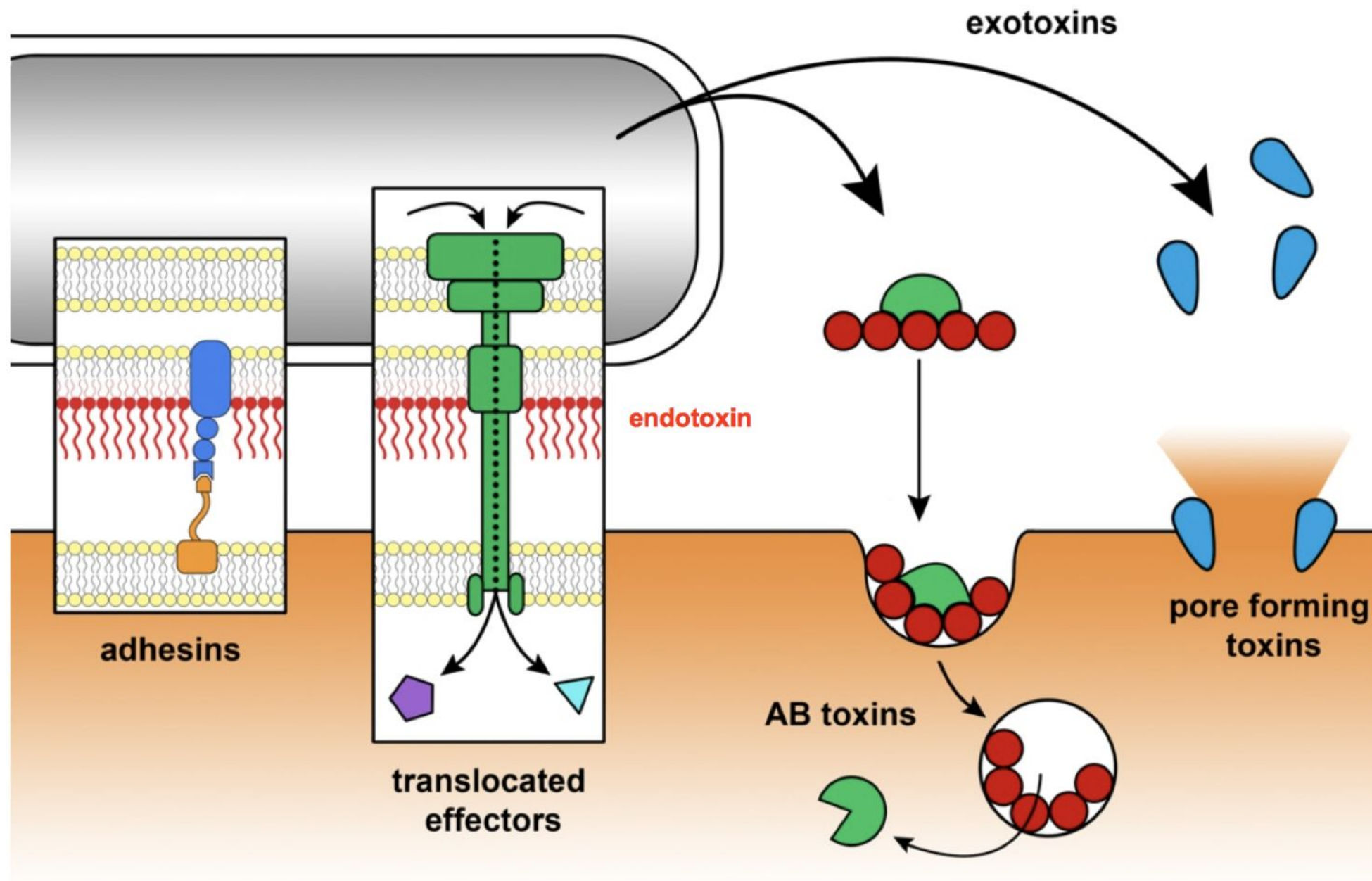
Jacques, D., McEwan, W., Hilditch, L., Price, A., Towers, G. and

James, L. (2016). HIV-1 uses dynamic capsid pores to import nucleotides and fuel encapsidated DNA synthesis. *Nature*,

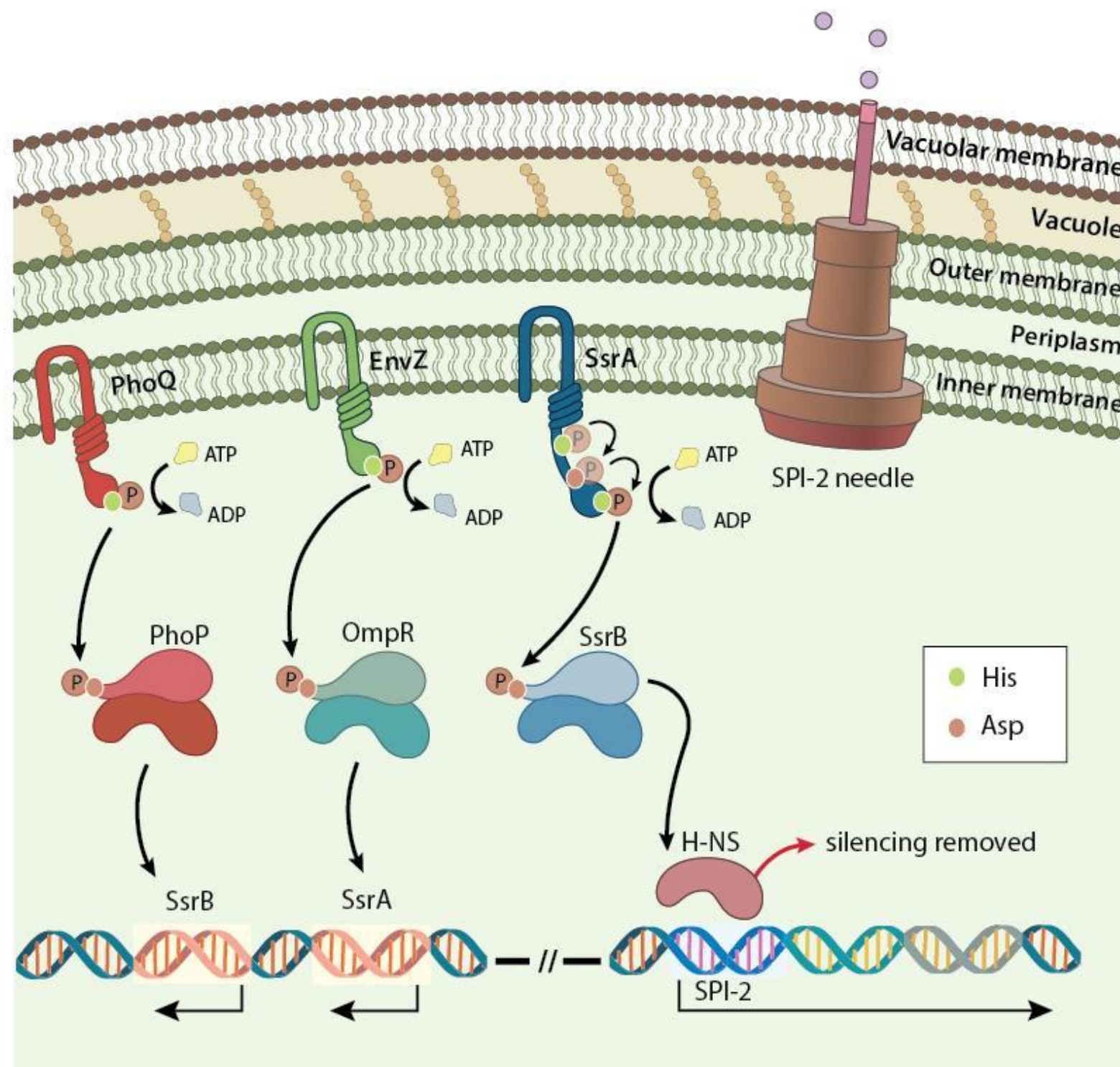


# Bacteria

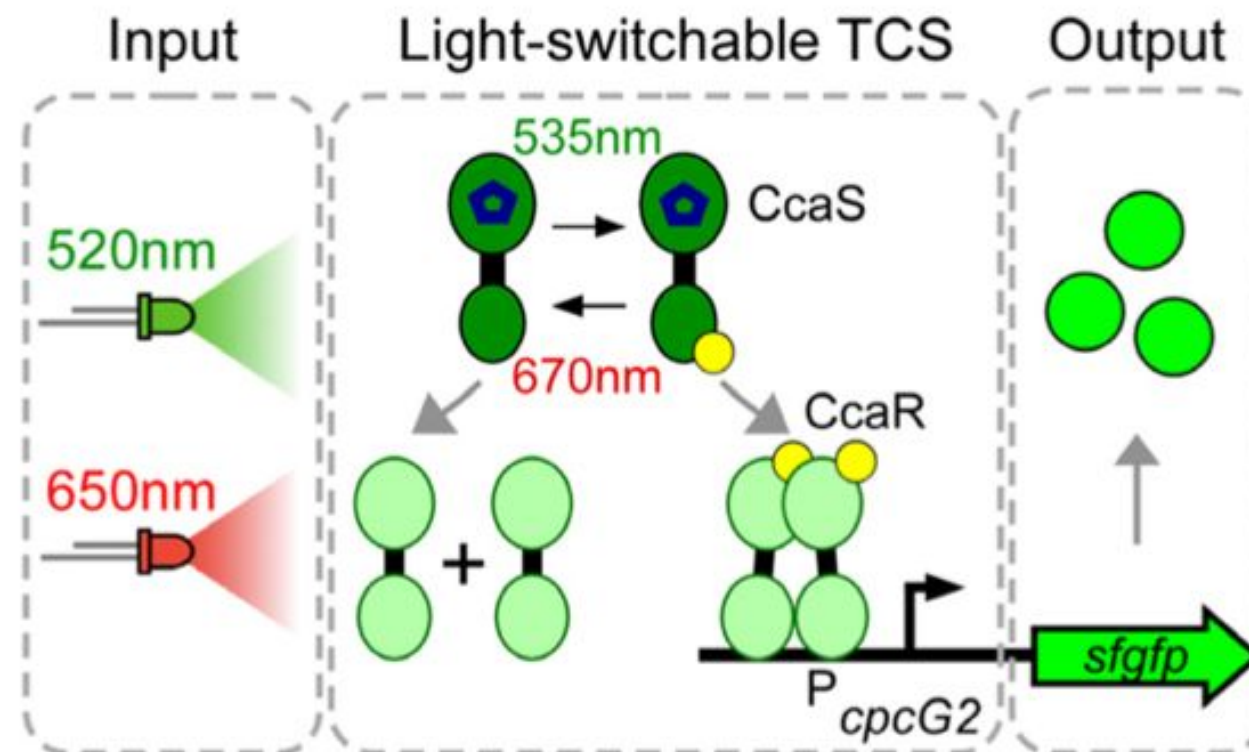
Virulence factors



# Regulation of virulence factors: two-component systems (TSS)



# A bit of synthetic biology...



Schmidl, S., Sheth, R., Wu, A. and Tabor, J. (2014). Refactoring and

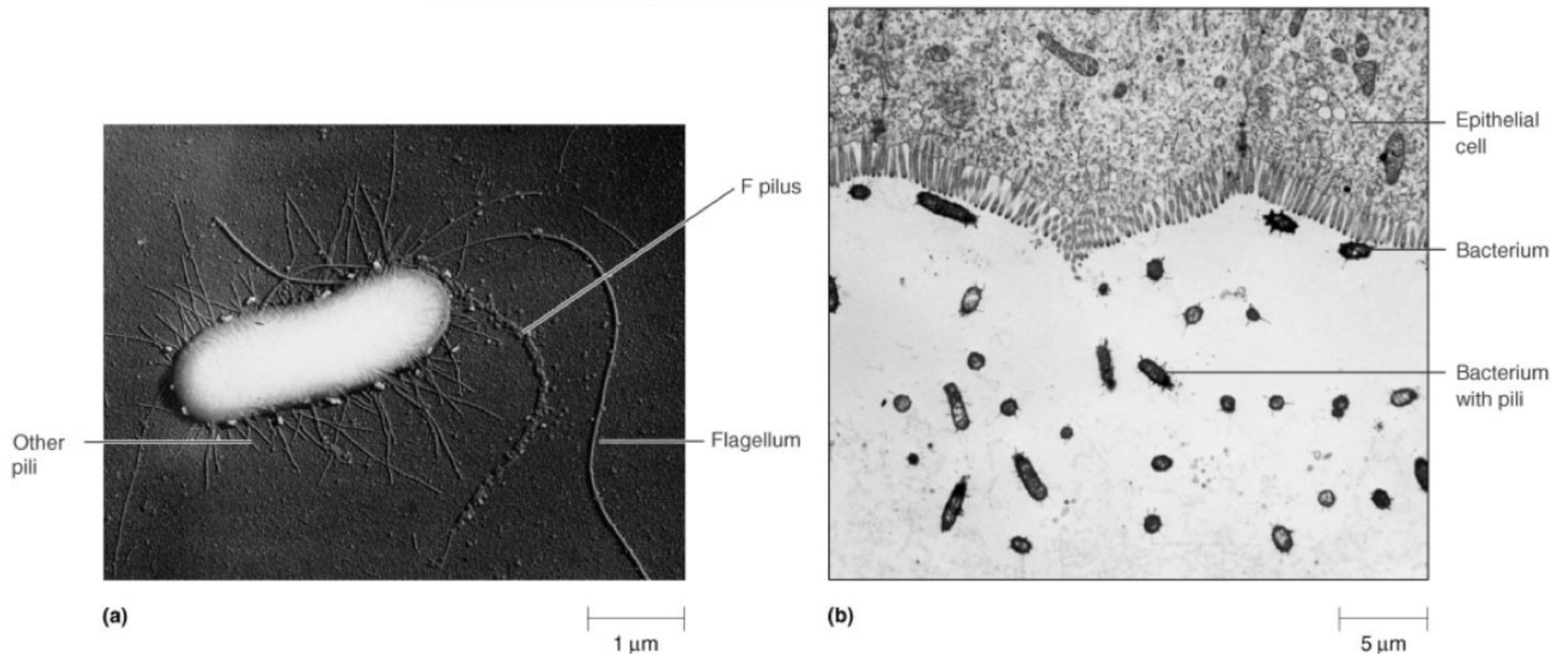
Optimization of Light-Switchable *Escherichia coli* Two-Component

Systems. *ACS Synthetic Biology*, 3(11), pp.820-831.



# Key events of pathogen-host interaction

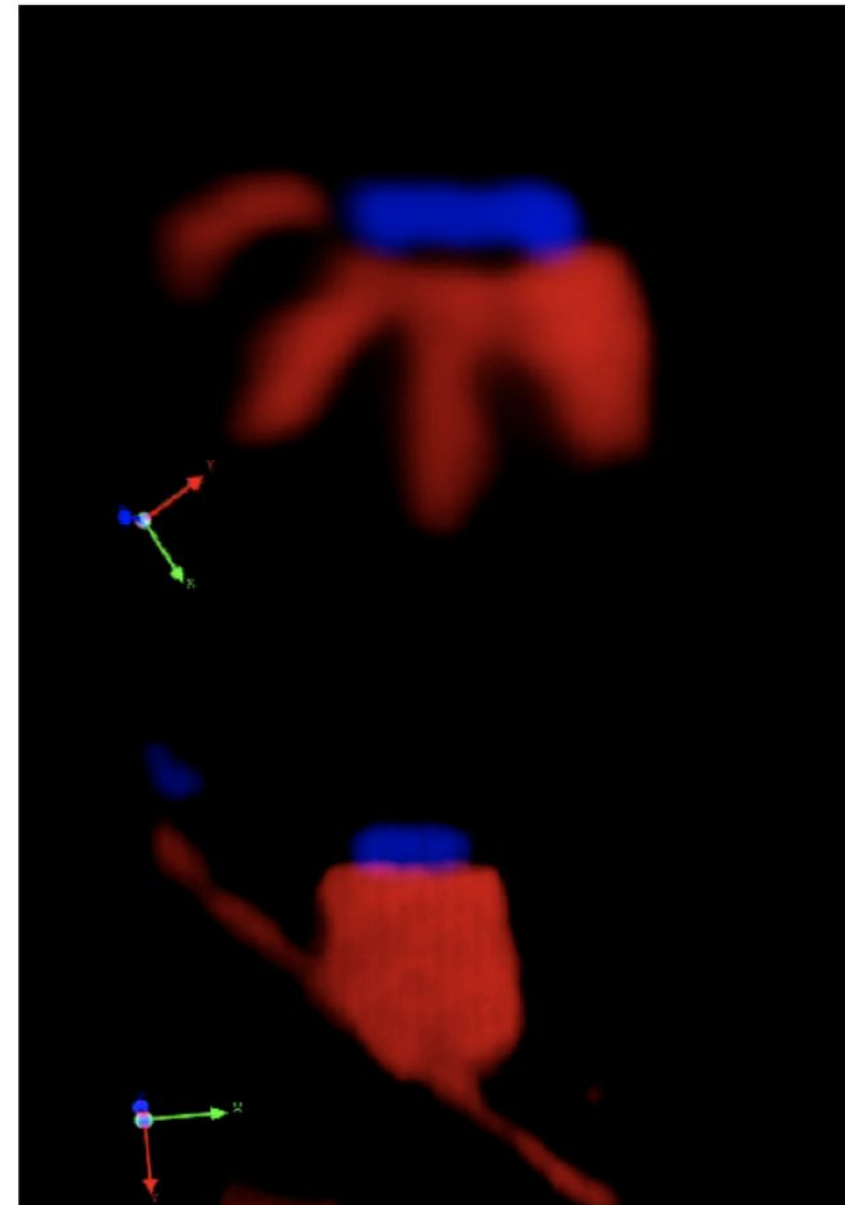
1. Colonisation - invasion
2. Multiplication
3. Transmission
4. Damage



Uropathogenic *E. coli* binding a kidney receptor with adhesins at the top of P-pili



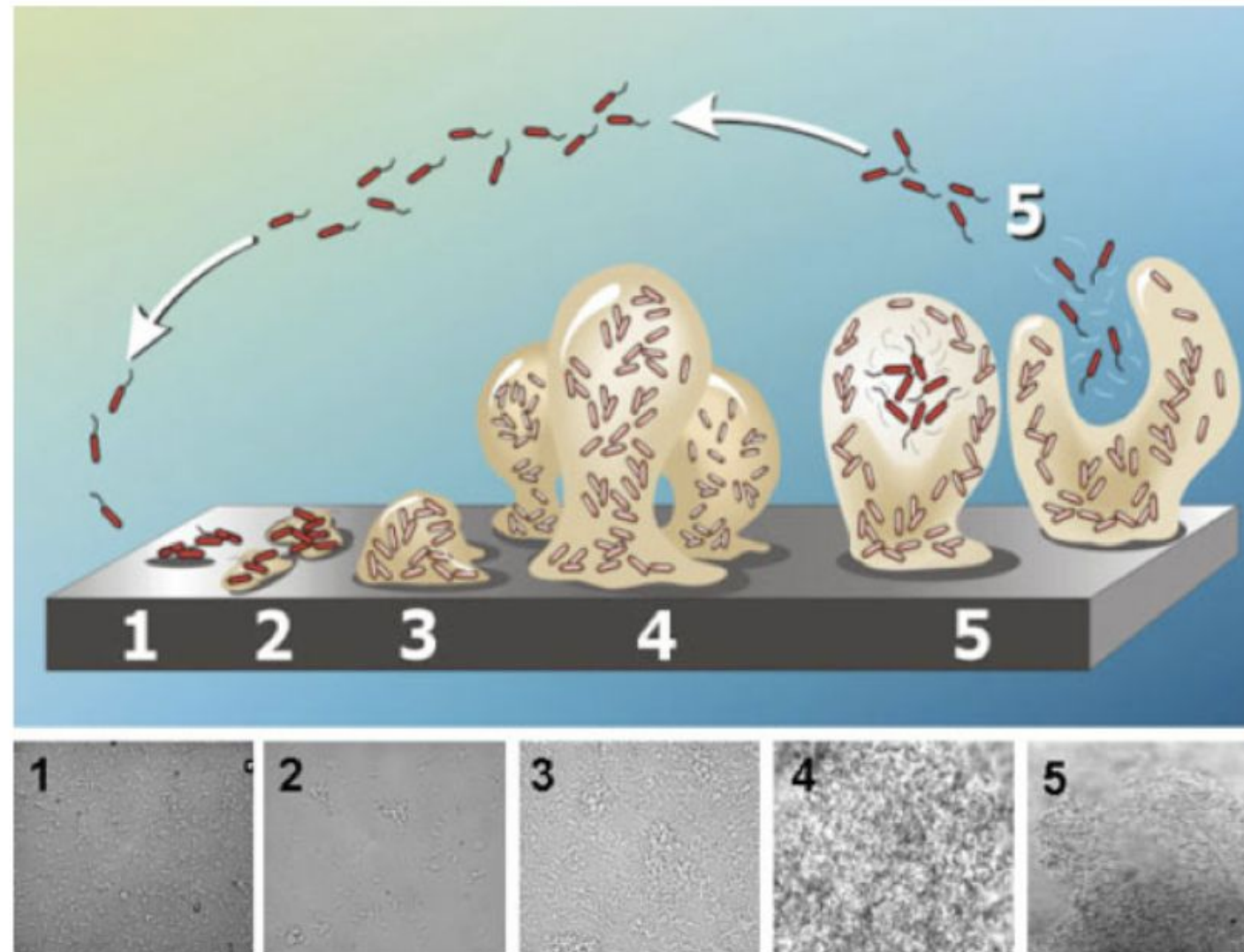
scanning electron microscopy



cytoskeleton  
enteropathogenic *E.coli*

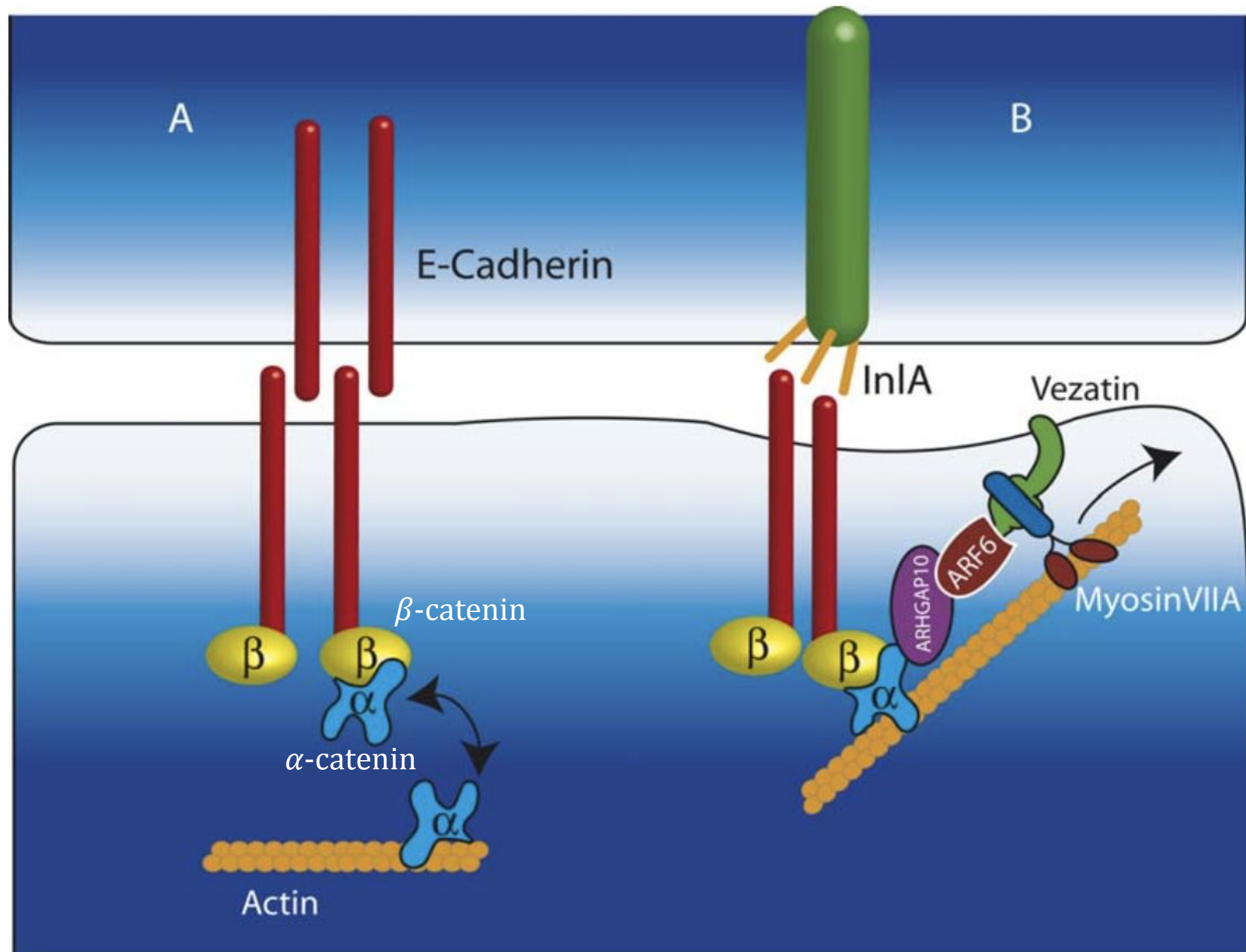
Enteropathogenic *E. coli* build specialised structures for adhesion

# Biofilms

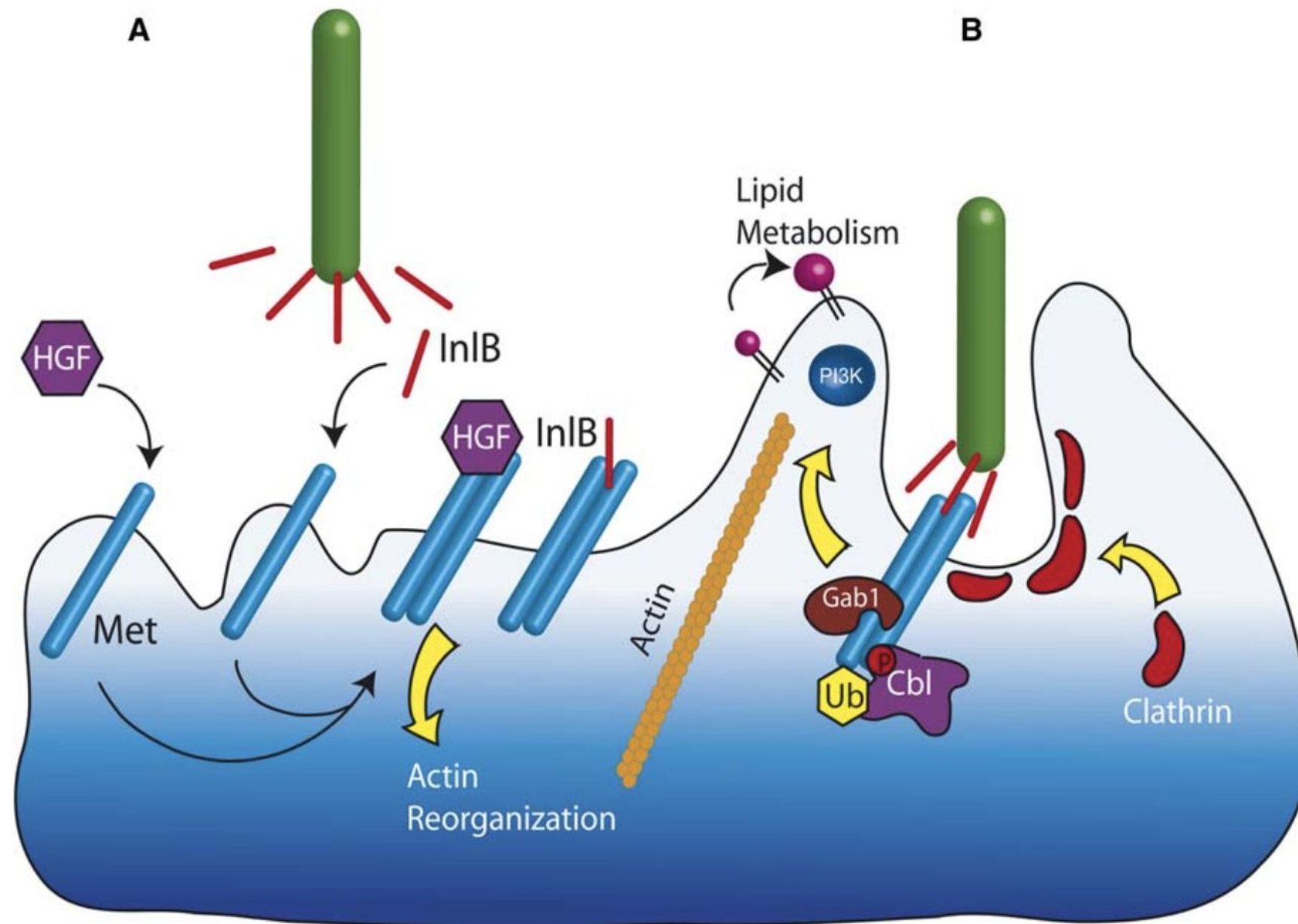


# Invasion

“Zipper mechanism”. *Listeria* invading non-phagocytic cells.



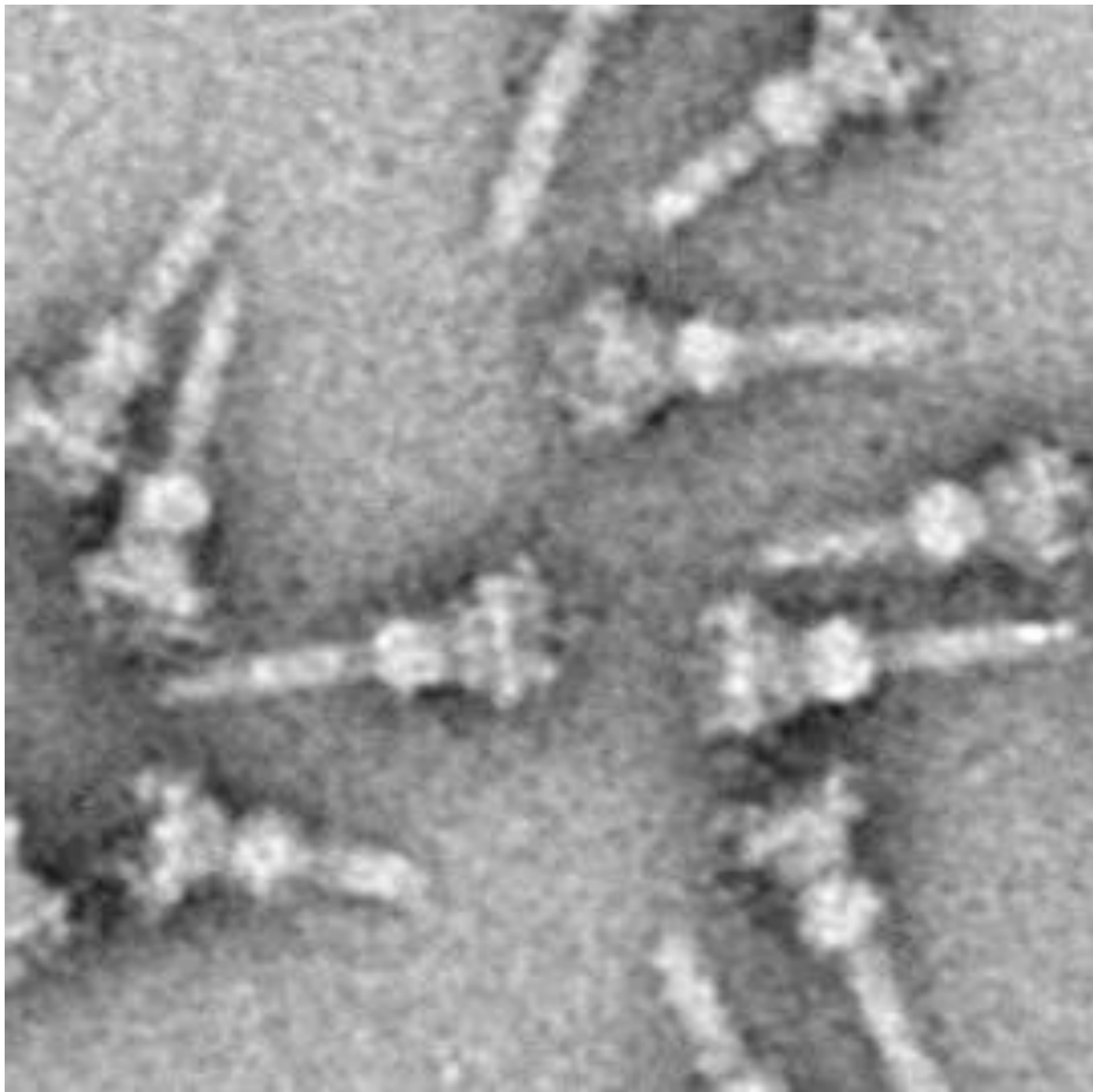




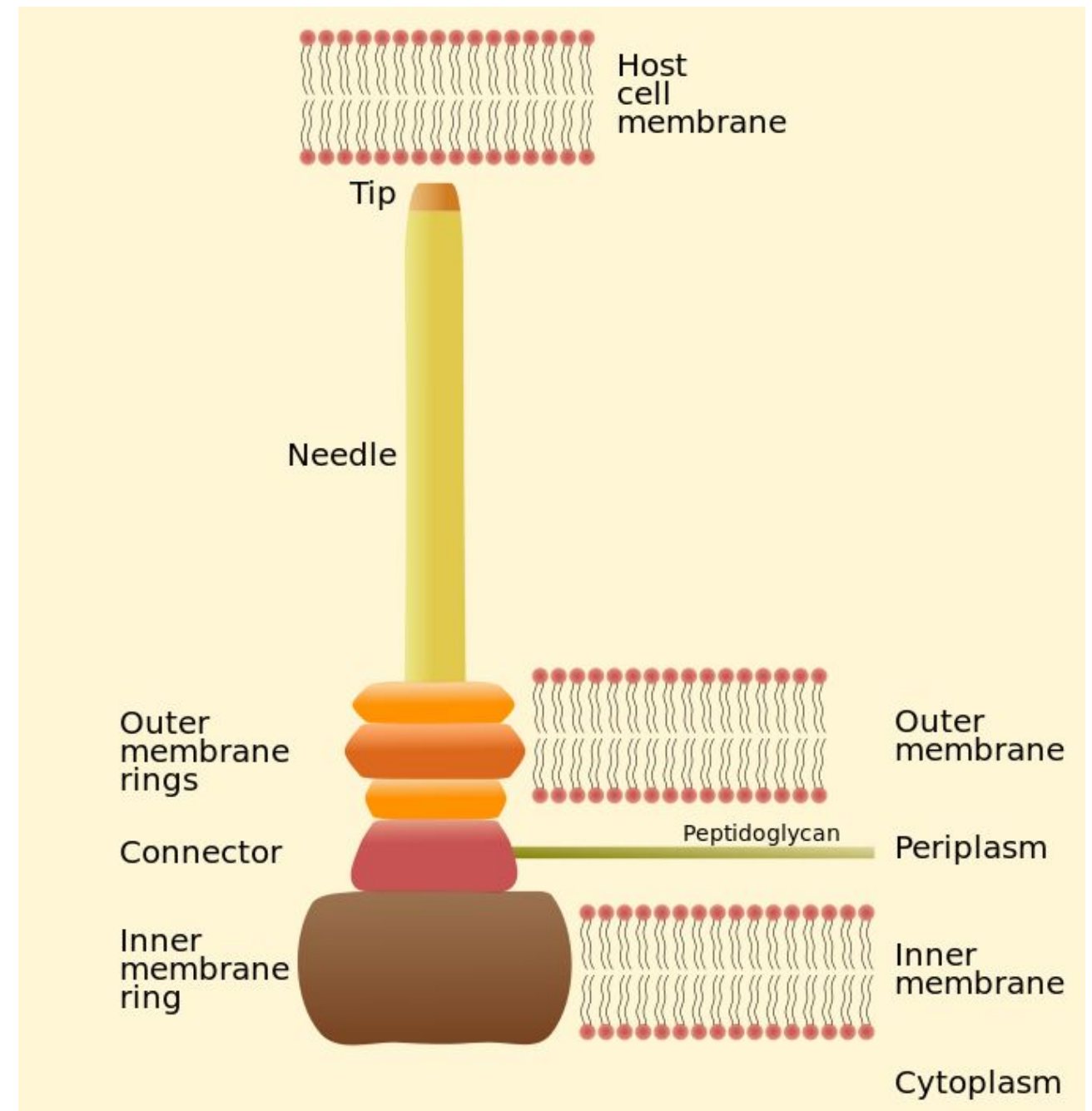
Bonazzi, M. and Cossart, P. (2006). Bacterial entry into cells: A role for the endocytic machinery. *FEBS Letters*, 580(12), pp.2962-2967.

“Trigger mechanism”. *Salmonella*.

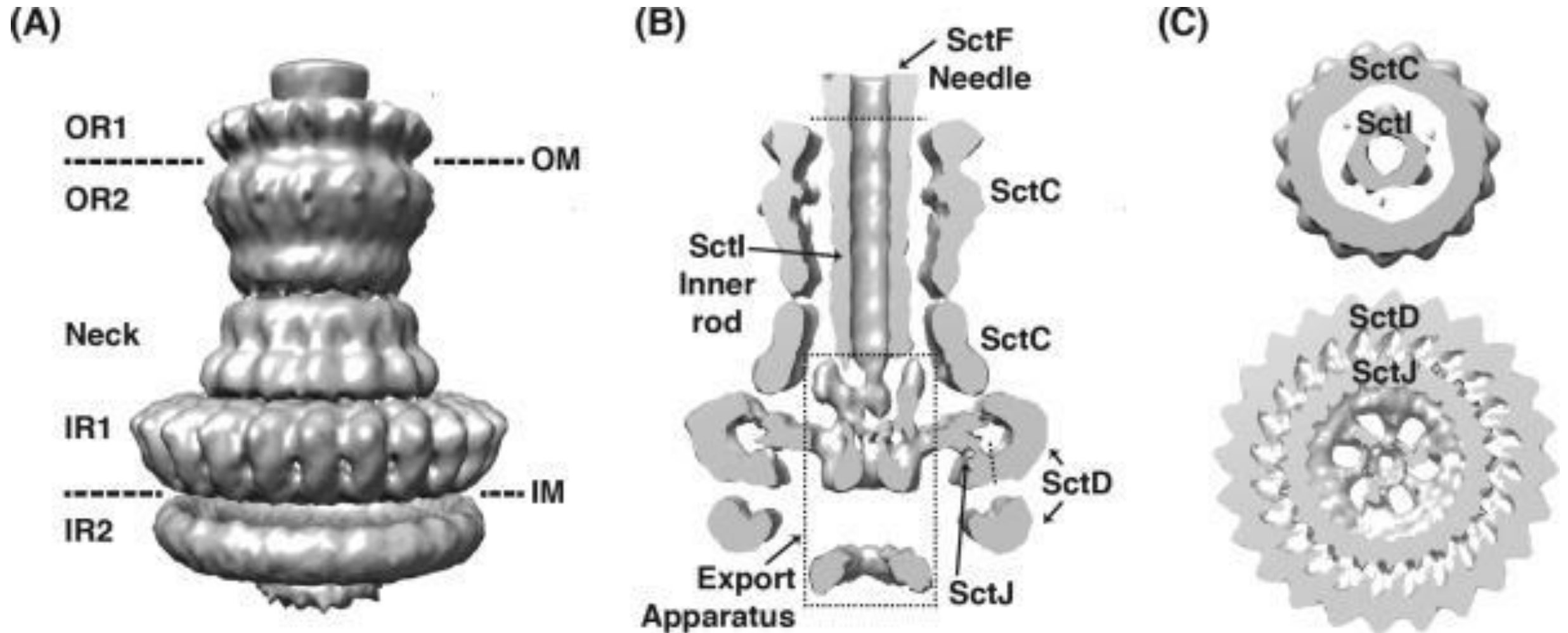
## Type III Secretion System



Transmission EM micrograph of *Salmonella* possessing T3SS



# Cryo-EM micrograph of T3SS



Abbreviations used: OR, outer ring; IR, inner ring; OM, outer membrane; IM, inner membrane. (B) An axial section through the map in (A). (C) Transverse sections through the map in (A) at the level of the neck (top) and IR1 (bottom).

Notti, R. and Stebbins, C. (n.d.). The Structure and Function of

Type III Secretion Systems. *Virulence Mechanisms of Bacterial*

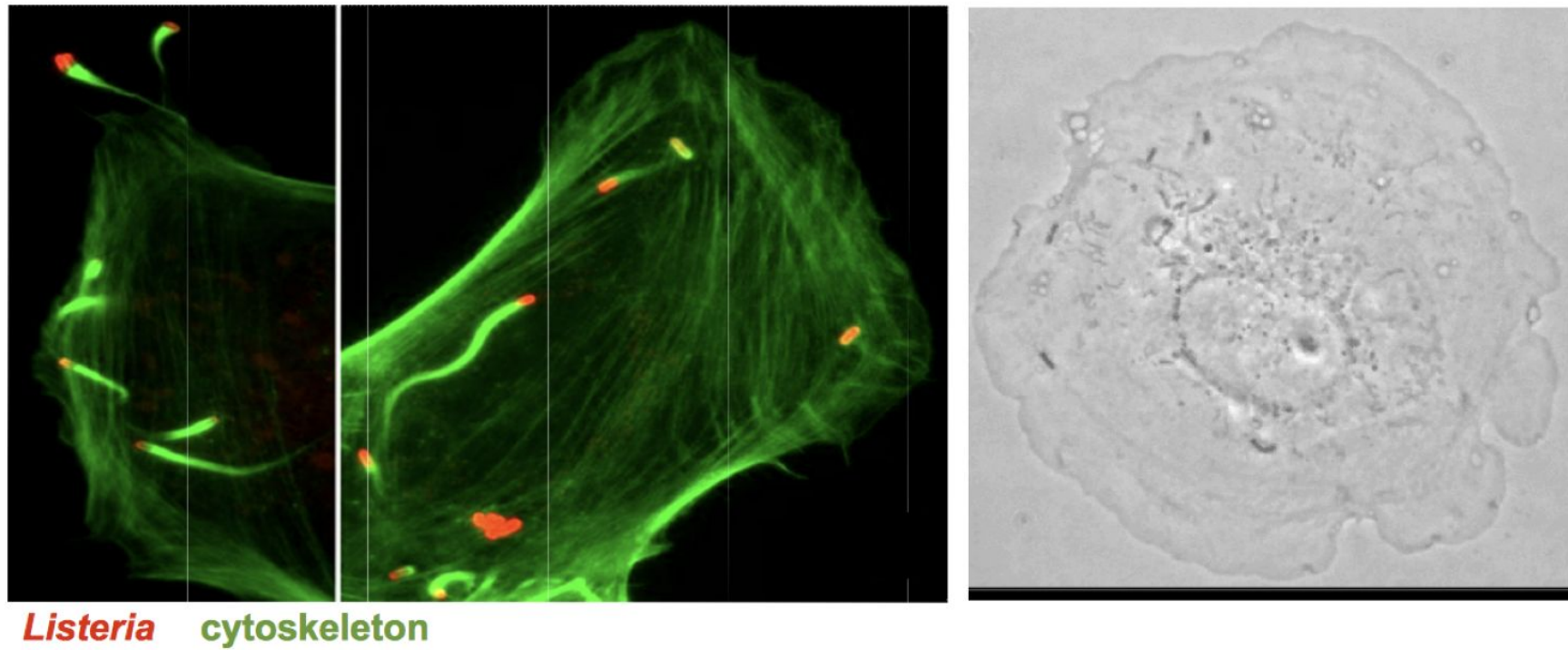
*Pathogens, Fifth Edition*, pp.241-264.



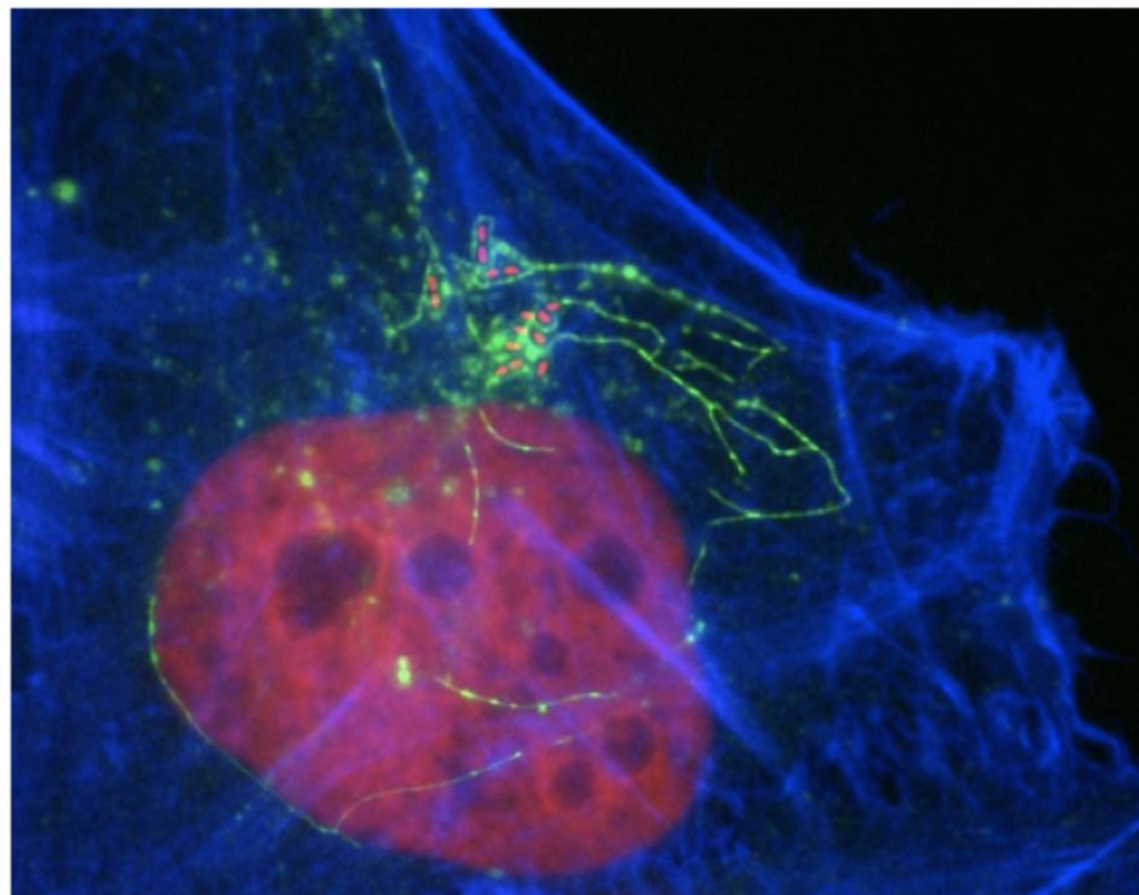




# What happens once bacteria are in?

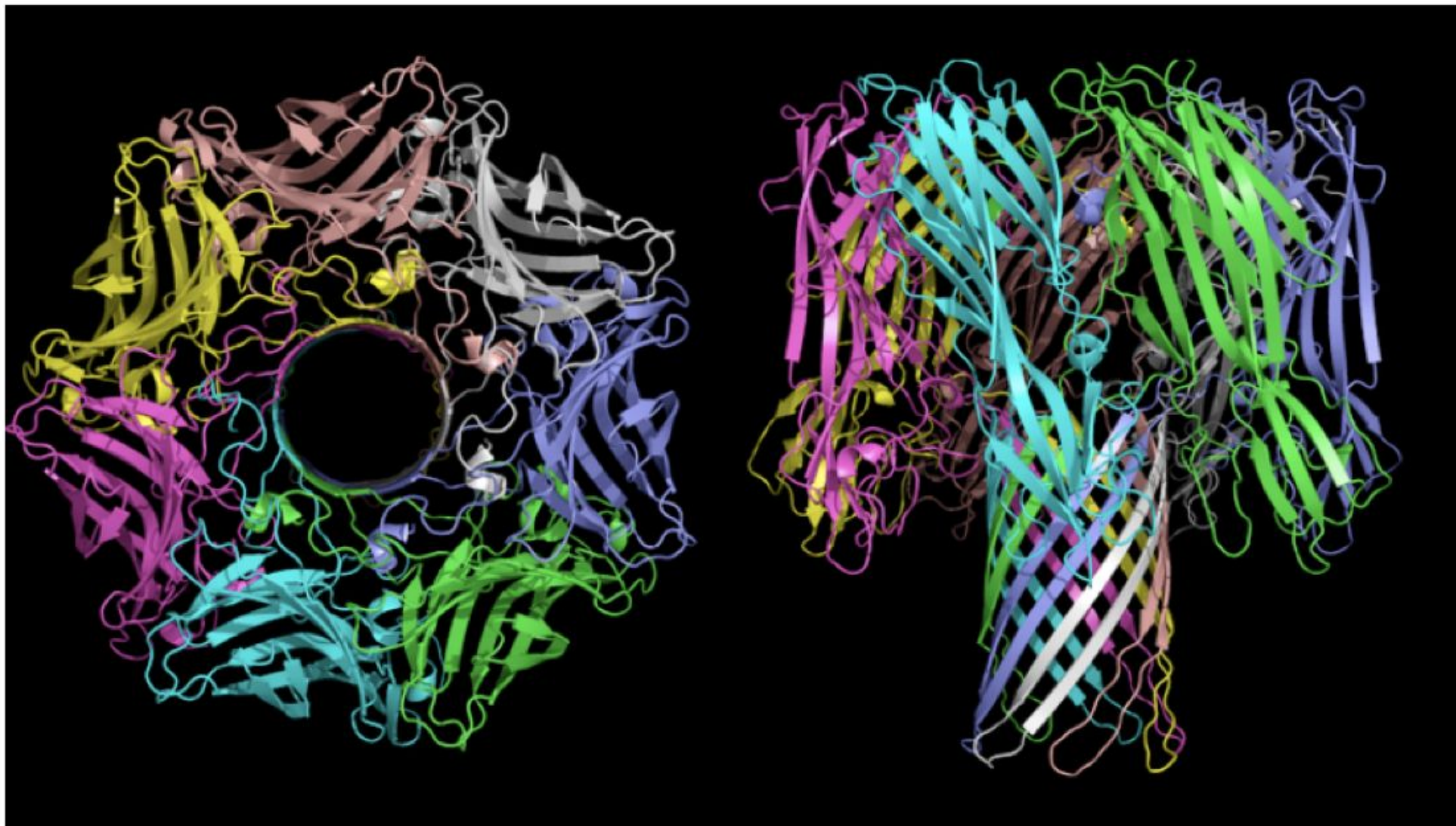


DNA  
cytoskeleton  
pathogen vacuole



# Damage caused by bacteria

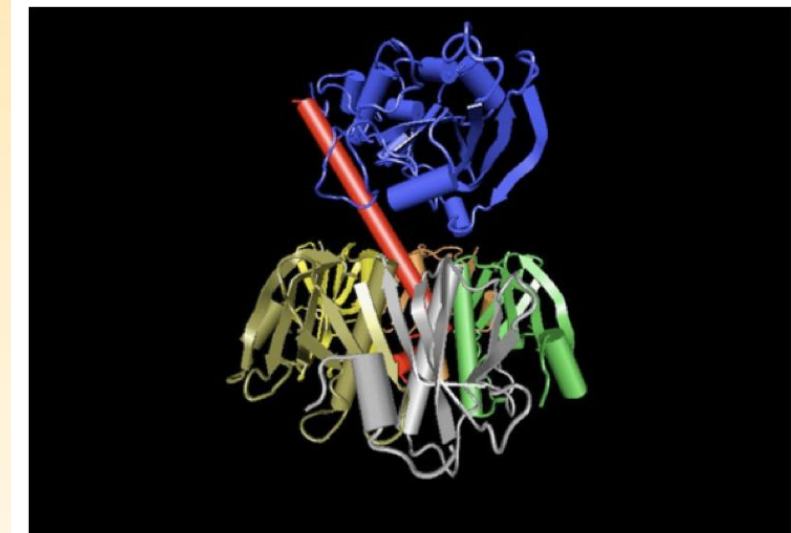
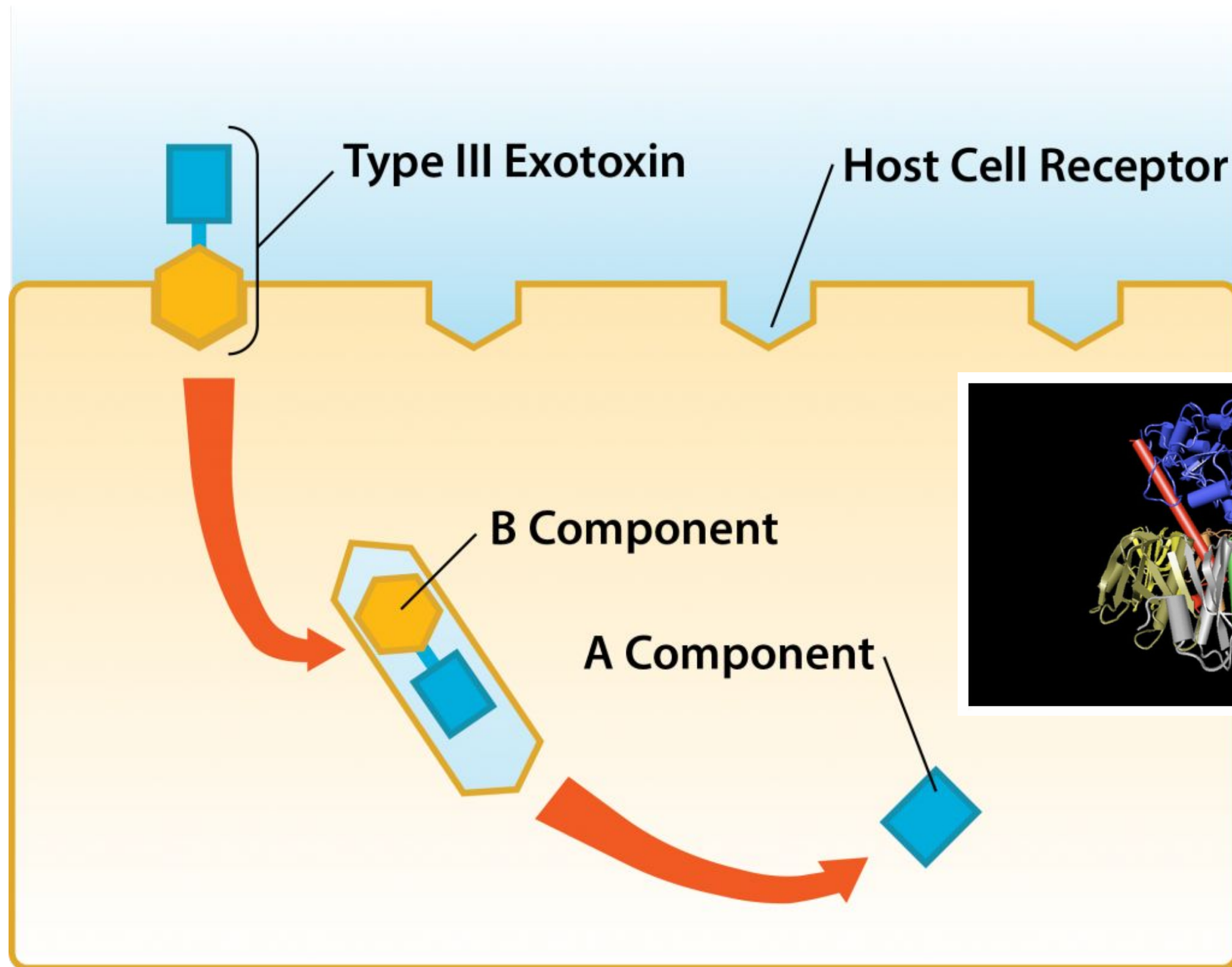
- **Direct** – from bacteria action
- **Indirect** – from host response



Cytolysin

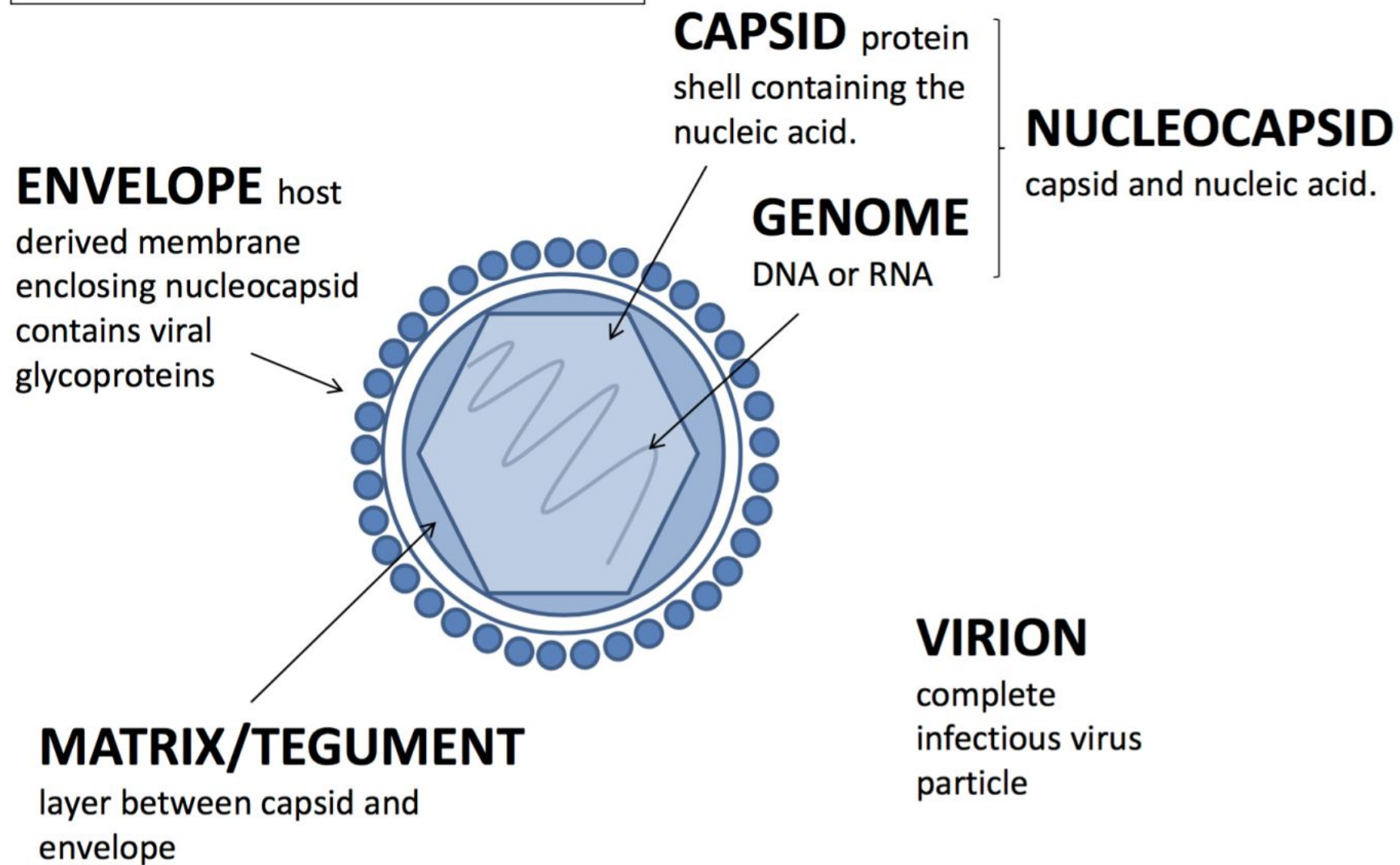


# AB toxins



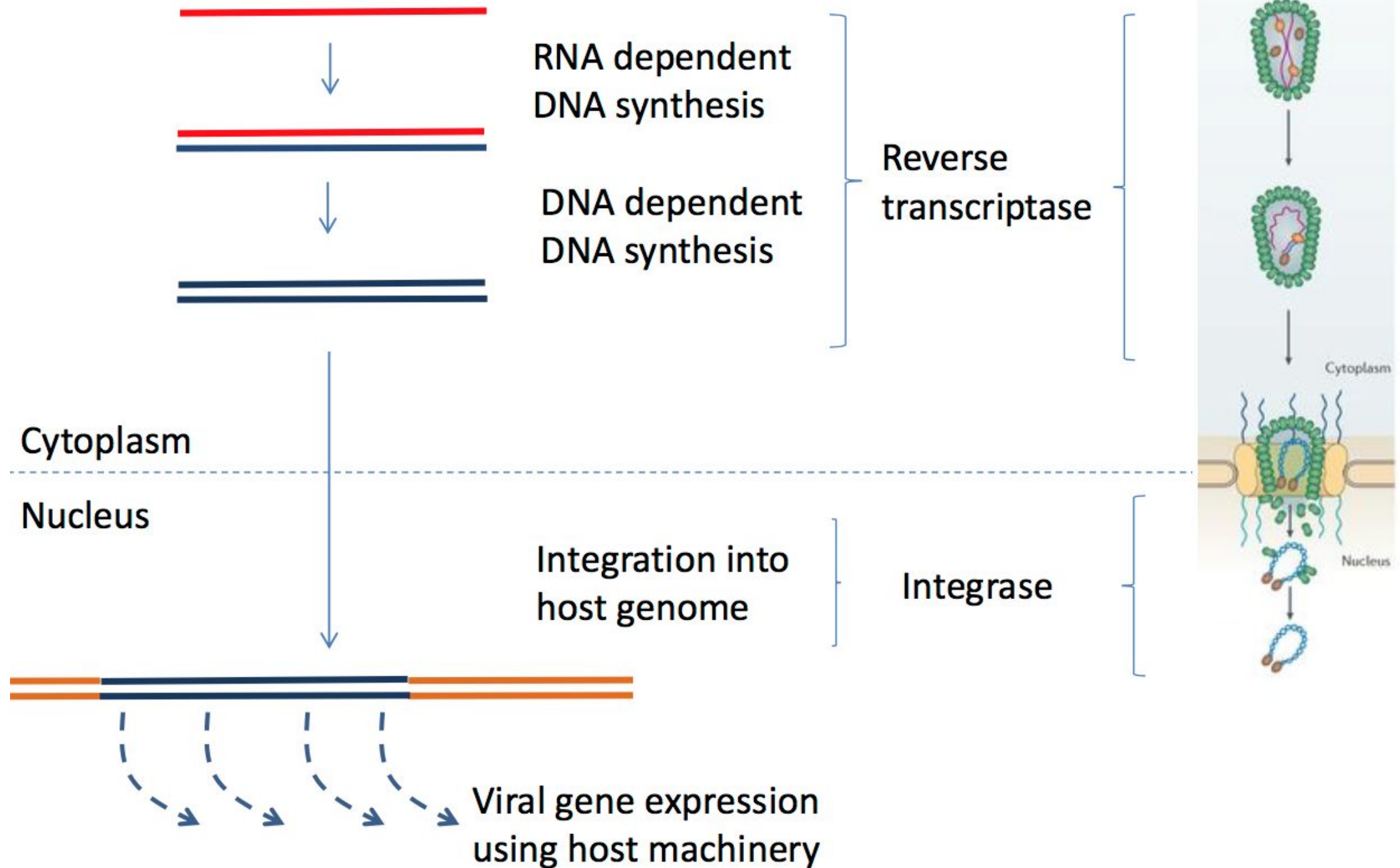
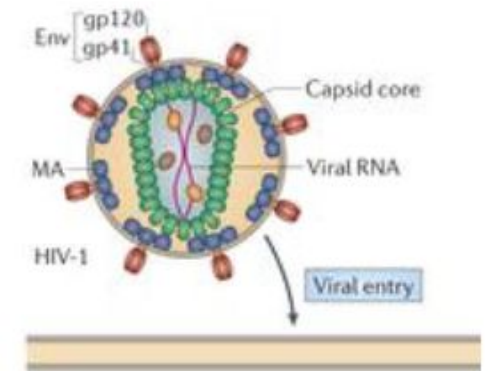
# Viruses

## Virus structure: terminology



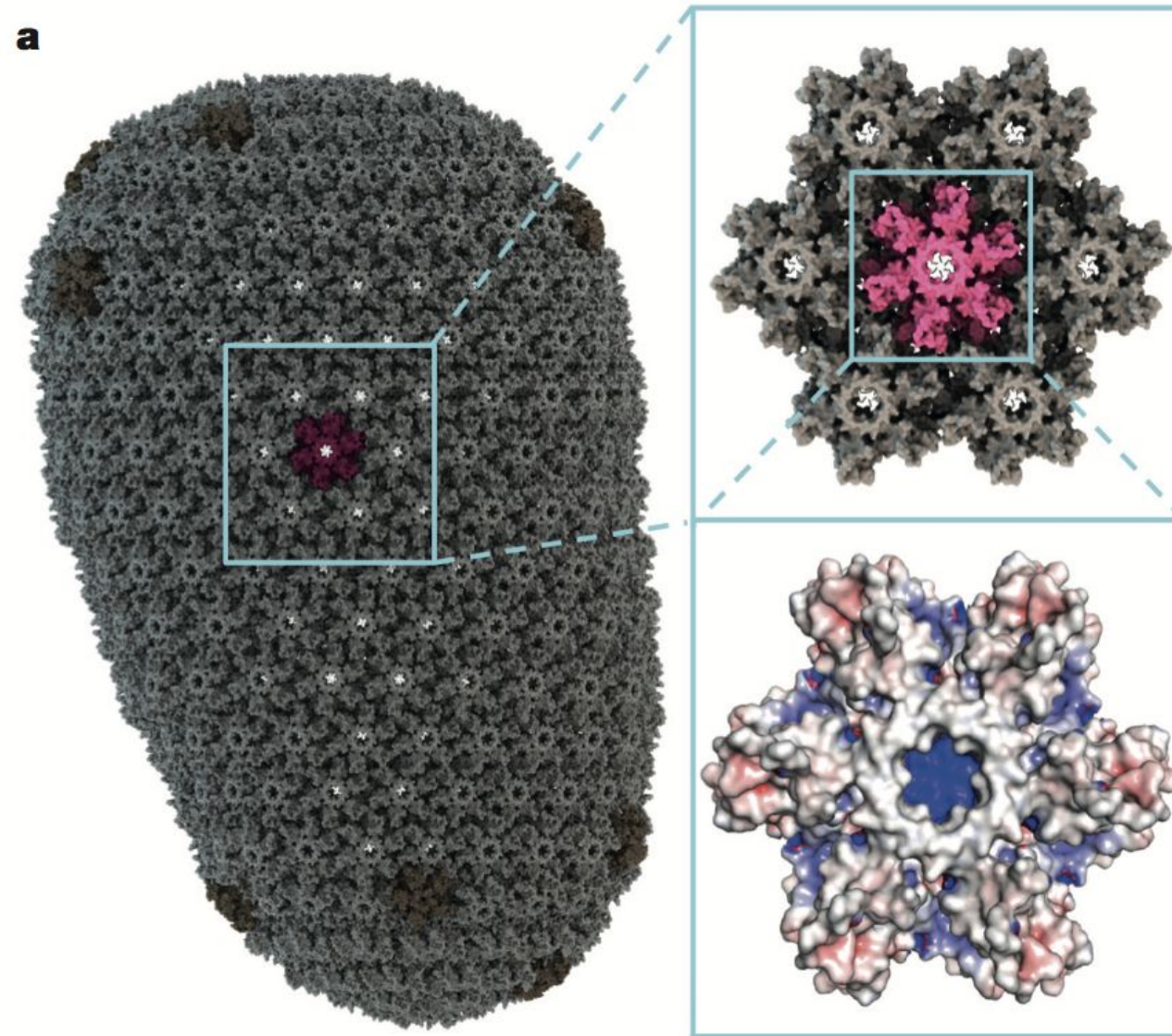
# Retroviruses - HIV

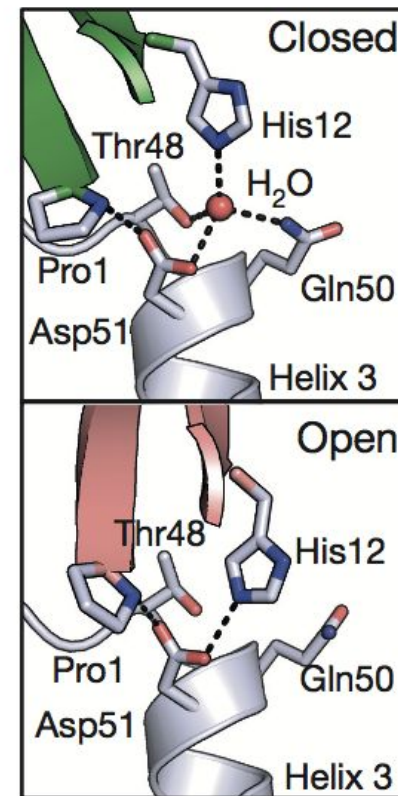
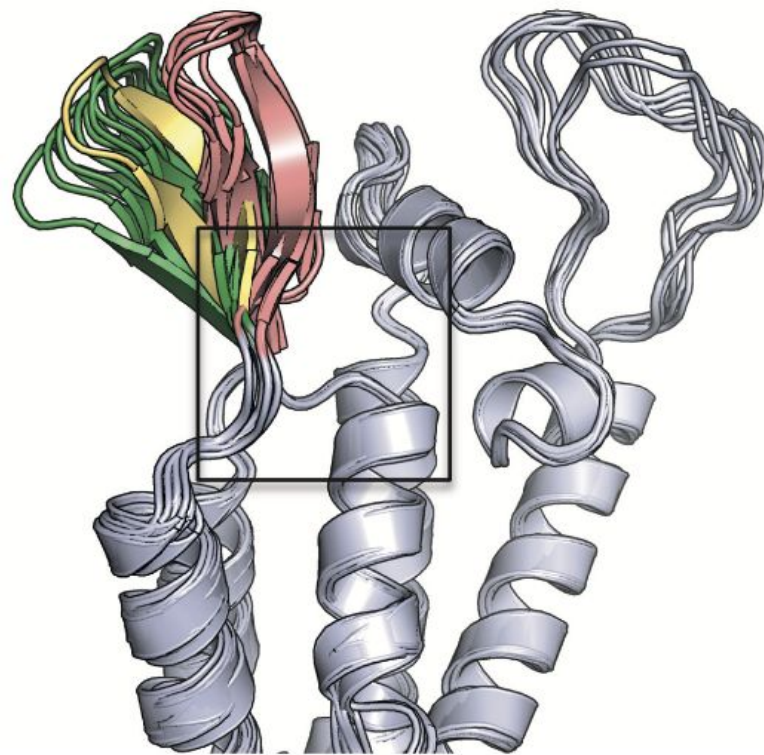
Replication enzymes  
contained in capsid





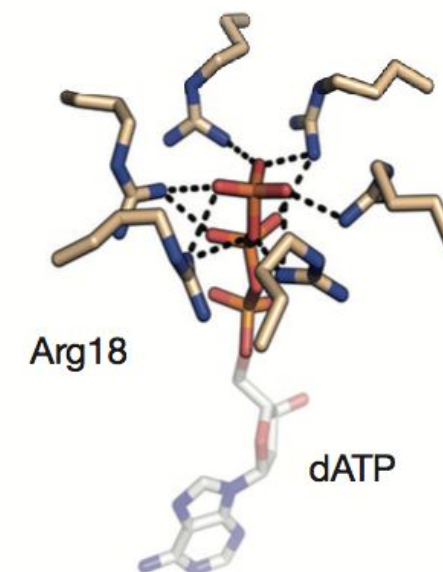
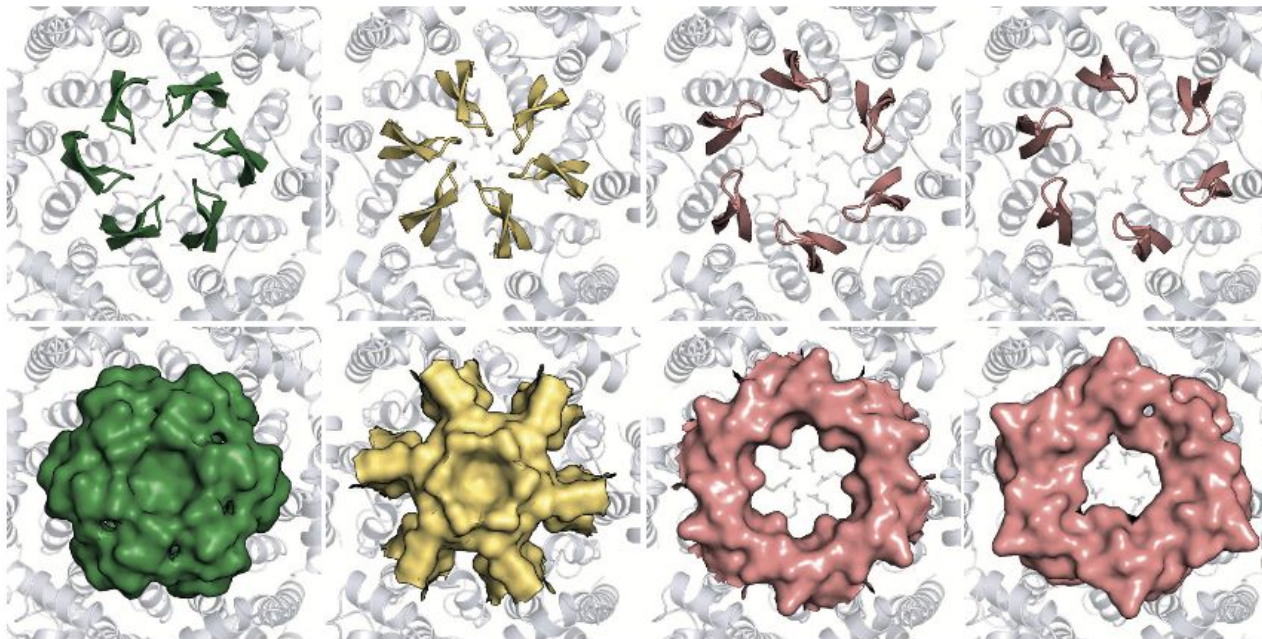
# HIV capsid



**a**

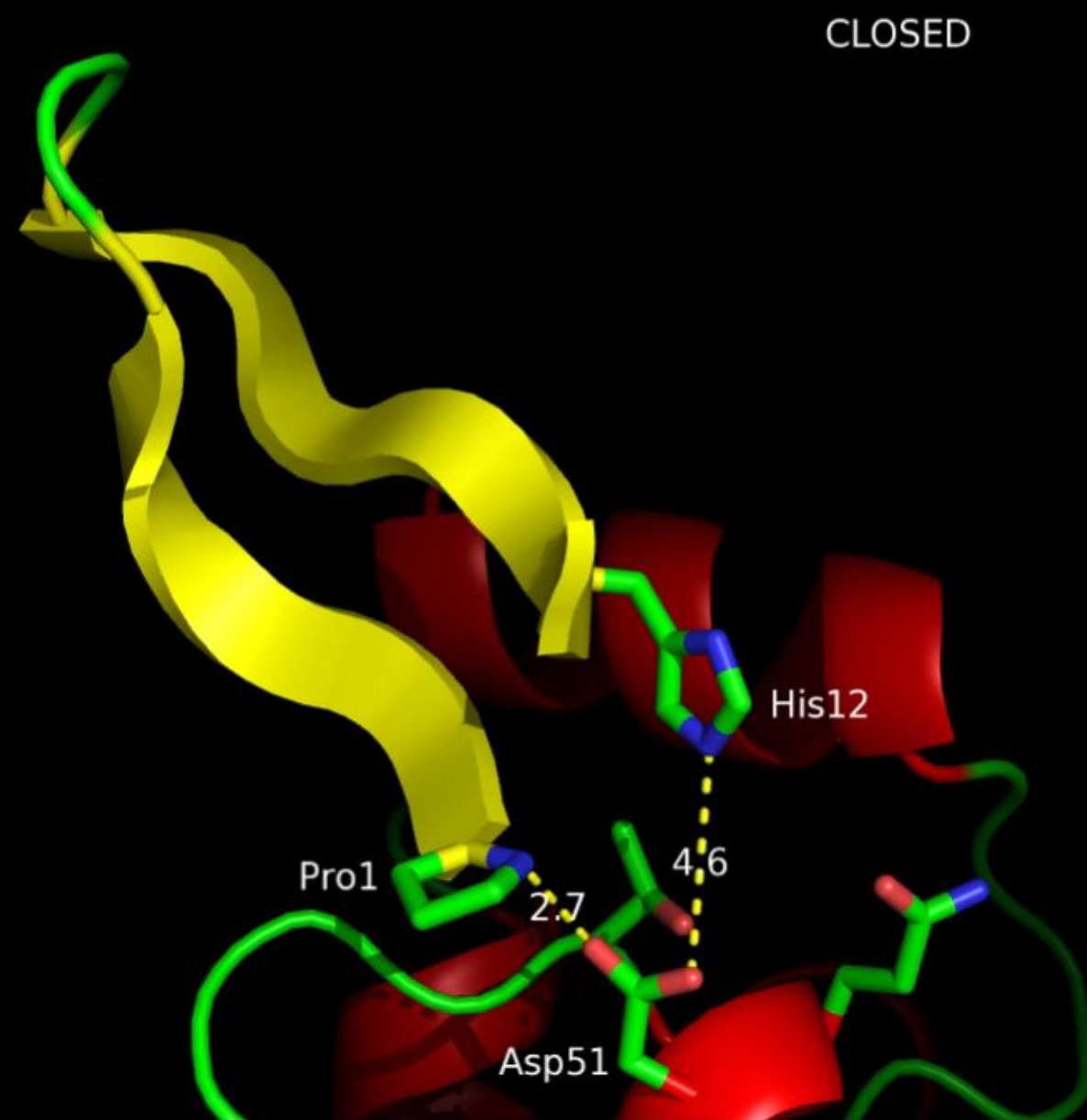
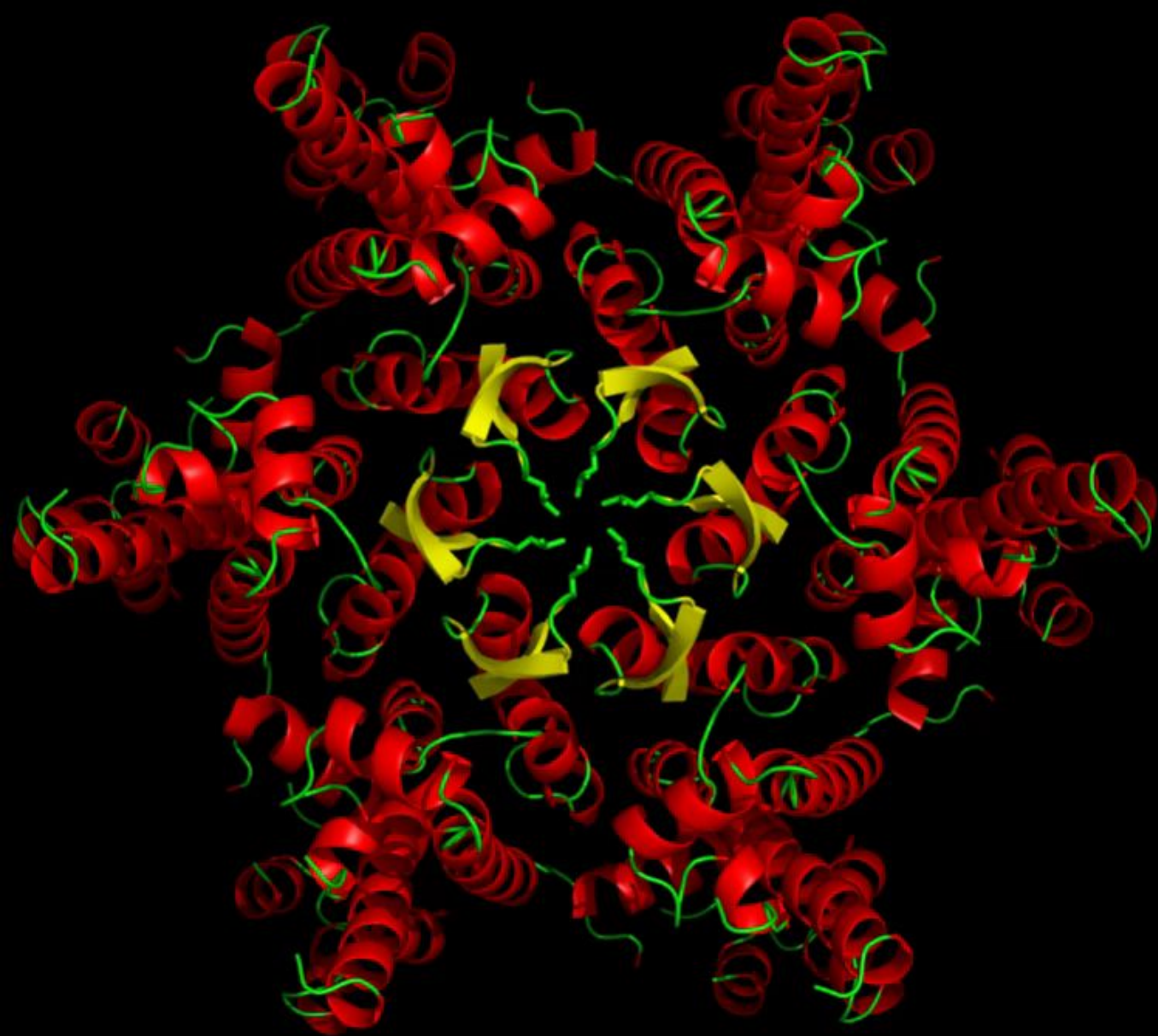
Closed

Open

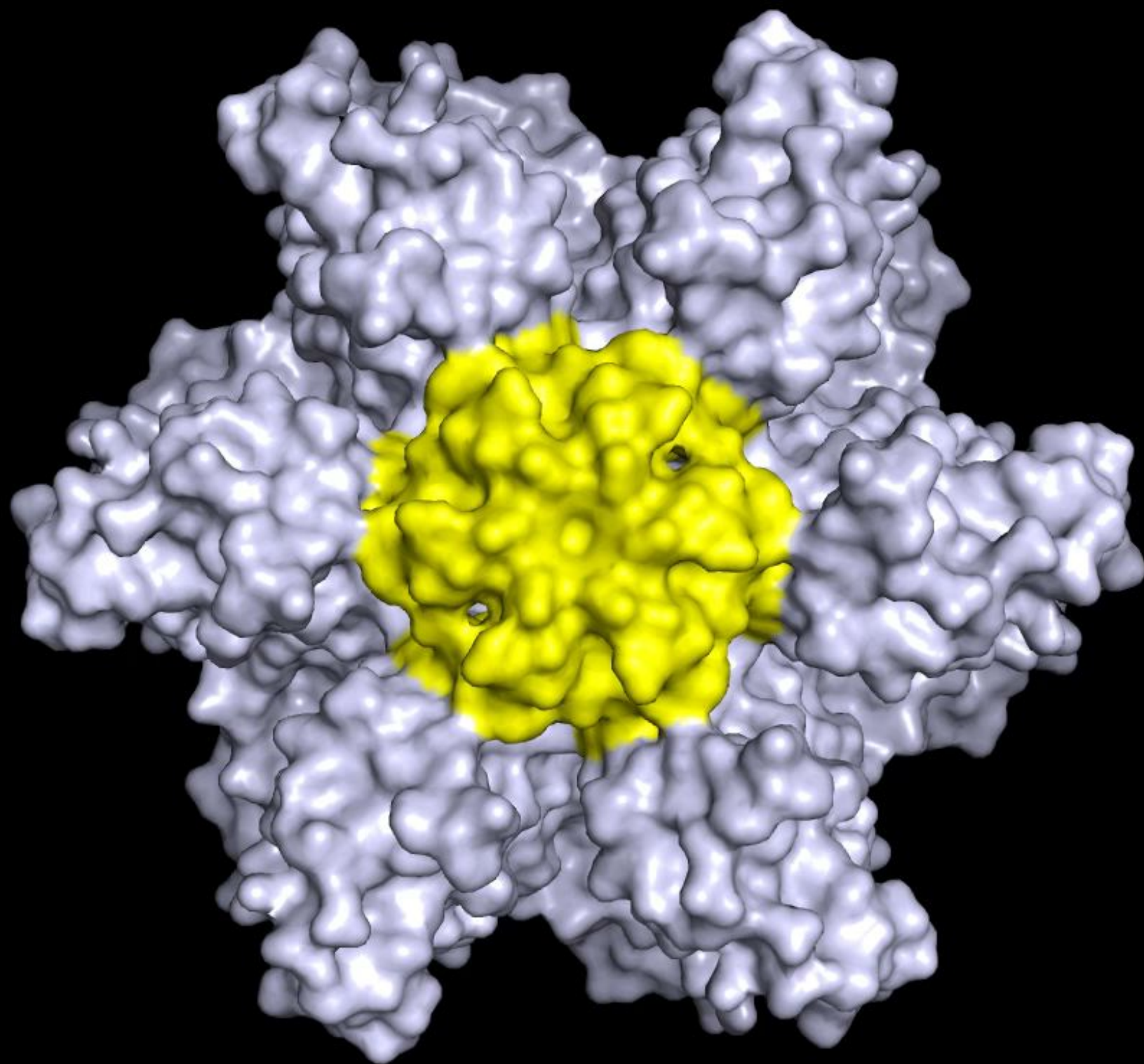
**b**Closed  
(CA<sub>hexamer</sub>)Intermediate  
(CA NTD)Open  
(CA NTD)Open  
(CA<sub>hexamer</sub>)

Beta-hairpin can adopt alternate conformations that differ by up to 15 Å.

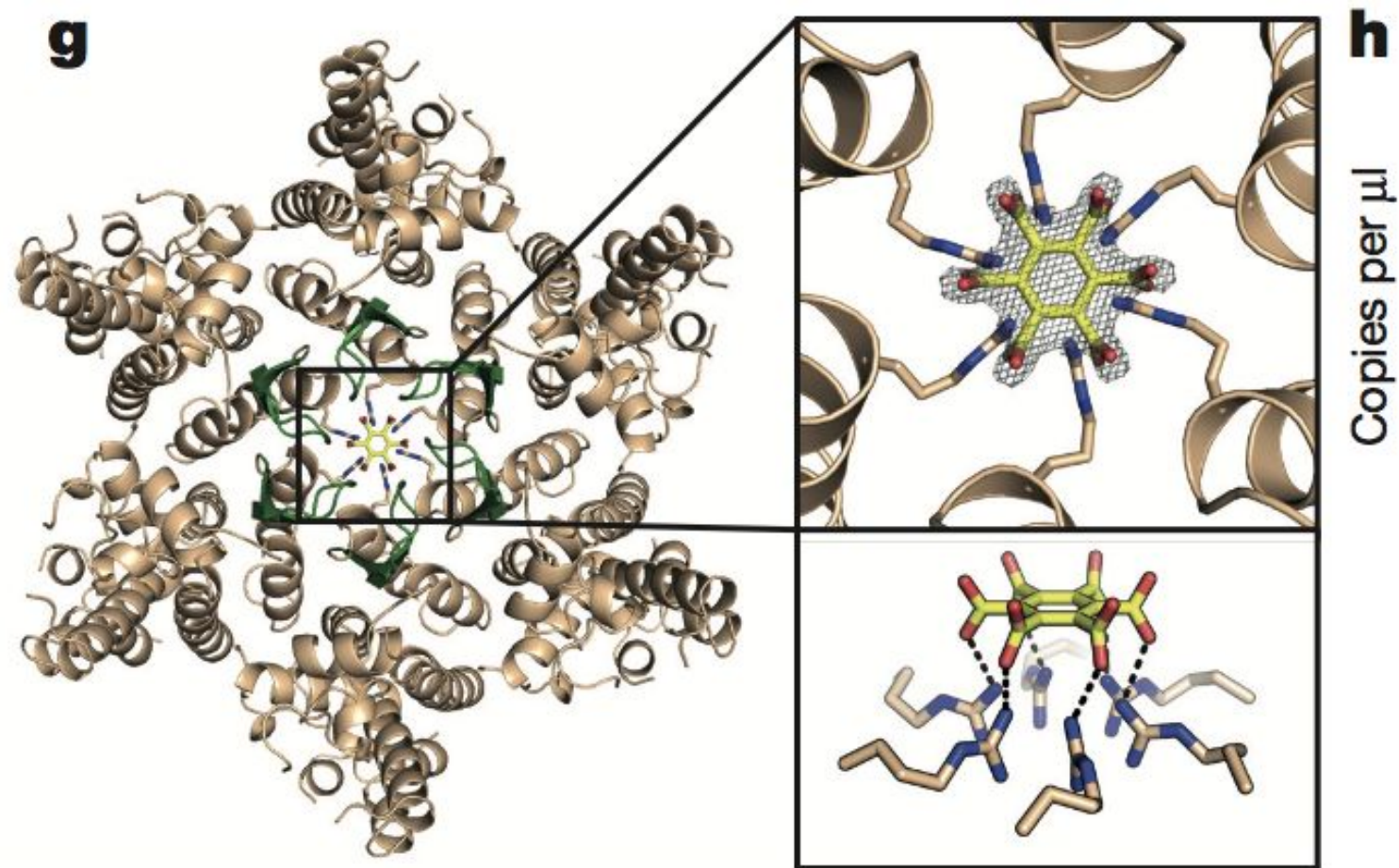








HIV-1 reverse transcription is inhibited by blockade of the capsid pore



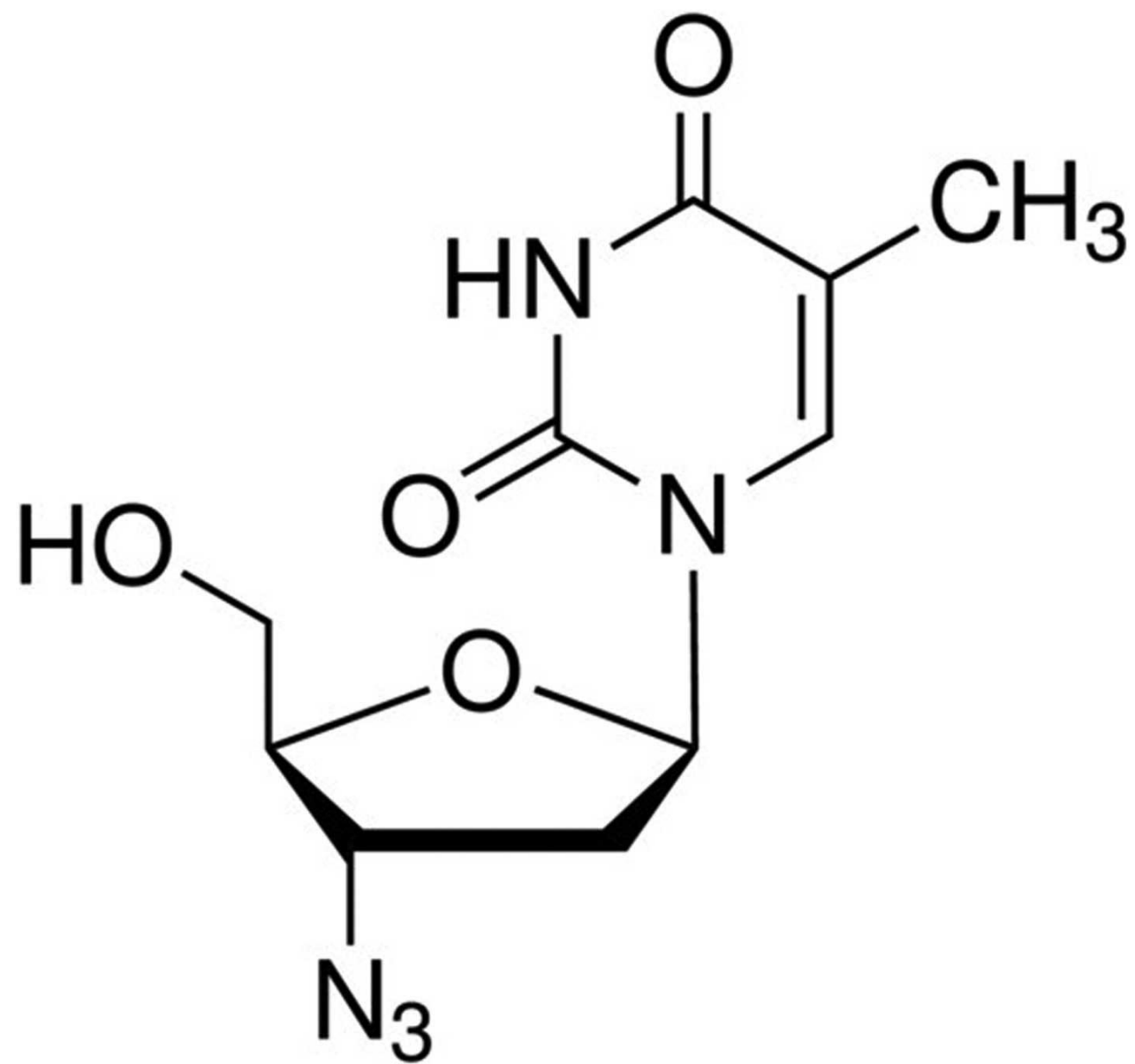
CA<sub>hexamer</sub> crystal structure in complex with  
hexacarboxybenzene, which is co-ordinated by R18

# Current approach to AIDS treatment

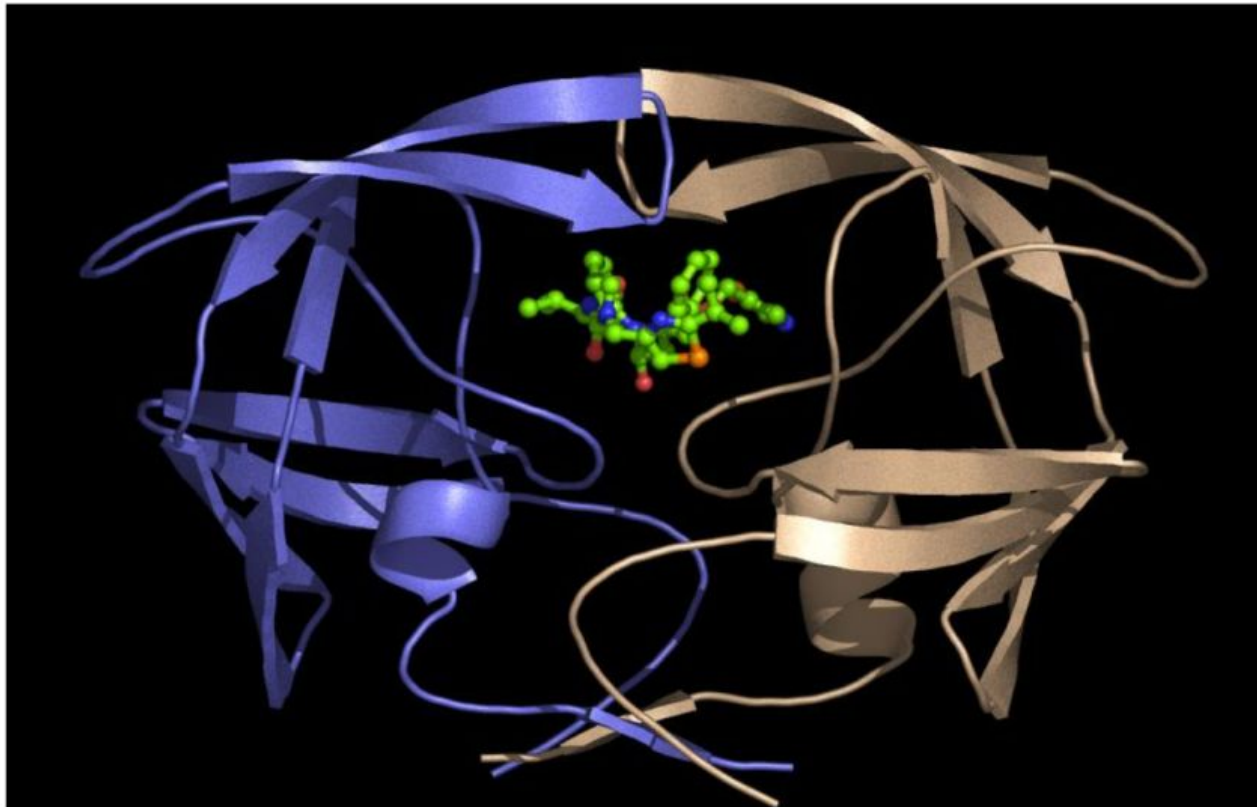
- Nucleoside Reverse Transcriptase Inhibitors
- Protease Inhibitors
- Fusion Inhibitors
- Highly Active Antiretroviral Therapy
- Non-Nucleoside Reverse Transcriptase Inhibitors



AZT



## Blocking assembly: protease inhibitors

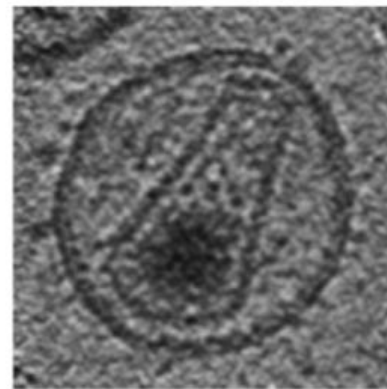
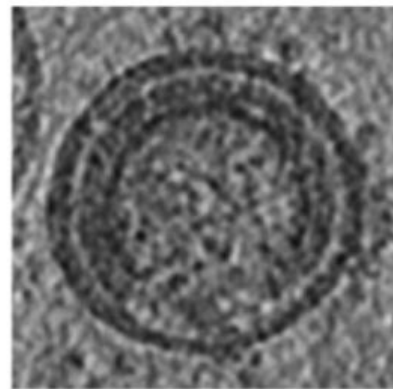
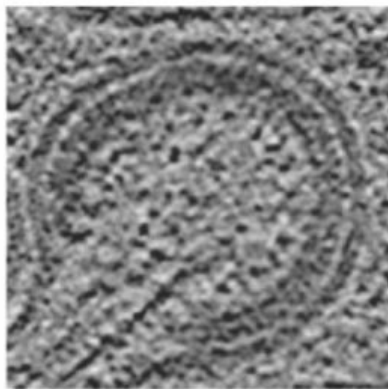


### HIV protease

Homo-dimeric  
aspartyl protease

Encoded by pol gene

Peptide mimics of  
cleavage sites are  
inhibitors



Cleaves polyprotein to  
produce capsid  
components