

Virology 1

Professor Wendy Barclay

Lecture learning objectives

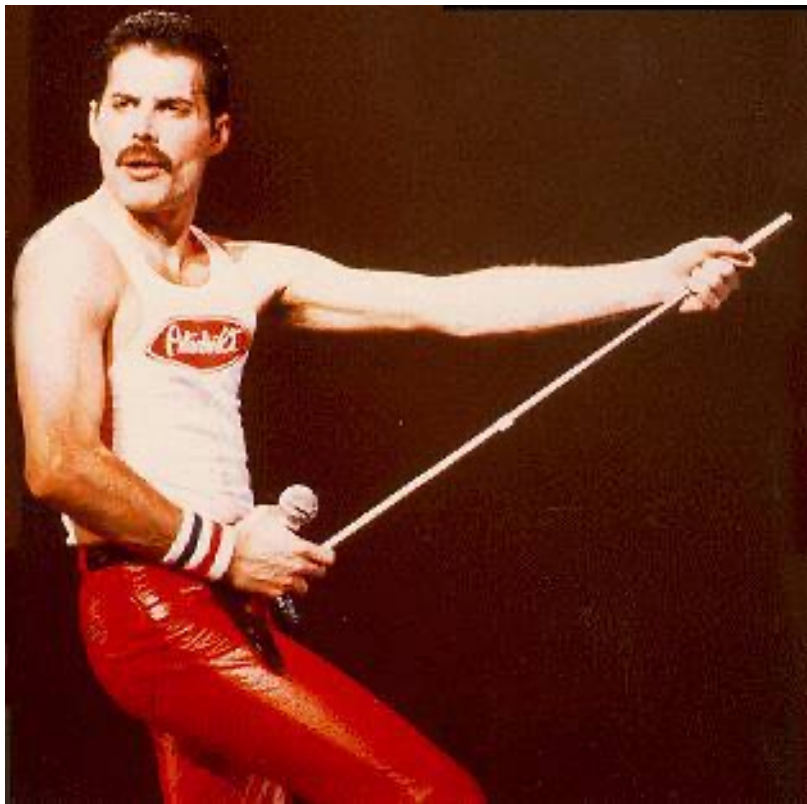
- Define the nature of viruses: their small size, dependence on a host and their structural and genetic diversity.
- Summarize a generic virus replication cycle.
- Explain how viruses are detected, cultivated and manipulated.

Which of these diseases is not associated with virus infection?

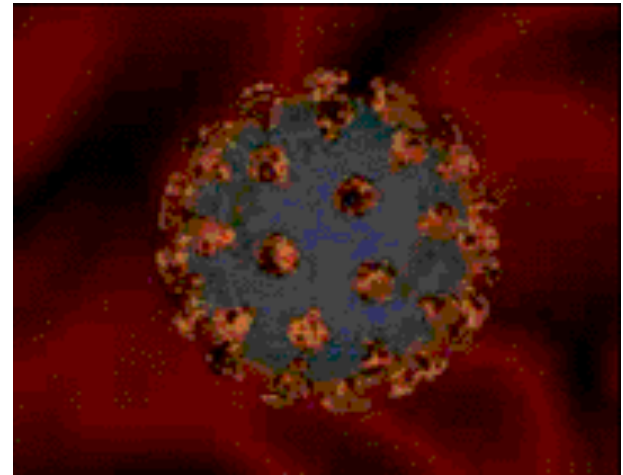
Smallpox
Chicken pox
cold sores
Poliomyelitis
colds and flu
cervical cancer
Encephalitis
microcephaly

Diarrhoea and vomiting
Rabies
Haemorrhagic fevers
Warts
Hepatitis
Leukaemia
Alzheimer's Disease

Infections of humans by viruses



3 billion nucleotides, 100,000 genes



10,000 nucleotides, 10 genes

The influenza pandemic of 1918 killed 50 million people.



Virus outbreaks

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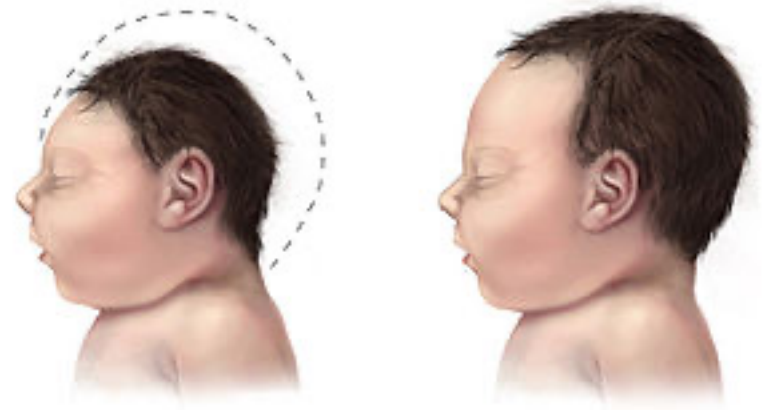
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Ebola crisis: Sierra Leone case number surpasses Liberia

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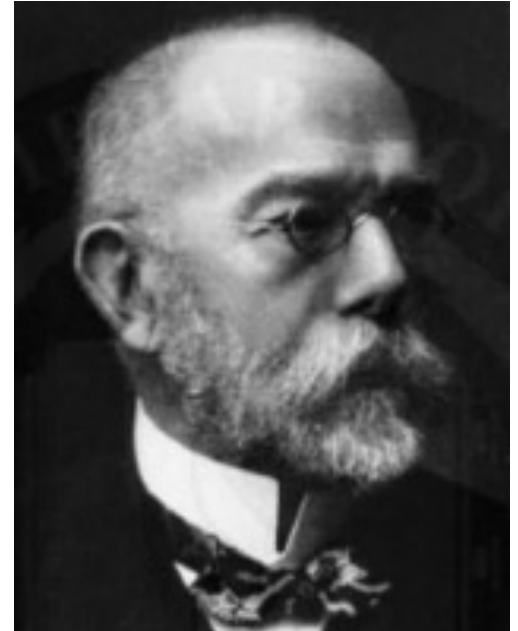


Sierra Leone is struggling to contain the deadliest-ever Ebola outbreak



Proving a virus causes a disease: Koch's Postulates

- The microorganism must be found in large numbers in all diseased animals, but not in healthy ones.
- The organism must be isolated from a diseased animal and grown outside the body in a pure culture.
- When the isolated microorganism is injected into other healthy animals, it must produce the same disease.
- The suspected microorganism must be recovered from the experimental hosts, isolated, compared to the first microorganism, and found to be identical.



Robert Koch

Yellow fever: spread by mosquitoes during the construction of the Panama Canal



Colonel Walter Reed 1901



Definition of a virus

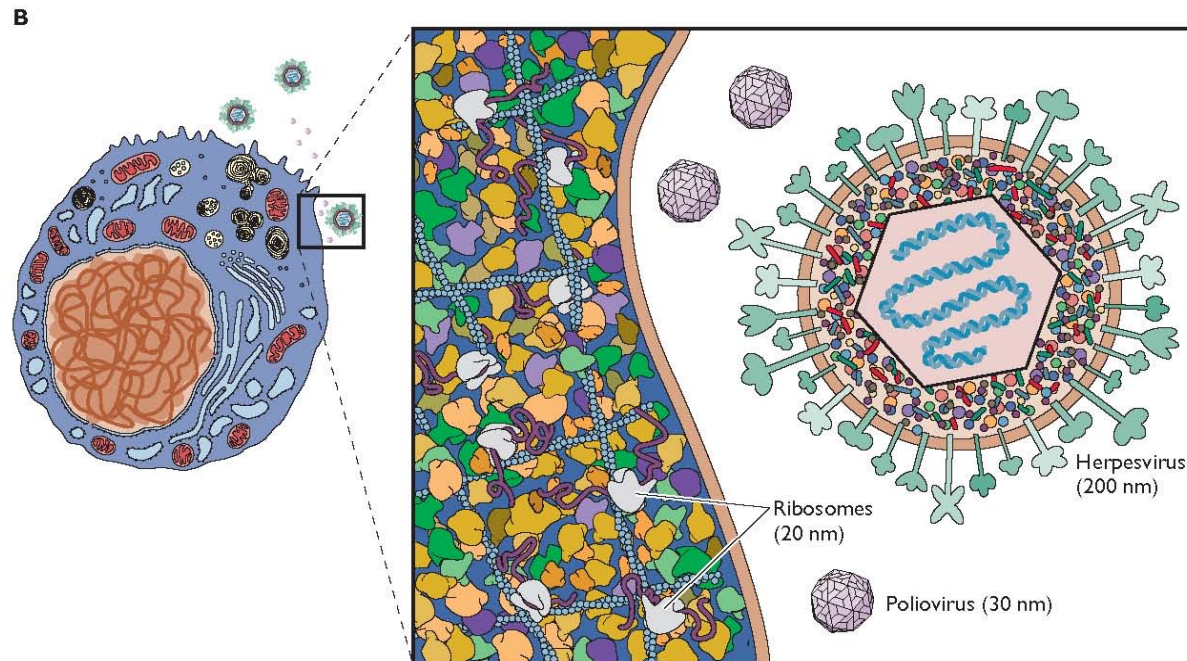
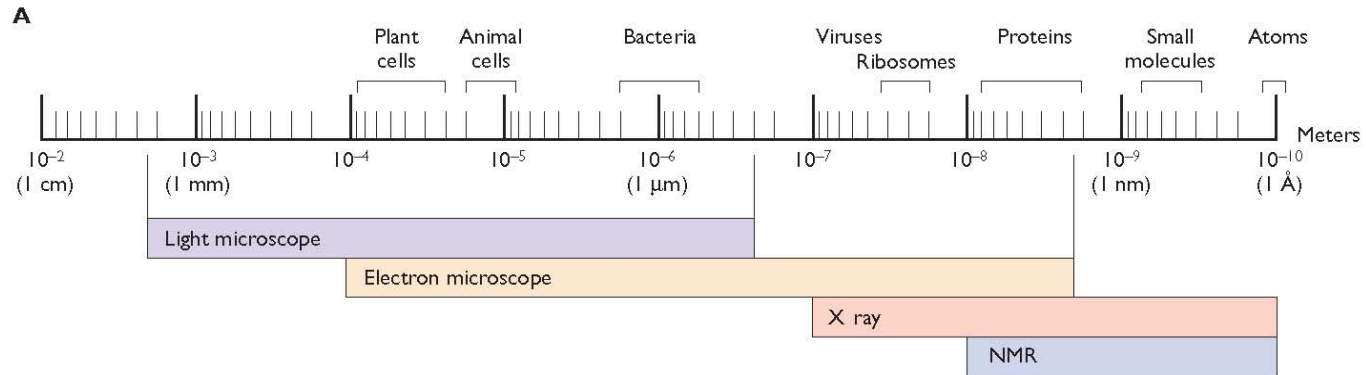
Viruses are infectious
OBLIGATE intracellular
PARASITES.

A virus has a genome that comprises DNA or RNA.

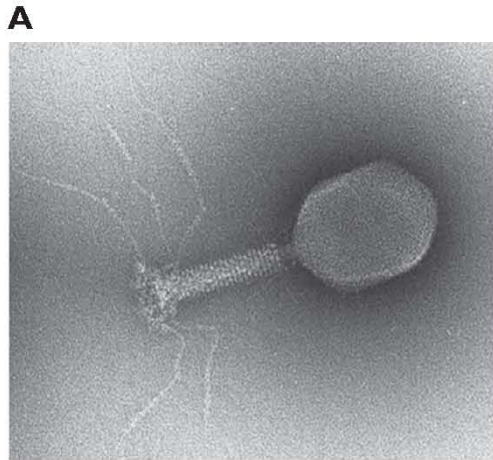
Within an appropriate cell, the viral genome is replicated and directs the synthesis, by cellular systems, of more viral components and genomes.

The components effect the transport of replicated viral genomes through the environment to new host cells.

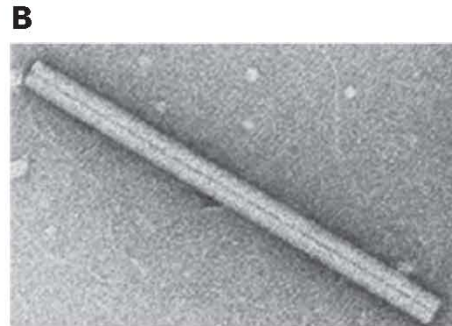
Virus particles or Virions are small



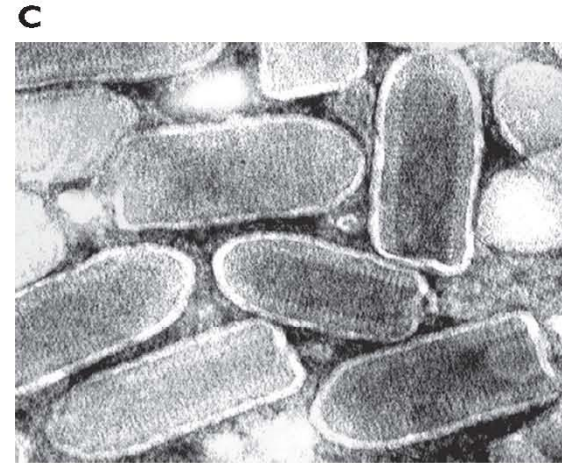
Electron micrographs of negatively stained viruses



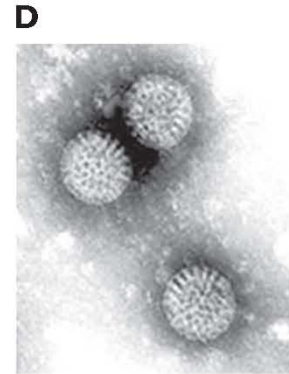
Bacteriophage T4



TMV

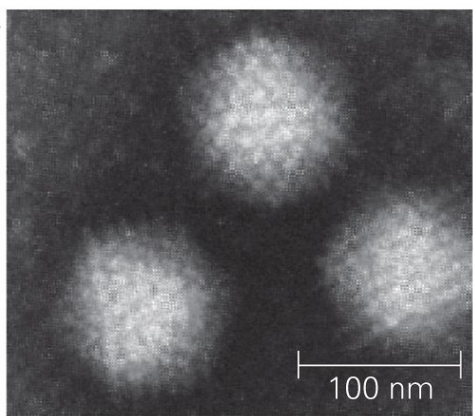


Rhabdovirus, VSV

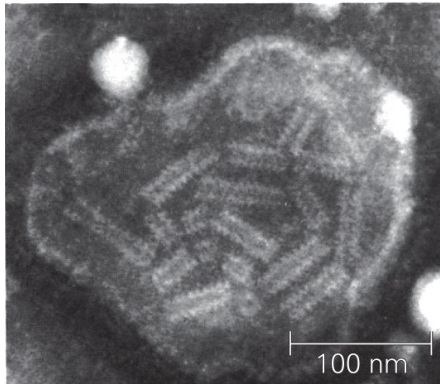


Rotavirus

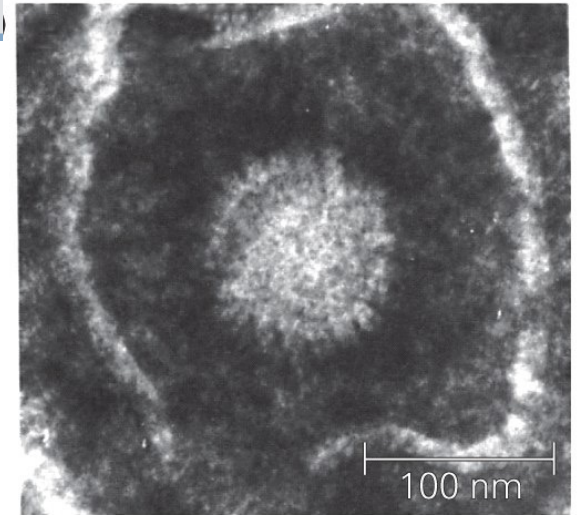
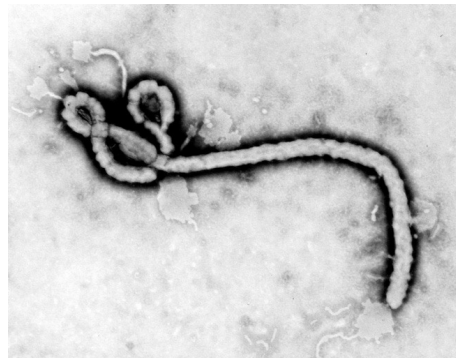
Virus Morphology



*Symmetrical protein **capsid***
Adenovirus
Picornavirus
Calicivirus
Non-enveloped



Enveloped
*Lipid **envelope** derived*
from host membrane
Pleiomorphic: measles virus
Typical shape: Ebola virus



Combination of capsid
and envelope
Herpes virus

Naming a virus

The disease

The person who discovered it

The place it was discovered

The part of the body affected
virus

The way it was spread

Poliovirus, rabies

Epstein Barr virus

Coxsackievirus

Rhinovirus, Hepatitis

Dengue, Influenza



The central dogma

DNA



RNA



protein

Genome

5' ATG- CCG-,,,,,, GAG- AAT- TAG 3'

Negative sense RNA 3' UAC-GGC-,,,,,,CUC-UUA-AUC 5'

mRNA 5' AUG- CCG-,,,,,, GAG- AAU- UAG 3'

Met- Pro,,,,,Asp-Ile- STOP

Consequences of viral genome type

- RNA viruses and retroviruses use their own polymerase to replicate. These lack proof reading capacity leading to high mutation rate.
- RNA viral genomes are limited in size due to inherent instability to RNA vs DNA. The largest RNA viruses are coronaviruses genome size around 30kb. RNA viruses often use complex coding strategies to make more proteins than expected from a small RNA genome.
- DNA viruses have genomes up to 100s kb. There is plenty of room for accessory genes that can modify the host immune response. These genes are often lost in passage in culture.
- Segmented genomes allow an additional easy form of recombination known as reassortment, but also impose more difficult packaging strategies. Influenza has 8 different RNA segments, rotavirus has 11!

A generic virus replication cycle

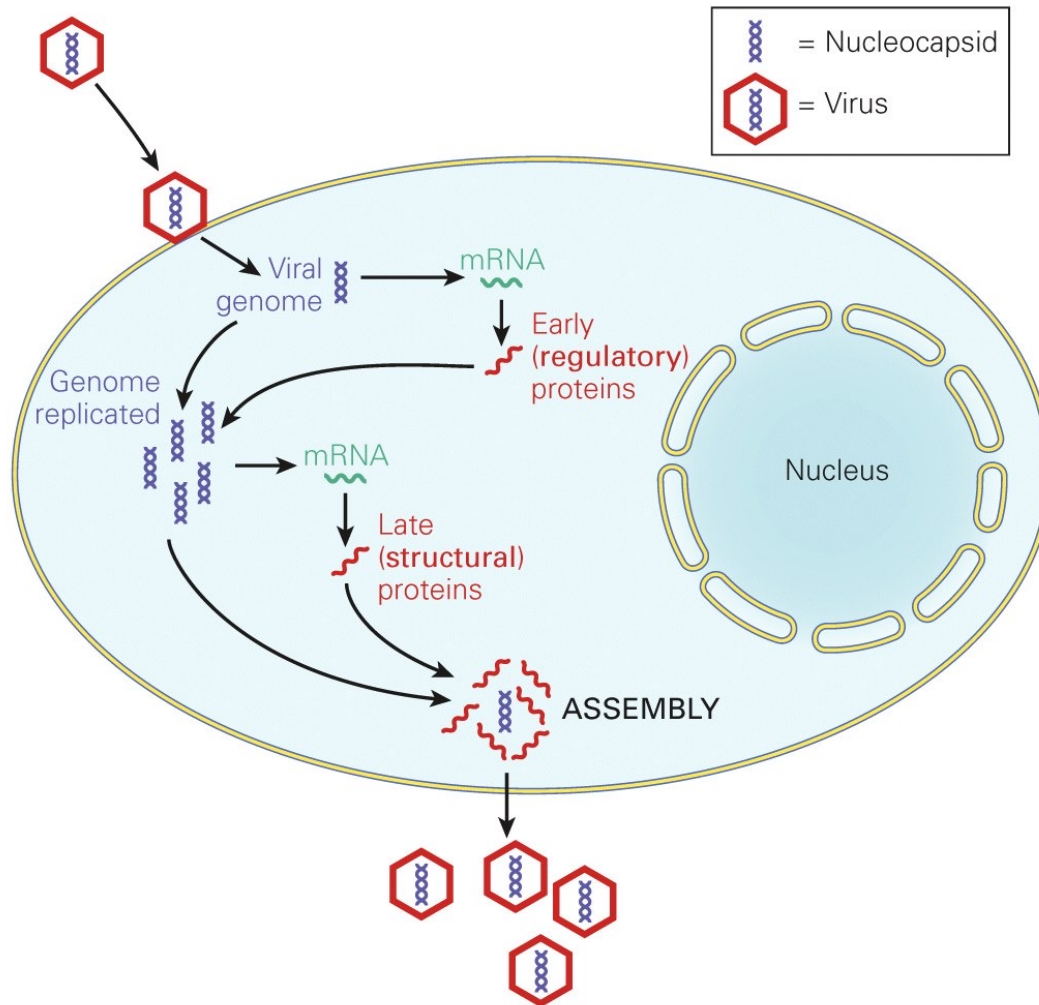
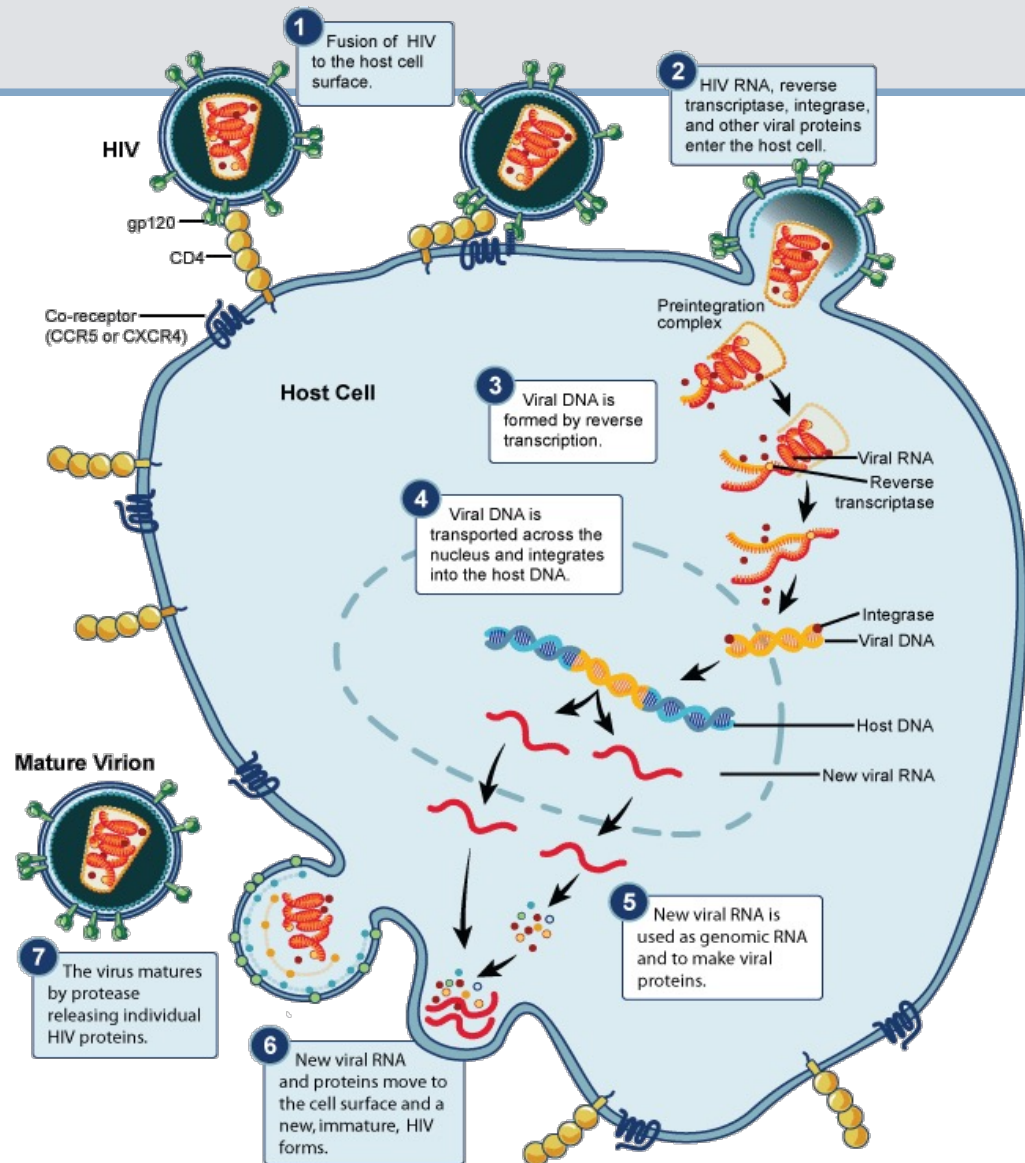
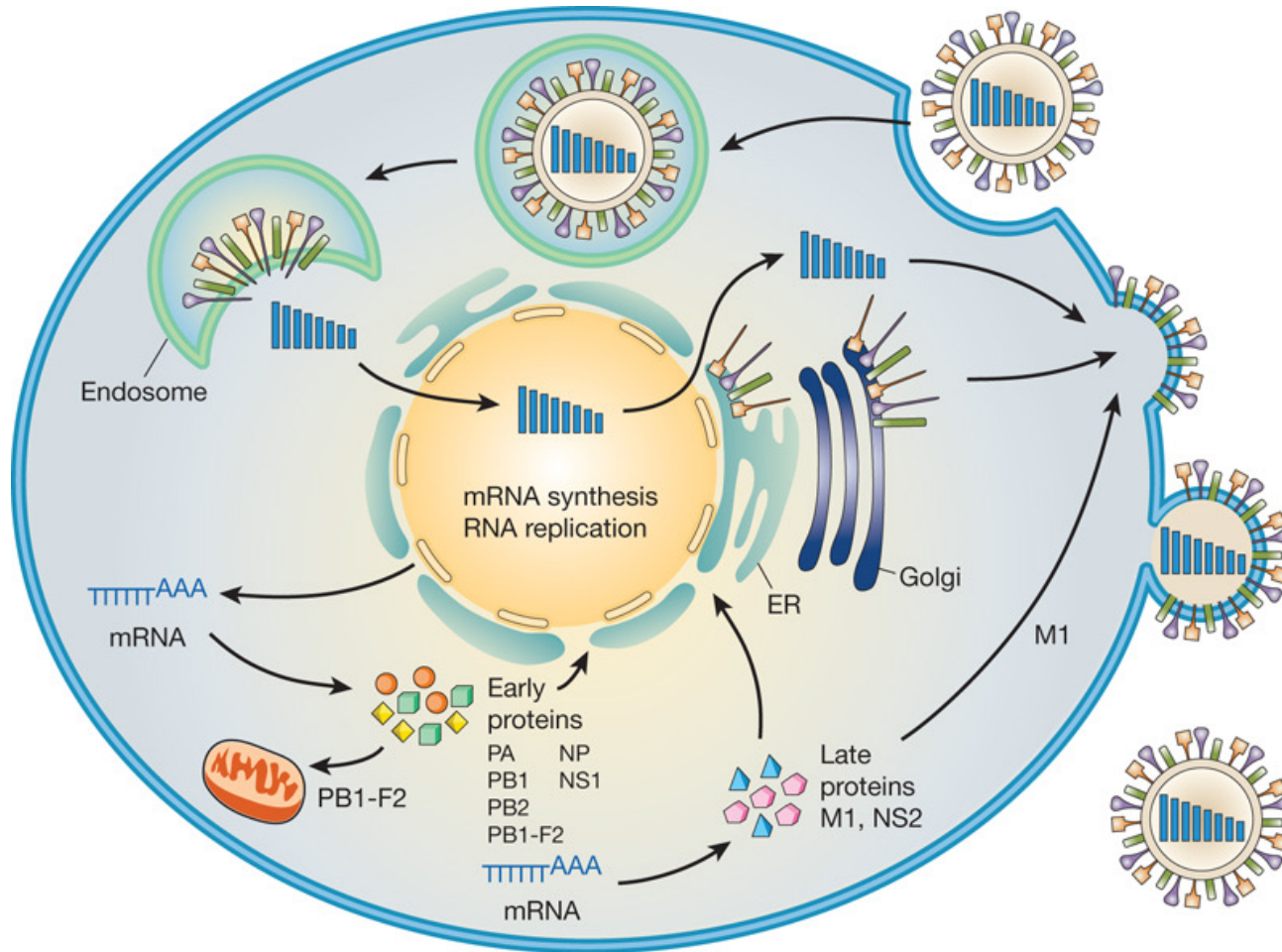


Figure 1.1 Viruses: Biology Applications Control (©2012 Garland Science)

The replication cycle of HIV-1

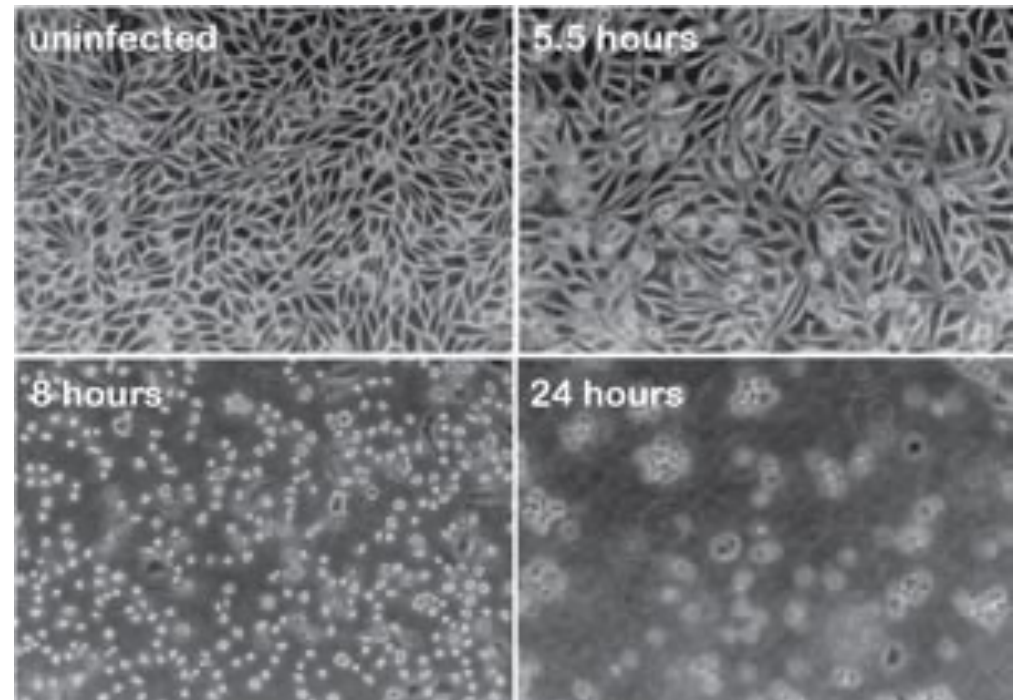


Influenza virus replication cycle



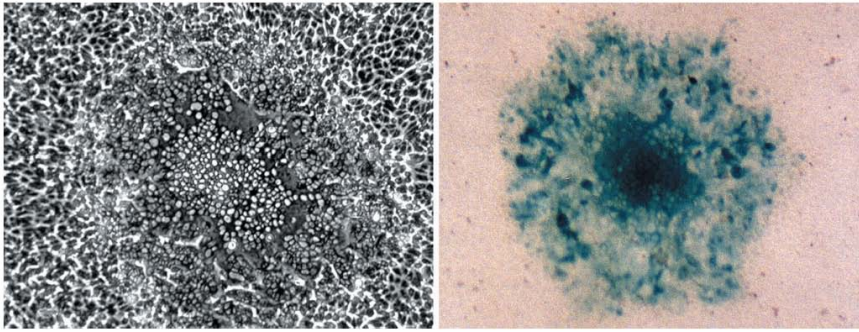
Investigating viruses in the laboratory

- **Cytopathic effect** is usually a result of the virus lysing the cell.
- This could be due to shut down of host protein synthesis or accumulation of viral proteins.

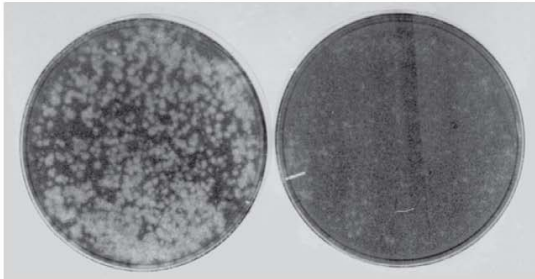


Viruses form plaques in cell monolayers

A



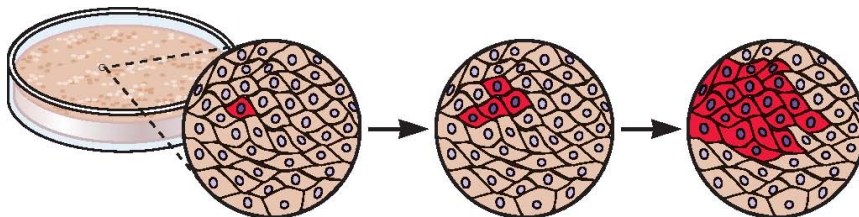
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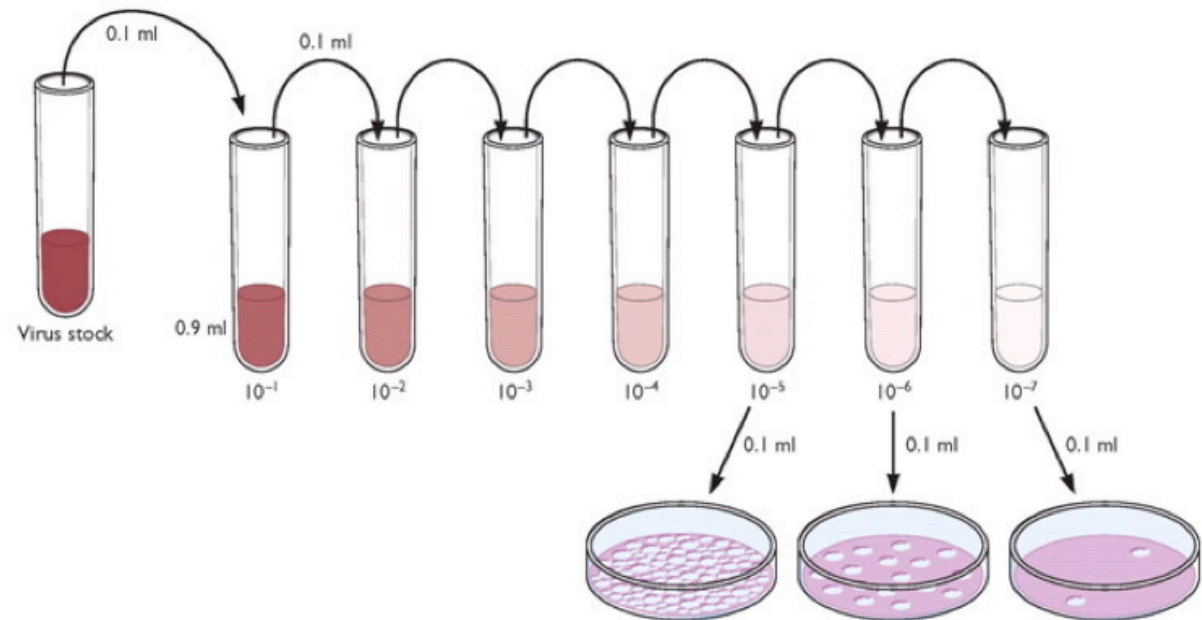
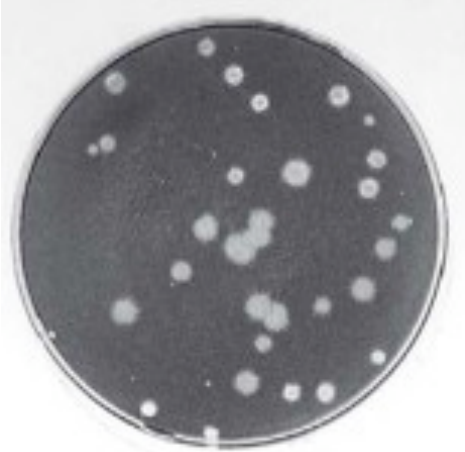
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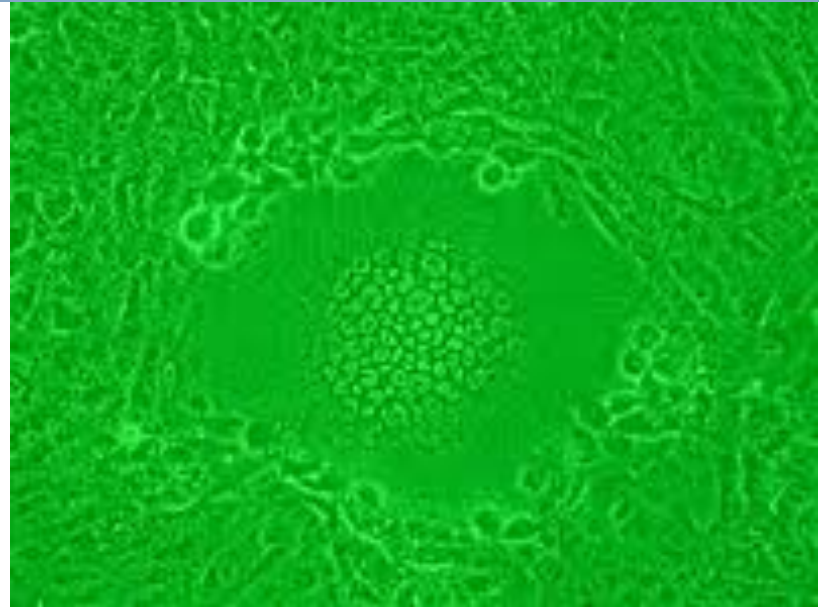


The plaque assay

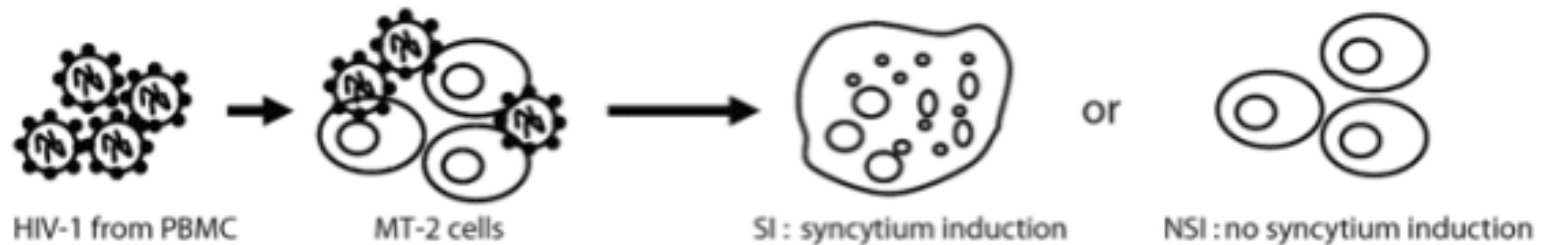


Syncytia

Viruses with surface proteins that can fuse at neutral pH often fuse cells together



MT-2 cell assay



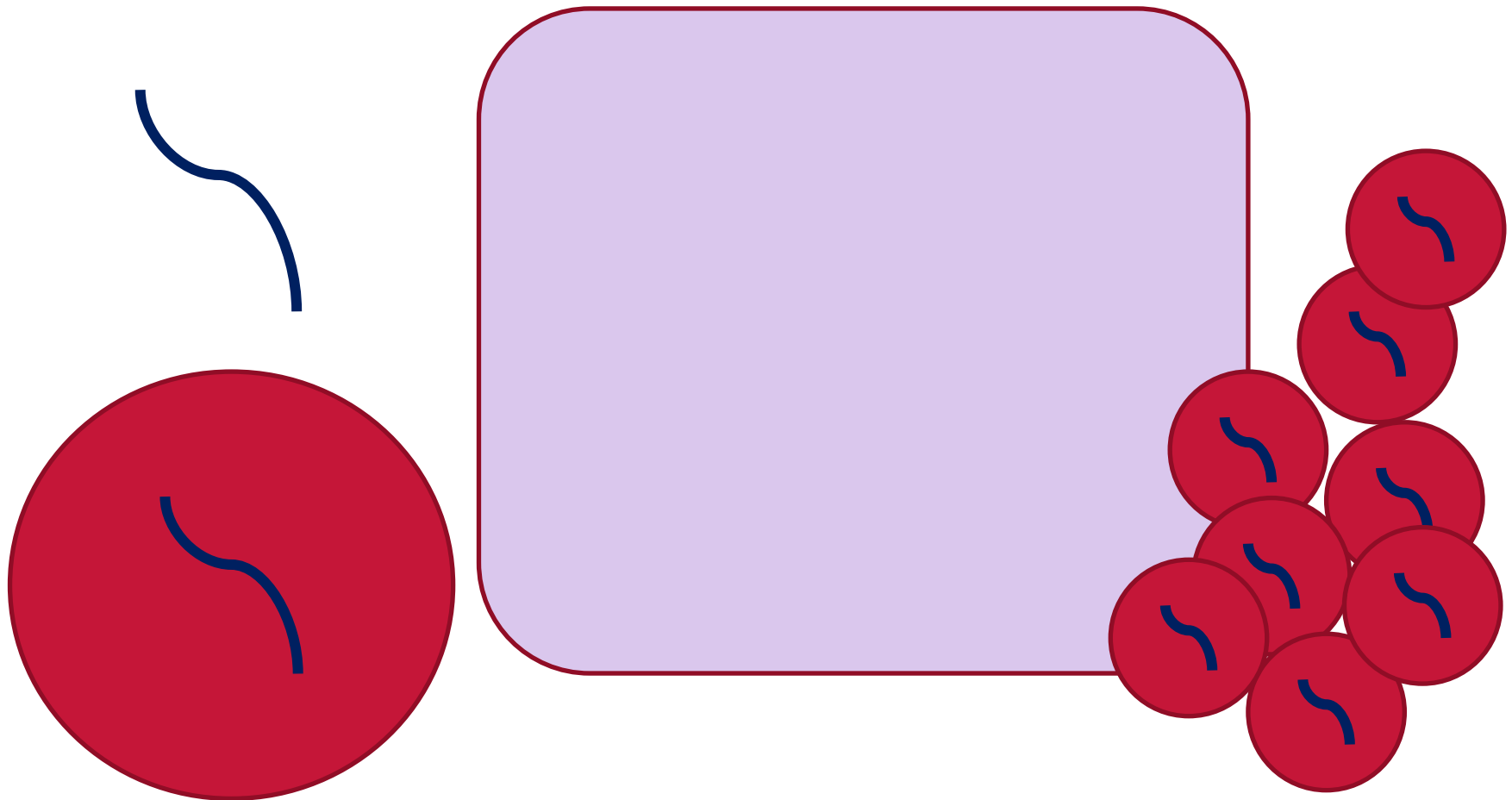
Viral diagnosis

- Detecting viral genome PCR
- Detecting viral antigen IFA, ELISA
- Detecting virus particles EM, HA
- Detecting virus cytopathic effect in cultured cells (Virus isolation)
- Detecting antibodies to virus (serology)

Manipulating viruses

- Virus genomes are so small they can be synthesized.
- When introduced into permissive cells they direct synthesis of all their component and new viruses are made *de novo*.
- This allows reverse genetics, the creation of viruses at will with engineered mutations in their genomes.

'New' viruses can be made in the laboratory

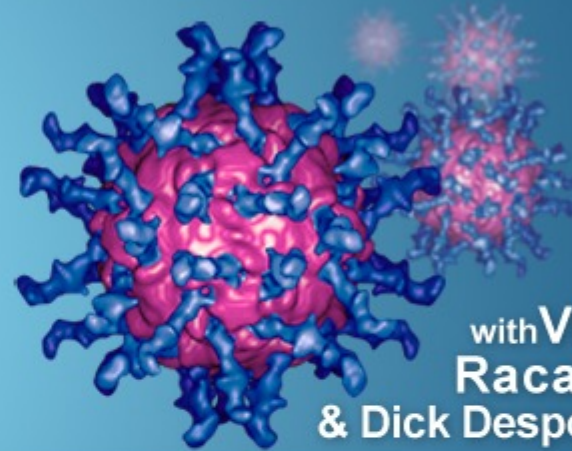


Sources of information

ABOUT EPISODES GUESTS LETTERS TRANSCRIPTS VIRAL VIDEO VIROLOGY 101 WEEKLY PICKS KUDOS

TWIV
THIS WEEK IN VIROLOGY

A netcast about viruses - the kind that make you sick



with **Vincent
Racaniello**
& **Dick Despommier**

<https://www.microbe.tv/twiv/>