



Reoviruses

Virion

Genome

Genes and proteins

Viruses and hosts

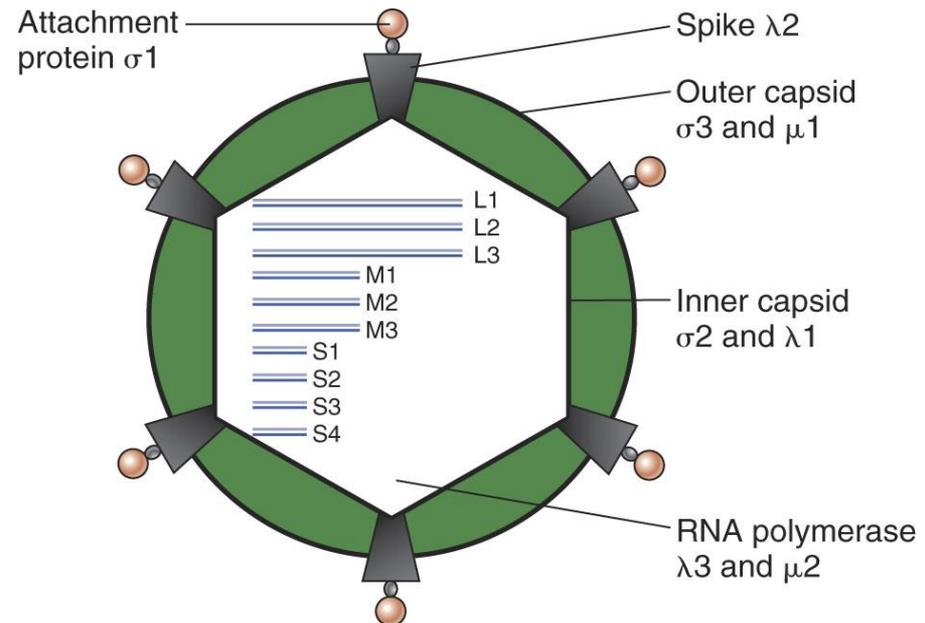
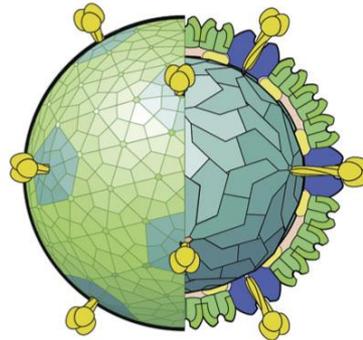
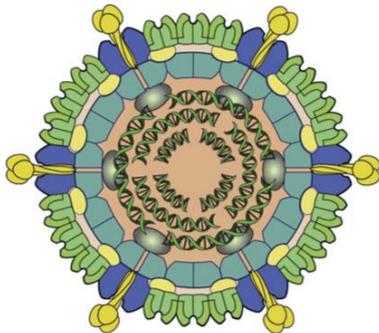
Diseases

Distinctive characteristics



Virion

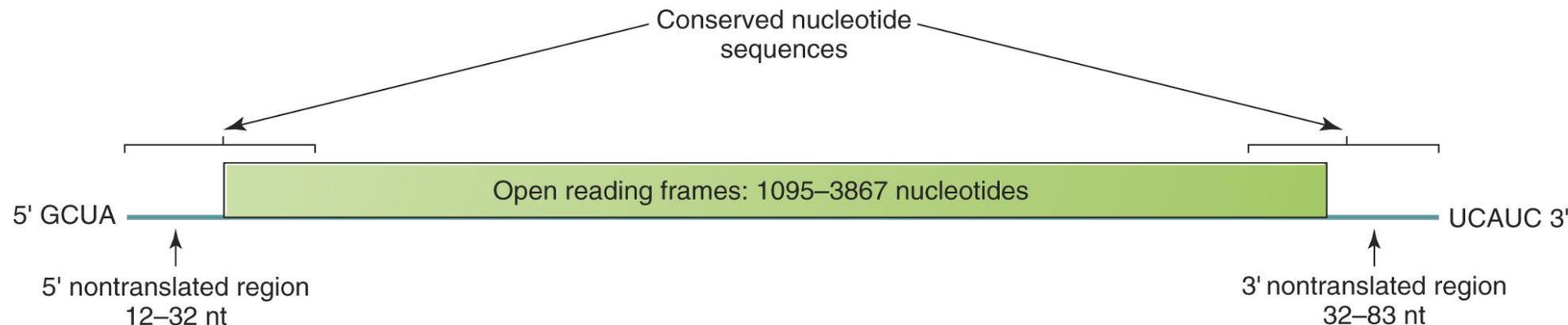
- Naked icosahedral capsid (T=13), diameter 60-85 nm
- Reovirus virions contain two or three concentric layers of capsid proteins
 - Inner capsid (T=1), or core, assembled from major ($\lambda 1$ and $\sigma 2$), and minor ($\mu 2$ and $\lambda 3$) proteins; RNA pol and capping enzymes
 - Outer capsid (T=13) constructed from complexes of $\mu 1$ and $\sigma 3$ and a spike made from pentamers of $\lambda 2$





Genome, Genes and Proteins

- Linear double-stranded RNA, 10-12 segments
- Total genome length 18-24 kb
- mRNAs are full length copies of each genome segment
- Typically one protein is encoded per genome segment
 - 6~8 capsid proteins
 - 3~6 nonstructural proteins



- General characteristics of a mammalian reovirus gene segment



Viruses and hosts

- Reoviridae from respiratory enteric orphan viruses
- 12 genera, including *Orthoreovirus*, *Rotavirus*, *Orbivirus*
- Infects humans (reoviruses types 1-3, rotaviruses, and Colorado tick fever virus), mammals, birds, fish, mollusks, plants, insects, and fungi

Genus	segments	Hosts
<i>Orthoreovirus</i>	10	Mammals, birds, reptiles
<i>Rotavirus</i>	11	Mammals, birds
<i>Orbivirus</i>	10	Mammals, birds, arthropods
<i>Coltivirus</i>	12	Mammals, arthropods
<i>Aquareovirus</i>	11	Fish, mollusks
<i>Cypovirus</i>	10	Insects
<i>Idnoreovirus</i>	10	Insects
<i>Fijivirus</i>	10	Plants, insects
<i>Oryzavirus</i>	10	Plants, insects
<i>Phytoreovirus</i>	12	Plants, insects
<i>Seadornavirus</i>	12	Insects, humans
<i>Mycoreovirus</i>	11–12	Fungi



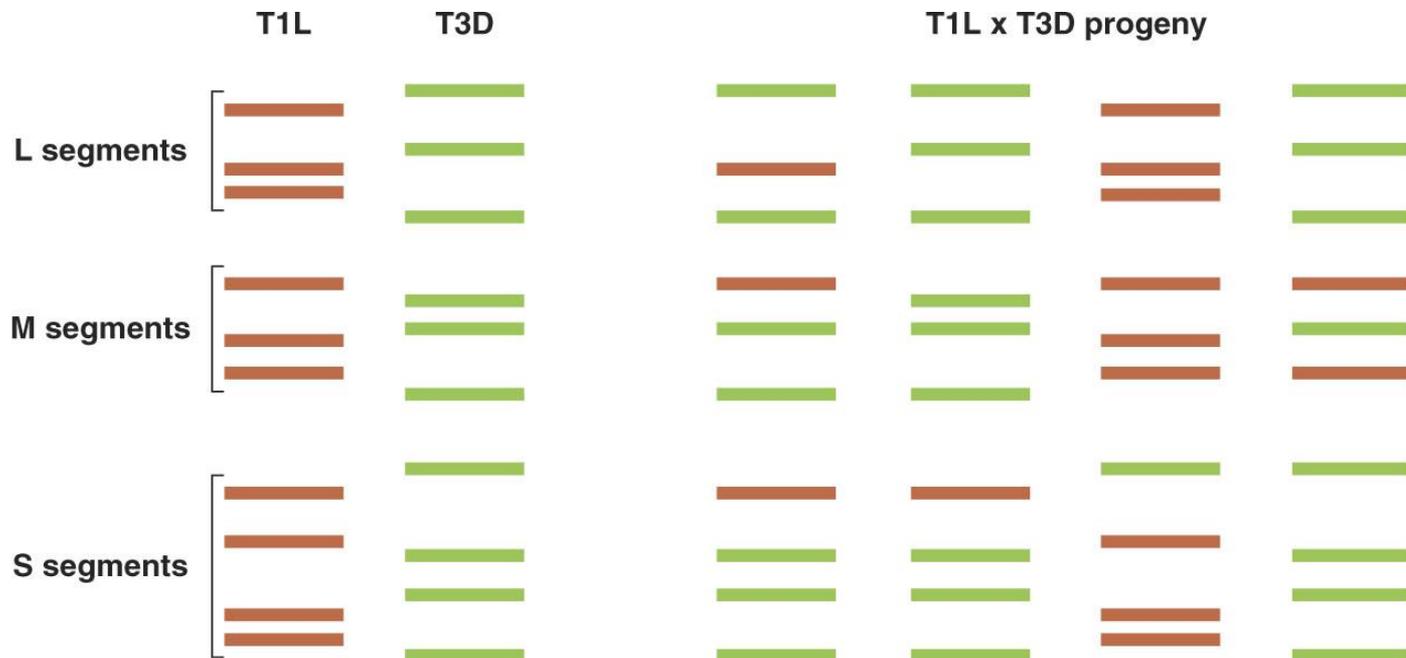
Diseases

- Members of genus *Orthoreovirus* cause little or no disease in humans
- Rotavirus is an important cause of gastroenteritis worldwide and infant mortality in the developing world
- Viruses spread between hosts by direct transmission, contaminated food or water, or arthropod vectors



Distinctive characteristics

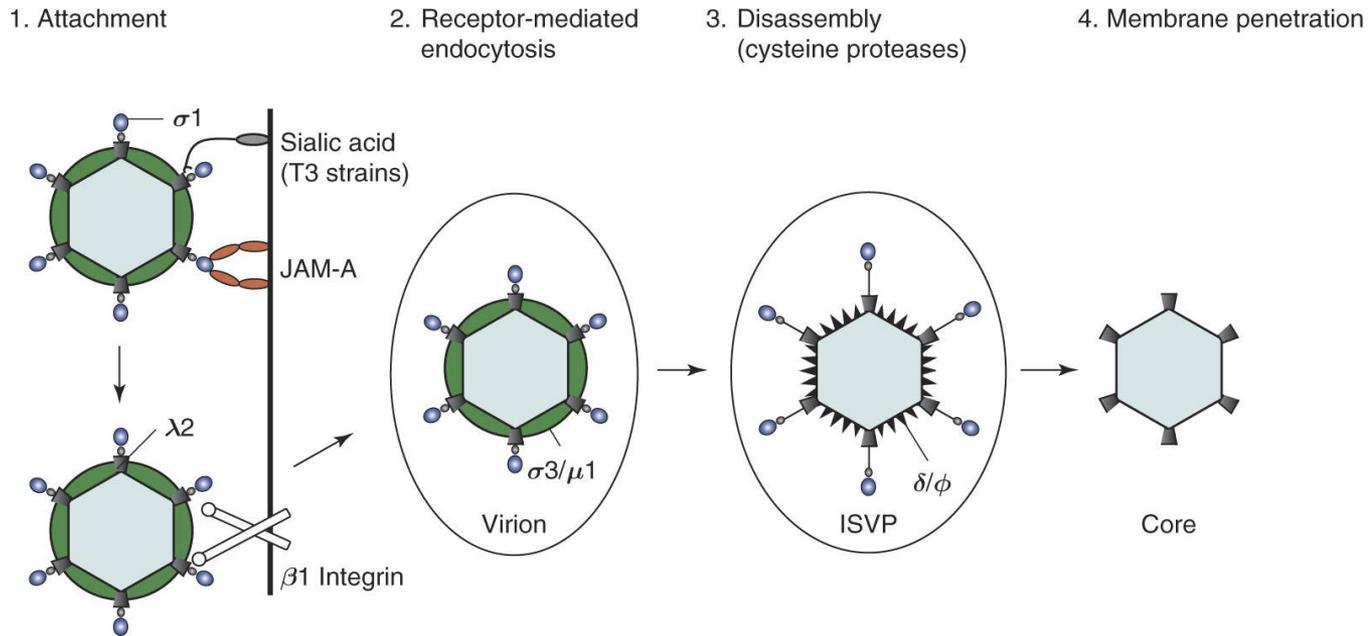
- *Reoviridae* have segmented genomes made of double-stranded RNA
 - 10-12 discrete linear segments of dsRNA
 - Three large (L) genes, three medium (M) genes and four small (S) genes
 - Mixed infections with different virus strains can result in **reassortant viruses**





Reovirus Entry

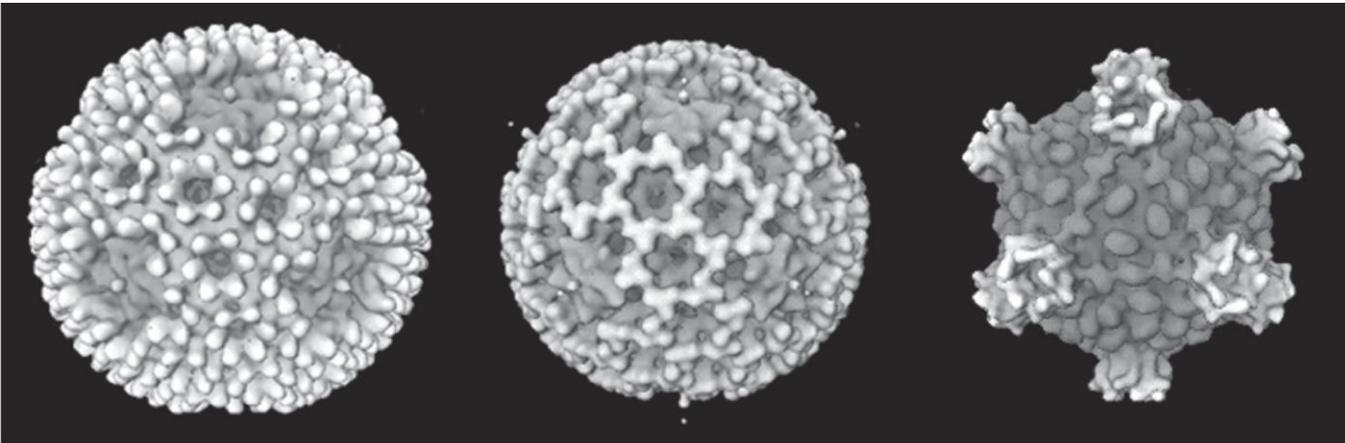
- The attachment protein binds to one or two cellular receptors
 - Sialic acid
 - Junctional adhesion molecule A (JAM-A); a protein located at tight junctions
- Clathrin-mediated endocytosis dependent on $\beta 1$ integrin
- During entry, the outer capsid is stripped from virions and the core is released into the cytoplasm





Reovirus Entry

- In endosomes, virions undergo partial degradation by cathepsins to form **infectious subvirion particles (ISVPs)**
- Disassembly can be viewed using cryoelectron microscopy



Virion

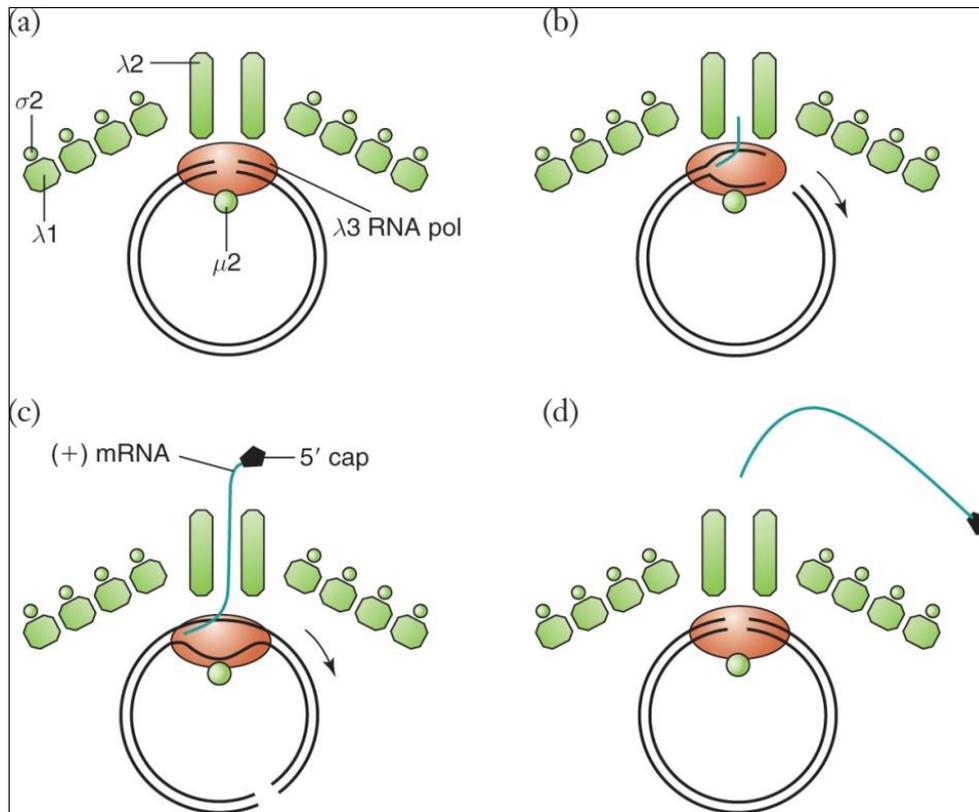
ISVP

Core



Reovirus Transcription

- Enzymes in the viral core synthesize and cap messenger RNAs
 - All 10 mRNAs are synthesized at the same time and passed up into the spike turret



Moving template model

- mRNA synthesis: $\lambda 3$ & $\mu 2$
- Capping: $\lambda 2$



Protein synthesis

- Translation of reovirus mRNAs is regulated
 - Proteins made from long mRNAs are made in lower abundance than those made from short mRNAs
 - Sequences surrounding the initiator AUG and differences in the length and secondary structure of 5' NTRs also account for different levels of synthesis of viral proteins



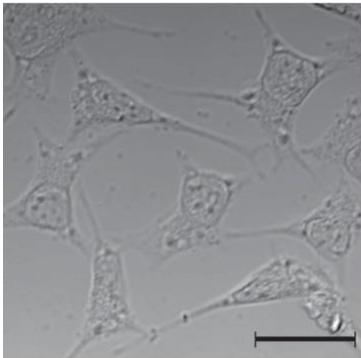
Distinctive characteristics

- Interferon and PKR: effects on viral and cellular protein synthesis
 - Reovirus dsRNA is a potent inducer of:
 - interferons which activate double-stranded RNA-dependent protein kinase R
 - 2', 5'-oligo(A) synthetase which activates ribonuclease L
 - The $\sigma 3$ protein modulates PKR activation
 - PKR regulation in cancer cells facilitates reovirus propagation;
oncolytic reoviruses

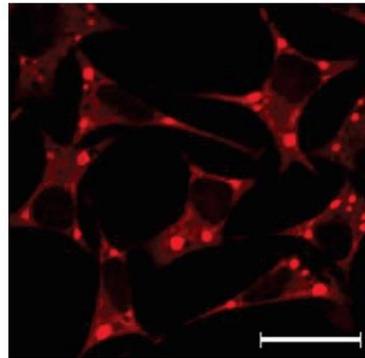


Genome replication and Virion assembly

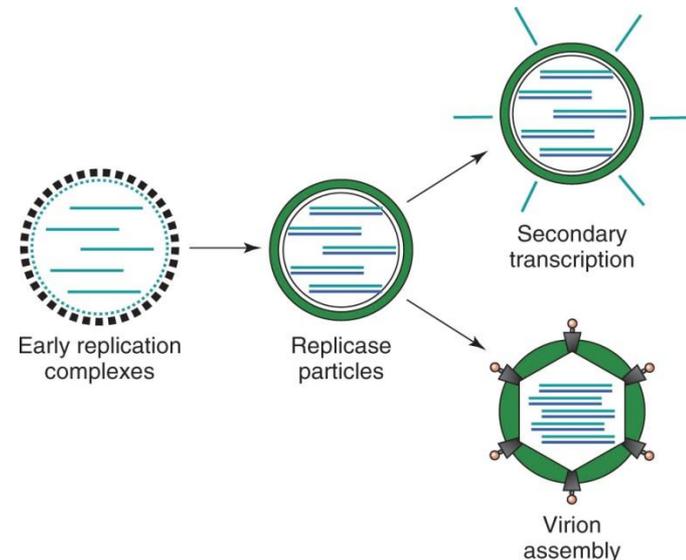
- Synthesis of progeny double-stranded genomes occurs within subviral particles
 - RNA replication and virion assembly take place in intracytoplasmic inclusion bodies called "virus factories"
 - mRNA bound to non-structural proteins and inner capsid proteins represent the first step in assembly; early replication complexes
 - Replicase particles then form, which are engaged in (-) strand synthesis
 - Secondary transcription particles then make additional (+) strand RNA
 - Outer capsids are formed when sufficient capsid proteins have been synthesized



(a)



(b)





Distinctive characteristics

- Reoviruses induce apoptosis via activation of innate immune response transcription factors NF- κ B and IRF-3
 - Caspases are also activated
 - Cell cycle is arrested by inactivation of cyclin-dependent kinases (CDK)
- Studies of reovirus pathogenesis in mice
 - Type 1 reovirus infection in ependymal cells lead to non-lethal hydrocephalus
 - Type 3 reovirus infection in neurons causes encephalitis
 - Reovirus also infects liver, bile duct and can cause myocarditis in mice
 - Infection of bile ducts causes ductal obliteration and jaundice



Plasmid-based reverse genetics

