Picorna Virus

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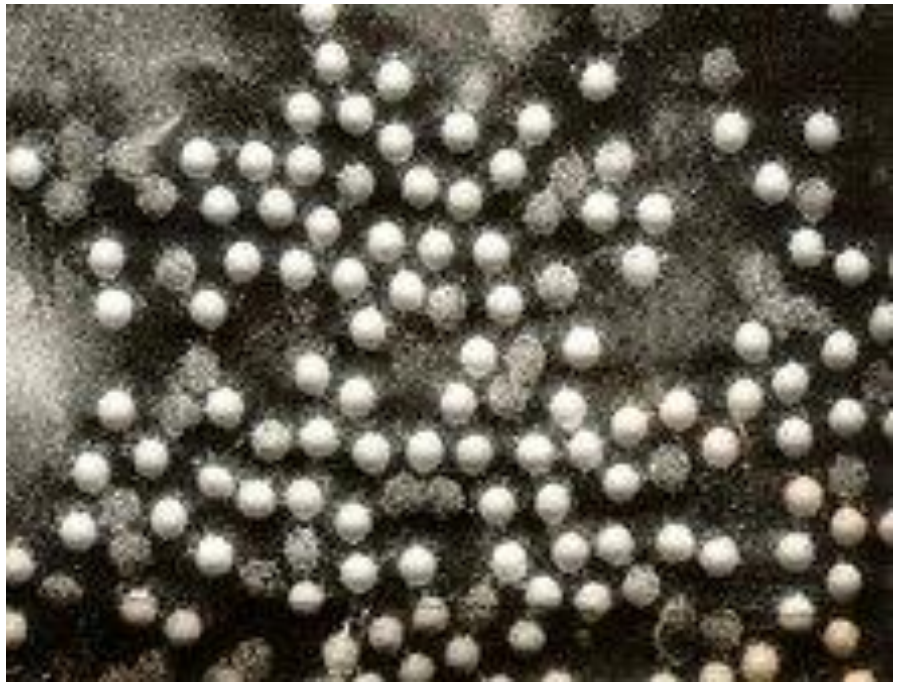
Introduction

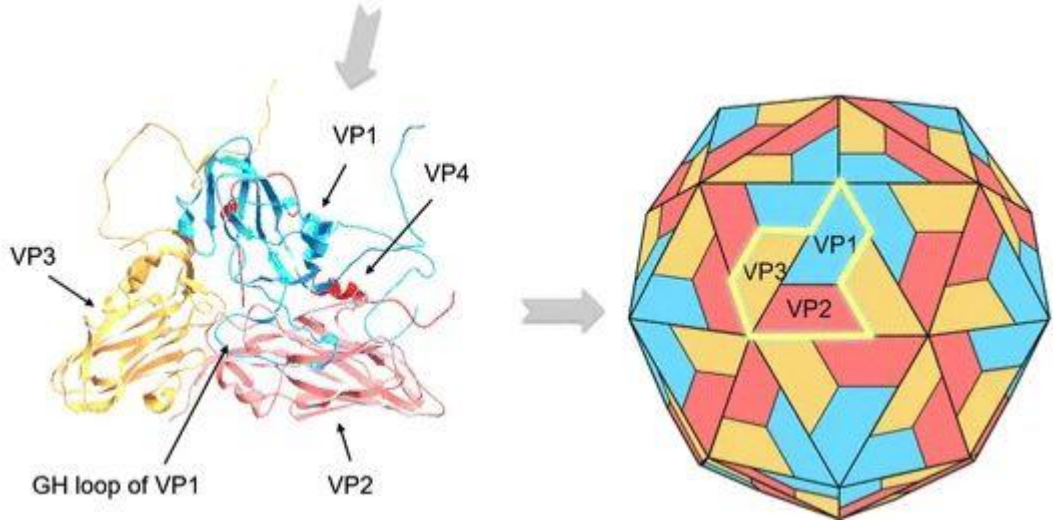
- The term Picornaviridae is derived from *pico*, which means small (typically, 18-30 nm), and RNA, referring to the single-stranded positive-sense RNA common to all members of the Picornaviridae family.
- Based on a number of properties including sequence homologies and acid sensitivity, there are nine genera within the *Picornaviridae*. Five of these infect humans:
  - Enteroviruses: Polio Virus
  - Rhinoviruses
  - Hepatoviruses- Hepatitis A
  - Parechoviruses
  - Kobuviruses

Classification

- Group: IV single strand RNA virus
- Realm: Riboviria
- Kingdom: Orthornavirae
- Phylum: Pisuviricota
- Class: Pisoniviricetes
- Order: Picornavirales
- Family: Picornaviridae

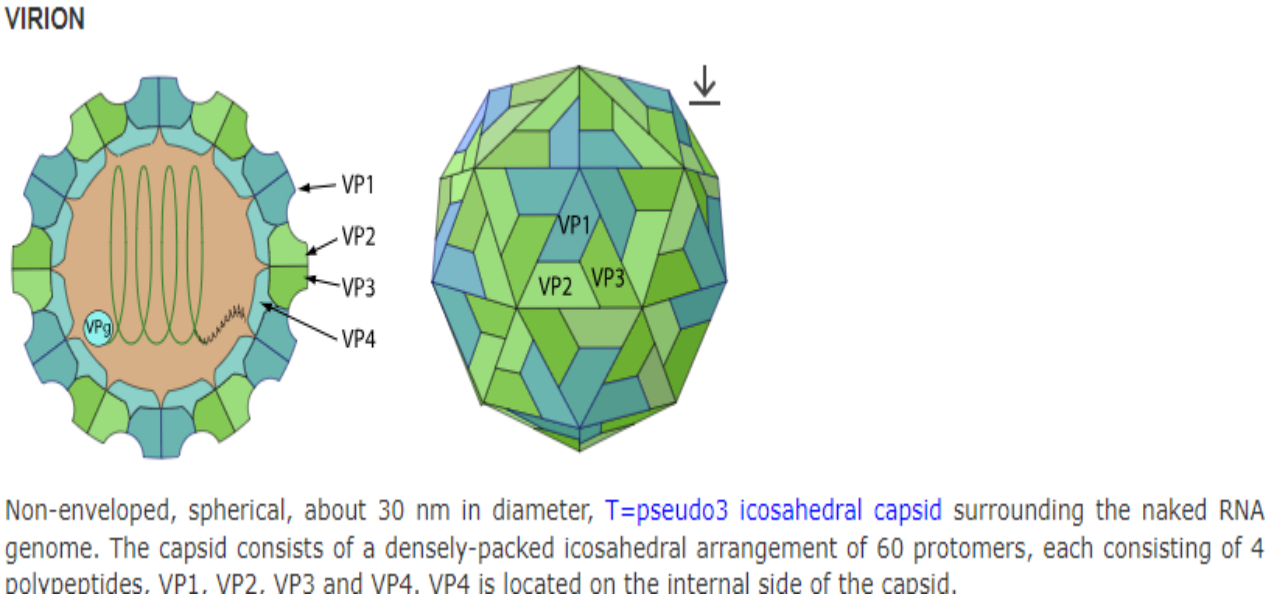
Structure





Structure

- Virions consist of a capsid, with no envelope, surrounding a core of ssRNA.
- 30–32 nm in diameter
- Picornaviruses have an icosahedral nucleocapsid There are 60 identical subunits (vertices) which contain five protomers. Each protomer is made up of one copy of four proteins, named VP1, VP2, VP3 and VP4. These proteins are made as a single polypeptide (polyprotein) which is cleaved by cellular proteases



Non-enveloped, spherical, about 30 nm in diameter, T=pseudo3 icosahedral capsid surrounding the naked RNA genome. The capsid consists of a densely-packed icosahedral arrangement of 60 protomers, each consisting of 4 polypeptides, VP1, VP2, VP3 and VP4. VP4 is located on the internal side of the capsid.

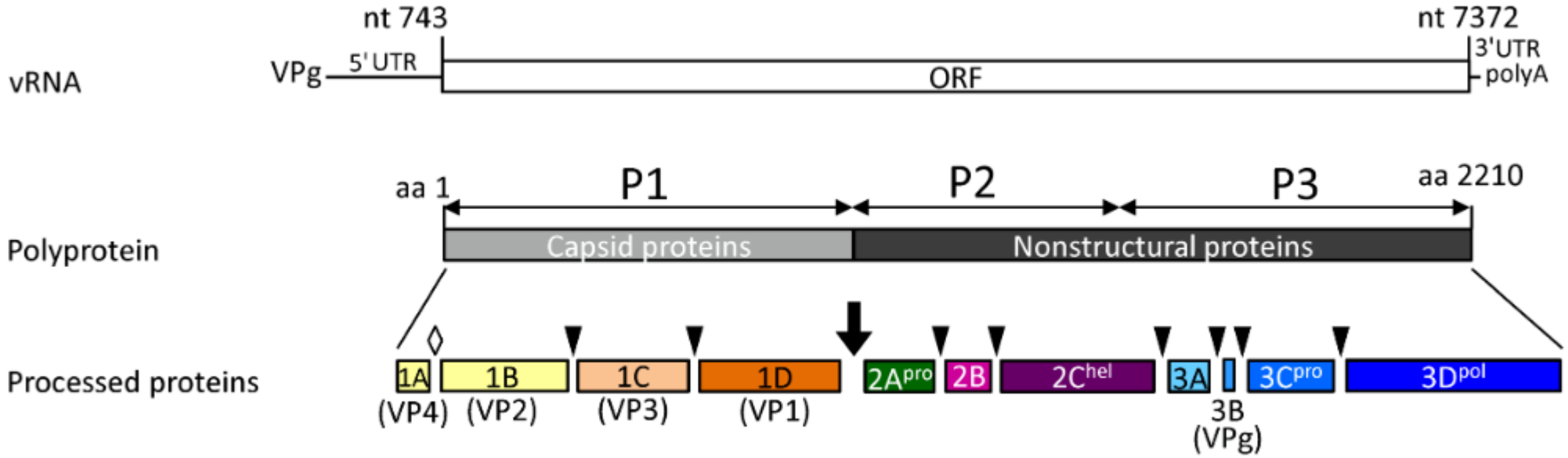
https://viralzone.expasy.org/

Genome

Genome: 6.7–10.1 kb and possessing a single long ORF

Viral RNA (vRNA) is polyadenylated and covalently linked to a virus-encoded protein (VPg) at its 5’-end. A single open reading frame (ORF) encoding a polyprotein is flanked on either side by untranlated regions (UTRs)

- 5' end have a viral protein called VPg. The large 5' leader sequence has considerable secondary structure that comes about by intramolecular base pairing and one of these structures is the internal ribosome entry site (IRES) which allows this RNA to bind to cytoplasmic ribosomes.



GENE EXPRESSION https://viralzone.expasy.org/97

- The virion RNA is infectious and serves as both the genome and viral messenger RNA. The IRES allows direct translation of the polyprotein.
- The polyprotein is initially processed by the viral proteases into three precursor proteins, P1, P2, and P3.
- Precursor P1 is then proteolytically cleaved to yield the structural proteins.
- Precursors P2 and P3 are processed into replicase, VPg, and a number of proteins that modify the host cell, ultimately leading to cell lysis.

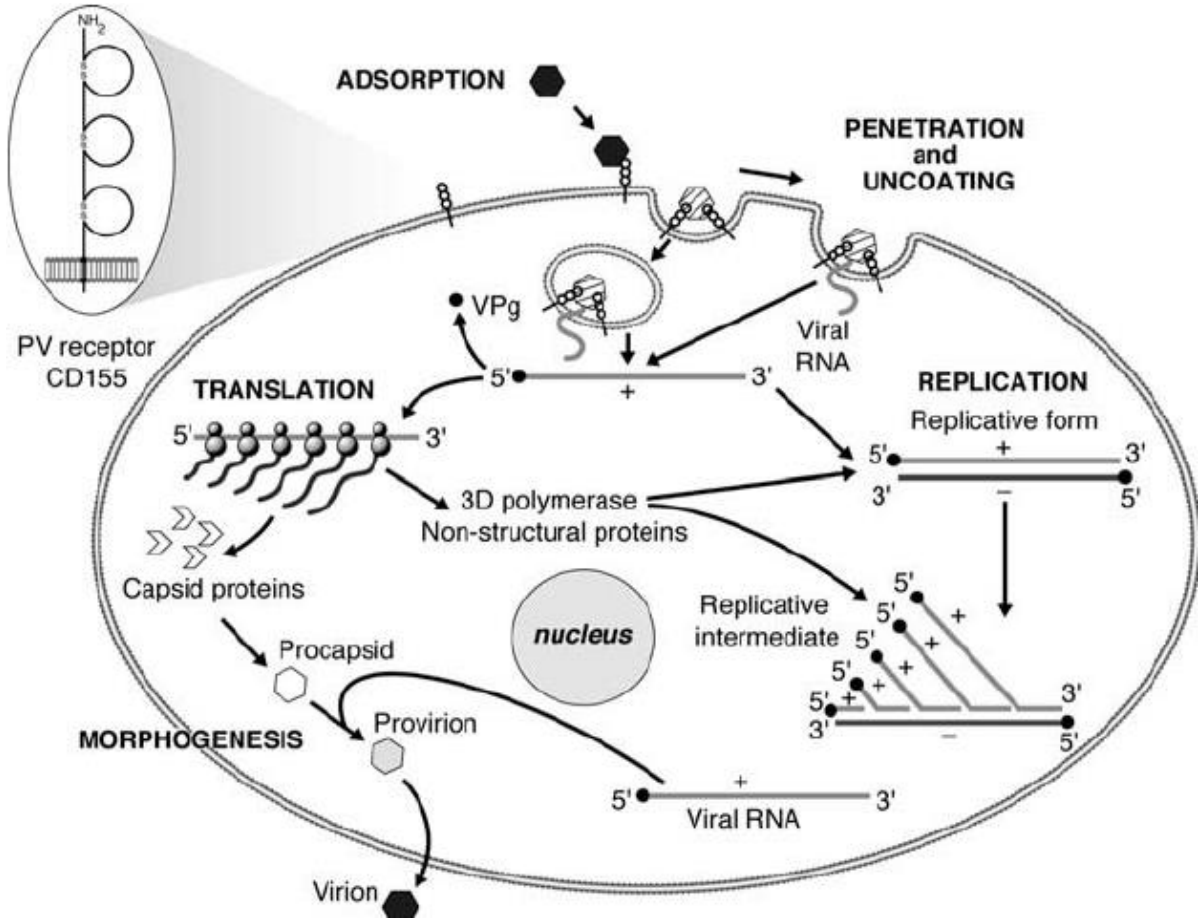
- ENZYMES
- RNA-dependent RNA polymerase [RdRp]
- VPG-type capping [VPg]
- NTPase-helicase [2C]
- Polyprotein major protease (Peptidase C3) [3Cpro, 2A]
- Virion maturation (Peptidase N8) [VP4]

Replication Cycle

- CYTOPLASMIC

- Attachement of the virus to host receptors mediates endocytosis of the virus into the host cell.
- The capsid undergoes a conformational change and releases VP4 that opens a pore in the host endosomal membrane and the viral genomic RNA penetrates into the host cell cytoplasm (the empty capsid remains intact).
- VPg is removed from the viral RNA, which is then translated into a processed polyprotein.
- Shutoff of cellular cap-dependent translation through the cleavage of translation initiation factors by viral protease.
- Replication occurs in viral factories made of membrane vesicles derived from the ER. A dsRNA genome is synthesized from the genomic ssRNA(+).
- The dsRNA genome is transcribed/replicated thereby providing viral mRNAs/new ssRNA(+) genomes.
- New genomic RNA is believed to be packaged into preassembled procapsids.
- Cell lysis and virus release.
- Maturation of provirions by an unknown host protease.

Replication Cycle



Blondel, B & Colbère-Garapin, F & Couderc, Therese & Wirotius, A & Guivel-Benhassine, F. (2005). Poliovirus, Pathogenesis of Poliomyelitis, and Apoptosis. Current topics in microbiology and immunology. 289. 25-56. 10.1007/3-540-27320-4_2.

Viral **Replication:**

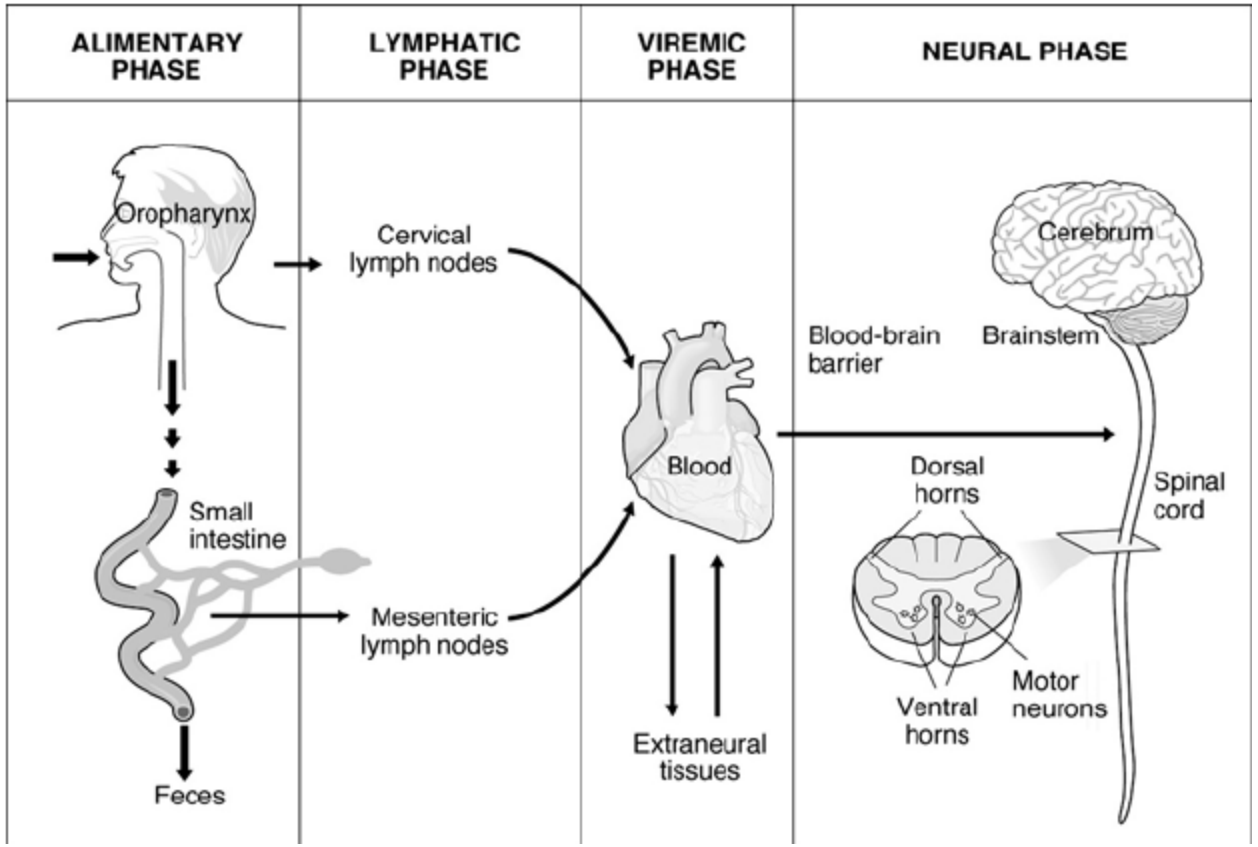
- RNA replication is primed by the VPg protein. It would mean that for each replicated RNA, one entire polyprotein has to be synthesized, because there is only one VPg per polyprotein..
- Genome replication occurs in two phases, first the minus strand is synthesized, which is in turn used as template to produce a lot of positive strand RNA genomes. Synthesis of negative strand presumably produces dsRNA.
- This dsRNA may be the replicative form of picornaviruses. It may be the template for (+) RNA synthesis by RNA strand displacement.

Poliomyelitis

- Poliovirus (PV), perhaps the most well studied of the Picornaviridae, is the causative agent of the crippling and sometimes fatal disease poliomyelitis
- Polio (poliomyelitis) mainly affects children under 5 years of age.
- One in 200 infections leads to irreversible paralysis. Among those paralysed, 5–10% die when their breathing muscles become immobilized.
- Post polio syndrome

Outcome	Proportion of cases[1]
No symptoms	72%
Minor illness	24%
Nonparalytic aseptic meningitis	1–5%
Paralytic poliomyelitis	0.1–0.5%
— Spinal polio	79% of paralytic cases
— Bulbospinal polio	19% of paralytic cases
— Bulbar polio	2% of paralytic cases

Pathogenesis



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Vaccine (wikipedia

- The first candidate polio vaccine, based on one serotype of a live but attenuated (weakened) virus, was developed by the virologist Hilary Koprowski.
- The second polio virus vaccine was developed in 1952 by Jonas Salk at the University of Pittsburgh, and announced to the world on 12 April 1955. The Salk vaccine, or inactivated poliovirus vaccine (IPV), is based on poliovirus grown in a type of monkey kidney tissue culture (vero cell line), which is chemically inactivated with formalin. After two doses of inactivated poliovirus vaccine (given by injection), 90 percent or more of individuals develop protective antibody to all three serotypes of poliovirus, and at least 99 percent are immune to poliovirus following three doses.[1]

Vaccine (wikipedia

- Subsequently, Albert Sabin developed another live, oral polio vaccine (OPV). It was produced by the repeated passage of the virus through nonhuman cells at subphysiological temperatures.
- The attenuated poliovirus in the Sabin vaccine replicates very efficiently in the gut, the primary site of wild poliovirus infection and replication, but the vaccine strain is unable to replicate efficiently within nervous system tissue.
- A single dose of Sabin's oral polio vaccine produces immunity to all three poliovirus serotypes in about 50 percent of recipients. Three doses of live-attenuated oral vaccine produce protective antibody to all three poliovirus types in more than 95 percent of recipients.
- 1988, the World Health Assembly adopted a resolution for the worldwide eradication of polio, marking the launch of the Global Polio Eradication Initiative (GPEI), spearheaded by national governments, WHO, Rotary International, the US Centers for Disease Control and Prevention (CDC) and UNICEF, and later joined by the Bill & Melinda Gates Foundation and Gavi, the Vaccine Alliance

Treatment

- There is no cure for polio, but there are treatments.
- The focus of modern treatment has been on providing relief of symptoms, speeding recovery and preventing complications