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Molecular Mechanism of Poliovirus Replication and Pathogenesis

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Poliovirus (PV), the causative agent of poliomyelitis, is a single stranded (plus sense) RNA virus. Humans are the only natural hosts of PV. After oral ingestion, the virus multiplies in the alimentary mucosa, and possibly in the tonsils and Peyer's patches. The virus then moves into the deep cervical and mesenteric lymph nodes and into the blood stream (viremia). The circulating virus invades the central nervous system (CNS) and replicates in neurons, particularly motor neurons. There are two possible dissemination routes through which PV can enter the CNS. One is virus permeation through the blood-brain barrier (BBB) and the other is virus transmission via peripheral nervous (neural pathway). Paralytic poliomyelitis occurs as a result of neuronal destruction by lytic replication of PV.

The development of a mouse model for poliomyelitis that is transgenic for the human PV receptor (CD155) has made it much easier to investigate the efficiency of the viral dissemination process in a whole organism. These studies have given an insight into the mechanisms of BBB permeation and neural transport. Strain specific neurovirulence levels, however, appears to depend mainly on the replicating capacity of the virus in the CNS rather than the dissemination efficiency.

The attenuating mutation within the IRES (internal ribosome entry site) on the RNA of the Sabin 1 vaccine strain of poliovirus was identified by constructing recombinant viruses between the Sabin 1 strain and the parental virulent Mahoney strain followed by neurovirulence test. This work opened a new avenue for elucidating the molecular mechanisms of the poliovirus pathogenesis. This discovery led to a concept "IRES activity-dependent virus tropism".

CD155 is not involved in the BBB permeation, but in the neural pathway. As for BBB permeation, PV is suggested to be incorporated into endosomes through a common pathway to that of transferrin. On the other hand, PV inoculated into skeletal muscle is incorporated into endosomes at synapses in a CD155-dependent manner as an infectious particle, and the PV-containing endosomes are retrogradely conveyed along microtubules in the axons with the aid of Tctex-1, a light chain-1 of cytoplasmic dynein complex, to the neuron cell body.

In addition, neural cells were found to possess protective response mechanisms against PV infection. This finding will be also discussed.