Gastrointestinal Influences on Poliovirus Replication, Dissemination and Pathogenesis in Mice

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Date Available: 12/12/2013
Summer 2011
Molecular Microbiology
Bibliography: pp. 164-190

Keywords: poliovirus; quasispecies; enteric virus; microbiota; intestinal bacteria; gastrointestinal tract; bottleneck; host barriers; viral trafficking; viral diversity

Enteric viruses are transmitted between individuals by fecal-oral spread. After oral acquisition, enteric viruses encounter a complex environment within the gastrointestinal (GI) tract, including pH changes, mucus, resident bacteria and a variety of epithelial and immune cell types. Little is known about how factors within and comprising the GI tract influence viral replication, dissemination and pathogenesis.

In order to assess the influence of the intestinal environment on enteric viruses, poliovirus was used as a model enteric virus. Following infection within the GI tract, poliovirus has the capacity to spread to the central nervous system (CNS). Poliovirus infection of the CNS is uncommon, but it can result in acute flaccid paralysis known as poliomyelitis in humans. Poliomyelitis can be mimicked in mice susceptible to poliovirus. Initial studies were performed in mice to examine poliovirus infection within and dissemination from the GI tract to extra-intestinal tissues, including blood and the CNS. By monitoring spread of a marked poliovirus population in susceptible mice, many host barriers to intra-host viral trafficking were identified. Type I interferon responses and intestinal epithelial cell integrity are host barriers that were found to restrict poliovirus. Infecting cells within the GI tract was also difficult for poliovirus, which further limited dissemination from the intestine to the blood and CNS. Bottlenecks were imposed on poliovirus while trafficking through and disseminating from the GI tract, possibly providing an explanation for the low incidence of poliomyelitis disease onset in humans following poliovirus infection.

Because the GI tract was a substantial barrier to poliovirus, studies were undertaken to characterize factors that limit poliovirus dissemination from the GI tract. The naturally-residing microbiota are amongst many other factors present within the GI tract that may influence poliovirus infection. Although suspected to limit poliovirus, intestinal microbiota augmented poliovirus infection in mice and cell culture by enhancing viral infectivity. The studies described herein demonstrate how host complexity imparts detrimental and beneficial influences on poliovirus acquired by the natural fecal-oral route.