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Poliovirus and Group C Enteroviruses: Knowledge Gaps Relevant to Eradication

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Abstract

Poliovirus eradication is one of the most challenging public health endeavors in modern times (www.polioeradication.org). Social, political, economic & scientific factors have made this goal elusive. When eradication goals were first established in 1988, there was little appreciation of viral RNA recombination, enterovirus species groups and their relevance to eradication. Now, it is clear that RNA recombination between live-attenuated vaccine strains of poliovirus and non-polio group C enteroviruses results in circulating vaccine-derived polioviruses (cVDPV) and corresponding outbreaks of paralytic disease, a significant obstacle to eradication. By understanding enterovirus species groups, it becomes clear that poliovirus capsid proteins can be eradicated; however, the remainder of poliovirus RNA genomes will survive indefinitely in other group C enteroviruses. To help address these obstacles to eradication, the Barton lab studies molecular features of 3Dpol involved in viral RNA replication and recombination. A dsRNA clamp of 3Dpol that holds RNA products of replication as they exit the polymerase plays important roles in the polyadenylation of viral RNA, the fidelity of RNA replication, ribavirin sensitivity and viral RNA recombination. In other experiments, we identified a group C enterovirus RNA involved in the inhibition of ribonuclease L, an antiviral endoribonuclease. The RNase L ciRNA plays important but largely unexplored roles in pathogenesis. Using novel deep sequencing methods,

Keywords:

we found that RNase L targets viral RNA encoding neutralizing epitopes of capsid proteins