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, we found that RNase L targets viral RNA encoding neutralizing epitopes of capsid proteins, sparing most other regions of viral RNA. These data suggest an important interplay between neutralizing antibodies, neutralization escape mutations and antiviral endoribonucleases. A better understanding of viral RNA recombination, enterovirus species groups and antiviral endoribonucleases should help achieve and maintain poliovirus eradication.

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The Intrathecal Antibody Response in Multiple Sclerosis Brain Does Not React Against Measles Virus

Deandra L Walker, Mark P Burgoon

Department of Neurology, University of Colorado School of Medicine, Aurora, CO

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) and is the most common disabling neurological disease of young adults. Although the cause of MS is unknown, genetic and epidemiological studies indicate that MS may be triggered by an environmental agent. The presence of intrathecally produced antibodies, which produce oligoclonal Ig bands in the CNS of MS patients, provides tools for investigating the target of the inflammatory response. In most of the CNS conditions with oligoclonal bands the target is known and the antibody is directed against an infectious, causative agent. For example, in subacute sclerosing panencephalitis, a measles virus (MV) infection of the brain, the oligoclonal bands and intrathecal antibodies are primarily directed against MV. In earlier studies of MS, we demonstrated that the intrathecal antibody response in MS brain does not react to varicella zoster or Epstein-Barr virus. The current study investigates the reactivity of the intrathecal antibody response in MS brain to MV. We isolated individual CD38+(+) plasma cells from MS brain to produce recombinant antibodies (rAbs). These rAbs likely represent oligoclonal bands and were used to immunostain MV-infected or uninfected monkey kidney (Vero) cells. Although many of the rAbs from MS brain reacted against auto-antigens in several mouse and human tissues, none of fifteen MS rAbs reacted against MV-infected cells. These results indicate that measles virus is not a disease-relevant antigen in MS.

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Poliovirus and Group C Enteroviruses: Knowledge Gaps Relevant to Eradication

Barton DJ, Kempf BJ, Cooper DA.

Department of Immunology and Microbiology, University of Colorado School of Medicine, Aurora, CO

The long-tailed pygmy rice rat (Oligoryzomys longicaudatus) is the reservoir host of Andes (ANDV) and Oran hantaviruses (Bunyaviridae). To examine transcriptome features of persistently infected rice rats, spleens