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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Current Disease and Epidemiologic Problems: What’s Hot?

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Included among the many current world problems are viral diseases of considerable significance and threat. This talk could not possibly cover them all but will discuss the emergence of Middle East respiratory syndrome in Saudi Arabia and nearby countries, ebolavirus hemorrhagic fever in West Africa, chikungunya in the Western Hemisphere, and the re-emergence of poliomyelitis.

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Transcriptome markers of viral persistence in naturally-infected Andes Hantavirus (Bunyaviridae) seropositive rice rats

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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

Poliovirus and Group C Enteroviruses: Knowledge Gaps Relevant to Eradication

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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 oligodendrocyte 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 oligodendrocyte 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 oligodendrocytes 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 examines transcriptome features of persistently infected rice rats, spleens

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

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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 oligodendrocyte 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 oligodendrocyte 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 oligodendrocytes 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 examines transcriptome features of persistently infected rice rats, spleens

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woodrats (Neotoma micropus) in the United States and has been preliminarily identified as a phlebovirus transmitted by the sand fly Lutzomyia anthophora. RGV is not known to cause disease in humans, but it could be detected by assays designed for HRTV or other phleboviruses. The goal of this study was to determine antigenic cross-reaction between RGV and other phleboviruses. A commercially available ELISA based sand fly fever antigen detection kit was tested for the ability to detect RGV and other New and Old-World phleboviruses, including attenuated Rift valley fever virus (RVFV) strain MP12, Punta Toro virus (PTV), Toscana virus, Aguacate virus, Anhanga virus, Arumowot virus, and Chagres virus. Immunocytochemistry and Western blotting were used to detect cross reactions between RGV, MP12, and PTV using rabbit anti-RVFV nucleocapsid protein and glycoproteins GC and GN, mouse monoclonal anti-PTV, and sheep polyclonal anti-MPV. The ELISA test detected cross reactivity for all phleboviruses excluding RGV, but Western blotting detected the presumed RGV nucleocapsid protein (N) using rabbit anti–RVFV-N serum, RGV-infected cells were also identified when labeled with this antibody. Our findings demonstrate assay specific antigenic cross reactivity between these phleboviruses, thus further characterization of the molecular targets of the cross-reaction is required for proper interpretation of serological assays.