

ISOLATION, CHARACTERIZATION, AND DIAGNOSIS OF MURINE NOROVIRUSES, A NEWLY RECOGNIZED PATHOGEN OF MICE

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ABSTRACT

Murine norovirus (MNV) is a newly recognized pathogen of mice. To assess the extent of MNV infection in laboratory mice, a high-throughput serologic diagnostic assay termed the multiplex fluorescent immunoassay (MFI) was developed and revealed that 22.1% of 12,639 serum samples from mice contained antibodies to MNV. These results indicate evidence of widespread MNV infection, making MNV the most prevalent viral pathogen in laboratory mice. Previously, murine norovirus 1 (MNV-1) was the only norovirus reported to infect research mice. We describe the isolation of 3 novel murine norovirus strains—MNV-2, MNV-3, and MNV-4—that caused persistent infections and prolonged fecal shedding in inoculated mice. These findings are markedly different from MNV-1 which causes only transient infections. Phylogenetic analysis confirmed that these novel MNV strains are related to MNV-1 even though they displayed different biologic behavior from that of MNV-1. We describe the use of microarrays, real-time RT-PCR and protein assays to identify perturbations in over 100 cytokines and chemokines involved in the inflammatory response, but we were unable to document any significant changes in MNV infected mice. Finally, we show serologic evidence suggestive of a rat norovirus infection by using a Western blot assay with MNV antigens that highlighted the 59 kDa major antigenic capsid protein of noroviruses.