Murine Norovirus

Norovoiruses are members of the family *Caliciviridae*, a non-enveloped single stranded RNA virus. Noroviruses have been associated with disease in several species including pigs, cattle, humans, and now mice. Noroviruses cause most of the non-bacterial, food-borne gastroenteritis in humans. The first murine norovirus known to infect mice (MNV-1) was identified in *Rag2*$^{-/-}$*/Stat*$^{-/-}$ mice in 2003 (Karst et al. Science 299:1575-1578). Experimentally infected mice with impaired innate immunity (*Rag2*$^{-/-}$*/Stat*$^{-/-}$, *Stat1*$^{-/-}$, *Stat1*$^{-/-}$, *Stat1*$^{-/-}$*/Pkr*$^{-/-}$, and *IFNαβγR*$^{-/-}$) were highly susceptible to MNV-1 induced lethality. Naturally exposed susceptible strains showed varying degrees of hepatitis, peritonitis, and pneumonia (Ward et al. Toxicologic Pathology 34:708-715 2006). Other immune-deficient strains such *RAG1*$^{-/-}$, *RAG2*$^{-/-}$, *Nu*, and *SCID* are resistant to MNV-1-induced lethality although the virus infection is persistent in these mice. In immunocompetent mice, MNV-1 only causes transient infection with no clinical signs reported to date. A recent report (Hsu et al. Comparative Medicine 56:247-251 2006 and information presented at the recent American Association for Laboratory Animal Science meeting) indicates that 22 to 30% of serum samples tested from various research institutes in North America contained antibody to MNV. This makes MNV-1 the most prevalent viral pathogen infecting mice. Also 40 to 50 strains of MNV have been isolated from geographically separate mouse facilities. MNV is the only norovirus that can be grown in culture. Sequence information on 21 of these strains has been deposited in Genbank. The strains are highly related (96 to 98% diversity) and show serologic cross-reactivity.

What is the MNV Status at NCI-Frederick?

The NCI-Frederick Animal Health Diagnostic and Molecular Laboratory now has a serologic and PCR assay for screening of MNV-1. Although the number of mice tested to date is low, with the exception of the Animal Production Area and Building 1048, all other Frederick NCI-facilities are seropositive for MNV-1. Testing elsewhere has also shown that mice housed in the Bethesda facilities and those at other NIH Institutes are also seropostive. The presence of the virus in our facilities has also been confirmed by PCR.

Summary

The high level of seropositive animals detected throughout the United States indicates that the virus is well adapted to its host and has been present in mice for a number of years. Interestingly, testing of mice from approved vendors has been negative whereas as those animals maintained in a research environment are highly positive. From information reported to date the overall biological impact of MNV-1 appears to be low and MNV-1 infections are transient and nonpathogenic except for the most severely immune-deficient mice. Susceptibility to disease is likely due to the lack of innate immune responses to infection. The general consensus from the many institutions that are positive for MNV is that there is no need to act hastily in trying to eliminate the virus, but to control spreading to highly susceptible strains by stringent husbandry procedures. Investigators need to be aware of the health status of their colonies and the confounding effect that MNV could have in the interpretation of results especially when using severely immune-deficient mouse models.