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## Mouse Norovirus (MNV)

Etiologic Agent – calicivirus, positive sense ssRNA nonenveloped, resistant to organic solvents and mild detergents, inactivated at  $3 < \text{pH} < 5$ , sensitive to UV irradiation and SporKlenz

### Introduction

Noroviruses are a group of genetically related and antigenically diverse viruses that infect both humans and animals. These viruses are responsible for the majority of acute nonbacterial gastroenteritis in humans. The disease is self-limiting and mild with symptoms of nausea, fever, vomiting and diarrhea lasting 24-48 hours. Transmission of the virus is by ingesting material contaminated from infected feces. These viruses infect and replicate in dendritic cells of the gastrointestinal tract where the elaboration of cytokines leads to the disease symptomology.

In 2003, SM Karst and CE Wobus two postdoctoral fellows in the laboratory of HW (Skip) Virgin at Washington University in St. Louis identified MNV-1, the first known mouse norovirus. Virgin's group showed that the mouse's ability to fight MNV-1 infection relied heavily on the innate immune system, the branch of the immune system that attacks invaders soon after they enter the body (Science 299:1575-1578). MNV-1 produces a transient infection with a short duration of fecal shedding in immunocompetent mice. Since the original description of MNV-1 three additional MNV strains have been identified that differ markedly in their pathogenicity producing persistent infections and prolonged shedding in feces of immunocompetent mice (CC Hsu et al 2006, Virus Genes vol.15:Epub). This group of viruses causes lethal infection in interferon  $\alpha$ - $\beta$ - $\gamma$ -receptor triple knockout mice, and in RAG/Stat-1 double knockout mice. Rag-1 KO mice did not become ill, however they were persistently infected. This suggests that the innate immune system is sufficient to protect mice from clinical disease associated with MNV infection. Histopathologic evaluation of immunodeficient mice that died from MNV inoculation demonstrated meningoencephalitis, cerebral vasculitis, pneumonia and hepatitis.

### Commercial Producers of Mice, Rodent Importation and Movement of Mice Between Animal Facilities and Animal Rooms

The following commercial producers of mice are testing for MNV and have shown to be free of this disease: Taconic, Charles River Laboratories, Harlan, and NCI. The Jackson Laboratory has shown their foundation colonies to be free of the disease but has not tested the production or research colonies (those which are sold) currently have no plan on doing so.

Approximately 80% of mice imported from other academic institutions that move through our clean quarantine area are harboring and actively shedding this virus.

The movement and sharing of transgenic mice between animal facilities within and between our vivaria has undoubtedly led to widespread dissemination of MNV within our institution. Even armed with our current knowledge of vivarium status CCM has not impeded the movement of mice at this time. This may change if widespread eradication is planned.

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MNV at the University of Virginia

In August of 2006 reagents became commercially available to test for the presence of antibodies to mouse noroviruses. The Center for Comparative Medicine incorporated that testing into our routine limited and comprehensive mouse panels for testing sera of sentinel mice placed in all animal rooms in all vivaria. There is one sentinel cage for each 120 mouse boxes so many room have multiple data entries. Modular clean quarantine is the space where we import mice, and have not stopped importation based on the presence of MNV antibodies. The table appended to this document is map of the mouse rooms infected with this virus as of the dates tested. Currently eradication of the virus is planned only for the Gene Targeting and Transgenic Facility. Due to the widespread occurrence of the virus in many vivarium rooms, and the prevalence of unique transgenic strains, a comprehensive plan to eradicate the virus from all facilities is no planned. If you need further information please contact me at 4-5058 or by e-mail at shf2b@Virginia.edu.

Sanford H. Feldman, DVM, PhD  
Director, Center for Comparative Medicine

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LOCATION	DATE COMPLETED	ACCESSION NO	SAMPLE NO	ROOM NO	MNV
Aurbach	11/15/06	2491	1	123	+
	11/15/06	2491	2	125	+
	11/15/06	2491	3	126	+
	11/15/06	2491	4	129	+
	11/15/06	2491	5	131	+
	11/15/06	2491	6	133	-
	11/15/06	2491	7	135	+
	11/15/06	2491	8	138	-
	11/15/06	2491	9	146	+
	11/15/06	2491	10	147	-
		12/13/06	2499	1	147
Gilmer	12/21/06	2501	1	180C	-
	12/21/06	2501	2	176C	+
	12/21/06	2501	3	178A	+
	12/21/06	2501	4	178A	+
Hospital	11/1/06	2489	1	1847	-
	12/5/06	2494	3	1843	-
	1/10/07	2518	1	1833	-
	1/10/07	2518	2	1834	-
	1/10/07	2518	3	1839	-
	1/10/07	2518	4	1843	-
	1/10/07	2518	5	1844	-
	1/10/07	2518	6	1845	-
	1/10/07	2518	7	1846	-
1/10/07	2518	8	1846	-	
Jordan	10/20/06	2471	1	211	-
	10/20/06	2471	2	213B	-
	10/20/06	2471	3	213C	-
	10/20/06	2471	4	213D	-
	10/20/06	2471	5	213E	-
	10/20/06	2471	6	213F	-
	10/20/06	2471	7	213G	-
	10/20/06	2471	8	216	-
	10/20/06	2471	9	217B	-
	10/20/06	2471	10	217D	-
	10/20/06	2471	11	217E	-
	10/20/06	2471	12	217F	-
	10/20/06	2471	13	217G	+
	10/20/06	2471	14	218	+
	10/20/06	2471	15	223B	+
	10/20/06	2471	16	223D	+
	10/20/06	2471	17	223G	+
	10/20/06	2471	18	223H	+
		1/2/07	2503	1	229
	10/20/06	2471	19	229	+

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LOCATION	DATE COMPLETED	ACCESSION NO	SAMPLE NO	ROOM NO	MNV
Modular	10/31/06	2476	1	Quarantine	-
	10/31/06	2477	2	Quarantine	+
	10/31/06	2478	3	Quarantine	+
	10/31/06	2479	4	Quarantine	+
	10/31/06	2480	5	Quarantine	+
	10/31/06	2481	6	Quarantine	-
	10/31/06	2482	7	Quarantine	-
	10/31/06	2483	8	Quarantine	-
	10/31/06	2484	9	Quarantine	-
	10/31/06	2485	10	Quarantine	+
	10/31/06	2486	11	Quarantine	-
	10/31/06	2487	12	Quarantine	-
	10/31/06	2487	13	Quarantine	+
	1/4/07	2504	1	Quarantine	-
	1/4/07	2505	1	Quarantine	-
	1/4/07	2506	1	Quarantine	-
	1/4/07	2507	2	Quarantine	-
	1/4/07	2508	3	Quarantine	-
	1/4/07	2509	4	Quarantine	-
	1/4/07	2510	5	Quarantine	-
	1/4/07	2511	6	Quarantine	+
	1/4/07	2512	7	Quarantine	-
	1/4/07	2512	8	Quarantine	-
	1/4/07	2513	9	Quarantine	-
	1/4/07	2513	10	Quarantine	-
	1/4/07	2514	11	Quarantine	-
	1/4/07	2514	12	Quarantine	-
	1/4/07	2515	13	Quarantine	-
	1/4/07	2516	14	Quarantine	-
	1/4/07	2517	1	Quarantine	+
	1/4/07	2517	2	Quarantine	+
	1/4/07	2517	3	Quarantine	+
	1/4/07	2517	4	Quarantine	+
	1/4/07	2517	5	Quarantine	+
	1/4/07	2517	6	Quarantine	+
	1/4/07	2517	7	Quarantine	+

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LOCATION	DATE COMPLETED	ACCESSION NO	SAMPLE NO	ROOM NO	MNV
MR4	11/8/06	2490	1	23	+
	11/8/06	2490	2	18	-
	11/8/06	2490	3	31	+
	11/8/06	2490	4	15	-
	11/8/06	2490	5	121B	-
	11/8/06	2490	6	168	-
	11/8/06	2490	7	168	-
	12/5/06	2493	1	168	-
	12/5/06	2493	2	168	-
	12/18/06	2497	1	18	+
	12/18/06	2497	2	17	-
	12/18/06	2497	3	11	+
	12/18/06	2497	4	121A	+
	12/18/06	2497	5	121E	+
	12/18/06	2497	6	121E	-
	12/18/06	2497	7	43C	+
	12/18/06	2497	8	43D	-
	12/18/06	2497	9	43B	-
	12/18/06	2497	10	19	+
	12/18/06	2497	11	23	+
	12/18/06	2497	12	147C	-
	12/18/06	2497	13	43E	-
	12/18/06	2497	14	147D	-
	12/18/06	2497	15	14	-
	12/18/06	2497	16	15	-
	12/18/06	2497	18	121F	-
	12/18/06	2497	19	144	-
	12/18/06	2497	20	37C	-
	12/18/06	2497	21	147B	-
	12/18/06	2497	22	13	-
	12/18/06	2497	23	13	-
	12/18/06	2497	24	147E	-
	12/18/06	2497	25	21	+
	12/18/06	2497	26	168	-
	12/18/06	2497	27	37A	-
	12/18/06	2497	28	121D	-
	12/18/06	2497	29	37B	+
	12/18/06	2497	30	121C	-
	12/18/06	2497	31	164	-
	12/18/06	2497	32	121B	-

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LOCATION	DATE COMPLETED	ACCESSION NO	SAMPLE NO	ROOM NO	MNV
MR5	10/12/06	2469	3	336	-
	10/20/06	2472	24	337	+
	11/10/06	2488	1	323	+
	11/10/06	2488	2	323	+
	11/10/06	2488	3	323	+
	11/10/06	2488	4	303	+
	11/10/06	2488	5	303	+
	11/10/06	2488	6	337	+
	11/10/06	2488	7	337	+
	11/10/06	2488	8	303	+
	11/10/06	2488	9	337	+
	11/10/06	2488	10	336	+
	11/10/06	2488	11	338	+
	11/10/06	2488	12	338	+
	11/10/06	2488	13	335	+
	11/10/06	2488	14	335	+
	11/10/06	2488	15	335	+
	11/10/06	2488	16	335	+
	11/10/06	2488	17	336	+
	11/10/06	2488	18	334	+
	11/10/06	2488	19	334	+
	11/10/06	2488	20	336	+
	11/10/06	2488	21	334	+
	11/10/06	2488	22	334	+
	11/10/06	2488	23	323	+
	11/10/06	2488	24	336	+
	11/10/06	2488	25	338	+
	11/10/06	2488	26	325	+
	11/10/06	2488	27	325	+
	11/10/06	2488	28	325	+
	11/10/06	2488	29	325	+
	11/10/06	2488	30	320	+
	11/10/06	2488	31	320	+
	11/10/06	2488	32	320	+
	11/10/06	2488	33	320	+