Mouse Kidney Parvovirus: A Newly Characterized Parvoviral Pathogen of Research Mice

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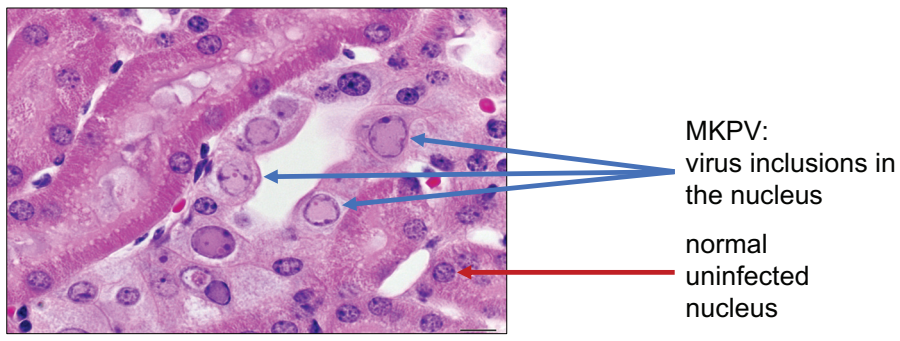
Introduction

- Anecdotal reports of inclusion body nephropathy (IBN) due to an unknown etiology for decades.
- Histopathologic lesions (epithelial intranuclear inclusions in renal tubules) observed in immunodeficient and immunocompetent mice.
- Recently, two independent research groups have attributed observed lesions to a new parvovirus of the *Chapparvovirus* genus.
- Mouse Kidney Parvovirus (MKPV) or Murine Chapparvovirus (MuCPV) are taxonomically the same species.
- Virus identified in both wild and laboratory mice.
- Virus is genetically divergent from other known mouse parvoviruses such as MVM and MPV.

Example of observed histologic lesions



Developing a PCR Diagnostic Test

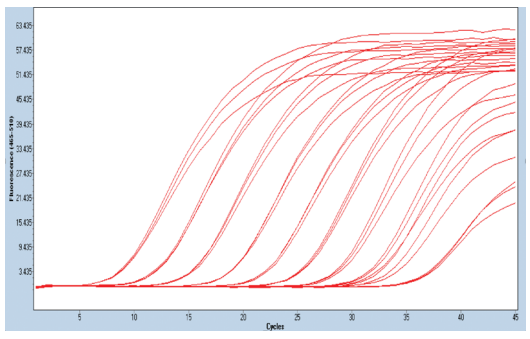
Assay Design

- The IDEXX BioAnalytics fluorogenic MKPV real-time PCR assay was designed to a target that is 100% conserved among the Murine chapparvovirus sequences obtained from both wild and research mice in the NCBI database.

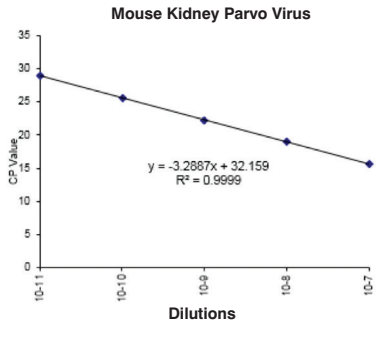
MKPV PCR Assay Validation Process

Analytical validation with serial dilutions of known positive controls included:

- Assay amplification efficiency of 95-105% (Figure A)
- Linearity over 5 points, calculated coefficient of variation (CV) of crossing points (Cp) ≤ 3% with CV calculated with absolute values ≤ 20%, r2 value ≥ 0.993 (Figure B)
- Amplification of ≤10 template molecules per PCR reaction
- Clinical validation involved testing serial dilutions of clinical samples, and target confirmation by sequence analysis.
- Clinical correlation study resulted in 100% positive real-time PCR results obtained for all histopathology samples tested.



A. Amplification Curves



B. Linearity Plot

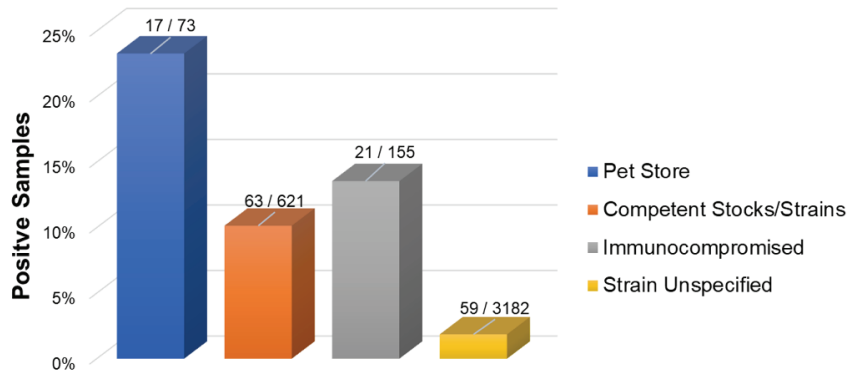
Sequence Analysis

MKPV PCR assay amplified virus in the feces and tissues from wild mice, pet store mice, immunocompetent and immunocompromised research mice.

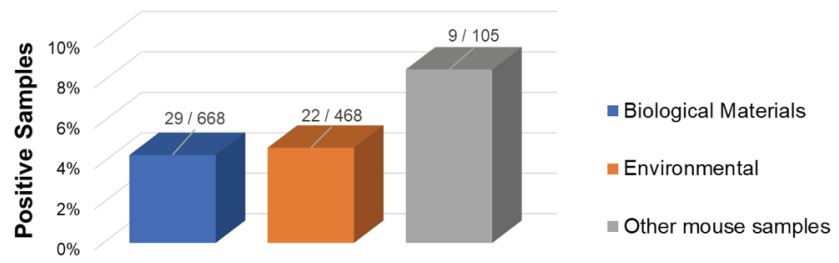
Sequence analysis was performed on virus from wild mice and research mice from 20 institutions in Canada, Europe, the Middle East, and the United States, and revealed multiple MKPV virus strains.

The MKPV PCR assay detects genetically divergent strains of MKPV, and serves as a useful tool in screening samples for MKPV.

Number of positive fecal samples as detected by real-time PCR



Number of positive non-fecal samples as detected by real-time PCR



Materials evaluated for this survey include:

- Biological materials – cell lines, tumors, tumor fragments, and Matrigel
- Environmental – rack filters and cage swabs
- Other mouse materials – kidneys, urine, unspecified mouse tissue, and pelt swabs

Detection by Dirty Bedding Sentinels

Colony Mice

- 3 cages naïve female nude mice (4 mice per cage)
- Mice housed in cages containing dirty bedding from a known positive colony for 2 weeks.
- MKPV was detected in the feces by real-time PCR for up to 12 weeks post exposure.

Sentinel Mice

- 3 cages of naïve ICR female mice (4 per cage)
- Mice housed on a separate rack from colony mice
- Sentinel mice exposed to 30 cc dirty bedding from colony cage every 2 weeks for 4 weeks.
- MKPV was detected in the feces by real-time PCR for up to 8 weeks post exposure.

Number of MKPV positive cages as detected by real-time PCR of feces

Mice	Time of Testing (Weeks)						
	0	2	4	6	8	10	12
Nude	0/3	ND	3/3	ND	3/3	ND	3/3
Sentinel	0/3	3/3	3/3	3/3	3/3	*	*

Table Legend

1. N/D = Time points not performed
2. * = time points that are pending testing

Summary

- MKPV infection has been detected in a wide range of mouse stocks and strains.
- MKPV can be detected in a variety of sample types including feces, urine, mouse tissues, rack filters, cage swabs and biological material such as cell lines and tumors.
- MKPV infection can be detected in soiled bedding sentinel mice as early as 2 weeks after exposure to dirty bedding.
- MKPV shedding was detected for up to 6 weeks in sentinel mice and 12 weeks in nude mice.