

Characterization of the humoral response to FIPV & FECV in naturally-infected cats Nicole Neely, Diego Castillo DVM, Sarah Cook DVM, Brian G. Murphy DVM, PhD School of Veterinary Medicine, University of California, Davis Department of Pathology, Microbiology, & Immunology



Hypothesis & Specific Aims

- Feline infectious peritonitis virus (FIPV) is a feline coronavirus responsible for the disease feline infectious peritonitis (FIP)
 - Arises from the feline enteric coronavirus (FECV) after it undergoes certain mutations
 - Mutations allow for the infection of macrophages
 - FIPV has four structural proteins: Spike, Nucleocapsid, Membrane, and Envelope
- Two serotypes exist, based on the Spike protein: FIPV I & FIPV II
- Long considered an untreatable, fatal disease
- Characterized by "wet" or "dry" forms involving fulminant vasculitis, cavitary effusions, and/or granulomatous inflammation of multiple organs
- Exhibits the property of "antibody-dependent enhancement (ADE)"
 - Antibodies facilitate the uptake of the virus into macrophages and contribute to vasculitis via type III hypersensitivity
 - Antibodies against Spike, Nucleocapsid, and Membrane have been demonstrated in previous literature
 - Epitopes of the Spike protein have been shown to contribute to ADE
- Recent research has revealed several modern antivirals with potential to actual efficacy against FIPV
 - GS-441524, GC376, nirmatrelvir, remdesivir, EIDD2801 (molnupiravir)
 - It is unknown if the humoral response of the cat affects treatment outcome

Materials & Methods

Hypothesis: The humoral response to feline infectious peritonitis (FIP) virus is associated with treatment outcome in cats naturally-infected with feline coronavirus & treated with antiviral therapeutics.

- Specific Aim 1: To characterize the humoral response to FIPV in naturally-infected cats on antiviral treatments.
- Specific Aim 2: To use traditional statistical methods to associate humoral response with response to antiviral therapy, mortality, & overall treatment outcome.



Blood & ascites fluid were collected from numerous cats, including participants in the VMTH clinical treatment in cats with feline infectious peritonitis (FIP)" and "Oral antiviral therapy for cats with feline infectious peritonitis (FIP)". Blood and ascites fluid were collected prior to the start of treatment.



Western Blot

- Four FIPV+ cats
- One FIPV survivor (post-experimental infection w/ serotype 1 & treatment with GS-441524)



Indirect ELISA

1. protein coated container

2. Antibodies bind to protein

3. Excess washed away

- Eight FECV-infected cats
- SPF cat (negative control)
- Monoclonal antibodies against FIPV nucleocapsid protein:
 - FIPV3-70
- CCV2-2

Results









Based on the results from the Western Blots & ELISAs:

Discussion

- A strong humoral response is elicited against N-protein & M-protein, including the various forms of glycosylation exhibited by M-protein
- The antibody profile against FIPV in ascites fluids seems to imitate that of serum
- The antibodies produced during acute infection with FIPV or FECV bind the same proteins, but the • response to FIPV is of significantly greater magnitude
- IgG is the predominant antibody produced against FIPV, with only small amounts of IgM & IgA
- The antibody profile may change over time post-infection, but strong immunity against N-protein is maintained
- The humoral response to FIPV I is not reliably detected on Western Blot, but ELISA data indicates that • this is likely artifactual & does not represent a real difference in feline humoral response

ELISA – FIPV Serum



Future Directions

The original goal of this study was to analyze feline humoral response and antiviral treatment outcome to seek potential associations between the two. Too few cats were enrolled during the period of this STAR project to achieve statistical power, but this analysis may be conducted once more cats are enrolled.

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