

## Characterization of the humoral response to FIPV & FECV in naturally-infected cats

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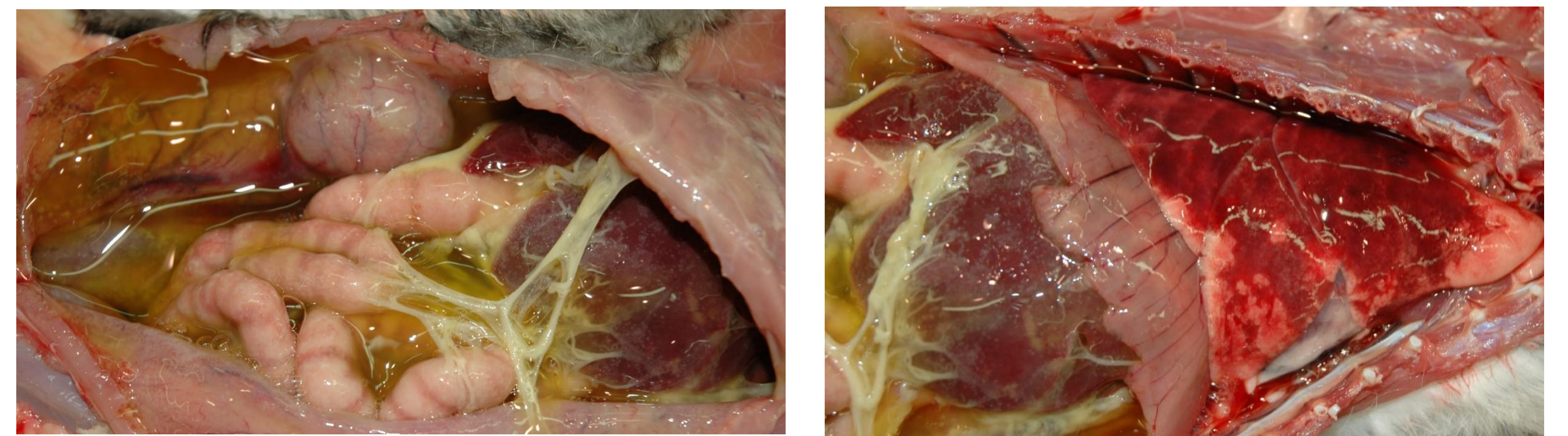
### Background

- 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, cavity 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

### Hypothesis & Specific Aims

**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.



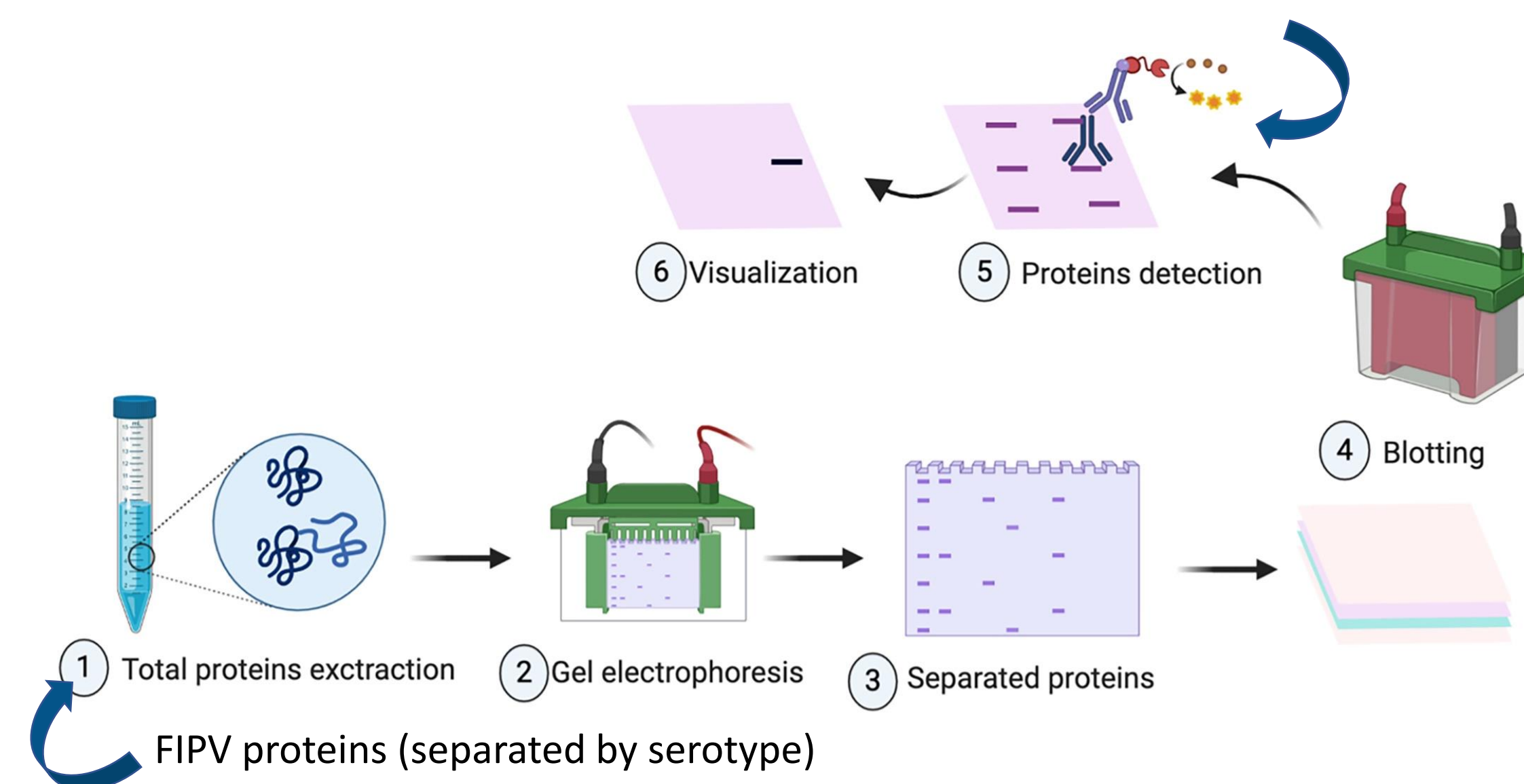
### Materials & Methods

Blood & ascites fluid were collected from numerous cats, including participants in the VMTH clinical trials “Combined stem cell & antiviral 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.

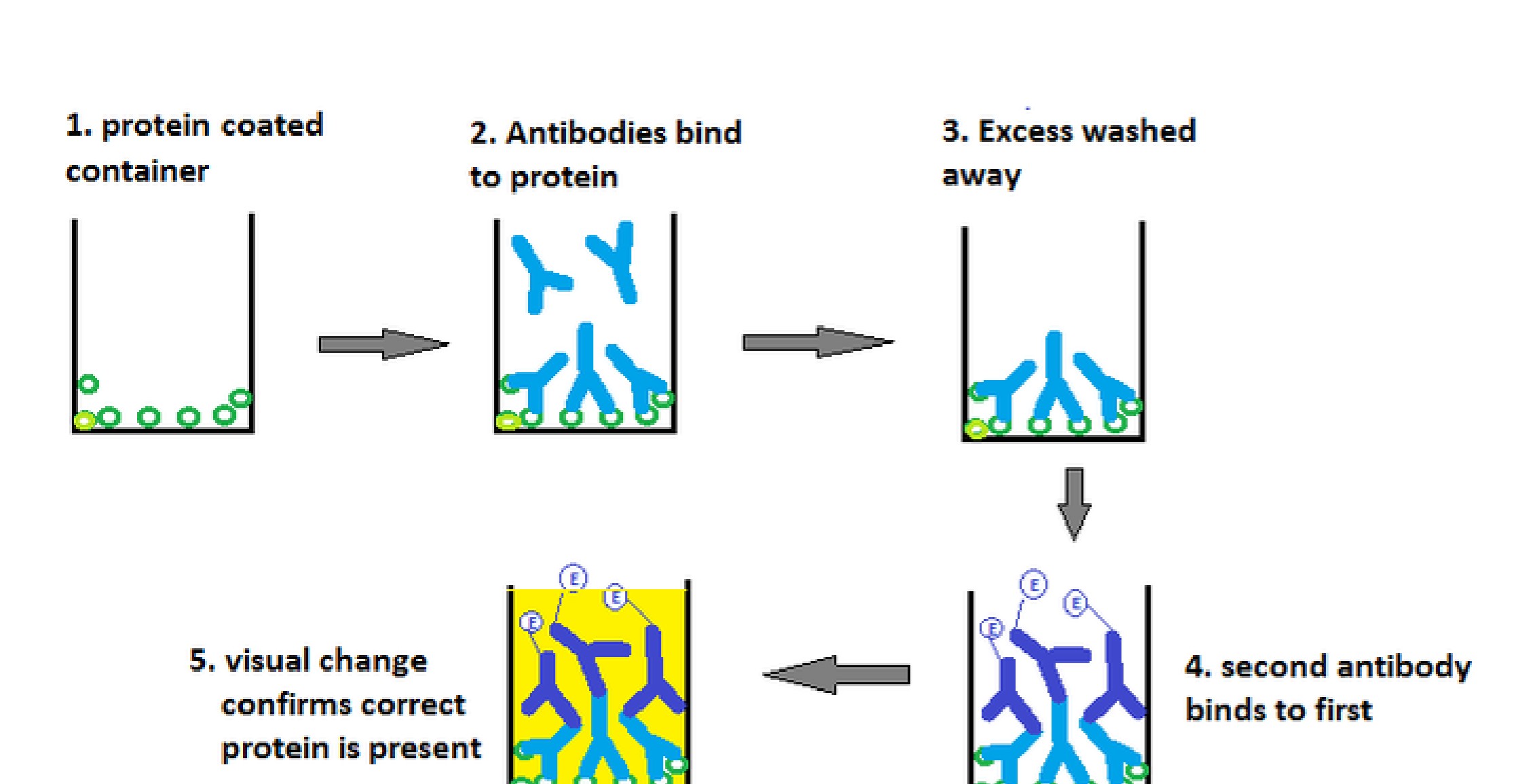
#### Cats

- Four FIPV+ cats
- One FIPV survivor (post-experimental infection w/ serotype 1 & treatment with GS-441524)
- Eight FECV-infected cats
- SPF cat (negative control)
- Monoclonal antibodies against FIPV nucleocapsid protein:
  - FIPV3-70
  - CCV2-2

#### Western Blot

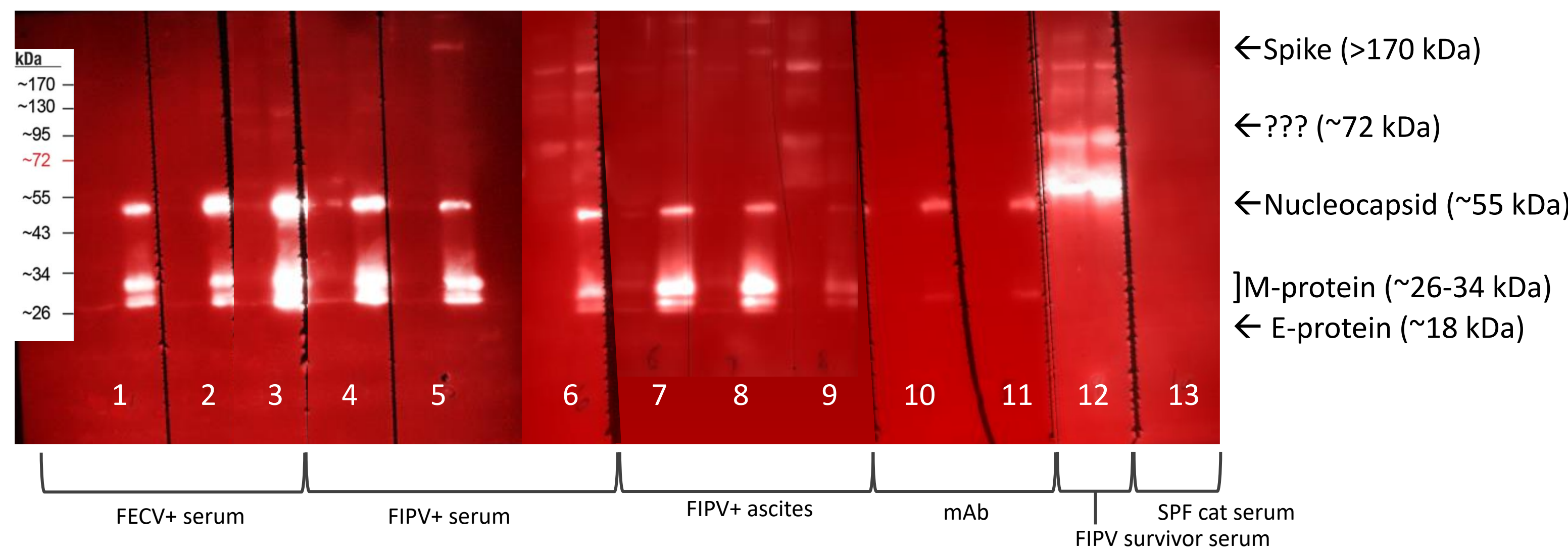


#### Indirect ELISA



### Results

#### Western Blot – FECV vs. FIPV Serum

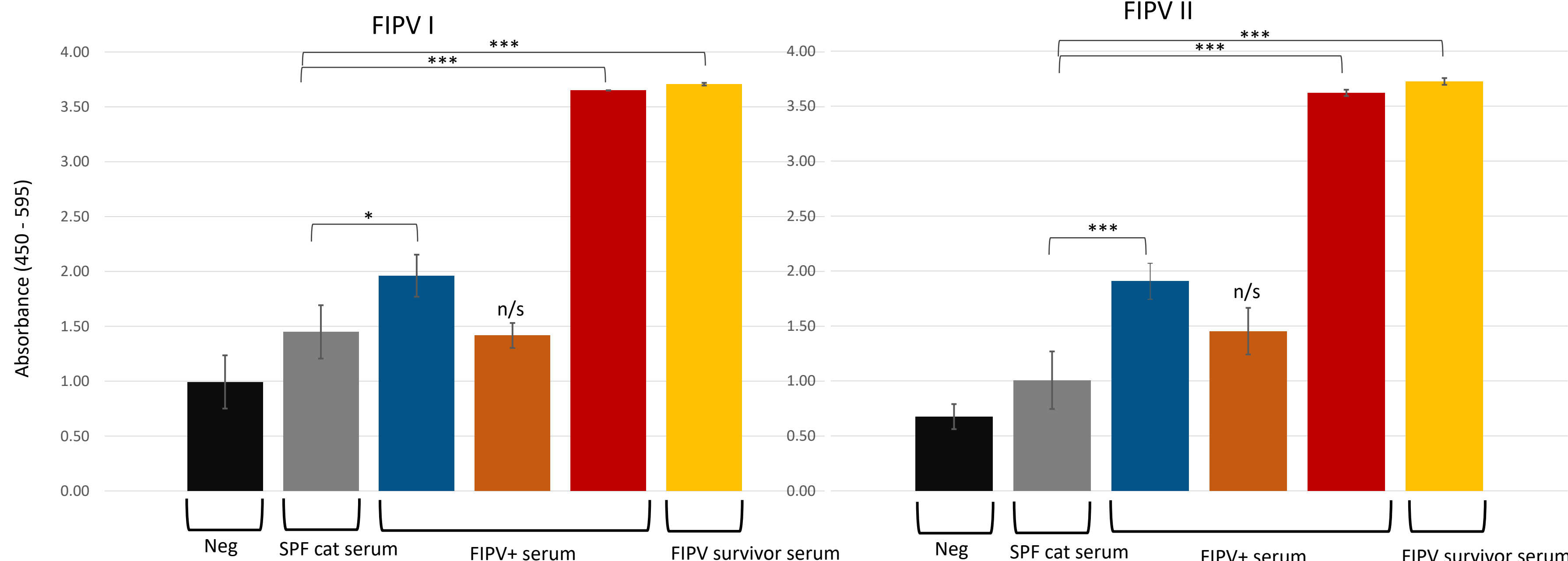


### Discussion

Based on the results from the Western Blots & ELISAs:

- 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.

### Acknowledgements

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