EFFICACY OF A SARS-CoV-2 RECOMBINANT VACCINE VIA SEROLOGIC RESPONSE IN CATS AND DOGS

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INTRODUCTION/BACKGROUND

To ensure preparedness in response to increasing reports of COVID-19 in companion animals, the team evaluated the efficacy and safety of a recombinant SARS-CoV-2 trimeric spike protein vaccine in cats and dogs when given subcutaneously using two doses 3 weeks apart, via the induction of antibodies with the ability to neutralize infectivity of SARS-CoV-2 *in vitro*.

METHODS

A DNA fragment encoding the extracellular domain of SARS-CoV-2 Spike protein was synthesized *de novo* to include mutations stabilizing the peptide in prefusion conformation, a domain to ensure trimeric conformation, and a purification tag. The resultant gene was cloned into pCDNA3.1. The resultant plasmid was used to transiently express the recombinant Spike protein in HEK cells with subsequent purification using the purification tag. The recombinant antigen was characterized by several assays including negative stain electron microscopy where the recombinant protein was demonstrated to have a tertiary structure in line with the SARS-CoV-2 Spike protein crystal structure.

Two vaccine serology studies were performed, one in cats and one in dogs, to assess the ability of the recombinant antigen formulated with proprietary Zoetis adjuvants to elicit robust antibody responses. Animals were randomly assigned to treatment groups using a generalized block design for the cats and a randomized complete block design for dogs. In each study, five animals were vaccinated subcutaneously with a true placebo and vaccines formulated with either Adjuvant #1 or Adjuvant #2, three weeks apart. Safety observations were conducted, and serum was drawn at various time points. Serologic responses were evaluated by an in-house SARS-CoV-2 Spike lateral flow assay (LFA), a SARS-CoV-2 Spike ELISA assay, and a SARS-CoV-2 serum neutralization (SN) assay performed externally.

Trt Group	No. of Animals	Vaccination				Blood Collection	End of Study
		Details	Day	Dose	Route		
T01	5	True Placebo Control	0, 21	1.0 mL	SC	0, 21, 42	42
T02	5	Recombinant Trimer Spike protein vaccine with Adjuvant 1*					
T03	5	Recombinant Trimer Spike protein vaccine with Adjuvant 2**					

SC – subcutaneous
* Commercial Adjuvant **Novel Zoetis Adjuvant

RESULTS

All vaccinated dogs and cats mounted a robust antibody response to the SARS-CoV-2 Spike antigen. Immune serum was also demonstrated to neutralize the SARS-CoV-2 virus *in vitro.*

Table 1. Canine Antibody Titers

Trt Group	SN Antibody Titer			ELISA Antibody Titer			LFA Assay*		
	Day 0	Day 21	Day 42	Day 0	Day 21	Day 42	Day 0	Day 21	Day 42
T01	<32	<32	<32	300	100	<1000	Neg	Neg	Neg
T01	<32	<32	<32	100	100	<1000	Neg	Neg	Neg
T01	<32	<32	<32	100	100	<1000	Neg	Neg	Neg
T01	<32	<32	<32	100	100	<1000	Neg	Neg	Neg
T01	<32	<32	<32	100	100	<1000	Neg	Neg	Neg
T02	<32	<64	>2048	300	8100	81000	Neg	Pos	Pos
T02	<32	272	>2048	100	8100	27000	Neg	Pos	Pos
T02	<32	55	563	100	8100	27000	Neg	Pos	Pos
T02	<32	536	>2048	100	2700	81000	Neg	Pos	Pos
T02	<32	<32	1026	100	8100	27000	Neg	Pos	Pos
T03	<32	489	>2048	100	8100	243000	Neg	Pos	Pos
T03	<32	441	>2048	100	8100	81000	Neg	Pos	Pos
T03	<32	258	>2048	100	8100	243000	Neg	Pos	Pos
T03	<32	538	>2048	100	8100	243000	Neg	Pos	Pos
T03	<32	160	>2048	100	24300	243000	Neg	Pos	Pos

* Qualitative only
Pos – positive; Neg - negative

Table 2. Feline Antibody Titers

Trt Group	SN Antibody Titer			ELISA Antibody Titer			LFA Assay*		
	Day 0	Day 21	Day 42	Day 0	Day 21	Day 42	Day 0	Day 21	Day 42
T01	<32	<32	<32	900	300	300	Neg	Neg	Neg
T01	<32	<32	<32	100	100	100	Neg	Neg	Neg
T01	<32	<32	<32	900	300	300	Neg	Neg	Neg
T01	<32	<32	<64	300	300	300	Neg	Neg	Neg
T01	<32	<32	<32	100	100	100	Neg	Neg	Neg
T02	<32	<32	>2048	300	24300	72900	Neg	Pos	Pos
T02	<32	<32	>2048	300	24300	72900	Neg	Pos	Pos
T02	<32	>2048	>2048	900	72900	72900	Neg	Pos	Pos
T02	<32	>2048	>2048	100	24300	72900	Neg	Pos	Pos
T02	<32	1371	>2048	300	24300	72900	Neg	Pos	Pos
T03	<32	558	>2048	900	8100	72900	Neg	Pos	Pos
T03	<32	>2048	>2048	300	24300	>218,700	Neg	Pos	Pos
T03	<32	361	>2048	300	24300	>218,700	Neg	Pos	Pos
T03	<32	550.5	>2048	300	8100	>218,700	Neg	Pos	Pos
T03	<32	>2048	>2048	300	8100	>218,700	Neg	Pos	Pos

* Qualitative only
Pos – positive; Neg - negative

CONCLUSIONS

The vaccines used in these studies were safe when administered to cats and dogs. They were efficacious in mounting an immune response as judged by the generation of serum neutralizing antibodies *in-vitro*.

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