May 2021

KOL Event

VAXART

UNLOCKING THE FULL POTENTIAL OF ORAL VACCINES

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Oral Vaccines Based on VAAST Platform

Selected Mucosal Adjuvant “Hard Wired” in Vector Delivery System

Non-replicating adenovirus with molecular adjuvant

ORAL VACCINES OFFERS IMPORTANT ADVANTAGES

- **Potentially disruptive impact across vaccine supply chain**
  - *Room temperature stable tablets*
  - *Ease of distribution*
- **Allows increased vaccination rates**
  - *Ease of administration*
  - *Patient acceptance*

INNOVATIVE PLATFORM FOR SYSTEMIC AND LOCAL IMMUNITY

- **Designed for wide range of recombinant antigens**
- **Local immunity is potential key differentiator**
  - *Protection at the mucosa of the gastrointestinal, respiratory tract*
  - *First line of Defense*

VAAST Oral Vaccines – Validated Platform In Humans

Approximately 500 Subjects Dosed to Date

Clinical Trials

Tablet Vaccines

Purpose:

- Safety
- Immunogenicity
- Dose ranging
- Efficacy

	Flu	RSV	Norovirus	COVID-19
SUBJECTS DOSED	245	46	171	35
SAFETY				
Favorable safety and tolerability profile				
EFFICACY				
Reduction in influenza illness comparable with the leading marketed quadrivalent intramuscular influenza vaccine				
BROAD IMMUNE RESPONSES				
Serum neutralizing antibodies (IgG), Systemic T cell responses				
MUCOSAL HOMING CELLS				
T cells, IgA positive B cells				

Liebowitz, et al, *Lancet ID*, 2020
Kim, et al, *JCI Insights*, 2018
Kim, et al, *Sci Reports*, 2016

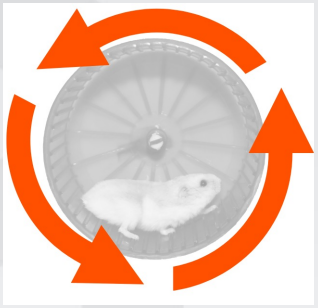
Vaxart – COVID Vaccine Issues

- Covid-19 is a significant health problem. Vaccines can be highly effective against the original parental strain

- Several limitations for roll-out of a needle solution during a pandemic
  - Need a qualified health care provider to administer
  - The first vaccines approved need to be kept frozen
  - We are all supposed to sequester and avoid contact
  - *All of this make the process of creating long-term herd immunity challenging*
- New coronavirus variants are appearing that may be able to circumvent vaccine induced immunity
  - Vaccine manufacturers have announced that they are making strain matched vaccines to address the potential variants
  - Can a cross-reactive vaccine be made to allow for better protection against future variants?

An Important Step is the time for injecting large populations: Vaxart Takes Away the Needles

Rapid Emergence of new SARS-CoV-2 strains



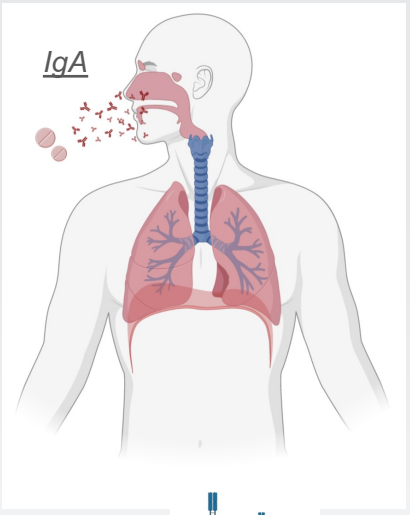
Vaccine Development

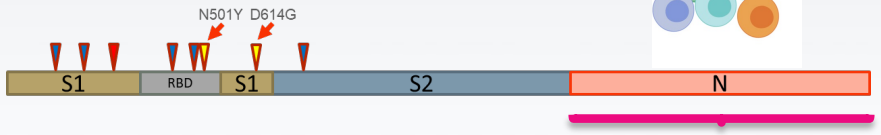
Rapid Distribution & Administration

Get Off The Wheel –
Shorten the Time to Herd Immunity

Vaxart's solution

- Room temperature stable tablet, easy to produce, distribute, and administer





- More conserved across strains
- Strong target for T cells

Dutta, et al, JV, 2020

VXA-COV2-101 Phase 1 Study Design and Schema

- Single Dose, Oral Tablet Study at Low and Medium Doses
- Small Sentinel Cohort that was boosted
- **Primary (Safety) and Secondary (Immunogenicity) Endpoints Met**

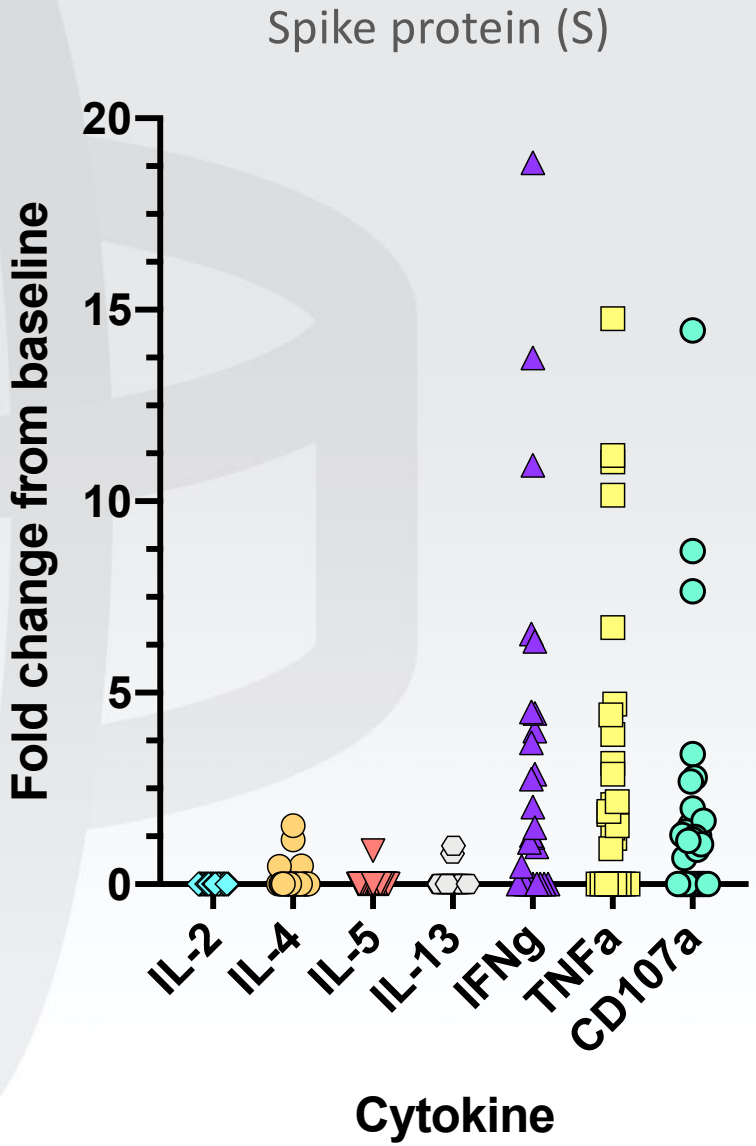
Treatment Group	Vaccine	Dose (±0.5 log)	No. of Doses	No. of Subjects
Cohort 1 (Sentinels)	VXA-CoV2-1	$1x10^{10}$ I.U.	2	5
	SMC Review of Safety Data through Day 8 Visit			
Cohort 2	VXA-CoV2-1	$1x10^{10}$ I.U.	1	15
Cohort 3	VXA-CoV2-1	$5x10^{10}$ I.U.	1	15
			Total	35

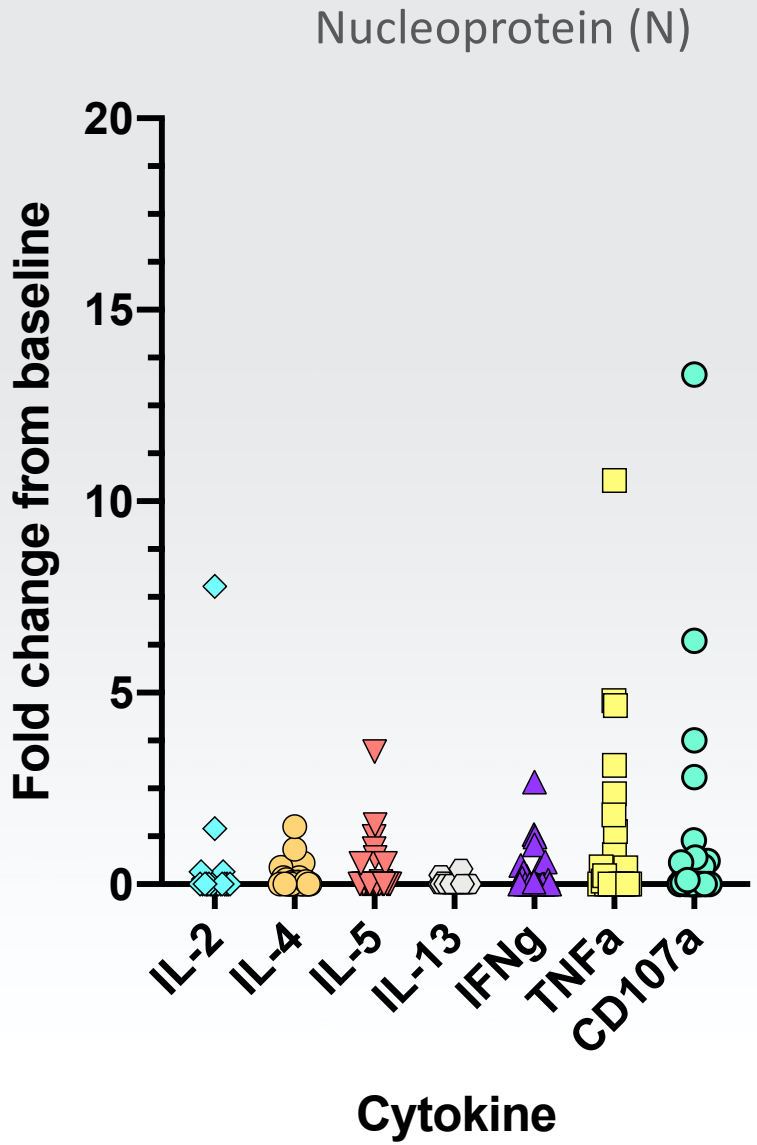
Solicited Symptoms Post Vaccination – Phase I

Solicited Symptom Days (1 – 8)	Low Dose (n=20)	High Dose (n=15)
No. (%) with Solicited Symptoms	4 (20)	10 (66.7)
Gastrointestinal Symptoms		
Diarrhea	0 (00)	4 (26.7)
Nausea	0 (00)	5 (33.3)
Vomiting	0 (00)	0
Abdominal Pain	1 (5.0)	2 (13.3)
General Symptoms		
Malaise/Fatigue	2 (10)	2 (13.3)
Myalgia (Muscle Pain)	1 (5.0)	1 (6.7)
Anorexia	0 (00)	2 (13.3)
Headache	3 (15)	2 (13.3)
Fever	0 (00)	1 (6.7)

- Most Solicited Adverse Events mild and transient; few moderates @ Days 2 to 6
- 6 Mild unsolicited AEs: sore throat, epistaxis, chills, dry sinus, back pain & testicular pain
- No SAEs or MAAEs reported to date

Vaxart's oral vaccine candidate shows preferential Th1 responses, inducing a strong CD8 cytotoxic response

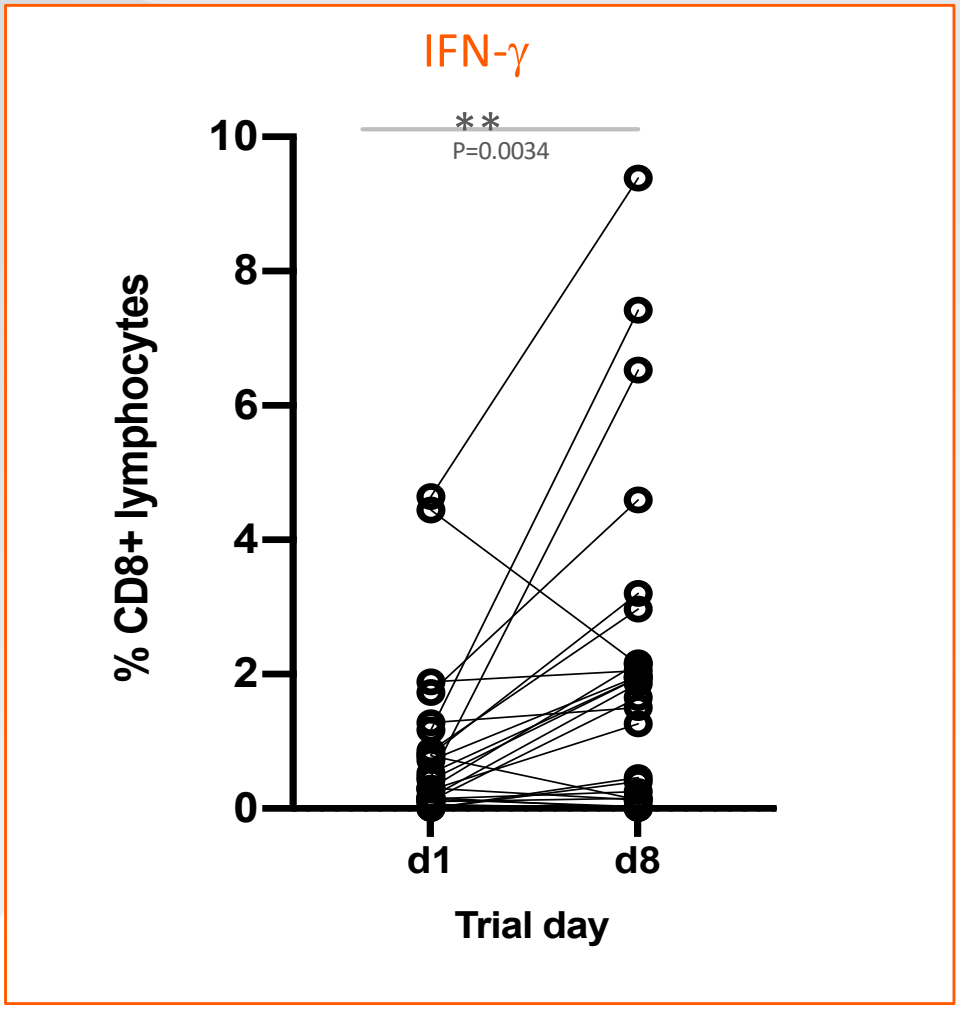


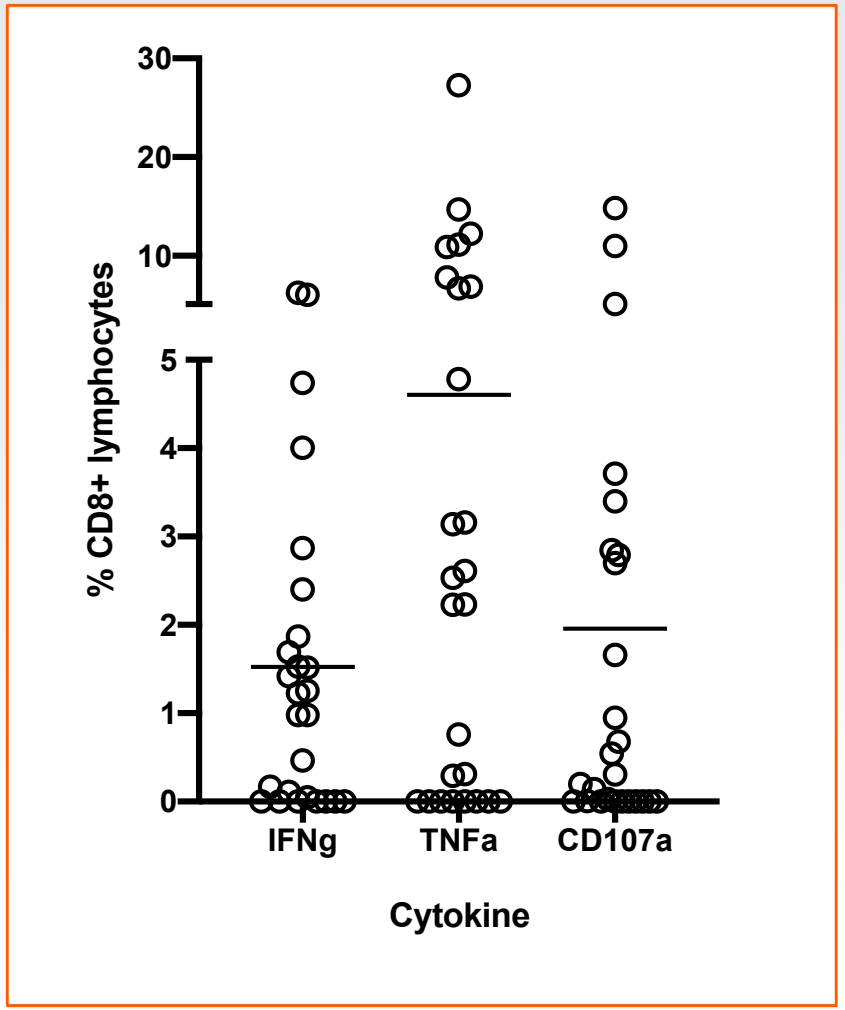


Restimulation with S or N peptide pools on PBMCs from pre and post vaccination. Th2 cytokines are CD4+ T cells, Th1 cytokines are CD8+ T cells. Fold change is calculated over the pre-vaccination sample.

Vaxart's Oral Vaccine candidate generates robust CD8 T cell responses

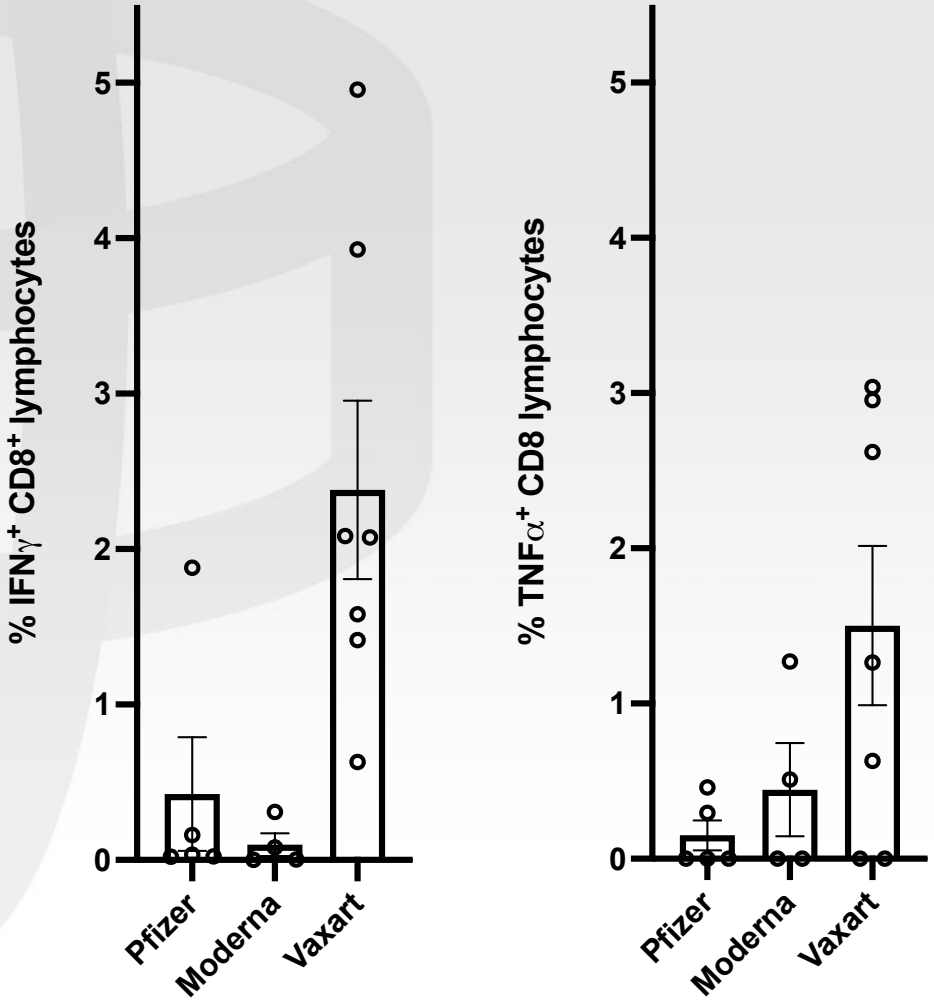
Vaxart's Oral Vaccine candidate generates high numbers of S specific IFN-γ, TNFα and CD107a producing T cells post immunization.





Vaxart's Oral Vaccine candidate generates robust CD8 T cell responses – Compares favorably to the mRNA vaccines

Induction of T cells responses measured 7 days after the first dose. Increase over day 1 for IFN-γ and TNFα are shown

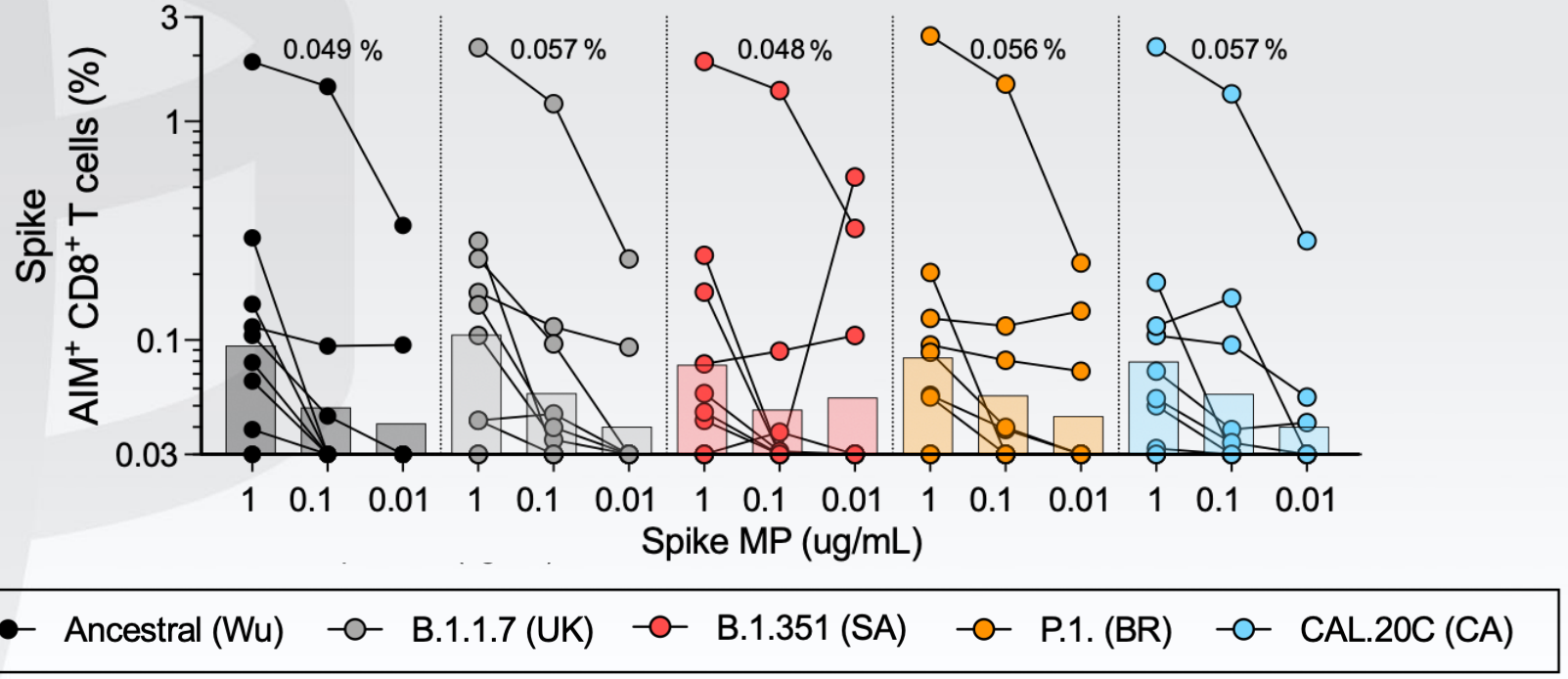


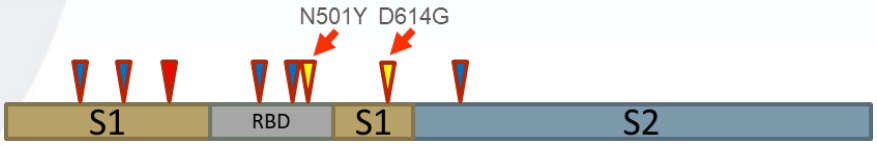
Frozen PBMC samples from Vaxart's Phase I trial were compared to PBMCs from volunteers that were immunized with the Pfizer or Moderna vaccines under EUA. Analysis was done at the same time points post immunization

Preliminary data

Do Vaccine Induced T cells Cross React Against other huCoV?

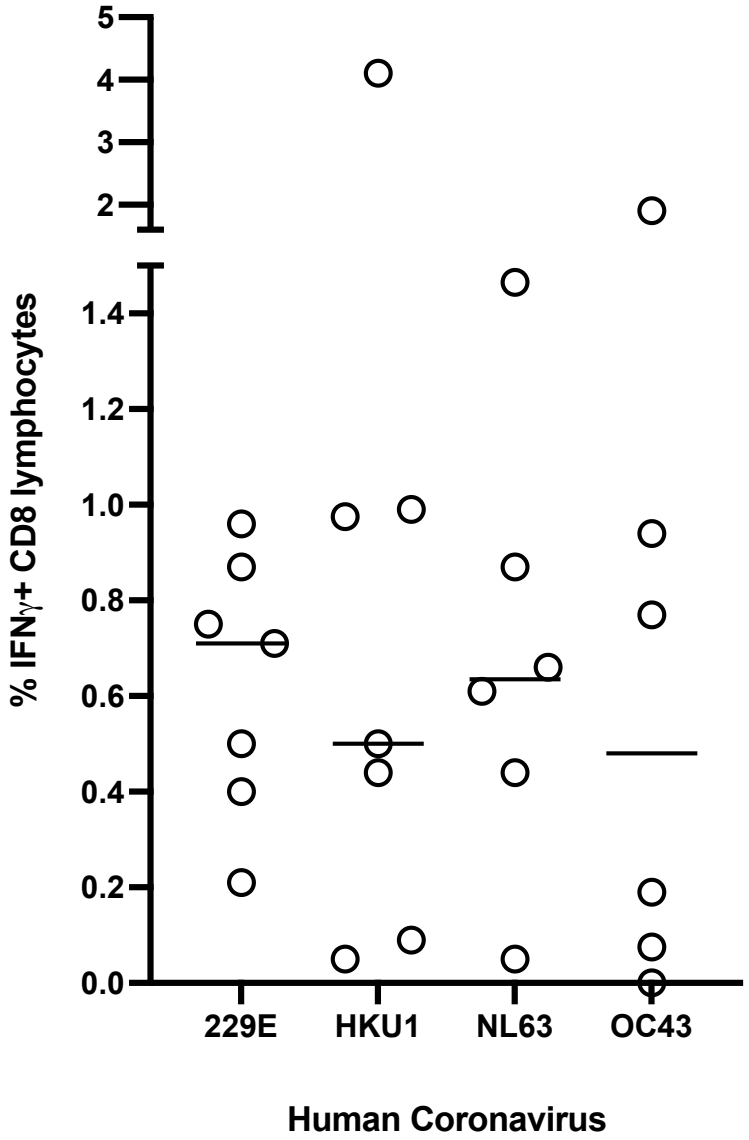
- Tarke, et al, (Biorxiv 2021) showed that mRNA vaccines create cross-reactive T cells against other SARS-CoV-2 variants of concern (see below)
- What about other Coronaviruses?





B.1.351 (South African S protein)

Future Proof: Vaxart's oral vaccine candidate generates cross reactive T cells to other endemic coronaviruses



% Identity compared to SARS-CoV-2

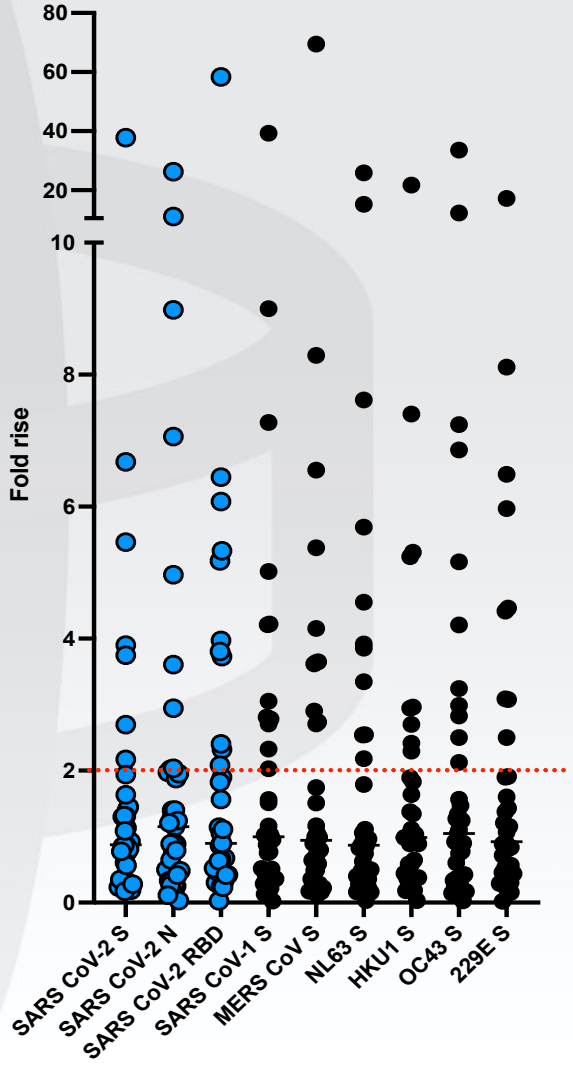
Virus	Genus	% identity
229E	alpha	65
NL63	alpha	65
HKU1	beta	68
OC43	beta	68
SARS-CoV	beta	82

Response is combined to both S & N peptides. Increase measured after subtracting background at day 0

Why T cells may be important for COVID

- Cross-protective and long-lasting
  - N protein responses to SARS-CoV-1 last 17 years after infection and cross-react to SARS-CoV-2 (Hellerstein, et al, Vaccine, 2020)
- People with agammaglobulinemia don't die of COVID and have a mild course of infection (Quinti, et al, J Allergy Clin Immunol, 2020)
- Mucosal T cells may be capable of blocking shedding and transmission
- Higher T cell responses correlated to protection against COVID disease in in prospective study of first responders (Wylie, et al, Medrxiv, 2020)
- Broader antigenic repertoire than antibody responses - T cell responses recognize at least 30-40 epitopes in each donor, as measured in 99 subjects. (Tarke, Cell Reports Medicine, Jan 21)

Vaxart immunized subjects have increased cross-reactive nasal IgA response to other coronaviruses



Increased IgA antibodies to SARS-Cov-2 also leads to increased antibody responses to the S protein of other coronaviruses including SARS-CoV-1, MERS, and endemic common cold viruses

Preliminary Data

Graph shows increase in nasal IgA at d29 over d1 sample, normalized for amounts of total IgA

Vaxart – Next Steps

- Dose ranging study to start around mid-year
- Phase II efficacy study later this year
- Evaluating new strain matched candidates in research
  - Made S only versions of the “California” and “South African” strains
  - Can our original vaccine approach provide protection as effectively as a strain-matched vaccine in animal models?

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