Oral Tablet Vaccination to SARS-CoV-2 Induces Long Lasting Cross-reactive Mucosal Antibody Responses in Humans

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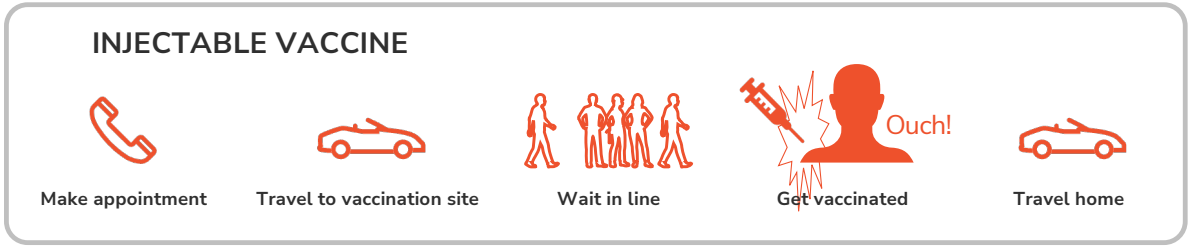
Room Temperature Oral Vaccine

Easy to Distribute – Easy to Take



VS

IgA is very potent molecule in the fight against infectious disease

Inhibition of transmission and viral shedding via mucosal IgA

- Reduced viral shedding by oral immunization in a human challenge study [1]
- Breast Milk IgA blocks norovirus diarrheal decrease in infants [2]
- **Transmission blocking: Mucosal-vaccinated hamsters protect naïve hamsters from infection and disease** [3]
- Mucosal IgA induction leads to reduced shedding of delta, omicron variants in hamster challenge studies

Generation of cross-reactive antibody responses in the mucosa

- Oral vaccination induces cross reactive nasal IgA against variants of concern and endemic coronaviruses in humans [4]
- Mucosal vaccination: cross-protection against beta, delta, and omicron variants in hamster models

1 Liebowitz, et al, *Lancet ID*, 2020

2 Labayo, et al, EClinMed, 2020

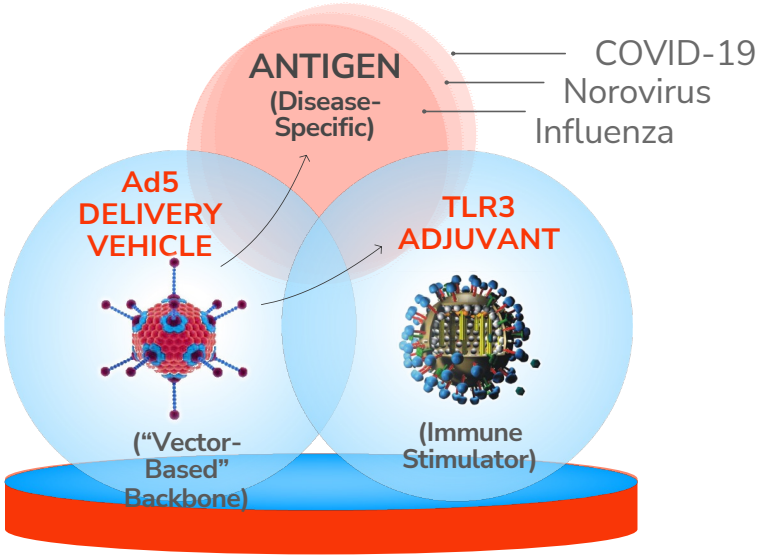
3 Langel, et al, *Sci Transl Med*, 2022

4 Tucker, et al, *World Vaccine Congress*, 2022

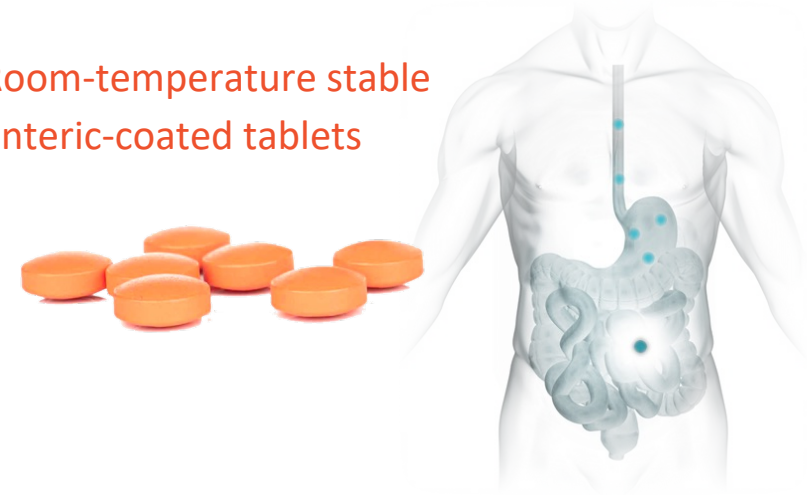
Vaxart Solution: Intestinal Delivery + Targeted Immune Activation: Non-replicating vector with molecular adjuvant

Key Issues to solve:

1. Replicating oral vaccines don't work well in the developing world
2. Protein delivered to the intestine is treated like food



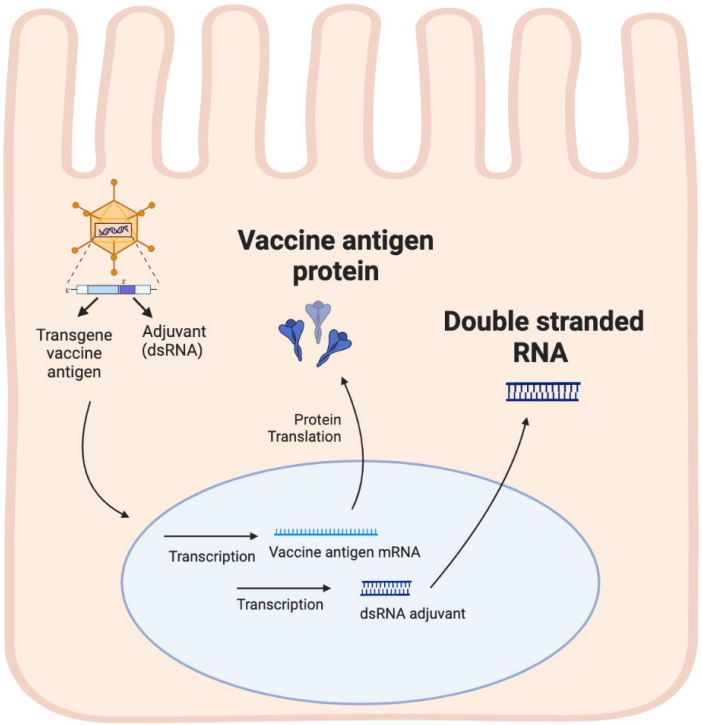
Room-temperature stable enteric-coated tablets



VAAST™: Vector-Adjuvant-Antigen Standardized Technology

Expression of protein antigen in exactly the same cell as the dsRNA (immune activator) creates a highly specific immune response

Epithelial cell expressing antigen and dsRNA



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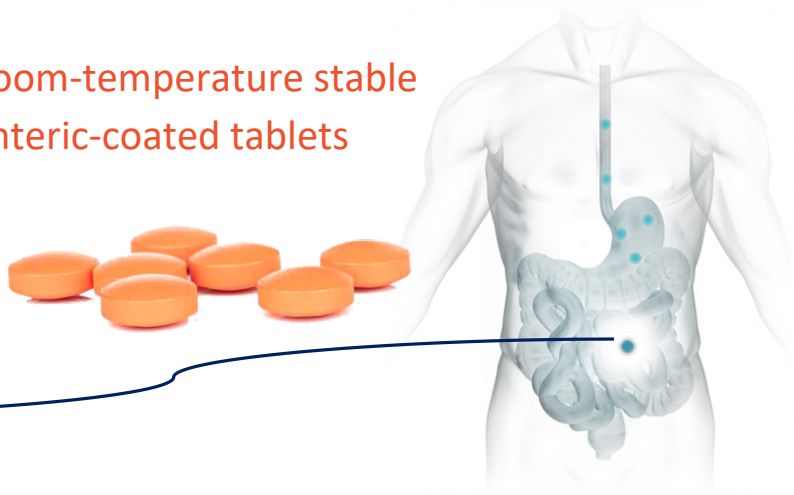


Oral Tablet Difference: cross-reactive and potent mucosal immune and systemic responses

Rapid Emergence of New SARS-CoV-2 Strains

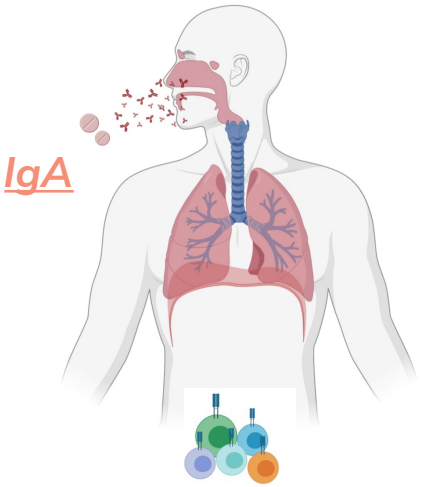
Distribution & Administration

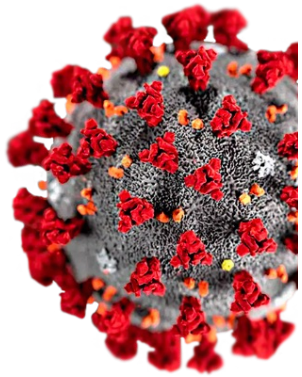
Vaccine Development

We are currently chasing the virus with vaccines like a hamster on a wheel

Oral Tablet is different

- Cross-reactive immune responses
- Tablets rather than injections





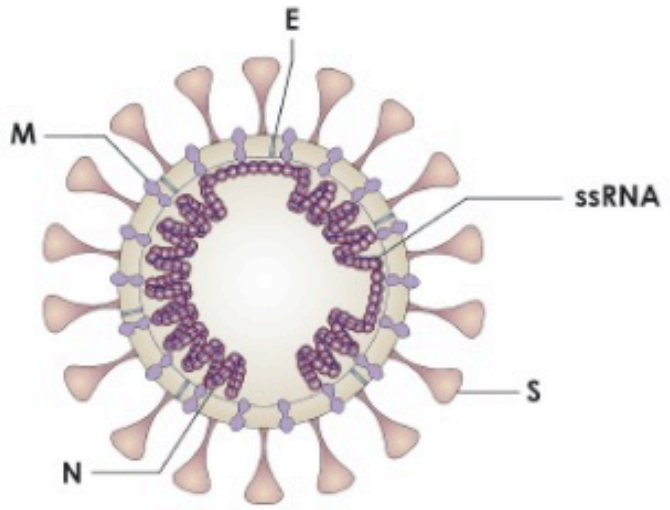
Vaxart Has Two Clinical COVID-19 Vaccine Candidates

VXA-CoV2-1.1-S (Expresses only S):
phase II study ongoing

- Goal is to improve the antibody responses

VXA-CoV2-1 (Expresses S+ N):
completed phase I

- Complete



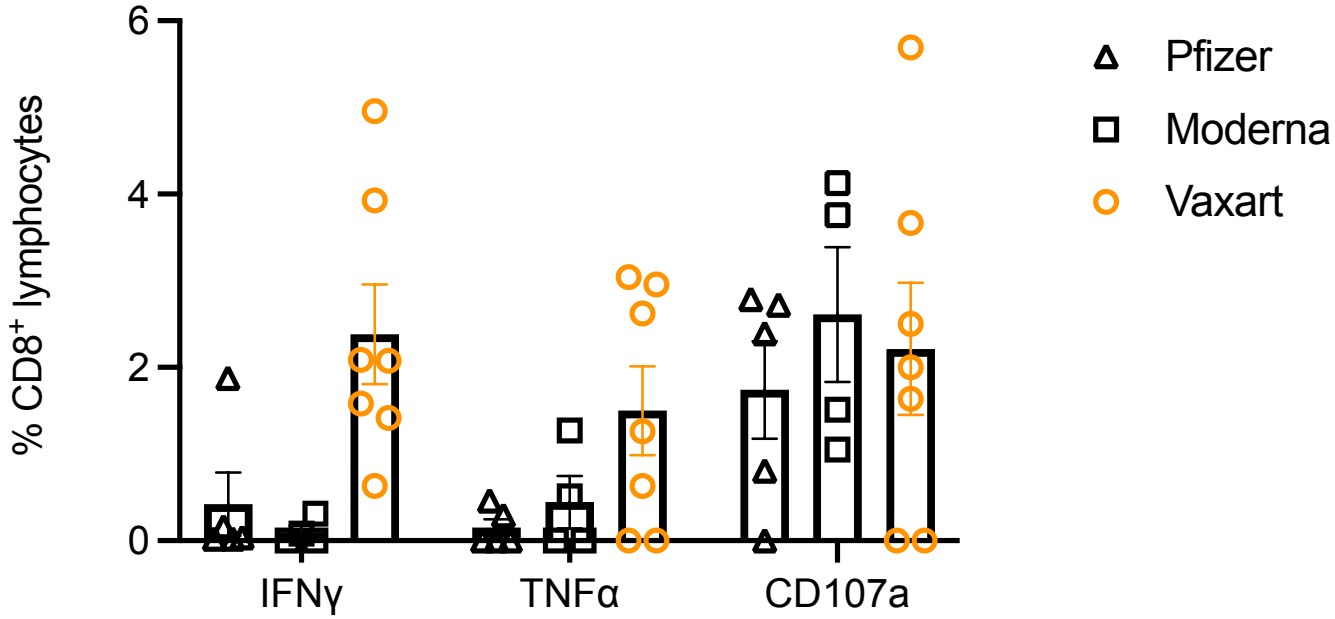
VXA-Cov2-1 Human Results

Phase I study results – rAd-S+N construct

- Small study (N=35, most subjects only given one immunization)
  - Well tolerated
  - Very robust, cross-reactive T cell response
  - Little serum IgG in the serum
  - IgA responses in the serum, saliva, and nasal against SARS-Cov-2 S protein

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

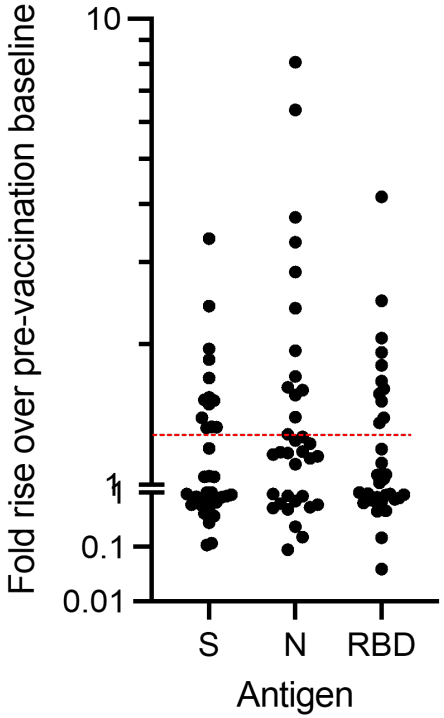
Induction of T cells responses measured 7 days after the first dose. Increase over day 1 for IFN-γ, TNFα and CD107a are shown

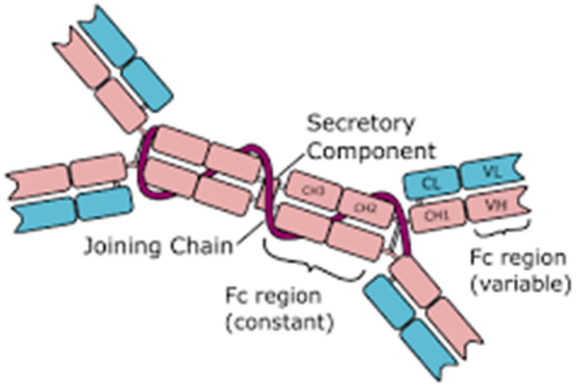


Pfizer, Moderna n=5, Vaxart n=7

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

VXA-COV2-1 (ED84) elicits a rise in secretory IgA



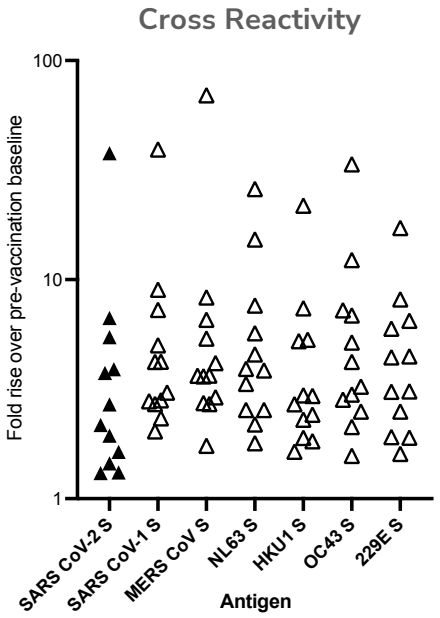


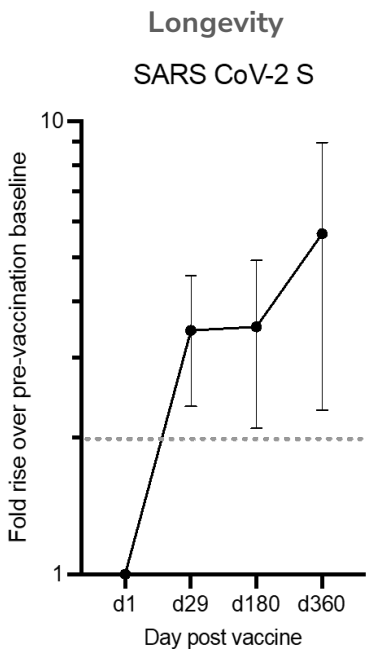
Secretory IgA has been shown to be superior over monomeric IgA at neutralizing in SARS-CoV-2 studies

VXA-CoV2-1 Induces Cross reactive and Long-Lasting Nasal IgA

Nasal IgA responses ***highly cross reactive against all coronaviruses***

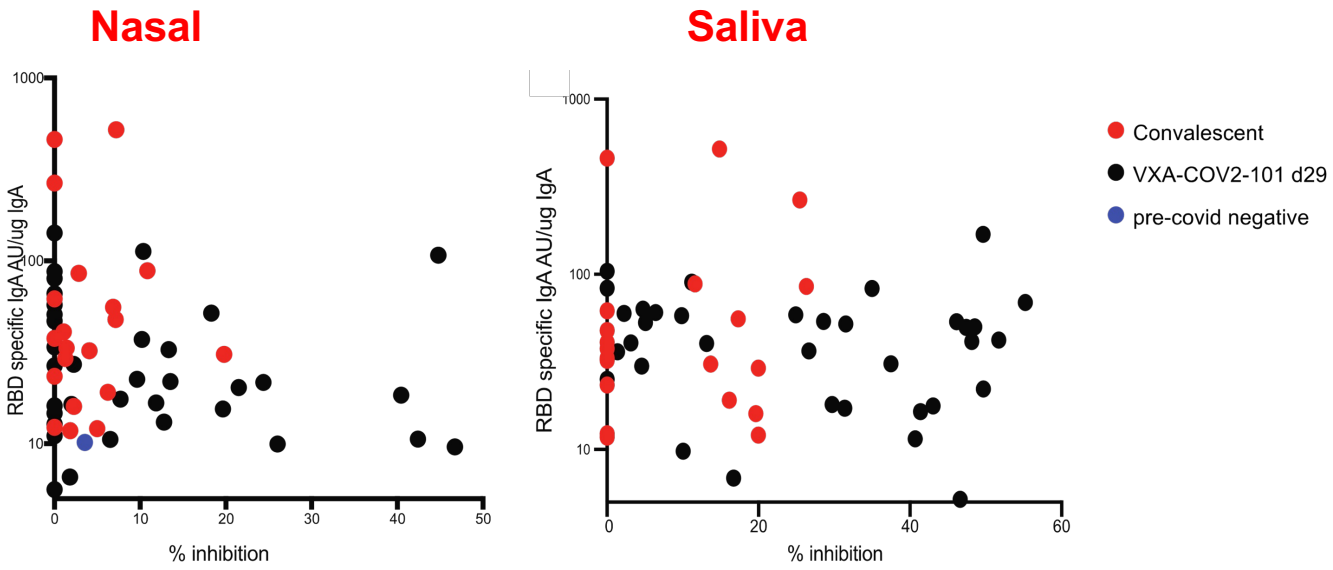
- 46% of subjects had a 1.5 fold increase or better against SARS-CoV2-S which also induced increased antibody responses to every Coronavirus tested





Langel, et al, *Sci Translational Med*, 2022

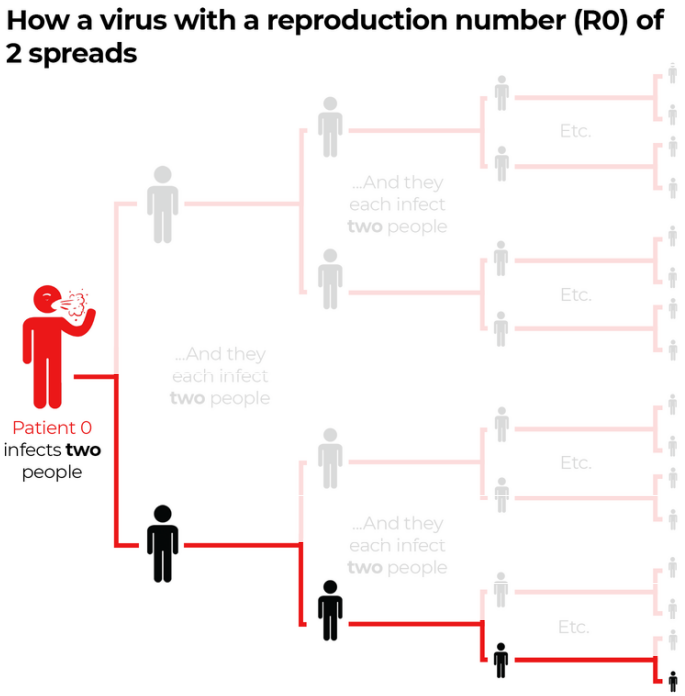
VXA-COV2-1 elicits IgA of a higher neutralizing ability than natural infection



nAb measured by sVNT assay

Johnson, et al, Medrxiv, 2022

A reduction in transmission may significantly impact pandemic control



theConversation.com

Estimated R0 values for SARS-CoV-2 Variants Worldwide

Delta	**6 < R0 < 7**
Omicron	**9.6 < R0 < 14.61**

Liu, et al. *Journal of Travel Medicine,* 2022

Can mucosal vaccination with Vaxart's oral tablet lower the R0 to less than 2?

Mucosal vaccination (rAd-S wuhan) protects hamsters from illness by SARS-CoV-2 And Reduces the Area Under the Curve (shedding vs time)

Vaccine: rAd5-S (S only)

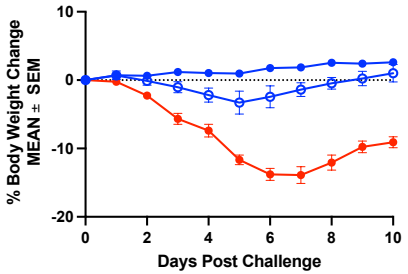
Vaccination

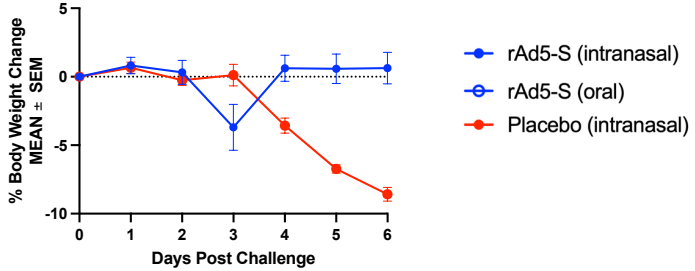
Challenge

Challenge: delta virus

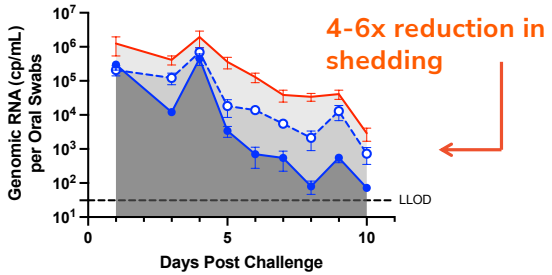
Challenge: omicron virus

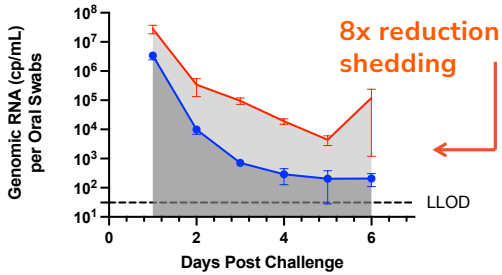
Weight Loss





Shedding





Vaccination elicited high levels of mucosal IgA and serum IgG in addition to protecting from disease

IgA can functionally block transmission

Generating a targeted immune response in the mucosa could reduce global disease

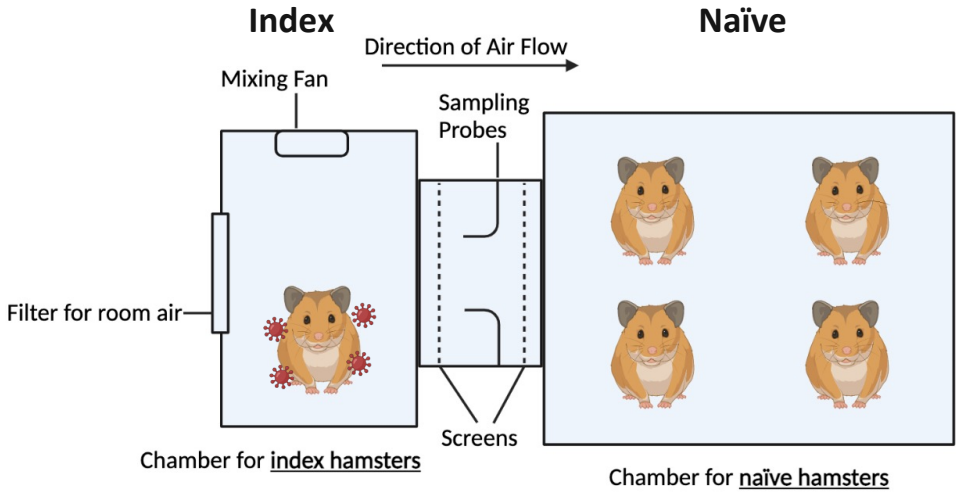
- Norovirus specific breast IgA milk can inhibit diarrhea disease in infants
  - Labayo, et al, EClinMed, 2020
- Studies with guinea pigs given IgA could be protected from transmission when in contact with infected animals
  - Seibert, et al, J. Virology, 2013
- We wanted to see if mucosal responses could block transmission in the other direction
  - Could a nasal mucosal response inhibit transmission to uninfected animals in a vaccine breakthrough – aerosol transmission model

Transmission study: Model vaccine breakthrough to naïve subjects

- Goal: Evaluate whether mucosal vaccination blocks transmission and shedding better than an injected vaccine for aerosolized viruses
- Method: Vaccinate animals, give high dose of SARS-CoV-2 (create vaccine breakthrough), expose to vaccine naïve animals for 8 hours

Index animals vaccination groups:

- Vaxart Oral rAd-S
- Vaxart Intranasal rAd-S
- Intramuscular S protein
- Placebo (Oral)



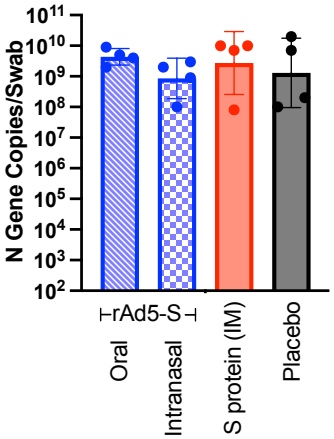
Transmission Blocking: Viral and disease burden is decreased in **naïve** animals exposed to mucosally vaccinated animals with breakthrough infections

Index Animals
Vaccine Breakthrough

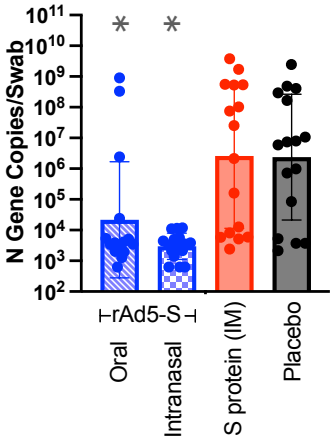
Aerosol exposure (8 hrs)

Naïve Animals
Unvaccinated

Day 1 post infection

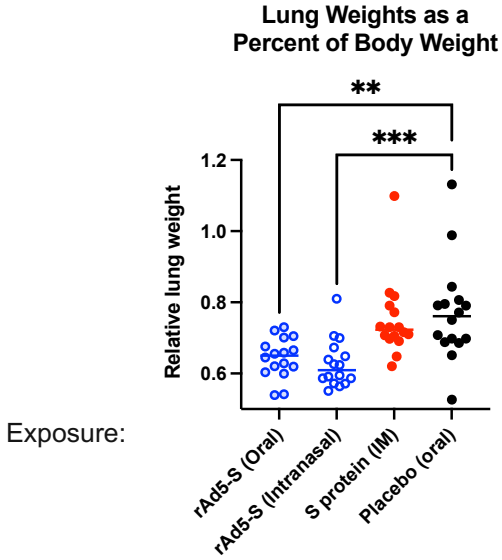


Day 1 post exposure



*** P <0.012 by Fishers' Exact**

Naïve Animals
protected from illness 5 days after exposure

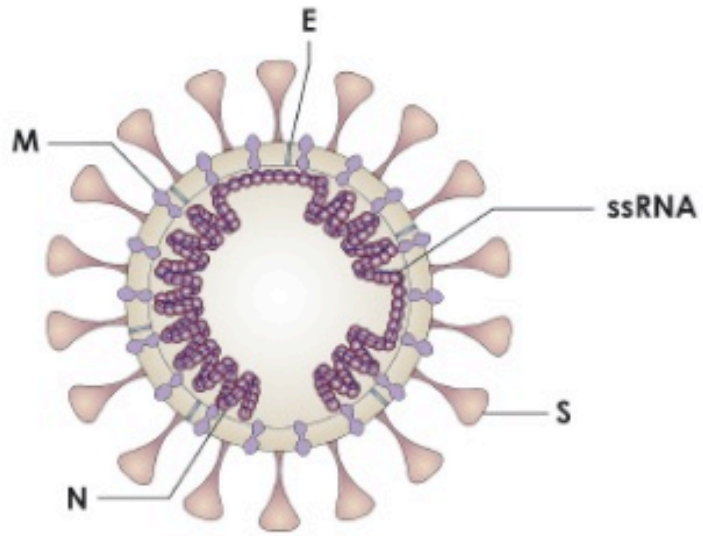


Langel et al, *Sci Translational Med* , 2022

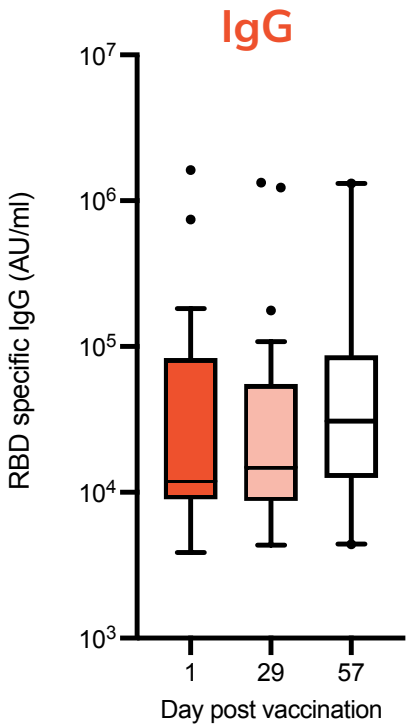
COVID-19: Vaccine Candidate VXA-CoV2-1.1-S

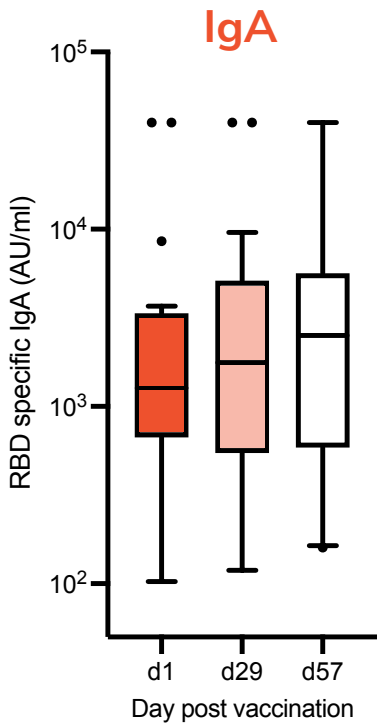
VXA-CoV2-1.1-S (Expresses only S): Completed Part 1 of Phase II

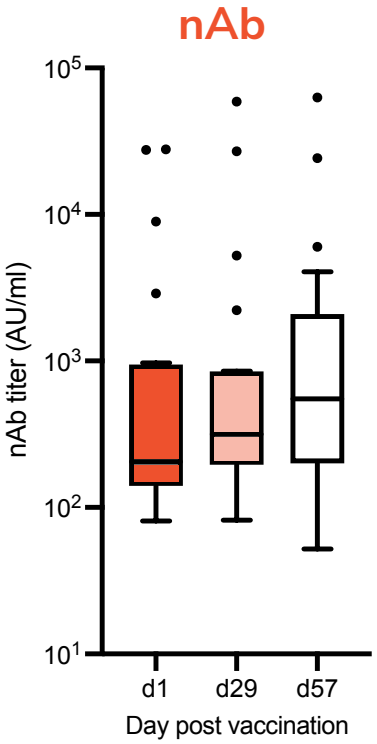
- Well Tolerated
- Better serum responses than S+N
- Ability to boost mRNA vaccines
- Makes cross reactive mucosal IgA



VXA-CoV2-1.1- S Boosts Serum & Neutralizing Responses in Vaccinated Individuals





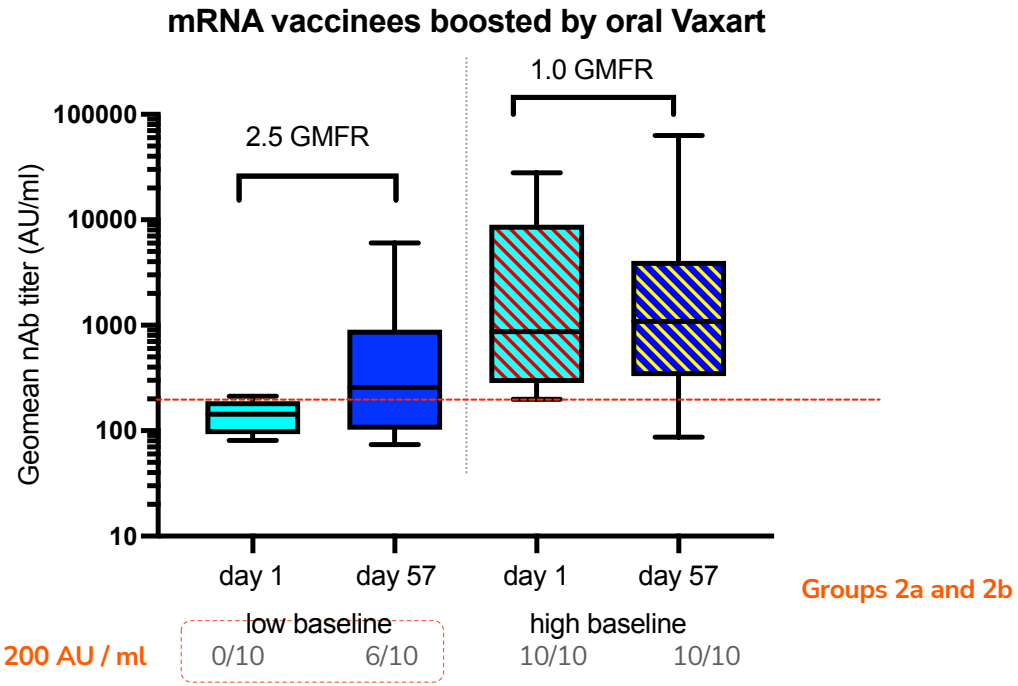


From those mRNA vaccinated, 18-55 cohorts

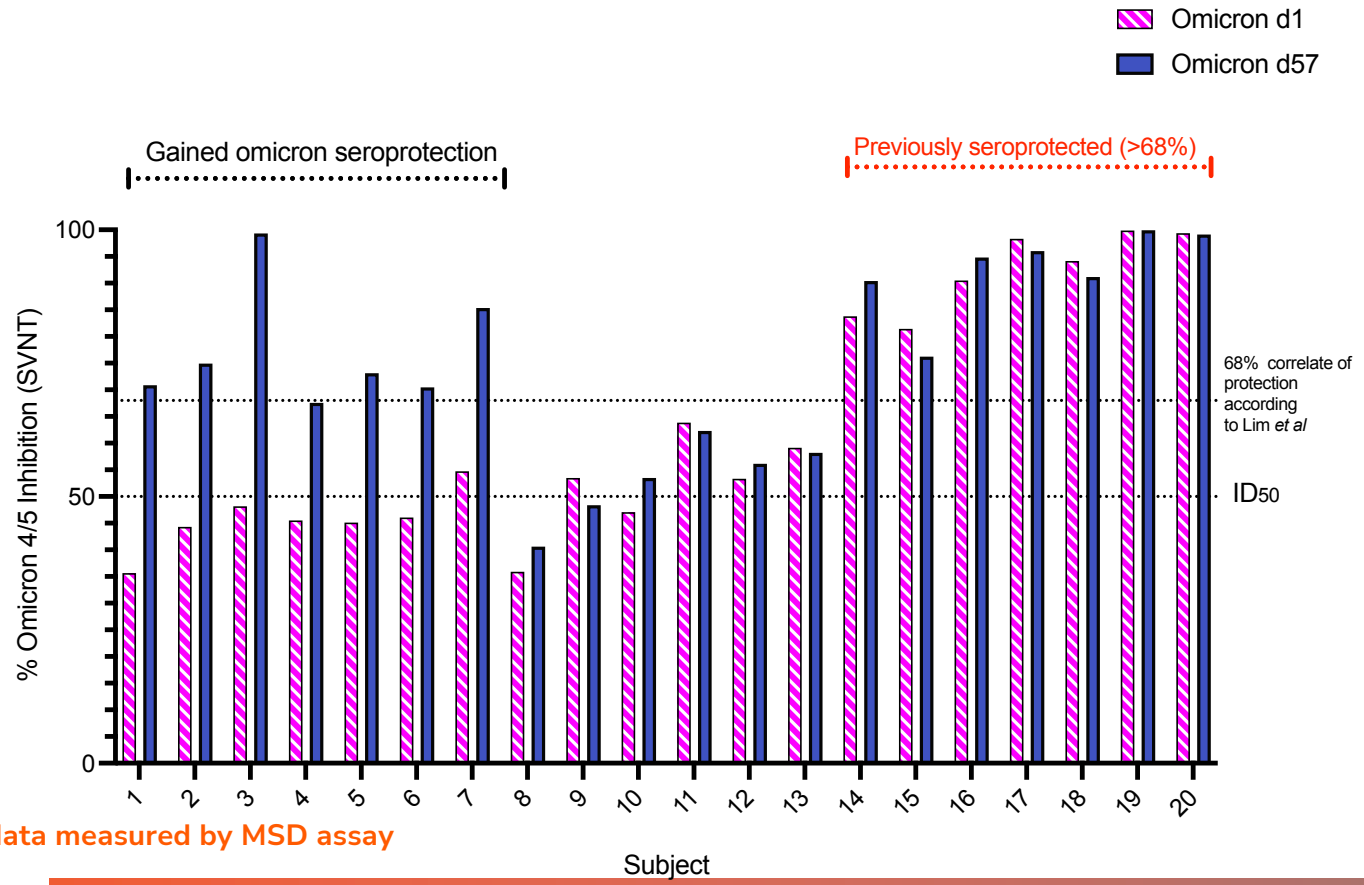
preliminary

VXA-CoV2-1.1-S Boosts mRNA Vaccines by increasing more the responses of subjects with lower baseline titers

Subjects with nAb titers ≥ 200 AU / ml increased from 50% at Day 1 to 80% at Day 57



Wuhan no longer circulating, but Vaxart's oral Wuhan vaccine increased "seroprotection" against Omicron 4/5

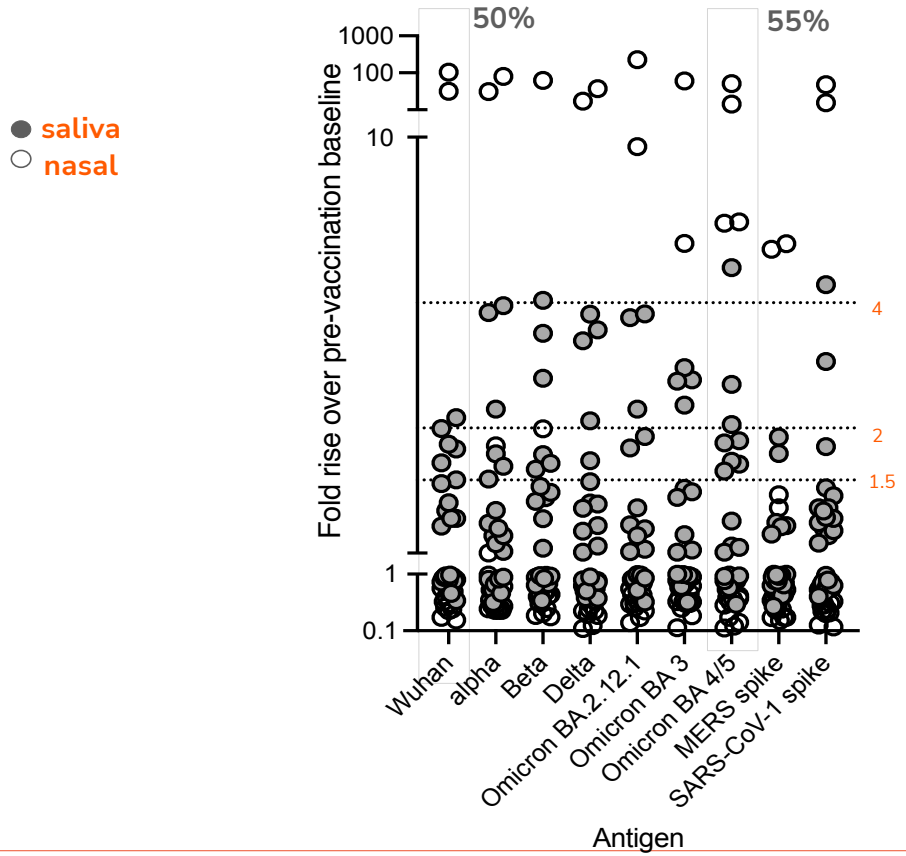


35% of subjects were "seroprotected" against Omicron 4/5 pre-vaccination, 70% post oral vaccination

sVNT data measured by MSD assay

Groups 2a and 2b

Mucosal responses in vaccinated individuals are cross-reactive to other SARS-CoV-2 variants AND other coronaviruses



- 50% of subjects had a mucosal response to wuhan
- 55% of subjects had a mucosal response to Omicron BA4/5

All responders to Wuhan had a response to omicron

Vaccinated 18-54
cohorts 2a & 2b

Preliminary data

Summary

- IgA can be potent in the prevention in infection and transmission, not readily elicited by mRNA vaccines
- First clinical trial with the vaccine expressing S and N proteins
  - Well-tolerated
  - Highly immunogenic on eliciting T cells. CD8 T-cell responses to the S protein are higher than those of injectable mRNA vaccines
  - Long lived IgA to SARS-CoV-2 induced in the nose and saliva
  - T cell and IgA were cross-reactivity to other coronaviruses observed, including to diverse endemic coronaviruses
- Second clinical trial with the vaccine expressing the S protein
  - Well-tolerated
  - Able to boost mRNA vaccines and induce increased nAb responses in the serum, both to wuhan and to the more recent BA4/5 variant
  - Induced cross-reactive IgA in the nose and saliva

Our vaccine platform induces mucosal IgA in humans, which we believe could have a substantial impact on pathogen transmission and global health

Acknowledgements and Thanks

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