Oral Tablet Vaccination to SARS-CoV-2 Induces Pan-coronavirus Nasal IgA Responses in Humans

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Vaxart

Society of Mucosal Immunology

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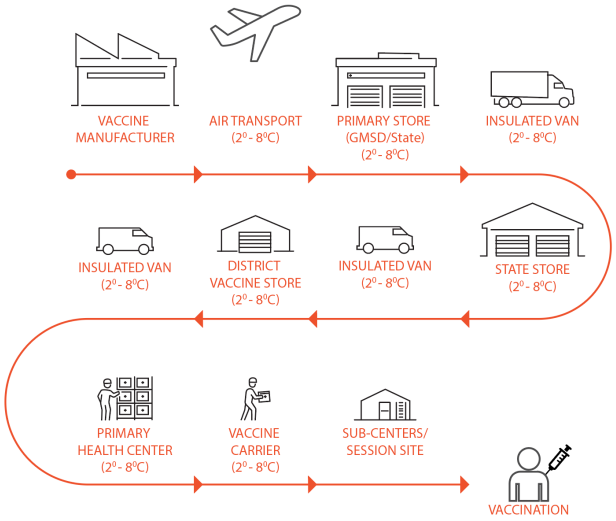
Goal: Develop a simple vaccine format that can have a significant impact on global vaccine protection and transmission

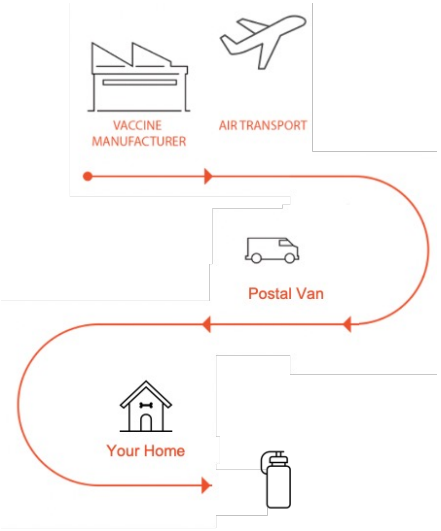


Vaccine as a pill

Ease of distribution and storage

Potentially more protective than injectable vaccines

Convenient mode of administration, rapid and painless



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

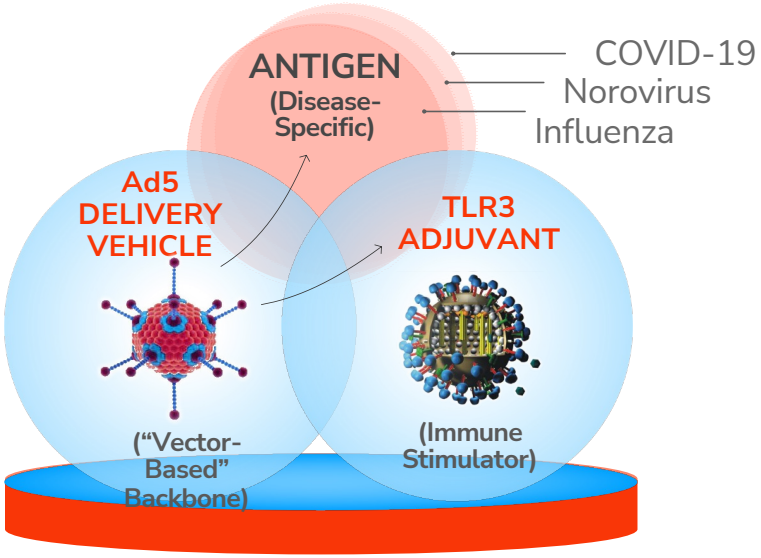
3 Langel, et al, *Sci Transl Med*, 2022

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

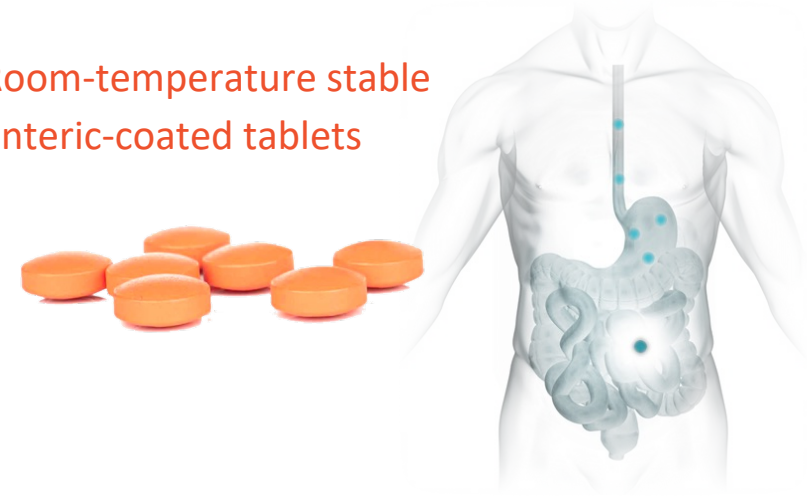
Vaxart Solution: Intestinal Delivery + Targeted Immune Activation: Non-replicating vector with molecular adjuvant

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



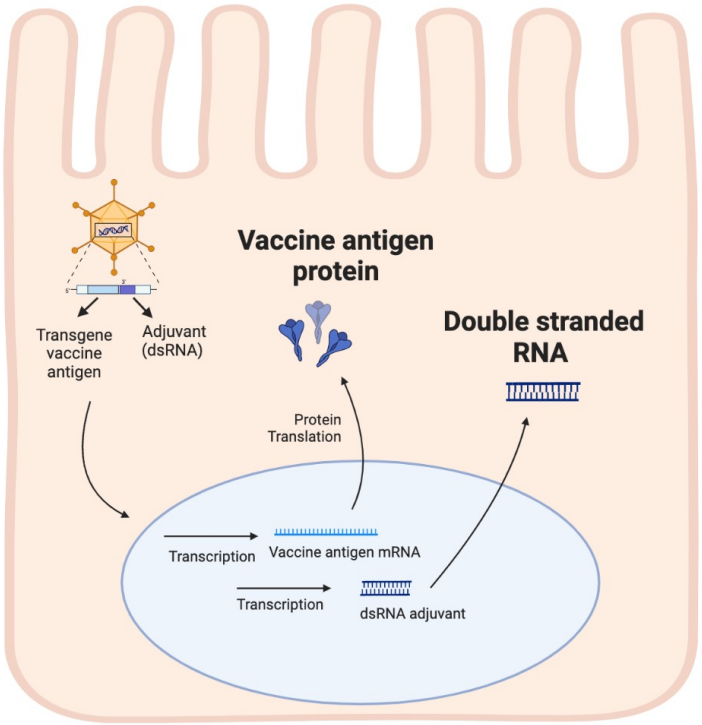
Room-temperature stable enteric-coated tablets



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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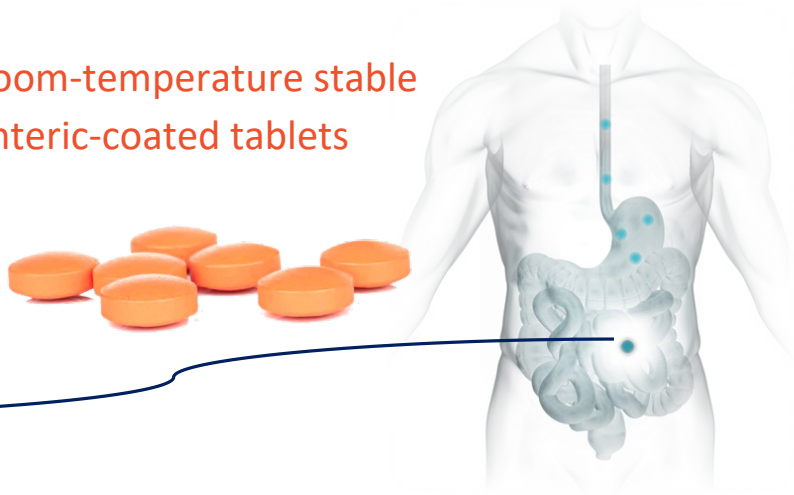


Oral Tablet Difference: cross-reactive and potent mucosal immune and systemic responses

Rapid Emergence of New SARS-CoV-2 Strains

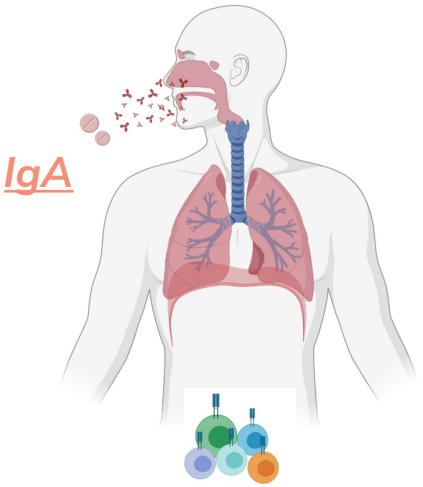
Distribution & Administration

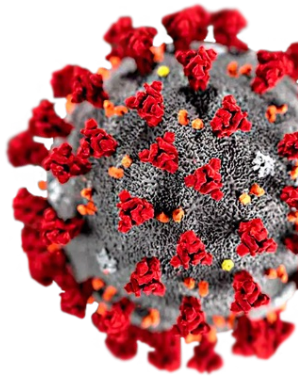
Vaccine Development

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





Human Influenza Challenge Study: Challenge after 90 days

- **A single dose administration of one of the following:**
  - Arm 1: VXA-A1.1 oral vaccine + placebo IM injection (n=60+extra)
  - Arm 2: QIV injection + oral placebo tablet (n=60+extra)
  - Arm 3: Placebo IM injection + oral placebo tablet (n=30+extra)
- **Subjects with baseline HAI titers ≤10**
- **Challenge post randomization after Day 90 (up to 120 days)**
  - A wild-type influenza A/Ca/2009/pH1N1 strain will be administered to subjects in all treatment groups
  - Virus was propagated on eggs, 3 passages, before use as a challenge virus
- **Primary endpoint**
  - Number and % of subjects protected against A/CA/2009/pH1N1 challenge by VXA-A1.1 compared to QIV and placebo

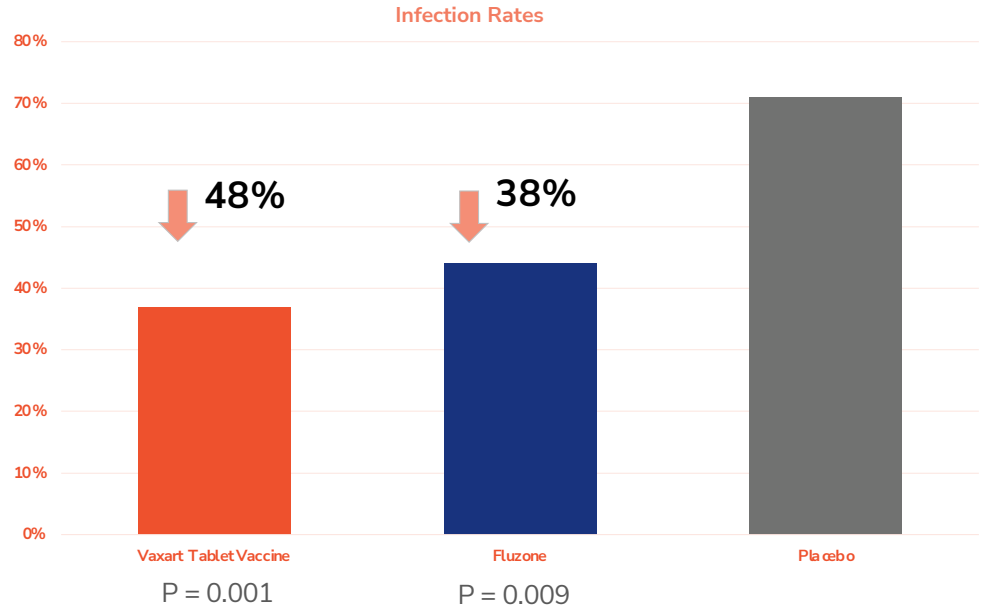
Liebowitz, et al, *Lancet ID*, 2020

Demonstration of Efficacy – Respiratory Virus Challenge in Humans

Oral Vaccine Candidate protected against influenza infection as well as market leading injected vaccine after influenza challenge

- Both vaccines protected against illness and infection
- Oral Vaccine had a different correlate of protection
  - Mucosal homing, antigen specific IgA B cells were found to be most important for protection
  - Very few were needed to get same level of protection as **very high serum neutralizing antibody** levels.

Reduced Infection Rates Trending Superior to Fluzone

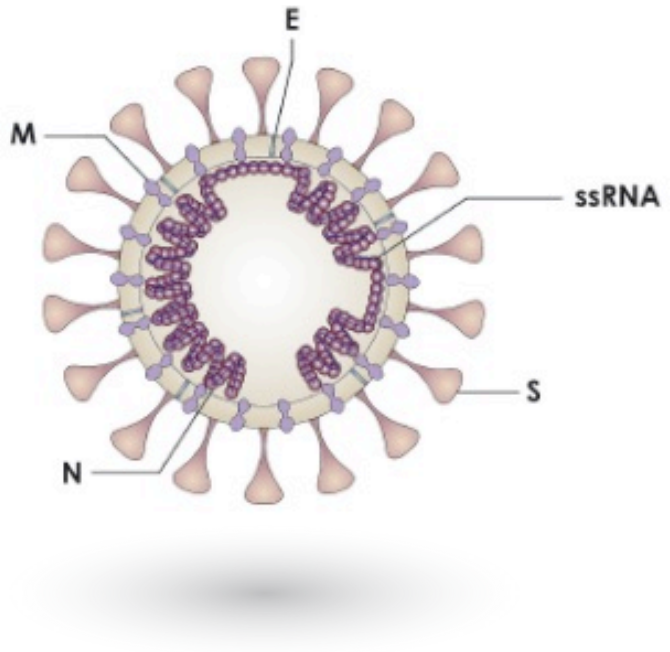


Liebowitz, et al, *Lancet ID*, 2020

Vaxart Has Two Clinical COVID-19 Vaccine Candidates

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

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



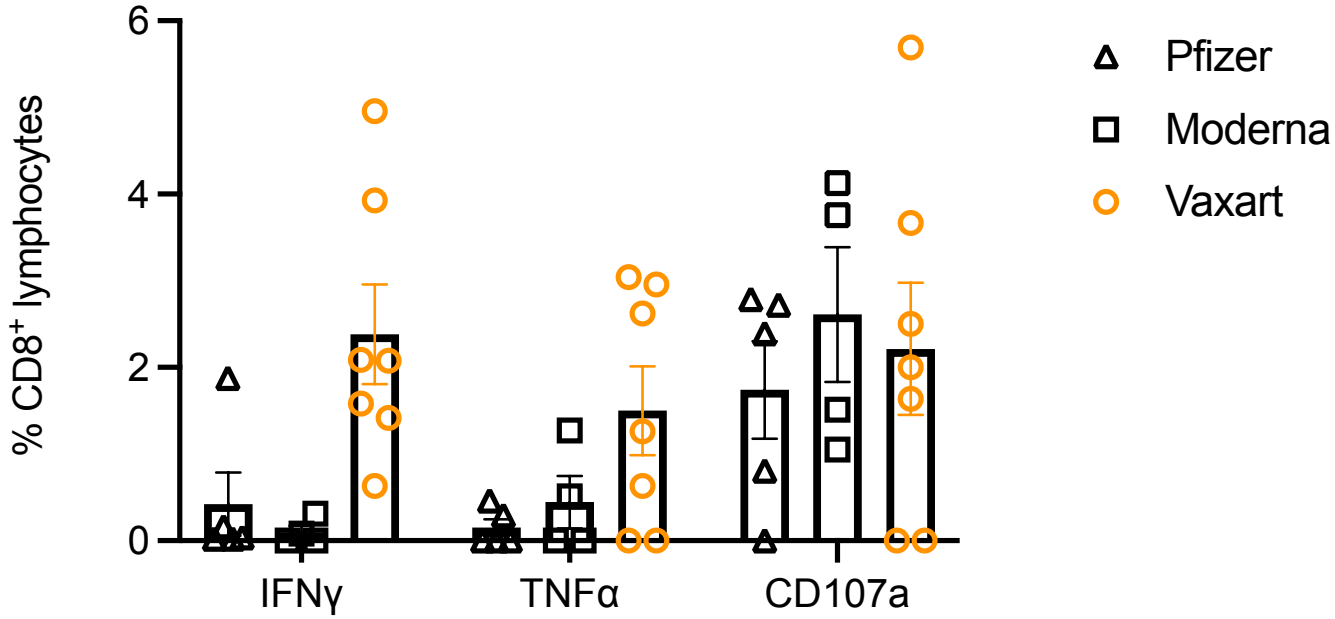
VXA-Cov2-1 Human Results

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
  - 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



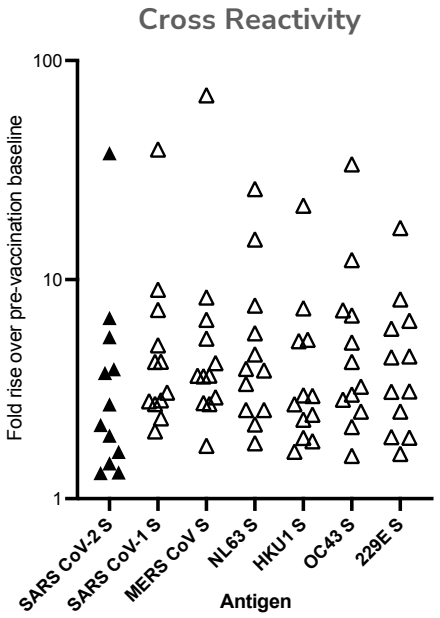
Pfizer, Moderna n=5, Vaxart n=7

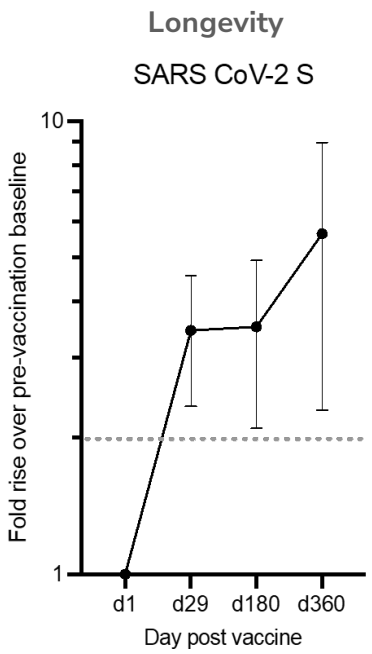
Frozen PBMC samples from Vaxart's Phase I trial were compared to PBMCs from volunteers that were immunized with the Pfizer or Moderna vaccines under EUA. Analysis was done at the same time points post immunization

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

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

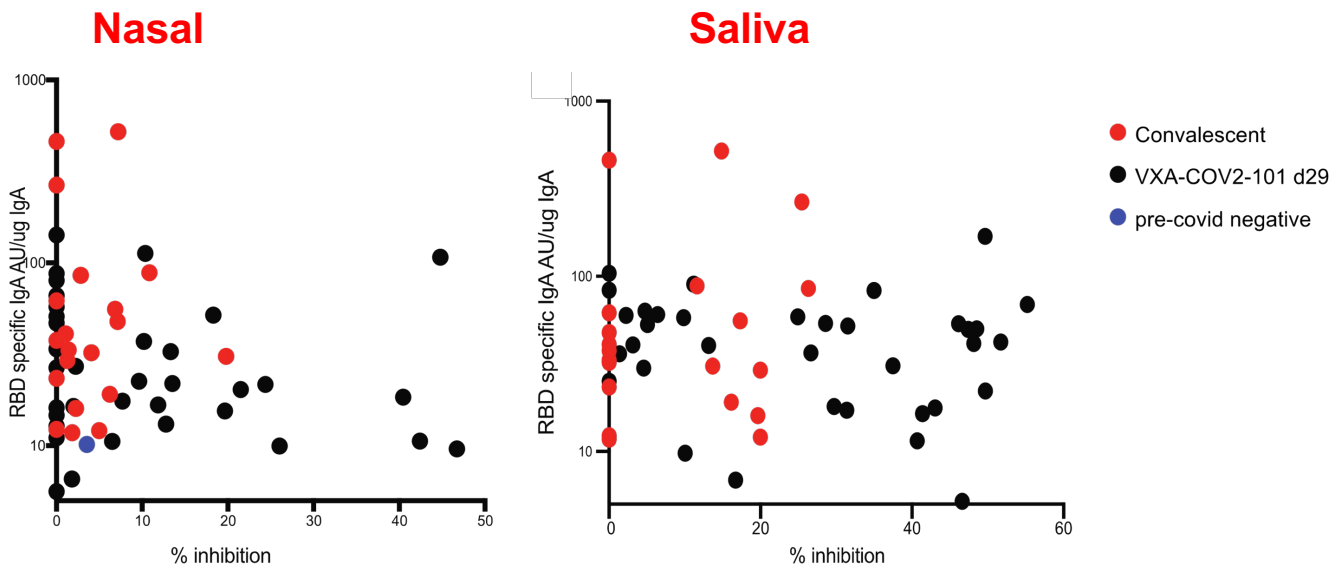
- 46% of subjects had a 1.5 fold increase or better against SARS-CoV2-S which also induced increased antibody responses to every Coronavirus tested





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, Biorxiv, 2022

Summary

- Vaxart oral tablet platform created a protective responses against a respiratory pathogen, with significant improvement against viral shedding following challenge compared to an injected vaccine
- SARS-CoV-2 indication - testing two different candidates
- First clinical trial with the vaccine expressing S and N proteins
  - 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 serum, nasal, and saliva
  - T cell and IgA were cross-reactivity to other coronaviruses observed, including to diverse endemic coronaviruses
- Currently evaluating a candidate in studies +/- mRNA vaccine priming

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

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Backup slides