



**A Phase 2 Double-Blind, Placebo-Controlled Study Showing
Oral Tableted Norovirus Vaccine VXA-G1.1-NN is
Immunogenic, Efficacious, and Reduces Viral Shedding
Following Norovirus Challenge**

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CONFIDENTIAL

Disclosure

- Dr. Tucker is an employee of Vaxart, a vaccine company

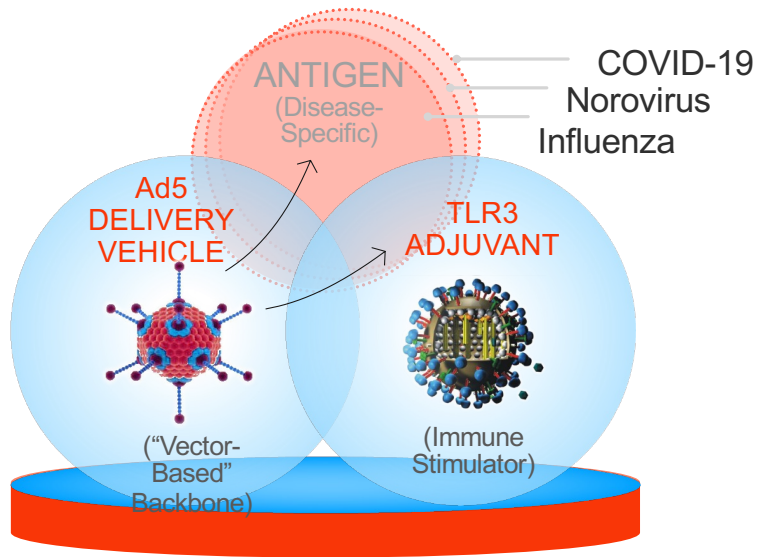
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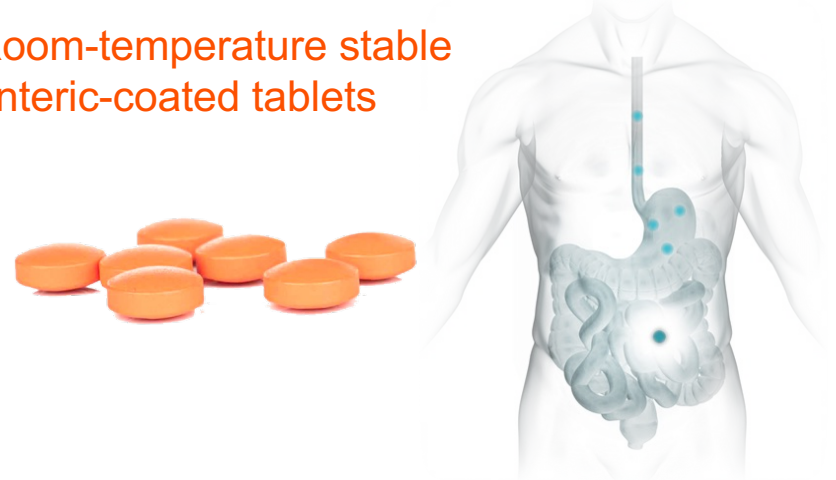
Vaxart Solution: Intestinal Delivery + Targeted Immune Activation: Non-replicating vector with molecular adjuvant

Key Issues solved by approach:

1. Adjuvant –creates immune responses to antigen choice
2. Doesn't create anti-vector immunity like injected vectors



Room-temperature stable enteric-coated tablets



VAAST™: Vector-Adjuvant-Antigen Standardized Technology

Norovirus: \$10 billion+ economic burden that presents a significant threat to children and seniors

Norovirus is a recognized U.S. public health priority

- Highly contagious – causes acute gastroenteritis leading to diarrhea, vomiting, stomach pain
- Leading cause of foodborne illness in the U.S.¹
- Priority for CDC and other public health thought leaders

Economic burden of disease concentrated in two groups

15%

of children under 5 catch norovirus annually²



3,000,000

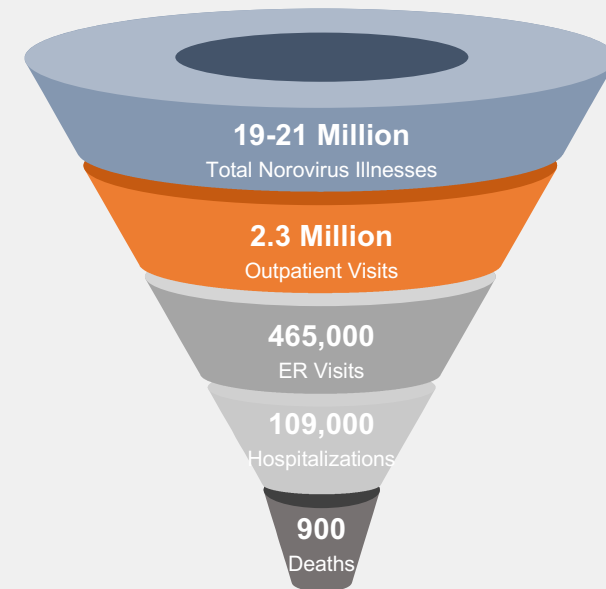
sets of parents need to take time from work to care for these children

7.5%

of age 65+ get sick, most hospitalizations in this group²

\$10.6 billion

U.S. economic burden



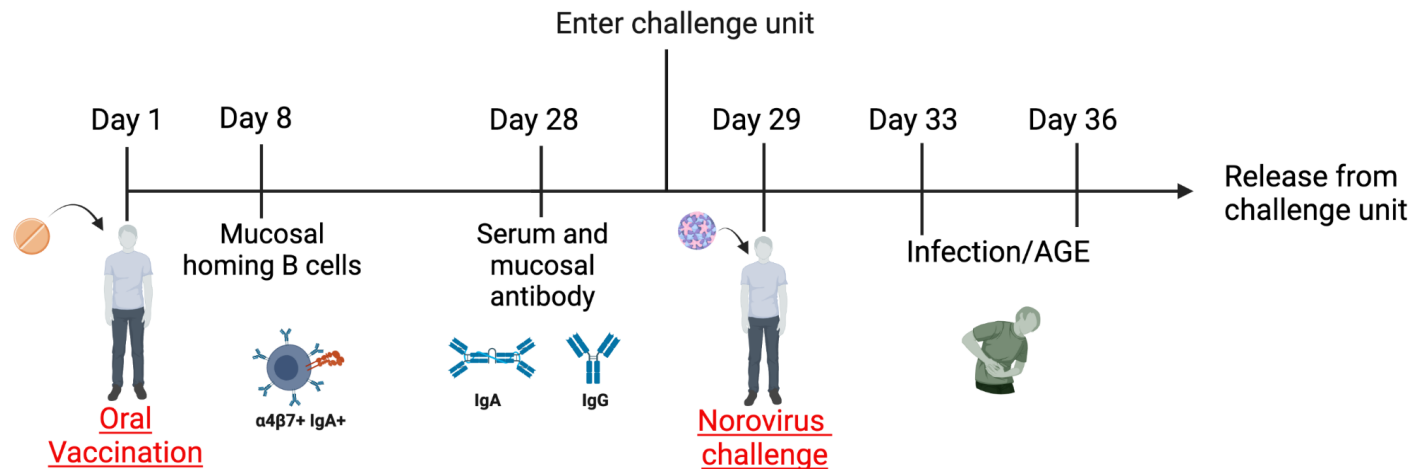
Source: 1) CDC Norovirus Illness: Key Facts & Figures; 2) Incidence of Norovirus and Other Viral Pathogens That Cause Acute Gastroenteritis (AGE) among Kaiser Permanente Member Populations in the United States, 2012–2013, Grytdal et al, PLOS 1, 2016

Source: CDC website (<https://www.cdc.gov/norovirus/burden.html>)

VXA-NVV-201: Norovirus GI.1 Challenge Study

Phase 2 double-blinded placebo controlled study

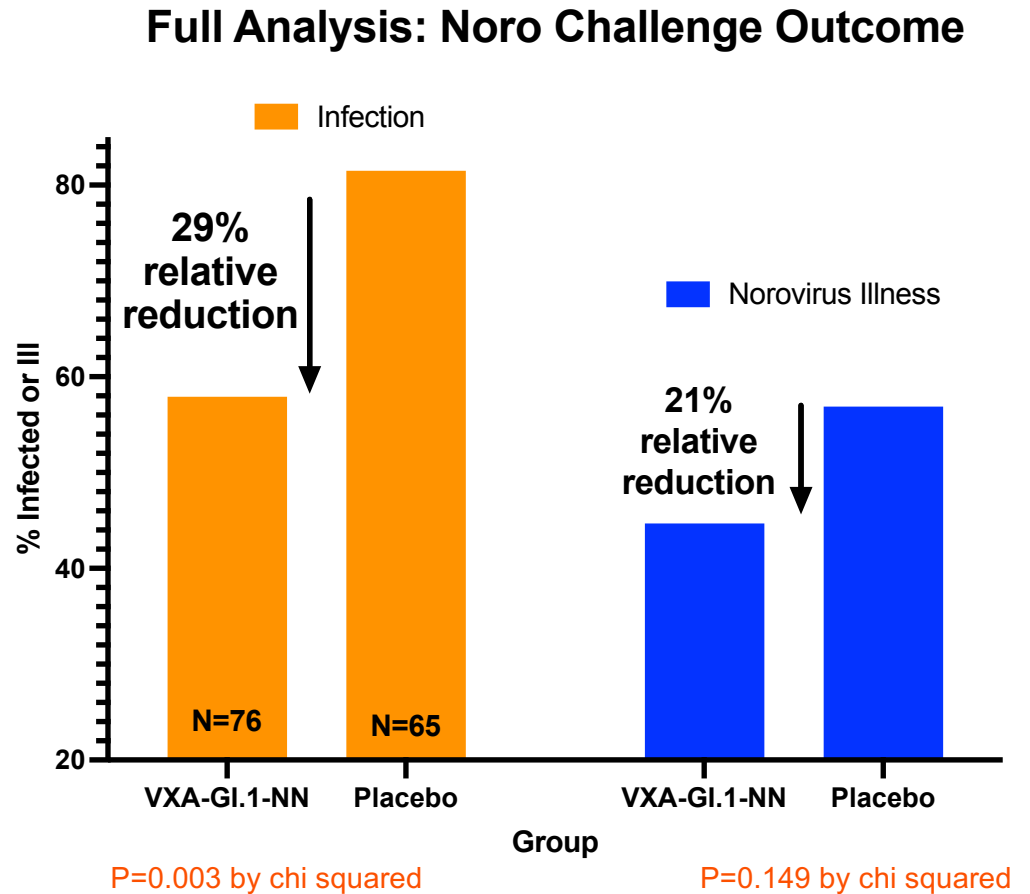
- GI.1 vaccine candidate or placebo, given to healthy subjects
- Given norovirus infection 29+ days after vaccination
- Determine infection and illness rates (AGE) in placebo and vaccinated subjects
- Measure immune parameters; determine which ones are important at predicting protection



Norovirus Challenge Study : Clinical Outcomes

Protection Against Infection and Illness by vaccination

- Primary Endpoint met for infection (P=0.003)
- Primary Endpoint not met (P=0.149) for Norovirus Illness

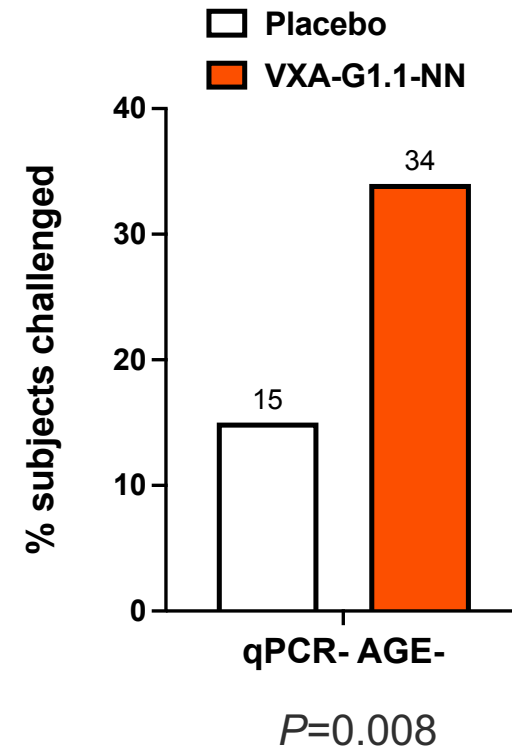


More VXA-G1.1-NN Vaccinated Subjects had no AGE or qPCR+ compared to Placebo

Odds Ratio for Vaccine Protection: 2.3

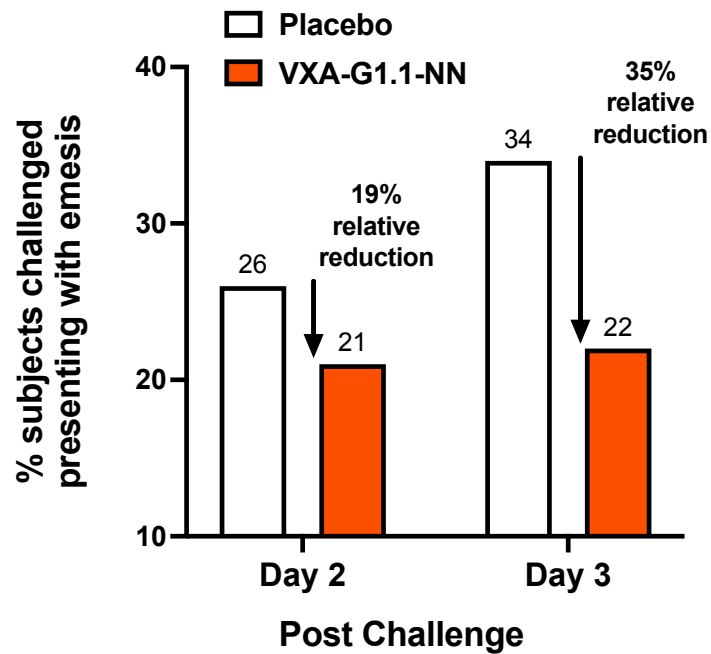
	number of subjects	#qPCR negative no AGE	% qPCR negative no AGE
placebo	65	10	15%
VXA-G1.1-NN	76	26	34%

Less symptomatic illness observed after VXA-G1.1-NN vaccination

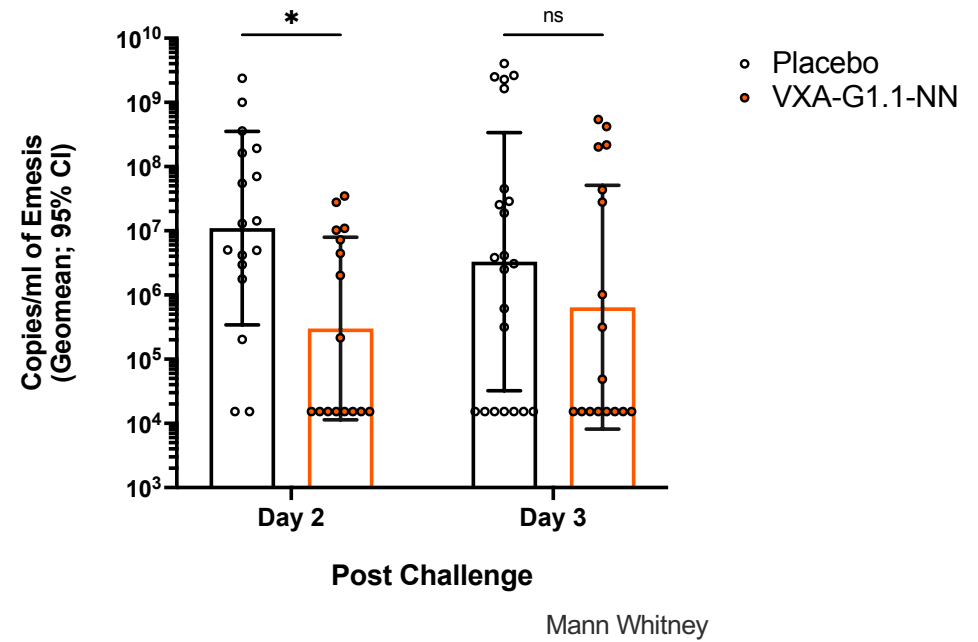


VXA-G1.1-NN Vaccination Reduce Emesis Frequency and Shedding

Incidence of Emesis



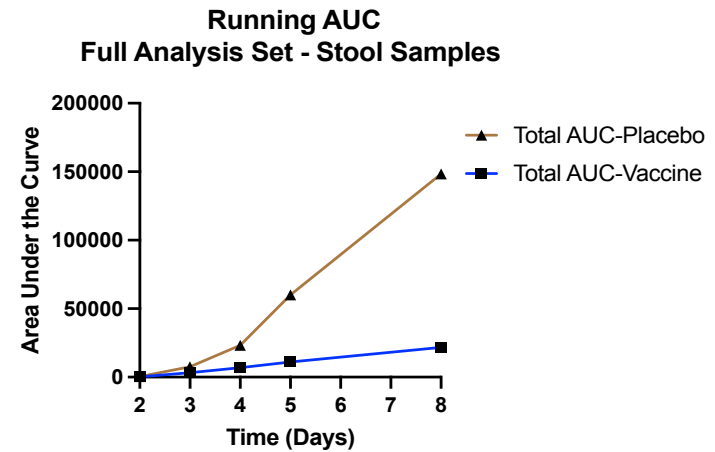
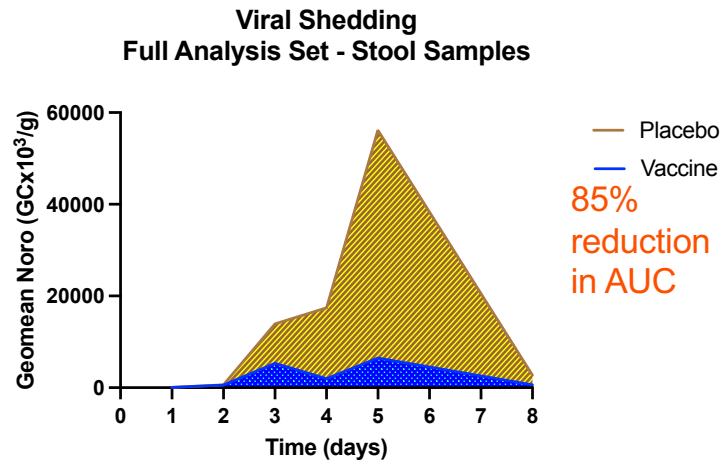
Viral Shedding in Emesis



Mann Whitney

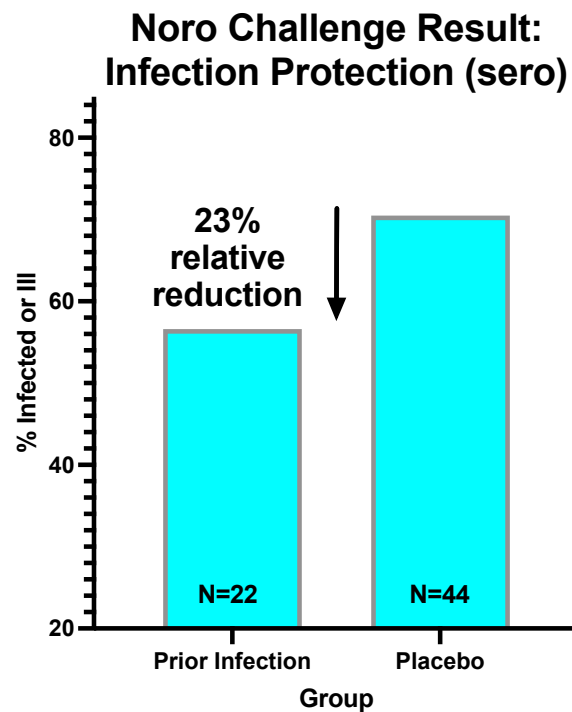
Cincinnati Children's Hospital

VXA-NVV-210 study demonstrated an 85% reduction in viral shedding



LOD is 256 copies per reaction or 1.52x10⁵ copies per mL

Using norovirus infection to prevent subsequent challenge is slightly protective



Norovirus Challenge study: Does norovirus infection prevent subsequent infection?

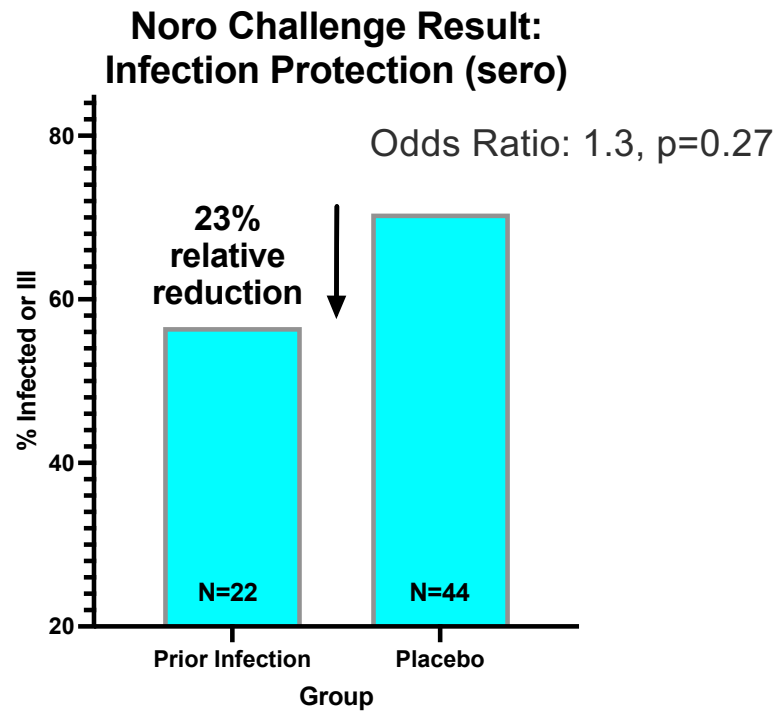
Seroconversion was used to define infection

- A four-fold or greater increase in serum titers post infection was defined as “infected”

Johnson, et al, JID, 1990

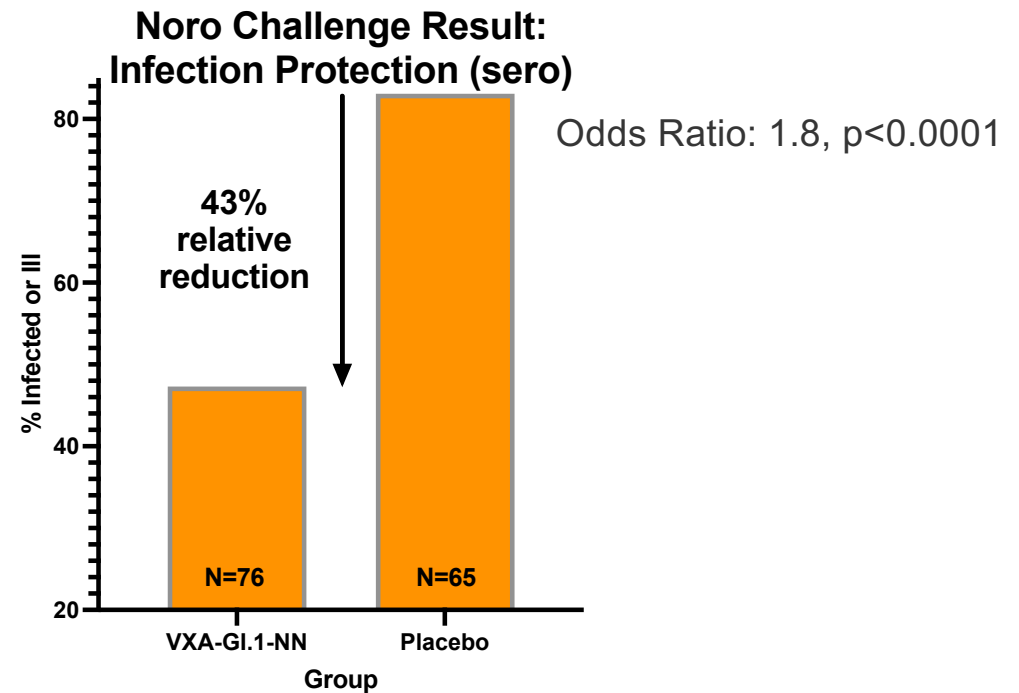
Using seroconversion definition, Vaxart oral vaccination appears to protect against infection better than norovirus infection in a challenge models

Johnson Challenge Study



Johnson, et al, JID, 1990

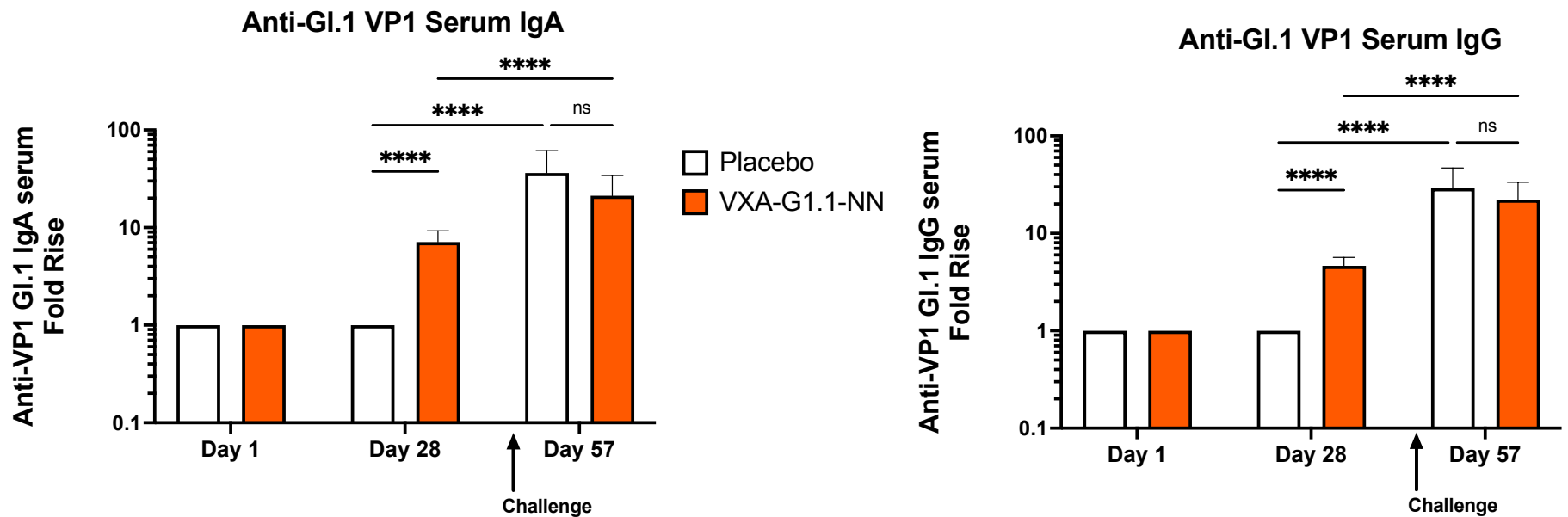
Vaxart Challenge Study



Separate studies not designed for comparison

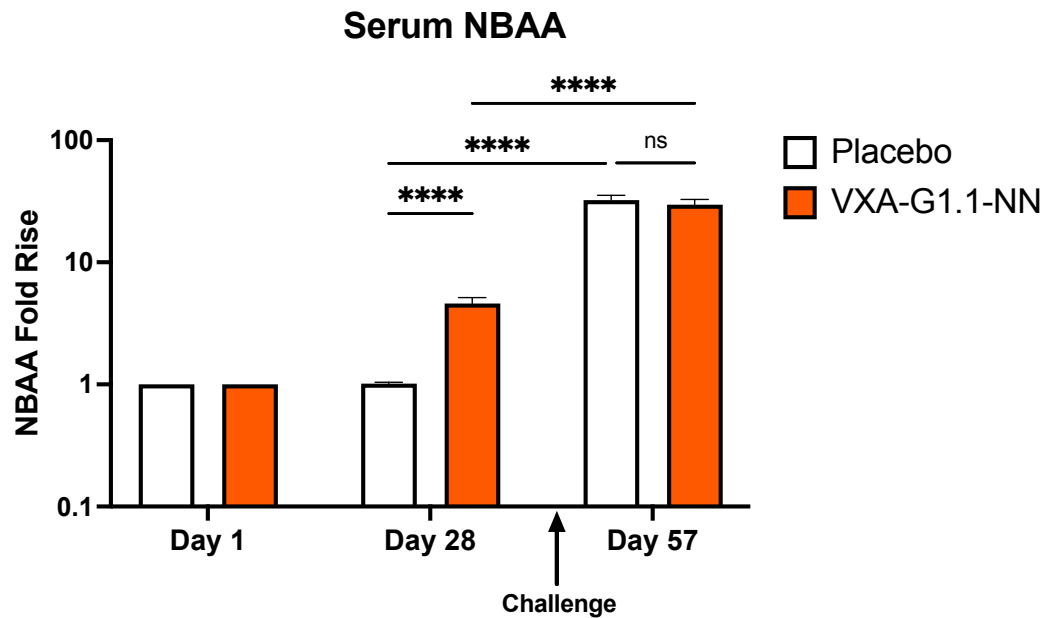
VXA-G1.1-NN Immunogenicity Endpoints

Norovirus VP1 specific IgA and IgG antibody increases 28 days after VXA-G1.1-NN Vaccination



Qualified MSD Assay
Conducted at PPD

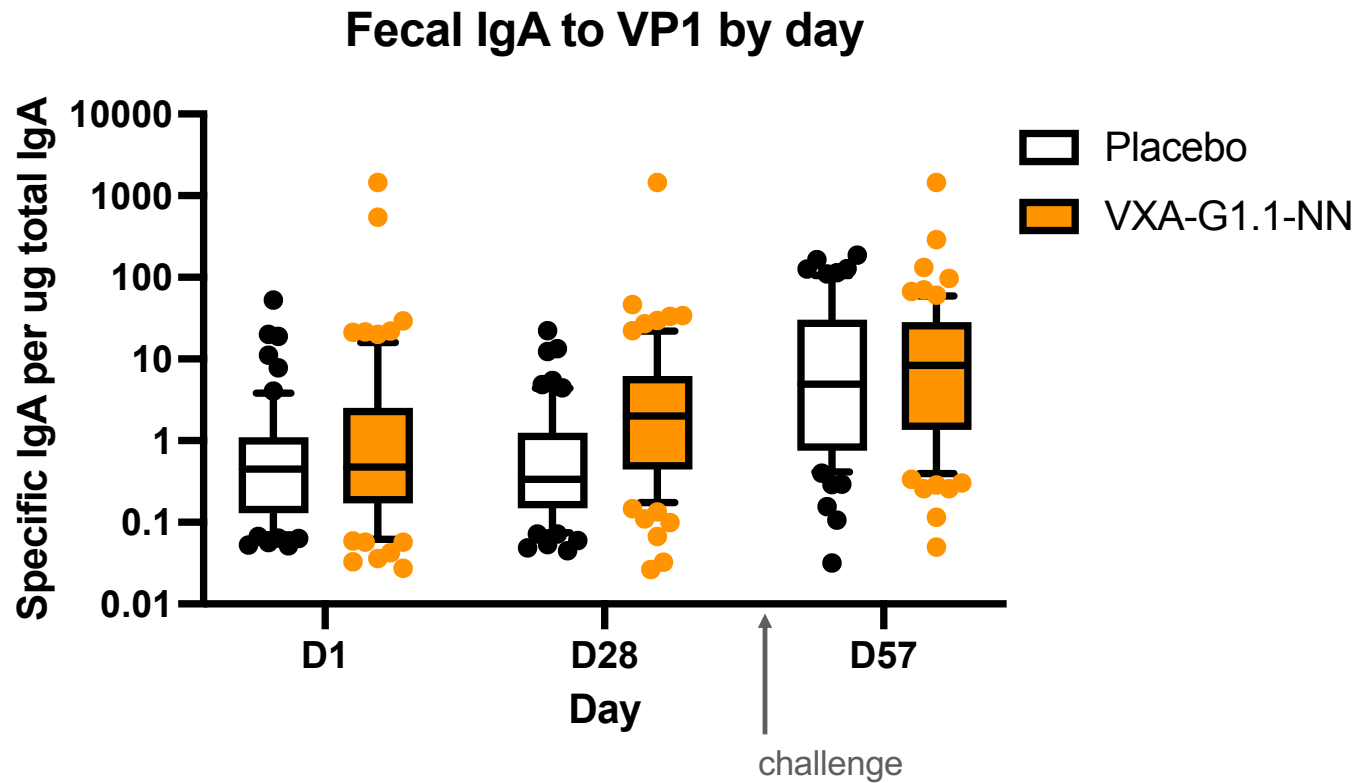
Norovirus functional antibody activity increases 28 days after VXA-G1.1-NN Vaccination



NBAA = norovirus blocking antibody assay
Similar to BT50

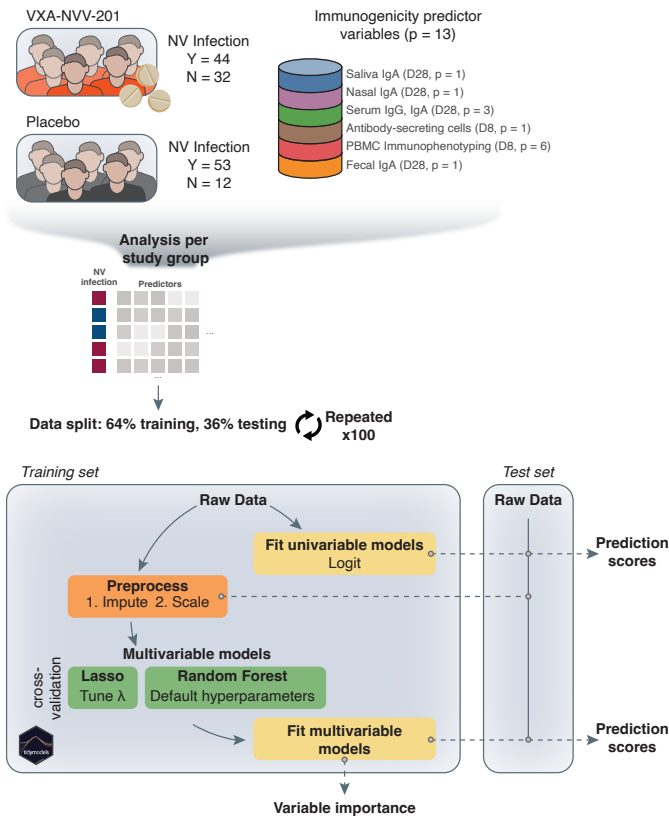
Qualified MSD Assay
Conducted at PPD

Fecal antibody increases 28 days after VXA-G1.1-NN Vaccination



Machine Learning Identifying Immune Correlates

Machine learning pipeline

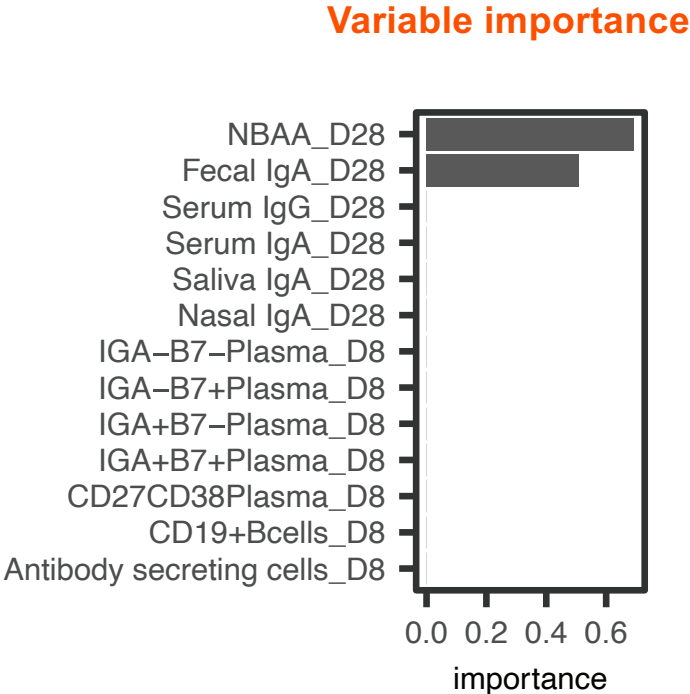
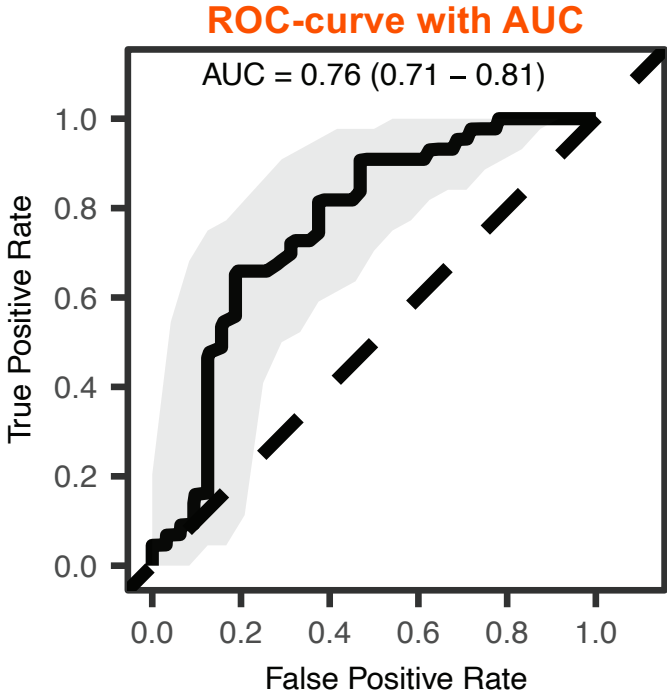
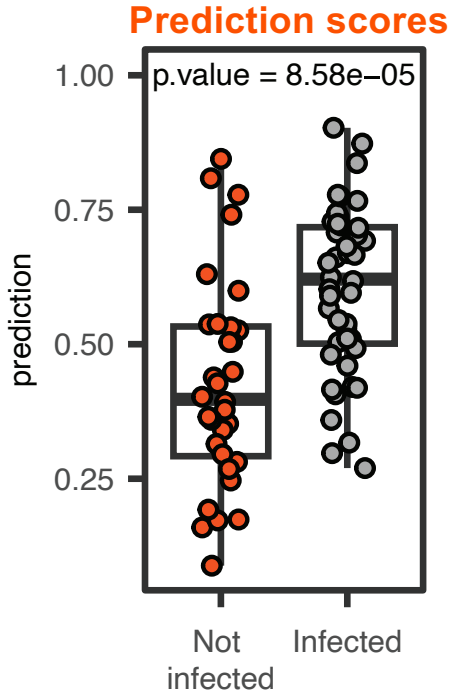


Analysis goals:

- Compare prediction performance of a range of individual markers and rank them (*Univariable logit models*)
- Address whether combining markers improves prediction (*Lasso, Random Forest*)

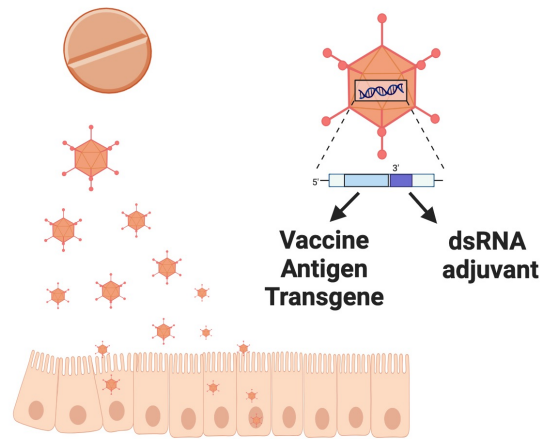
References
Liebowitz D et al., Lancet ID 2020
McIlwain DR et al., Cell Host Microbe 2021
Benkeser D et al. Sci Transl. Med. 2023

Lasso logistic regression shows the importance of quality antibody responses and fecal IgA in vaccinees



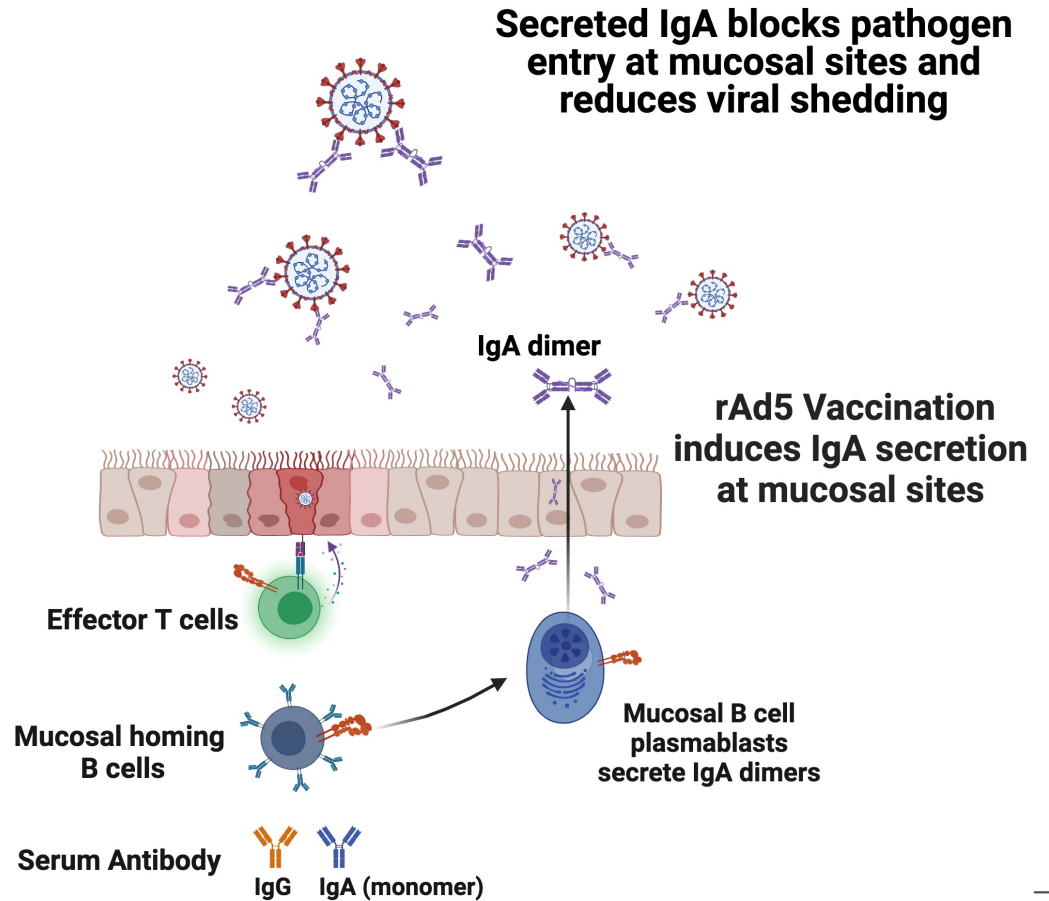
Vaxart Vaccine Proposed Mechanism: Make IgA - Block Infection

Oral rAd5
Vaccine Tablet



Delivered to
Small Intestine
(Ileum)

Vaccination generates
systemic and mucosal
immune responses



Conclusions

- Norovirus oral vaccination induces mucosal and systemic immune responses
- Norovirus oral vaccination protects against shedding and infection in a human challenge model
- Protection most tightly associates with making a functional antibody response to norovirus **and fecal IgA**
 - Because of the strong induction of mucosal IgA due to the oral vaccination and potential read through into the serum, suggests that **functional fecal IgA is probably critical for protection** against norovirus infection

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