Mucosal rAd5 Immunization Against SARS-CoV-2 Spike Elicits Cross-Reactive Nasal and Serum Neutralizing Antibodies and Protects Against Beta Variant Challenge in Non-Human Primates

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Vaxart Inc.

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Oral Vaccine Solution: Non-replicating rAd5 vector containing target antigen and a molecular adjuvant delivered by tablet

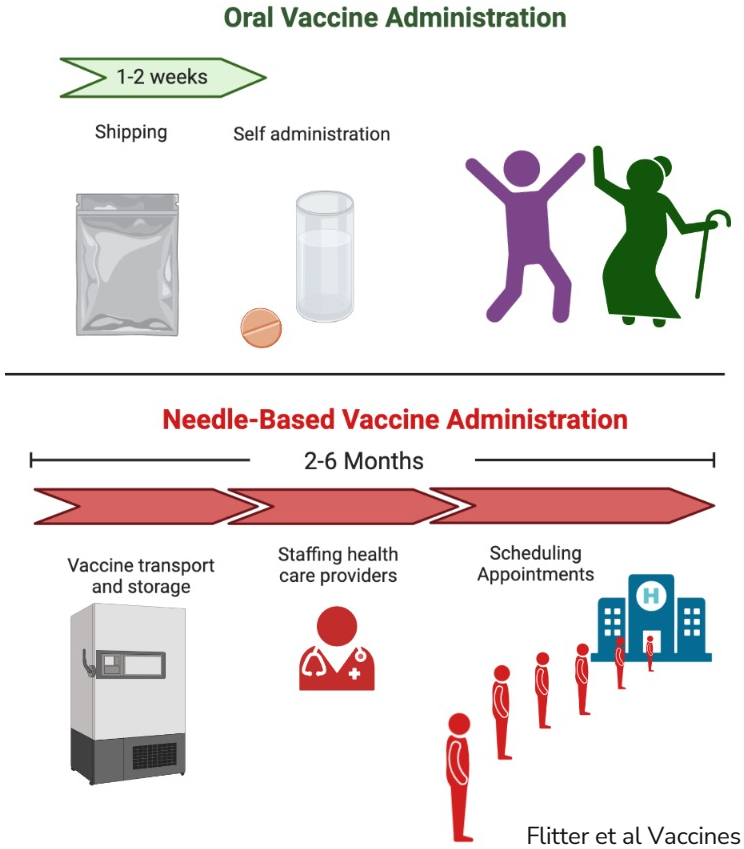
Different than traditional vaccines

Tablets are convenient mode of administration

- Self administration eliminates burden on health care infrastructure
- Quick distribution to the population

Room temperature stable eliminates cold chain

- Aids global distribution
- Longer shelf life without refrigeration



Flitter et al Vaccines 2022

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Activates mucosal immune responses

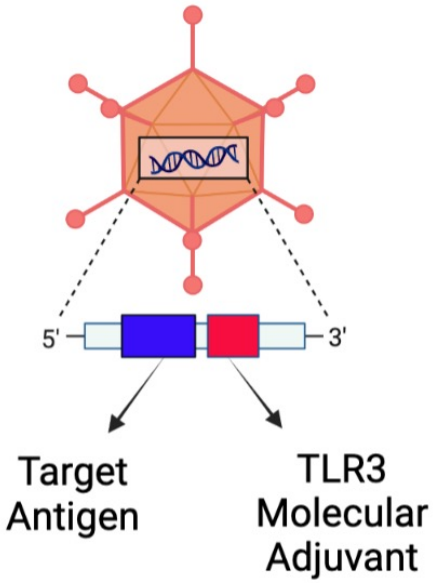
- Antigen specific IgA at mucosal surfaces in preclinical and clinical trials
- Reduced viral shedding, transmission and protects against disease

Lebowitz et al Lancet ID, 2020

Langel et al STM 2022

rAd5 Vector

- **Replication deficient E1/E3 deletion**
- **Delivered to intestinal ileum**

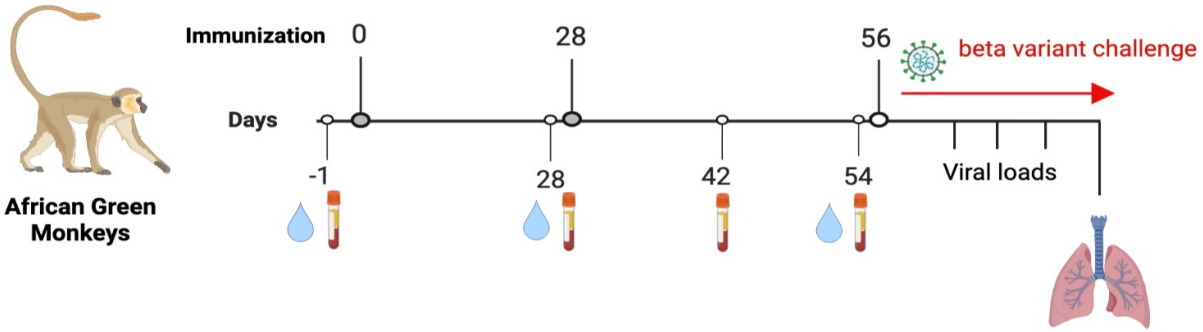


Vaccine administration and SARS-CoV-2 Challenge

Questions:

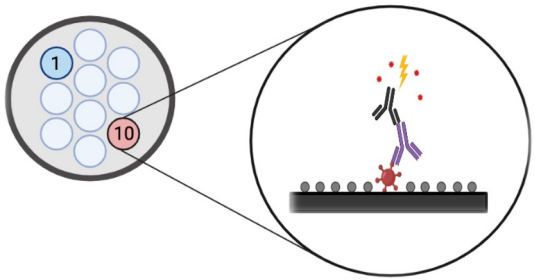
- **Can Wuhan based vaccine be cross protective against challenge?**
- **Is a variant specific approach needed?**

Group	Prime	Boost
1	PBS	PBS
2	rAd5 S (Wuhan) + N	rAd5 S (Wuhan) + N
3	rAd5 S (Wuhan)	rAd5 S (Wuhan)
4	Wuhan S Protein (IM)**	rAd5 S (Beta)
5	rAd5 S (Beta)	rAd5 S (Beta)



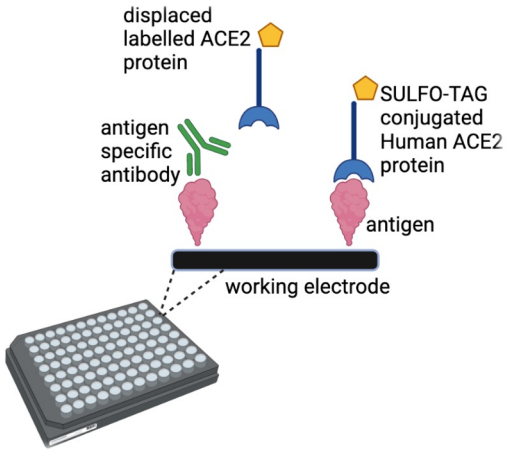
Evaluation of antibody responses, viral loads and shedding

Quantity



Multiplexed MSD

Functional Activity



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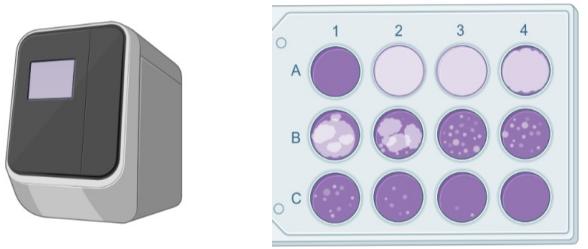
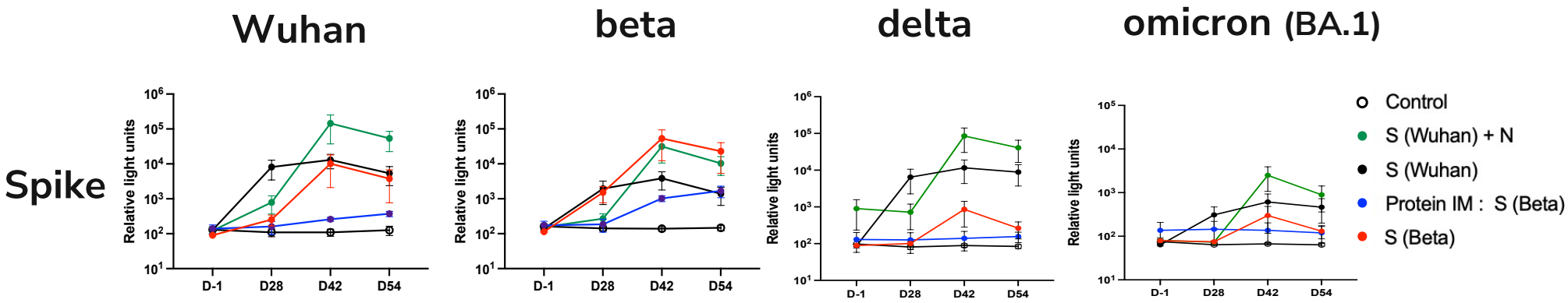
Protection



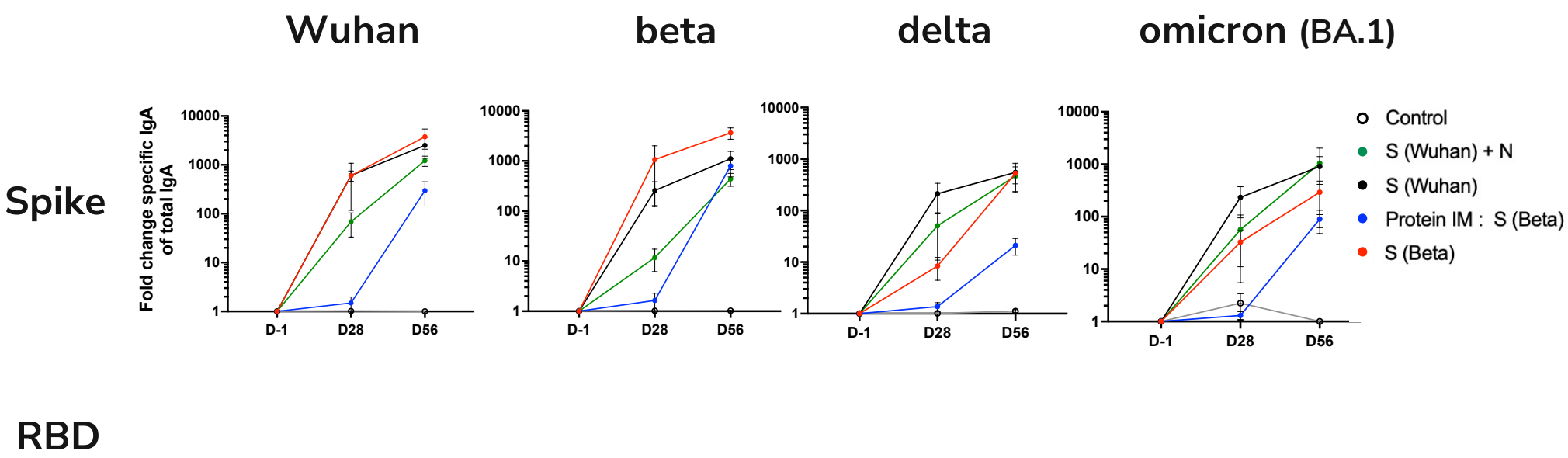
qPCR and TCID50

rAd5 mucosal immunization generates cross reactive serum IgG to full length spike and RBD of multiple VOC

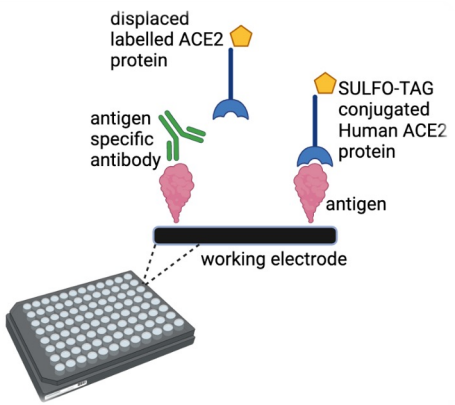


Serum IgA responses had similar trends

Significant increases in cross reactive nasal IgA are generated following mucosal vaccination to spike and RBD of mutilple VOC



Boost immunization enhances neutralizing antibody activity in the nasal compartment



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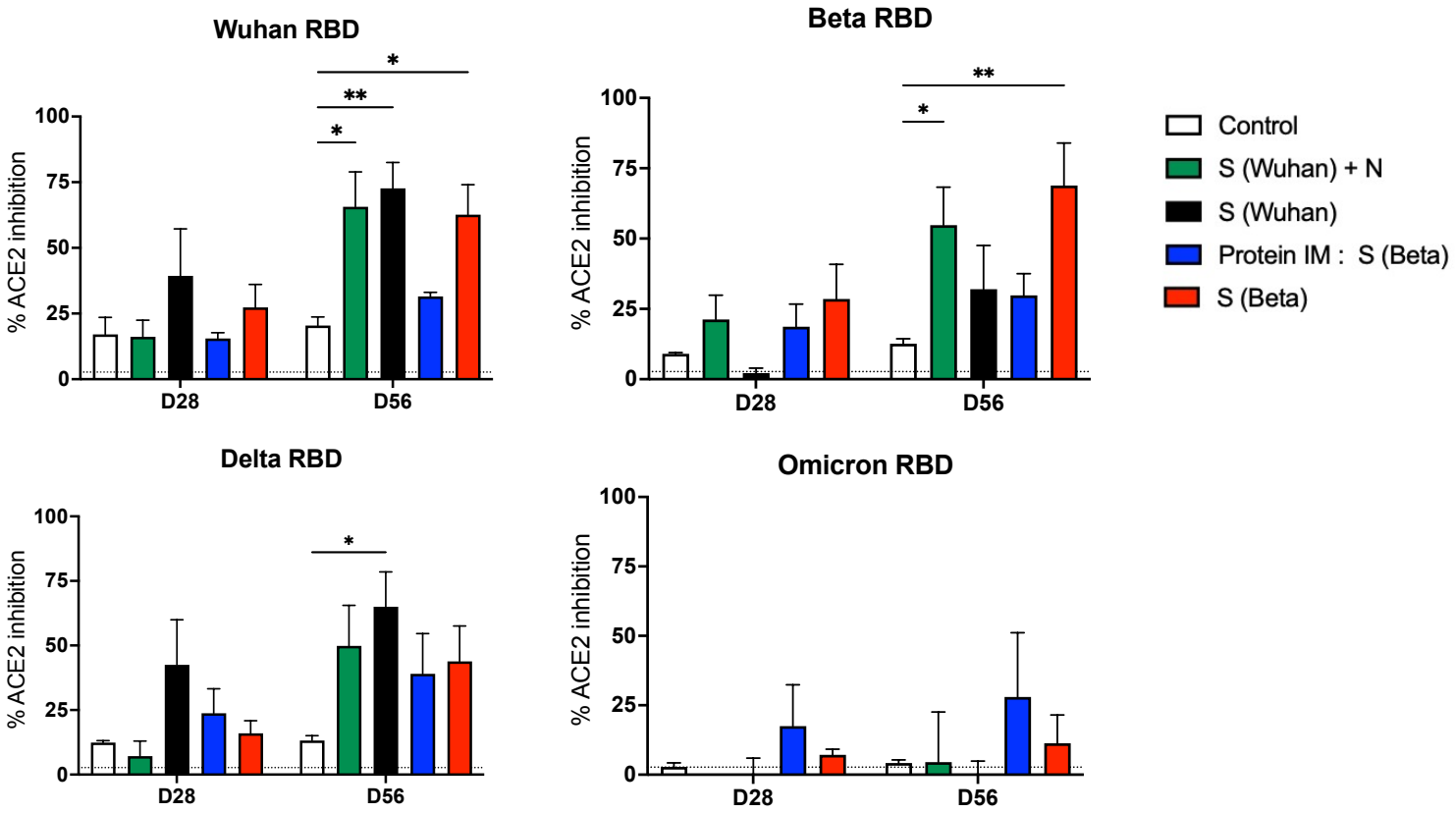
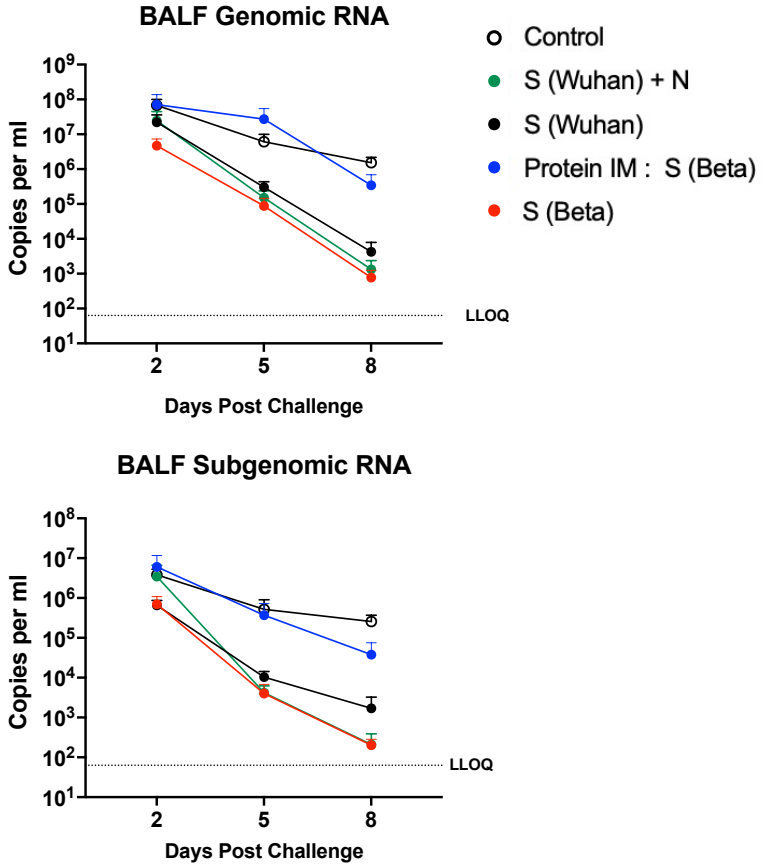
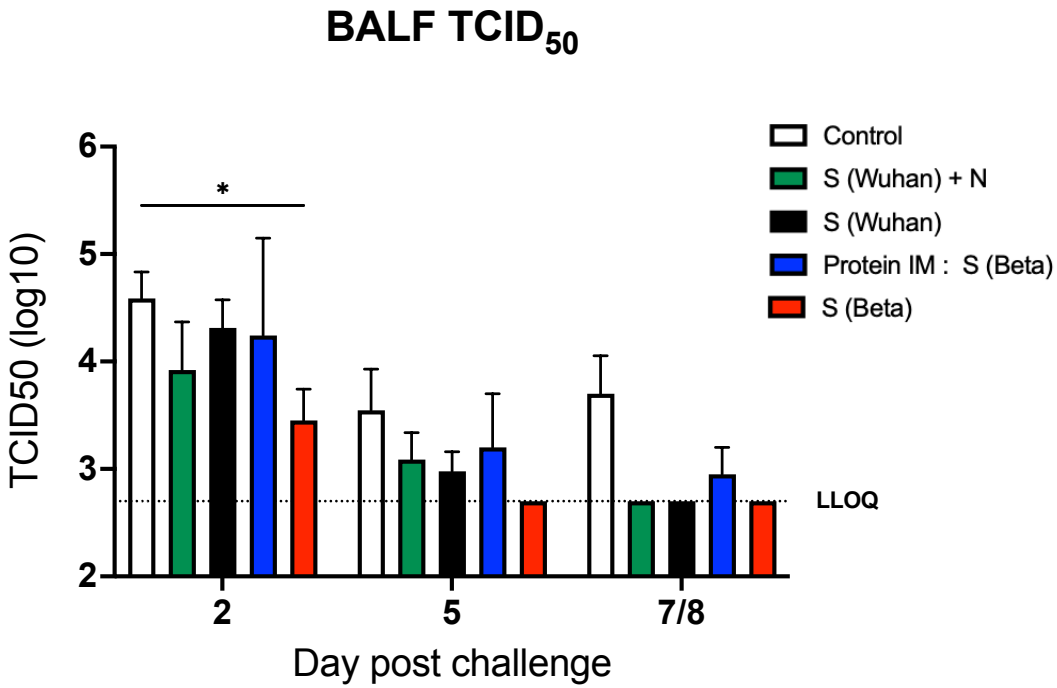
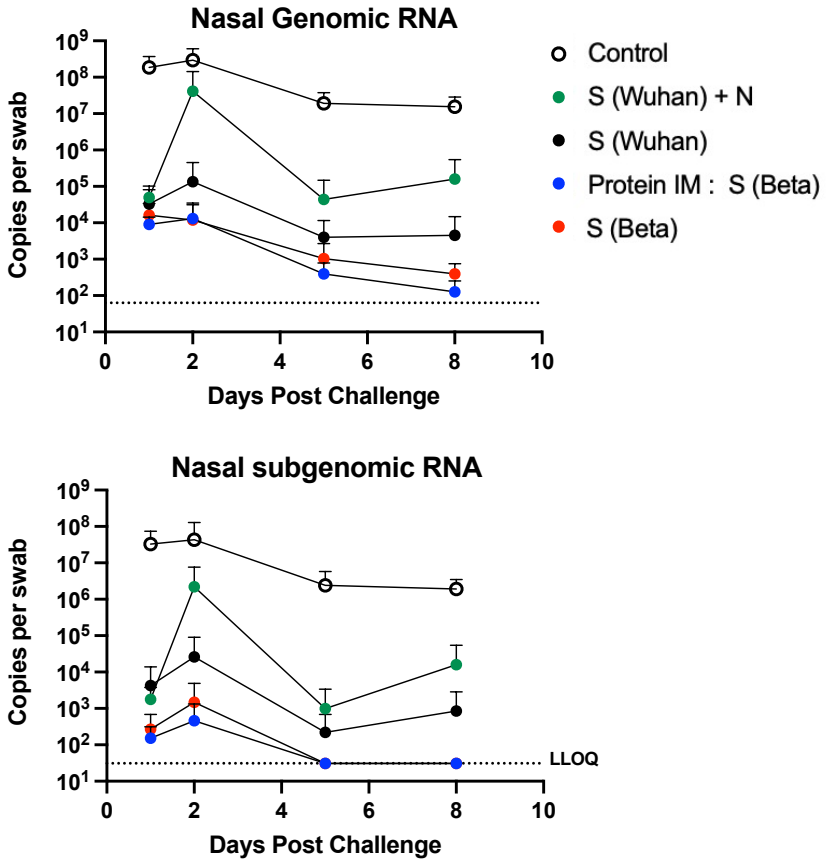


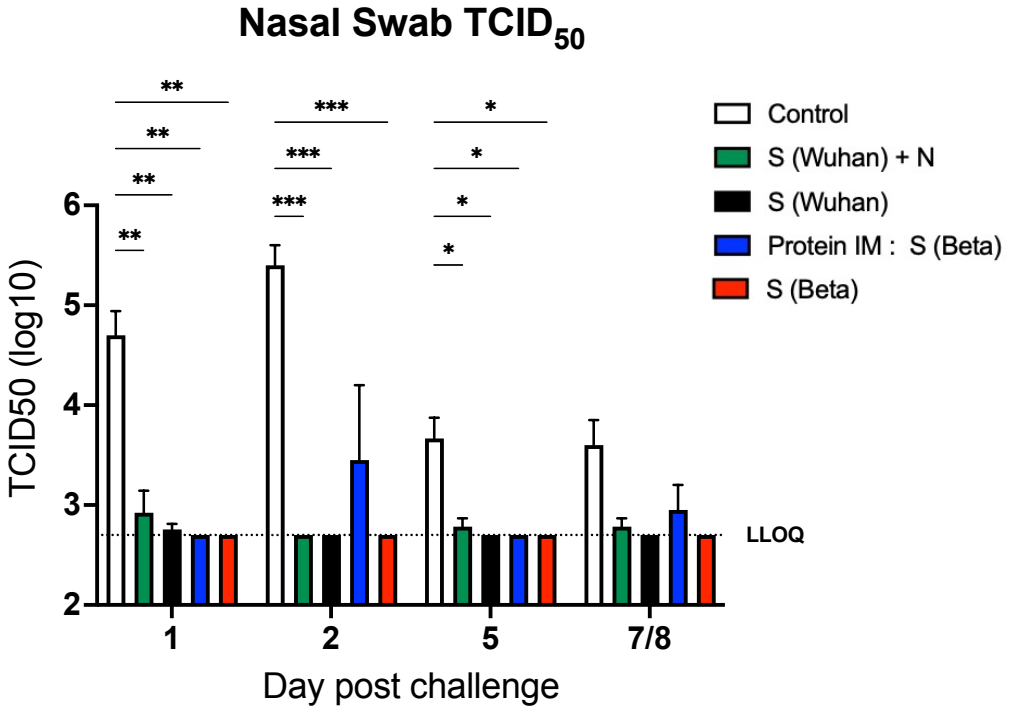
Mucosal vaccination reduces viral loads in the lung





Significantly reduced viral replication and shedding is detected in immunized animals



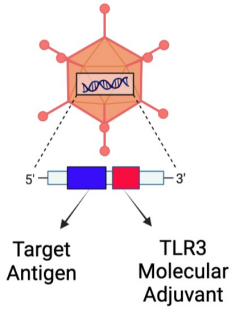


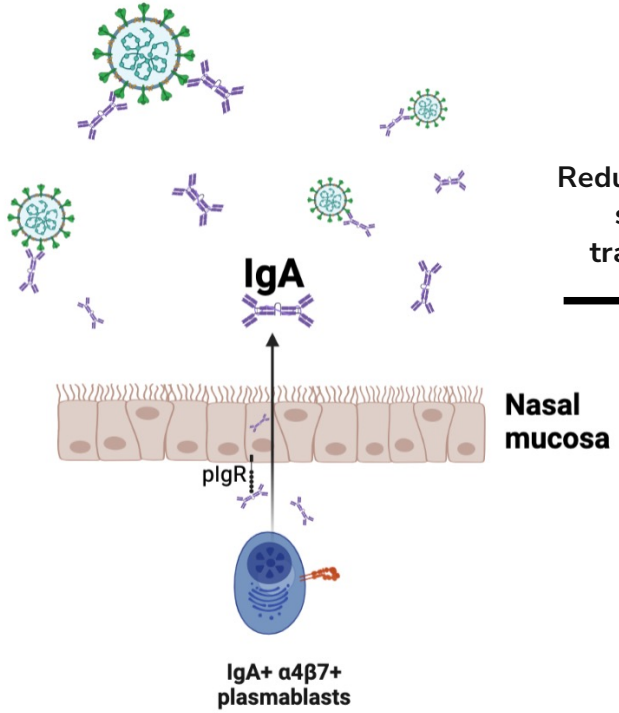
Summary

- **All rAd5 vaccines tested were immunogenic in African Green Monkeys**
  - S (Wuhan) + N and S (Wuhan) vaccines induced highly cross-reactive serum IgG and mucosal IgA responses to multiple variants of concern
  - S (Beta) vaccination induces strong matched antibody responses to homologous spike protein, however this vaccine approach generated less systemic cross-reactive humoral response to delta and omicron
- **Viral shedding in the nasal passages was significantly reduced in immunized animals following beta variant SARS-CoV-2 challenge**
  - Even mismatched S (Wuhan)+ N and S (Wuhan) vaccines significantly reduced viral shedding in the nose by TCID50
- **Functional nasal IgA antibody responses were enhanced with prime and boost rAd5 mucosal immunization**

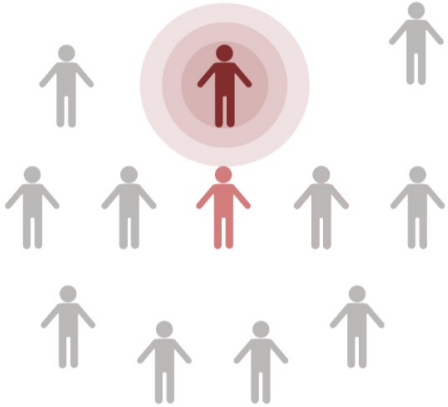
Mucosal rAd5 vaccination induces functional IgA responses that reduce viral shedding and transmission

rAd5 mucosal immunization





Reduction in viral shedding transmission



Liebowitz et al Lancet ID, 2020

Langel et al STM 2022

Johnson et al MedRxiv 2022

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Bioqual