

ADULT IMMUNISATION FORUM

2023

This event will start at 8:30am AWST

22 JUNE 2023

8:30AM–5:00PM AWST



IMMUNISATION
COALITION

SESSION 1



Katie Attwell

Impact of COVID
Vaccine Mandates



Rod Pearce

Pandemic's Impact
on GPs



Lauren Bloomfield

Vaccine Safety and VE



David Muller

Complete
Protection By A
Single Dose Skin
Patch Delivered
SARS-CoV-2 Spike
Vaccine



Ken Griffin

APNA Workforce
Survey:
Vaccination by
Primary Health
Care Nurses

David Muller

Complete protection by a single dose
skin patch delivered SARS-CoV-2 spike
vaccine



Advance Queensland Industry Research Fellow
School of Chemistry and Molecular Biosciences
University of Queensland

COVID-19 Pandemic

- SARS-CoV-2 emerged in late 2019
- Respiratory pathogen that causes COVID-19 disease
- 759,408,703 Confirmed cases
- 6,880,233 deaths

180 vaccines in clinical development

199 vaccines in pre-clinical development

Vaccines approved for use in people in less than 1 year.

Novel vaccination platforms have been granted emergency use.



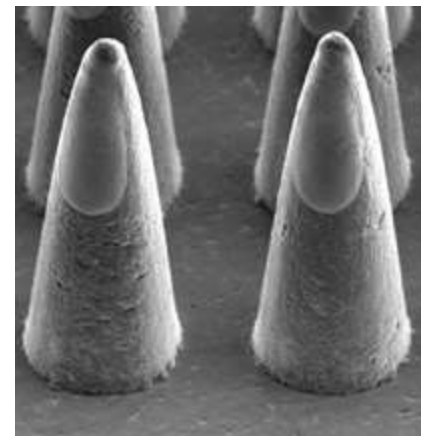
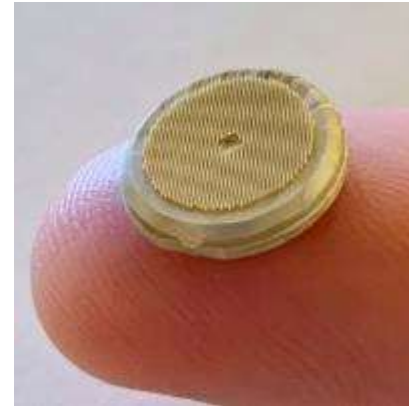
Flight paths out of major airports over a 48hr period

All approved vaccines are:

- **limited by cold chain**
- **require highly trained medical staff**

Needle free vaccine solution – The Vaxxas High density Microarray patch (HD-MAP)

- Polymer HD-MAP (patch)
- Cutaneous delivery, targets APCs to enhance immune responses
- Dried vaccine formulation to eliminate / reduce cold-chain
- Short application time
- No needle/syringe
- Potential for self-administration





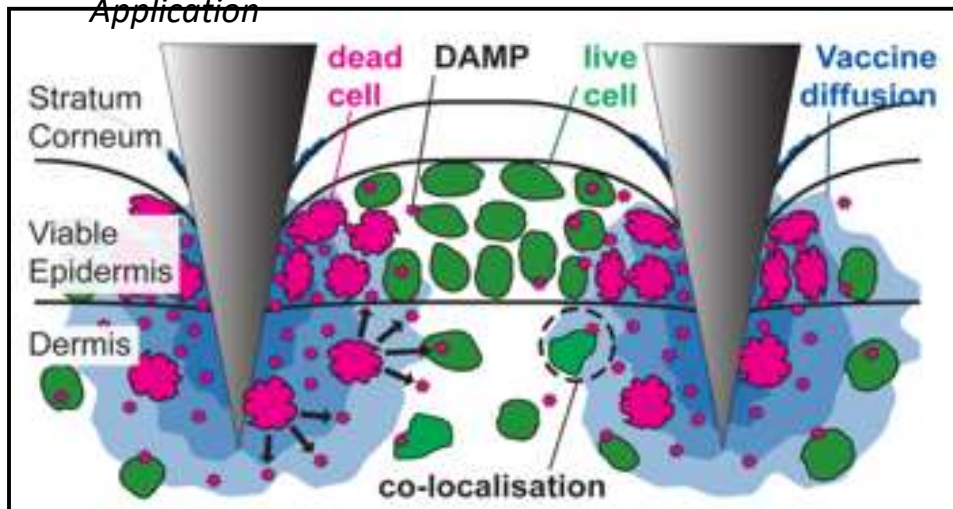
EXAMPLE
1 DOSE SINGLE USE NON-STERILE
CONTAINS NO NEEDLE PROTECTION
STORE AT 2-8°C

TE 304, LEVEL 3
AUSTRALIA

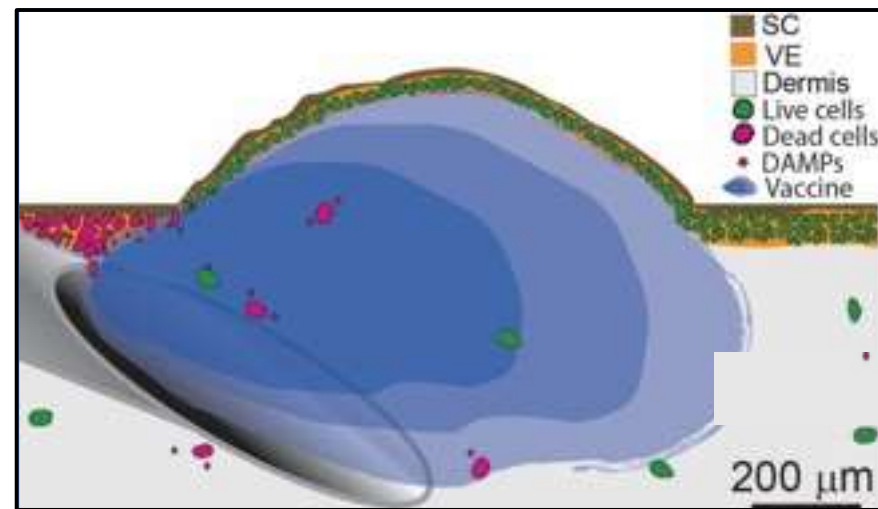
HD-MAP Mode of Action:

Co-localising vaccine, DAMPs, PAMPs and live skin immune cells

*Vaxxas HD-MAP
Application*



ID-Injection



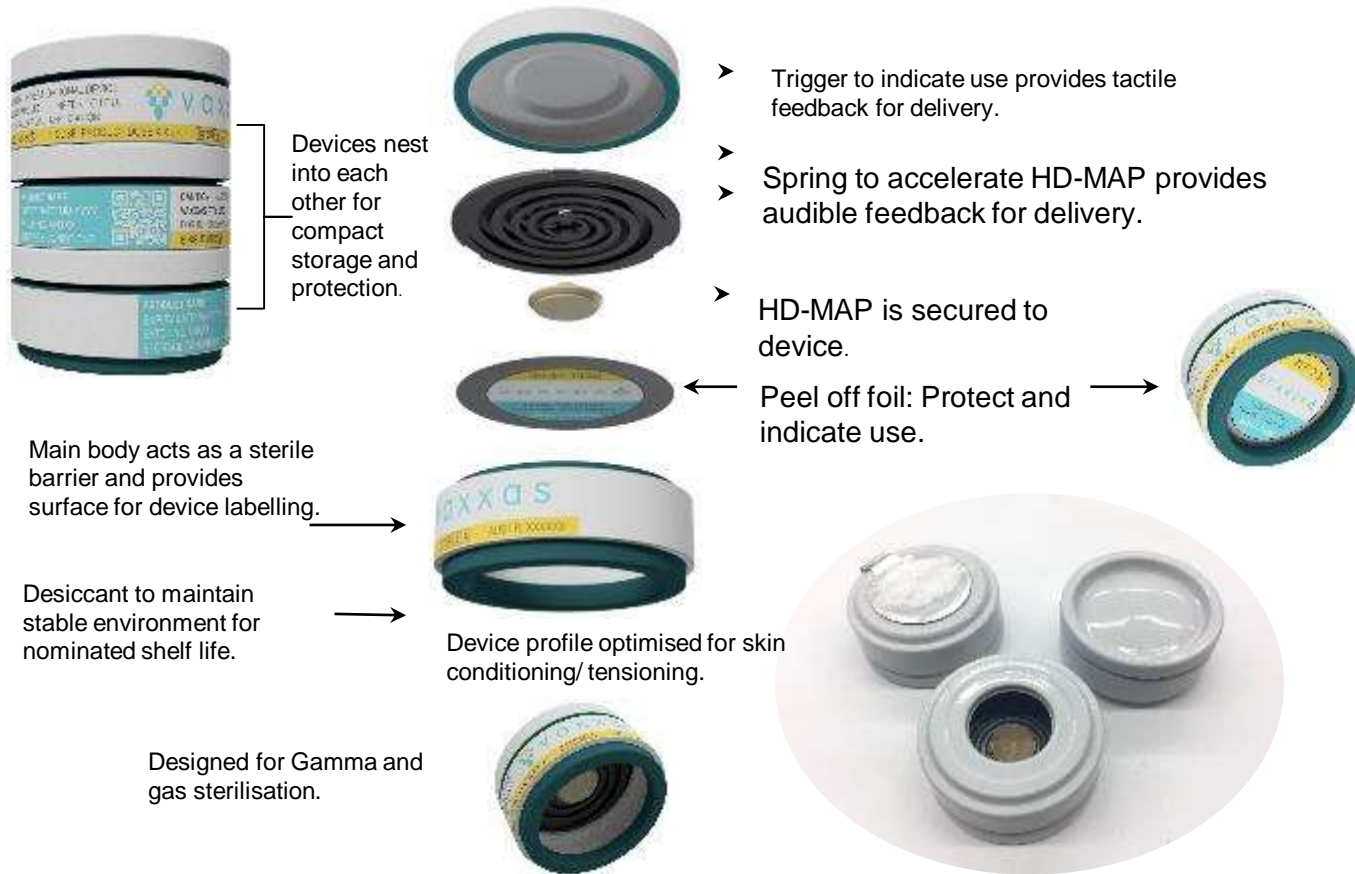
Dynamic application (20 meters / sec.)

- Controlled, consistent skin penetration
- Direct targeting of vaccine to epidermis & dermis

Localized cell death 30X > ID injection:

Rapid release of innate alarm signals in presence of live APC's

Manufacturing Scale



SARS-CoV-2 S “Hexapro”

RESEARCH

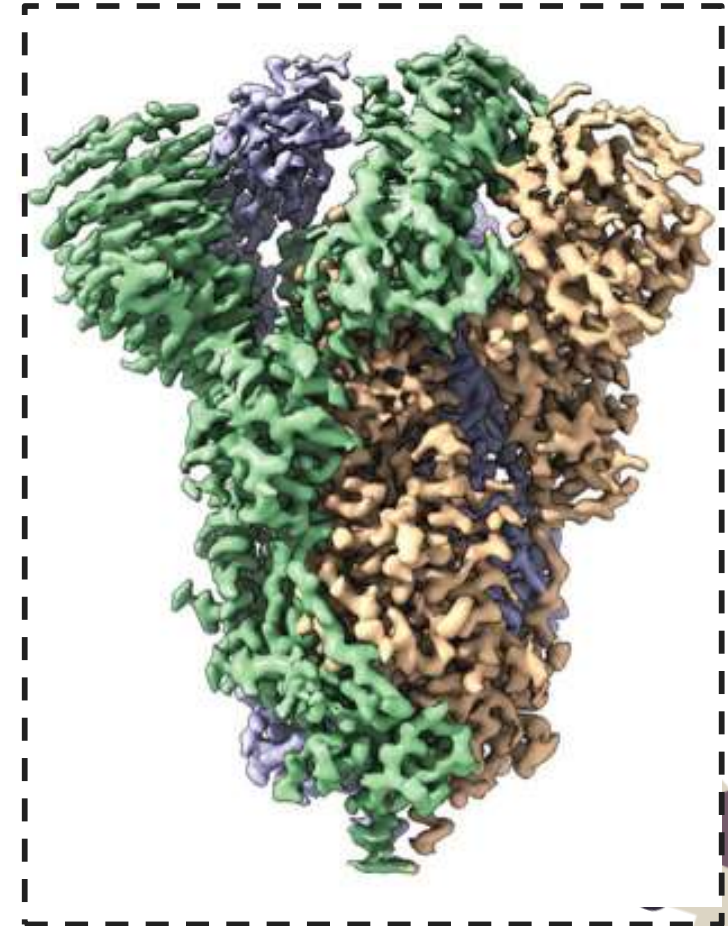
CORONAVIRUS

Structure-based design of prefusion-stabilized SARS-CoV-2 spikes

Ching-Lin Hsieh¹, Jory A. Goldsmith¹, Jeffrey M. Schaub¹, Andrea M. DiVenere², Hung-Che Kuo¹, Kamyab Javanmardi¹, Kevin C. Le², Daniel Wrapp¹, Alison G. Lee¹, Yutong Liu², Chia-Wei Chou¹, Patrick O. Byrne¹, Christy K. Hjorth¹, Nicole V. Johnson¹, John Ludes-Meyers¹, Annalee W. Nguyen², Juyeon Park¹, Nianshuang Wang¹, Dzifa Amengor¹, Jason J. Lavinder^{1,2}, Gregory C. Ippolito^{1,3}, Jennifer A. Maynard^{2*}, Ilya J. Finkelstein^{1,4*}, Jason S. McLellan^{1*}

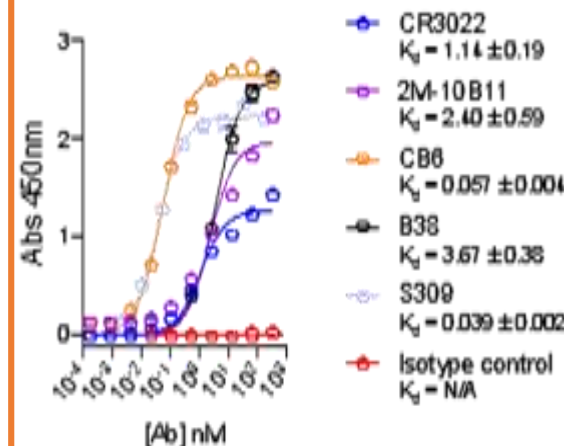
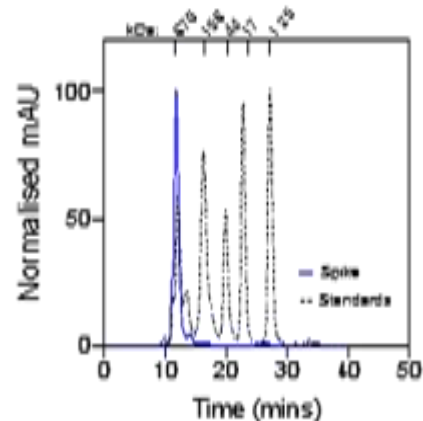
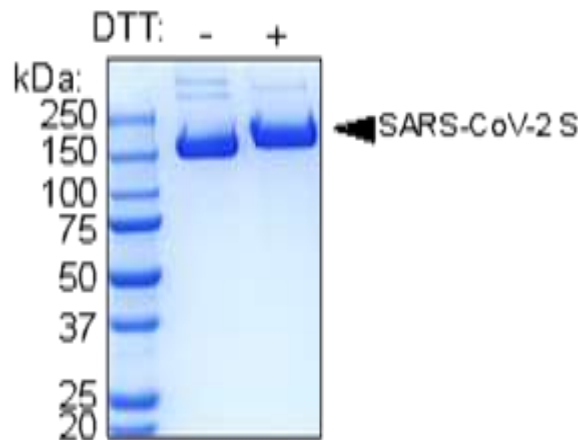
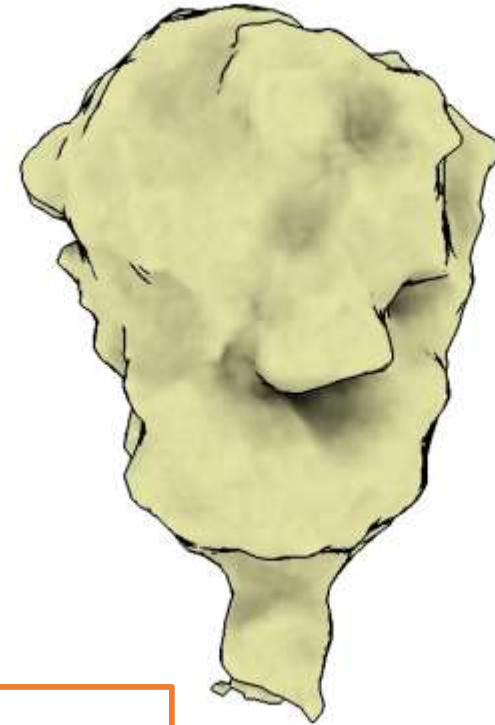
What is it?

- Pre-fusion stabilized SARS-CoV-2 S protein
- Stabilised by:
 - 6 proline substitutions
 - T4 bacteriophage fibritin Foldon trimerization domain
 - Cleavage site mutated to GSAG



SARS-CoV-2 spike

- Suitability of Hexapro for HD-MAP delivery:
 - ✓ Easy to express and purify in GMP cell lines (Expi293F™)
 - ✓ Thermostable
 - ✓ Easy to update in response to novel variants



SCIENCE ADVANCES | RESEARCH ARTICLE

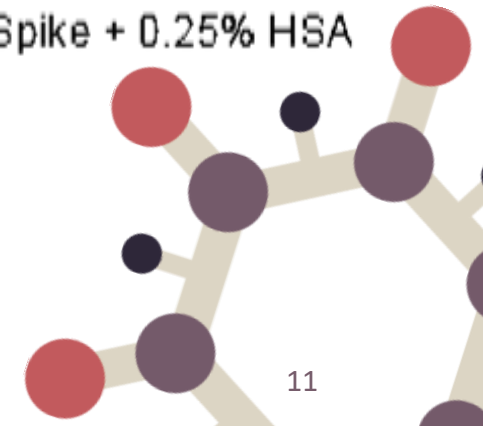
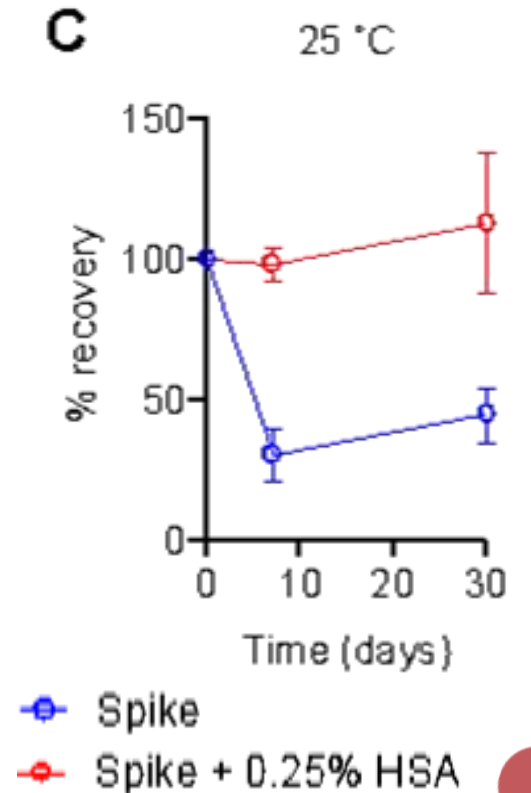
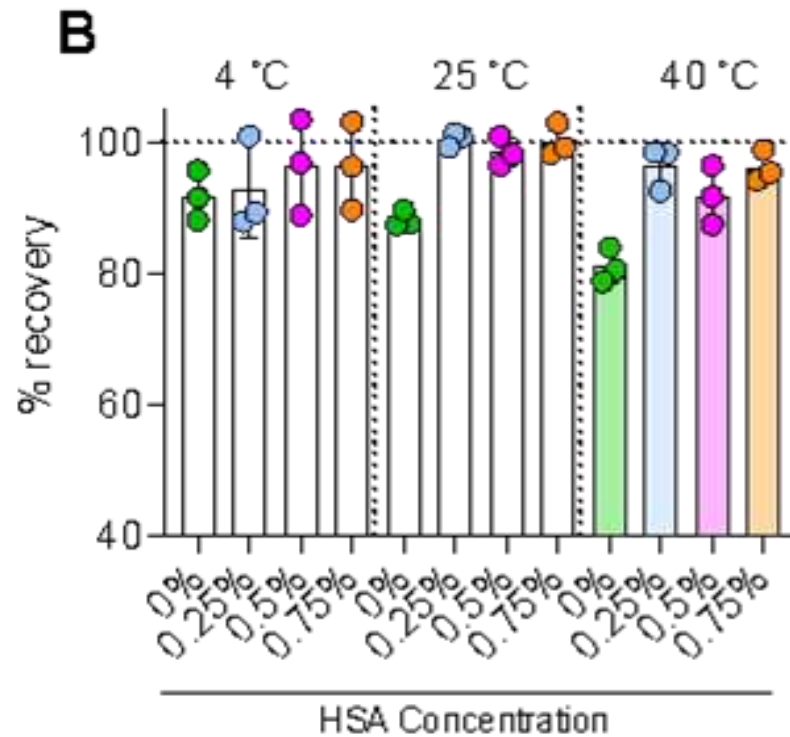
CORONAVIRUS

Complete protection by a single-dose skin patch-delivered SARS-CoV-2 spike vaccine

Christopher L. D. McMillan^{1†}, Jovin J. Y. Choo^{1†}, Adi Idris², Aroon Supramaniam², Naphak Modhiran¹, Alberto A. Amarilla¹, Ariel Isaacs¹, Stacey T. M. Cheung¹, Benjamin Liang¹, Helle Bielefeldt-Ohmann^{1,3,4}, Armira Azuar¹, Dhruba Acharya², Gabrielle Kelly², Germain J. P. Fernando^{1,5}, Michael J. Landsberg^{1,3}, Alexander A. Khromykh^{1,3}, Daniel Watterson^{1,3}, Paul R. Young^{1,3}, Nigel A. J. McMillan², David A. Muller^{1*}

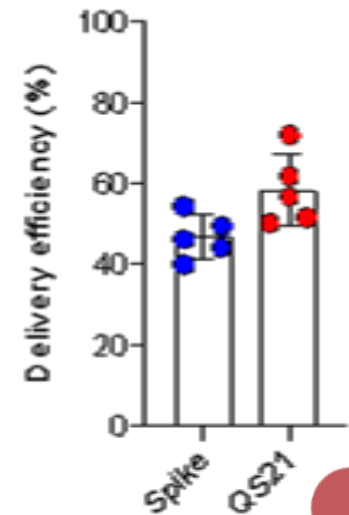
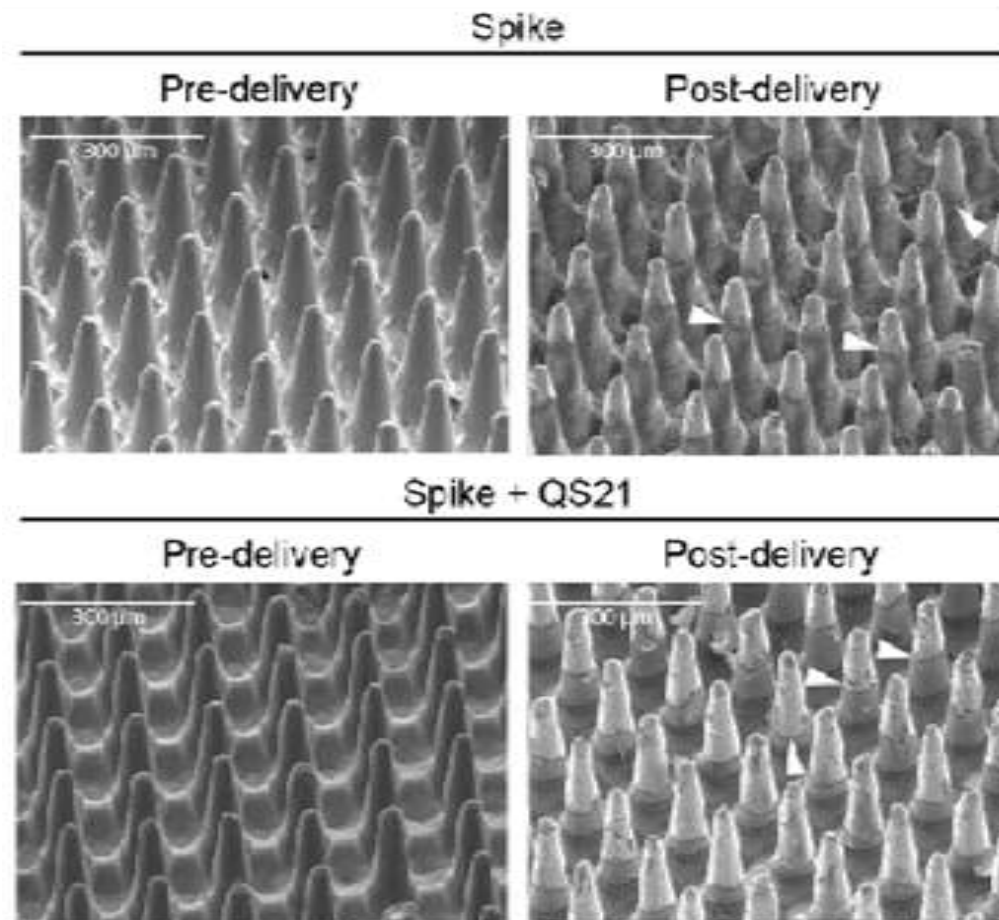
Thermostability, HD-MAP Coating and Delivery

- Limited formulation screen was performed and identified HSA as the lead excipient
- Stability outside of the cold chain:
 - 30 days at 25 °C: 100%
 - 7 days at 40 °C: 95%



Thermostability, HD-MAP Coating and Delivery

- Limited formulation screen was performed and identified HSA as the lead excipient
- Stability outside of the cold chain:
 - 30 days at 25 °C: 100%
 - 7 days at 40 °C: 95%
- HSA formulation has excellent coating morphology
 - 50-60% delivery efficiency



Mouse immunogenicity study design:

Aim:

Deliver a stabilized SARS-CoV-2 Spike protein vaccine candidate, Hexapro, via HD-MAP

Study overview:

Mice received 2 doses, 3 weeks apart.

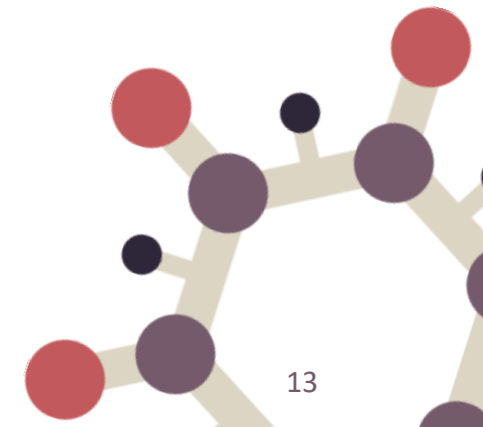
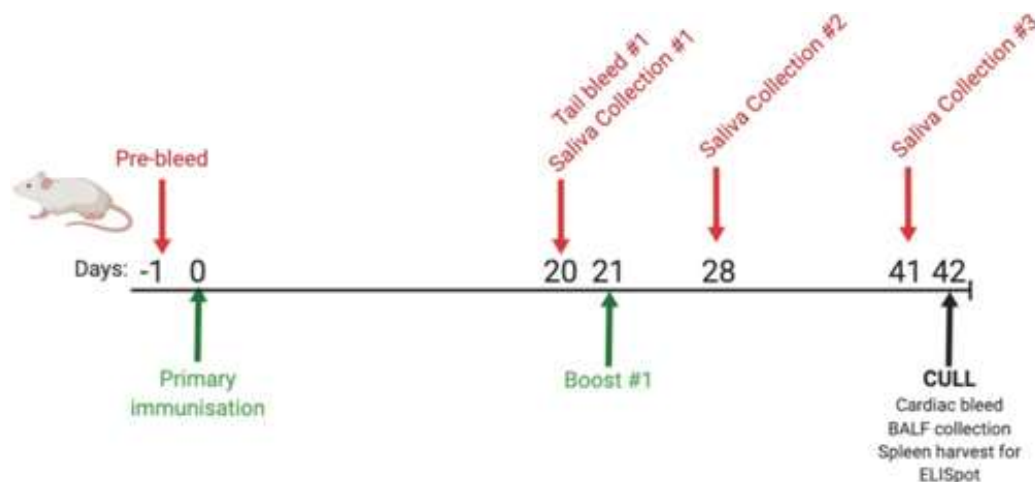
HD-MAP vs ID (+/- adjuvant)

Serum samples collected:

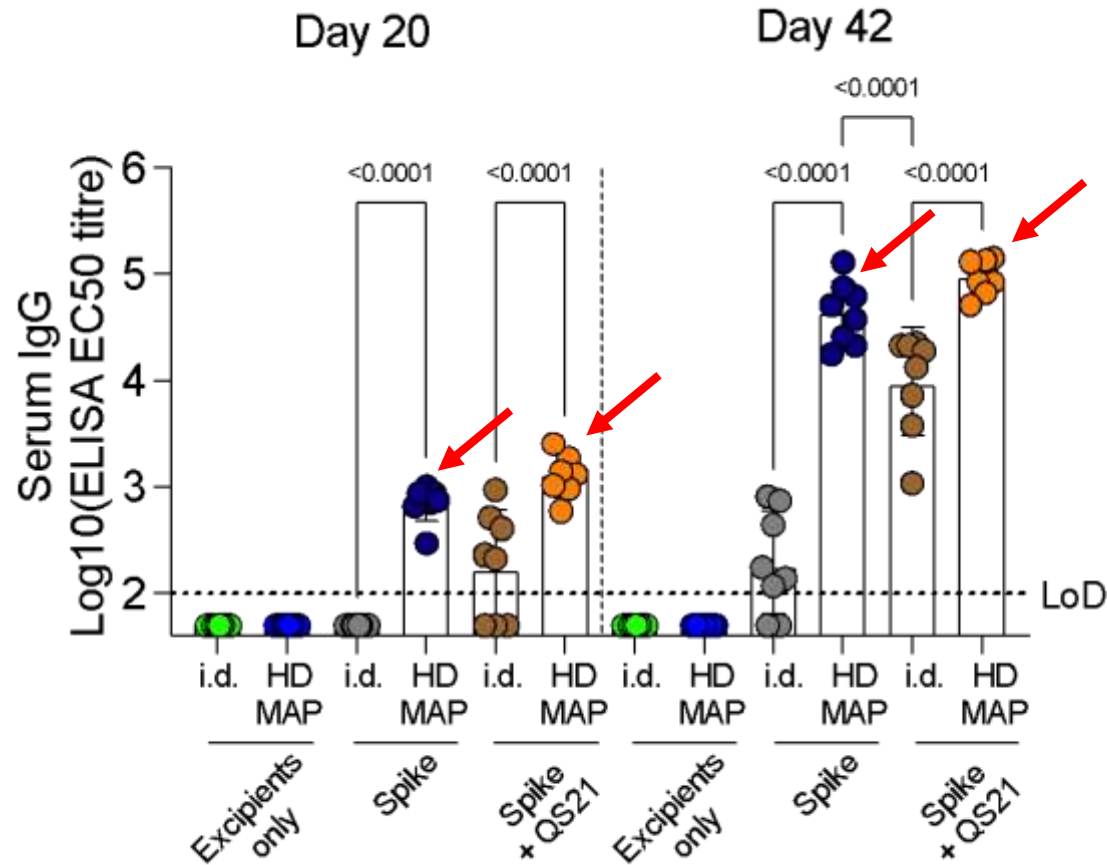
Days -1, 20 and 42

BALF collected day 42

Group	Vaccine	Adjuvant	Delivery	n
1	Excipients only	-	HD-MAP	8
2	Hexpro Spike (2 µg)	-	HD-MAP	8
3	Hexapro Spike (2 µg)	QS21 (3 µg)	HD-MAP	8
4	Excipients only	-	ID	8
5	Hexapro Spike (2 µg)	-	ID	8
6	Hexpro Spike (2 µg)	QS21 (3 µg)	ID	8
Total				48



Immunogenicity of Spike delivered via HD-MAP

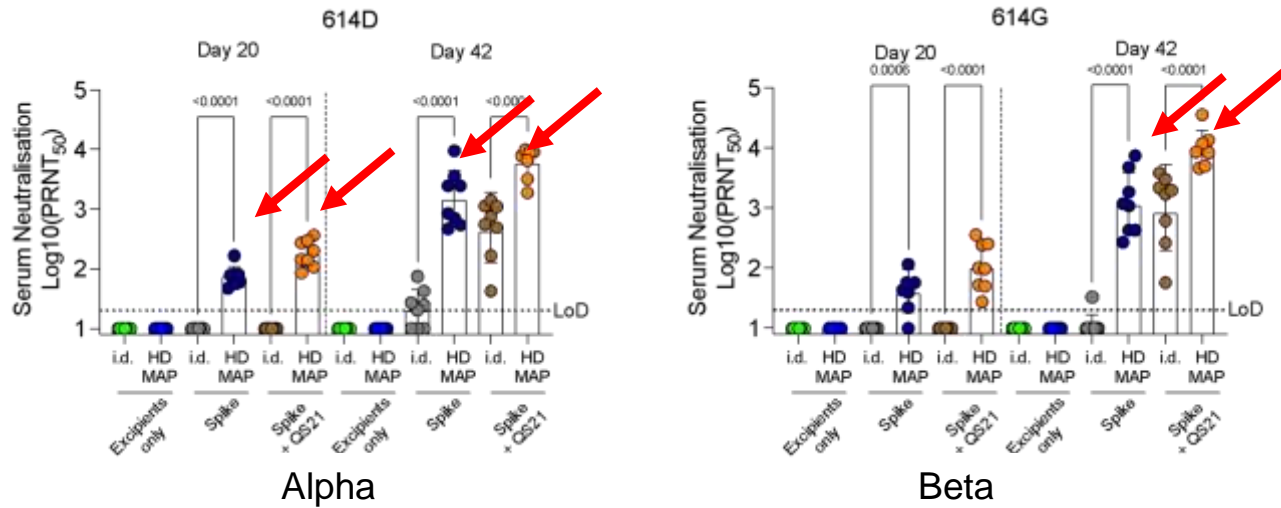


ELISA:

IgG levels measured in serum and BAL fluid via ELISA

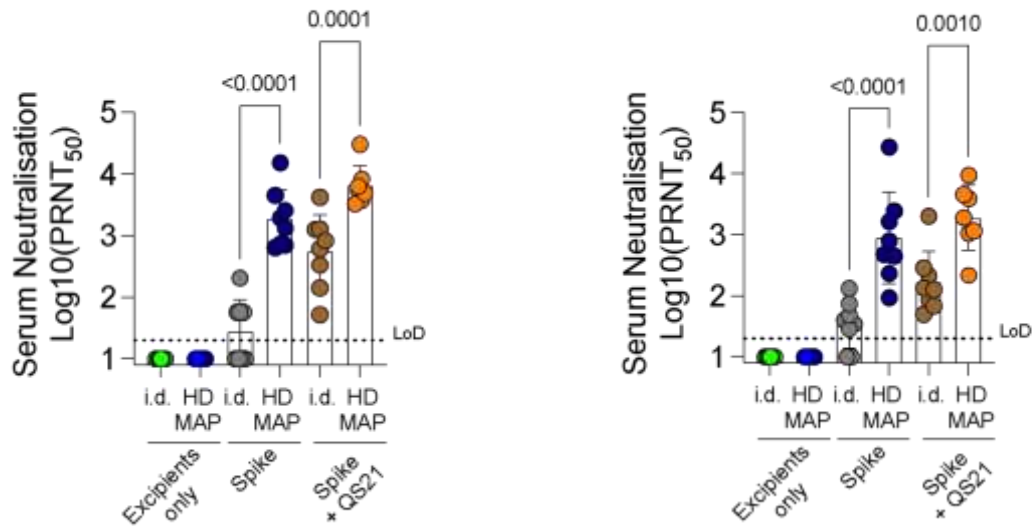
- HD-MAP was more immunogenic than i.d. in all groups
- Unadjuvanted HD-MAP delivery of spike was as immunogenic as QS21-adjuvanted

Serum neutralisation of virus



Alpha

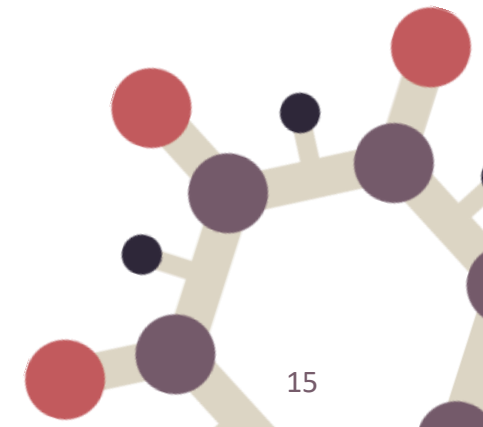
Beta



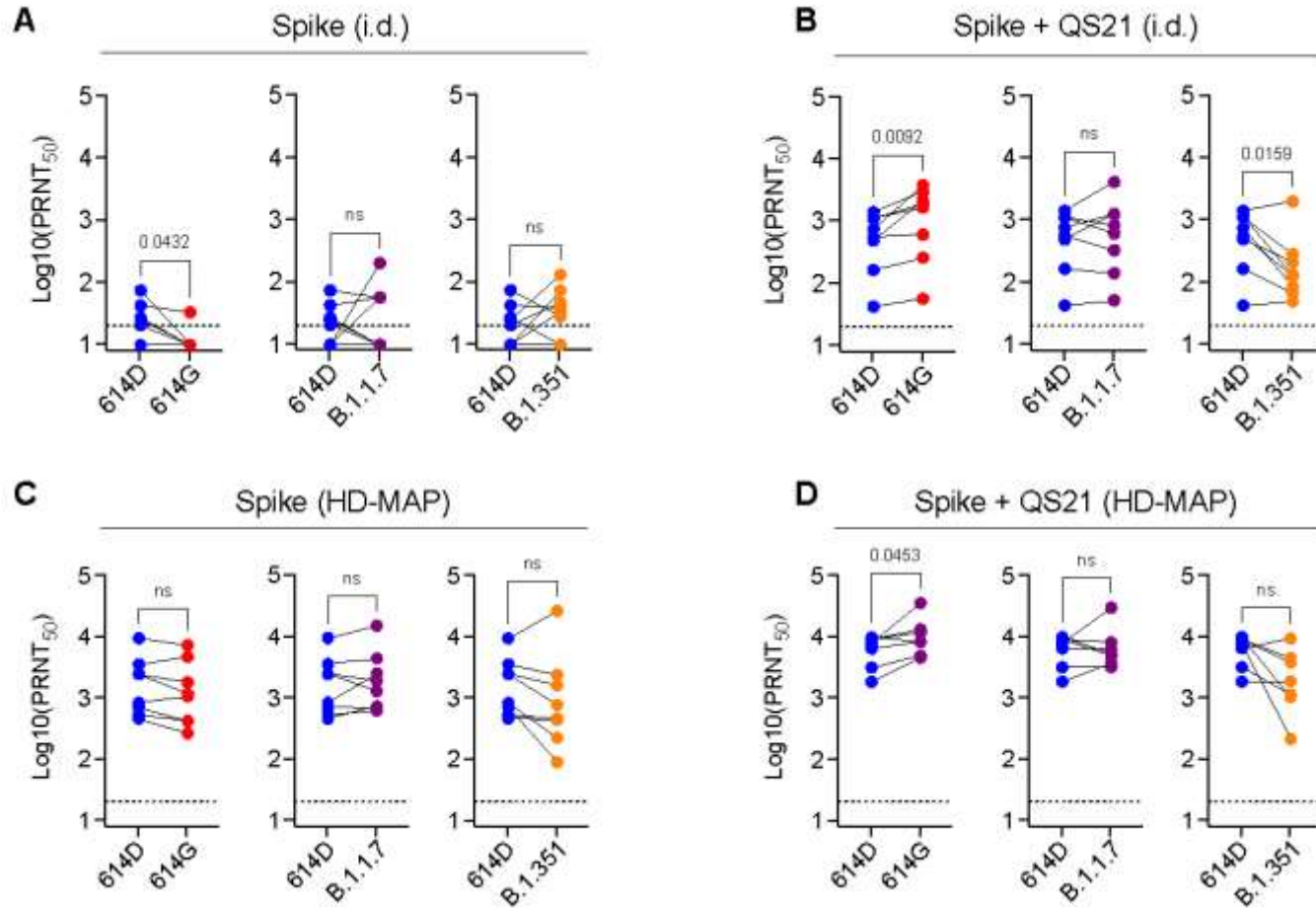
Virus Neutralisation:

Virus neutralization measured via PRNT against SARS-CoV-2 virus isolates:

- 614D (wild-type, reference strain)
- 614G (contains G at residue 614)
- B.1.1.7 (alpha variant – day 42 serum only)
- B.1.351 (beta variant – day 42 serum only)



Serum neutralisation of virus

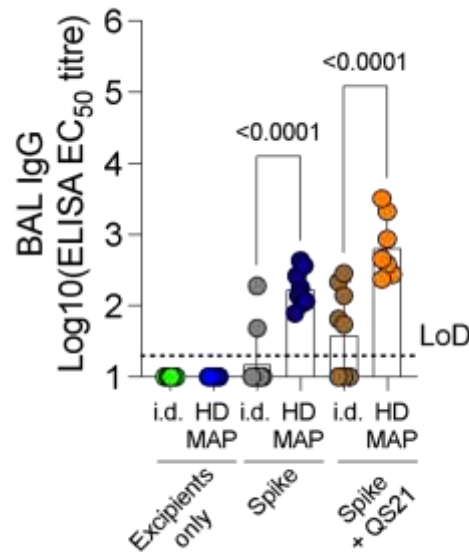


Virus Neutralisation:

Virus neutralization measured via PRNT against SARS-CoV-2 virus isolates:

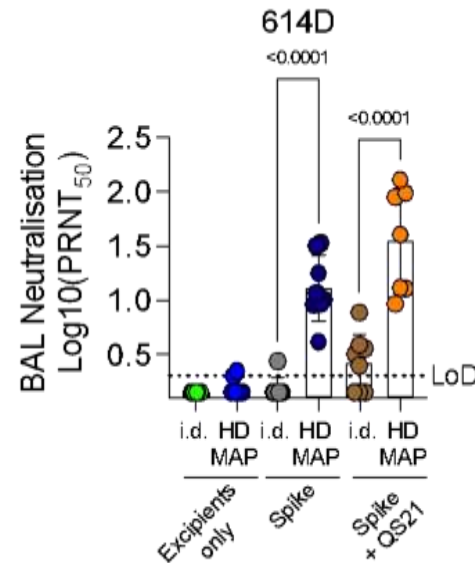
- 614D (wild-type, reference strain)
 - 614G (contains G at residue 614)
 - B.1.1.7 (Alpha variant– day 42 serum only)
 - B.1.351 (Beta variant – day 42 serum only)
- HD-MAP groups showed neutralization after 1 dose, even in unadjuvanted groups
 - After 2 doses, adjuvanted i.d. groups showed neutralization, though this was lower than the HD-MAP groups

Virus neutralising antibody in the lungs



IgG in BAL fluid:

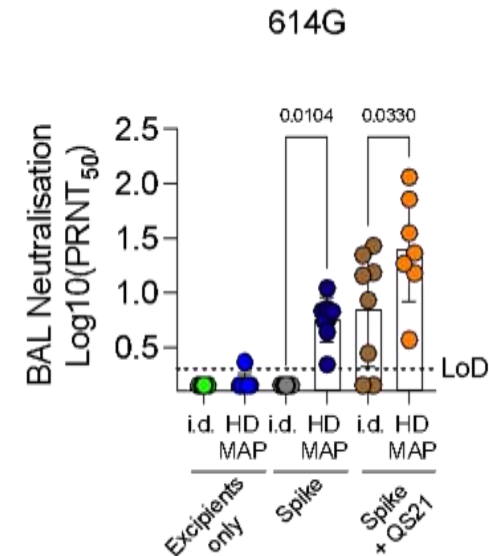
- IgG present in the BAL in all HD-MAP-immunized mice



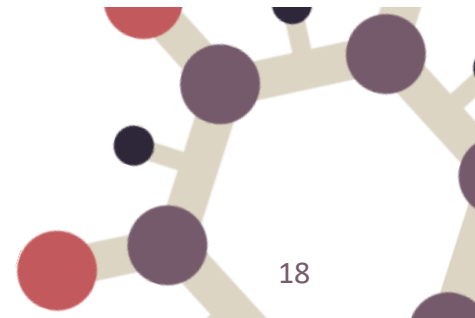
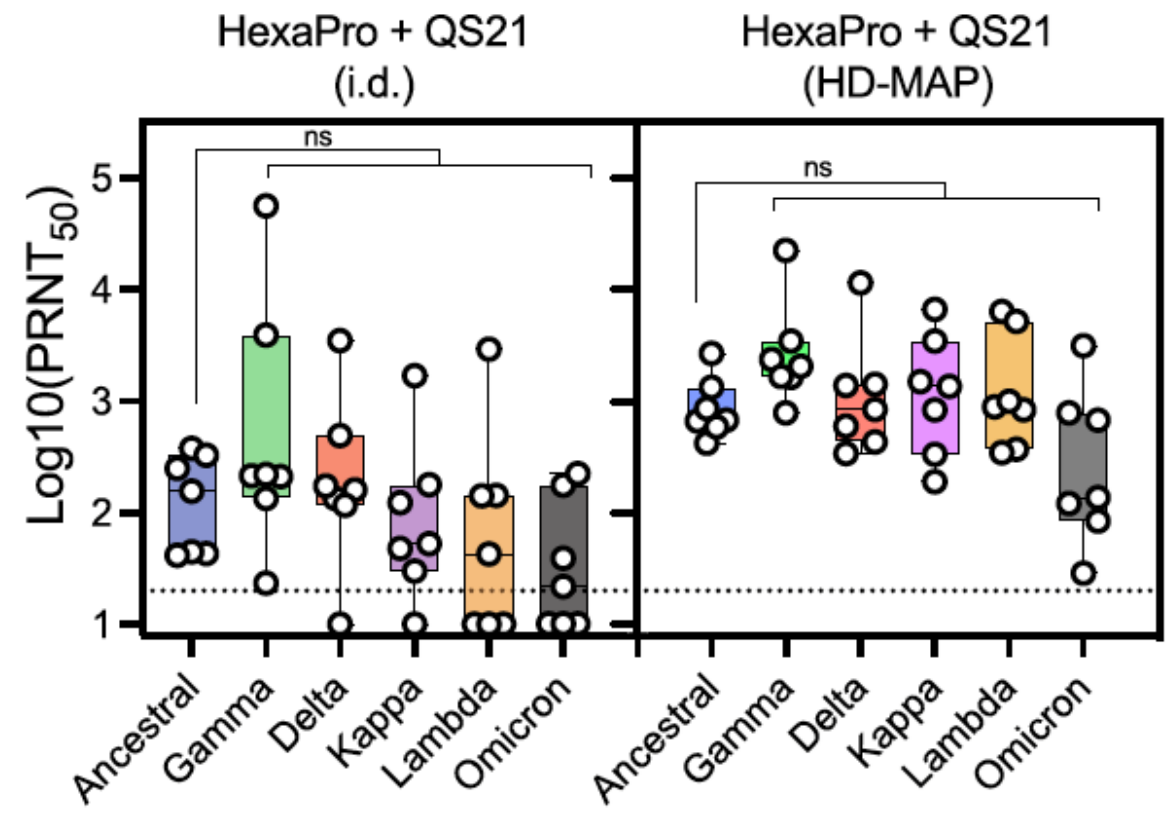
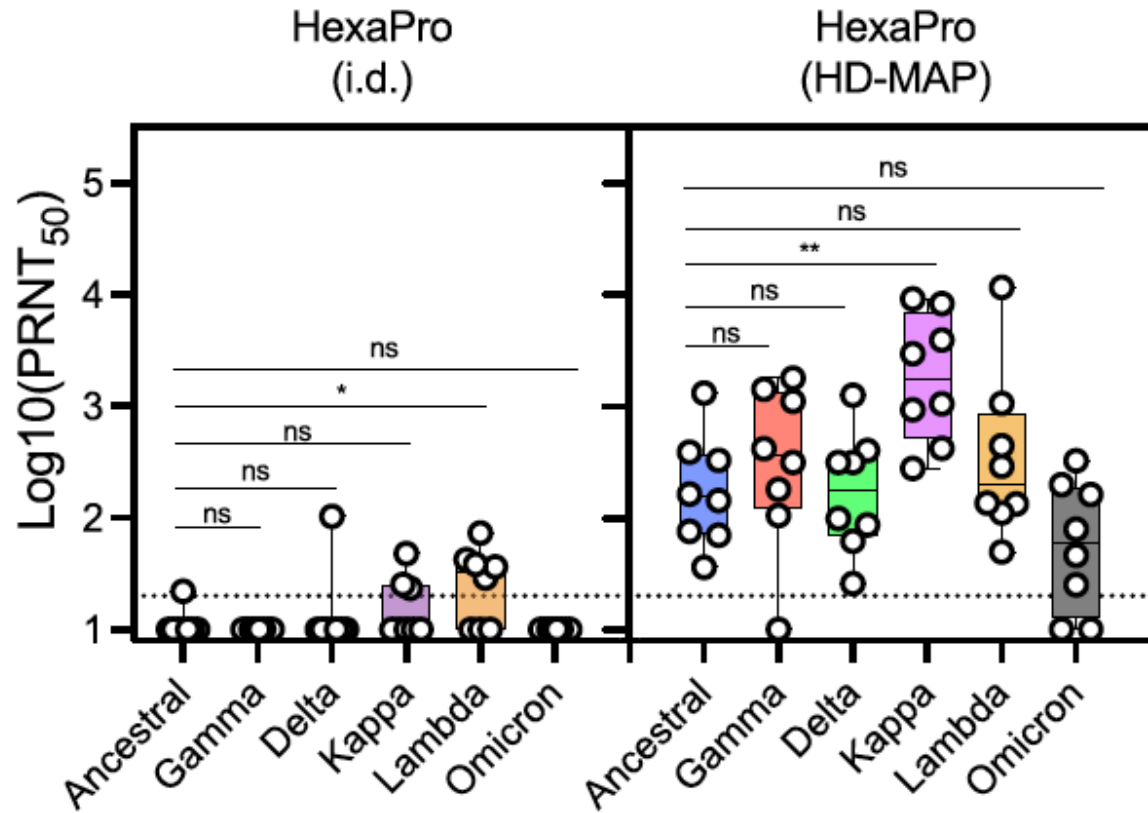
Virus Neutralisation:

Virus neutralization of BAL fluid measured via PRNT against SARS-CoV-2 virus isolates:

- 614D (wild-type, reference strain)
- 614G (contains G at residue 614 – now dominant variant)
- Higher neutralization in HD-MAP groups



What about more recent variants?



Evaluation of HD-MAP spike induced protection from SARS-CoV-2 infection

Aim:

Demonstrate that HD-MAP delivered Spike can protect mice (K18-hACE2 mice) from SARS-CoV-2 infection.

Study overview:

Mice received 1 or 2 doses via HD-MAP (+/- adjuvant)

Serum samples collected on days -1, 20 and 41

Challenge on day 42

Readouts:

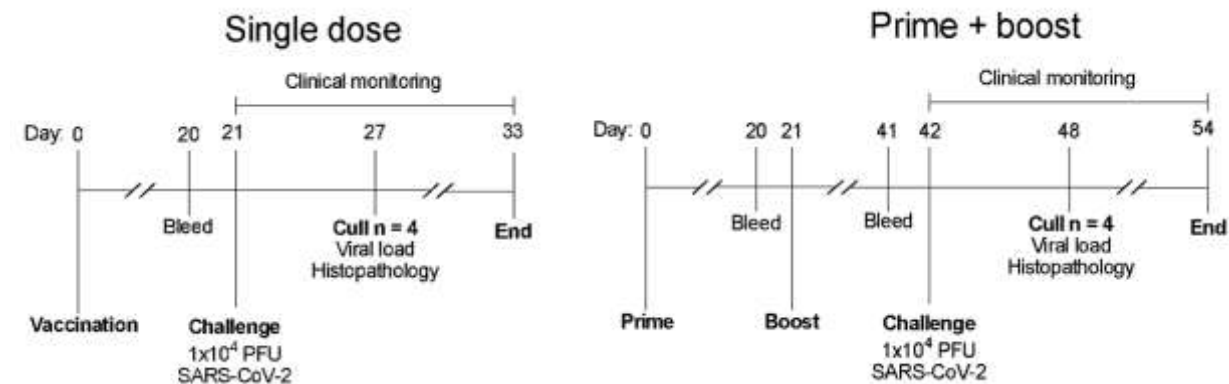
Survival + weight loss

Lungs:

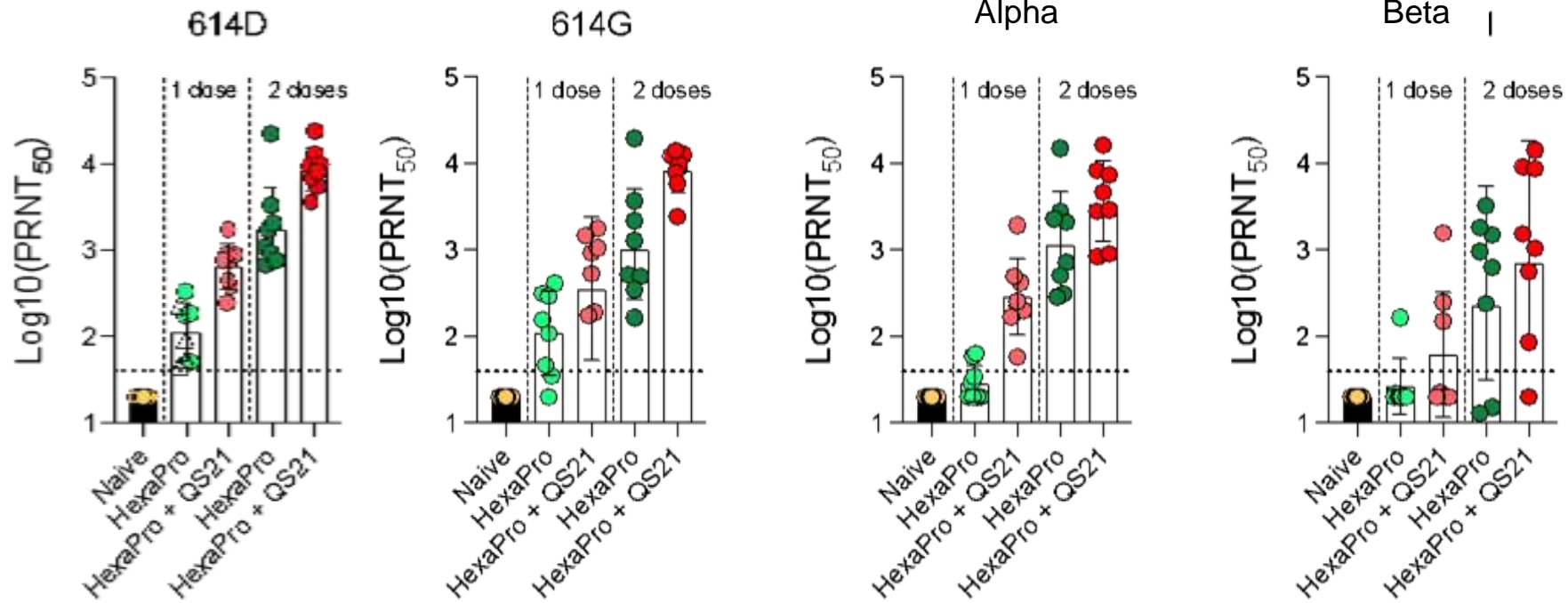
Viral load on day 6 via plaque assay (n=4)

Serum IgG via ELISA and PRNT

Group	Vaccine	Adjuvant	No. of Doses	Delivery	n	Challenge virus
1	-	-	-	HD-MAP	8	2 x 10 ⁴ PFU of SARS-CoV-2 (VIC-01)
2	Hexapro spike (2 µg)	-	1	HD-MAP	8	
3	Hexapro spike (2 µg)	QS21 (3 µg)	1	HD-MAP	8	
4	Hexapro spike (2 µg)	-	2	HD-MAP	8	
5	Hexapro spike (2 µg)	QS21 (3 µg)	2	HD-MAP	8	
Total					40	



Virus neutralisation

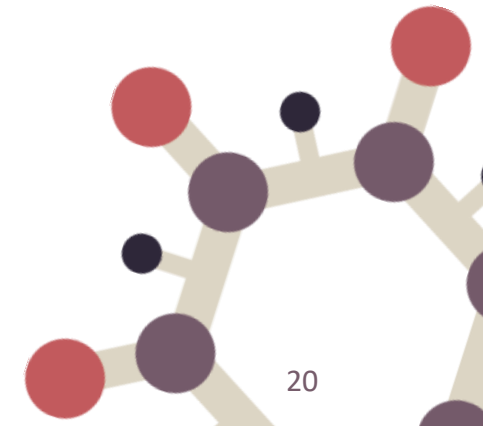


- Immunogenicity:

- Similar ELISA EC₅₀ titres as the BALB/c animal experiment

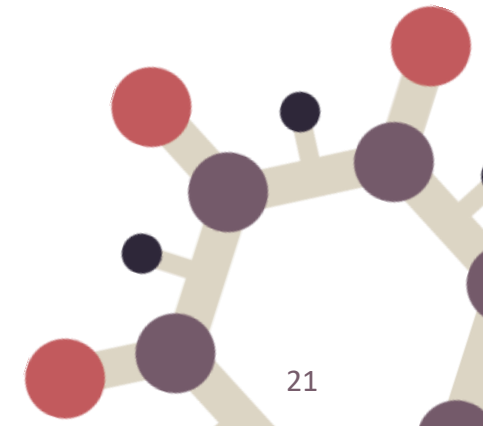
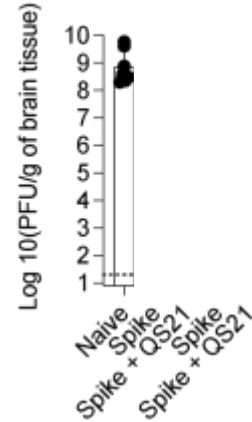
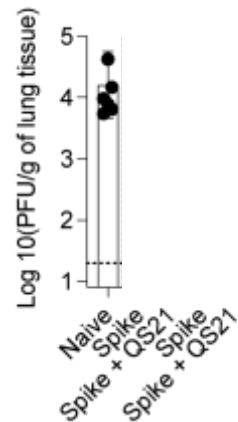
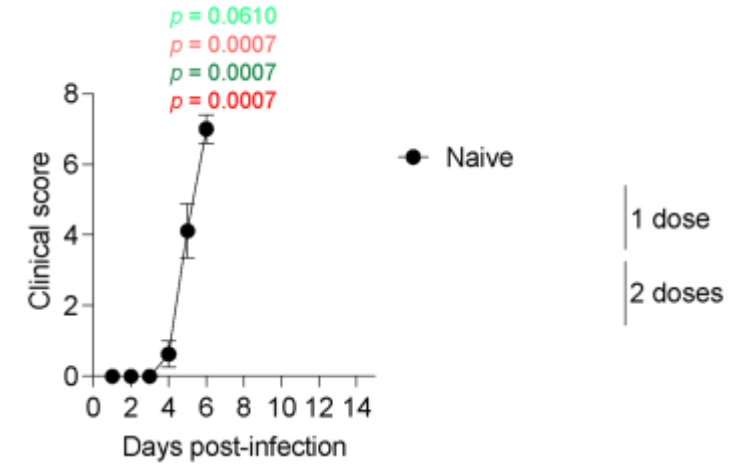
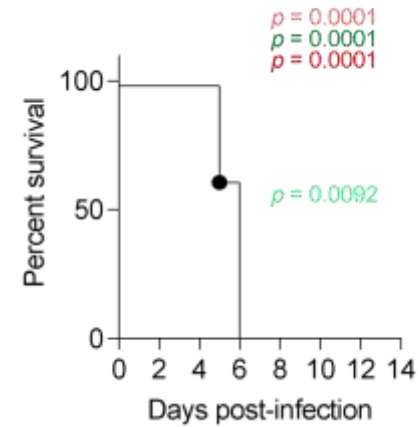
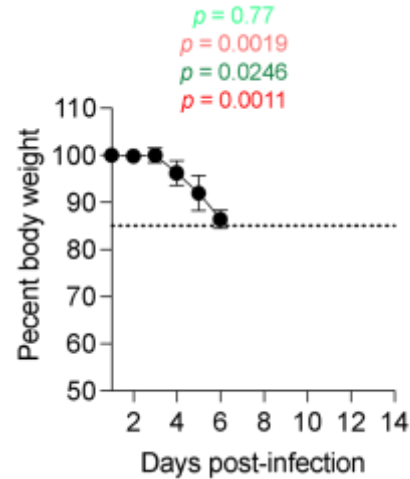
- Virus neutralisation:

- Good neutralization of 614D, 614D and B.1.1.7 isolates
- Lower neutralization of Beta isolates – mouse strain difference?



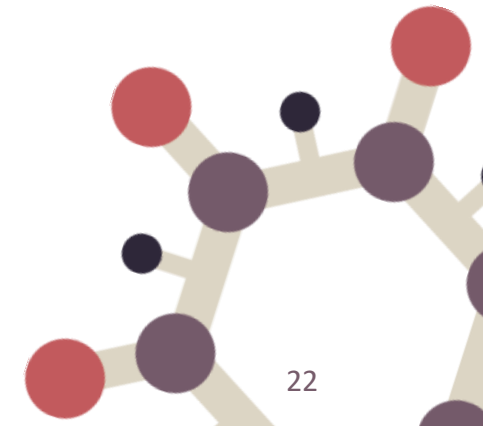
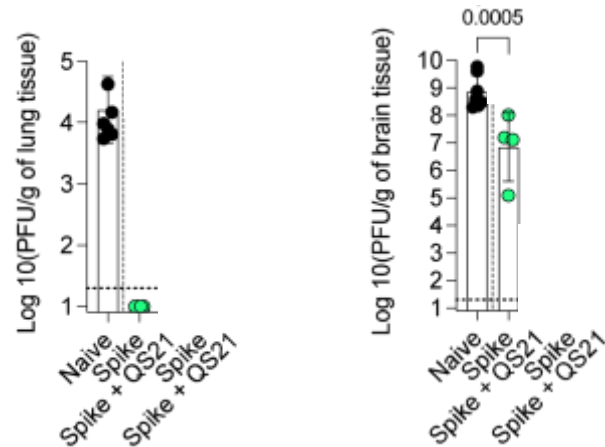
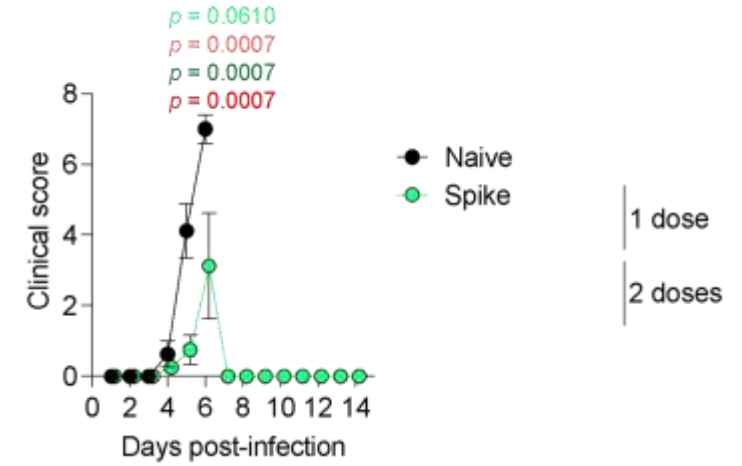
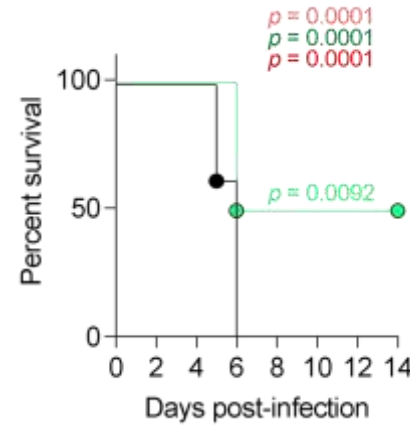
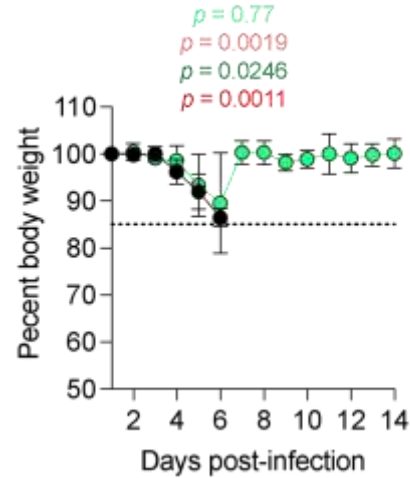
Protection from lethal SARS-CoV-2 challenge

- 1-dose groups:
 - 50% survival in unadjuvanted groups
 - 100% survival and protection from weight loss and clinical signs of infection in adjuvanted groups
- 2-dose groups:
 - 100% survival and protection from weight loss and clinical signs of infection in both unadjuvanted and adjuvanted groups
 - No virus detected in lungs or brain



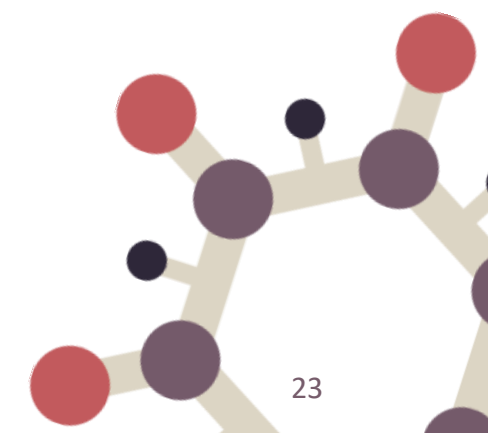
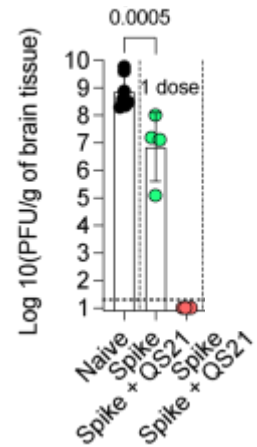
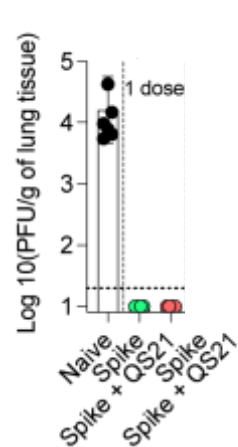
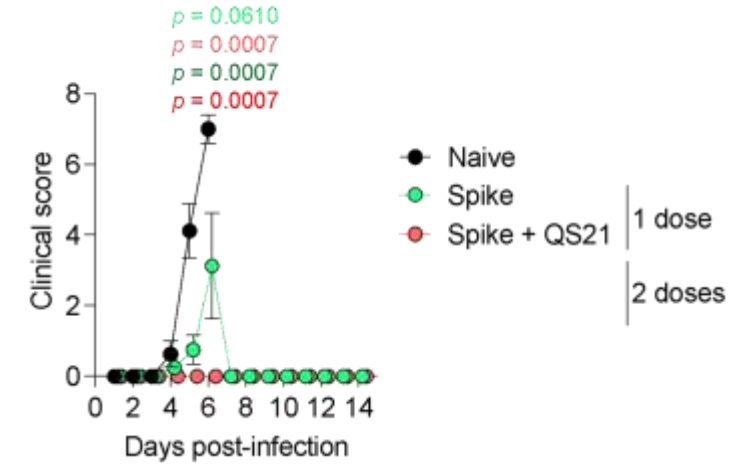
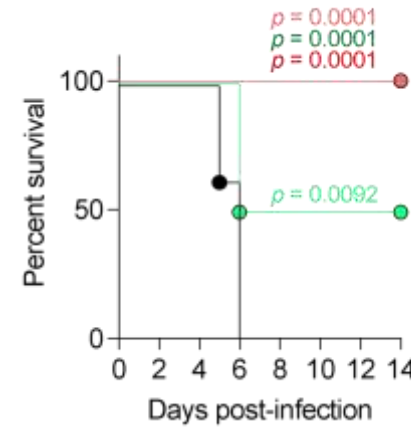
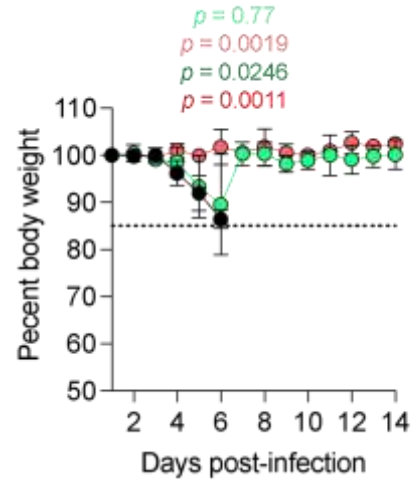
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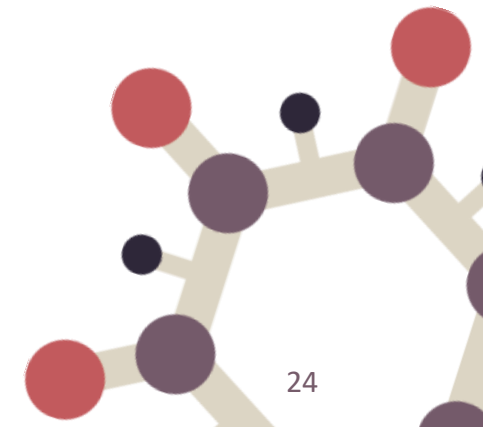
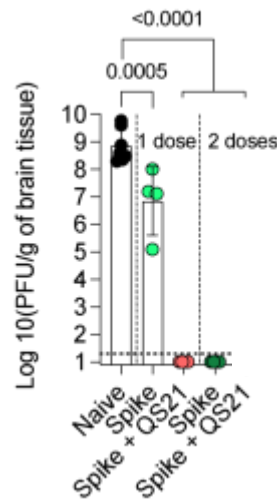
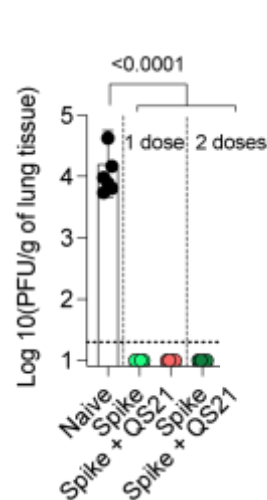
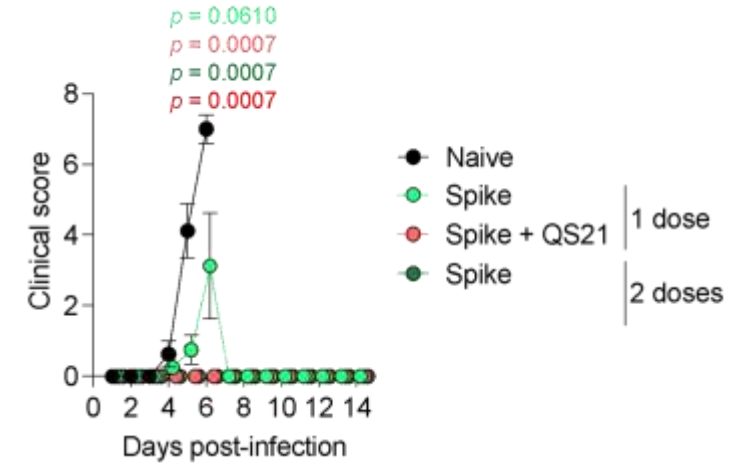
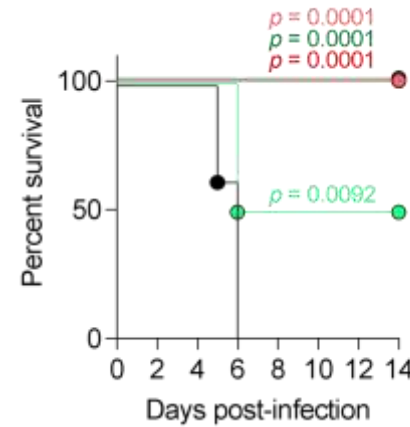
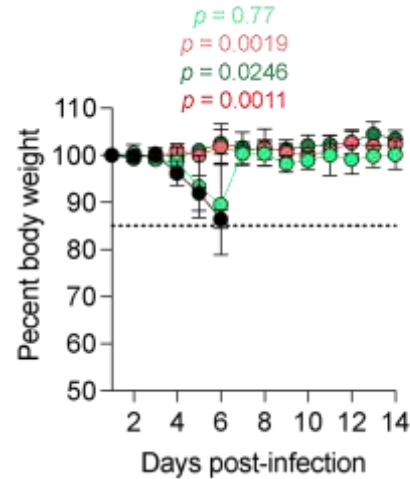
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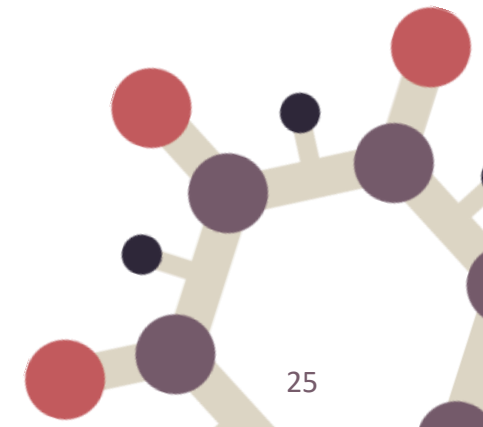
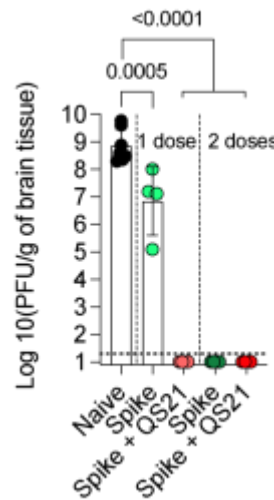
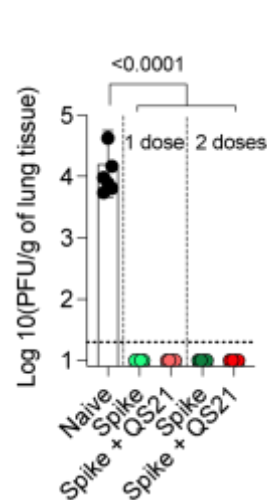
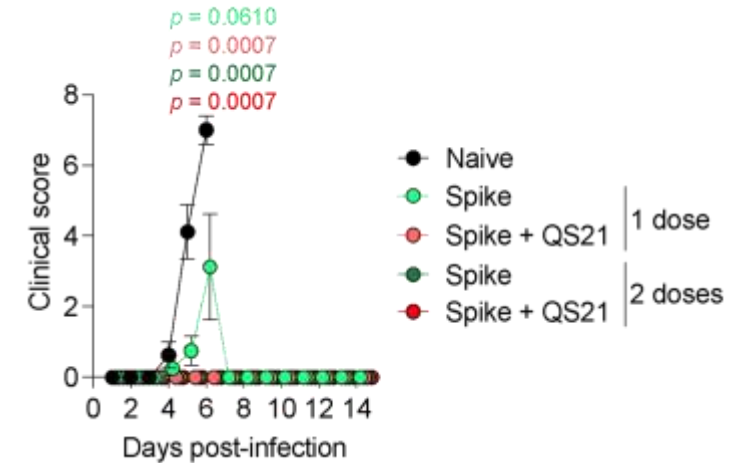
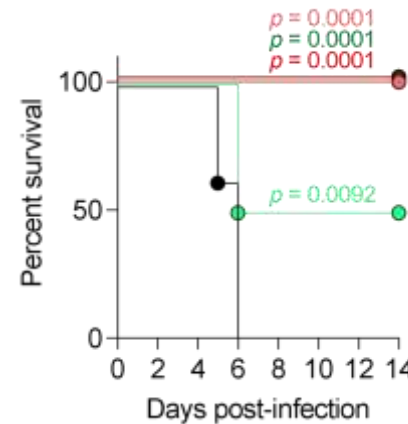
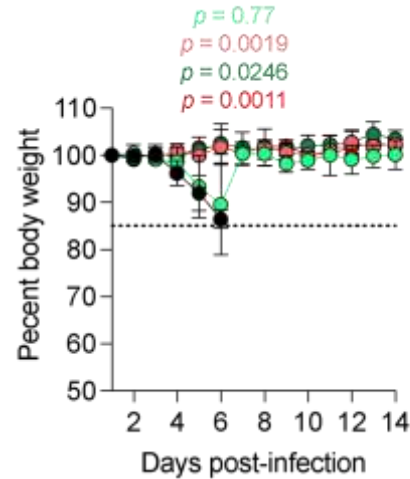
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Conclusions

✓ Excellent stability profile

95% recovery after storage of HD-MAPS for **1 week at 40°C and 30 days at 25°C**

✓ HexaPro HD-MAPs induce **neutralizing antibodies after 1 dose**, boosted after 2 doses

Response is **faster and more potent than ID injection**.

Adjuvant (QS21) not required

Serum neutralized 614G, Alpha, Beta, Delta, Kappa, Lambda, and Omicron variants

✓ HD-MAPs protect from lethal SARS-CoV-2 challenge :

100% survival and **protection from weight loss and clinical signs of infection** after a **single**

Hexapro HD-MAP dose with adjuvant or two doses of HexaPro HD-MAP, either with or without adjuvant.

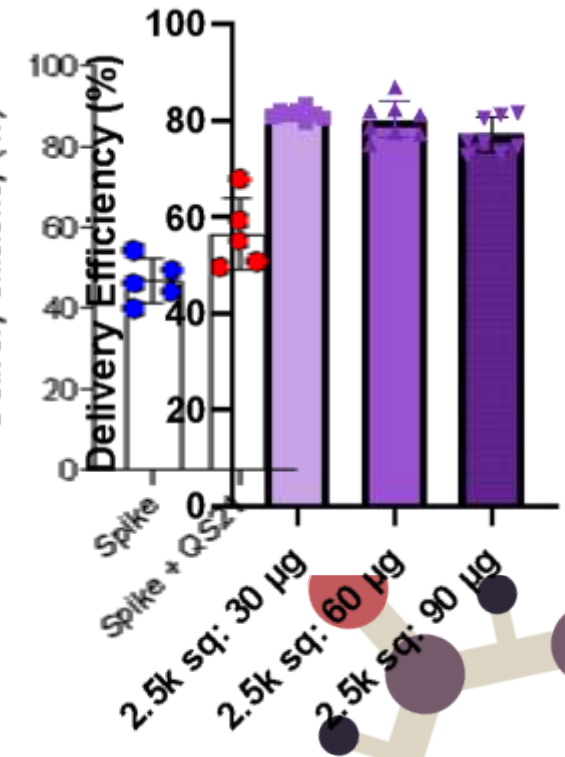
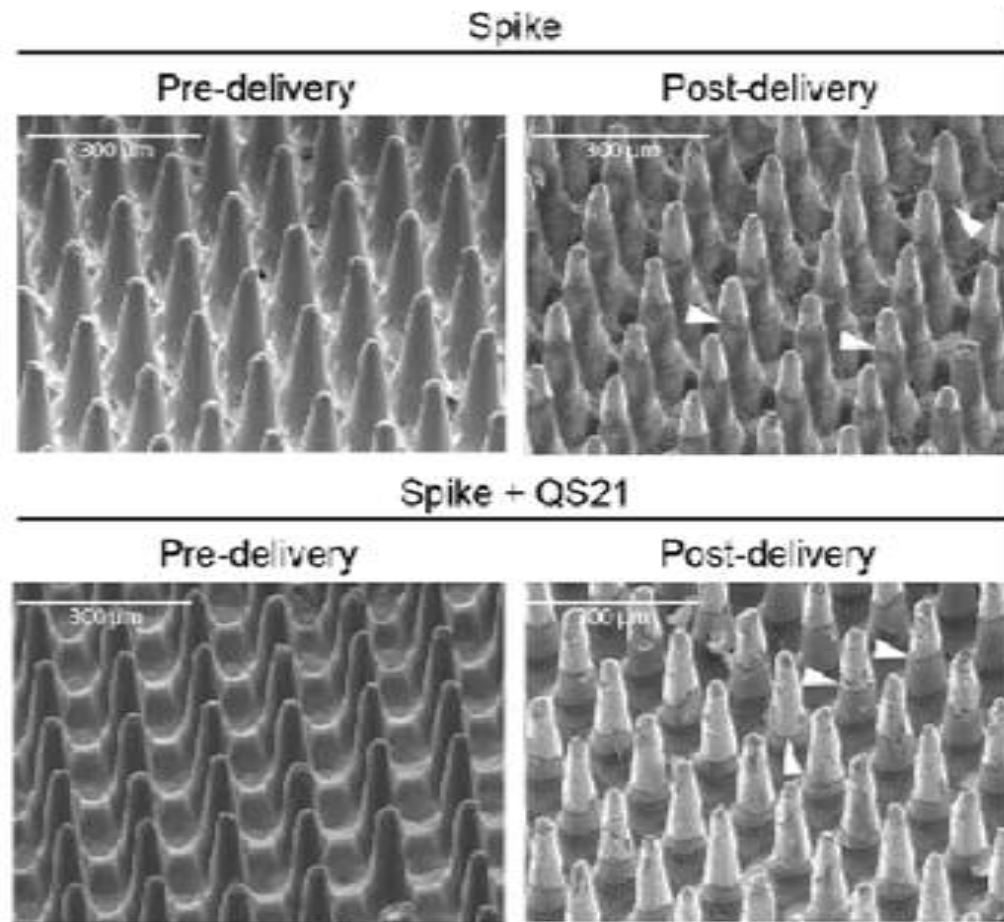
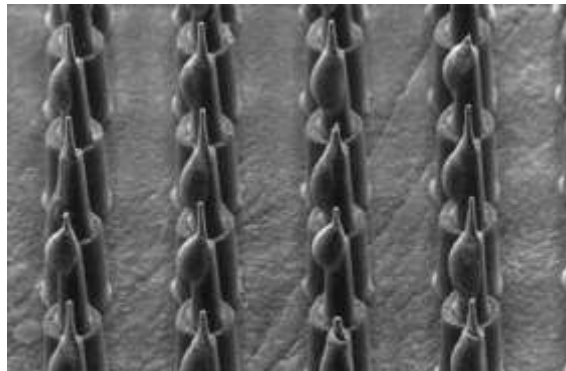
✓ **Formulations and assay transferred to Vaxxas for phase 1 clinical evaluation of Hexapro as a HD-MAP COVID-19 booster**



Translation of Preclinical to Clinical

Vaccine coating optimisation

- Transition from research style jet coating to printing vaccine to projection tips
 - Formulation 0.25 % HSA
 - Direct printing resulting



Translation of Preclinical to Clinical

Aim:

Demonstrate that HD-MAP delivered HexaProSpike can act as a booster dose.

Study overview:

Participants received 1 dose of 15 or 45 µg via HD-MAP

Readouts:

Bleeds and saliva collected at 0, 7, 28, 56, 90 for immunogenicity

Serum IgG, virus neutralisation, saliva IgA

- Study requirements

Inclusion criteria: Inclusion participants who have received COVID mRNA vaccine no less than four (4) months prior

Exclusion criteria: participants who have been had COVID since the last vaccination

On study entry requirement: On study COVID screening

Groups	HD-MAPs	Dose
Group 1 (n=15)	1 x Hexapro HD-MAP 2 x uncoated HD MAPs	15 µg
Group 2 (n=15)	3 x Hexapro HD-MAPs	45 µg
Group 3 (n=14)	3 x uncoated HD-MAPs	control



Estimating the Economic and Public Health Impact of Microarray Patch (MAP)-Administered Vaccines in Pandemics

White Paper by Avalere Health; March 2022

White Paper by Avalere Health; March 2022

“Through dose-sparing capabilities, streamlined storage and distribution, and simplified administration, MAP vaccines could mitigate the public health and economic consequences of future pandemics.”

White Paper by Avalere Health; March 2022

If We Had Used MAPs at Start of SARS-CoV-2 Pandemic

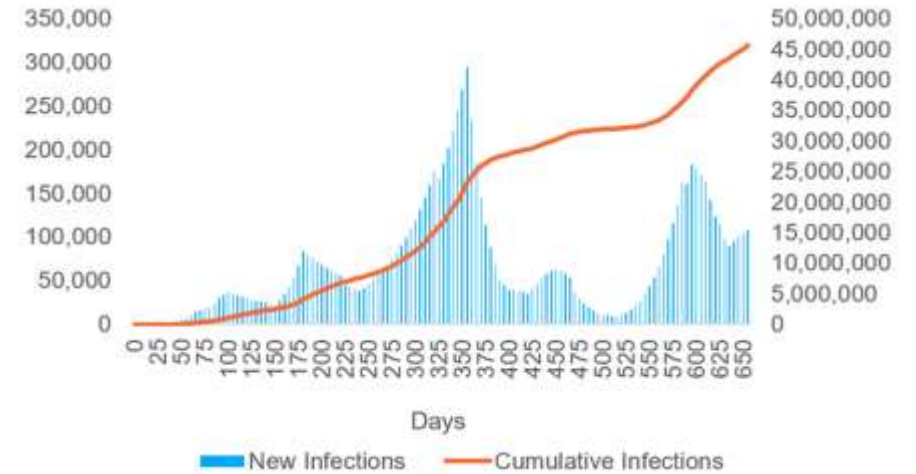
16.4 million
fewer cases

200,000
fewer deaths

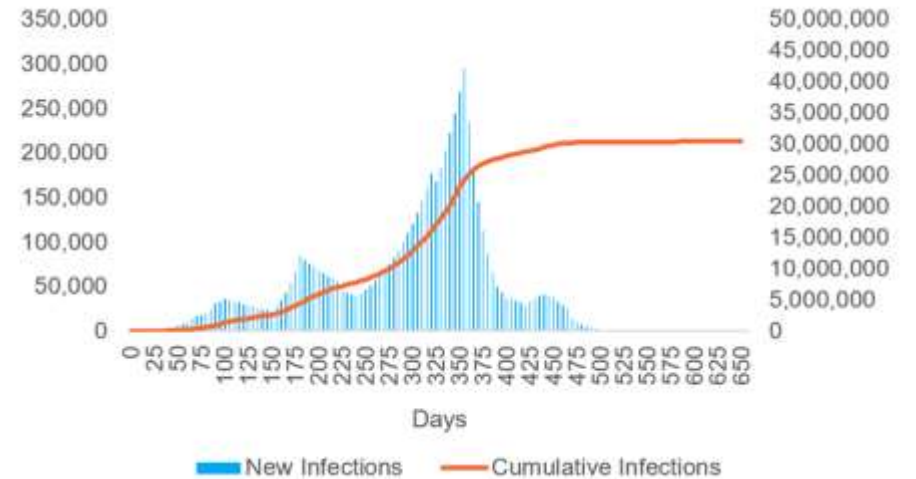
Reduced duration by **150** days

>\$500 billion reduction
in 2-year US economic impact

Baseline Infections, New and Cumulative

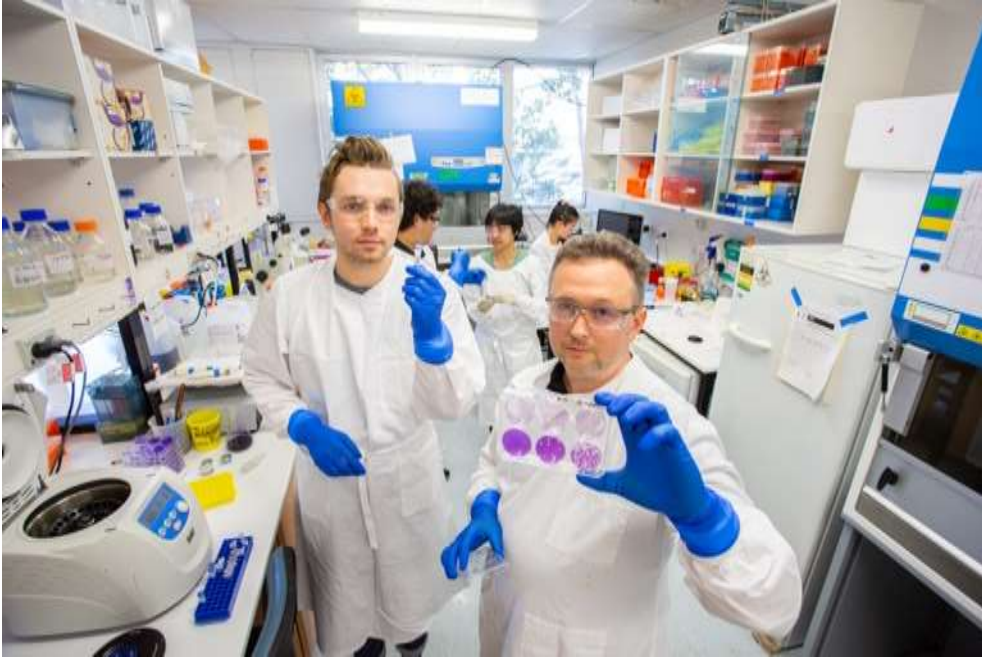


Infections with MAPs, New and Cumulative

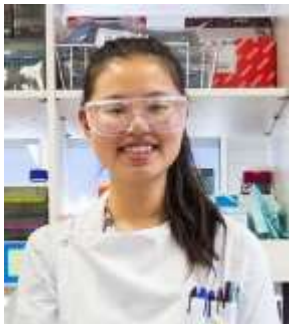


Acknowledgements

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Guneet Bindra



Briony Joyce



Paul Young



Aleksandra Todorovic



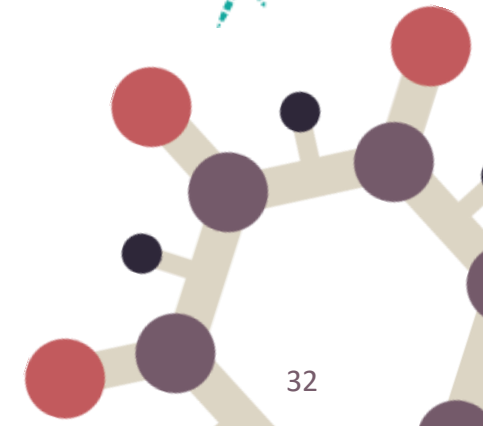
Danushka Wijesundara
Vaxxas@UQ



Andrea Corner



Create change



WE WOULD LIKE TO THANK THE FOLLOWING COMPANIES
FOR SUPPORTING THIS EVENT



THANK YOU

Thank you to our speakers and the audience for engagement and questions.

There will be a very short survey coming after the event closes and we look forward to hearing your feedback.

The next IC event will be “*Title*” on DATE.

Subscribe to the Immunisation Coalition Newsletters for more information.

Good evening and stay safe.