The effect of vaccine platform on boosting of the immune response to SARS-CoV-2

Alex Sigal

Africa Health Research Institute

University of KwaZulu-Natal

CAPRISA

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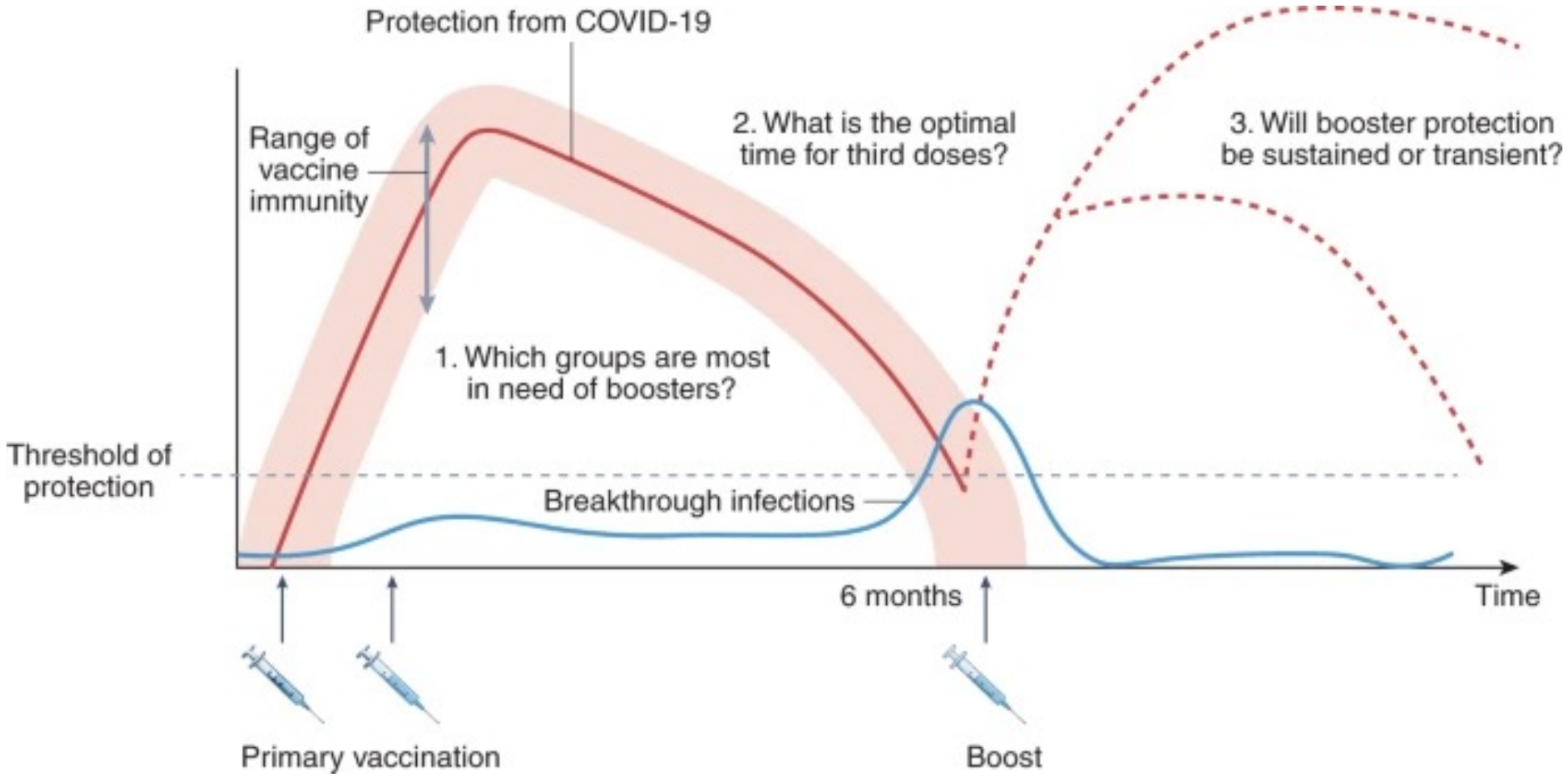
Booster after Sisonke

Boosting is key to maintain antibodies but how best to do it in everyone is still an open question

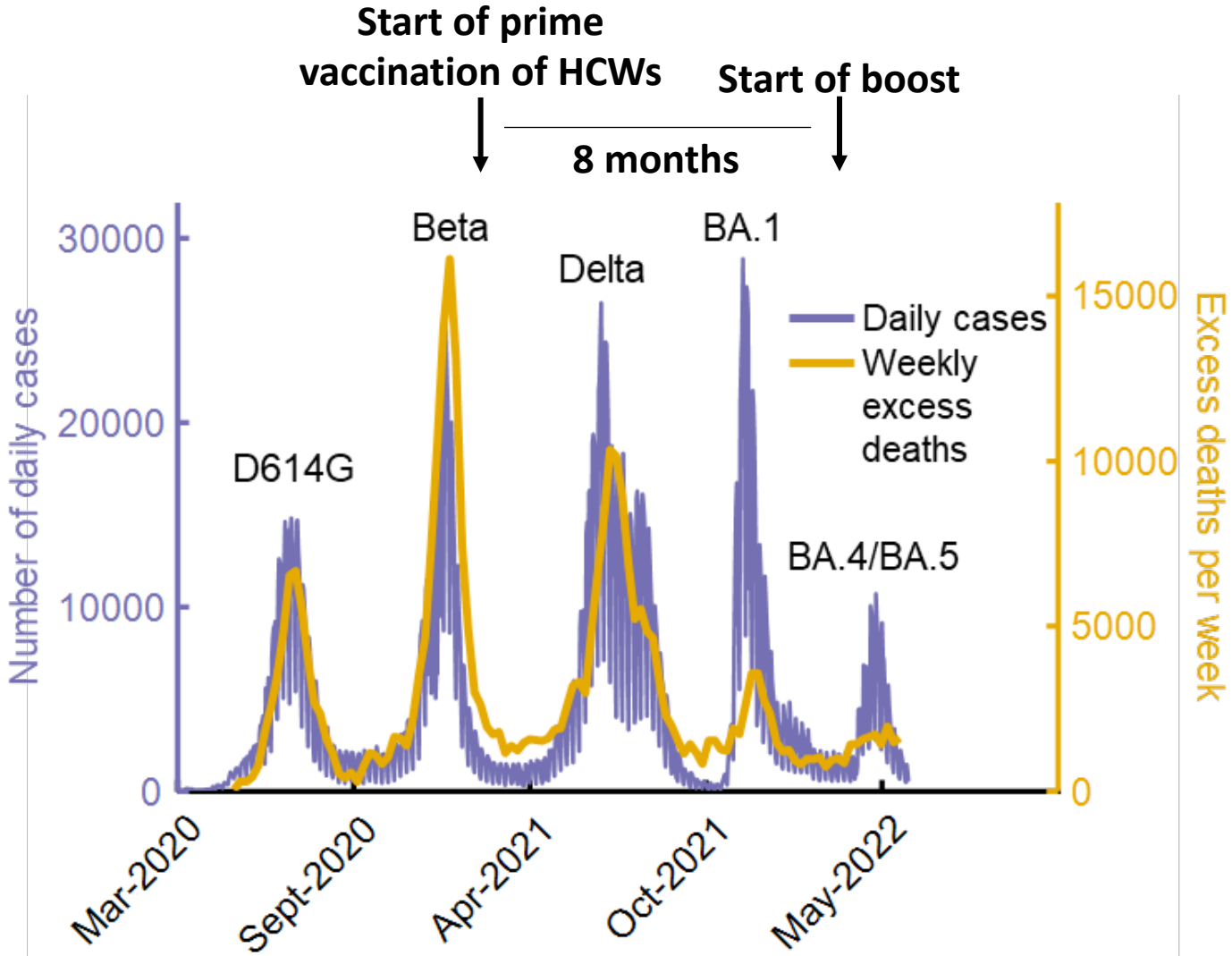


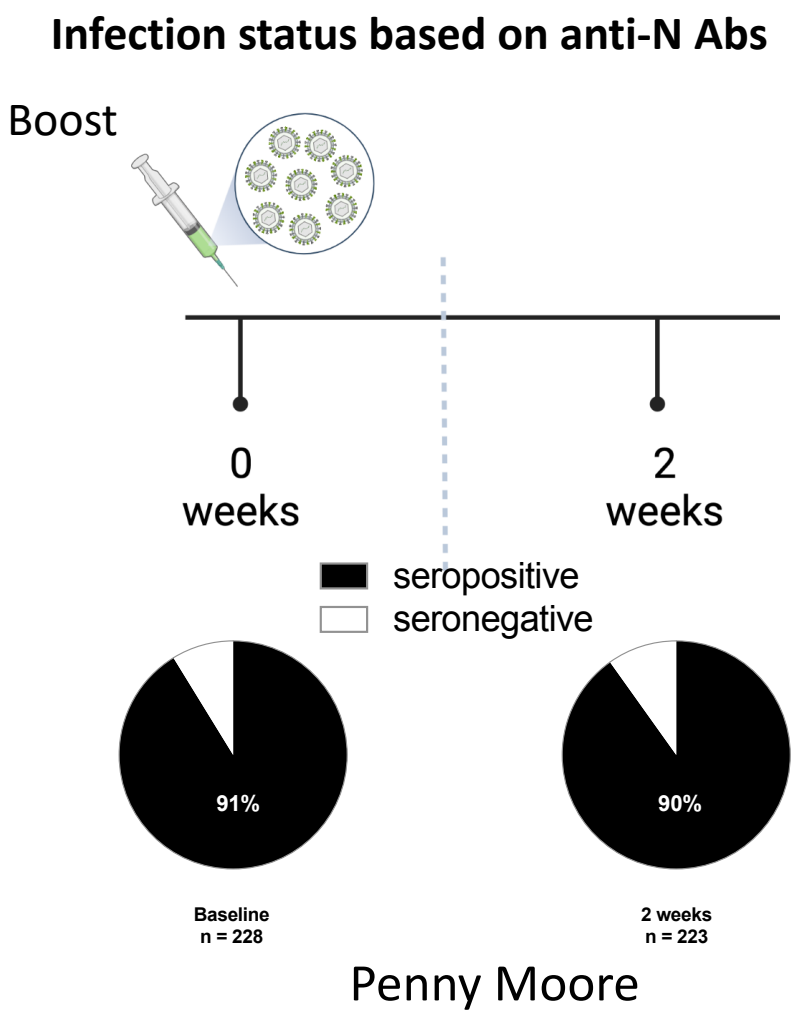
Juno and Wheatley, *Nature Medicine volume 27, p1874–1875 (2021)*

Purpose of the BaSiS immuno-bridging trial

- To test whether J&J Ad26.CoV2.S adeno-vectored vaccine (homologous boost) or Pfizer BNT162b2 mRNA vaccine (heterologous boost) works better at boosting Ad26.CoV2.S prime immunity
- To test whether HIV interferes with vaccine immunogenicity
- To test whether halving the dose makes a difference

Most most participants will have hybrid immunity





Penny Moore

We investigated the booster response in people living with HIV and HIV negative trial participants

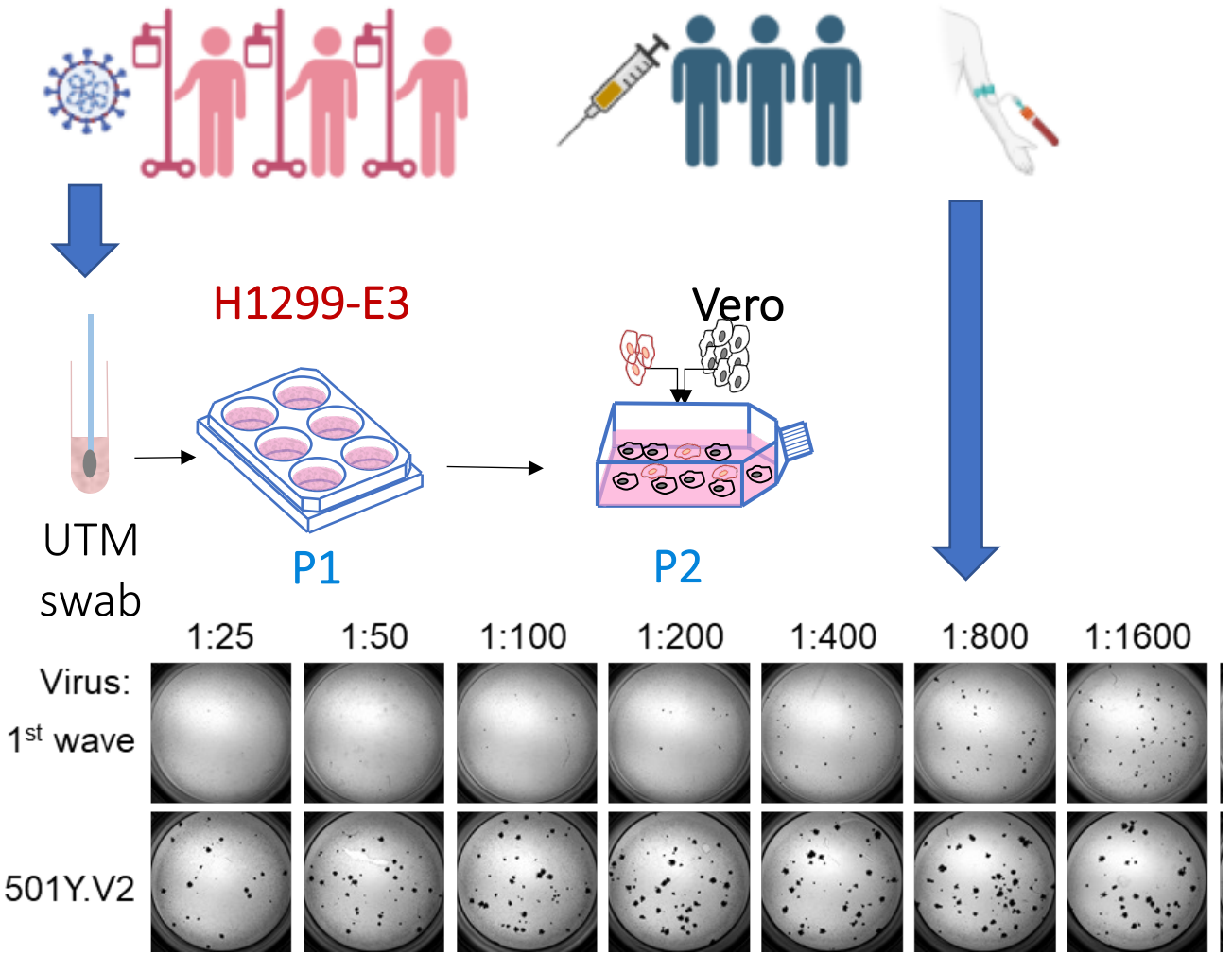
	Pfizer BNT162b2 FULL DOSE	Pfizer BNT162b2 HALF DOSE	J&J Ad26.COV2.S FULL DOSE	J&J Ad26.COV2.S HALF DOSE
	31	37	36	31
Age	45 (38-52)	45 (37-50)	42 (36-45)	39 (35-44)
Female	21 (68%)	33 (89%)	30 (83%)	31 (100%)
Vacc. – Boost. (days)	273 (259-287)	272 (260-294)	264.5 (253-288.5)	266 (255-282)
PLWH	**16 (52%)**	**18 (49%)**	**19 (53%)**	**16 (52%)**
Baseline				
CD4 (PLWH only)	**627 (542-874)**	**697 (401-757)**	**708 (564-938)**	**638 (471-754)**
Viremic	1 (8%)	3 (17%)	0 (0%)	3 (20%)

We used neutralization of live virus to detect the levels of SARS-CoV-2 neutralizing antibodies

1) Cohort/trial

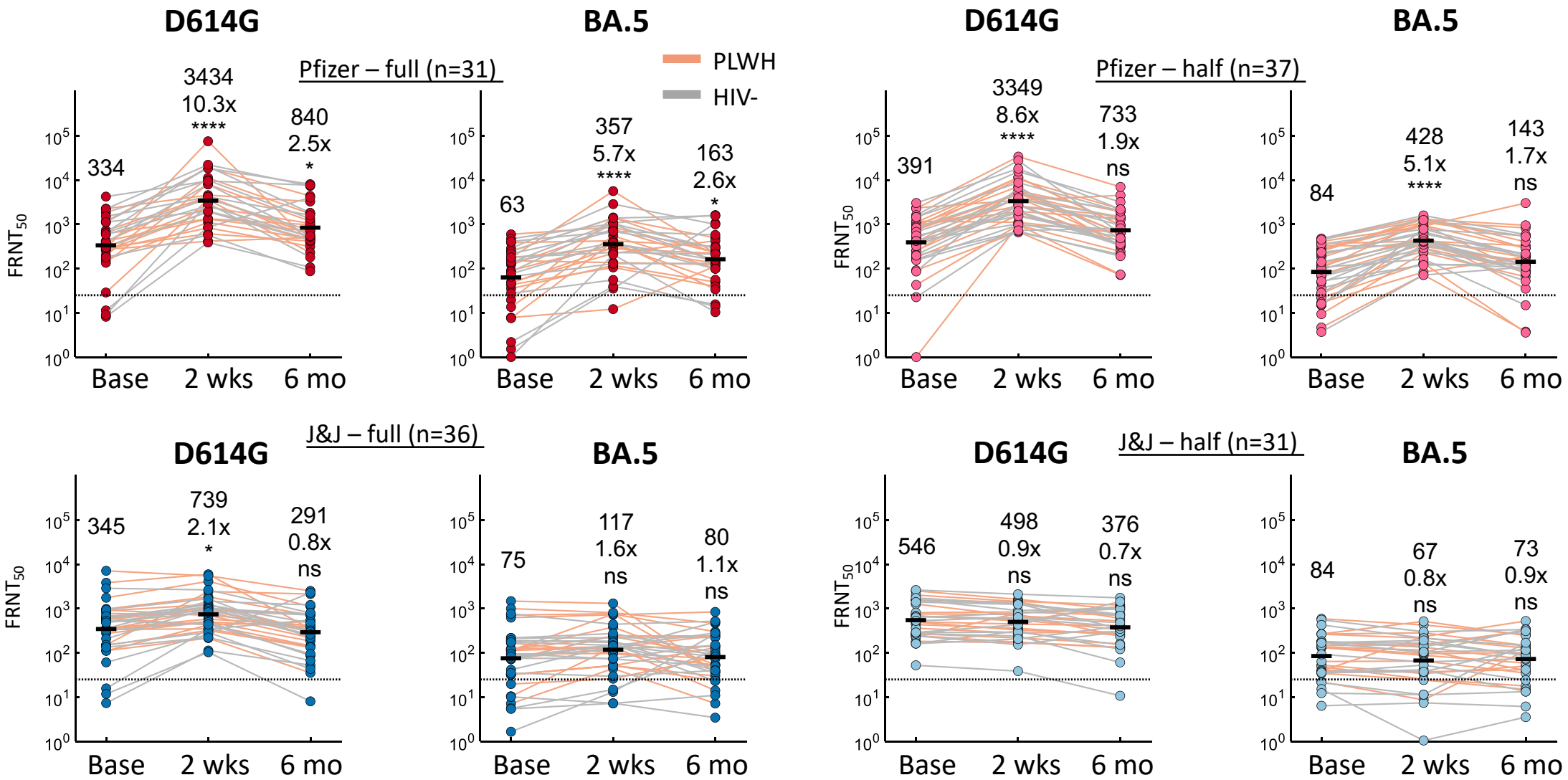
2) Pathogen isolation in BSL3 and sequencing

3) Live virus assays: antibodies/ pathogenicity

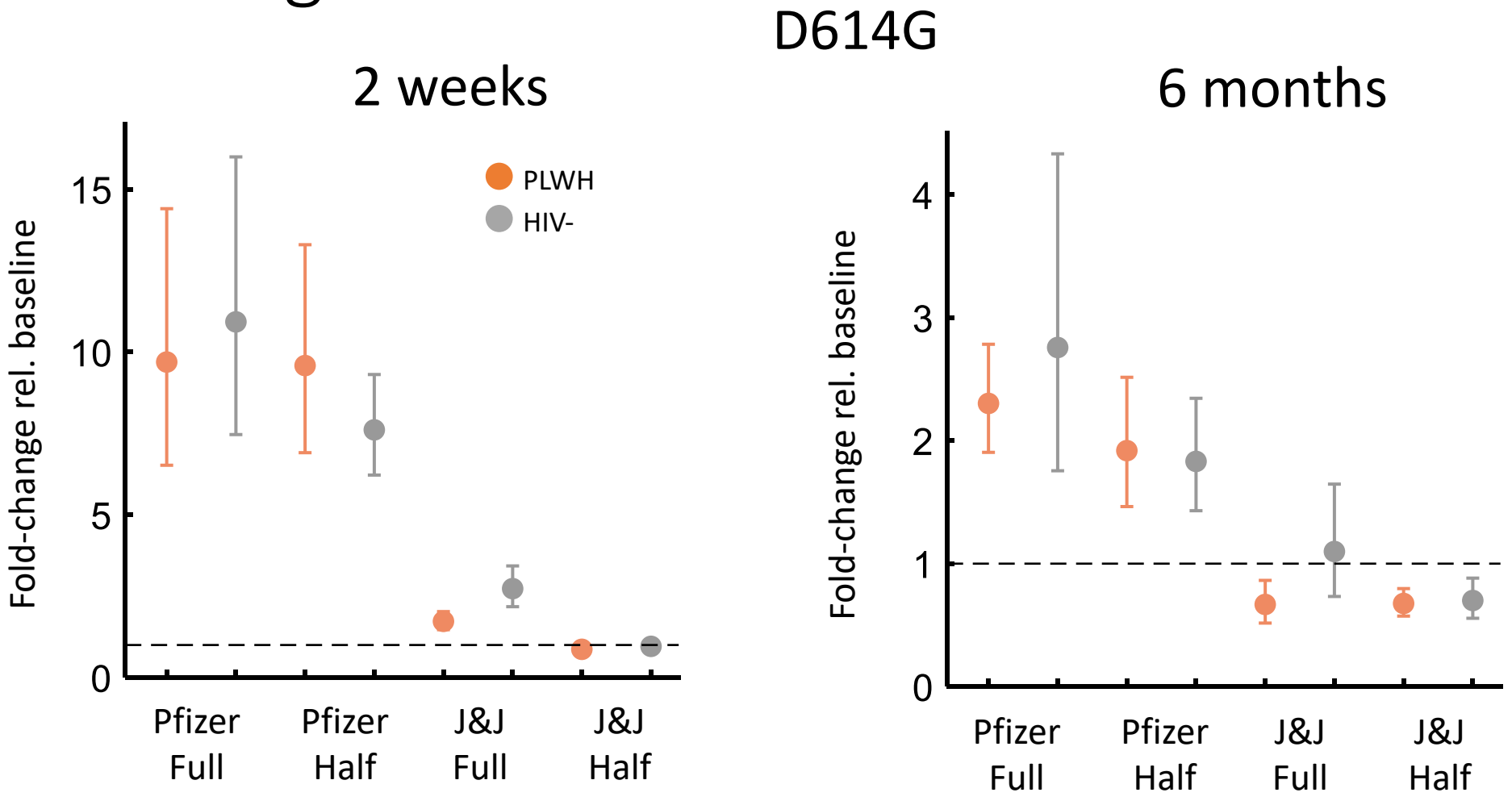


Cele…Sigal, *Nature* 2021; 593(7857):142-146

Full dose BNT162b2 results in the highest fold-increase after boosting



HIV status has a minor effect on boosting in all boost regimens



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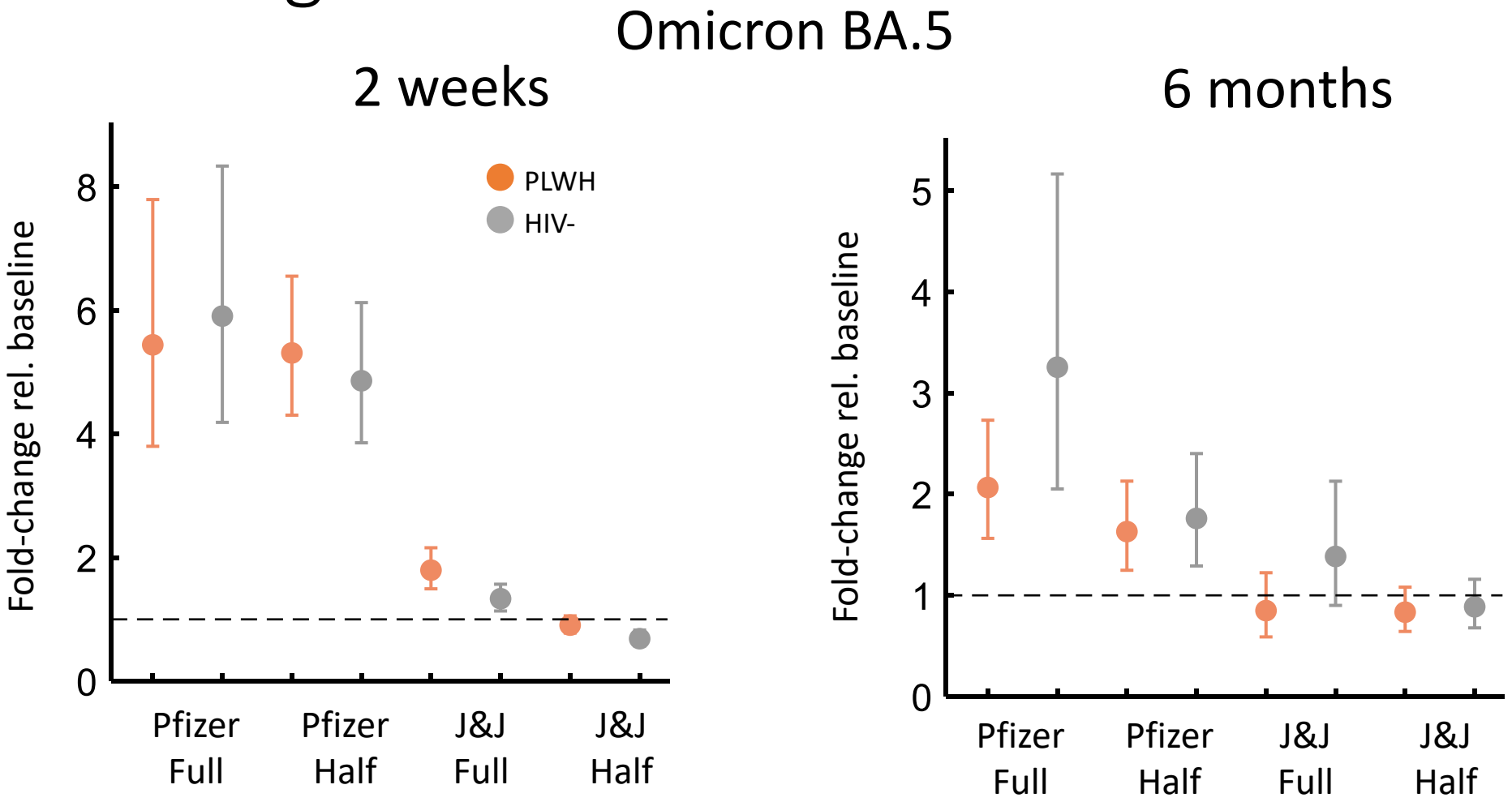
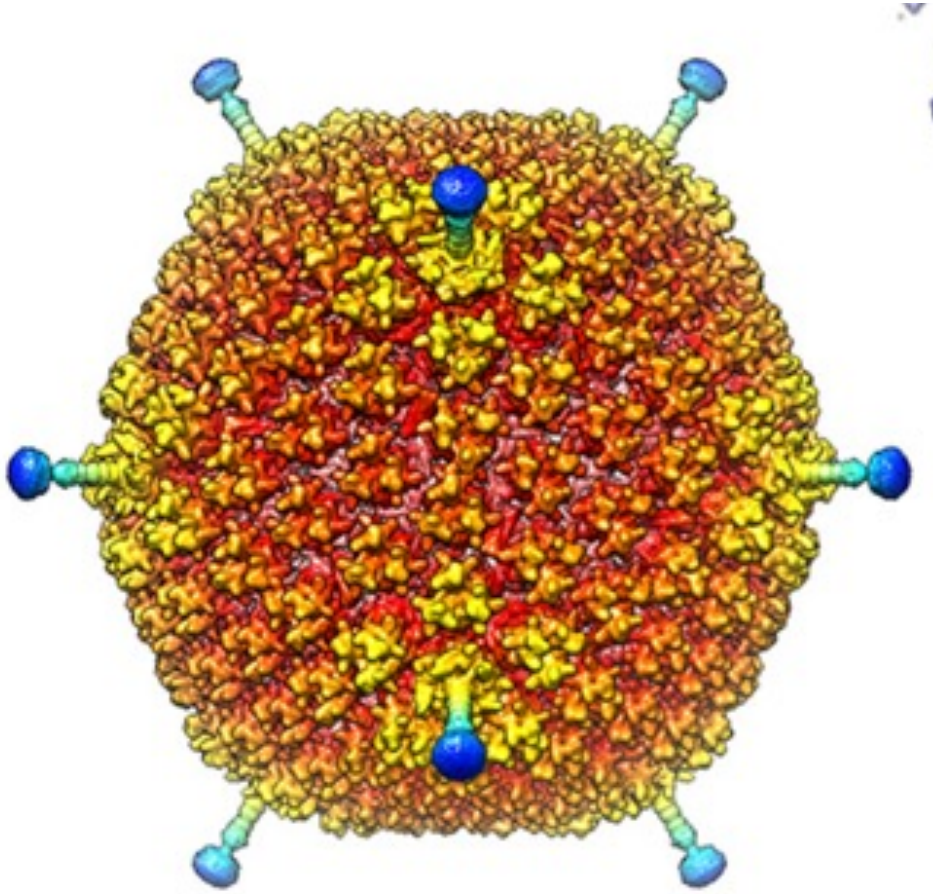
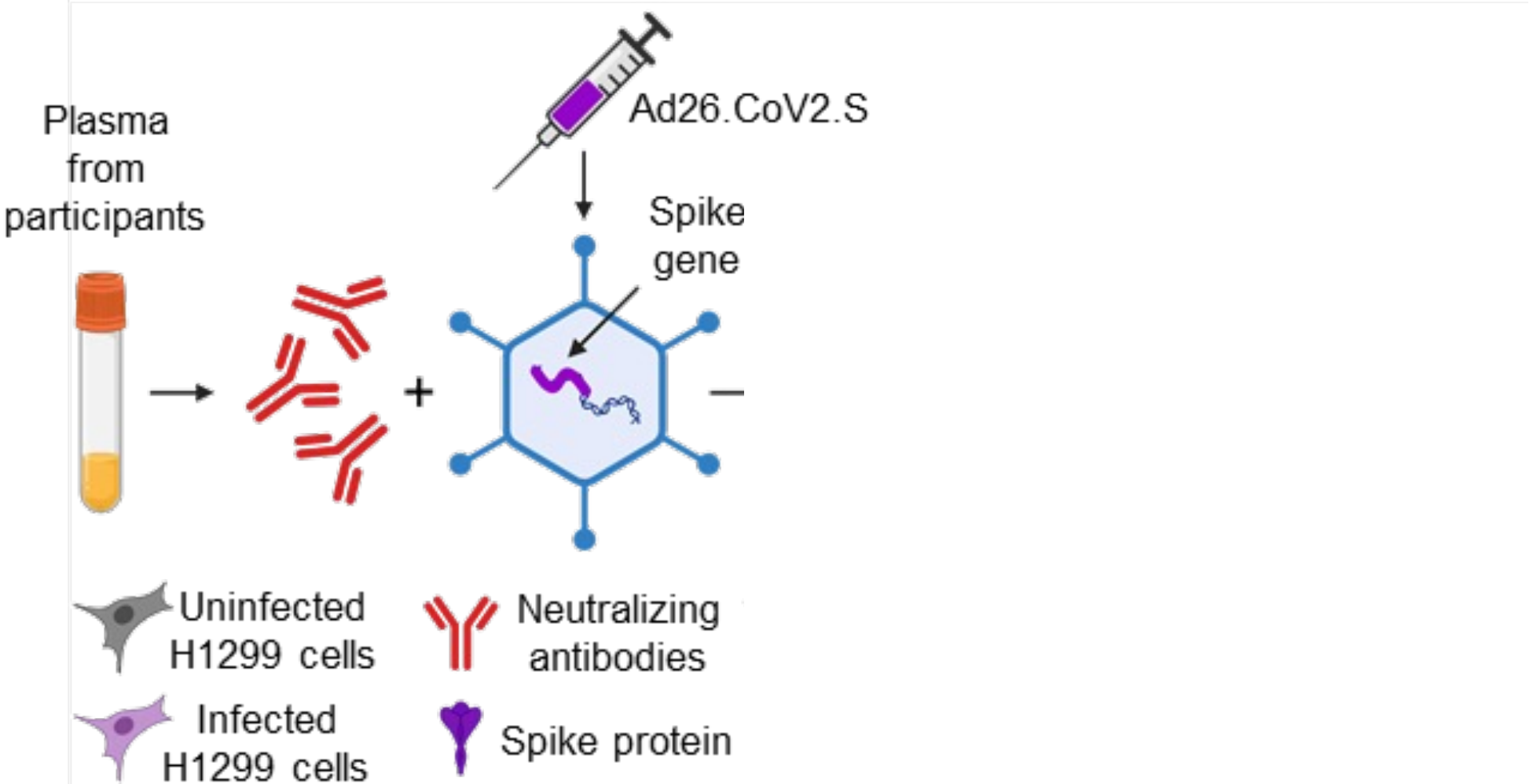


Why didn’t Ad26.CoV.2 give a better response?

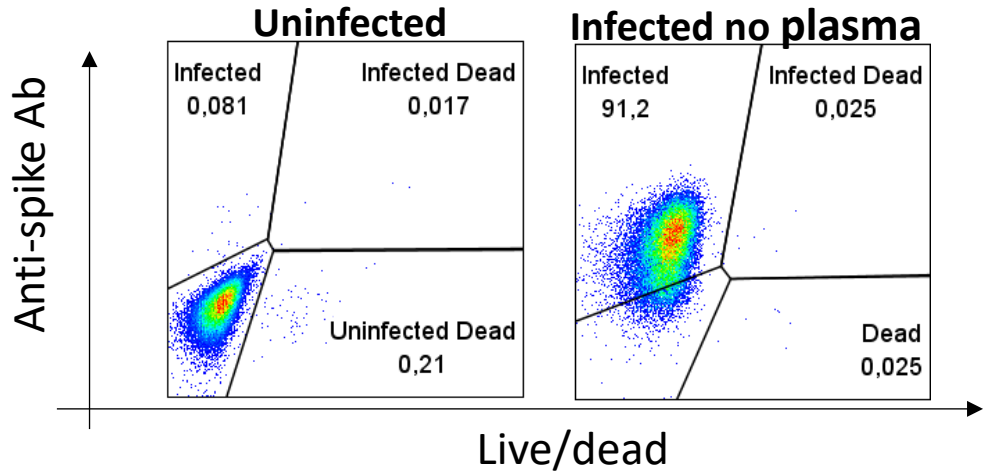
Ad26.CoV2.S is a virus and would be expected to trigger an immune response to itself and therefore be less effective on second administration



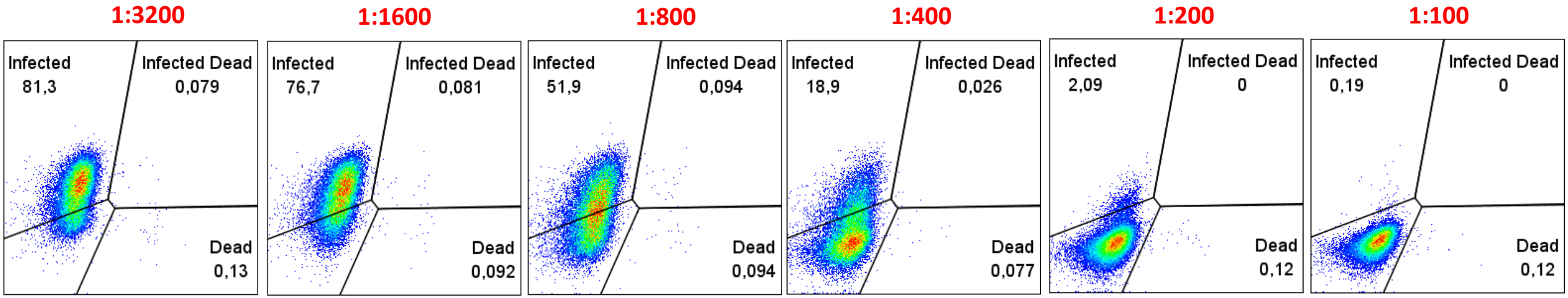
Developed a system to detect successful infection by Ad26.CoV2.S



Addition of vaccinated plasma decreases Ad26.CoV2.S infection in a concentration dependent manner



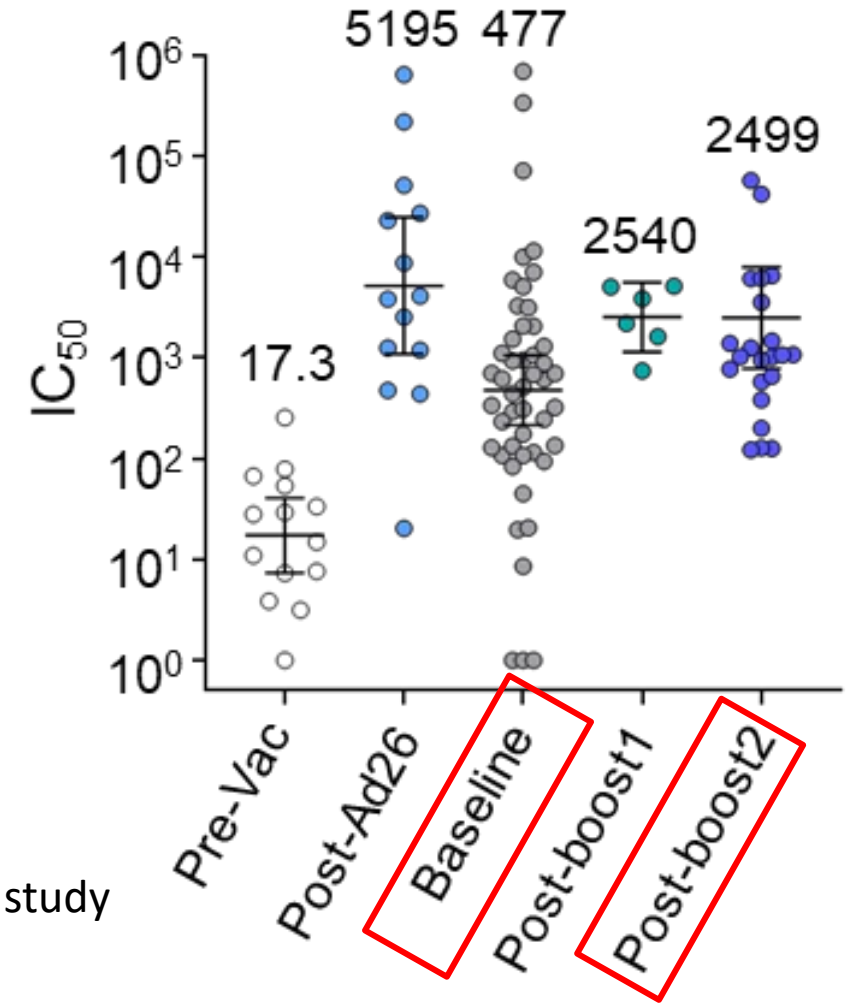
Participant 5735-1052 baseline plasma



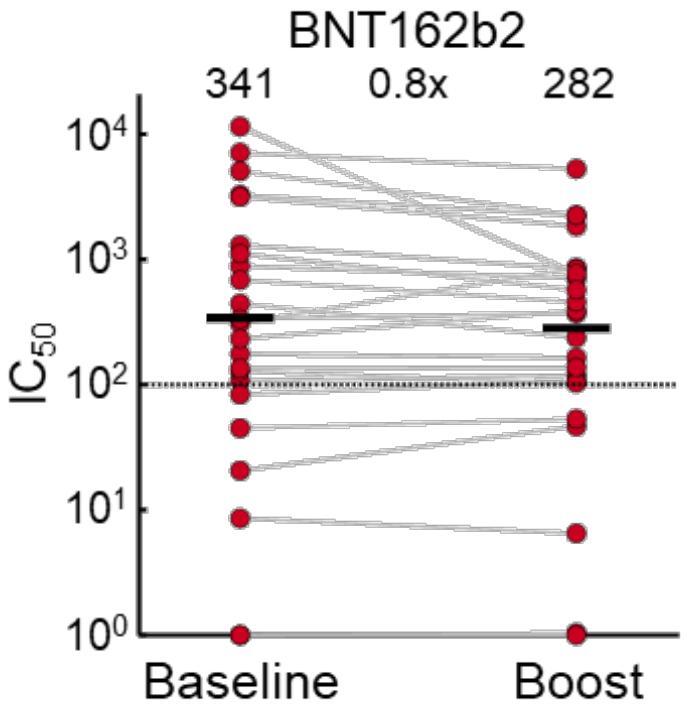
Criteria to determine whether anti-vector immunity interferes with Ad26.CoV2.S boosting

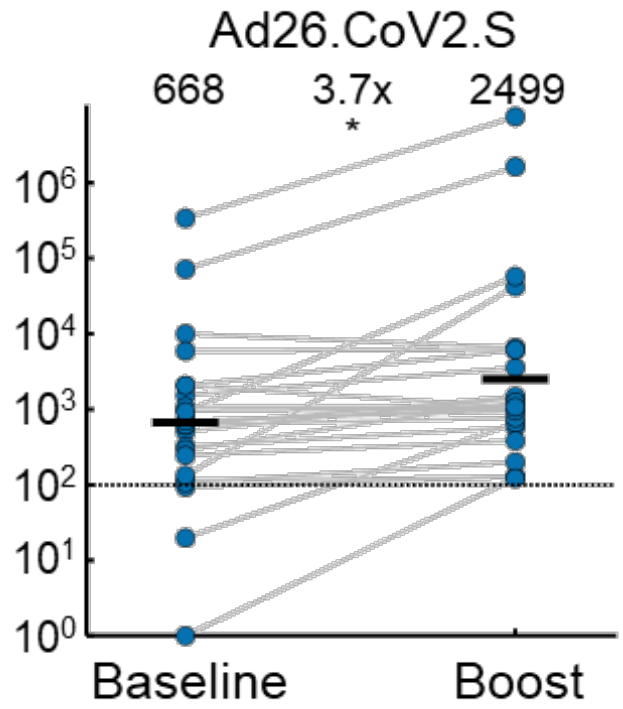
- ☐ Does Ad26.CoV2.S vaccination increase antivector immunity?
- ☐ Does boosting with Ad26.CoV2.S further increase immunity?
- ☐ Does Ad26.CoV2.S immunity inversely correlate with ability of boost to elicit neutralizing antibodies?

Increase in anti-vector neutralization after prime vaccine and booster dose



BaSiS study





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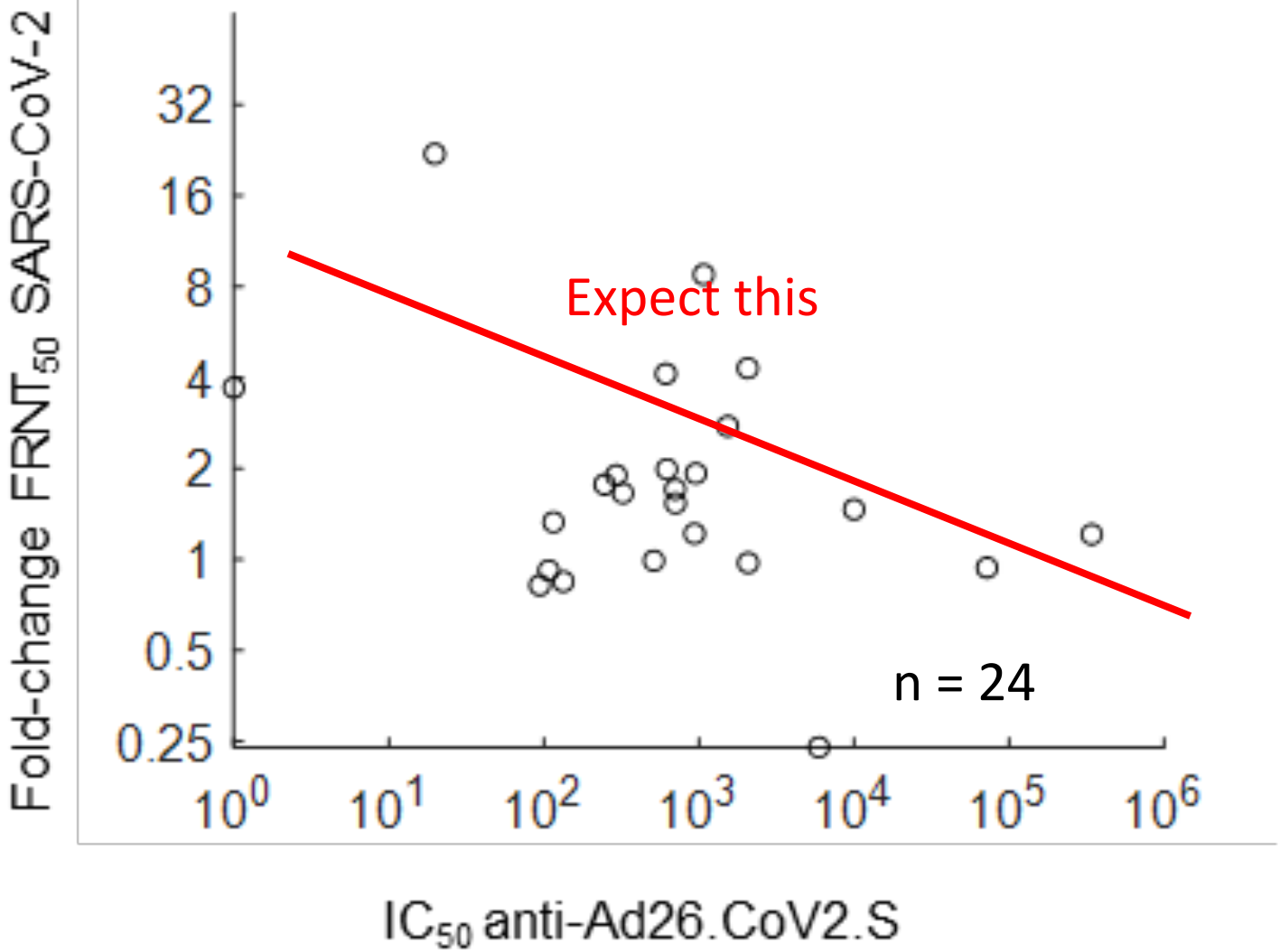
SARS-CoV-2 neutralization post-Ad26.CoV2.S boost does not correlate to anti-Ad26 neutralization response



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Not the first to see lack of correlation

PLOS MEDICINE

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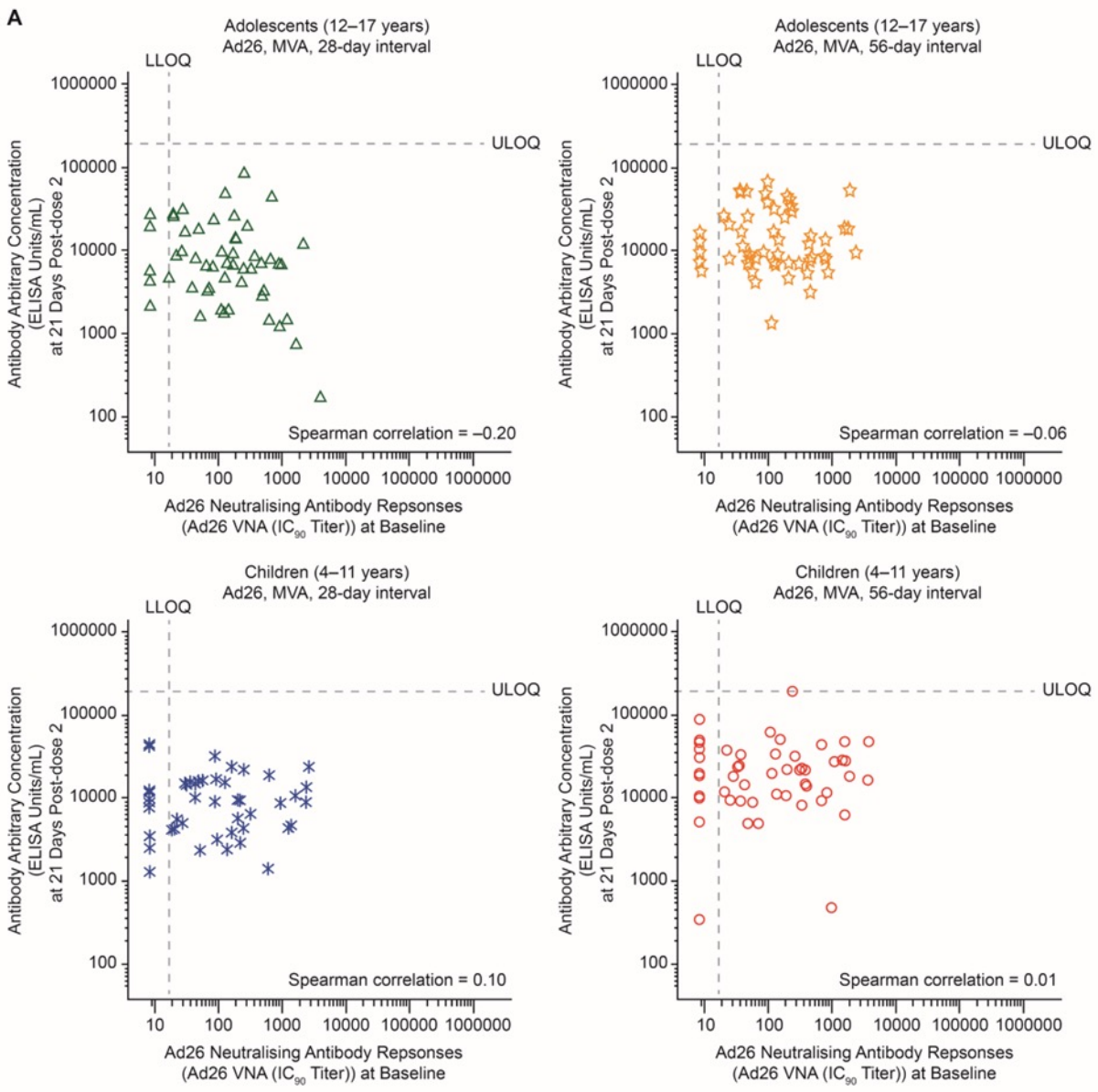
RESEARCH ARTICLE

Safety and immunogenicity of 2-dose heterologous Ad26.ZEBOV, MVA-BN-Filo Ebola vaccination in healthy and HIV-infected adults: A randomised, placebo-controlled Phase II clinical trial in Africa

Houreratou Barry, Gaudensia Mutua, Hannah Kibuuka, Zacchaeus Anywaine, Sodiomon B. Sirima, Nicolas Meda, Omu Anzala, Serge Eholie, Christine Bétard, Laura Richert, Christine Lacabaratz, M. Juliana McElrath, Stephen De Rosa, [...], the EBL2002 Study group * [view all]

Published: October 29, 2021 • https://doi.org/10.1371/journal.pmed.1003813



Conclusions

- Full dose Pfizer BNT162b2 boosting is the most effective way to boost anti-SARS-CoV-2 neutralizing antibody levels of people vaccinated with Ad26.CoV2.S
- HIV infection does not have a significant impact on the neutralizing response to a booster dose in predominantly HIV controlled participants
- Anti-Ad26 vector immunity is strongly increased after a Ad26.CoV2.S prime vaccination and further increased after Ad26.CoV2.S boosting
- No significant correlation between level of anti-vector immunity and elicited SARS-CoV-2 neutralization

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