Viral Vectored Vaccines

Global Vaccine and Immunization Research Forum 2023
Incheon, Republic of Korea, 28-30 March 2023

Jerry Sadoff MD
Janssen Infectious Diseases and Vaccines
Johnson & Johnson

Advantages of non-replicating viral vector delivery of vaccine antigens

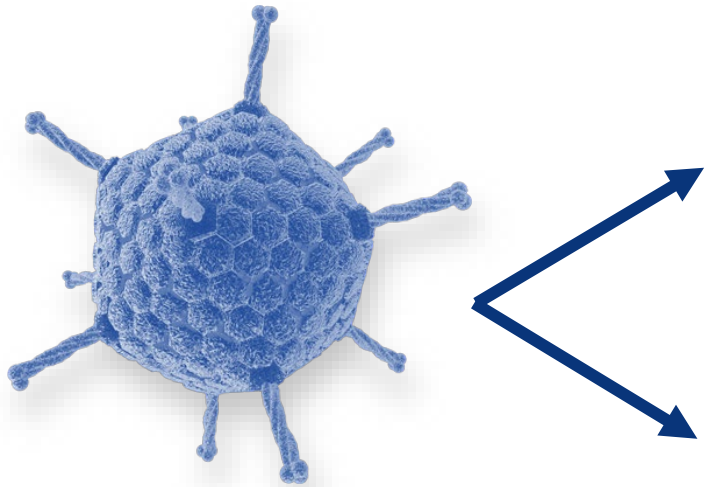
- Closer to natural infection compared to non-living vaccines
  - Lower burst of antigen than mRNA or protein based vaccines
  - Longer duration of antigen secretion
  - Vaccine antigen on the surface of cell and/or secreted from cell
    - Human cell production & processing
    - Presented in context of human cell similar to natural viral infection
- Provides persistent immune responses and booster responses
- Induction of functional and memory CD4 & CD8+ T cells in humans
- Induction of durable functional neutralizing antibody & antibodies with Fc mediated functions
- Can be delivered nasally to induce local upper respiratory immunity
- Generally well tolerated & can be given safely to immunosuppressed individuals in contrast to replicating vaccines
- Stability at 4-8 degrees
- Generic Manufacturing scalability for mass production

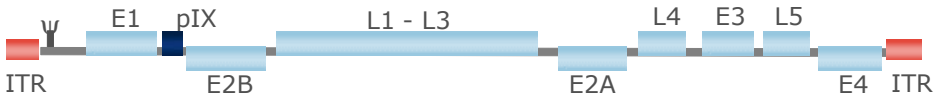
Disadvantages of non-replicating viral vector delivery of vaccine antigens

- Takes 5-12 months from DNA sequence identification to CTM & large scale manufacturing
- Antibody response to priming regimen may be quantitatively lower than protein or mRNA vaccines which does not apply to cellular responses probably related to lower levels of antigen delivery
- Ptential role of pre-existing or induced anti-vector immunity (not observed thus far)
- Very rare adverse event of VITT associated with Adeno-vectored COVID-19 vaccines which were not seen in developing world for Janssen vaccine

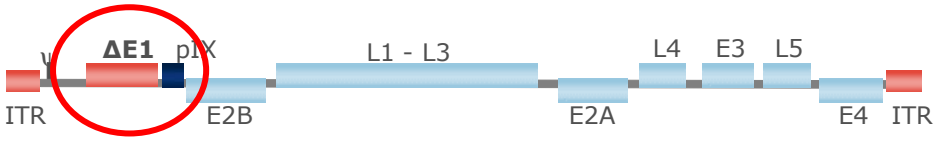
Non-replicating Adenovirus technology

- A replication deficient adenovirus as vaccine platform





Wild-type virus (**replication proficient**)



E1-deleted virus (**replication deficient**)

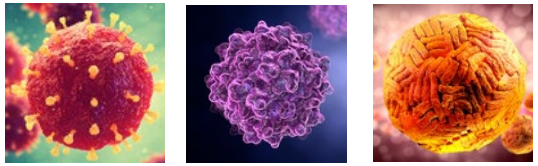
E3 can also be deleted to create more space for transgene insertion

Adenovirus

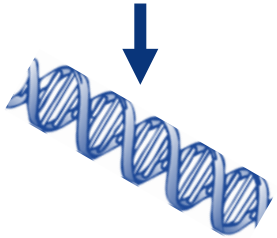
- Over 50 distict serotypes that can cause a wide range of (mild) illnesses, including respiratory infections
- Disease is usually self-limiting but can lead to complications in immuno-comprimised individuals
- > 80% between 1 and 5 years of age have antibody to one or more serotypes

AdVac Technology

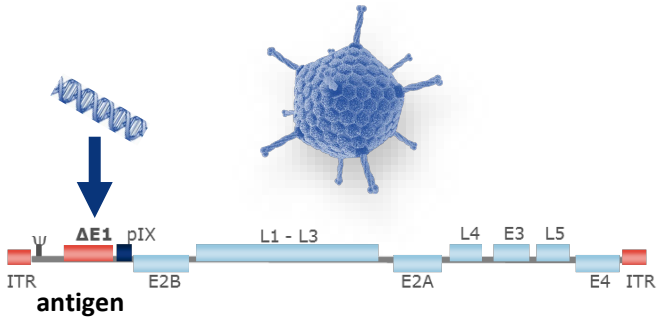
- Replication deficient Adenoviral vectors can be used as vaccine technology for delivery of antigens in human cells



Pathogen

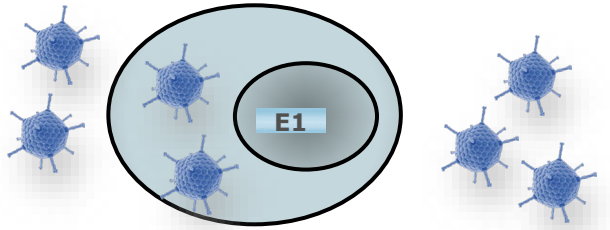


Isolate DNA coding for antigen of interest



E1-deleted Adenovirus encoding antigen of interest

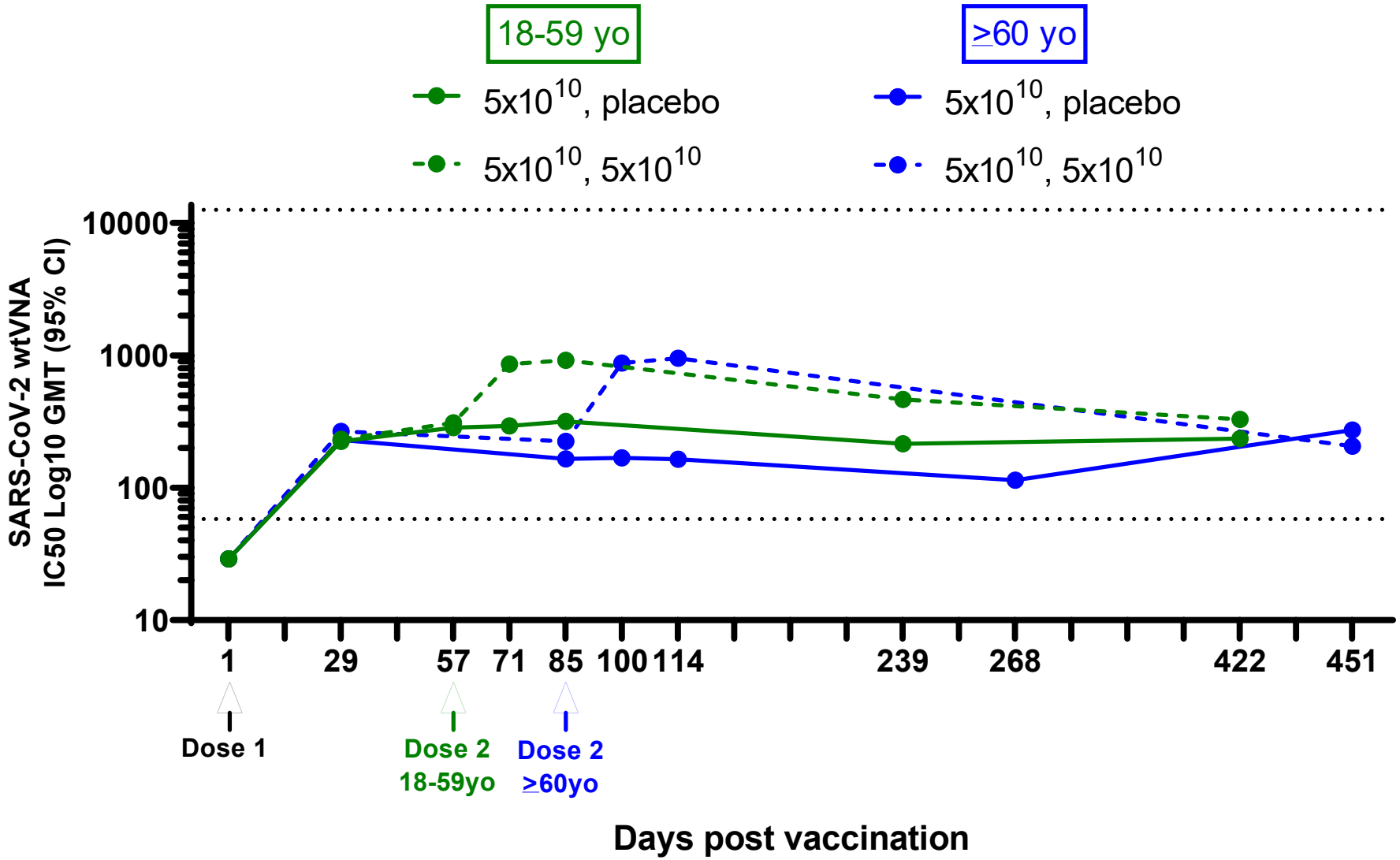
Replication on PER.C6® cells which supply E1 in trans



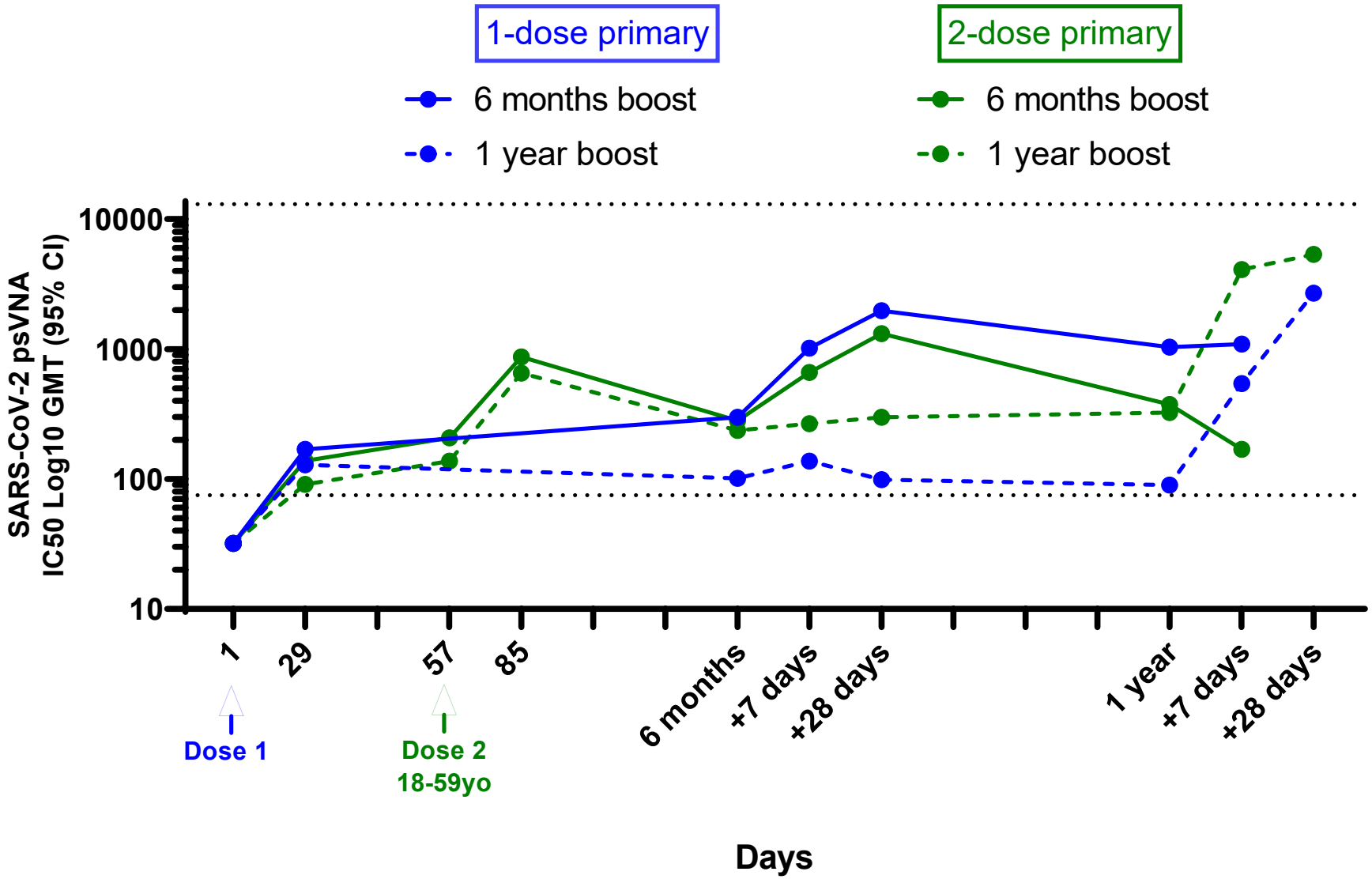
Vaccine Manufacturing

BMC Proc. 2015; 9(Suppl 9): P76.

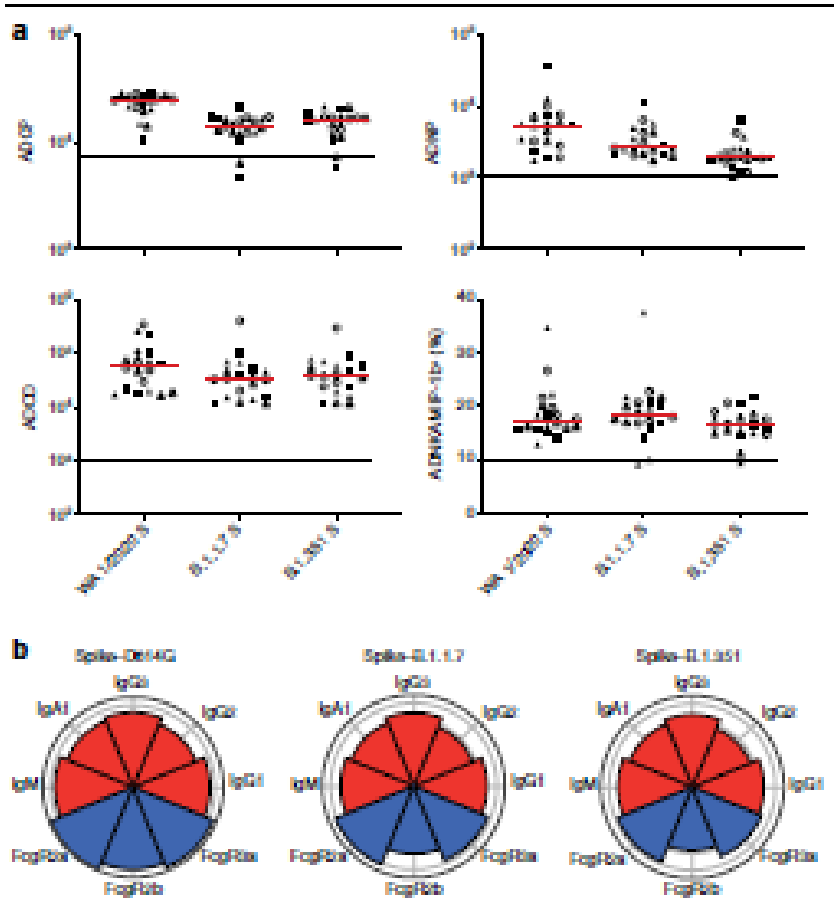
Neutralizing antibody (wtVNA) responses in 18-58 & ≥65 years old who received one or 2 doses of Ad26.COV2.S ($5x10^{10}$vp)



D614G neutralizing antibody (psVNA) responses in 18-55 years old who received 1- or 2-doses of Ad26.COV2.S as primary vaccination, and were boosted at 6 months or 1 year post primary vaccination



Systems Serology responses (ADCP, ADNP, ADCD, ADNKA) against SARS-COV-2 variants WA1/2020 (D614G), B1.1.1.7, B.1.351 indued by AD26 vectored vaccine on day 71

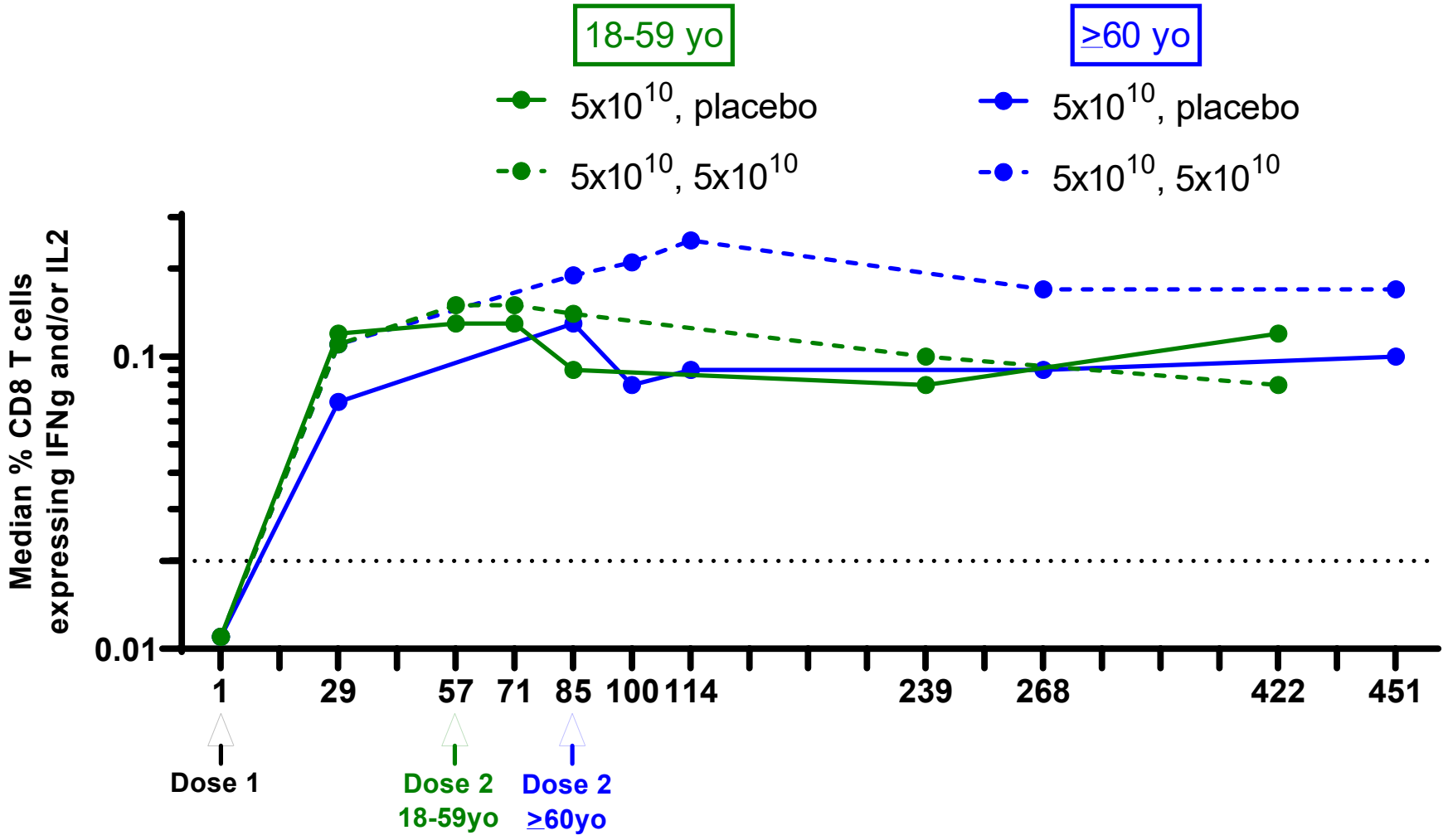


Alter et al, Nature | Vol 596 | 12 August 2021

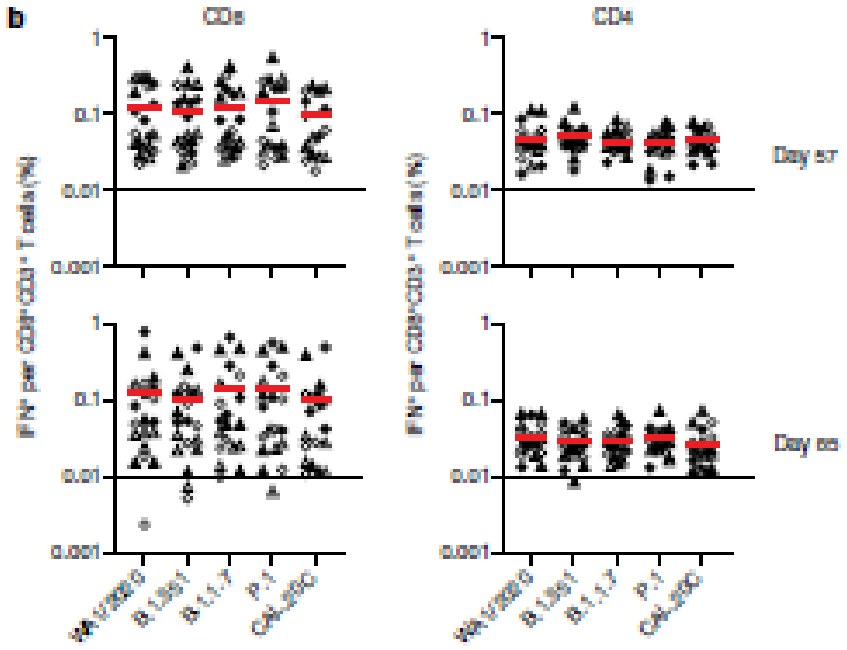
Results overall show induction of relatively similar levels of Fc functionalities independent of viral variant.

Nightingale plots showing the median levels of WA1/2020 (D614G, B.1.1.7, B.1.351 spike specific Isotype (IgM, IgA, IgG1, IgG2 and IgG3) in red and FcγR2a, FcγR2b and FcγR3a in blue

CD8 T cell responses in 18-55 and ≥65 years old who received one or 2 doses of Ad26.COV2.S ($5x10^{10}$vp)



Ad26.COV2.S Vaccine induced Cellular Immune CD4 & CD8 Responses to SARS COV-2 variants WA1/2020 (D614G), B.1.351 B1.1.1.7, P.1, CAL.20G



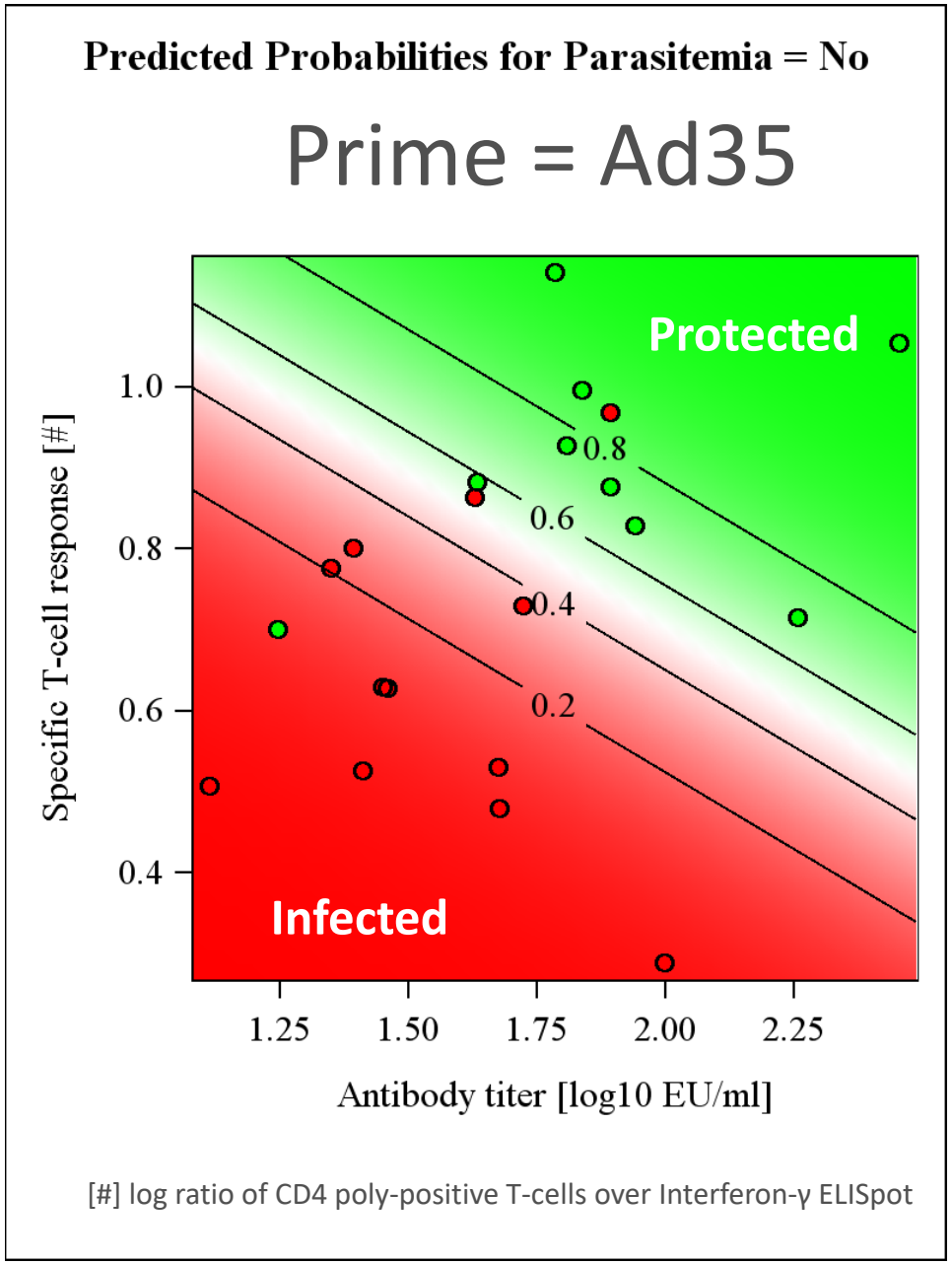
Vaccine induced CD4+ T cells and CD8+ T cells react at similar levels across the 5 variants tested

Suggests targets of cellular immunity are more invariant to strain variation than neutralizing antibody targets

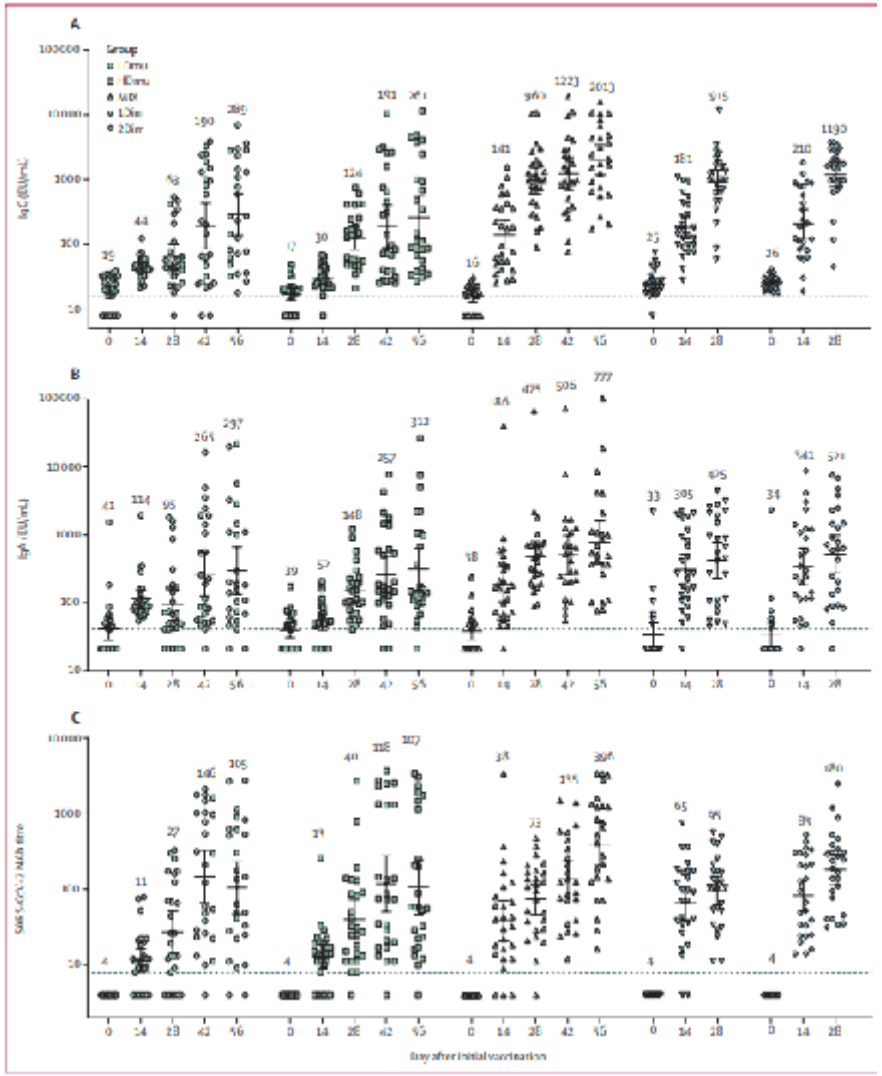
Alter et al, Nature | Vol 596 | 12 August 2021

AD35 Prime RTSS malaria vaccine boost induces Antibody & T cells

- Pre-specified logistic regression of parasitemia on antibodies and T-cells (CD4 poly-positives and Interferon-γ ELISpot)
- Significant contribution of T-cells for Ad35 prime (but not for RTS,S prime)
- ***Proof-of-principle*** *shown of T-cells as correlate-of-protectionin malaria for Ad35*



Serum IgG, IgA and Neutralizing Antibody responses to Nasal Administration of an Adeno 5 vectored COVID vaccine which also induces T cell responses



Wu et al. lancet/infection Vol 21 December 2021

Conclusions concerning non-replicating Adeno Vectored Vaccines

- Vaccines well tolerated
  - Can safely be used in immunosuppressed individuals
  - Extremely rare VITT has been seen with COVID-19 vaccines expressing S antigen
  - Almost never seen in developing world.
- Are similar in antigen release to live vaccines but can be utilized in immunosuppressed individuals
- They induce durable neutralizing, Fc mediated antibody, memory T cell responses and durable functional CD4 and CD8 responses as primary regimens or as boosters to other vaccines (mRNA, killed, protein)
- Non-replicating Adeno Vectored vaccines can be delivered nasally
- The vaccines are stable at 4-8 degrees C
- Can be manufactured in large scale
- Cannot be manufactured in the same time frame as mRNA vaccines