

Interpreting NAb Assays and Animal Models

Dan H. Barouch, M.D., Ph.D.

Director, Center for Virology and Vaccine Research

Beth Israel Deaconess Medical Center

William Bosworth Castle Professor of Medicine

Harvard Medical School

Ragon Institute of MGH, MIT, and Harvard

WHO Global Consultation on Omicron, Geneva, Switzerland

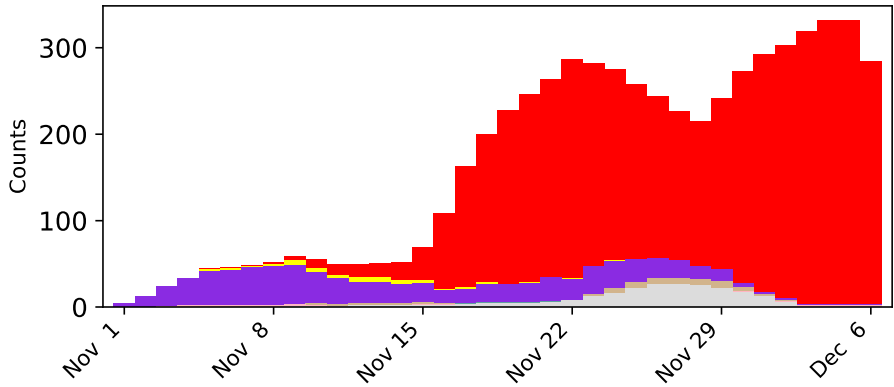
December 14, 2021

Omicron: BA.1 and BA.2 South Africa

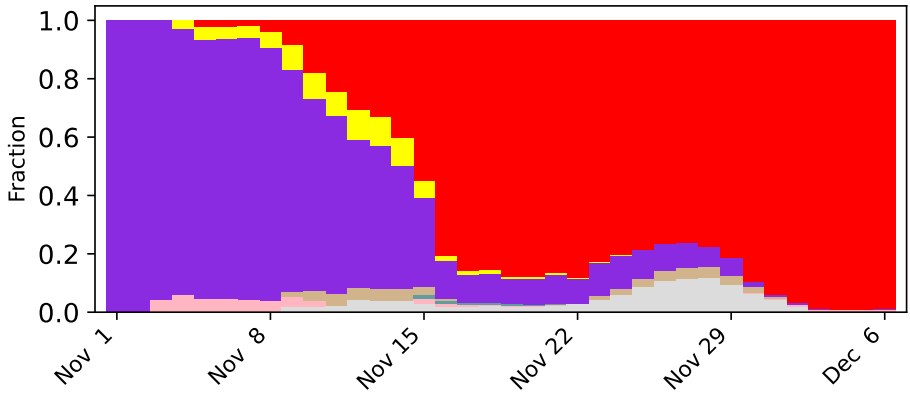
Enabled by data from the South African
contributions to GISAID
and cov.lanl.gov



South-Africa: 938 sequences



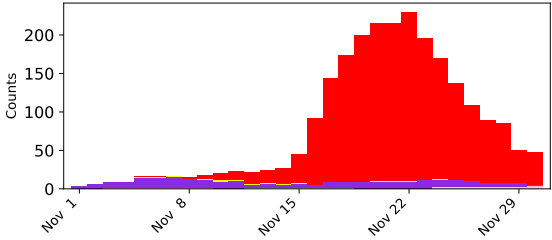
South-Africa: 938 sequences



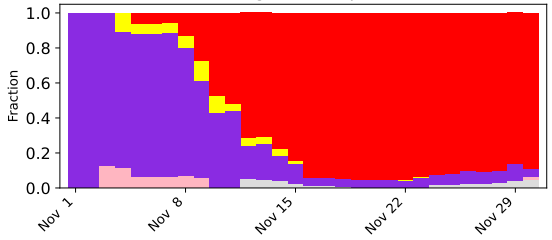
- Omicron
- B.1.640
- B.1.1.318
- C.1.2
- Delta
- Delta_AY.122
- Delta_AY.4.2
- Delta_AY.35
- Delta_AY.47
- Delta_AY.98.1
- Delta_AY.33
- Delta_AY.26
- Delta_AY.25
- Gamma
- Mu
- Lambda
- Beta
- Alpha
- other



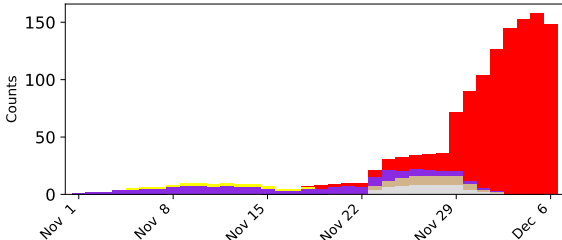
Gauteng: 359 sequences



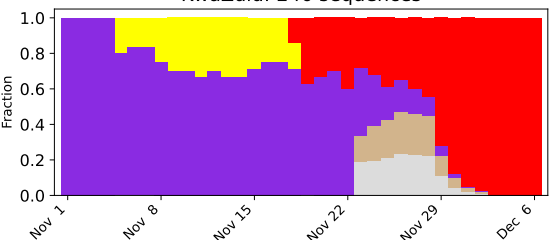
Gauteng: 359 sequences



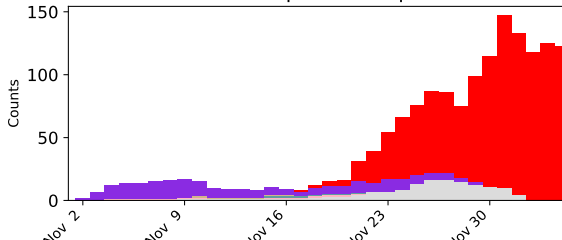
KwaZulu: 246 sequences



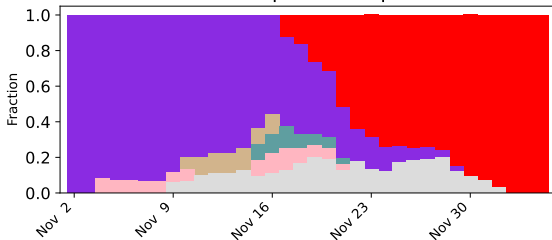
KwaZulu: 246 sequences



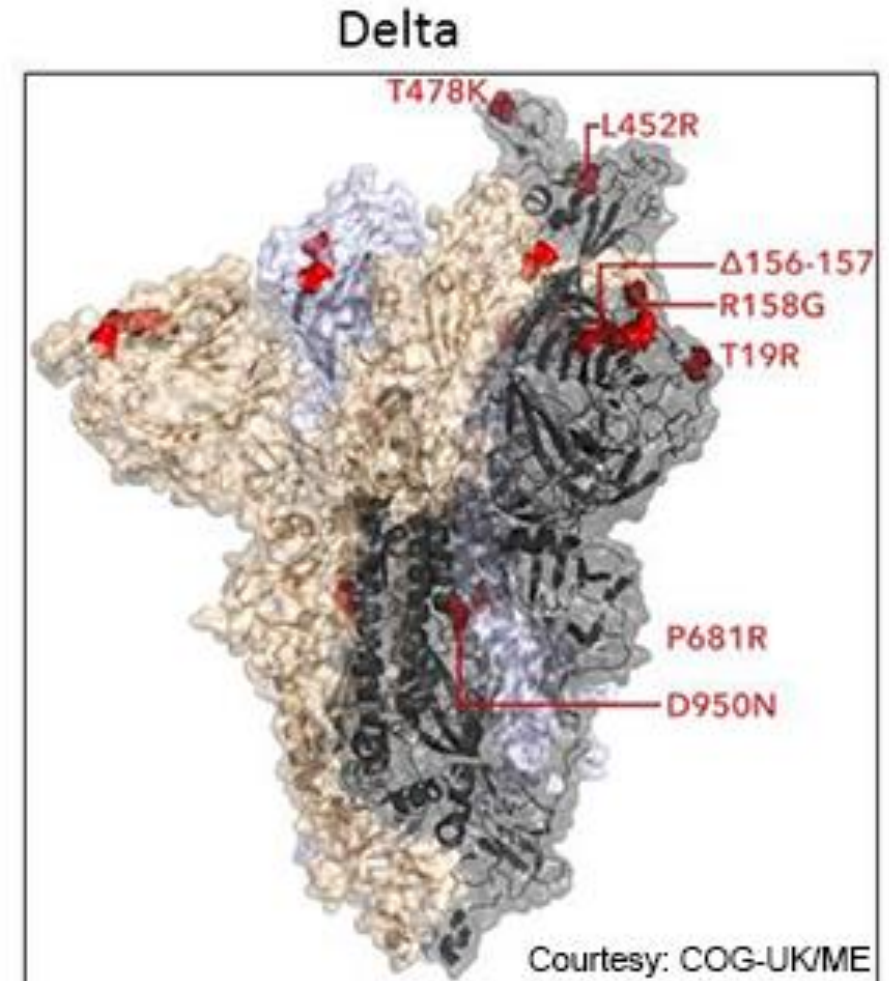
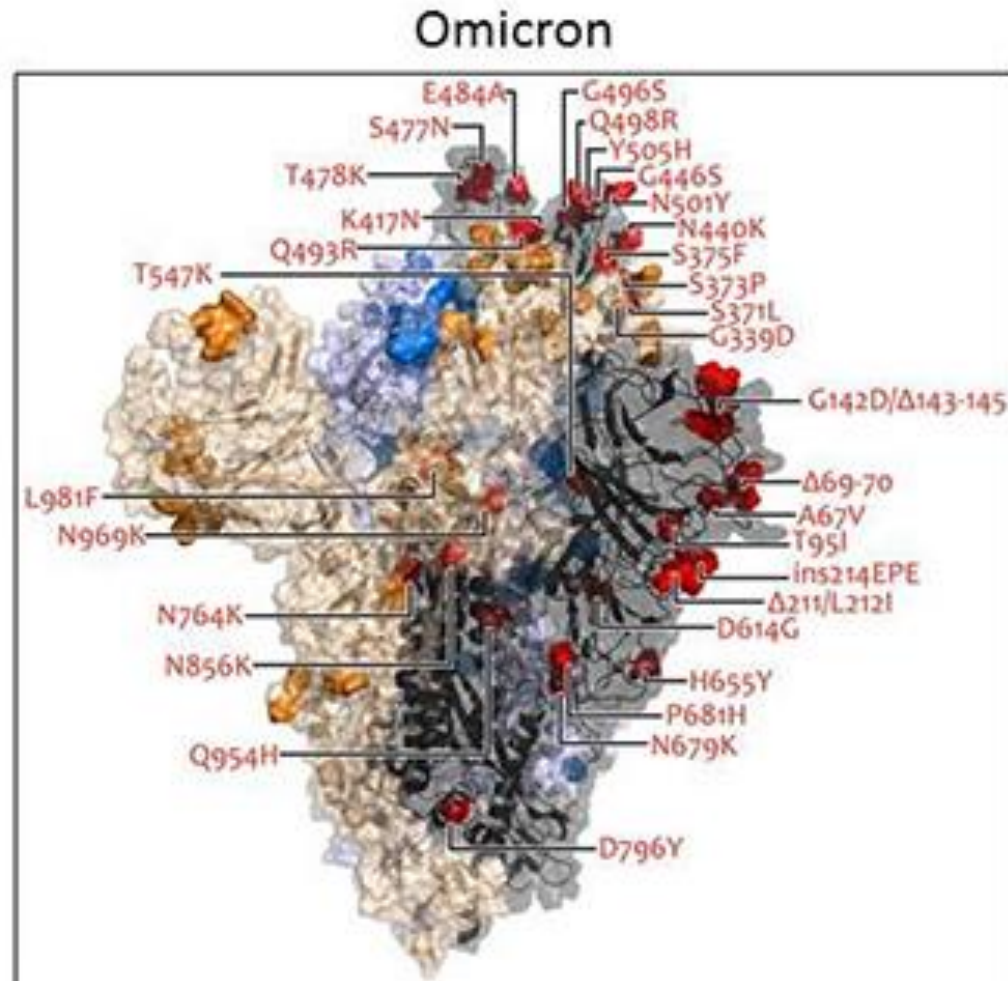
Western-Cape: 252 sequences



Western-Cape: 252 sequences



Omicron vs. Delta Spike Mutations



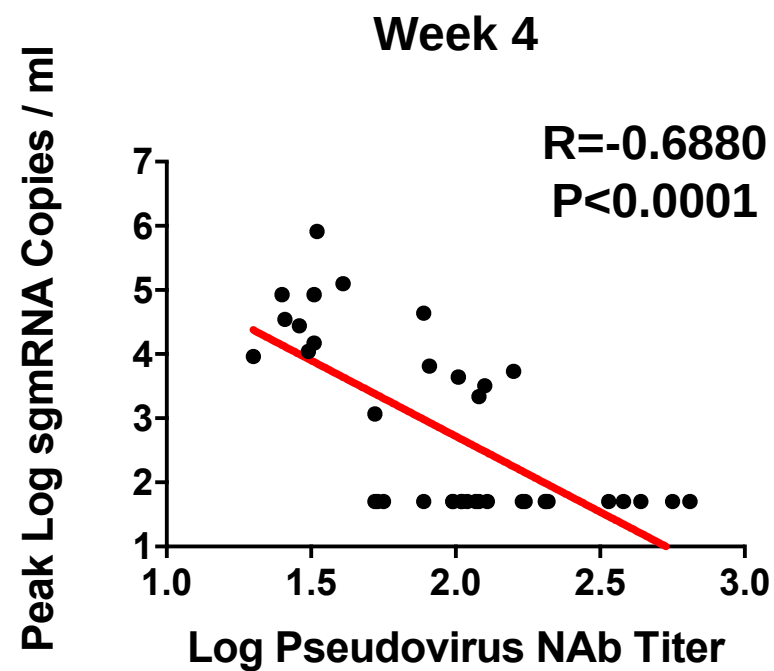
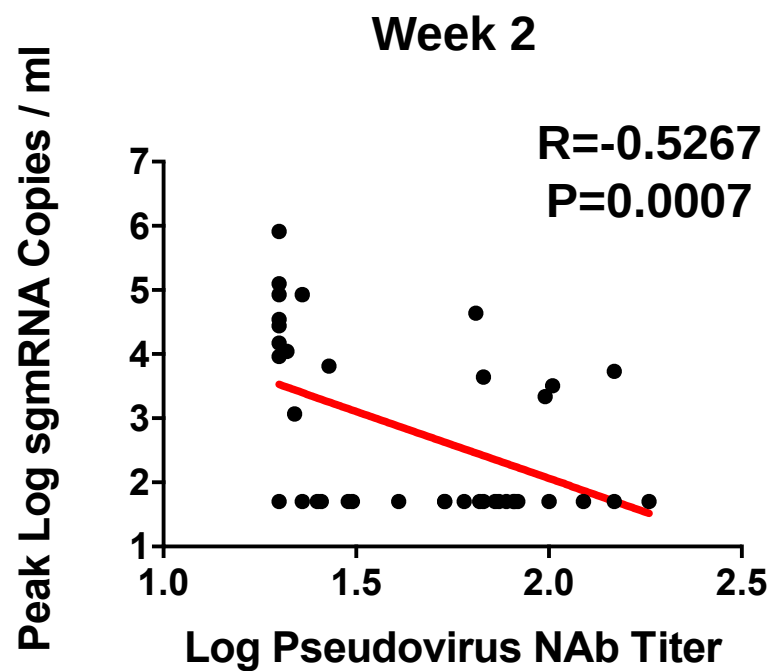
Select Key Questions for the Omicron Variant

- **Severity of illness?**
- **Transmissibility?**
- **Evasion of immune responses?**
 - Natural immunity
 - Vaccines
 - mAbs

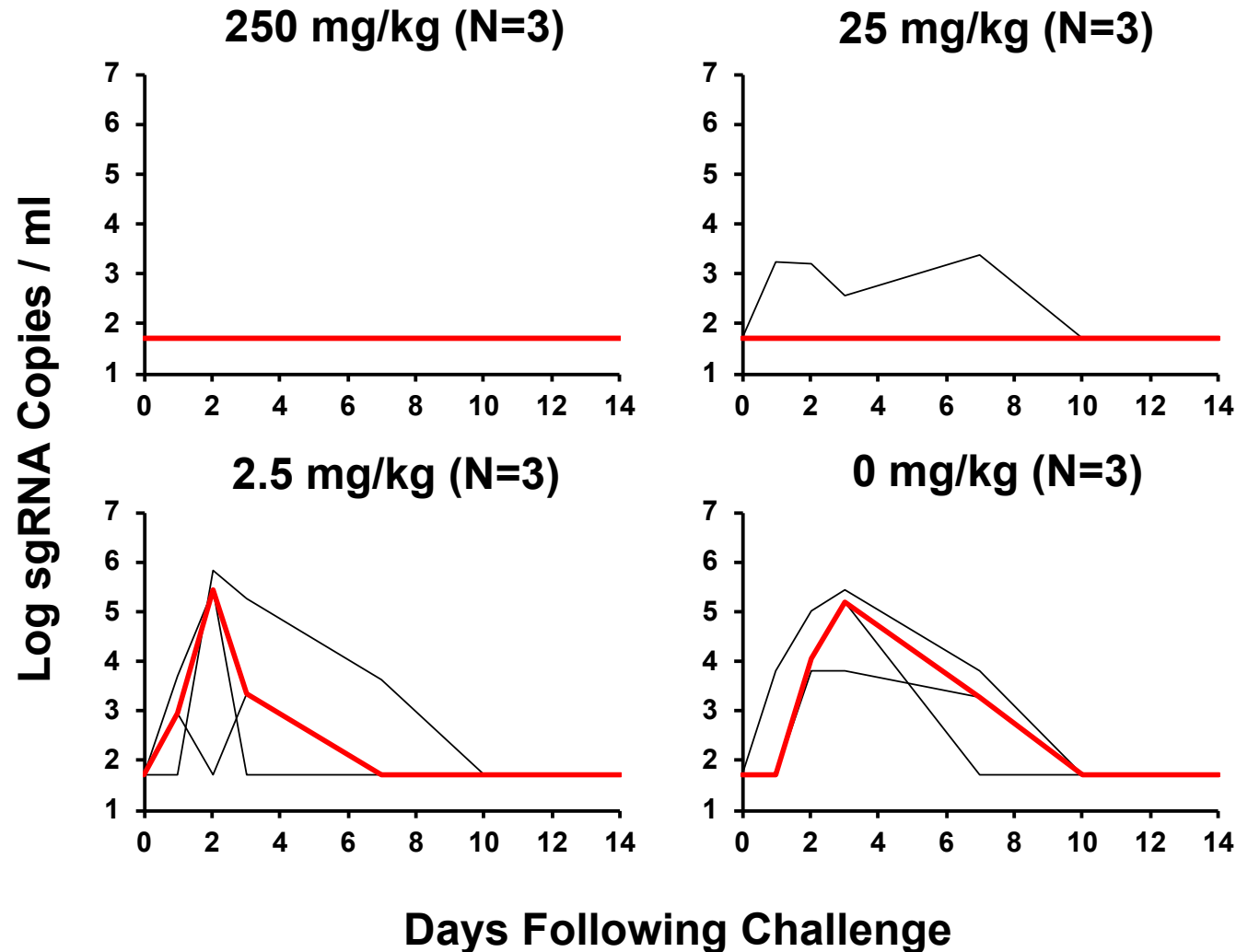
To What Extent Does the Omicron Variant Escape from Current Vaccines?

- **Many groups have now reported decreased NAb titers to the Omicron variant, and partial restoration with boosting**
- **Less data available for binding and other functional antibodies and T cell responses to the Omicron variant**
- **At least two studies have reported preliminary vaccine effectiveness against the Omicron variant (UK, RSA)**

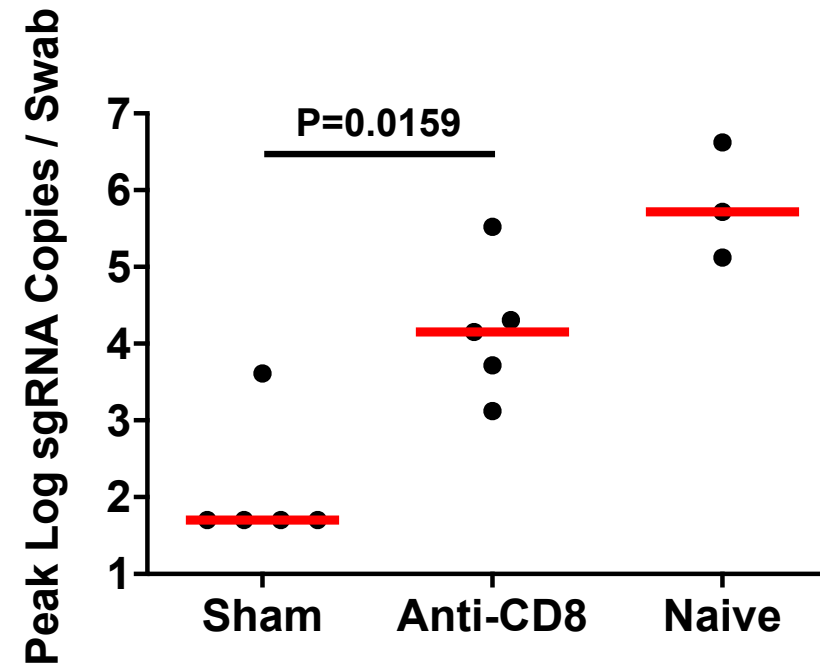
Pseudovirus NAbS Correlate with Protection Against SARS-CoV-2 WA1/2020 Challenge in Rhesus Macaques



Dose-Dependent Adoptive Transfer of Purified IgG Protects Against SARS-CoV-2 in Rhesus Macaques



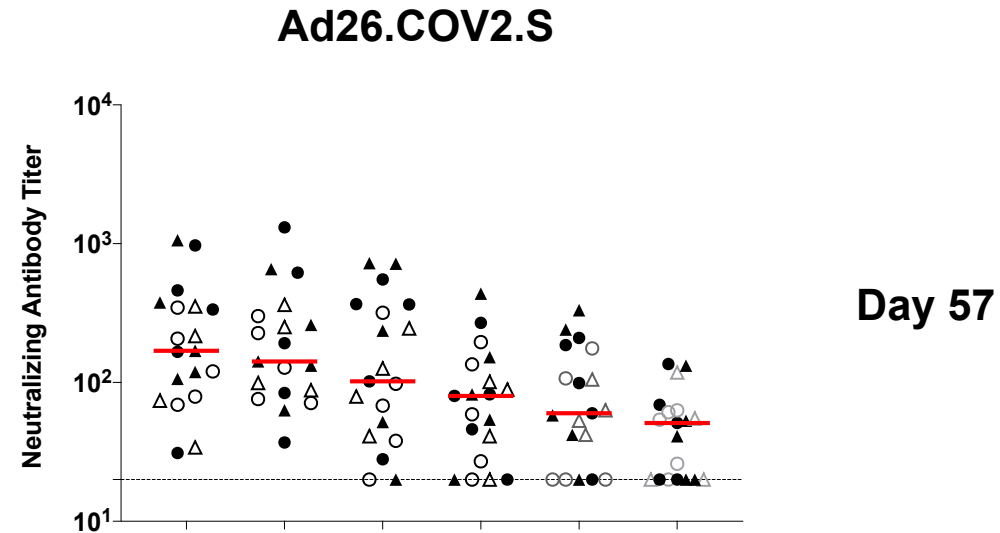
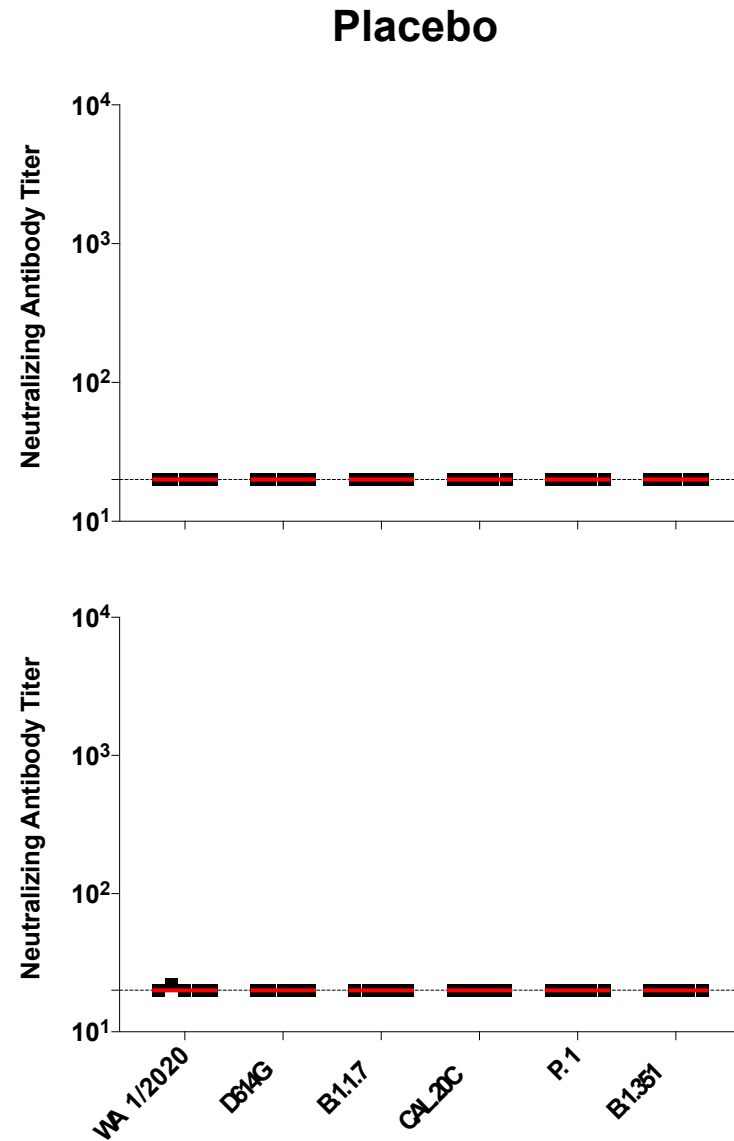
CD8 Depletion Partially Abrogates Protection of Natural Immunity Against SARS-CoV-2 in Rhesus Macaques



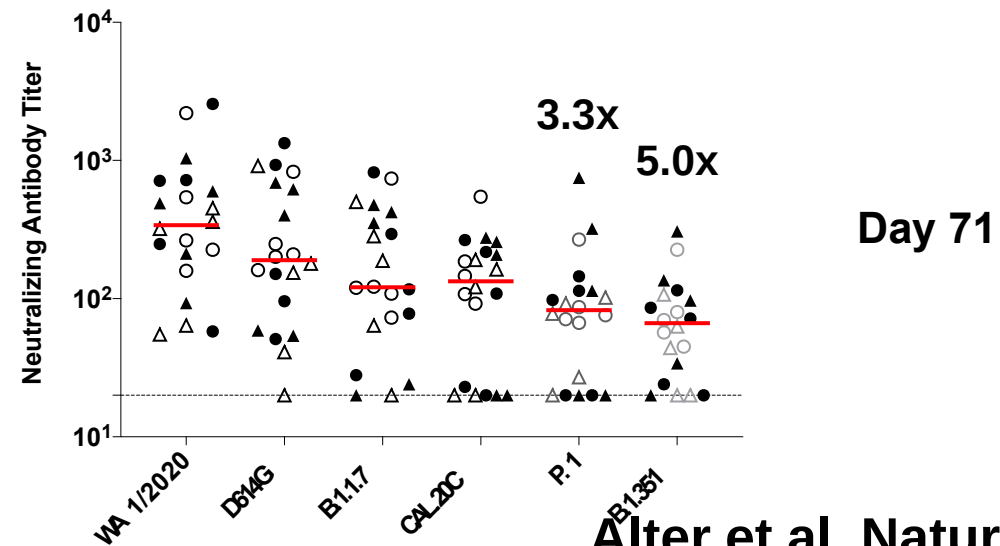
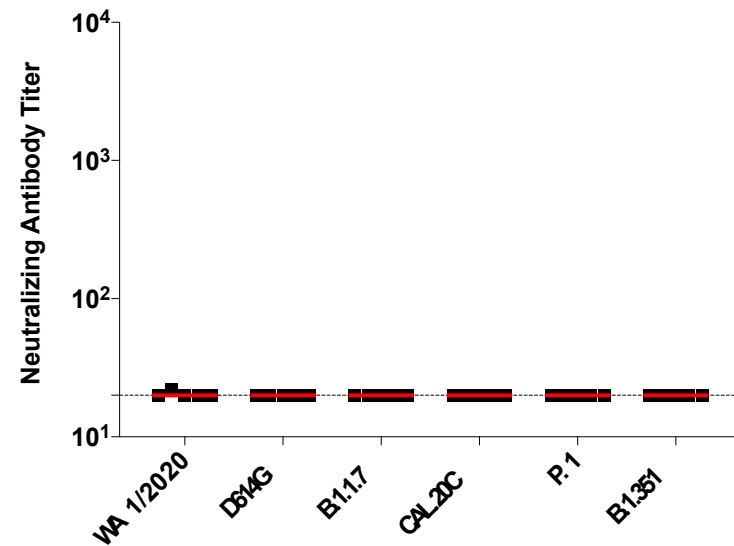
IgG Adoptive Transfer and CD8 Depletion Studies

- **Purified IgG protects macaques against SARS-CoV-2 challenge in a dose-dependent fashion**
- **CD8 depletion reduced protection against re-challenge in convalescent macaques with waning Ab titers**
- **These data suggest that Abs alone can protect, but cellular immune responses contribute when Ab titers are borderline or subprotective**

Immunogenicity of Ad26.COVS.S Against SARS-CoV-2 Variants: Neutralizing Antibody Responses

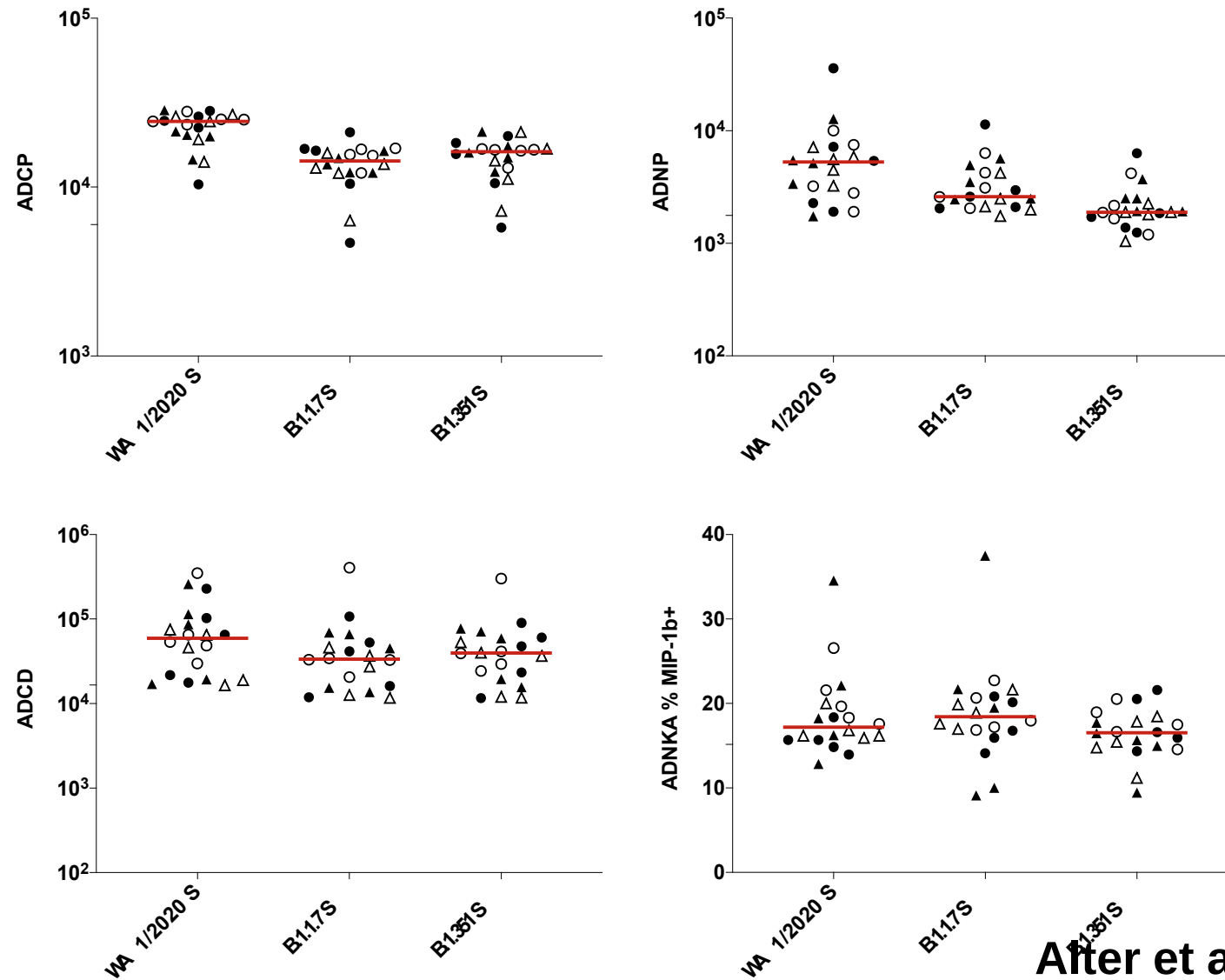


Day 57



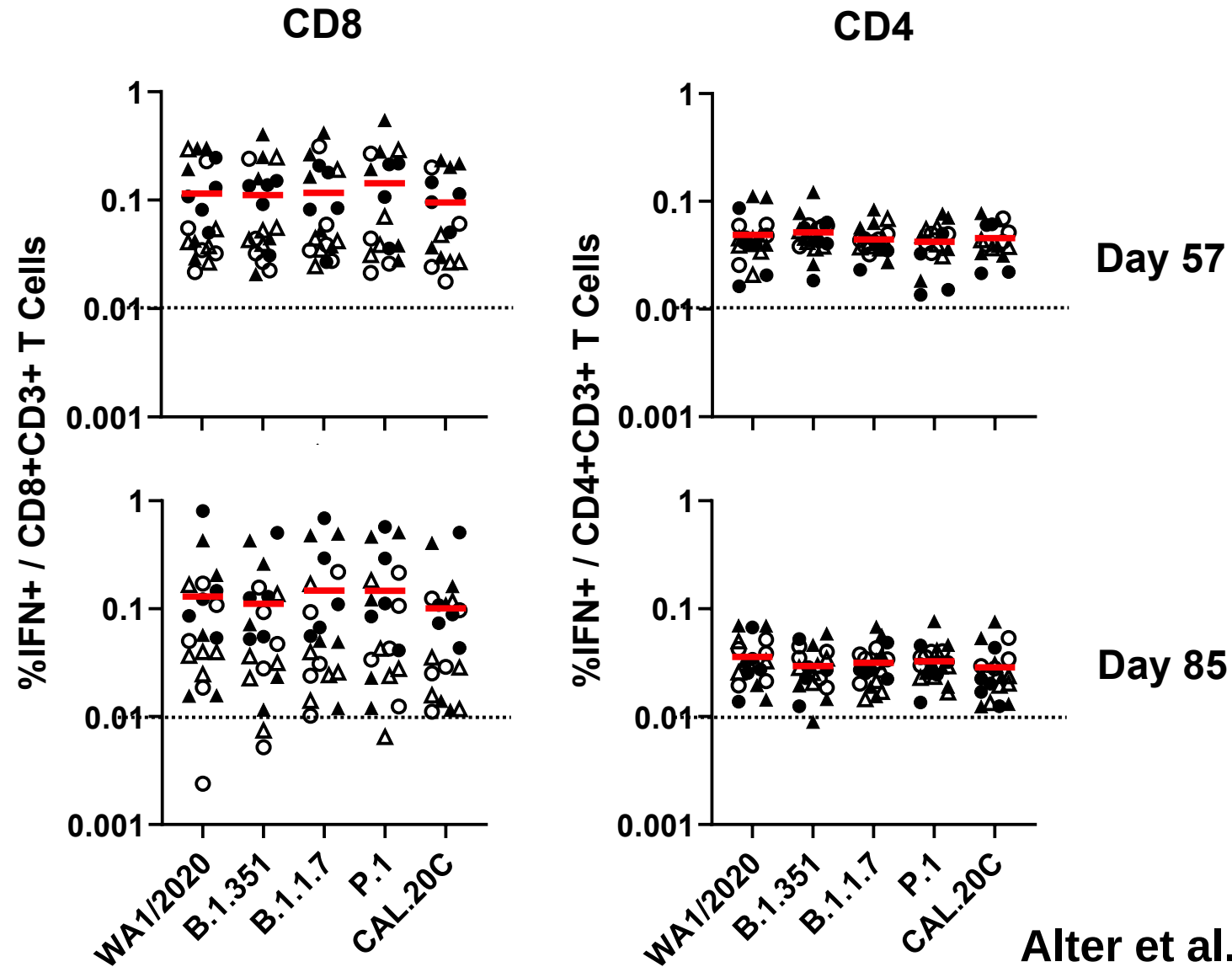
Day 71

Immunogenicity of Ad26.COVS.S Against SARS-CoV-2 Variants: Fc Functional Antibody Responses



After et al. Nature, June 9, 2021

Immunogenicity of Ad26.COVS.S Against SARS-CoV-2 Variants: CD8 and CD4 T Cell Responses



Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants

- Substantial impact of variants on NAb responses
- Less impact of variants on binding and Fc functional antibodies
- No impact of variants on CD8 T cell responses
- Cellular immune responses may be more preserved than NAb responses against Omicron

Setting the Stage for Omicron Studies

- **Neutralizing antibody responses, if present at high titers, will likely provide protection against infection**
- **However, the magnitude and durability of neutralizing antibody responses against Omicron with current vaccines may be reduced**
- **Other antibody functions and cellular immune responses may show greater cross-reactivity against Omicron and may contribute to protection against severe disease**
- **Correlates of protection in humans against variants remain unclear**

Acknowledgements

Beth Israel Deaconess

Ai-ris Collier
Sabrina Tan
Jingyou Yu
Jinyan Liu
Abishek Chandrashekar
Erica Borducchi
Lisa H. Tostanoski
Katherine McMahan
Catherine Jacob-Dolan
Aiquan Chang
Tochi Anioke
Michelle Lifton
Joseph Nkolola
Kathryn Stephenson

Janssen / J&J

Mathieu Le Gars
Jerald Sadoff
Anne Marit de Groot
Dirk Heerwegh
Frank Struyf
Macaya Douoguih
Johan Van Hoof
Hanneke Schuitemaker
Mathai Mammen
Paul Stoffels

Ragon Institute

Galit Alter
Caroline Atyeo
Sally Shin

Funding

BARDA/J&J
Ragon Institute
MassCPR
NIAID

All Trial Volunteers!