Vaccine-Induced Antibody Protection Against SARS-COV-2

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Initial Experiments on Natural and Vaccine Immunity

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RESEARCH ARTICLES

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SARS-CoV-2 infection protects against rechallenge in rhesus macaques

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DNA vaccine protection against SARS-CoV-2 in rhesus macaques

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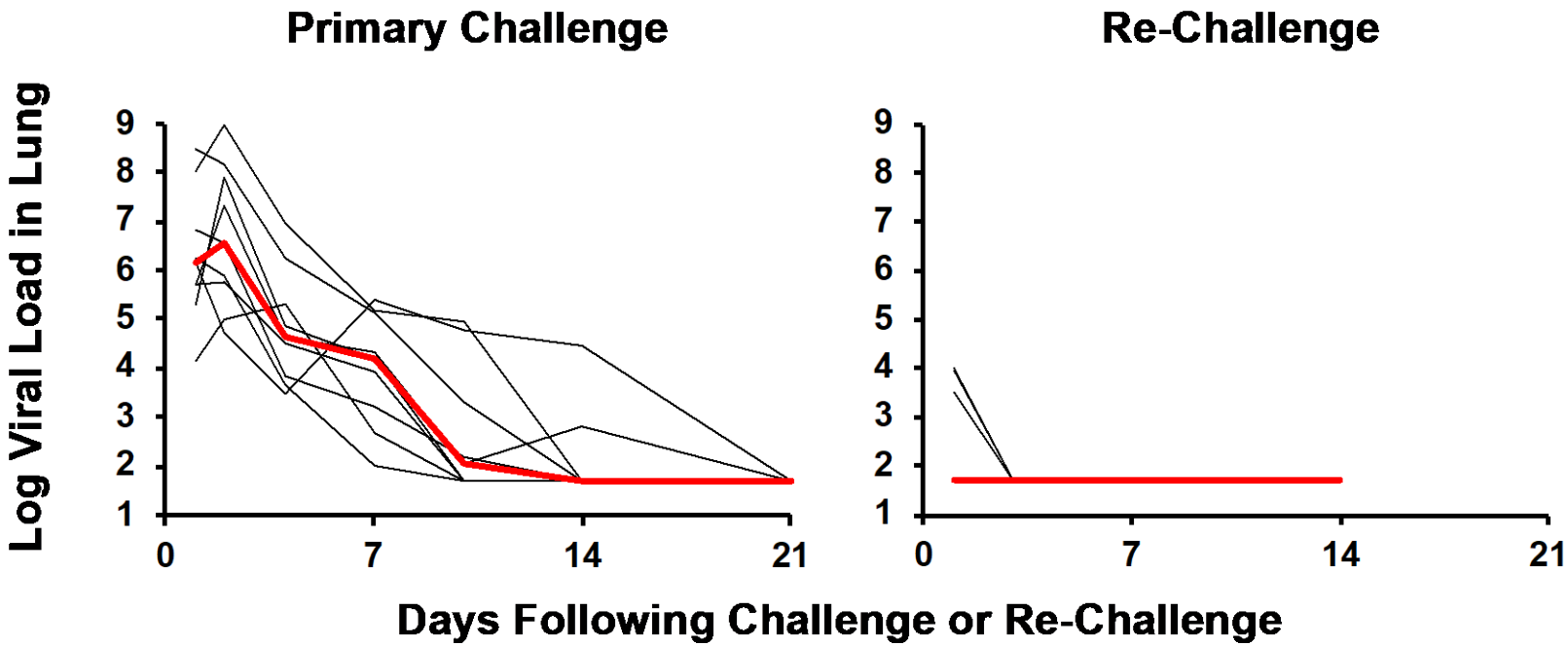
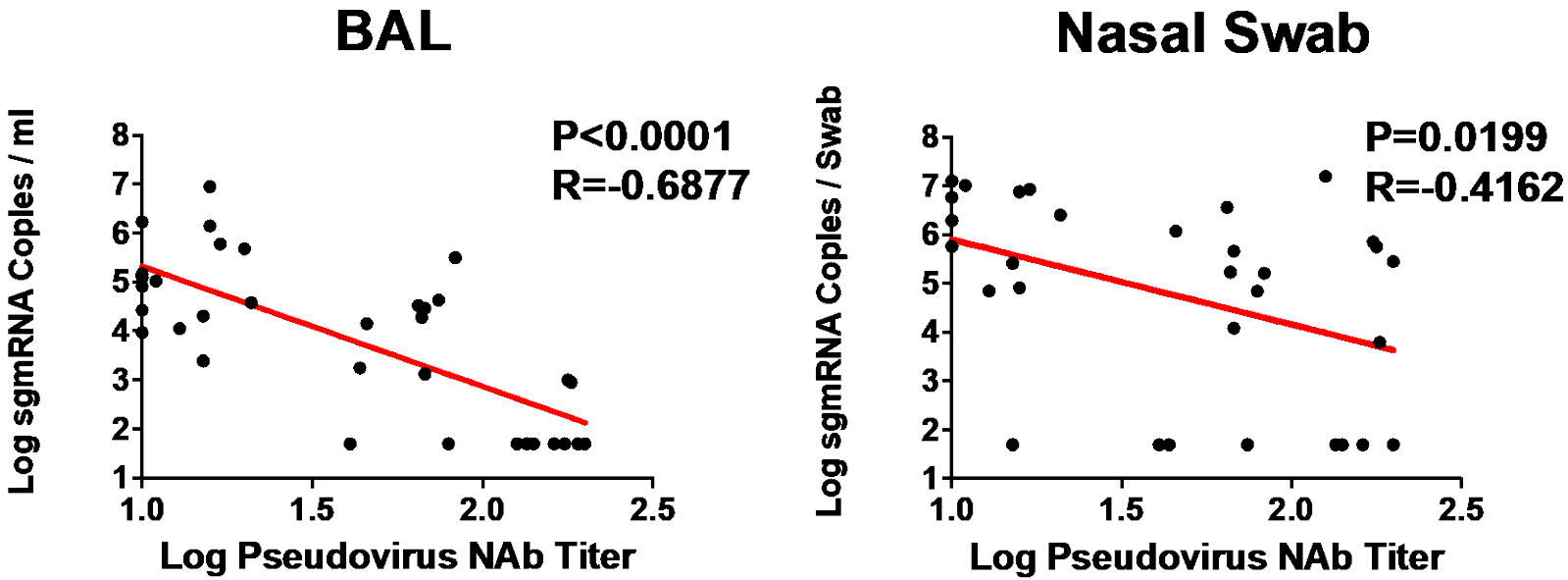
Chandrashekar et al. Science May 20, 2020; Yu et al. Science May 20, 2020

Natural Immunity: SARS-CoV-2 Infection Protects Against Re-Challenge in Rhesus Macaques



Chandrashekar et al. Science May 20, 2020

Vaccine Immunity: DNA Vaccine Induced NAb Titers Correlate with SARS-CoV-2 Protection in Macaques



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Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques

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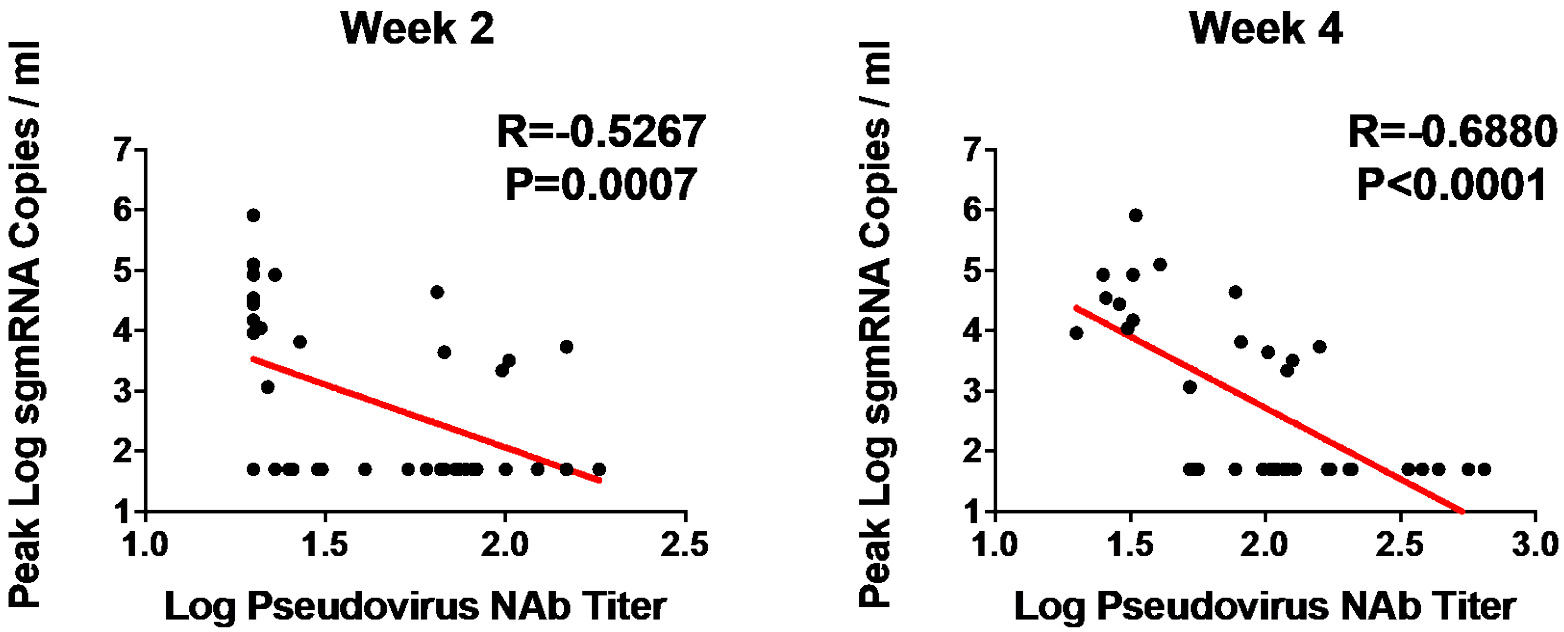
Noe B. Mercado, Roland Zahn, Frank Wegmann, Carolin Loos, Abishek Chandrashekar, Jingyou Yu, Jinyan Liu, Lauren Peter, Katherine McMahan, Lisa H. Tostanoski, Xuan He, David R. Martinez, Lucy Rutten, Rinke Bos, Danielle van Manen, Jort Vellinga, Jerome Custers, Johannes P. Langedijk, Ted Kwaks, Mark J. G. Bakkers, David Zuijdgeest, Sietske K. Rosendahl Huber, Caroline Atyeo, Stephanie Fischinger, John S. Burke, Jared Feldman, Blake M. Hauser, Timothy M. Caradonna, Esther A. Bondzie, Gabriel Dagotto, Makda S. Gebre, Emily Hoffman, Catherine Jacob-Dolan, Marinela Kirilova, Zhenfeng Li, Zijin Lin, Shant H. Mahrokhian, Lori F. Maxfield, Felix Nampanya, Ramya Nityanandam, Joseph P. Nkolola, Shivani Patel, John D. Ventura, Kaylee Verrington, Huahua Wan, Laurent Pessaint, Alex Van Ry, Kelvin Blade, Amanda Strasbaugh, Mehtap Cabus, Renita Brown, Anthony Cook, Serge Zouantchangadou, Elyse Teow, Hanne Andersen, Mark G. Lewis, Yongfei Cai, Bing Chen, Aaron G. Schmidt, R. Keith Reeves, Ralph S. Baric, Douglas A. Lauffenburger, Galit Alter, Paul Stoffels, Mathai Mammen, Johan Van Hoof, Hanneke Schuitemaker & Dan H. Barouch

Mercado et al. Nature July 30, 2020

NAb Titers Correlate with Protection in Macaques: Ad26 SARS-CoV-2 Vaccine



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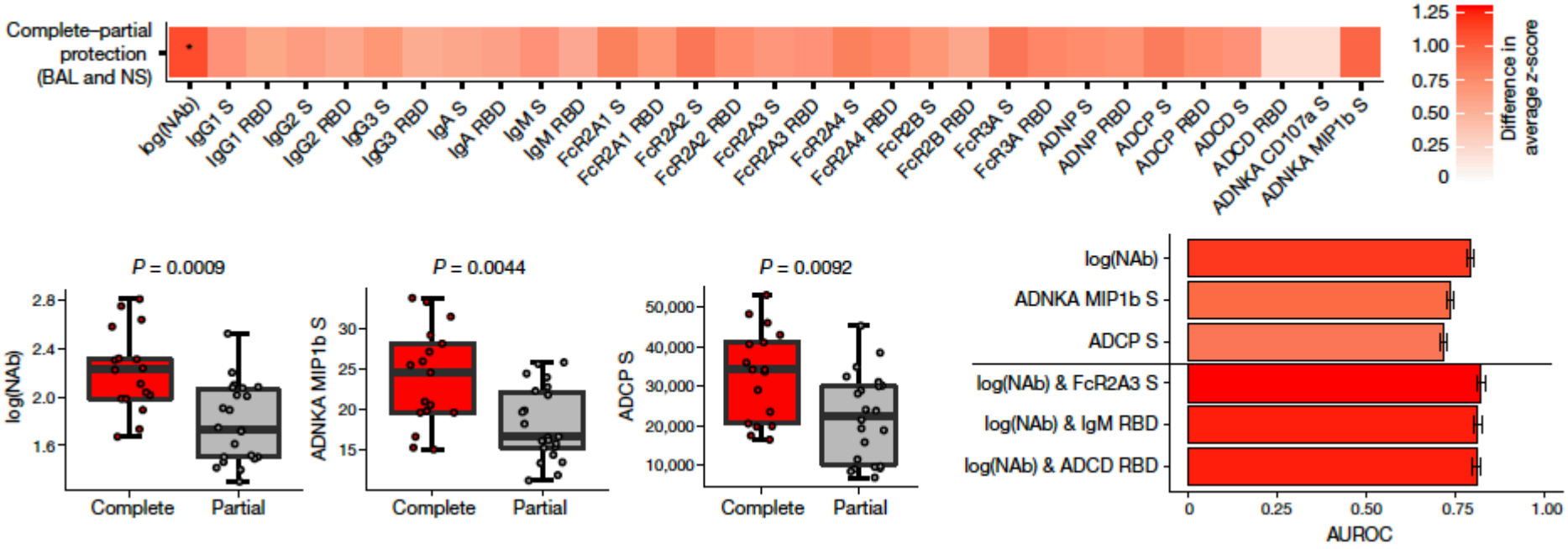
Binding and Fc Functional Antibody Titers Also Correlate with Protection in Macaques



Mercado et al. Nature July 30, 2020

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Correlates of protection against SARS-CoV-2 in rhesus macaques

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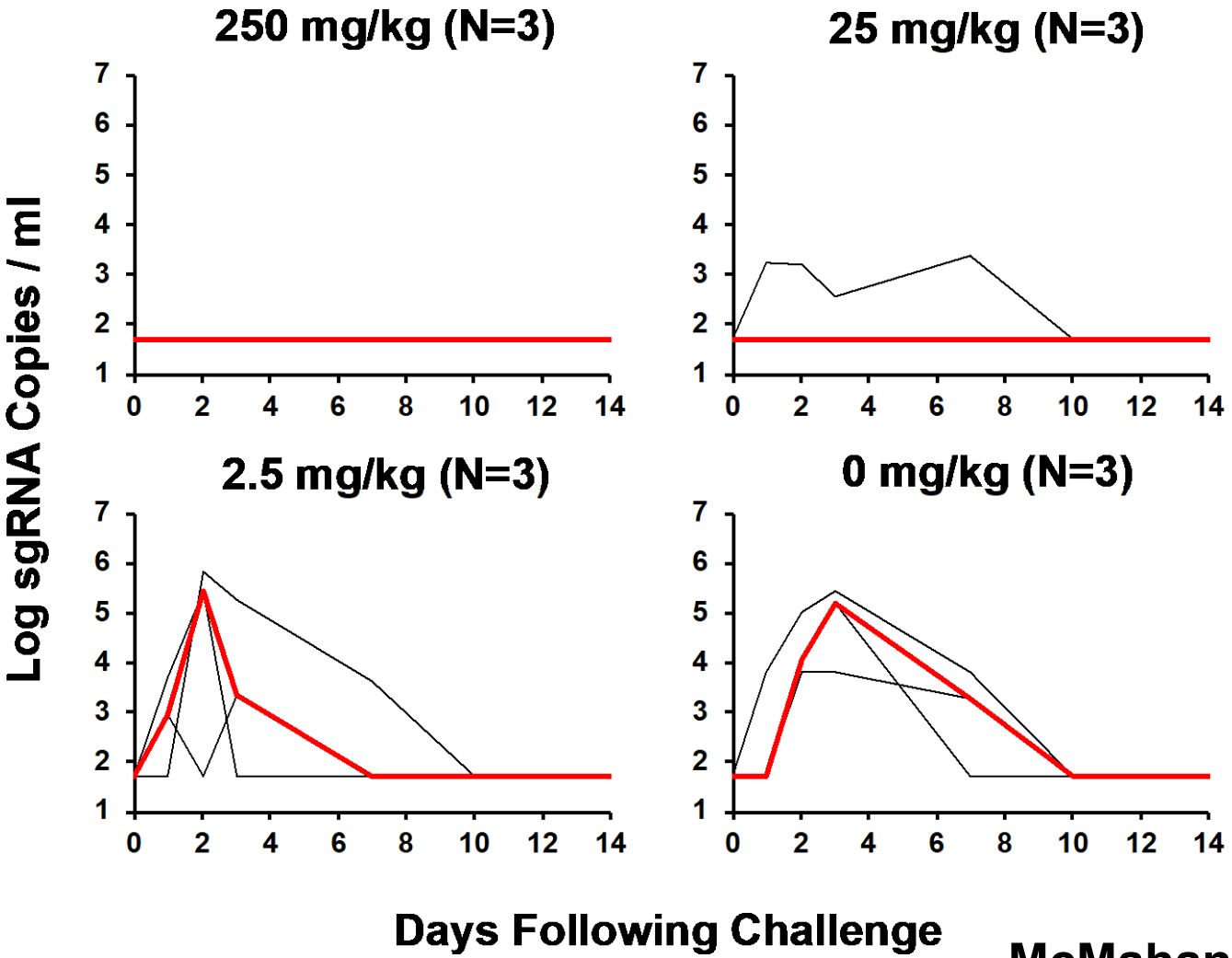
McMahan et al. Nature Dec 4, 2020

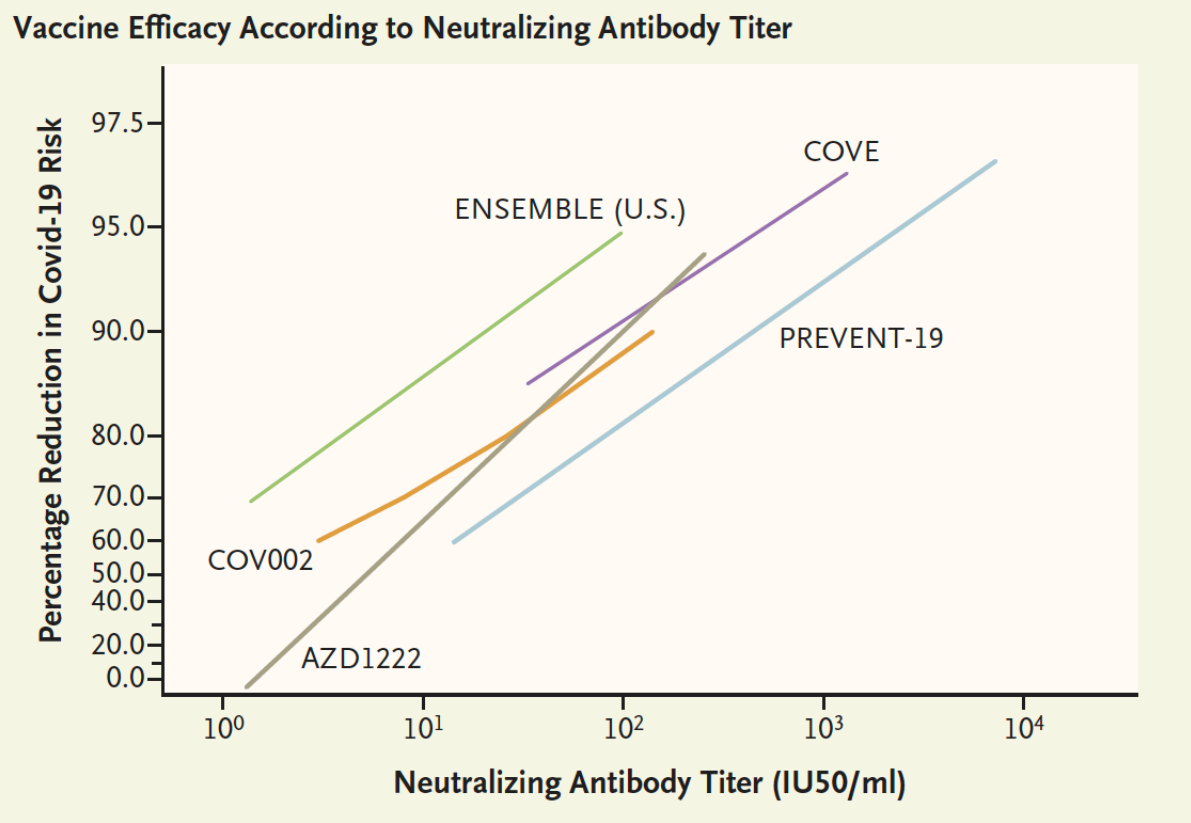
NAb Titers Correlate with Protection in Macaques: Adoptive Transfer of Purified IgG



McMahan et al. Nature Dec 4, 2020

A Covid-19 Milestone Attained — A Correlate of Protection for Vaccines

Peter B. Gilbert, Ph.D., Ruben O. Donis, Ph.D., Richard A. Koup, M.D., Youyi Fong, Ph.D., Stanley A. Plotkin, M.D., and Dean Follmann, Ph.D.



- **NAb titers correlated with protection in the phase 3 efficacy trials against ancestral virus**

Gilbert et al. NEJM 2022; 387:2203-2206

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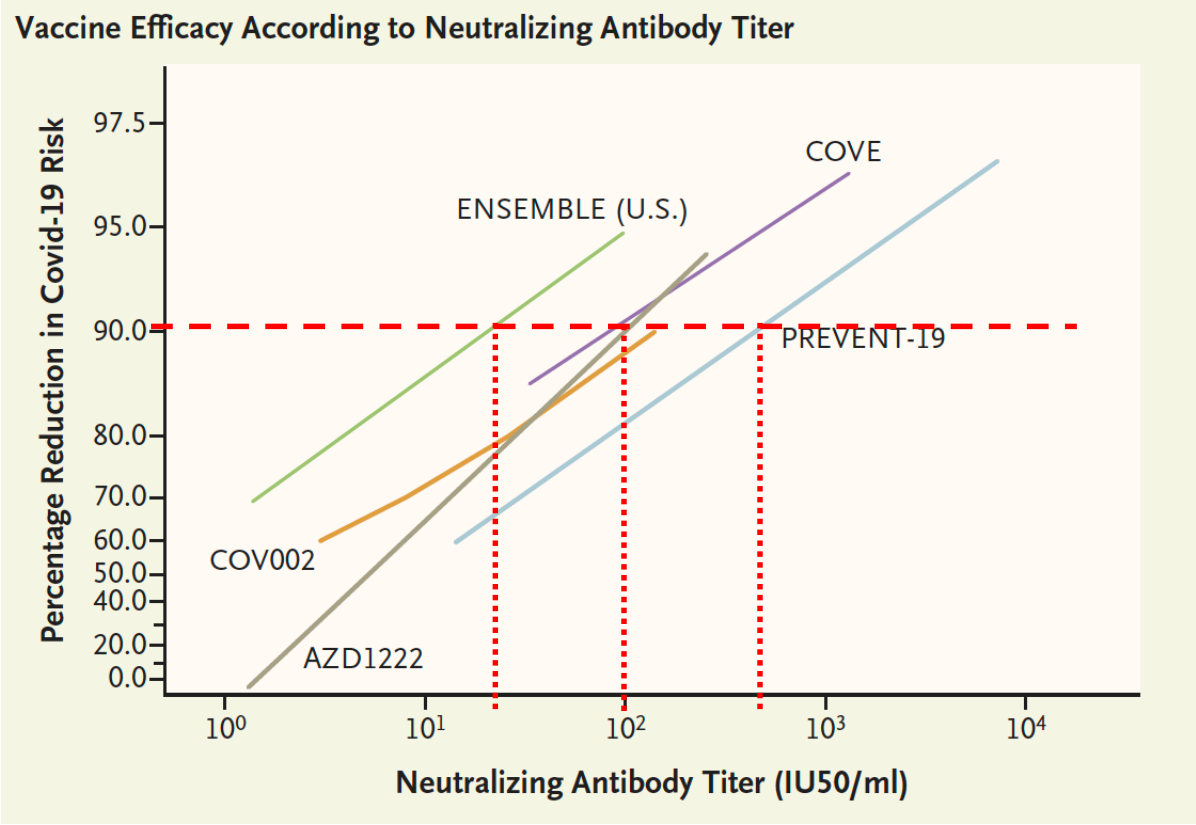
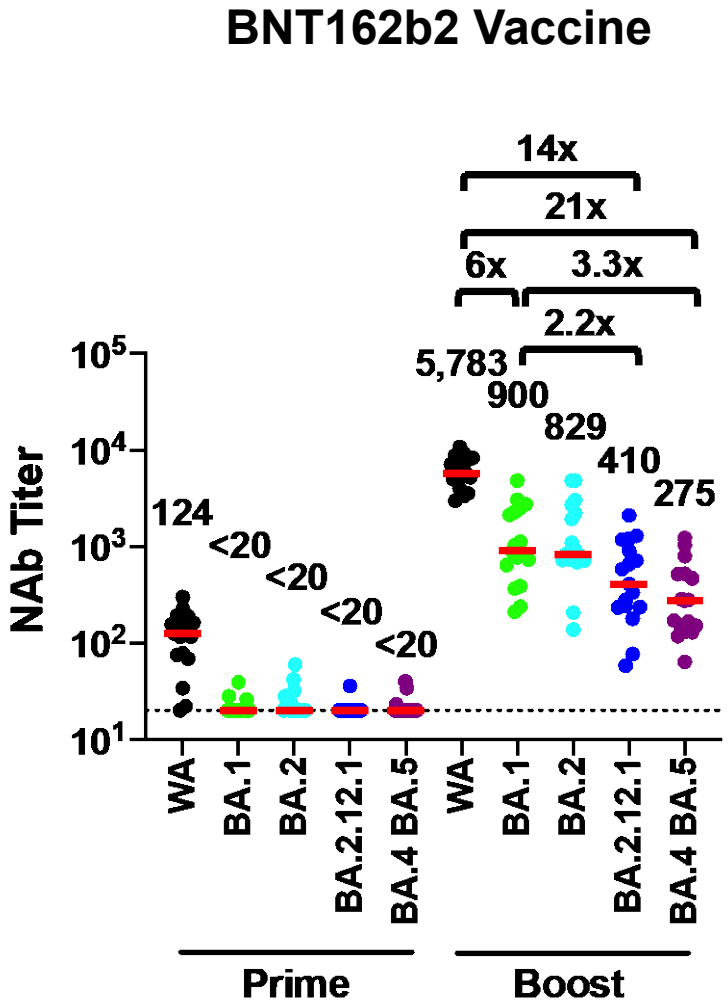


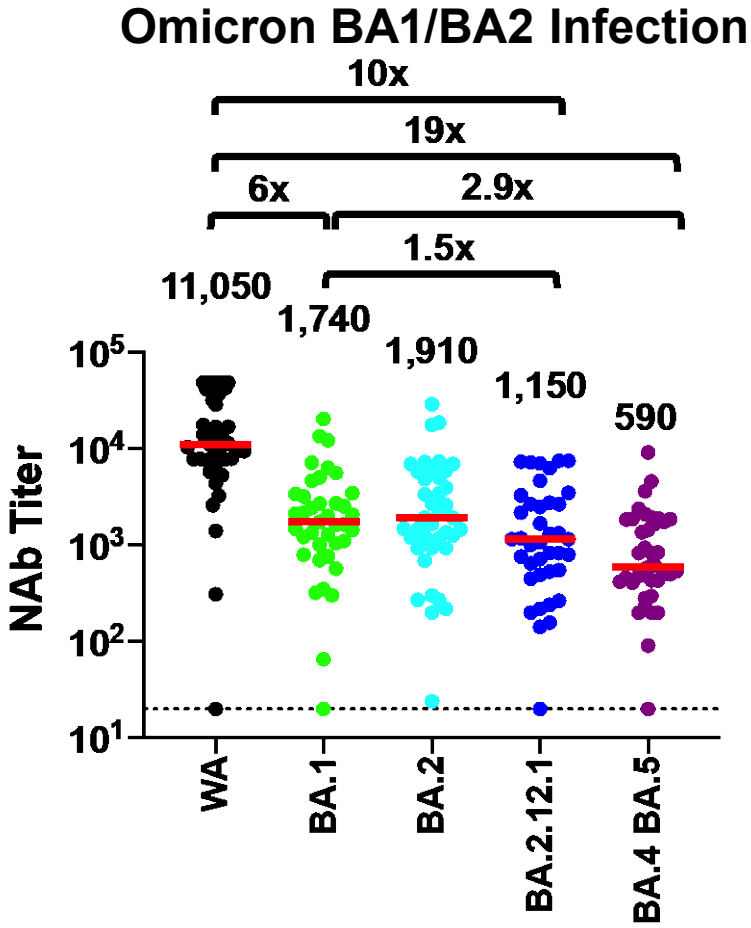
- **NAb titers correlated with protection in the phase 3 efficacy trials against ancestral virus**
- **But platforms differ: J&J required 5-fold lower and NVX required 5-fold higher NAb titers for similar protection as Moderna**
- **Suggests role of T cells in protection**
- **Omicron increased transmissibility and reduced incubation period impact correlates**
- **Recent real-world data show that NAb titers of 100 do not protect against Omicron**

➢ **These NAb correlates do not hold for variants**

Gilbert et al. NEJM 2022; 387:2203-2206

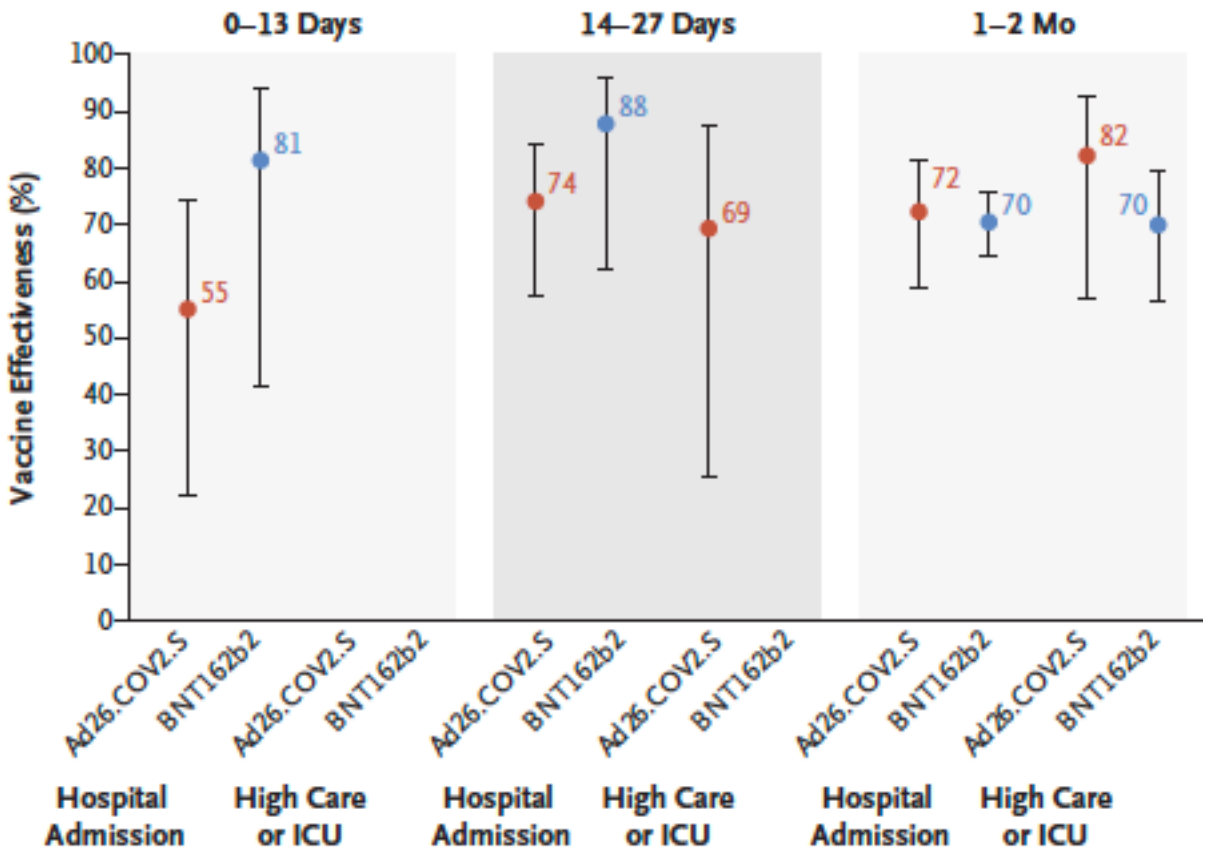
Neutralization Escape of BA.1, BA.2, BA.5 Variants





Hachmann et al. NEJM 2022; 387:86-88

Vaccine Protection Against Omicron Hospitalization and ICU Admission in South Africa in the Absence of NAbs



Gray et al. 2022 NEJM May 4, 2022

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Vaccines Elicit Highly Conserved Cellular Immunity to SARS-CoV-2 Omicron

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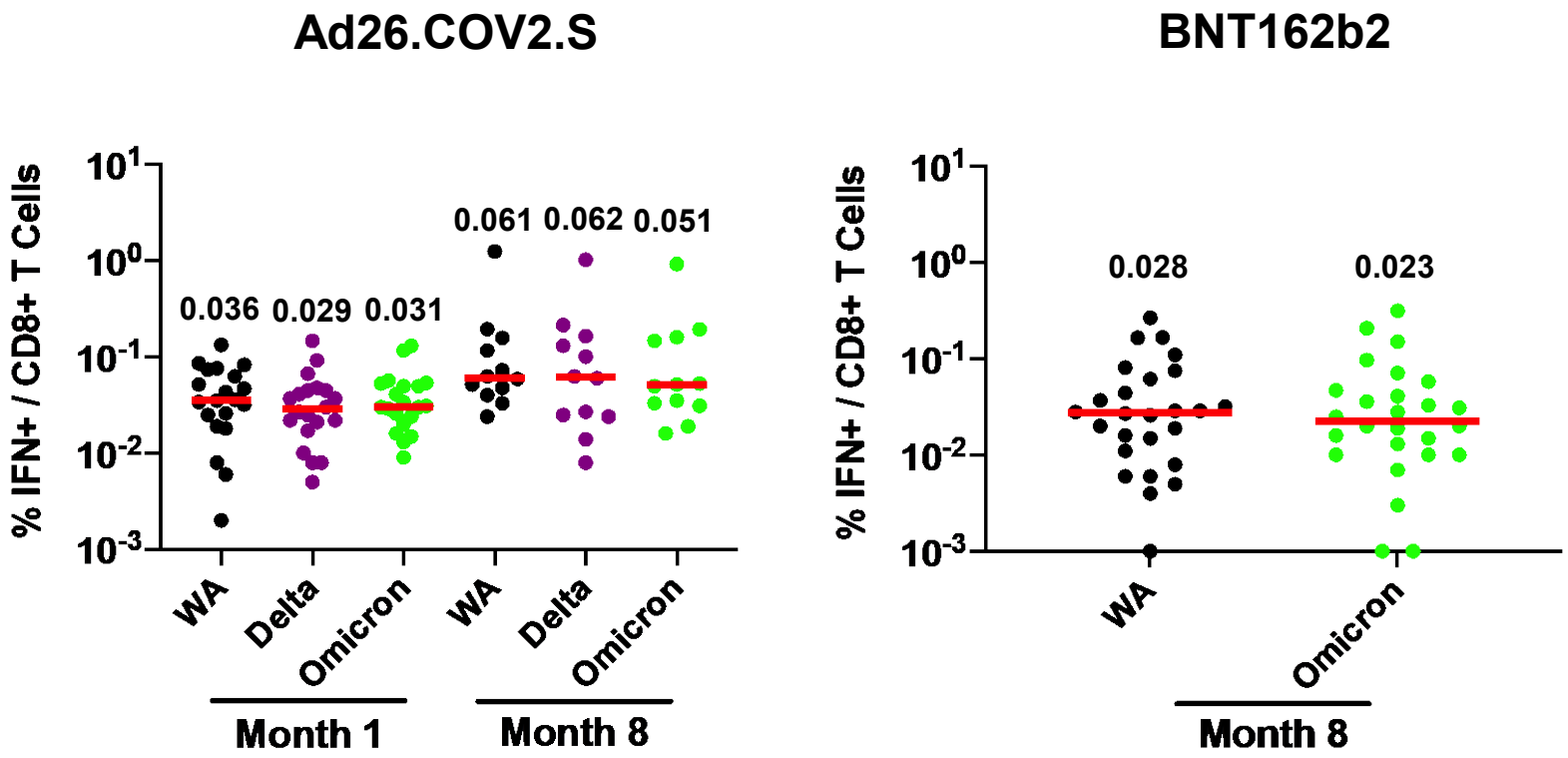
Jinyan Liu, Abishek Chandrashekar, Daniel Sellers, Julia Barrett, Catherine Jacob-Dolan, Michelle Lifton, Katherine McMahan, Michaela Sciacca, Haley VanWyk, Cindy Wu, Jingyou Yu, Ai-ris Y. Collier & Dan H. Barouch

Liu et al. Nature, January 31, 2022

Vaccine-Elicited CD8 T Cell Responses are Highly Cross-Reactive to Omicron



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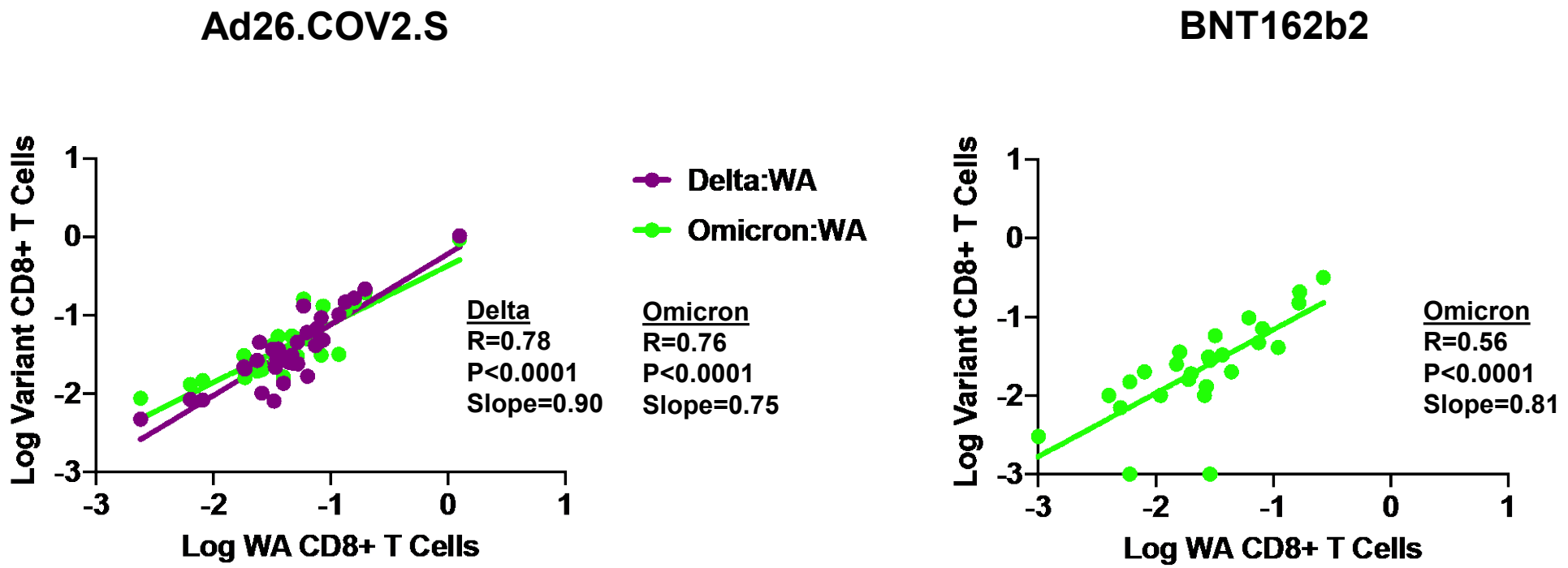

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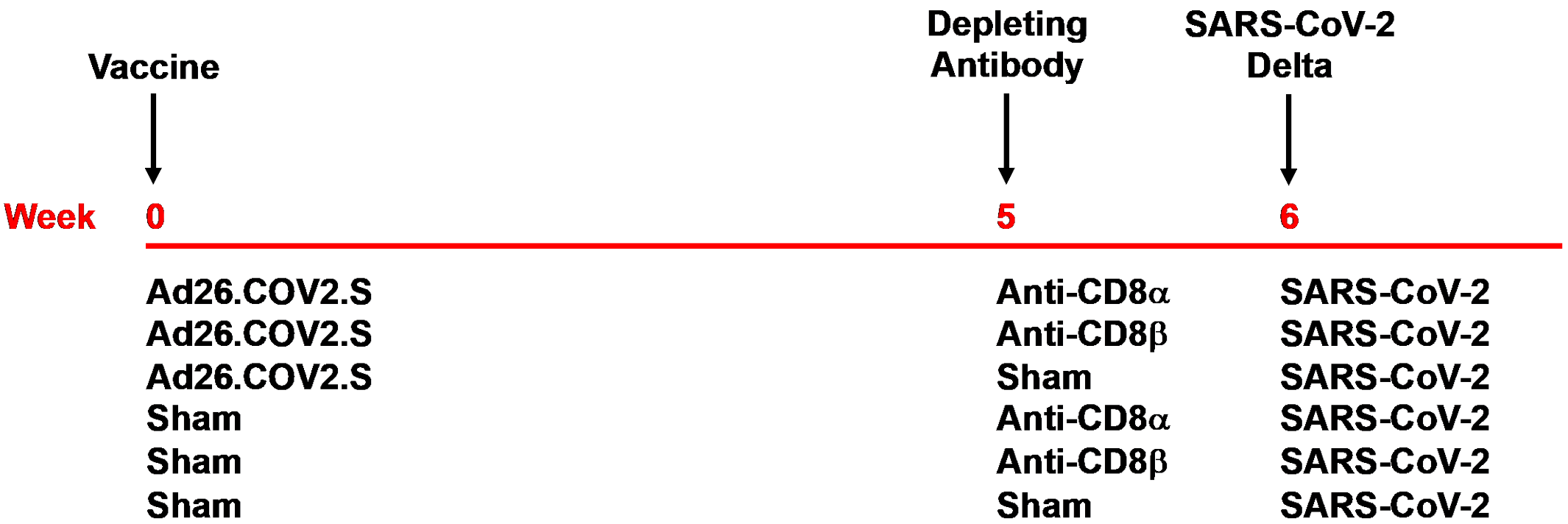
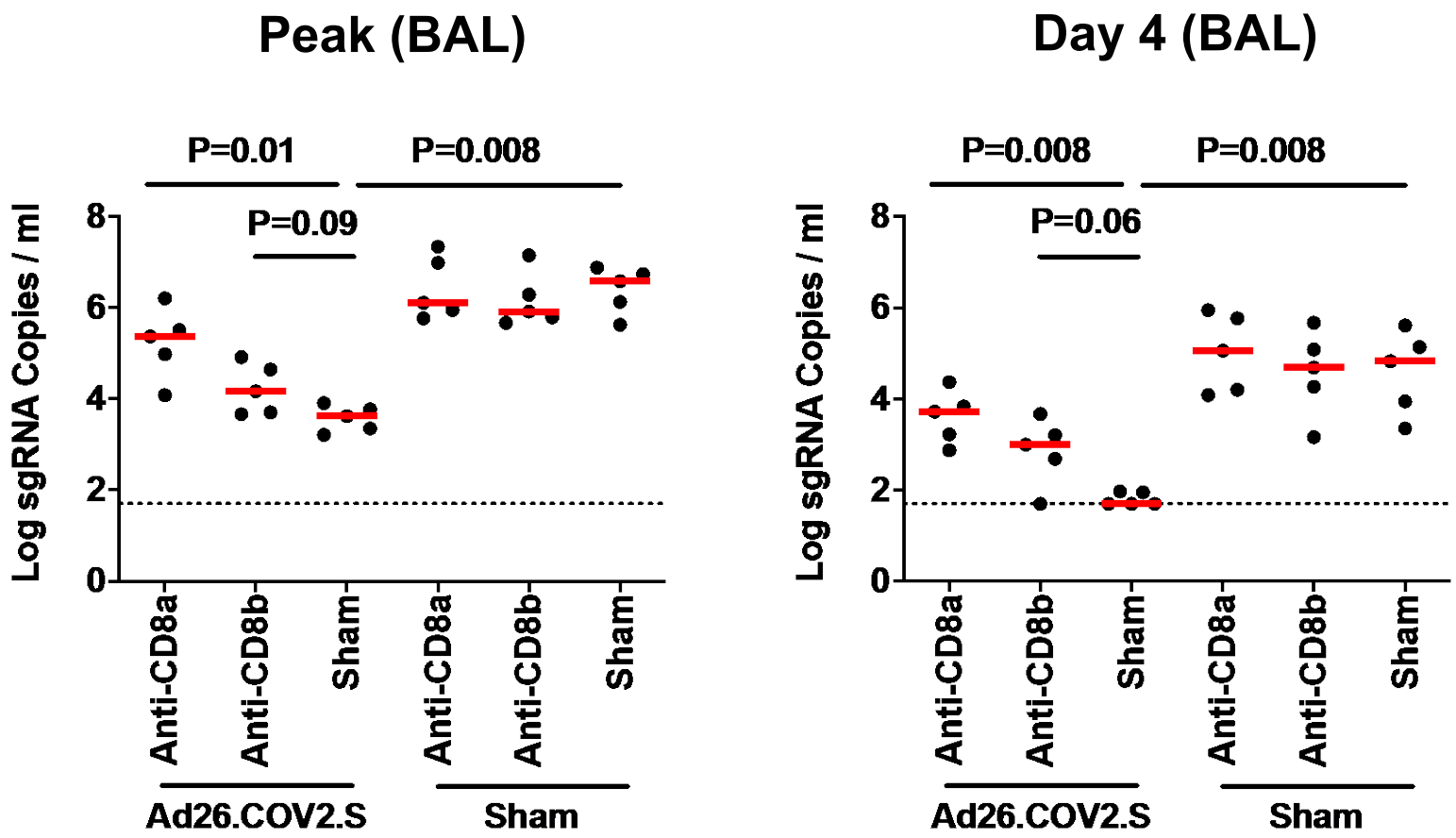
In Vivo CD8 T Cell Depletion to Evaluate Mechanistic Correlates of Protection Against Delta in Macaques



Liu et al. Sci. Immunol. Aug 9, 2022

In Vivo CD8 T Cell Depletion Reduces Vaccine Protection Against SARS-CoV-2 Delta in Macaques



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Correlates of Protection for COVID-19 Vaccines: Conclusions

- Neutralizing, Fc functional, and binding antibodies correlate with protection against SARS-CoV-2
- Data from macaques and humans suggest that both antibodies and CD8 T cells, and not antibodies alone, are important for vaccine protection
- CD8 T cell responses demonstrate substantially greater durability and cross-reactivity against variants than neutralizing antibody responses
- Short-term NAb responses are important, but durability of Ab and T cell responses critical for protection against severe disease with variants

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