Vaccine Protection Against the SARS-CoV-2 Omicron Variant in Macaques

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

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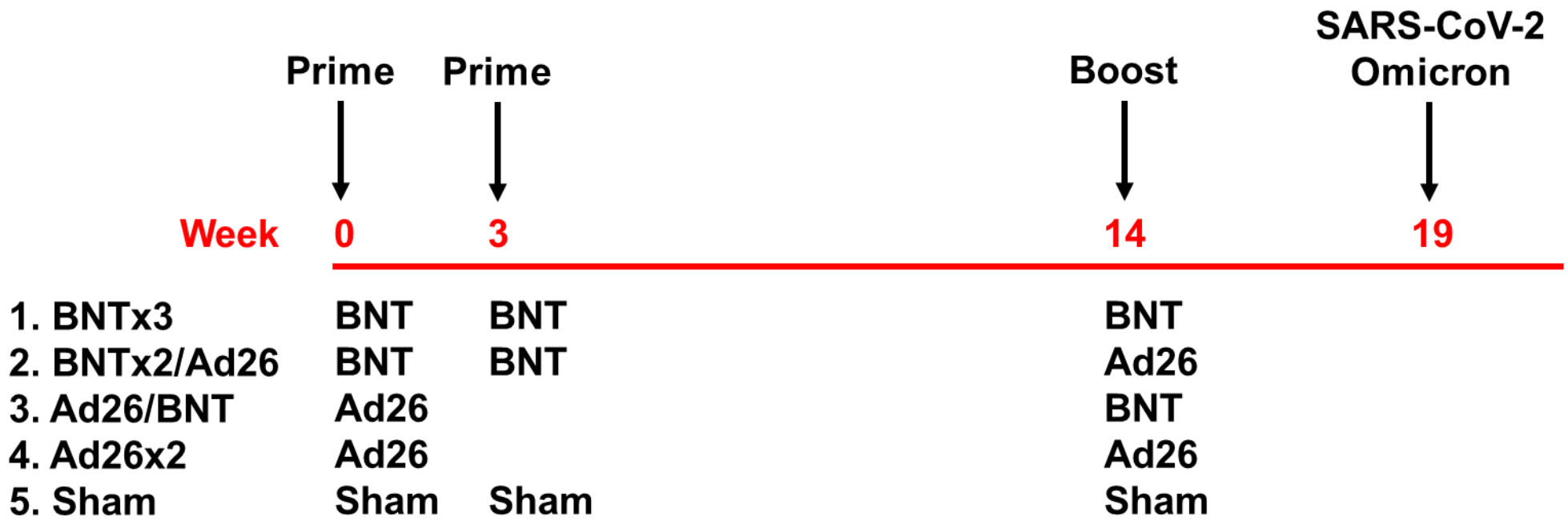
- **Goal: To evaluate the protective efficacy and immune correlates of mRNA and adenovirus vaccines against Omicron**

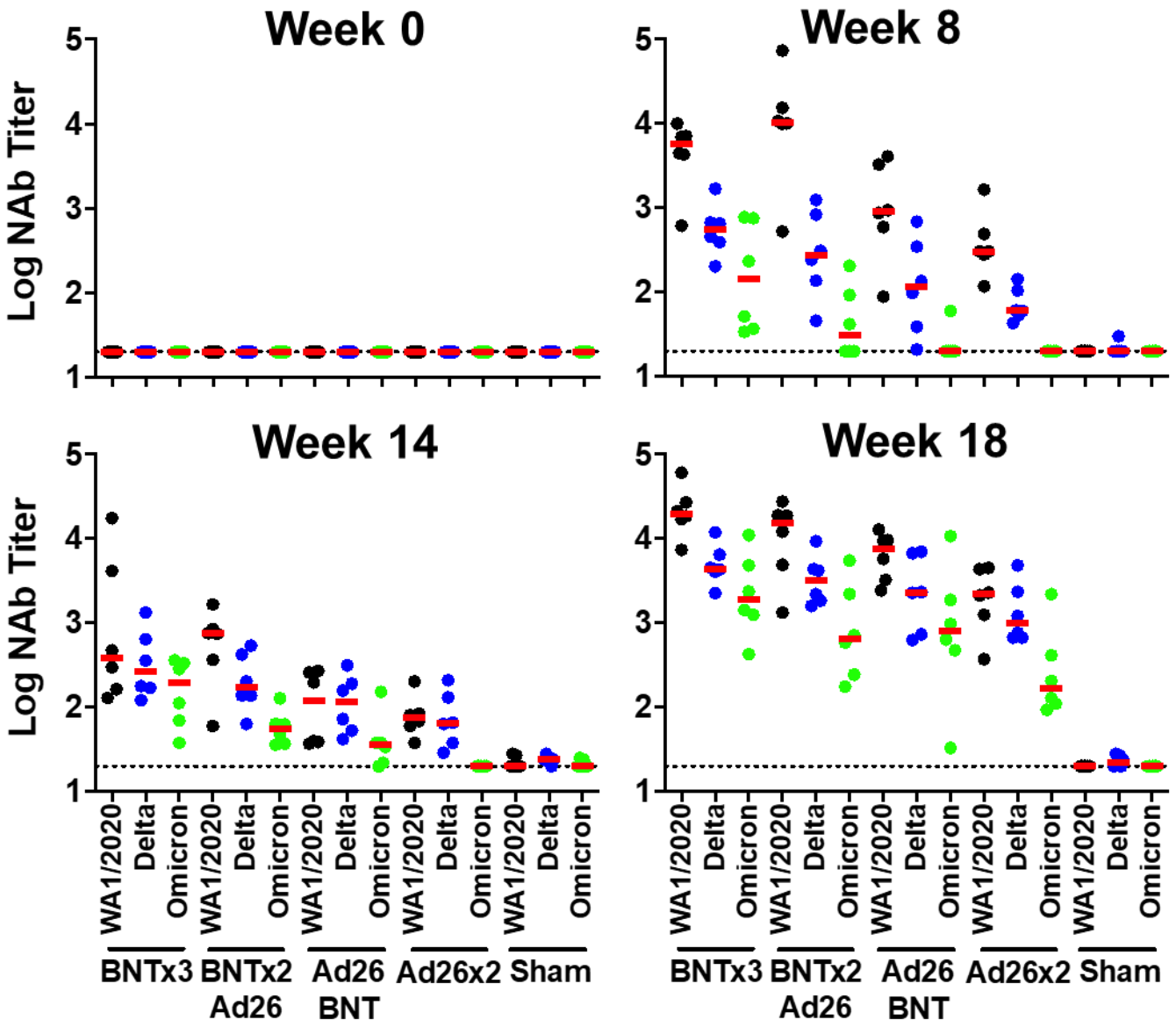
- **30 cynomolgus macaques (N=6/group)**
  - **BNTx3:** **BNT162b2 (week 0, 3, 14)**
  - **BNTx2/Ad26:** **BNT162b2 (weeks 0, 3), Ad26.COV2.S (week 14)**
  - **Ad26/BNT:** **Ad26.COV2.S (week 0), BNT162b2 (week 14)**
  - **Ad26x2:** **Ad26.COV2.S (week 0, 14)**
  - **Sham:** **Sham (weeks 0, 3, 14)**

- **High-dose 10^6 PFU SARS-CoV-2 Omicron challenge at week 19 by the IN+IT routes (challenge stock provided by Mehul Suthar, Emory)**

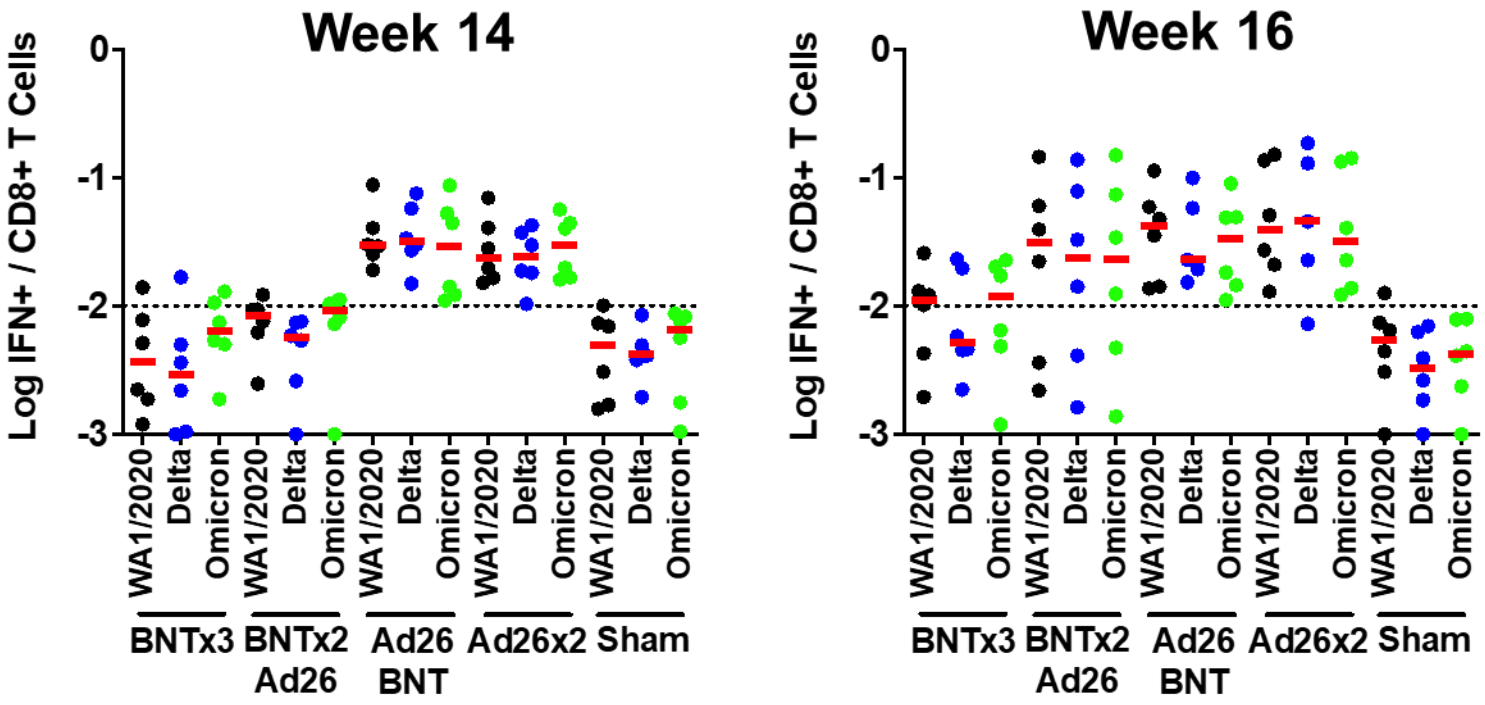
Study Outline



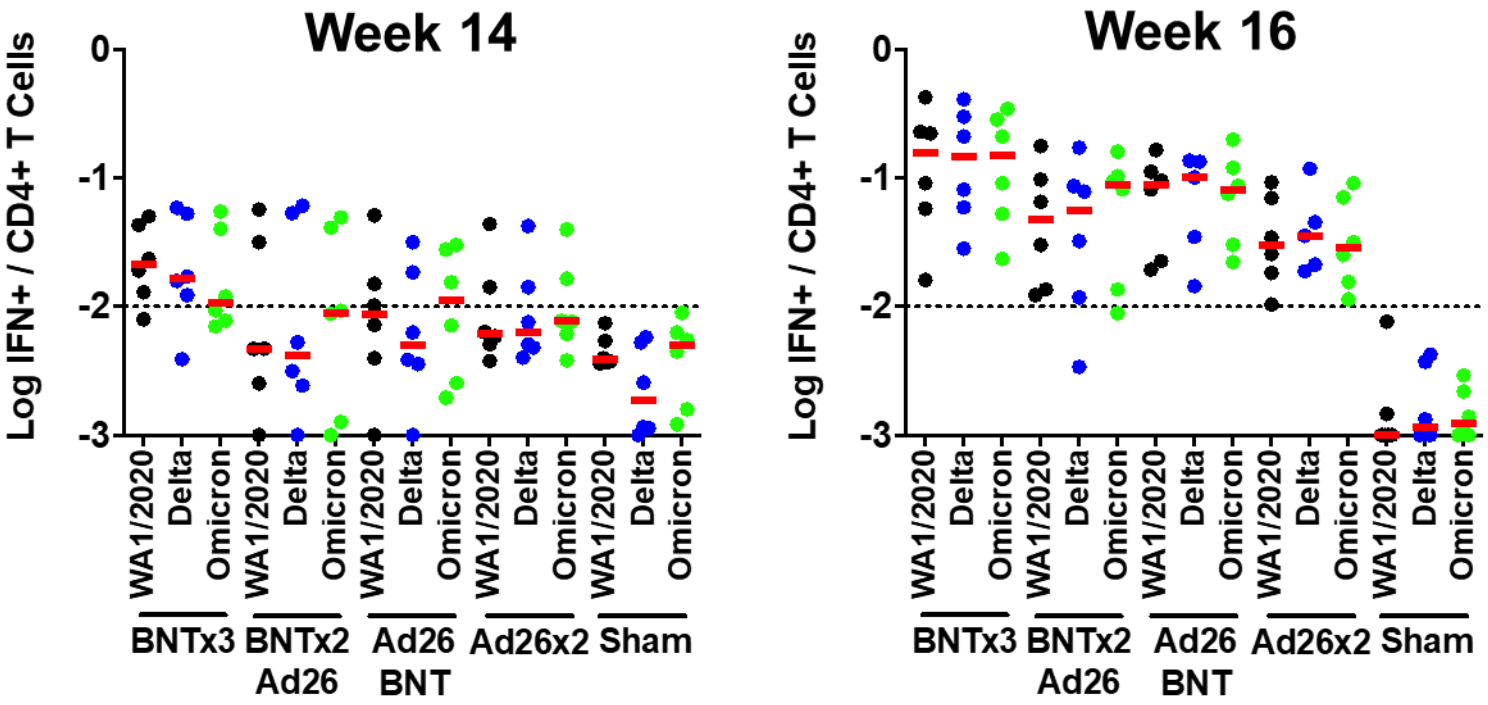
Pseudovirus NAb Responses



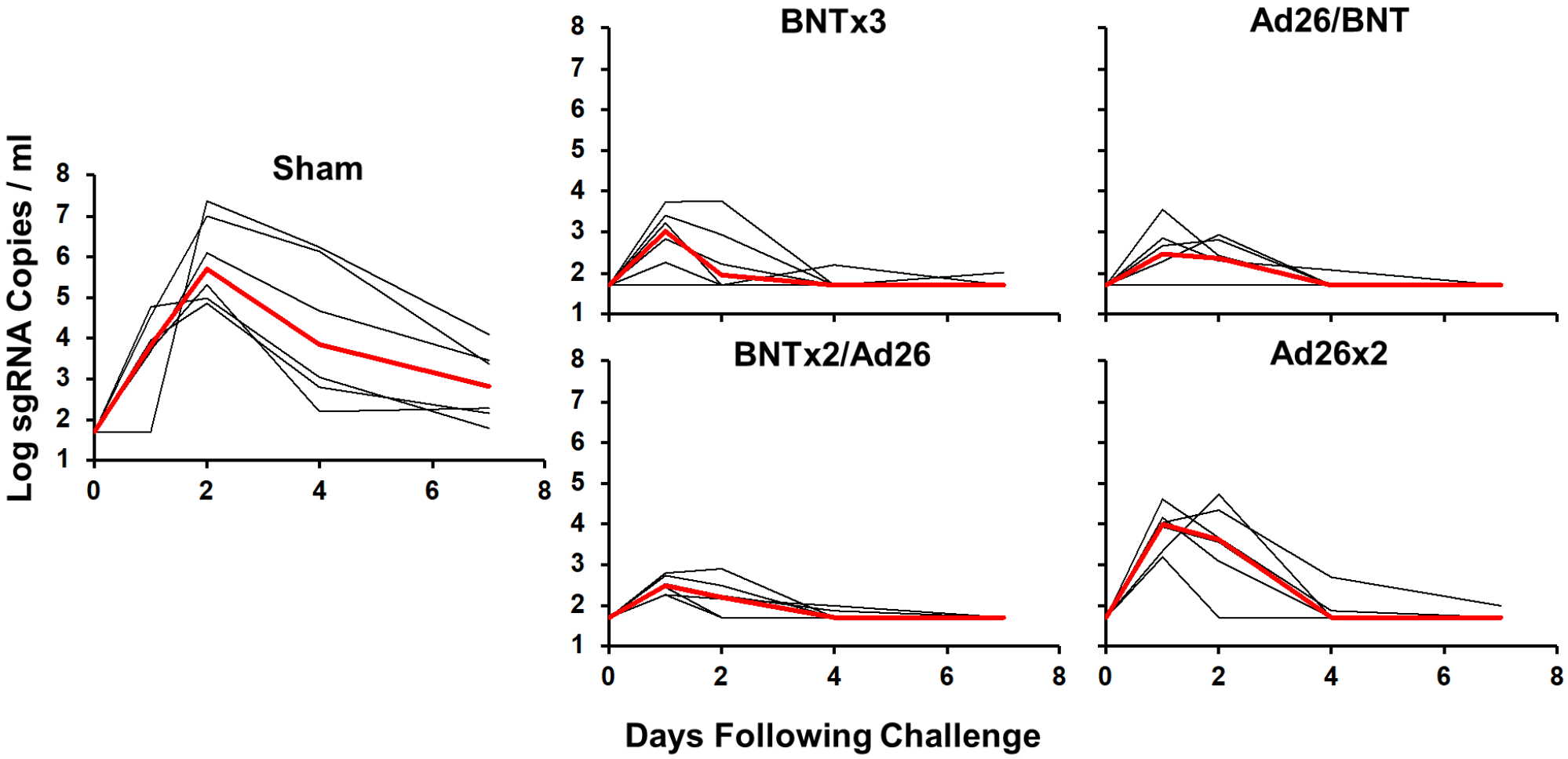
CD8+ T Cell Responses



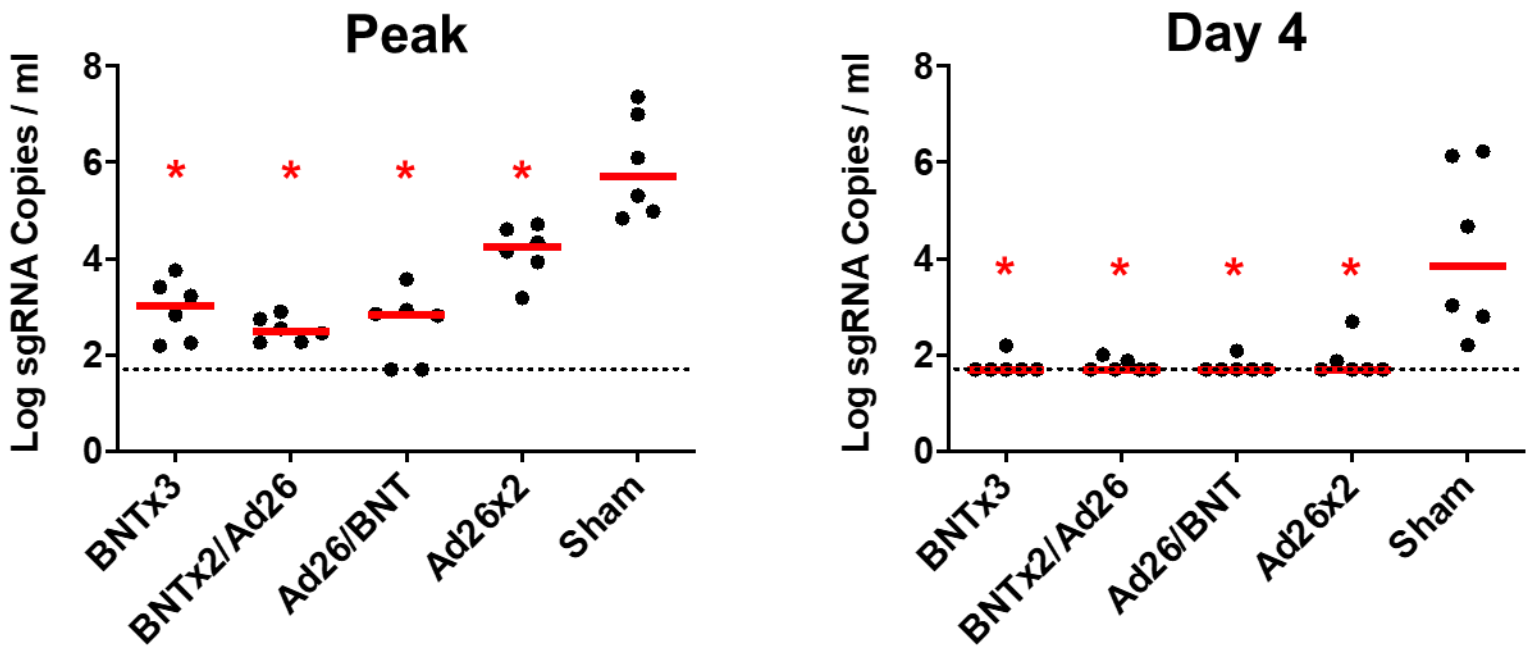
CD4+ T Cell Responses



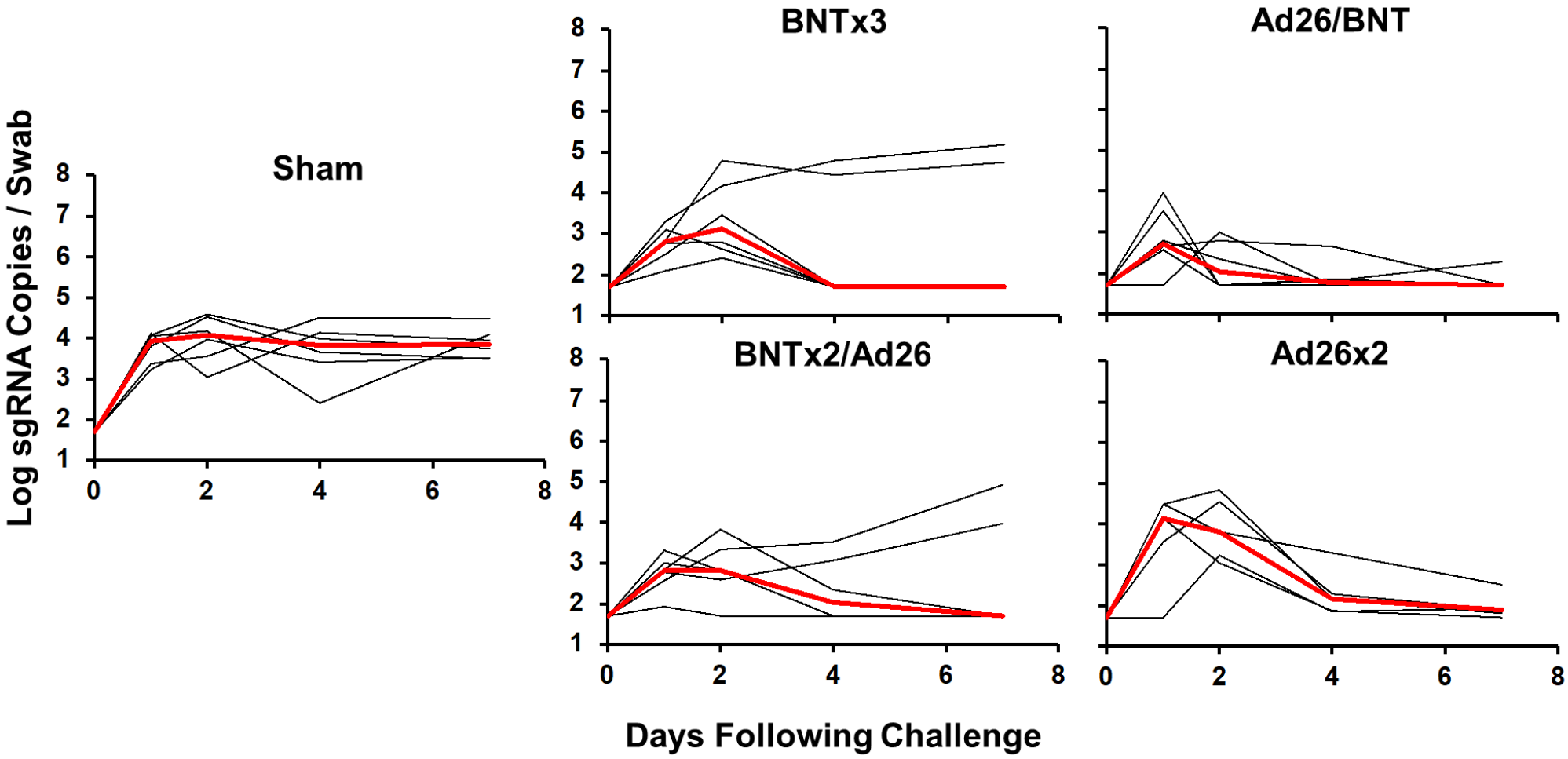
Viral Loads (sgRNA) in BAL



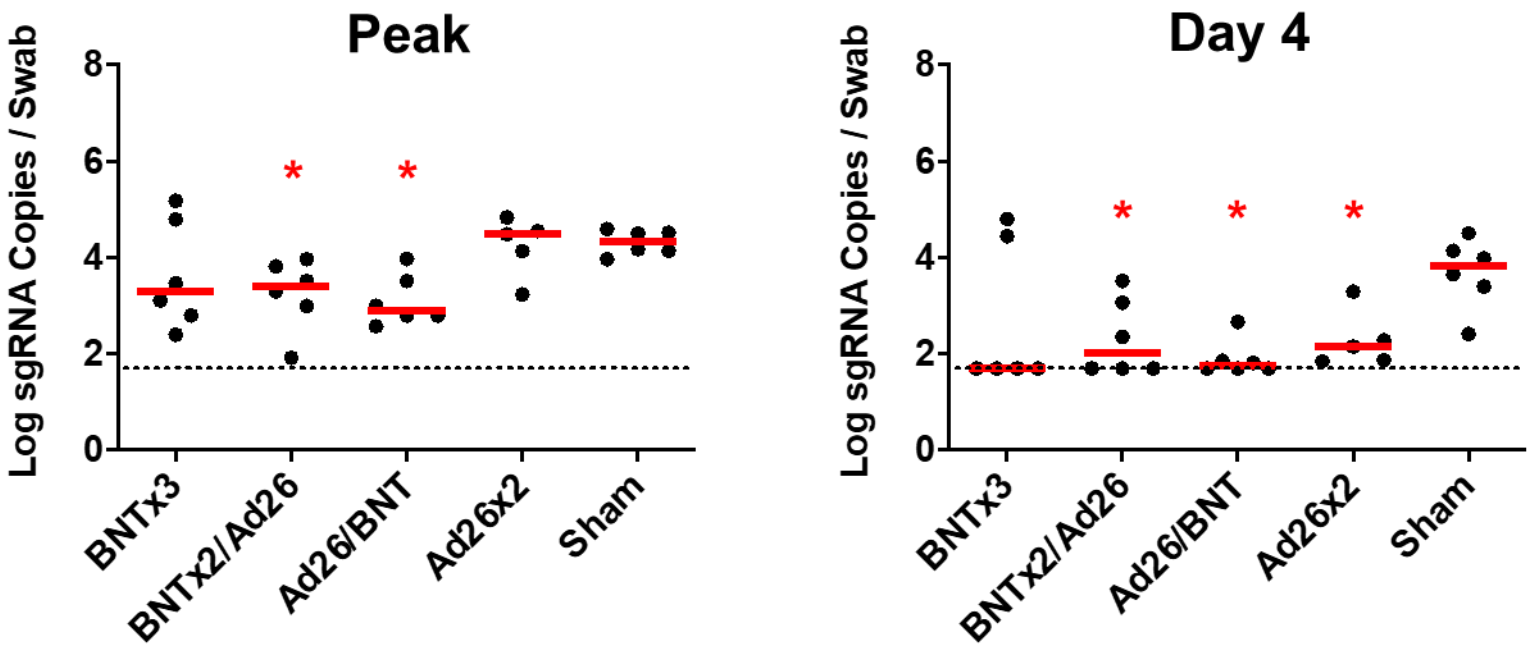
Peak and Day 4 Viral Loads (sgRNA) in BAL



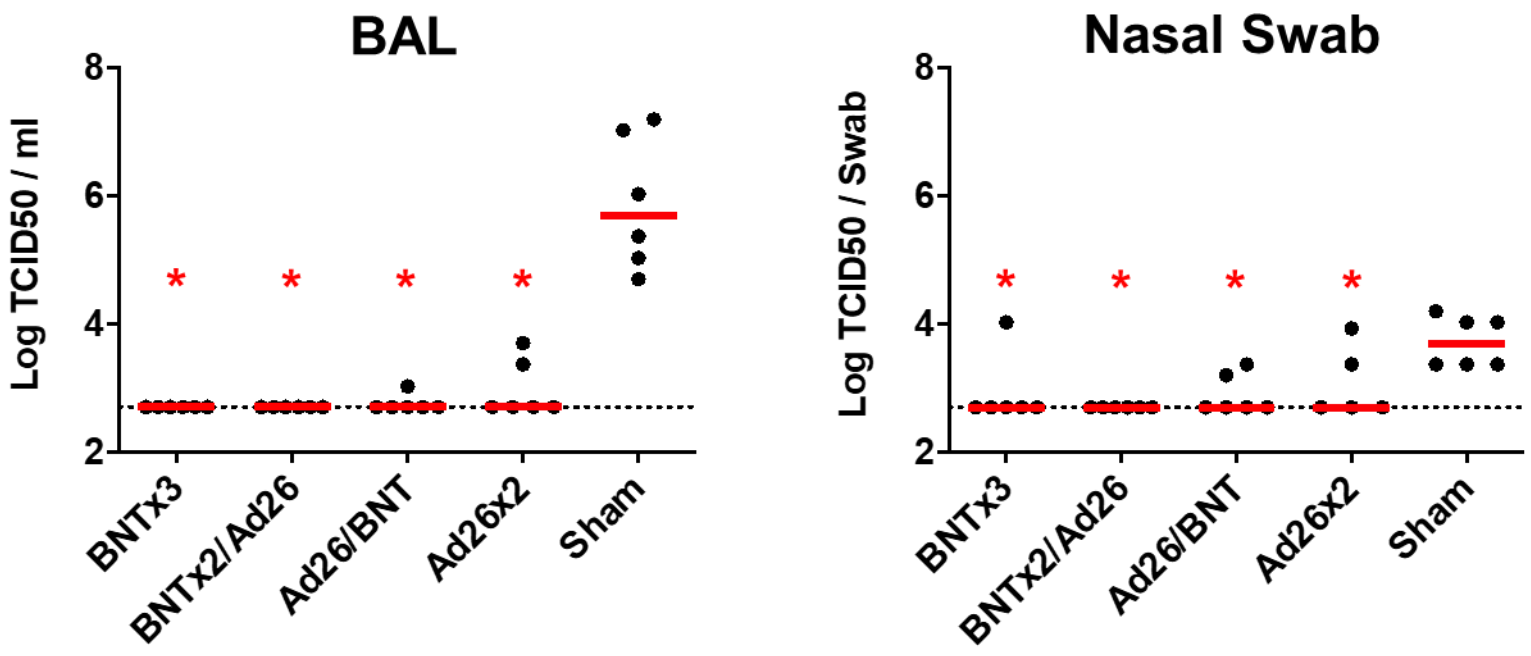
Viral Loads (sgRNA) in Nasal Swabs



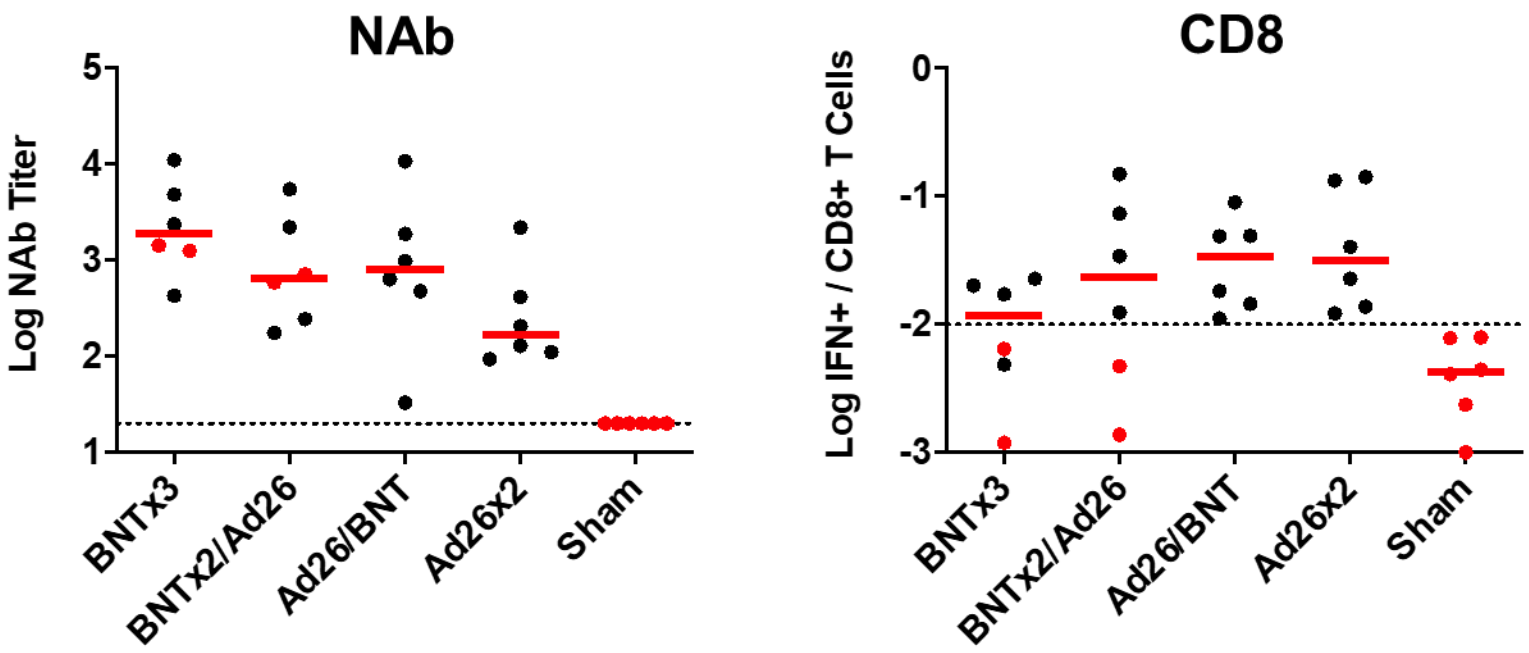
Peak and Day 4 Viral Loads (sgRNA) in Nasal Swabs



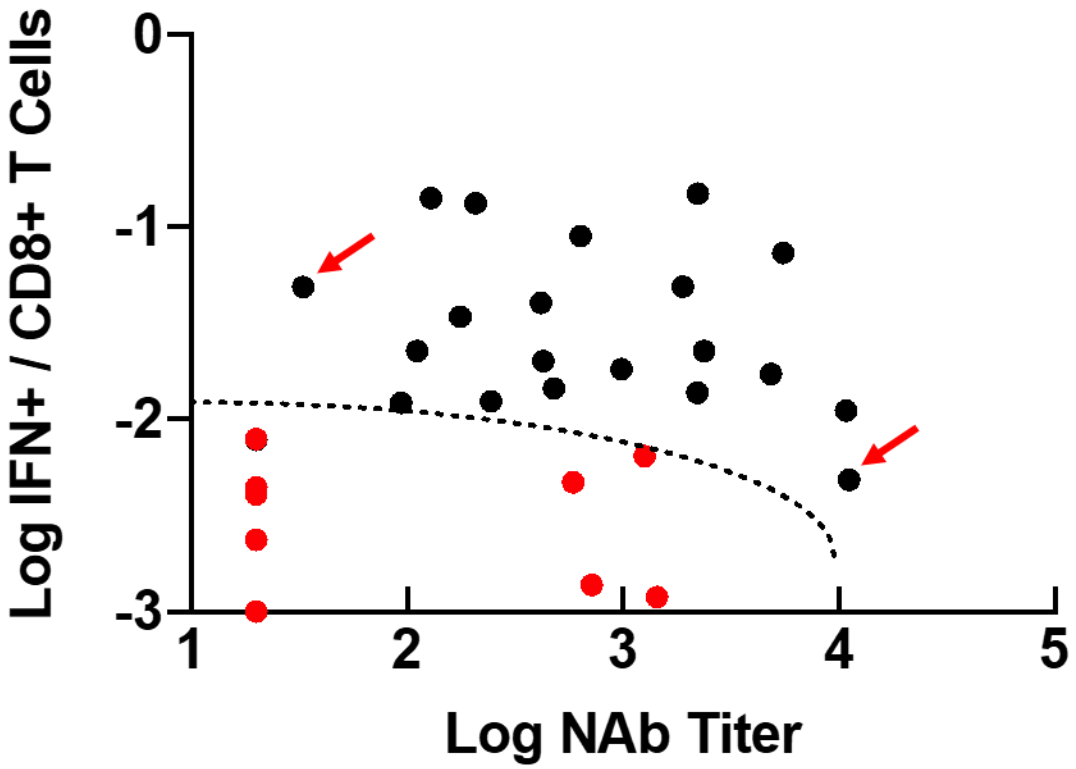
Day 2 Infectious Virus Titers (TCID50)



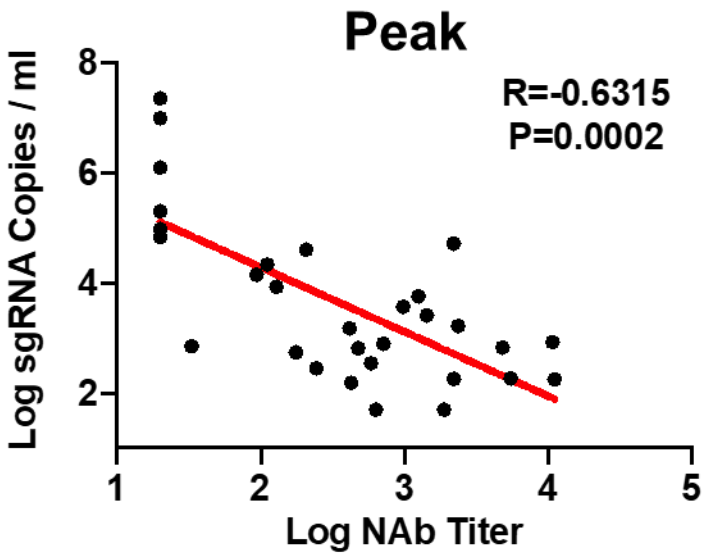
Immunologic Profile of Vaccine Failures

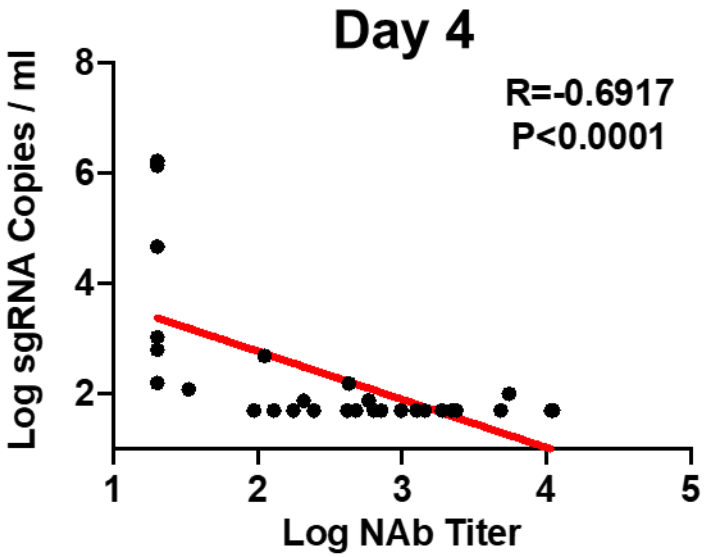


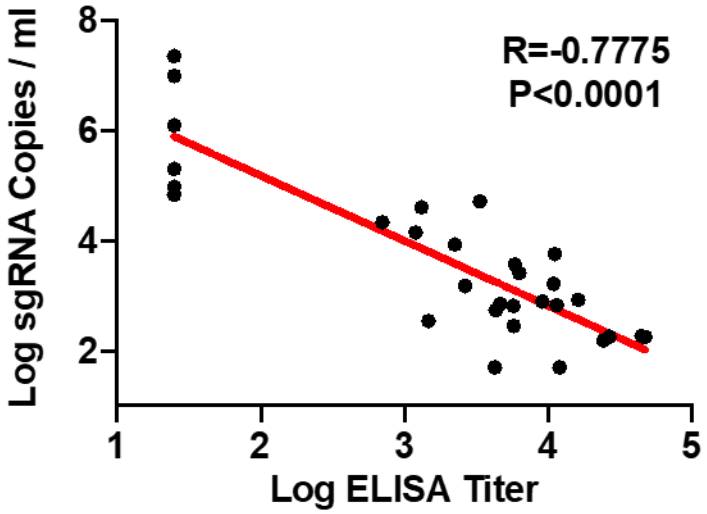
Immunologic Profile of Vaccine Failures Suggests Role of Antibodies and CD8 T Cells in Protection

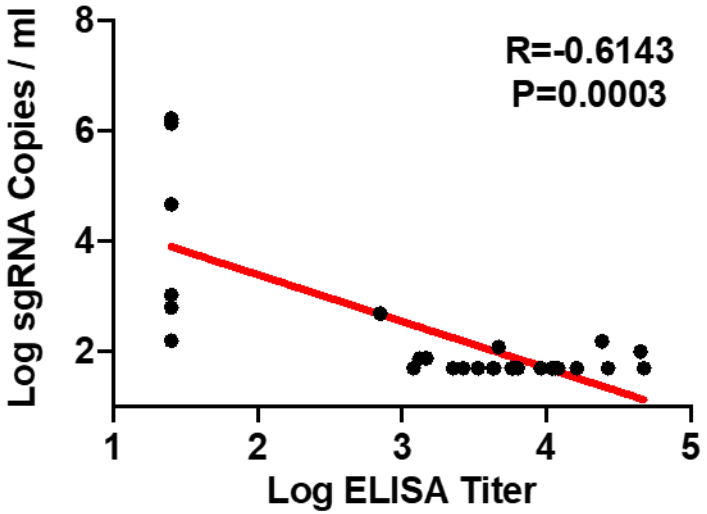


Antibody Correlates of Protection

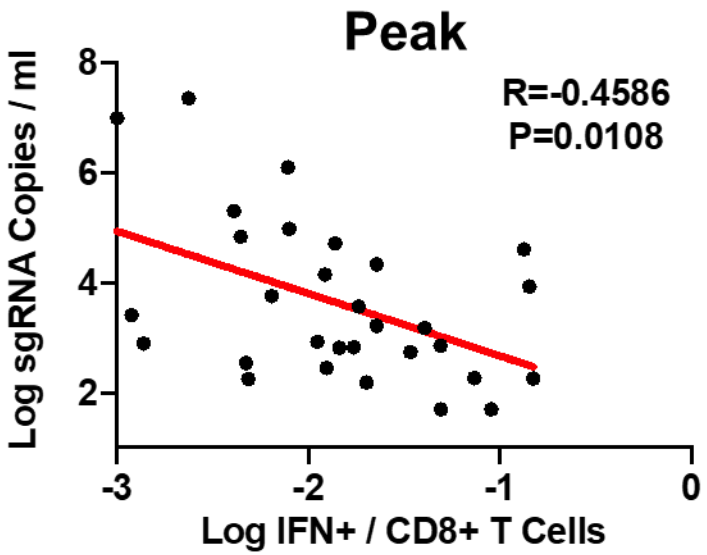


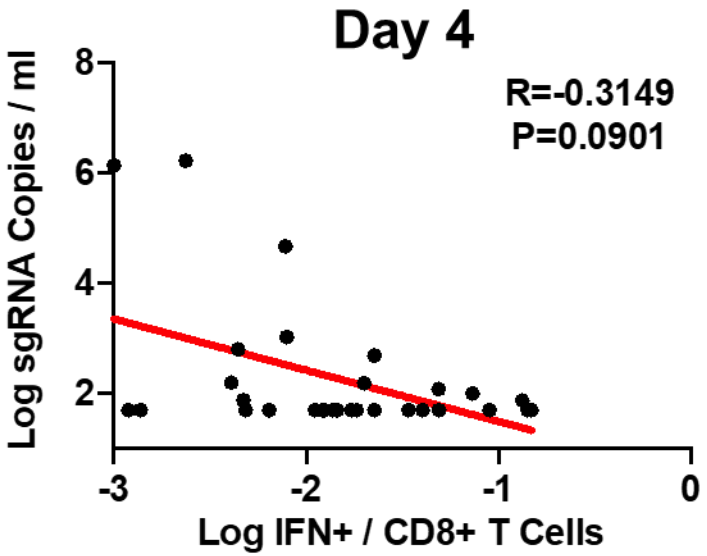


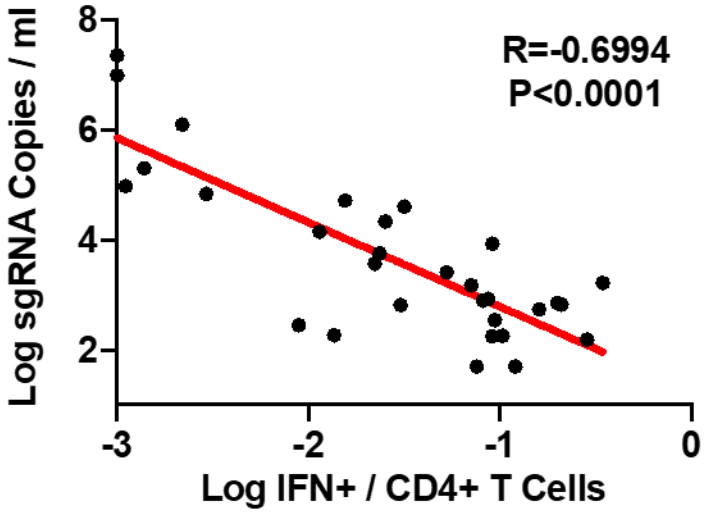


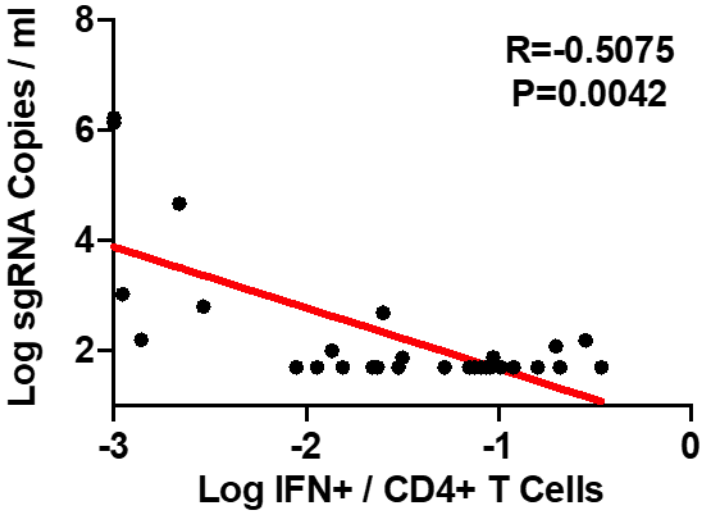


T Cell Correlates of Protection









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- **Rapid virologic control in vaccinated macaques in lower respiratory tract following SARS-CoV-2 Omicron challenge**
- **Significant virologic control by heterologous vaccine regimens (BNT/Ad26, Ad26/BNT) in upper respiratory tract**
- **BNT162b2 induced higher antibody responses; Ad26.COV2.S induced higher CD8 T cell responses**
- **Both antibody and CD8 T cell responses correlated with virologic control; virologic failure in upper respiratory tract associated with moderate NAb titers and low CD8 T cell responses**

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