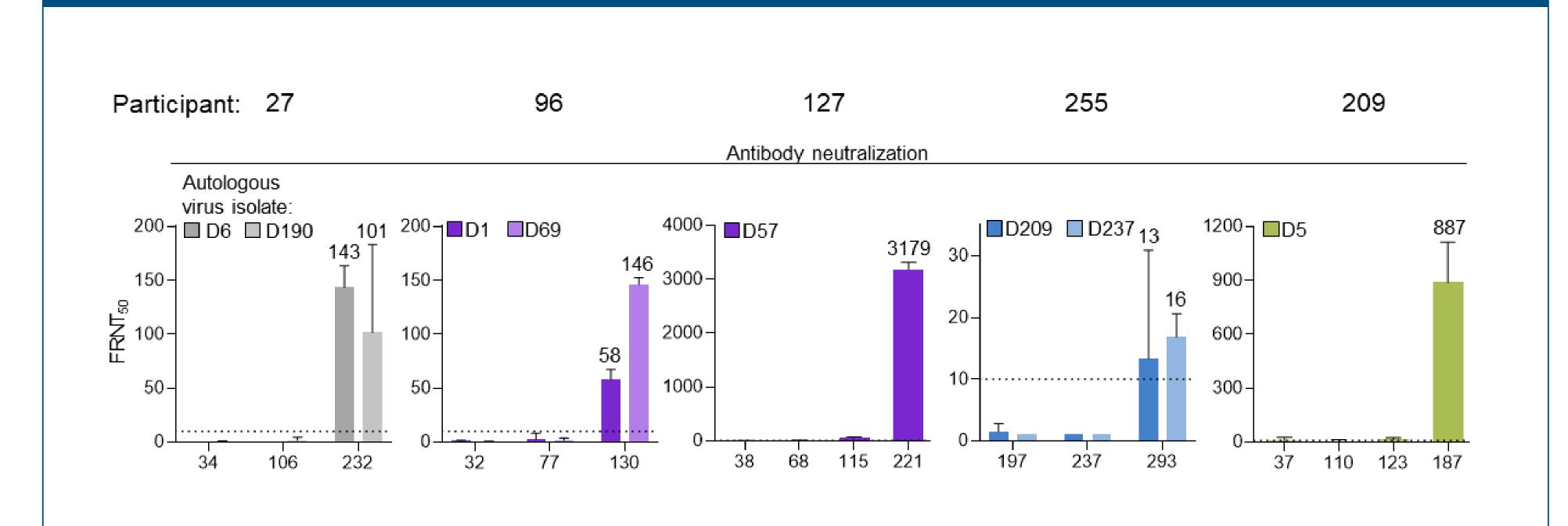
Emergence of neutralizing antibodies associates with clearance of SARS-CoV-2 during HIV-mediated immunosuppression

Farina Karim^{1,2}, Catherine Riou^{3,4}, Mallory Bernstein¹, Zesuliwe Jule¹, Gila Lustig⁵, Strauss van Graan^{6,7}, Roanne S. Keeton³, Janine-Lee Upton¹, Yashica Ganga¹, Khadija Khan^{1,2}, Kajal Reedoy¹, Matilda Mazibuko¹, Katya Govender¹, Kershnee Thambu¹, Nokuthula Ngcobo¹, Elizabeth Venter^{6,7}, Zanele Makhado^{6,7}, Willem Hanekom^{1,8}, Anne von Gottberg^{9,10}, Monjurul Hoque¹¹, Quarraisha Abdool Karim^{5,12}, Salim S. Abdool Karim^{5,12}, Nithendra Manickchund¹³, Nombulelo Magula¹⁴, Bernadett I. Gosnell¹³, Richard J. Lessells^{5,15}, Penny L. Moore^{6,7}, Wendy A. Burgers^{3,4}, Tulio de Oliveira^{5,15,16,17}, Mahomed-Yunus S. Moosa¹³, Alex Sigal^{1,2,5}

Background

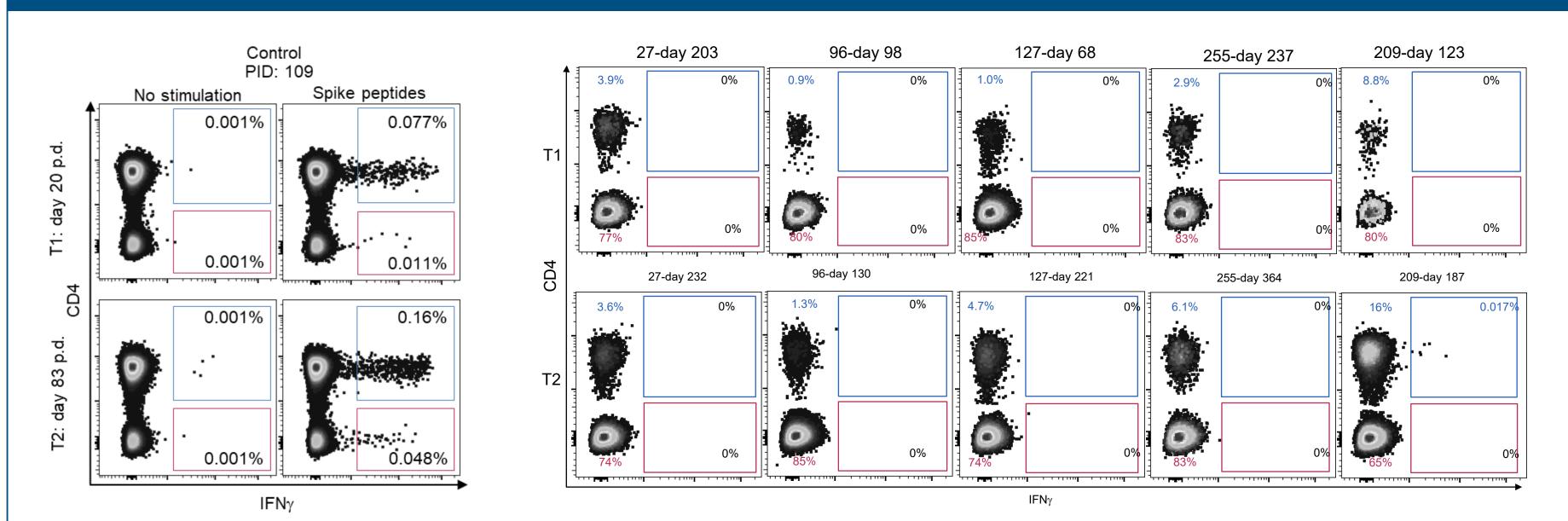
- Emergence of new variants through SARS-CoV-2 evolution compromises the effectiveness of current vaccines.
- •Persistent SARS-CoV-2 infection because of immunosuppression may drive accelerated SARS-CoV-2 evolution and it is therefore critical to understand how such persistent infections can be cleared.
- While adaptive immunity is known to be required for SARS-CoV-2 clearance, the relative contribution of neutralizing antibodies and T cells to clearance in immunosuppression is not well understood.
- •Here we examined whether neutralizing antibody and T cell responses are associated with the clearance of persistent SARS-CoV-2 infection in people recovering from advanced HIV-mediated immunosuppression through adherence to HIV antiretroviral therapy.

SARS-CoV-2 clearance in advanced HIV disease immunosuppression associates with neutralizing antibody response



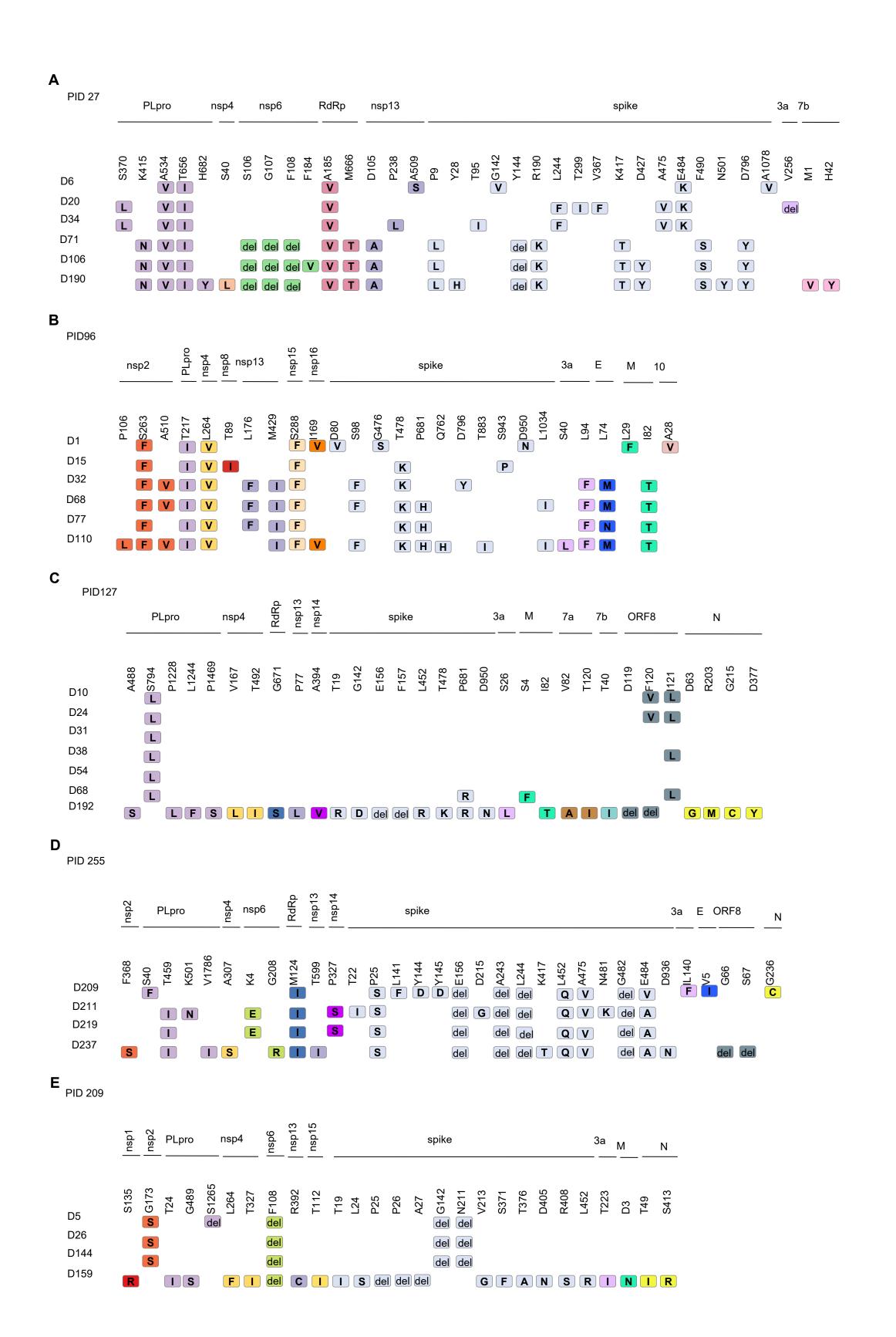
Neutralization by plasma from each participant sampled at different timepoints of SARS-CoV-2 infection with virus isolated from the same participant. One to two autologous viruses were tested per participant and are indicated top left on each graph by day of isolation post-diagnosis. Numbers above bars are geometric mean FRNT50, and error bars are geometric mean standard deviations of FRNT50.

SARS-CoV-2 specific T cell responses in controls and advanced HIV disease



Flow cytometry results showing CD4 (blue) and CD8 T cell (red) frequencies in advanced HIV disease participants at two timepoints (T1, pre-SARS-CoV-2 clearance; T2, post-SARS-CoV-2 clearance).

Substitutions or deletions in SARS-CoV-2 sequences of advanced HIV disease participants through time



Horizontal axis indicates the SARS-CoV-2 protein where substitution or deletion occurred relative to the infecting strain and vertical axis is the time postdiagnosis the viral isolate was obtained.

- Neutralizing antibodies may be required for SARS-CoV-2 clearance in recovery from HIV mediated immunosuppression.
- Successful management of HIV is necessary to curtail evolution of co-infecting pathogens.

¹Africa Health Research Institute, Durban, South Africa. ²School of Laboratory Medicine and Medical Sciences, University of KwaZulu-Natal, Durban, South Africa. ³Institute of Infectious Disease and Molecular Medicine, Division of Medical Virology, Department of Pathology, University of Cape Town, Observatory, South Africa. ⁴Wellcome Centre for Infectious Diseases Research in Africa, University of Cape Town, Observatory, South Africa. ⁵Centre for the AIDS Programme of Research in South Africa, Durban, South Africa. ⁶SAMRC Antibody Immunity Research Unit, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. ⁷National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa. 8Division of Infection and Immunity, University College London, London, UK. 9Centre for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa. 10 School of Pathology, University of the Witwatersrand, Johannesburg, South Africa. 11 KwaDabeka, South Africa. 12 Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, United States. 13 Department of Infectious Diseases, Nelson R. Mandela School of Clinical Medicine, University of KwaZulu-Natal, Durban, South Africa. 14 Department of Internal Medicine, Nelson R. Mandela School of Medicine, University of Kwa-Zulu Natal, Durban, South Africa. 15KwaZulu-Natal Research Innovation and Sequencing Platform, Durban, South Africa. 16Centre for Epidemic Response and Innovation, School of Data Science and Computational Thinking, Stellenbosch University, Stellenbosch, South Africa. ¹⁷Department of Global Health, University of Washington, Seattle, USA.













