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Louies Liu
Assistant Editor
VIRUSES

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Dear Louies

Manuscript entitled: "**Longitudinal IgA and IgG response, and ACE2 binding blockade, to full length SARS-CoV-2 spike protein variants in a population of Black PLWH vaccinated with ChAdOx1 nCoV-19**"

Authors: *Muneerah Smith, Gaurav Kwatra, Alane Izu, Andrew JM Nel, Clare L. Cutland, Khatja Ahmed, Vicky Baillie, Shaun L. Barnabas, Qasim Bhorat, Carmen Briner, Erica Lazarus, Keertan Dheda, Lee Fairlie, Anthonet Koen, Shabir Madhi, Jonathan Blackburn*

Further to our previous email correspondence, I would now like to submit the above manuscript for publication in *Viruses* as a Brief Report.

It is commonly accepted that vaccines against SARS-CoV-2 have been pivotal in overcoming the Covid-19 pandemic, yet understanding the subsequent outcomes and immunological effects remain crucial, especially for at-risk groups such as people living with human immunodeficiency virus (HIV) (PLWH) and people of African descent. Epidemiological studies suggest that people of black African descent are at increased risk of severe COVID-19 disease and death, with an adjusted hazard ratio of 1.4-1.7 for death in African Americans. Seroprevalence studies in South Africa - which has a high prevalence of HIV infection - suggest that prevalence of SARS-CoV-2 reached 80%, but with low mortality.

In the present manuscript, we report the longitudinal (Day 0, Day 28 and Day 42) IgA and IgG antibody titres, as well as antibody-mediated angiotensin converting enzyme 2 (ACE2) binding blockade, against the SARS-CoV-2 spike (S) protein after 1 and 2 doses of the ChAdOx1 nCoV-19 vaccine in a population of Black PLWH. We report that PLWH ($N$ = 103) did not produce an anti-S IgA response after infection or vaccination, but anti-S IgG was detected in response to vaccination and infection, with the highest level detected for infected vaccinated participants. The anti-IgG and ACE2 blockade assays revealed that both vaccination and infection results in IgG production, however, only vaccination results in a moderate increase in ACE2 binding blockade to the ancestral S protein. Vaccination with a previous infection resulted in the greatest anti-S IgG and ACE2 blockade for the ancestral S protein, whereas a lower response was observed for the B.1.351, then B.1.1.7 S protein variants.

The striking absence of measurable anti-S IgA response in blood following vaccination or natural infection in PLWH reported in this manuscript may reflect a fundamental difference in B-cell responses in PLWH due to perturbation of $CD4^+$ T-cell responses, or may simply reflect a shorter-lived anti-S IgA response in PLWH than in HIV-negative participants. Either way, this perturbed anti-S IgA response may impact on susceptibility to SARS-CoV-2 infection in PLWH. We therefore believe that this Brief Report will fit within the scope of *Viruses* and that it will be of interest to your broad readership.

I confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal.

I further confirm that all authors have approved the manuscript and agree with its submission to *Viruses*.

Yours sincerely

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