Higher coronavirus antibody responses pre-pandemic in Africa than in Thailand

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ABSTRACT

COVID-19 clinical manifestations range from asymptomatic to severe disease. Prior immune responses to human coronaviruses may affect individual responses to SARS-CoV-2. We surveyed coronavirus responses pre-pandemic in individuals from Kenya, Nigeria, Tanzania, Uganda and Thailand; 81% were people living with HIV (PLWH).

Specimens were screened for SARS-CoV-2 Spike S2 subunit IgG responses. Selected samples were tested using a bead-based immunoassay that profiled the specificity, isotype and subclass of antibody responses to coronavirus, flavivirus and HIV antigens. Wilcoxon rank sum tests were performed to compare responses across antigens and participant group.

We screened 1,875 samples (one per individual) collected between 2013 and October 2019: 1,630 samples were from Africa (87%) and 245 from Thailand. 6.99% of participants (n=131, 116 from Africa (89%) and 15 from Thailand) showed responses above the naïve signal threshold and were further tested (Fig.1). Using a signal to noise ratio of >10 as a cut-off value, 44, 27 and 42 samples showed IgG responses to the Spike protein of SARS-CoV-2, SARS-CoV-1 and MERS-CoV respectively, while 7, 9 and 4 samples showed responses to Nucleocapsid for these same antigens. Some individuals had higher responses than those seen in SARS-CoV-2 convalescent individuals. We found a strikingly different pattern of reactivity in Africa compared to Thailand (Fig. 2). Antibody responses were significantly higher in the African participants compared to Thai participants across antigens corresponding to SARS-CoV-2 ($p<0.001$), SARS-CoV-1 ($p<0.001$) and MERS-CoV ($p<0.01$). Similar patterns were seen for IgG subclasses, IgA and IgM. The difference was less pronounced for the four endemic coronaviruses, nonetheless anti-Spike responses were significantly higher in African participants for HKU1 and OC43 ($p\leq0.018$). In addition, mapping responses to 21 flavivirus antigens showed the highest reactivity in Thailand and in Nigeria.

Our serosurvey of pre-pandemic samples showed that there were significantly higher antibody responses against coronaviruses, including SARS-CoV-2, in Africa than in Thailand. Profiling flavivirus responses showed that the difference between the two regions was not due to a higher background reactivity across African samples. Further analysis is needed to explain pre-pandemic SARS-COV-2-like antibody responses among African participants and explore implications for geographic diversity in disease severity.

BACKGROUND

Pre-pandemic samples from three cohorts were surveyed:

- RV254 in Thailand: PLWH who started ART during HIV acute infection
- RV329 in Kenya, Nigeria, Tanzania, and Uganda: PLWH who started ART during chronic infection; ~ 15% were people without HIV
- RV466 in Nigeria: participants diagnosed with acute febrile infections

METHODS

Prescreen

- 1,630 samples from Africa and 245 from Thailand collected between 2013 and October 2019
- SARS-CoV-2 Spike S2 subunit IgG responses were measured

Multiplex bead-based immunoassay

- 131 samples showing responses above the naïve signal threshold
- Antibody responses against 23 human coronavirus antigens and 11 detection reagents (IgG, IgG1-IgG4, IgA, IgM, FcgR2A, 2B, 3A, 3B) were measured
- Samples were also tested against a flavivirus panel and a HIV-1 panel

- SARS-CoV-2-like responses detected before the pandemic
- Higher reactivity against outbreak coronaviruses among African participants
- No association between coronavirus responses and HIV-1 viral load or CD4 count in PLWH

RESULTS

6.99% of participants showed IgG responses above the naïve signal threshold against SARS-CoV-2 S2

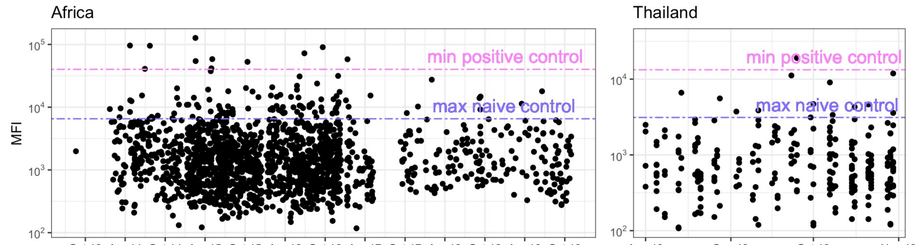

Fig. 1: IgG responses against SARS-CoV-2 Spike S2 mapped on samples collected between 2013 and October 2019

- Samples selected for further testing:
  - 7.11% samples from African participants and 6.12% of Thai participants

Higher coronavirus-specific responses among African participants than among Thai participants

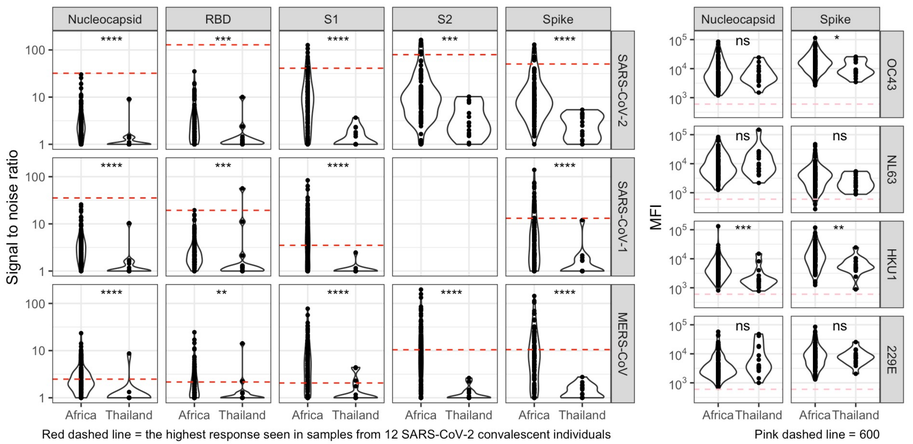

Fig. 2: IgG responses in 116 African and 15 Thai samples against three outbreak coronaviruses reported as signal to noise ratios (left) and against 4 common human coronaviruses reported as adjusted MFI (right). Symbols in each panel indicating statistical significance for Wilcoxon rank sum tests: ns: p > 0.05, *: p <= 0.05, **: p <= 0.01, ***: p <= 0.001, ****: p <= 0.0001

No correlation between coronavirus-specific responses and HIV-1 viral load among PLWH

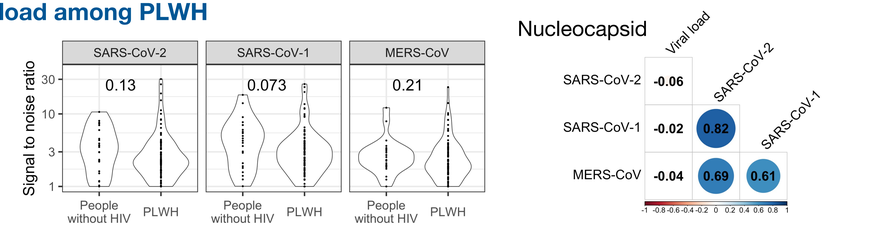

Fig. 3: Three outbreak coronaviruses Nucleocapsid IgG responses in 23 people without HIV and 92 PLWH in Africa (left) and correlation matrix of viral load at visit from PLWH and the responses (right). The values in the figure show p values of Wilcoxon rank sum tests (left) and Spearman's ρ (right).

- No evidence of different coronavirus responses associated with HIV-1 status

Different profiles for outbreak coronaviruses, flavivirus and HIV-1 specific responses in Thai and African participants

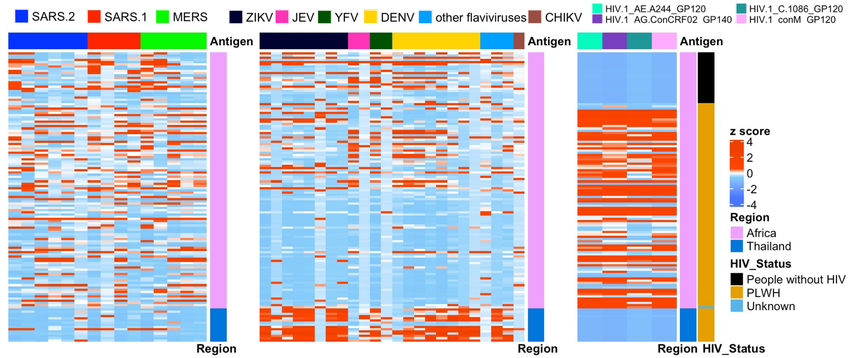

Fig. 4: IgG responses against outbreak coronaviruses (left), flaviviruses (middle) and HIV-1 (right). The heatmap shows the normalized MFI values of each antigen by column and each sample by row.

- The higher coronavirus reactivity across African samples was not associated with overall high reactivity for other antigens

CONCLUSION

- Coronavirus-specific antibody profile from pre-pandemic samples shows significantly higher reactivity among African participants than Thai participants, especially for outbreak coronaviruses
  - The responses did not associate with viral loads or CD4 counts in PLWH
- High reactivity in African samples specific to coronaviruses and not seen for flaviviruses or HIV-1 antigens

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