Divergent systemic and mucosal SARS-CoV-2 adaptive immunity in African adults without HIV

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Background

The upper (URT) and lower (LRT) respiratory tracts are the principal sites of SARS-CoV-2 infection and severe COVID-19 disease, respectively.

While serum anti-Spike antibody levels are associated with a reduced risk of reinfection, the mechanistic correlates of airway protection remain unclear.

To evaluate the relationship between systemic immune correlates of protection and SARS-CoV-2 airway mucosal immune responses.

Methods

A prospective cohort study that recruited previously SARS-CoV-2–infected adults in Malawi.

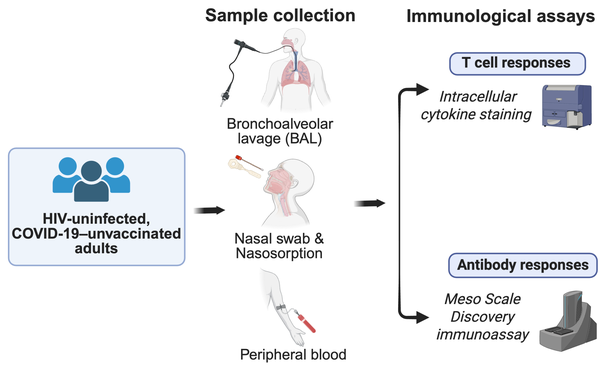


Figure 1: Study design and sample collection

Demographics

Table 1: Participant demographic characteristics

Characteristic	N = 43[1]
Age (years)	29 (24, 37)
Sex	
Female	20 (47%)
Male	23 (53%)
Vaccination status	
Unvaccinated	28 (65%)
Vaccinated	15 (35%)
Number of doses	
1	11 (73%)
2	4 (27%)

[1]Median (Q1, Q3); n (%)

Systemic SARS-CoV-2 IgG correlates of protection **better reflect lower than upper airway immune responses.**

SARS-CoV-2-specific antibody and T cell responses

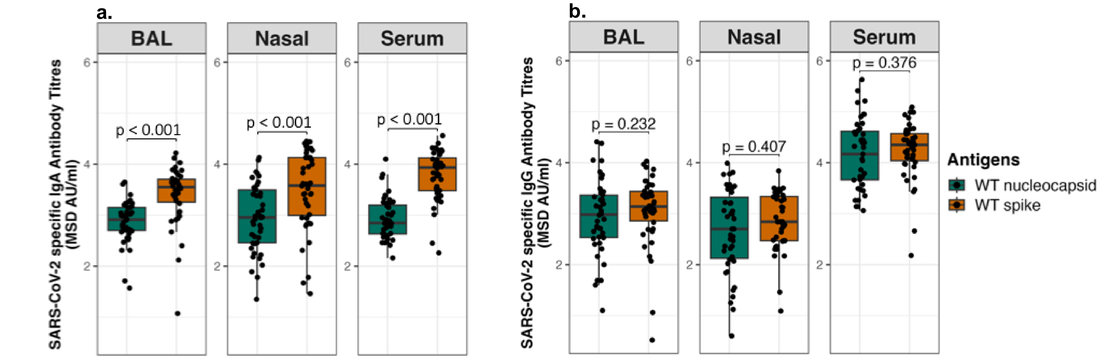


Figure 2. Detectable Wildtype (WT) nucleocapsid (N) and spike (S)–specific IgA and IgG across systemic and mucosal compartments.

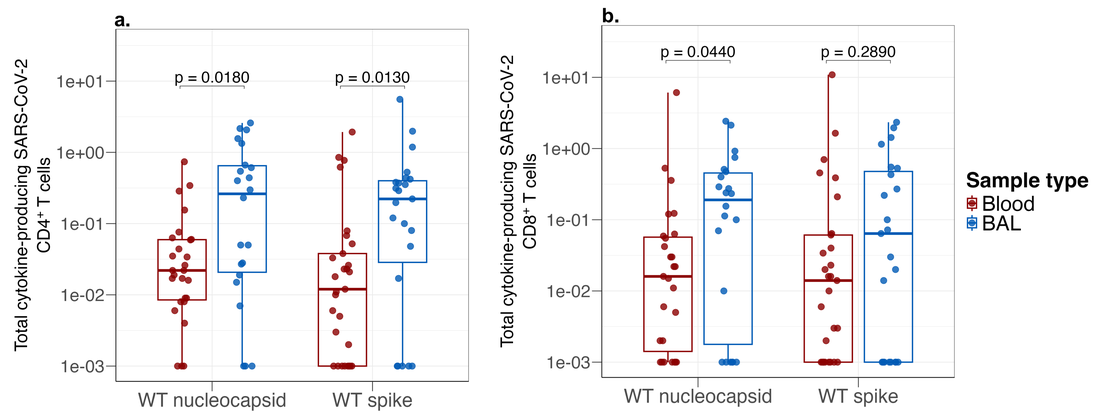


Figure 3: Higher frequencies of S- and N-specific CD4⁺ T cells were observed in the LRT than in blood.

Correlation of systemic and mucosal SARS-CoV-2–specific immune responses

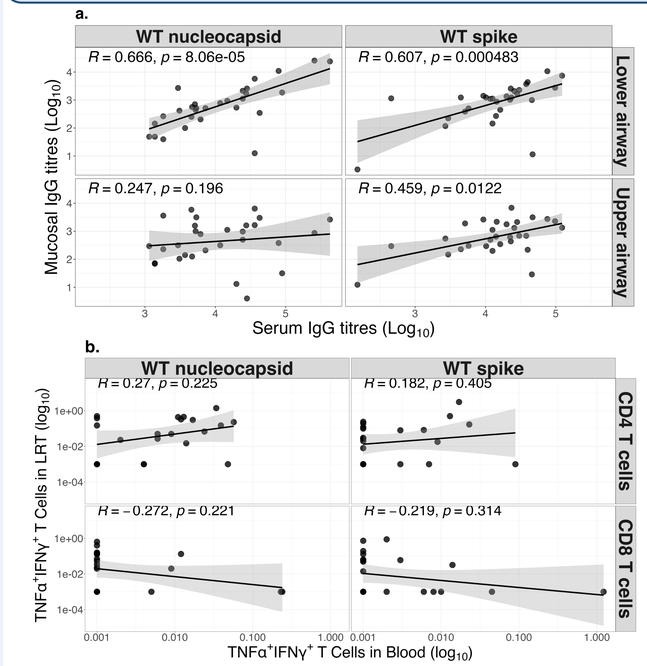


Figure 4: IgG correlates strongly between serum and LRT, weakly with URT; T cells show no correlation between compartments.

Conclusion

Serum anti–S and anti–N SARS-CoV-2–specific IgG correlates more strongly with LRT than URT antibodies, supporting its use as a surrogate marker for lower airway disease rather than upper airway infection.

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Blood antibodies against SARS-CoV-2 better reflect immunity in the lungs than in the nose.