Delineating factors associated with asymptomatic primary SARS-CoV-2 infection

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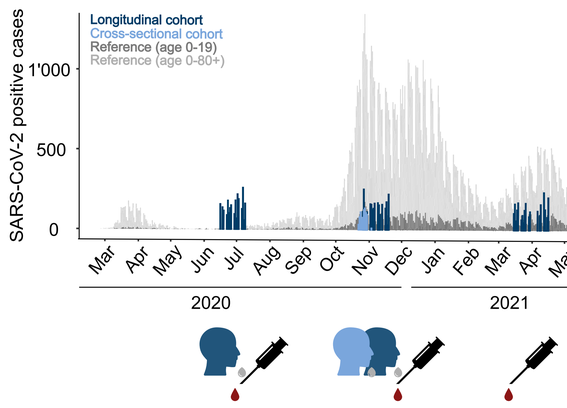
Systemic and mucosa SARS-CoV-2 and HCoV immunity in primary SARS-CoV-2 infection are linked with reduced vira load and asymptomatic infection

BACKGROUND

SARS-CoV-2 infection leads to a broad range of clinical manifestations, from no symptoms to critical illness. Pre-stimulated innate defenses, rapid induction of SARS-CoV-2 responses and **pre-existing cross-reactive immunity** to circulating human coronaviruses (HCoV) may early dampen SARS-CoV-2 infection, preventing symptomatic disease.

Here we explore SARS-CoV-2 and HCoV antibody impact on asymptomatic infection in individuals first encountering SARS-CoV-2 in March 2020-March 2021 participating in a **longitudinal pediatric cohort** (n=2917) and **a cross-sectional adult and children diagnostic cohor**t (n=882) in Switzerland.

METHODS AND RESOURCES



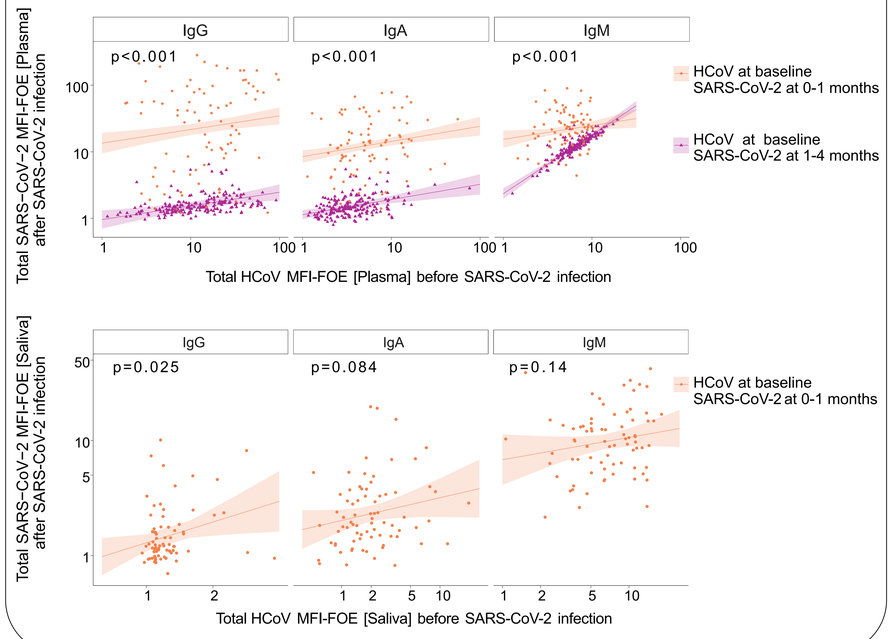
We assessed longitudinally collected saliva (n=4'993) and serum (n=7'486) samples by multifactorial profiling with the ABCORA 2 test (Abela et al. Nat Comm 2021). This provided information on IgG, IgA, and IgM reactivity to four SARS-CoV-2 antigens (RBD, S1, S2, and N) and the S1 protein of HCoV-HKU1 in saliva and plasma samples. A time-matched cohort was remeasured with ABCORA 5 to additionally record IgG, IgA and IgM responses to S1 to HCoV-HKU1, HCoV-NL63, HCoV-OC43. Mucosal (saliva) and systemic (plasma) neutralization activity was assessed against wildtype SARS-CoV-2, Alpha, Delta and Omicron (BA.2).

ACKNOWLEDGEMENTS

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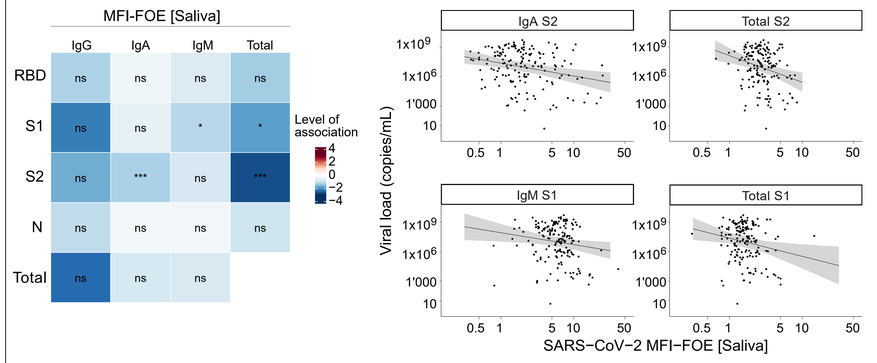
RESULTS

Pre-existing high HCoV antibody response links with higher mucosal and systemic SARS-CoV-2 responses following infection



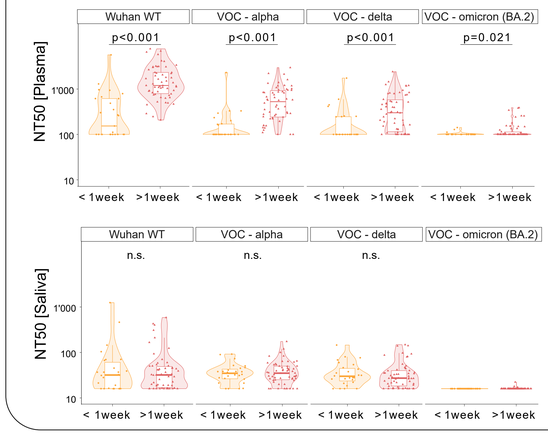
Mucosal Ab response has a significant impact on viral suppression

Inverse association between SARS-CoV-2 antibody levels and virus load in saliva



Saliva total Ig S2, total Ig S1, and IgM S1 (<0.001, p<0.001, p=0.02, p=0.01 respectively) are inversely associated with salivary viral load in PCR positive individuals (n=177).

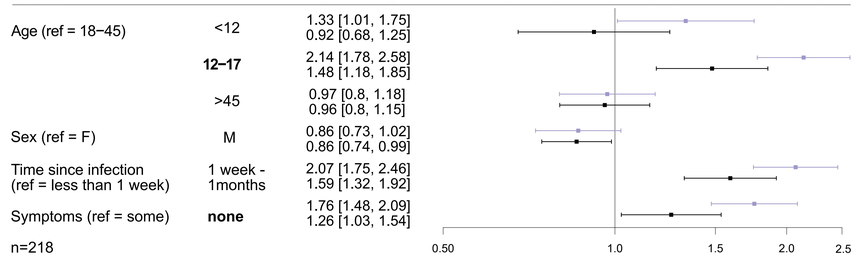
Low but broad neutralization activity in saliva



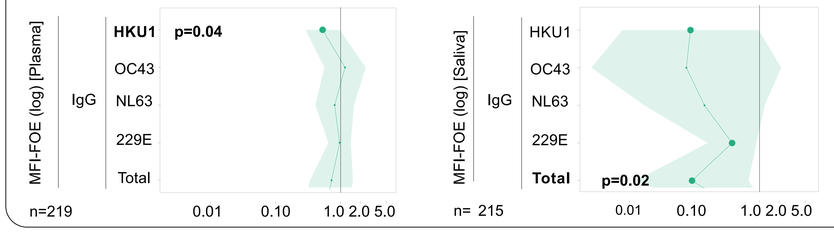
Plasma neutralization activity shows typical decrease for all three VoCs.

Saliva neutralization activity is modest but retains breadth against Alpha and Delta.

Higher levels of saliva IgG S2 in asymptomatic infection



Higher pre-existing HCoV antibody activity in plasma and saliva is linked with lower frequency of symptoms



CONCLUSIONS

Our study reveals interdependencies of systemic and mucosal SARS-CoV-2 and HCoV immunity following primary SARS-CoV-2 infection and locates reactivities linked with reduced viral load and asymptomatic infection.