Cross-reactive antibodies in SARS-CoV-2 infection and vaccination

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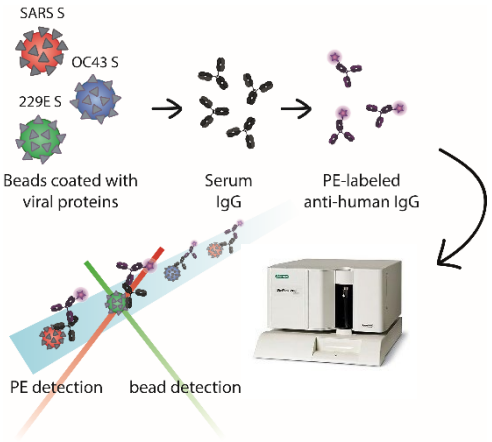
Background

There are still many unknowns about the role of SARS-CoV-2 antibodies in the immune response after infection, but evidence is appearing that previous human coronavirus (HCoV) infections may play an important role. SARS-CoV-2 is very similar in sequence to SARS (77% spike protein sequence identity), less similar to MERS (31%) and most distinct in sequence from the common cold human coronaviruses HKU1, OC43, 229E and NL63 (25-30%).

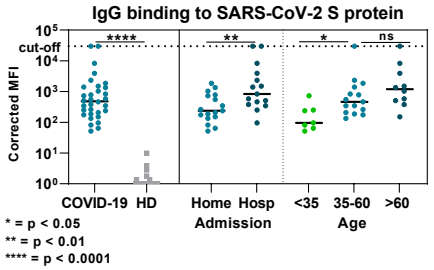
Methods

Recombinant trimeric spike proteins (S) of all 7 HCoVs were expressed, purified and coupled to beads. Using a custom Luminex assay, we investigated spike protein-specific IgG antibody levels in serum of COVID-19 patients, healthy donors and cynomolgus macaques immunized with a SARS-CoV-2 spike nanoparticle vaccine.



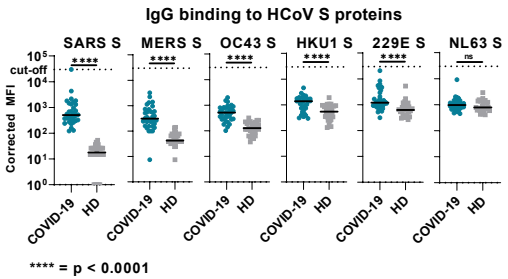
Results

Characterization of IgG binding to SARS-CoV-2 Spike protein in a COVID-19 patient cohort



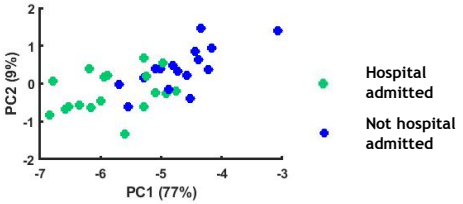
IgG binding to SARS-CoV-2 S was characterized in a cohort of 33 convalescent COVID-19 patients. A potent antibody response was observed, with higher S-specific IgG levels in hospitalized patients compared to the non-hospitalized group and increased IgG levels in older age groups.

Higher levels of cross-binding antibodies in COVID-19 patients compared to healthy donors



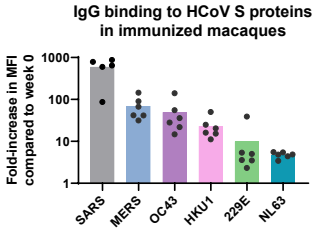
In the same cohort, IgG binding to all other HCoV S proteins except NL63 was found to be significantly higher compared to healthy donors.

Differentiation between hospitalized and non-hospitalized patients based on cross-binding



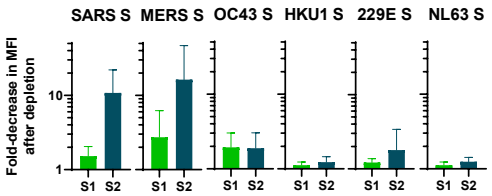
A principle component analysis was performed using log-transformed MFI values for IgG binding to all HCoV S proteins except SARS-CoV-2 as input. The plot shows clustering of the hospitalized and non-hospitalized patients.

Immunized macaques generate detectable cross-binding antibodies to all HCoV S proteins



To confirm the possibility of induction of cross-binding antibodies by SARS-CoV-2 S protein, we investigated cynomolgus macaques which received a total of three SARS-CoV-2 S nanoparticle immunizations in 12 weeks and compared antibody binding to all HCoV with pre-immunization samples. All animals generated detectable IgG to all HCoV spike proteins.

Cross-binding antibodies to SARS, MERS and 229E target the S2 domain more than S1



Patient sera were depleted using recombinant SARS-CoV-2 S1 and S2 subdomain proteins to further confirm the presence of cross-binding antibodies and to get an indication of their target location on the S protein. We saw a stronger decrease in IgG binding after S2 depletion for SARS, MERS and 229E.

Conclusion

This study demonstrates that SARS-CoV-2 infection elicits cross-reactive HCoV antibody responses and that the induction of such responses by a vaccine seems a feasible goal. These cross-reactive antibodies and their role in future HCoV-infections need to be further investigated because the induction of cross-binding antibodies might be of great value especially for vulnerable populations such as HIV-infected individuals.

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