NATURAL KILLER CELL-MEDIATED ADCC IN SARS-COV-2 INFECTION AND VACCINATION

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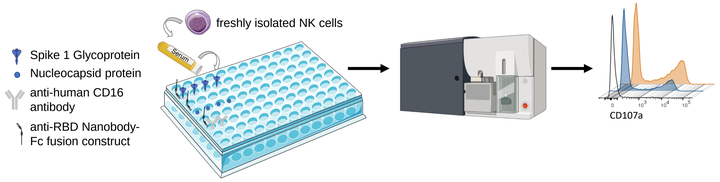
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BACKGROUND

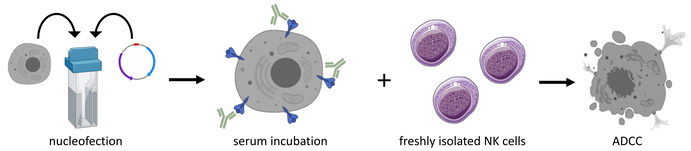
COVID-19, caused by SARS-CoV-2, has emerged as a global pandemic. To better understand the role of NK cells in COVID-19, we characterized NK cell-mediated ADCC against SARS-CoV-2 spike-1 (S1) and nucleocapsid (NC) protein. Furthermore, antibody-induced NK cell responses were compared between natural SARS-CoV-2 infection and BNT162b2 vaccination.

METHODS

Serum samples were collected from COVID-19 resolvers and BNT162b2 vaccine recipients by the University Medical Center Hamburg-Eppendorf, Hamburg, Germany. NK cell activation was analyzed using the plate-bound degranulation assay and flow cytometry to determine CD107a surface expression, the marker for NK cell degranulation.



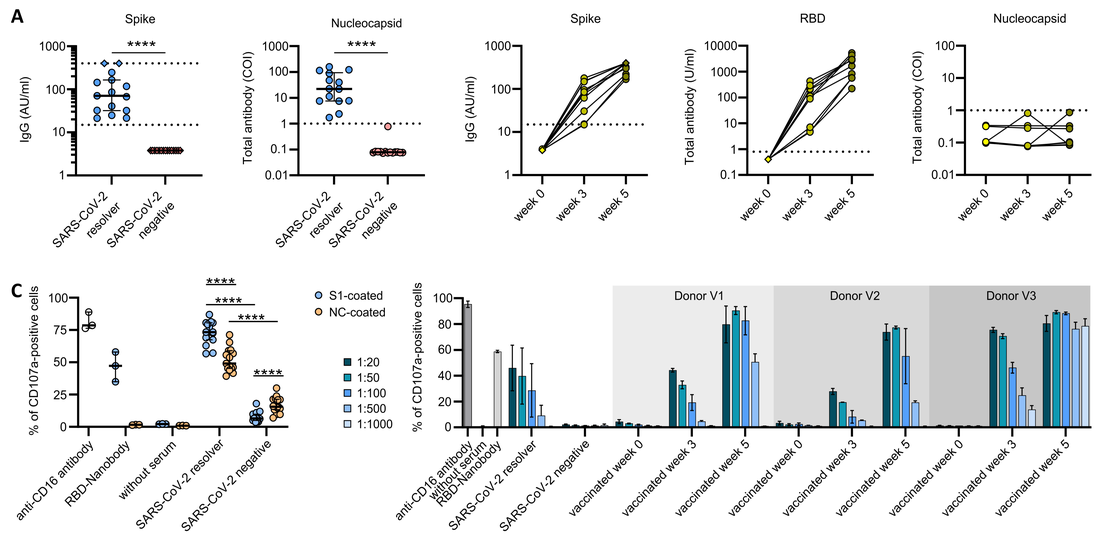
Raji cells were modified via nucleofection to induce cell surface expression of the S1 receptor-binding domain (RBD) and target cell killing was analyzed using flow cytometry.

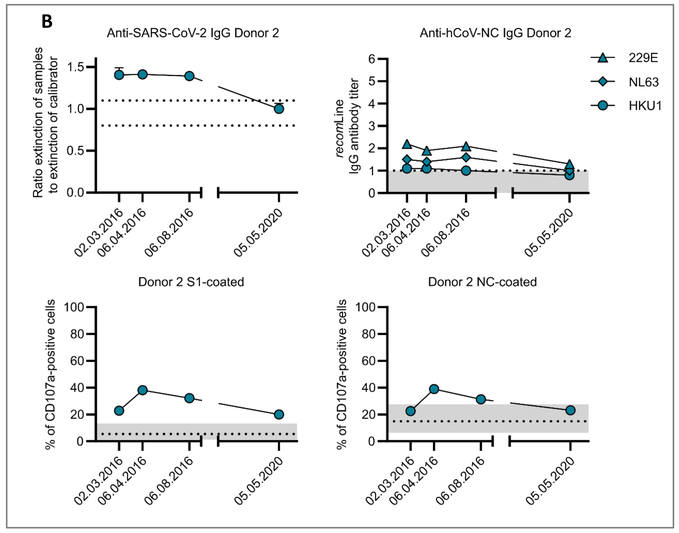


RESULTS

Antibodies induced by SARS-CoV-2 infection and BNT162b2 vaccination mediate strong NK cell activation. In addition, NK cell responses are stronger at higher serum dilutions after vaccination compared to natural SARS-CoV-2 infection. Serum collected prior to the COVID-19 pandemic shows SARS-CoV-2 cross-reactive antibodies, induced by endemic coronaviruses, capable of activating NK cells. NK cell activation by SARS-CoV-2-directed antibodies results in NK cell-mediated ADCC and lysis of RBD-expressing Raji cells.

Antibodies induced by **SARS-CoV-2** infection and BNT162b2 **vaccination** mediate strong antibody-dependent cellular cytotoxicity (**ADCC**) of NK cells.





CONCLUSIONS

While the induction of neutralizing antibodies has been described in COVID-19, other functional activities of SARS-CoV-2-directed antibodies are insufficiently understood. This study shows strong ADCC activity of antibodies induced by natural SARS-CoV-2 infection and an even stronger antibody-induced NK cell activation after BNT162b2 vaccination. Furthermore, we show that cross-reactive antibodies induced by endemic coronaviruses can induce NK cell-mediated ADCC in SARS-CoV-2 infection

A) Spike and NC antibody titers in SARS-CoV-2 resolvers, healthy individuals and BNT162b2 vaccine recipients determined by sandwich assay.

B) Cross-reactive antibodies in pre-COVID-19 serum sample after infection with endemic human coronaviruses. Pre-COVID-19 cross-reactive antibodies stimulated CD107a expression by NK cells. Dotted lines in the upper panel mark the threshold level for positive antibody titer. Dotted lines in the lower panel mark the mean value and the grey area represents the range of results observed in SARS-CoV-2 negative serum samples.

C) left: CD107a expression in response to S1 and NC protein-directed serum antibodies in SARS-CoV-2 resolvers and healthy individuals.

right: CD107a expression in response to SARS-CoV-2 spike protein.

D) RBD expression in mock- and RBD-nucleofected Raji cells and binding of SARS-CoV-2-directed antibodies in serum of COVID-19 resolvers towards the RBD.

E) RBD-mediated antibodies induce CD107a expression in SARS-CoV-2 resolvers and vaccinated individuals and result in increased killing of target cells.