SARS-CoV-2 Natural Infection Elicits Cross-Reactive Immunity to OC43

Micaela Garziano [1], Claudia Vanetti [2], Sergio Strizzi [2], Irma Saulle [1], Maria Luisa Murno [2], Fiona Limanaqi [2], Valentina Artusa [1], Mario Cano Fiestas [2],Pasquale Ogno [2], Mario Clerici [1],Daria Trabattoni [2], Mara Biasin [2]
[1]University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, [2]University of Milan, Department of Biomedical and Clinical Sciences, Milan, Italy

BACKGROUND

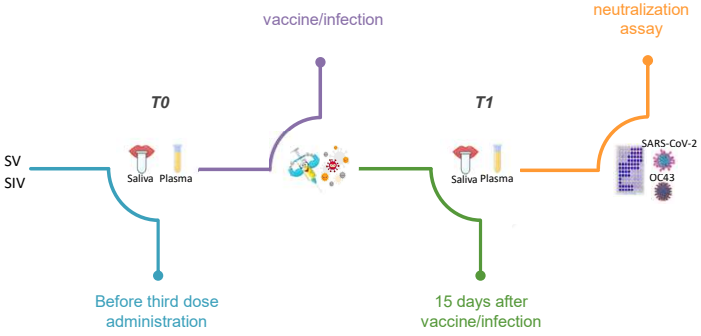
The recent SARS-CoV-2 pandemic renewed interest in other previously discovered non-severe acute respiratory syndrome human coronaviruses. Among these, OC43 is a seasonal human coronaviruses widely diffused in the global population (90% seroprevalence in adults), mostly responsible for mild respiratory symptoms [1]. As OC43 protective immunity is short lasting [2], the aim of this study was to verify if systemic and mucosal SARS-CoV-2 humoral immunity elicited either by natural infection and/or vaccination confers protection against a new OC43 re-infection.

METHODS

Neutralization assay using plasma and saliva samples of 49 SARS-CoV-2-vaccinated (SV) subjects who were never naturally infected and received three doses of BNT162b2 RNA vaccine were performed against "wild type" SARS-CoV-2 lineage B.1 (EU) and OC43 in VeroE6 cell lines. The same analyses were carried out on saliva and plasma samples from 25 SARS-CoV-2-infected and vaccinated subjects (SIV).

Sampling was carried out immediately before (T0) and 15 days (T1) post third-dose administration (SV) or 15 days post-infection (SIV).

Groups	Subjects	Sex M	Sex F
SV=SARS-CoV-2 vaccinated with 3 doses of vaccine	49	15	34
SIV=SARS-CoV-2 infected after 2 doses of vaccine	25	13	12

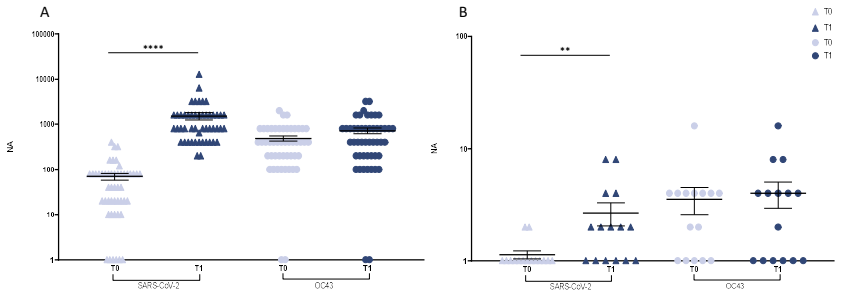


SARS-CoV-2 **Neutralizing Activitiy** triggered by natural infection proved to be **cross-reactive** and **protective** against OC43

RESULTS

1. Neutralizing Activity (NA) against SARS-CoV-2 and OC43 in SV

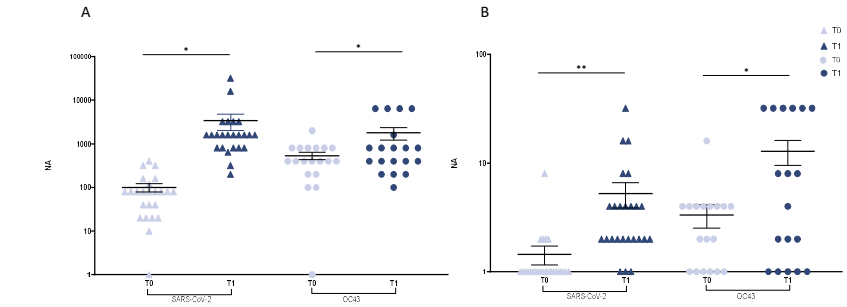
Following third dose vaccine administration, NA titer against SARS-CoV-2 significantly increased in plasma samples ($p<0.0001$) (Fig. 1A). Conversely, NA against OC43 was not modified in response to third dose SARS-CoV-2 vaccine administration (Fig. 1A). The same trend was observed analyzing saliva samples ($p<0.01$). *p < 0.05, **p < 0.01, ***p < 0.001,****p < 0.0001



2. Neutralizing Activity (NA) against SARS-CoV-2 and OC43 in SIV

Statistically significant differences were observed against both SARS-CoV-2 ($p<0.05$) and OC43 ($p<0.05$) in plasma samples from SIV (Fig. 2A). Likewise, the hybrid immunity induced by both natural infection and vaccination in SIV resulted in an increased NA in saliva samples against SARS-CoV-2 ($p<0.01$) and OC43 (saliva $p<0.05$) as well (Fig. 2B).

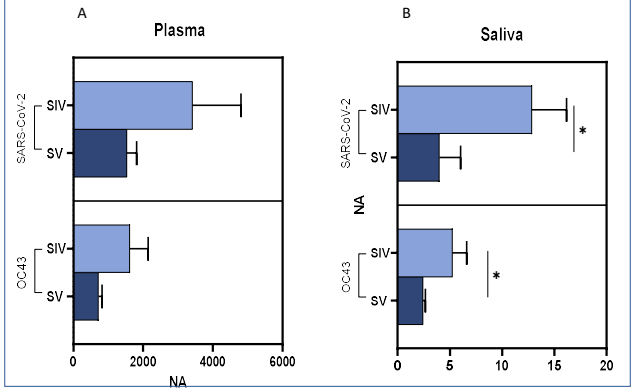
*p < 0.05, **p < 0.01, ***p < 0.001,****p < 0.0001



3. Comparison of NA against SARS-CoV-2 and OC43 in SV and SIV

NA in plasma from SIV is pointedly higher than that displayed by SV against both SARS-CoV-2 and OC43, though differences did not reach statistically significant differences (Fig 3A). Contrariwise, such variations were statistically different in saliva samples as NA against both SARS-CoV-2 and OC43 was more robust in SIV compared to SV ($p<0.05$ for both viruses) (Fig. 3B).

*p < 0.05, **p < 0.01, ***p < 0.001,****p < 0.0001



CONCLUSIONS

Our data indicate that, compared to vaccine-induced immunity SARS-CoV-2 natural infection elicits a broader and cross-reactive immunity, which results in protection from OC43 at both systemic and mucosal level. As the oral cavity represents the main entry route for coronaviruses, these results support the development of a pan-coronavirus vaccine to prevent new infections and re-infections [3].

REFERENCES

[1]The impact of pre-existing cross-reactive immunity on SARS-CoV-2 infection and vaccine responses
Sam M. Murray, Azim M. Ansari, John frater, Paul Klenerman, Susanna Dunachie, Eleanor Barnes, Ane Ogbe
Nat Rev Immunol. 23, pages304–316 (2023)

[2] Seasonal coronavirus protective immunity is short-lasting
Artur W.D. Edridge, Joanna Kaczorowsaka, Alexis C.R. Hoste, Margreet Bakker, Michelle Klein, Katherine Loens, Maarten F. Jebbink, Amy Matser, Cormac M. Kinsella, Paloma Rueda, Margareta Leven, Herman Goossens, Maria Prins, Patricia Sastre, Martin Deijs, Lia van der Hoek
Nat Med. 26, pages1691–1693 (2020)

[3] SARS-CoV-2 epitopes inform future vaccination strategies
Areez Shafqat, Mohamed H. Omer, Omar Ahmad, Mahnoor Niaz, Humzah S. Abdulader, Shameel Shafgat, Ali Hassan Mushtaq, Abdullah shaik, Ahmed N. Elshaer, Junaid Kashir, Khaled Alkattan, Ahmed Yaqinuddin
Front. Immunol. 2022; 13: 1041185.

ADDITIONAL KEY INFORMATION

micaela.garziano@unimi.it