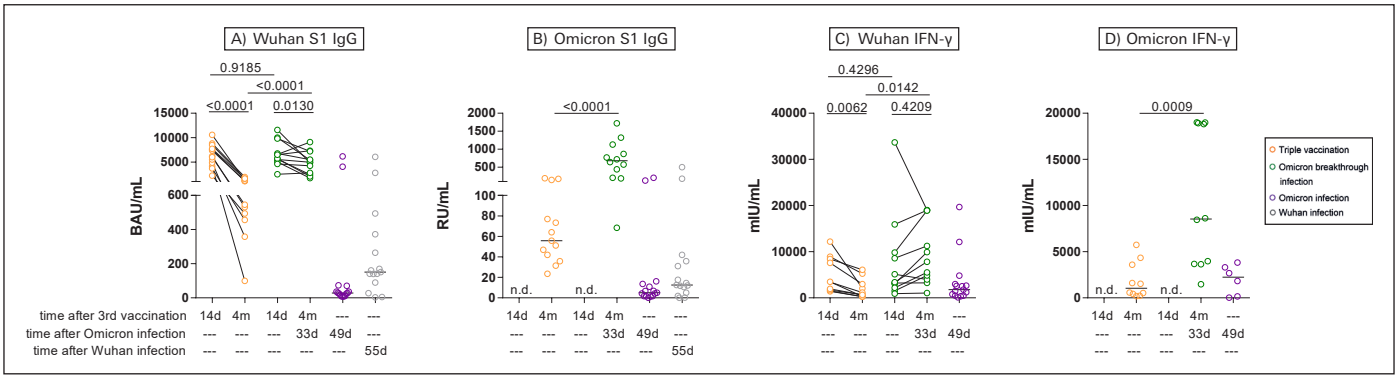
Humoral and cellular responses to SARS-CoV-2 Omicron infection in vaccinated and antigen-naïve individuals

G. Morillas Ramos[1], A. Cossmann[1], E. Grage-Griebenow[2], S. Hohensee[2], L. Hetzel[1], M.V. Stankov[1], and G.M.N. Behrens[1,3]

[1]Department for Rheumatology and Immunology, Hannover Medical School, Hannover, Germany
[2]Institute for Experimental Immunology,affiliated to EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany*
[3]German Center for Infection Research (DZIF), Partner Site Hannover-Braunschweig, Hannover, Germany



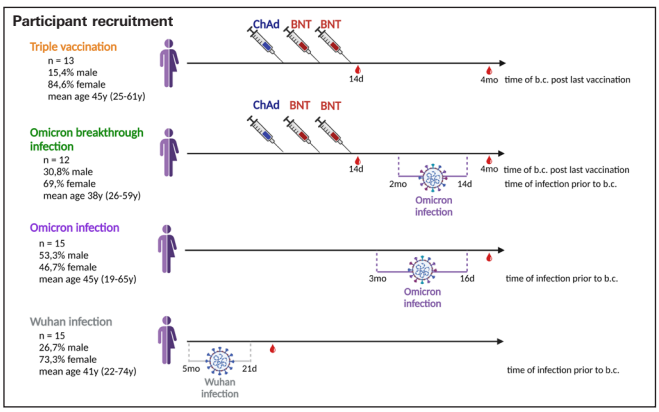
(A, B) Anti-S1 IgG and (C, D) IFN-γ levels measured by ELISA and IGRA based on (A, C) Wuhan S1 or (B, D) Omicron S1 antigen in ChAdOx1/BNT162b2/BNT162b2 triple vaccinees without Omicron breakthrough infection (orange) or after Omicron breakthrough infection (green), and in non-vaccinated individuals after Omicron (purple) or Wuhan (grey) infection; paired t-test (within groups) or two-way ANOVA followed by Sidak's multiple comparison (between groups); horizontal lines represent group median

Introduction

SARS-CoV-2 Omicron variants, which dominate the COVID-19 pandemic since early 2022, are B cell immune escape variants that elude the defence mechanisms induced by first-generation vaccines or infection with earlier variants. This study investigated the effect of Omicron infections on the humoral and cellular immunity in COVID-19-vaccinated versus antigen-naïve individuals.

Methods

Blood samples were collected from triple-vaccinated (ChAdOx1/BNT162b2/BNT162b2) individuals without (n = 13) or with (n = 12) Omicron breakthrough infection and from unvaccinated individuals after Omicron (n = 15) or Wuhan infection (n = 15). Anti-spike IgG was measured using the EUROIMMUN Anti-SARS-CoV-2 QuantiVac ELISA and Omicron ELISA, which are based on the S1 domain of the Wuhan and Omicron variant, respectively. Interferon-gamma (IFN-γ) release was quantified using the EUROIMMUN Quan-T-Cell SARS-CoV-2 kit employing stimulation tubes with antigens based on the Wuhan S1 protein, and compared to alternative stimulation tubes containing Omicron S1 antigen.



Results

In vaccinees without SARS-CoV-2 infection, a significant decrease in anti-S1 IgG (minus 85.9%, $P < 0.0001$, Fig. A) and IFN-γ release (minus 73.3%, $P = 0.0062$, Fig. C) was observed within 3.5 months following the third vaccine dose. Omicron breakthrough infections contracted 2 to 3.5 months after the third vaccination restored anti-spike IgG and IFN-γ release to levels similar or above those measured 2 weeks post vaccination ($P = 0.0130$ and $P = 0.4209$, Fig. A, C). In antigen-naïve individuals, Omicron infection led to IFN-γ release assay (IGRA) results resembling those detected in the triple-vaccinated group 3.5 months after the third dose (Fig. C), whereas anti-S1 IgG levels were significantly lower than those in vaccinees (but within the range of those detected in the Wuhan infection group, Fig. A). Inter-ELISA and inter-IGRA comparison revealed very similar spike-specific results, irrespective of whether the test systems were based on antigens derived from the Wuhan (Fig. A, C) or the Omicron variant (Fig. B, D).

Conclusion

There are substantial differences in immunity after Omicron infection in vaccinated and unvaccinated individuals. Considering the gradual decrease in immunity over time, unvaccinated individuals post Omicron infection are likely to have poor cross-protection against existing and possibly emerging SARS-CoV-2 variants. The detection of Omicron-induced immune responses in primed and antigen-naïve individuals supports the use of Omicron-adapted COVID-19 vaccines.

*EUROIMMUN owns patents, patent applications and utility models relating to the diagnosis or differential diagnosis of a SARS-CoV-2 infection or vaccination, such as EP3869199.