Comparison of T-cell and humoral responses to SARS-CoV-2 infection and vaccination among healthcare workers in the Czech Republic

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N = 90		T-SPOT.COVID IGRA (combined S and N)		
		pos	bdl	neg
Quan-T-Cell IGRA	pos	81 (90.0%)	2 (2.2%)	5 (5.6%)
	bdl	2 (2.2%)	0	0
	neg	0	0	0
P-value (symmetry test)		0.082		
Overall agreement[a]		94.4% (95% CI: 87.5–98.2%)		

Table 1: Comparison between qualitative results obtained using IGRAs (T-SPOT.COVID vs. Quan-T-Cell); [a]borderline results were considered positive; CI, confidence intervall

Group[a]	N	Days from last immunization impulse, median (IQR)	Humoral immunity[b]		T-cell-mediated immunity[b]			
			IgG ELISA	VNT	Quan-T-Cell	T-SPOT (total)	T-SPOT (S)	T-SPOT (N)
Omicron unvaccinated	6	209 (138–221)	33.3% (4/2/0)	100% (0/2/4)	100% (0/1/5)	100% (0/0/6)	83.3% (1/1/4)	100% (1/1/4)
Wuhan/Apha/Delta unvaccinated	6	315 (310–616)	83.3% (1/0/5)	83.3% (1/0/5)	100% (0/0/6)	100% (0/0/6)	83.3% (1/0/5)	100% (0/2/4)
Reinfected unvaccinated	6	263 (201–316)	100% (0/0/6)	100% (0/0/6)	100% (0/0/6)	66.6% (2/0/4)	66.6% (2/0/4)	50.0% (3/0/3)
Vaccinated convalescents	50	238 (204–307)	100% (0/0/50)	100% (0/0/50)	100% (0/1/49)	100% (0/1/49)	100% (0/1/49)	84.0% (8/4/38)
Vaccinated uninfected	22	286 (284–304)	100% (0/0/22)	100% (0/0/22)	100% (0/0/22)	86.4% (3/1/18)	86.4% (3/2/17)	54.5% (10/2/10)
Total	90	284 (209–307)	94.4% (5/2/83)	98.8% (1/2/87)	100% (0/2/88)	94.4% (5/2/83)	92.2% (7/4/79)	75.6% (22/9/59)

Table 2: Subgroup analysis according to the infection variant; [a]assignment of the SARS-CoV-2 variants is conjectural (derived from the date of PCR positivity); [b]test results are presented as % positive (negative/borderline/positive), borderline results were considered positive for the calculation of the overall positivity; IQR, interquartile range; VNT, virus neutralization test

Introduction

This prospective cohort study investigated the humoral and cellular immune response among employees of the Public Health Institute Ostrava following infection with SARS-CoV-2 or vaccination against COVID-19 during the last 2 years. The aim of the study was to compare two interferon-gamma (IFN-γ) release assays (IGRAs) for the evaluation of SARS-CoV-2-specific cellular immunity.

Methods

Between August and October 2022, blood samples were collected from 90 Czech healthcare workers with a history of laboratory-confirmed SARS-CoV-2 infection (PCR or antigen test dating back 3 weeks to 2 years) and/or COVID-19 vaccination. Participants were grouped based on infection dates (dominant SARS-CoV-2 variant) and vaccination status. Antibodies were determined using the EUROIMMUN Anti-SARS-CoV-2 ELISAs (anti-S1/RBD IgG and IgA) and an in-house virus neutralization test (VNT). IFN-γ release was measured using the Oxford Immunotec T-SPOT.COVID assay (stimulation: spike S and nucleocapsid N antigen) and the EUROIMMUN Quan-T-Cell SARS-CoV-2 kit (stimulation: antigens based on the S1 protein). A symmetry test and Kruskal-Wallis test at a significance level of 5% were used for statistical evaluation.

Results

Out of the 90 samples, the Quan-T-Cell IGRA identified 88 (97.8%) as positive and 2 as borderline positive, compared to 83 (92.2%) positives, 2 borderline positives and 5 negatives detected by the T-SPOT assay. The distribution of results is shown in Fig. 1. The qualitative agreement between both IGRAs was 94.4% (95% CI: 87.5–98.2%), implying that there was no statistically sigificant difference between the methods ($P = 0.082$, Table 1). Comparison of immune responses with respect to the variant of the past infection (Table 2) revealed very good overall agreement (83.3–100% in all subgroups) of both IGRAs with VNT and anti-S IgG, with the only exception that 4/6 subjects in the subgroup of unvaccinated Omicron convalescents were devoid of IgG while T-cell responses were detectable.

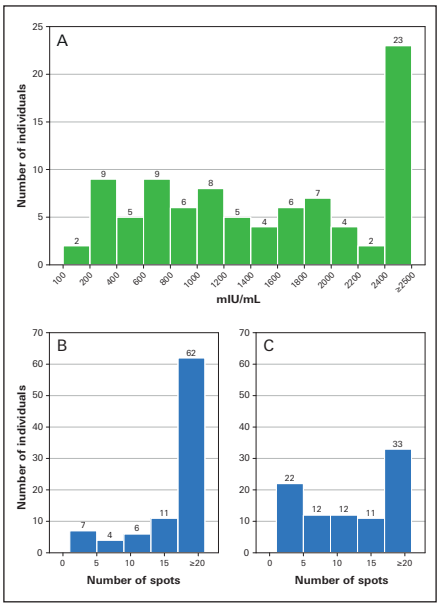

Fig. 1: Distribution of IGRA results: (A) Quan-T-Cell (≤100 mIU/mL neg, 100–200 mIU/mL bdl, ≥200 mIU/mL pos) and T-SPOT.COVID with (B) S and (C) N (≤4 neg, 5–7 bdl, ≥8 pos)

Conclusion

Both IGRAs showed comparable performance. Based on the possibility to evaluate N protein-stimulated effector cell responses, the T-SPOT assay is able to differentiate past SARS-CoV-2 infections, while the Quan-T-Cell assay is not. Both IGRAs appear to provide higher sensitivity than IgG-specific assays. This applies particularly to unvaccinated persons who contracted only SARS-CoV-2 Omicron variant infection but is also likely to be relevant to other patient groups. Therefore, testing for cellular immunity can be recommended for immunocompromised persons.

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

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