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Cellular immunity against SARS-CoV-2 is predominantly boosted in vaccinated individuals with no history of infection

Running title: Cellular immunity and the serological status

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The authors declare that there are no competing interests related to the present work.

Dear Editor,

Despite a substantial reduction in humoral immunity, COVID-19 vaccines still show robust protection against severe COVID-19 disease, even against highly mutated variants (1, 2). Accumulating evidence suggests that T cell response plays a key role in the protection against severe disease (i.e., hospitalization and death) (1, 3, 4). Two recent papers published in Journal of Infection (5, 6) found that the cellular immunity as assessed with an interferon gamma (IFNγ) release assay (IGRA) declined progressively 6 to 12 months after full vaccination with various COVID-19 vaccines, especially in those with no history of SARS-

CoV-2 infection. In the present study, we would like to confirm these findings and to show the impact of the second booster administration on the cellular immunity; a feature not explored in the two above-mentioned studies.

On September 2022, 54 participants of the CRO-VAX-HCP study (7) received the second and bivalent adapted BNT162b2 booster. Forty were females (median age = 51.0 years; IQR = 43.3–58.8) and 14 were males (median age = 52.5 years; IQR = 43.8–59.8). Age was not different between females and males (p = 0.60, Man-Whitney test). Most of the participants (45/54; 83.3%) had a history of SARS-CoV-2 infection. Blood was collected in lithium heparin and serum separator tubes (BD Vacutainer, Becton Dickinson, New Jersey, USA) just before and 28 days after the booster administration. The study was approved by a central ethical committee (CHU UCL Namur, Yvoir, Belgium; approval number: 2020-006149-21). Total antibodies against the NCP (Roche Diagnostics) were measured using the Elecsys Anti-SARS-CoV-2 assay. Results above 1.0 cut-off index (COI) were considered positive and indicates a previous SARS-CoV-2 infection. Moreover, the T cell-mediated immune response was assessed using the cobas IGRA SARS-COV-2 Tubes and the Elecsys IGRA SARS-CoV-2 assay (Roche Diagnostics). The test measures the release of interferon gamma (IFNγ) from T cells in response to an *in vitro* SARS-CoV-2 stimulation in whole blood samples which have been formerly in contact with SARS-CoV-2 coated antigens (8). Median and interquartile range (IQR) were used to present the data. A Mann-Whitney test was used to assess the impact of the second booster on cellular immunity. A multiple comparison test was used to evaluate the effect of anti-NCP levels on the cellular immunity. Results were categorized as < 1.0 COI, 1.0 to 10.0 COI and >10.0 COI. A Spearman correlation was also performed for the comparison between anti-NCP and IFNγ. Statistical analyses were performed using GraphPad Prism 9.5.1 (GraphPad Software, Massachusetts, USA). $p < 0.05$ was considered statistically significant.

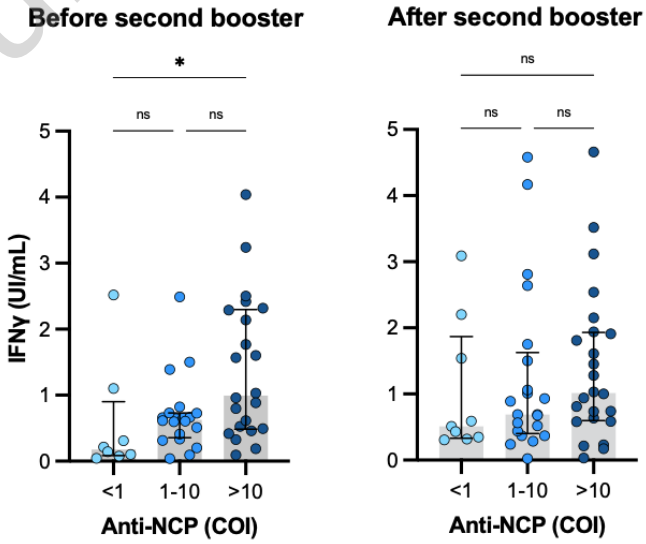
Before the second booster administration, we found a significant and positive correlation between anti-NCP and IFNγ (r = 0.39 (95%CI = 0.11–0.61), p = 0.005). Individuals with negative anti-NCP had significantly lower levels of IFNγ as compared to individuals with high anti-NCP, i.e. >10.0 COI (INFγ level of 0.18 versus 1.00 IU/mL, p = 0.007). These data are consistent with those published by Bonnet *et al.* and Pighi *et al.* (5, 6). One month after the bivalent booster administration, a significant increase in IFNγ was only observed for individuals with no history of SARS-CoV-2 infection (from 0.18 to 0.51 IU/mL, fold-increase = 2.85, p = 0.04). Mean fold increase 28 days after the bivalent booster in individuals with positive anti-NCP were close to 1 (i.e., 1.09 and 1.02) (**Table 1 and Figure 1**). Additionally, the correlation between anti-NCP and IFNγ was no longer significant after the second booster administration (r = 0.14 (-0.14-0.40), p = 0.30).

Based on these findings, we confirm that individuals with no history of SARS-CoV-2 infection presented a reduced cellular immunity but were those that were more susceptible to benefit from a second booster in terms of cellular immunity. These findings need to be confirmed in other studies with a larger population.

Table 1: INFγ levels before and after the bivalent booster in subjects with low (< 1.0 COI), intermediate (1-10 COI) and high (> 10 COI) anti-NCP antibodies.

Anti-NCP (COI)	Before booster	After booster	Fold-increase	P value
<1 (n = 9)	0.18 IU/mL 95%CI: 0.08–0.90	0.51 IU/mL 95%CI: 0.33–1.87	2.85	0.04 (*)
1–10 (n = 21)	0.63 IU/mL 95%CI: 0.36–0.73	0.69 IU/mL 95%CI: 0.40–1.6	1.09	0.22 (ns)
>10 (n = 24)	1.00 IU/mL 95%CI: 0.48–2.30	1.02 IU/mL 95%CI: 0.60–1.93	1.02	0.97 (ns)

Figure 1: Comparison of INFγ levels before and after the bivalent booster in subjects with low (< 1.0 COI), intermediate (1-10 COI) and high (> 10 COI) anti-NCP antibodies. Results were only statistically different before booster administration between subjects with low and high anti-NCP antibodies.



References:

1. Wherry EJ, Barouch DH. T cell immunity to COVID-19 vaccines. Science. 2022 Aug 19;377(6608):821-2. PubMed PMID: 35981045. Epub 20220818.
2. Moss P. The T cell immune response against SARS-CoV-2. Nat Immunol. 2022 Feb;23(2):186-93. PubMed PMID: 35105982. Epub 2022/02/03.
3. Ledford H. 'Killer' immune cells still recognize Omicron variant. Nature. 2022 Jan;601(7893):307. PubMed PMID: 35017690. Epub 2022/01/13.
4. Lippi G, Mattiuzzi C, Henry BM. Is cellular immunity the future key for deciphering and monitoring COVID-19 vaccines efficacy? Journal of Laboratory and Precision Medicine. 2022;7.
5. Pighi L, Henry BM, De Nitto S, Salvagno GL, Lippi G. Cellular immunity against SARS-CoV-2 depends on the serological status. J Infect. 2023 Apr 14. PubMed PMID: 37060925. Pubmed Central PMCID: PMC10102536. Epub 20230414.
6. Bonnet B, Chabrolles H, Archimbaud C, Brebion A, Godignon M, Dutheil F, et al. Comparative T and B immune responses of four different anti-COVID-19 vaccine strategies 6 months after vaccination. Journal of Infection. 2022 2022-05-01;84(5):e45-e7.
7. Favresse J, Gillot C, Bayart JL, David C, Simon G, Wauthier L, et al. Vaccine-induced binding and neutralizing antibodies against Omicron 6 months after a homologous BNT162b2 booster. J Med Virol. 2023 Jan;95(1):e28164. PubMed PMID: 36131356. Pubmed Central PMCID: PMC9538323. Epub 2022/09/22.
8. Salvagno GL, Pighi L, Henry BM, Valentini M, Tonin B, Bragantini D, et al. Assessment of humoral and cellular immunity after bivalent BNT162b2 vaccination and potential association with reactogenicity. Clin Chem Lab Med. 2023 Feb 2. PubMed PMID: 36722026. Epub 2023/02/02.

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Authors state no conflict of interest.
Informed consent
All subjects recruited provided written informed consents for participation.
Ethical approval
The study was approved by a central ethical committee (CHU UCL Namur, Yvoir, Belgium; approval number: 2020-006149-21).

Declaration of Competing Interest

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Authors state no conflict of interest.