ALTERED FEATURES OF B AND T CELL RESPONSES TO BNT162 VACCINE IN HEMODIALYSIS PATIENTS

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BACKGROUND

This study aim to define the trajectories of SARS-CoV-2 vaccine-induced humoral, B, CD4⁺ and CD8⁺ T cell responses in patients receiving hemodialysis.

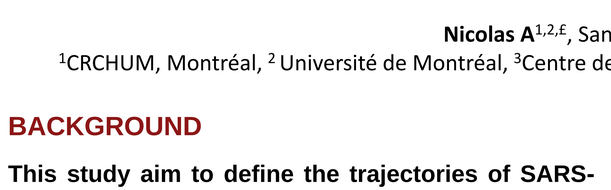
People receiving hemodialysis (HD) are highly vulnerable to SARS-CoV-2 infection and develop lower antibody responses to SARS-CoV-2 mRNA vaccines. However, the underlying immune defects are poorly understood.

METHODS

We followed 20 HD patients who received 2 doses of mRNA vaccines 5 weeks apart at:

- Baseline (**B**), before vaccination
- 4 weeks after dose 1 (**D1**),
- 4 weeks after dose 2 (**D2**),
- 12 weeks after dose 2 (memory, **M2**).

Health-care workers (HCW, two doses 16 weeks apart) served as controls. All participants were SARS-CoV-2 naïve.



To examine associations between different arms of immunity , we characterized:

- Humoral responses by receptor-binding domain (RBD) ELISA
- RBD-specific B-cell responses by flow cytometry
- Spike (S)-specific CD4 and CD8 T-cell responses by 16-h activation-induced marker (AIM) assays
- Effector functions of S-specific CD4 and CD8 T-cells by 6-h intracellular staining (ICS).

ADDITIONAL KEY INFORMATION

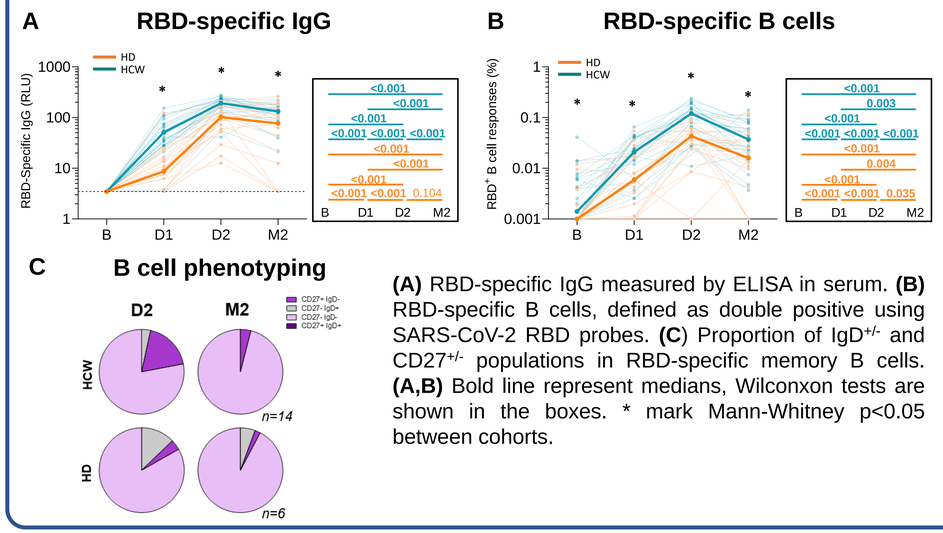
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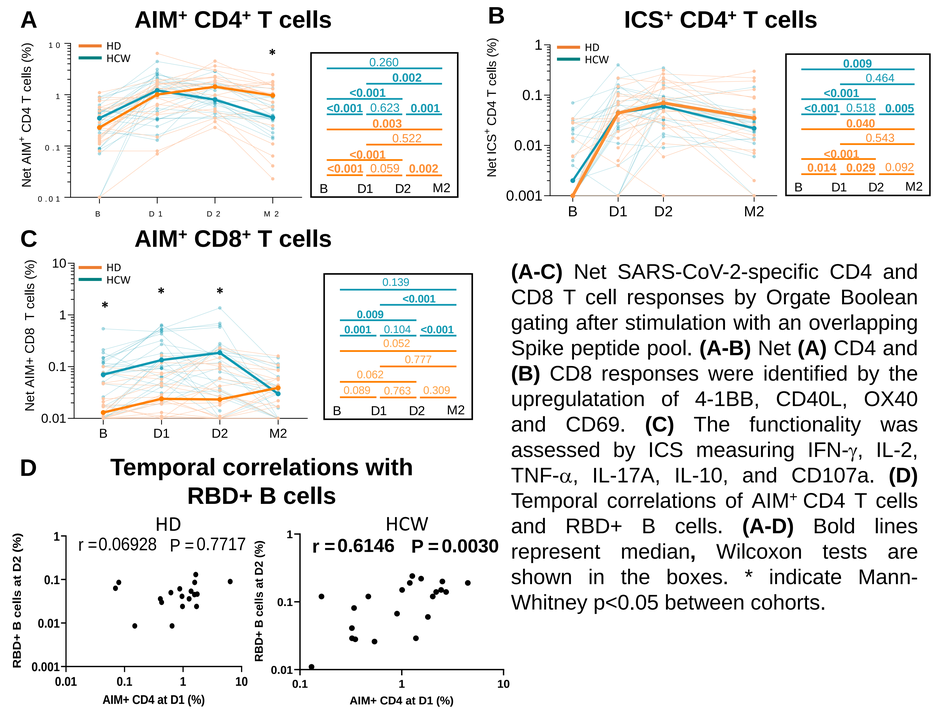
RESULTS

Figure 1. HD developed poor antibody and B cell responses after vaccination in comparison of HCW



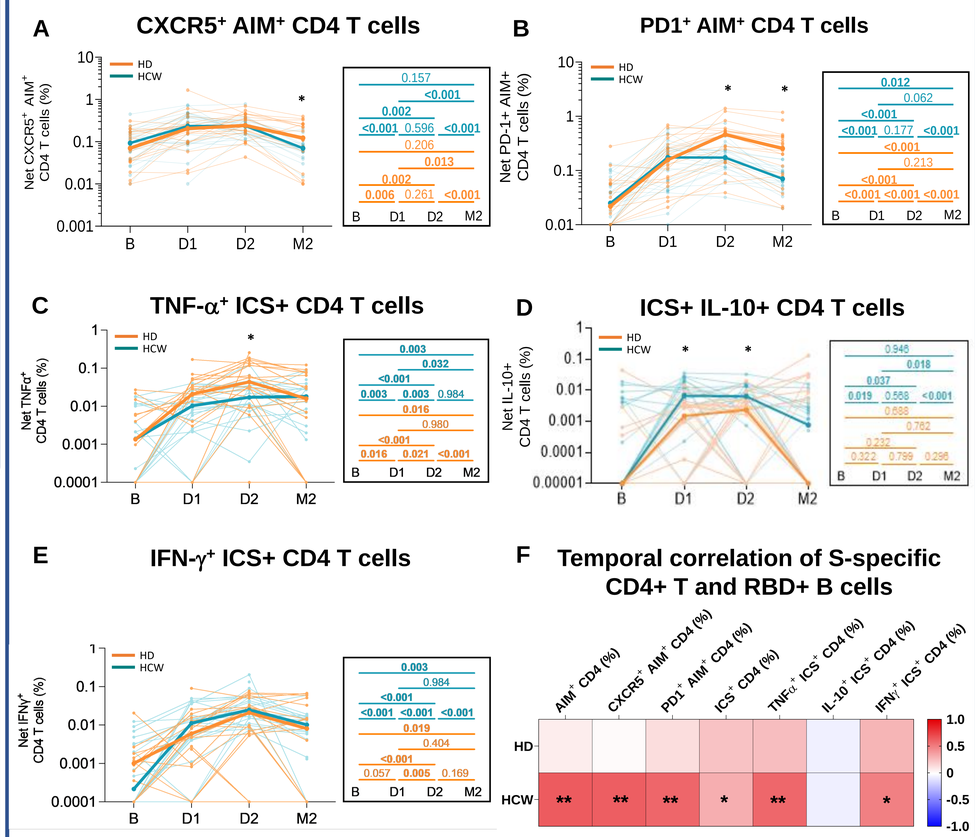
(A) RBD-specific IgG measured by ELISA in serum. **(B)** RBD-specific B cells, defined as double positive using SARS-CoV-2 RBD probes. **(C)** Proportion of IgD$^{+/-}$ and CD27$^{+/-}$ populations in RBD-specific memory B cells. **(A,B)** Bold line represent medians, Wilconxon tests are shown in the boxes. * mark Mann-Whitney p<0.05 between cohorts.

Figure 2. HD develop normal CD4 cell responses, but with no temporal association with B cell responses, and fail to elicit CD8 responses



(A-C) Net SARS-CoV-2-specific CD4 and CD8 T cell responses by Orgate Boolean gating after stimulation with an overlapping Spike peptide pool. **(A-B)** Net **(A)** CD4 and **(B)** CD8 responses were identified by the upregulatation of 4-1BB, CD40L, OX40 and CD69. **(C)** The functionality was assessed by ICS measuring IFN-γ, IL-2, TNF-α, IL-17A, IL-10, and CD107a. **(D)** Temporal correlations of AIM⁺ CD4 T cells and RBD+ B cells. **(A-D)** Bold lines represent median, Wilcoxon tests are shown in the boxes. * indicate Mann-Whitney p<0.05 between cohorts.

Figure 3. In HD patients, SARS-CoV-2 specific CD4 T responses are characterized by increased frequency of CXCR5+, PD-1+ and TNFa cells, fewer IL-10 and failed temporal association with RBD-B cells



(A-E) Longitudinal net **(A)** CXCR5⁺ AIM⁺, **(B)** PD-1⁺ AIM⁺, **(C)** TNF-α⁺ ICS⁺ **(D)** IL-10 ICS⁺ and **(E)** IFN-γ⁺ ICS⁺ CD4⁺ responses. **(F)** Temporal correlation of S-specific CD4+ T cells at D1 and RBD⁺ B cells at D2. **(A-E)** Bold lines represent median, Wilcoxon tests are shown in the boxes. * indicate Mann-Whitney test p<0.05 between cohorts.

CONCLUSIONS

Vaccination of hemodialysis patients with mRNA vaccine results in poor antibody, B cell and CD8 responses. Hemodialysis patients reach similar level of CD4 T cells responses than HCW but enriched in CXCR5⁺, PD-1⁺, TNF-α⁺, and diminished in IL-10⁺. In contrast to HCW, no temporal association were found between these S-specific CD4 T cell populations and RBD+ B cells, suggesting an impaired cross-talk between both cell types.

Further investigation are required to correlate protection after additional doses.