

SARS-CoV-2 spike-specific B cell responses in chronic lymphocytic leukaemia

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Introduction

Chronic lymphocytic leukaemia (CLL) is associated with secondary immunodeficiency and infections remain the major cause of mortality in CLL patients. Disease-driven immune dysfunction and immunosuppressive therapies have been suggested to underly this immunodeficiency. While altered non-malignant B cell composition is present already in the early stages of CLL, it is unknown how this impacts foreign antigen-specific B cell differentiation, such as to SARS-CoV-2 vaccination, in untreated and chemotherapy-receiving patients.

Aim

To characterise the development and phenotype of SARS-CoV-2 spike protein-specific B cells following vaccination in CLL patients compared to healthy controls (HCs) in relation to the overall non-malignant B cell landscape.

Materials and Methods

We recruited CLL patients who met the WHO 2017 and the International Workshop on CLL diagnostic criteria; CLL patients were either treatment naïve (CLL-TN) (n=23) or chemotherapy-receiving (CLL-CTx) (n=11). The control group (HC, n=16) was composed of age- and sex-matched individuals. All study participants received at least 2 doses of SARS-CoV-2 vaccine and time post-vaccination was comparable between groups. Using flow cytometry, we phenotyped B cells, including SARS-CoV-2 spike protein-specific, among peripheral blood mononuclear cells. Anti-SARS-CoV-2 spike IgG levels were determined by ELISA. The data were analysed with GraphPad Prism 10. Results were considered statistically significant at $p < 0.05$.

Results

Despite the considerable expansion of the malignant B cells and prominent alterations in peripheral B cell subsets in patients with CLL, the absolute numbers of circulating SARS-CoV-2 spike-specific B cells were comparable between CLL-TN, CLL-CTx and HCs (Figure 1). That B cell response to SARS-CoV-2 spike protein was maintained, was supported by anti-SARS-CoV-2 IgG levels that were comparable between groups. Furthermore, when interrogating the phenotype of spike-specific B cells, approximately half were IgG-class-switched in all groups, suggesting preserved B cell differentiation pathways to SARS-CoV-2 vaccination in CLL (Figure 2).

Figure 1. SARS-CoV-2 spike-specific immunity. (a) Representative flow cytometry plots and box and whisker plots demonstrating the frequencies and absolute numbers of spike⁺ B cells, (b) box and whisker plots showing serum levels of anti-spike IgG in treatment naïve CLL patients (CLL-TN), chemotherapy-receiving CLL patients (CLL-CTx) and healthy controls (HC).

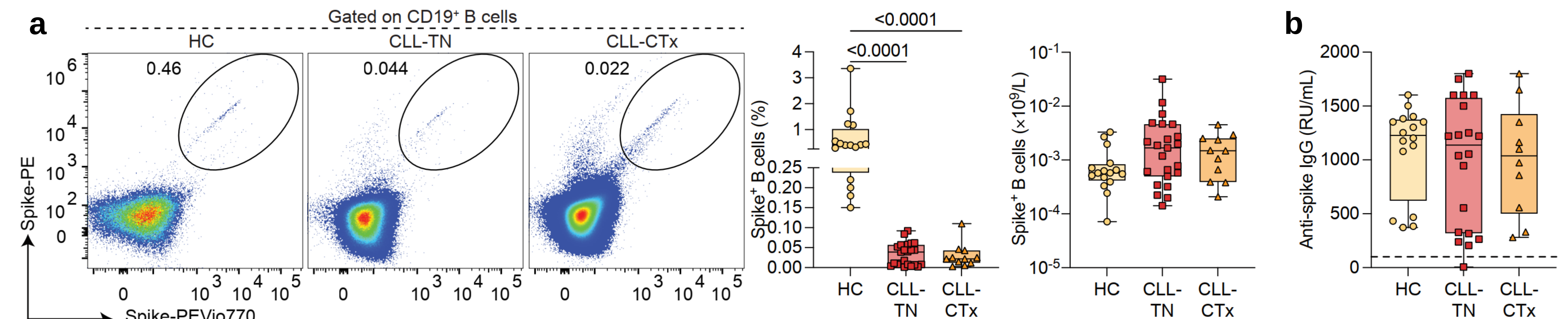
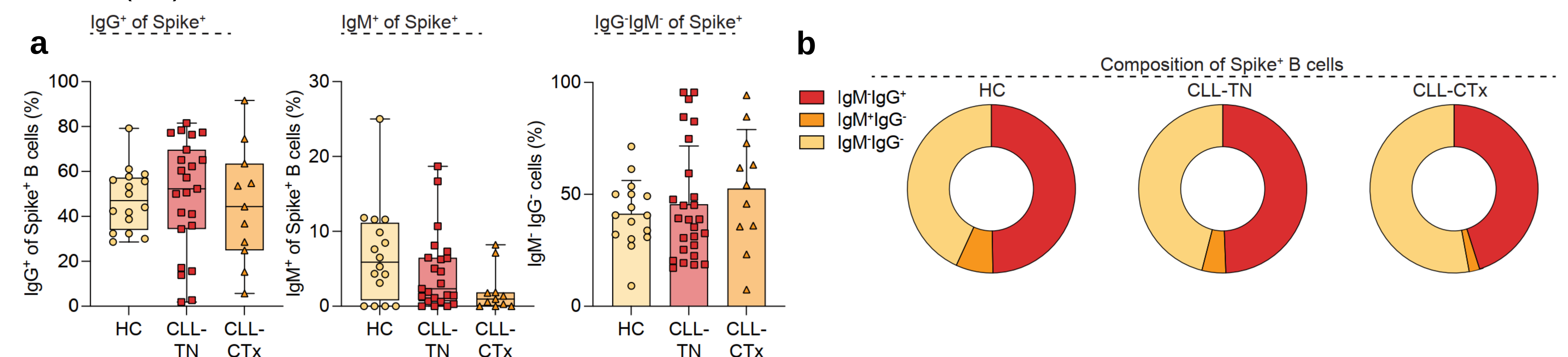


Figure 2. Composition of SARS-CoV-2 spike-specific B cells. (a) Box and whisker plots demonstrating the frequencies of IgG⁺, IgM⁺ and IgG-IgM⁺ among spike⁺ B cells, (b) parts-of-whole charts demonstrating the IgG/IgM subset composition of spike⁺ B cells in treatment naïve CLL patients (CLL-TN), chemotherapy-receiving CLL patients (CLL-CTx) and healthy controls (HC).



Conclusions

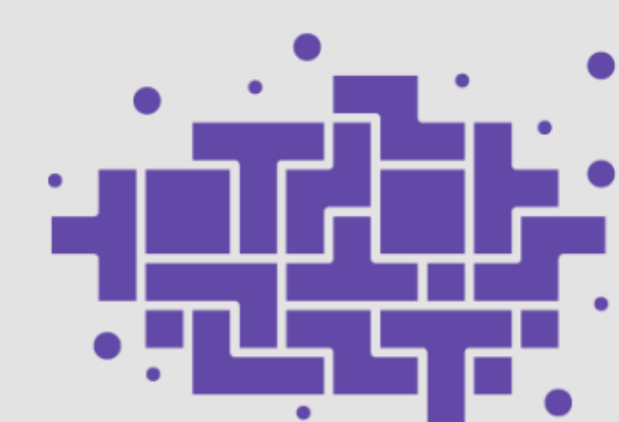
These data suggest that despite the major alterations in B cell subsets, the ability of the B cell compartment to give rise to SARS-CoV-2 spike-specific B cells is preserved in patients with CLL. We hypothesize that this may be related to the level of T cell help provided for B cell activation, compared to, for example, polysaccharide antigens that are by definition T cell independent.

Acknowledgment

We thank the volunteers who donated blood for this study, the clinical laboratory staff who participated in the sample collection and processing and Dr Dagnija Straupmane, Head of United laboratory, Pauls Stradiņš Clinical University Hospital for advice and technical expertise.



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PROJECTS

This work is funded by the Latvian Council of Science Fundamental and Applied Research Project Grant No Izp-2022/1-0080