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Phototherapy decreases the levels of circulating IgG3+ B cells in Clinically Isolated Syndrome; an early form of Multiple Sclerosis

Disease-modifying therapies (DMT) targeting B cells are amongst the most effective for preventing multiple sclerosis (MS) progression. IgG3 antibodies and their uncharacterised B cell clones are predicted to play a pathogenic role in MS. Identifying subsets of IgG3+ B cells involved in MS progression could improve diagnosis, inform timely disease intervention, and may lead to new DMTs that target B cells more specifically.

We designed a 31-parameter B cell-focused mass cytometry panel to interrogate the role of peripheral blood IgG3+ B cells in conversion from clinically isolated syndrome (CIS) to MS. We also investigated the effect of narrowband UVB on these subsets. Nine distinct CD20+IgD–IgG3+ B cell subsets were identified. Significant changes in the proportion of CD21+CD24+CD27–CD38– and CD27+CD38hiCD71hi memory B cell subsets correlated with changes in serum IgG3 levels and time to conversion from CIS to MS. The same CD38– double negative B cell subset was significantly elevated in a second cohort of MS patients with active forms of the disease. A third CD21+CD24+CD27+CD38– subset was elevated in patients with active MS, whilst narrowband UVB phototherapy significantly reduced the proportion of this switched-memory B cell subset.

In conclusion, we have identified previously uncharacterised subsets of IgG3+ B cells and shown them to correlate with autoimmune attacks on the CNS. Our results highlight that interventions (e.g. phototherapy) that reduce these populations of IgG3+ B cells protect CIS patients from transitioning to MS. These findings justify consideration for subsets of IgG3+ B cells as biomarkers and/or mediators of disease progression in MS, as well as future targets of novel immunotherapies.