INCREASED FOLLICULAR HELPER T CELL REGULATES AUTOANTIBODY HYPOSIALYLATION IN GLUCOSE-6-PHOSPHATE ISOMERASE INDUCED ARTHRITIS

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Background: Circulating follicular helper T (Tfh) cells were reported to be increased and promote B cell activation and antibody production in rheumatoid arthritis. Recently, IL-23-Tfh17 cells axis and hyposialylation of antibodies were proved to be linked to the inflammation of experimental and rheumatoid arthritis. However it remains uncertain how Tfh, including IL-17 producing Tfh (Tfh17), is associated to arthritis and whether its function includes promotion of antibody hyposialylation.

Objectives: The aim of this study is to explore the relation between Tfh and autoantibody hyposialylation in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA), which mouse model was dependent on T cells, B cells and IL-17.

Methods: 1. Fluclution of Tfh and its subsets in draining lymph nodes (dLNs) were assessed by FACS analysis. 2. To elucidate Tfh function in ex-vivo, naive B cells were co-cultured with Tfh and the ratio of differentiated plasmablast was quantified. Anti–GPI antibody production from plasmablast was measured in the existence of Tfh. 3. The titers of anti–GPI antibodies in GIA sera were measured by ELISA. 4. DCs were stimulated with purified anti–GPI antibodies from day 7 (arthritis onset phase) and day 28 (resolving phase) GIA to examine the pathogenicity change of antibody. MRNA of ST6 beta-galactoside alpha-2,6-sialyltransferase 1 (st6gal1), the responsible protein for antibody hyposialylation, in plasmablast was quantified by PCR and detection of sialic acid in anti–GPI antibody was performed by lectin blotting. 5. Naive B cells were co-cultured with Tfh and the st6gal1 expression in differentiated plasmablast was measured by flow cytometry.

Results: 1. Tfh cells were increased in GIA. It peaked at day 7, the onset of arthritis, and Tfh17 was specifically increased at the same time. Moreover, OX40 expression in Tfh17 was higher than other subsets. IF showed that Tfh and Tfh17 were accumulated in germinal centre of dLNs. As counterparts, plasmablats and plasma cells were most increased at day 7 as well. 2. When co-cultured with Tfh, the frequency of differentiated plasmablast was much higher than other conditions, and anti–GPI antibody production was up-regulated in the existence of Tfh and GPI. 3. Conflicting with the results above, anti–GPI antibody titers in the sera were gradually elevated even after day 7 and this elevation continued while GIA peaked out. 4. DCs produced higher level of TNF–alpha when stimulated with the antibody from day 7 GIA than day 28. St6gal1 expression in plasmablast was significantly decreased at day 7 and recovered at day 28. In addition, the day 7 antibodies were tended to be contain less sialic acid. 5. Decreased expression of st6gal1 was observed in differentiated plasmablast co-cultured with Tfh.

Conclusions: Tfh, especially Tfh17 were increased in the induction phase of arthritis. Also, Tfh could have a crucial role in the development of arthritis via plasmablast activation and regulation of autoantibody hyposialylation in GIA.

Disclosure of Interest: None declared