THU0077

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-Th17 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 auto-antibody 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. Fluctuation of Tfh and its subsets in draining lymph nodes (dLNs) were analysed and expression of co-stimulatory molecules were assessed among these subsets. Their localization were examined by immunofluorescence (IF) staining. In order to explore the counterpart reaction, serial changes of plasmablast and plasma cell population in dLNs were also analysed.
2. To elucidate Tfh function in ex-vivo, naïve 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 sialylation, in plasmablast was quantified by PCR and detection of sialic acid in anti-GPI antibody was performed by lectin blotting.
5. Naïve 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, plasmablasts 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

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THU0078

BERBERINE AMELIORATES BONE EROSIONS IN COLLAGEN-INDUCED ARTHRITIS RAT MODELS VIA SUPPRESSING THE EXPRESSION OF IL-17A

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Background: Rheumatoid arthritis (RA) is a chronic progressive disease characterised by synovial inflammation, autoantibody production, cartilage and bone destruction. Bone erosions are a key feature of RA reflecting both disease severity and disease progression. An imbalance between Th17 and regulatory T cells (Treg cells) has been extensively recognised in both patients and model animals

of RA. Oral administration of berberine, an isoquinoline alkaloid, has been showed to ameliorate various symptoms of autoimmune diseases including RA.

Objectives: To verify whether berberine may prevent bone erosions during RA progression and to explore the potential mechanisms in Collagen-induced arthritis (CIA) rat model.

Methods: The severity of arthritis was expressed as mean arthritic index on a 0–4 scale according to the following criteria: 0=no oedema or swelling; 1=slight oedema and erythema limited to the foot and/or ankle; 2=slight oedema and erythema from the ankle to the tarsal bone; 3=moderate oedema and erythema from the ankle to the tarsal bone; and 4=severe oedema and erythema from the ankle to the entire leg. Each limb was graded, and thus the maximum possible score was 16 for each animal. The threshold score of rats with established CIA is 2. The CIA rats were divided into 3 groups: placebo group (n=4), low dose berberine group (50 mg/kg/day, n=4) and high dose berberine group (200 mg/kg/day, n=4). Placebo and berberine were intragastrically administered to all rats for 4 and 8 weeks after the CIA models were established. TNF-α, IL-1β, IL-6, IL-17A, and IgG in the serum were measured by ELISA kits (purchased from Abcam). The hind paws of rats were scanned by micro CT (Scanco, Switzerland).

Results: The thickness of the swollen hind paws was reduced in the high dose berberine group (200 mg/kg/day) compared with the placebo group (Fig A). No significant differences were observed in the levels of TNF-α, IL-1β, and IL-6 between the three groups. However, the levels of IL-17A and IgG were significantly decreased in the high dose berberine group when compared with the placebo group (Fig A). Micro CT data revealed that berberine could significantly improve the microstructure of CIA rats including the bone volume ratio (BV/TV), areal bone mineral density (aBMD) and trabecular separation (Tb Sp) (Fig B and C). Development of bone erosion had also been partially prevented.

Figure 1 A; B microstructure; C 3D reconstruction

Conclusions: Berberine attenuated the symptoms of CIA rats and may prevent bone erosion progression by suppressing IL-17A in CIA. Human studies are required to confirm whether it may serve as a potential treatment for RA in the future.

Disclosure of Interest: None declared

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THU0079

ADIPONECTIN AGGRAVATES BONE EROSION BY PROMOTING OSTEOPONTIN PRODUCTION IN SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS

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Background: We have previously reported that adiponectin (AD), an adipokine that is secreted by adipocytes, correlates closely with progressive bone erosion in rheumatoid arthritis (RA). The exact mechanism of AD towards promoting joint destruction remain unclear.