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 involved in the development of arthritis. 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. Fluctuation of Tfh and its subsets in draining lymph nodes (dLNs) were analysed by flow cytometry. 2. The titers of anti-GPI antibodies from day 7 (arthritis onset phase) and day 28 (resolving phase) were measured. 3. The expression of st6gal1 in dLNs was quantified by PCR and detected by sialic acid analysis. 4. The stimulated GPI antibody production from plasmablasts was measured in the existence of Tfh.

Results: 1. Tfh cells were increased in GIA. It peaked at day 7, the onset of arthritis, and then gradually elevated even after day 7 and this elevation continued while GIA peaked out. 2. The titers of anti–GPI antibodies in GIA sera were measured by ELISA. 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) to GIA. The titers of anti–GPI antibodies in GIA sera were measured by ELISA. 5. Naïve B cells were co-cultured with Tfh and the st6gal1 expression in differentiated plasmablasts was measured by flow cytometry.

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.

BACKGROUND: Rheumatoid arthritis (RA) patients have loss of muscle mass. The balance between muscle protein synthesis and degradation is regulated by cytokines and growth factors, named myokines, such as irisin and myostatin. Myokines are mainly expressed by skeletal muscle and exert systemic effects promoting crosstalk among different tissues. Irisin increases cortical bone mass and its low levels are related to muscle atrophy and obesity.1, 2 While myostatin is a negative regulator of muscle growth and regeneration and has a direct role in osteoclastogenesis of inflammatory bone destruction.3, 4

OBJECTIVES: To evaluate serum levels of irisin and myostatin and body composition of RA patients and controls.

METHODS: 122 female patients with RA, mean age 53 years, mean disease activity score (DAS28) 4.09, mean disease duration 11.2 years and mean body mass index 27.33 kg/m² were included. 69 age and sex-matched healthy subjects were enrolled as control group. Irisin (Phoenix Pharmaceuticals) and myostatin (R and D Systems) serum levels were evaluated by ELISA. Fat mass index (FMI[Kg/m²]) and appendicular lean mass index (ALMI[Kg/m²]) were assessed by total body dual-energy x-ray absorptiometry. Student’s t test and Spearman correlation were performed. Significance was set at p<0.05.

Table 1. Irisin and myostatin serum levels of RA patients and controls

<table>
<thead>
<tr>
<th>Irisin (mean ±SD)</th>
<th>Myostatin (mean ±SD)</th>
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<tbody>
<tr>
<td>RA patients treated with biologics</td>
<td>31.7±17.69*</td>
</tr>
<tr>
<td>RA patients non-treated with biologics</td>
<td>25.9±8.89</td>
</tr>
<tr>
<td>Controls</td>
<td>30±10.95</td>
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</table>

Results: RA patients had decreased serum levels of irisin (25.6±12.25 vs 30.36 ±10.95 ng/ml; p<0.05) and myostatin (3011.28±1271.11 vs 4049.0±1610.01 pg/ml; p<0.05), decreased ALMI (6.09±0.88 vs 6.50±1.10; p<0.05) and increased FMI (11.26±3.30 vs 9.44±2.65; p<0.05), compared to controls. No correlations were observed among irisin and myostatin levels and ALMI and FMI. Of the 122 RA patients, 40 were analysed for the use of biologic medication. Serum levels of irisin and myostatin were different between RA patients treated and non-treated with biologics (table 1).

DISCUSSION: Low levels of irisin and myostatin in RA patients are associated with a negative impact on body composition. In patients treated with biologics, a significant decrease in irisin and myostatin levels were observed. Further analyses are needed for a better comprehension of irisin and myostatin roles in RA, and to verify their correlation to other RA features.

REFERENCES:

Disclosure of Interest: None declared