Objectives: Osteopontin (OPN) is required for osteoclast recruitment. We hypothesised that AD exacerbates bone erosion by inducing OPN expression in synovial tissue. This study aimed to evaluate a novel role for AD in RA.

Methods: The serum levels of AD and OPN were determined in 38 RA, 40 osteoarthritis (OA) patients, and 20 healthy controls using enzyme-linked immunosorbent assay (ELISA). AD and OPN production were measured by double immunofluorescence of RA and OA synovial tissue. Quantitative real-time PCR and immunofluorescence were used to evaluate the mRNA and protein expression levels of OPN in RA synovial fibroblasts (RASFs) and OA synovial fibroblasts after preincubation with AD, respectively. Migration of the RAW264.7 osteoclast precursor cell line was assessed using the Transwell migration assay and co-culture system. Bone destruction and osteoclastogenesis were assessed by immunohistochemistry, microcomputed tomography, and tartrate-resistant acid phosphatase (TRAP) staining in AD-treated collagen-induced arthritis (CIA) mice with and without AD.

Results: AD stimulation of RASFs increased OPN production in a dose-dependent manner. RA patients treated with biologics showed decreased serum levels of OPN compared to non-treated patients. AD stimulation of OA synovial fibroblasts induced migration and OPN expression, while OPN silencing with siRNA reduced the number of TRAP-positive osteoclasts and the extent of bone erosion in the AD-treated CIA mice. When bound to integrin α2β1, OPN functioned as a mediator of AD and osteoclasts.

Conclusions: Our study provides new evidence of AD involvement in bone erosion. AD induces the expression of OPN, which recruits osteoclasts and initiates bone erosion. These data highlight AD as a novel target for RA treatment.

Disclosure of Interest: None declared


THU0081 IDENTIFICATION OF NOVEL AUTOANTIBODIES IN THE SYNOVIAL FLUID FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic, autoimmune and inflammatory joint disease with a poorly understood etiology. Despite widespread diagnostic use of anti-citrullinated protein antibodies and rheumatoid factor, there is strong demand for novel biomarkers to improve the diagnosis of this disease.

Objectives: The purpose of present study is to investigate novel autoantibodies in the synovial fluid of RA patients.

Methods: 1) Using LISA (Serological identification of antigens by recombinant cDNA expression cloning), we identified ten and several antigens from sera of RA patients. 2) Three epitope sites in the candidate antigens proteins were predicted and 18 mer peptides were synthesised. 3) Synovial fluid of the knees was obtained from 48 RA and 48 osteoarthritis (OA) patients. 4) Furthermore, AlphaLISA was used to analyse the antibody levels in synovial fluid using synthetic polypeptide as antigens.

Results: Significantly higher proportion of antibodies against lamin A (LMNA, RA 1987±1392 VS OA 672±3975, p<0.000001) and cell growth-regulating nucleolar protein (CGRN, RA 1987±1331 VS OA 1061±6391, p<0.000007) were found in synovial fluid of RA as compared with OA.

Conclusions: We identified two novel autoantibodies in the knee synovial fluid of RA patients. These antibodies would have the potential to become diagnostic biomarkers of RA.

Disclosure of Interest: None declared


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THU0080 SERUM IRISIN AND MYOSTATIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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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 through amino acid, energy, and immune system metabolism.

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></th>
<th>Irisin (mean ±SD)</th>
<th>Myostatin (mean ±SD)</th>
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<tbody>
<tr>
<td>RA patients treated with biologics</td>
<td>31,71±7,69*</td>
<td>2484,6±1114,90*</td>
</tr>
<tr>
<td>RA patients non-treated with biologics</td>
<td>25,93±6,89</td>
<td>3261,6±1156,28*</td>
</tr>
<tr>
<td>Controls</td>
<td>30,36±10,95</td>
<td>4049,0±1610,01</td>
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Results: RA patients had decreased serum levels of irisin (25,61±2,25 vs 30,36 ±10,95 ng/ml; p<0.05) and myostatin (3011,28±1271,11 vs 4049,08±1610,01 pg/ml; p<0.05), decreased ALMI (6,09±1,08 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).

Conclusions: RA patients presented loss of lean mass and gain of fat mass, as well as lower irisin and myostatin serum levels, in comparison with controls. Additionally, the use of biologic medication by patients impacted on myokines serum levels. 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


THU0082 IMPAIRED LEFT VENTRICULAR RELAXATION AND ITS ASSOCIATION WITH INFLAMMATORY MARKERS IN COLLAGEN-INDUCED ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) experience an increased risk of developing heart failure with a preserved ejection fraction. Although there is some evidence to support a role of chronic inflammation in the pathogenesis of impaired left ventricular (LV) function in RA,1 the direct effects of inflammatory cytokines on the LV function in collagen-induced arthritis (CIA) (an experimental model most similar to RA) require further elucidation.

REFERENCES:

Disclosure of Interest: None declared