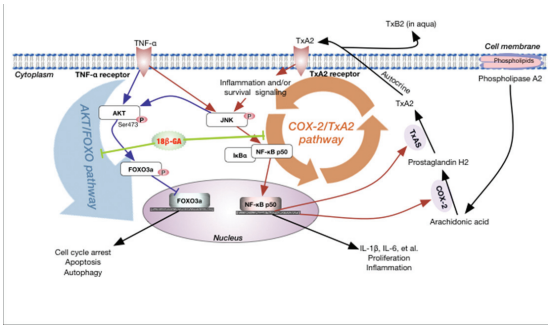
anti-proliferation effects of different treatments. To further study the potential mechanism, TNF-α-induced *in vitro* model was applied. With different treatments, cell proliferation was detected using MTS, meanwhile, cell cycle distribution and apoptosis were examined by flow cytometric analysis. Western blotting and real-time quantitative PCR were conducted to evaluate many moleculars that involved in interested pathways like COX-2/TxA2 pathway and AKT/FOXO3a pathway.
Results: The paw swelling volume and histological data indicate that 18β-GA administration attenuates arthritis severity in rats with CIA. Lower level of IL-1β, IL-6, and TxB2 were observed in serum of 18β-GA group as compared with model group. In addition, synovial immunohistochemistry data shows that 18β-GA decreased about half of PCNA intensity induced by collagen. However, *in vivo*, all data exhibited no significant differences among groups with monotherapy and combination therapy. In *vitro,* 18β-GA inhibited the mRNA and protein levels of COX-2 and TxAS that induced by TNF-α in MH7A cell line. Both p-JNK and NF-κ B1 (p50) were inhibited by 18β-GA as well as TxAS siRNA transfection. Moreover, 18β-GA inhibited MH7A proliferation in a time- and dose- dependent manner from MTS assay. Flow cytometric analysis revealed that 18β-GA induced cell apoptosis and caused G1-phase cell cycle arrest. Finally, AKT and FOXO3a were predominantly phosphorylated by TNF-α, whereas such effect was blocked by18β-GA treatment.



Abstract AB0127 – Figure 1

Conclusions: This study has for the first time shown that 18β-GA has an inhibitory role in synovial cell inflammation and proliferation, which is, at least in part, dependent on the regulation of COX-2/TxA2pathway and AKT/FOXO3a pathway. Thus,18β-GA should be regarded as a new potential drug candidate for RA therapy.

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AB0128 CXCL1, BUT NOT AUTO-ANTIBODIES OR CD4+CCR6+ MEMORY TH CELLS WITHIN BLOOD, IS A MARKER TO DIFFERENTIATE MICE INTO COLLAGEN INDUCED ARTHRITISPOSITIVE OR NEGATIVE PRIOR TO CLINICALLY MANIFEST DISEASE

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Background: There is currently a knowledge gap on early pathogenesis prior to Rheumatoid Arthritis (RA) diagnosis. Additionally, current medication available for RA treatment has not been developed for prevention. Collagen induced arthritis (CIA) could aid in extending knowledge on early RA pathogenesis and testing the preventive effects of medicines.
Objectives: In this study we sought a marker that can differentiate mice prior to clinically manifest disease into their future CIA status with the aim to facilitate research into early disease processes and preventive treatment strategies.
Methods: Blood was obtained at time points prior (days 12 and 19) and after clinically manifest disease (days 27 and 35) during CIA. Antibodies against bovine and mouse collagen type II (mCII) were measured from plasma by ELISA. $CD4^+CCR6^+$ memory Th cells as well as other T cell types were determined in blood. Cytokines and chemokines were detected in plasma by Luminex. Mice were divided into CIA negative and CIA positive groups based on CIA score reached on day 35.
Results: Antibodies against mCII of the IgG2a isotype differed prior to clinically manifest disease but are not suitable as a differentiation marker. $CD4^+CCR6^+$ memory Th cells in blood differed only at day 35. The same holds for IL-6, TNFα and CXCL2. In contrast, CXCL1 differed prior to clinically manifest disease with an AUC significantly better (p=0.003) than random.
Conclusions: Here we identified CXCL1 as a marker that can differentiate mice prior to clinically manifest disease into CIA positive and CIA negative mice. This might help facilitate research into early disease processes and preventive pre-clinical treatment strategies.
Disclosure of Interest: None declared
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AB0129 ASSESSMENT OF MORPHOLOGY OF THE EARLY AND LATE STAGE OF JUVENILE RHEUMATOID ARTHRITIS

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Background: One of the current problems of modern rheumatology is chronic inflammatory diseases of the knee joint in children. With juvenile rheumatoid arthritis (JRA), an uncontrolled inflammatory process can lead to the formation of contractures and deformities of the limbs
Objectives: Our aim is to study morphology of the early and late stage of juvenile rheumatoid arthritis
Methods: In total, 81 knee joint surgery was performed on 71 children of the child age in connexion with the JRA. The average age of the patients was 11 years (6–14). To verify the diagnosis during diagnostic arthroscopy, a multifocal biopsy from 7 points was performed. Pathomorphological study of the material was performed according to the conventional histological method of studying soft tissues
Results: The results of the pathomorphological examination were analysed for the time frame of the appearance of the JRA. Pathomorphological early and late synovitis criteria were found. Early criteria (typical for the first three months after the JRA debut) – the phenomenon of necrosis in synoviocytes and the subintimal layer, palisade-like cell structures in the sub-synovial layer, synoviocyte proliferation, fibrinoid superimpositions on the surface of the cover layer, productive endovascular endo- lytic endotheliosis, lymphocyte infiltration and plasmocytes. Late criteria (duration of the disease – more than 3–6 months): marked plasmacytic infiltration with the formation of lymphoid nodules with a hermetic centre, activation of fibrinoid and sclerotic processes with the formation of extensive fibrinoid necrosis with perifocal sclerosis, the formation of rheumatoid nodules, productive synovial hyperplasia, deposition of amyloid masses, formation of pannus granulation tissue with destructively invasive growth articular cartilage and synovium
Conclusions: Determining the stage of JRA is of great clinical importance for the early initiation of treatment and prevention of irreversible destructive complications. The proposed new method for determining the prevalence of pathological changes in the synovial membrane of the knee joint in children with JRA using a combined arthroscopic and pathomorphological evaluation of pathological changes in synovium in 7 joints allows to accurately determine the prevalence of the pathological process in the synovium, which has macroscopically only local manifestations

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AB0130 SERUM LEPTIN AND ADIPONECTIN LEVELS IN RHEUMATOID ARTHRITIS PATIENTS, THEIR ASSOCIATION WITH INFLAMMATORY PROCESS

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Background: It is well known that such bioactive substances as leptin and adiponectin are involved in different pathologic process including inflammation. At the same time, in a number of studies it was demonstrated anti-flammatory properties

of adipokines. Many studies have shown increasing leptin level and reducing adiponectin level in patients with rheumatoid arthritis (RA) compared with healthy ones. On the other hand the roles of adipokines in pathogenesis of autoimmune disorders are still controversial due to their both pro-inflammatory and anti-inflammatory effects.
Objectives: The aim of this study was to evaluate adipokine levels in patients with RA and to assess their association with the activity of inflammatory process
Methods: The study included 62 patients with RA and 35 practically healthy sex and age matched persons of control group. The diagnosis of RA was established according to the ACR 2010. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) were used to assess inflammation. Disease activity and functional impairment were evaluated using the Disease Activity Score (DAS28). Serum leptin and adiponectin levels were studied by immunoassay using standard sets (DRG", Germany and "Orgenium", Finland). Results are expressed as mean ±standard error of the mean. Spearman's r was used to calculate correlations between markers of disease activity (ESR, CRP, DAS28) and serum adipokine levels. A p value<0.05 was considered statistically significant for all tests
Results: It was found that the mean value of leptin and adiponectin levels were 20.7±12.3 ng/ml and 2.47±1.34 ng/ml respectively in patients with RA and 6.47 ±3.17 ng/ml and 4.21±1.4 ng/ml respectively in the control group. Thus, the leptin level in patients with RA was 3.2 times higher, and adiponectin level was 1.7 times lower than in healthy individuals. Levels of adipokins were associated with the activity of the inflammatory process. Thus, serum concentration of leptin level was increased (r=0.33 and r=0.35) and adiponectin level was decreased (r=−0.25 and r=−0.24) with the increasing of ESR and CRP. Similar patterns were observed for the integral index of RA activity DAS28. In particular, DAS28 was 1.6 times higher in subjects with leptin levels above 44.7±9.4 ng/ml than in the group of patients with leptin levels below 44.7±9.4 ng/ml. The correlation analysis has also confirmed the close association between the leptin and adiponectin levels with DAS28 activity index (r=0.37 and r=−0.28, respectively).
Conclusions: Disadipokineemia in patients with RA is characterised by the increasing of serum leptin level and the decreasing of serum adiponectin level and is closely related to the activity of the inflammatory process.
Disclosure of Interest: None declared
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AB0131 RHEUMATOID FACTOR IS DETECTED ON CIRCULATING EXTRACELLULAR VESICLES IN A SUBPOPULATION OF RHEUMATOID ARTHRITISPATIENTS WITH A MORE SEVERE DISEASE PHENOTYPE

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Background: Extracellular vesicles (EVs) play a role in cell-cell communication and contain numerous signalling molecules inside and on their cell membrane. Although their function remains to be elucidated, evidence accumulates that EVs play a regulatory role in immunity during health and disease. They contain numerous proteins, lipids, RNA, DNA and sometimes cell organelles such as mitochondria. In a recent study was shown that Immunoglobuline M-Rheumatoid factor (IgM-RF) is present on milk derived exosomes.[1] High IgM-RF levels in Rheumatoid Arthritis (RA) predict a more severe disease and comorbidities, probably due to their involvement in immune complex formation and activation of complement (crucial mediators of the effector phase of inflammation in the pathogenesis of RA).
Objectives: In this study we investigate whether RF +EVs are detectable in the circulation of RA patients and if this relates to parameters of disease activity.
Methods: EVs were isolated from platelet-free plasma of 38 RA patients and from age and sex-matched 24 healthy controls (HC) by size exclusion chromatography. EV markers (tetraspanins) were detected by Western blot and miRNA content by RT-qPCR. Particle size and concentration were measured by electron microscopy and nanosight tracking analysis. Protein concentration was determined by micro-BCA. RF levels were measured using a commercial ELISA. The percentage of RF +EVs was determined by measuring bound and unbound PHK labelled EVs to Protein L magnetic beads in a fluorometer.
Results: Mean EV particle size, concentration and protein content were not different between RA patients and HC. 27 of the 38 RA patients were classified as RF+ (>10 IU/ml) and of the clinical parameters studied only their erythrocyte sedimentation rate (ESR) was higher (31 vs 14 mm/hr). In 14 RF +patients, RF was detectable on a small portion of EVs not exceeding 4% of the total number of circulating EVs. Interestingly, RA patients with RF +EVs showed higher disease activity as assessed by patient global health assessment using a visual analogue scale (63 vs 31), blood C-reactive protein (22 vs 9 mg/L) and ESR (43 vs 19 mm/hr) levels, than RA patients with undetectable RF +EVs.
Conclusions: This study shows for the first time that in a subpopulation of RA patients RF is present on EVs, which might originate from their B-cells. The higher disease activity in RA patients expressing RF on their EVs suggests that RF +EVs are involved in RA pathogenesis.

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AB0132 FRAXINELLONE ATTENUATES RHEUMATOID INFLAMMATION IN MICE

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Background: Fraxinellone is isolated from *Dictamnus dasycarpus*, a traditional herbal medicine that attenuates inflammatory conditions.[1,2] Recent studies have suggested that fraxinellone has a potential therapeutic effect in animal models with inflammatory diseases.[3–5]
Objectives: We aimed to evaluate the therapeutic effect of fraxinellone on inflammatory arthritis and identify the underlying mechanisms.
Methods: Fraxinellone (7.5 mg/kg) or a vehicle control was injected into mice with collagen-induced arthritis (CIA). The severity of arthritis was evaluated clinically and histologically. The differentiation of CD4 +T cells and CD19 +B cells was investigated in the presence of fraxinellone. Osteoclastogenesis after fraxinellone treatment was evaluated by staining with tartrate-resistant acid phosphatase (TRAP) and by measuring the mRNA levels of osteoclastogenesis-related genes.
Results: Fraxinellone attenuated the clinical and histologic features of inflammatory arthritis in CIA mice. Fraxinellone suppressed the expression of interleukin-17, and T helper 17 cell-related transcription factors (RORγt and phosphorylated STAT3) in CD4 +T cells. CD19 +B cells showed lower expression of activation-induced cytidine deaminase (AID) and Blimp-1 after treatment with fraxinellone. The formation of TRAP-positive cells and the expression of osteoclastogenesis-related markers were reduced in the presence of fraxinellone. Inhibition of interleukin-17 and osteoclastogenesis was also observed in experiments using human peripheral mononuclear cells.
Conclusions: Fraxinellone alleviated synovial inflammation and osteoclastogenesis in mice. The therapeutic effect of fraxinellone was associated with the inhibition of cellular differentiation and activation. The data suggests that fraxinellone could be a novel treatment for inflammatory arthritis, including rheumatoid arthritis.

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