biphosphonates on the one hand, with the MIC of all control groups on the other hand, revealed significant differences (p < 0.002).

Results: The analysis, using the paired t-test, the average MIC values in the combined group using biphosphonates and the pooled control group, confirmed that the BMD in the zone of intervention in the biphosphonate group was significantly higher than in the control: 0.320 ± 0.008 g / cm², respectively, versus 0.285 ± 0.019 g / cm² (p = 0.002). If the group was excluded from the analysis, where the defect was not filled, the tendency to differences remained: 0.320 ± 0.008 g / cm² vs. 0.308 ± 0.002 g / cm² (p = 0.11).

Mean BMDs of the whole segment with the use of biphosphonates also proved to be significantly higher than in the control, both with the inclusion in the analysis of the group without replacement of the defect, and with its exclusion. Thus, when all control groups were included in the analysis, the mean MIC values in the group with biphosphonates were 0.30 ± 0.01 g / cm² vs. 0.272 ± 0.12 g / cm² (p < 0.001). When excluding from the analysis of the group without replacement of the defect, the MIC values were respectively: 0.307 ± 0.01 g / cm² versus 0.285 ± 0.01 g / cm² (p = 0.01).

Conclusion: Relative to the control, an increase in BMD in the group using biphosphonates excludes the possibility of their negative impact on the process of bone formation. The marked positive bone balance confirms the ability of biphosphonates to maintain the remodeling mechanism at the physiological level.

References: Local application of biphosphonates, osteoelastic materials, biocomposite material, bone implant reconstruction, bone formation.

Disclosure of Interests: None declared

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Rheumatoid arthritis - aetiology, pathogenesis and animal models

AB0082 INHIBITION OF TGFβ1 SIGNALING USING SB-505124 BLOCKS TH17 DIFFERENTIATION AND RESTORES THE TH17/TREG BALANCE IN VIVO, BUT DOES NOT SUPPRESS EXPERIMENTAL ARTHRITIS

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Background: TGFβ1 is an important growth factor that promotes the differentiation of TH17 helper T cells (Th17) as well as regulatory T-cells (Treg). Due to its dual role, the potential of TGFβ1 as therapeutic target is unclear.

Objectives: In this study we aimed to investigate the effect of inhibition of TGFβ1 signaling with the ALK5 inhibitor SB-505124 on human Th17 differentiation in vitro, on cytokine production by human rheumatoid arthritis (RA) synovial explants, and study the effects of local SB-505124 treatment in vivo during innate immune and Th17-driven experimental arthritides.

Methods: Magnetic sorted naïve human T cells were differentiated into Th17 cells with CD3/CD28 activation beads, IL-2, TGFβ1, IL-1β, IL-23, anti-IL-4 and anti-IFNγ and cultured for 4 days; Human RA synovial samples were collected for in vitro experimentation after informed consent. SB-505124 was added as a potential new drug for autoimmunity and Th17-driven arthritides. In addition, SB-505124 was used to inhibit acute joint inflammation during SCW-arthritis (T-cell independent model); Interestingly, SB-505124 reduced Th17 levels in draining lymph nodes (dLN) during IL-1β/BSA arthritis while increased levels of Tregs were observed. Surprisingly, despite this skewed Th17/Treg balance, this did not result in suppression of joint inflammation and destruction in this Th17-driven arthritides model, whereas anti-IL-17 antibody treatment showed significant therapeutic effects.

Results: SB-505124 potently reduced human Th17 differentiation in vitro by decreasing IL-17 and RORγt gene expression and IL-17 protein production. SB-505124 significantly suppressed IL-6 and TNFα production by human RA synovial explants. In addition, SB-505124 dose-effectively inhibited acute joint inflammation during SCW-arthritis (T-cell independent model). Interestingly, SB-505124 reduced Th17 levels in draining lymph nodes (dLN) during IL-1β/BSA arthritis while increased levels of Tregs were observed. Surprisingly, despite this skewed Th17/Treg balance, this did not result in suppression of joint inflammation and destruction in this Th17-driven arthritides model, whereas anti-IL-17 antibody treatment showed significant therapeutic effects.

Conclusion: We revealed suppressive effects of SB-505124 on human Th17 differentiation and the Th17/Treg balance in arthritic mice. However, SB-505124 did not suppress joint inflammation and destruction. This indicates that despite the importance of TGFβ1 in Th17 differentiation, targeting TGFβ1 signaling is not enough to suppress experimental arthritides.

Disclosure of Interests: None declared

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AB0083 STUDY OF THE ROLE OF ANGIPOETIN-LIKE PROTEIN TYPE 4 IN METABOLIC DISORDERS CAUSED BY INFLAMMATION IN RHEUMATOID ARTHRITIS

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Background: Objectives: To assess the potential role of angiopoietin-like protein type 4 (ANGPTL4) in metabolic disorders caused by inflammation in rheumatoid arthritis (RA).

Methods: The study included 88 patients with significant RA, 64 patients with other rheumatic diseases (RD) (36 patients with osteoarthritis (OA); 28 patients with psoriatic arthritis (PsA)); 17 patients with ankylosing spondylitis (AS)) and 32 healthy individuals. Estimation of ANGPTL4 was carried out by enzyme immunoassay using the commercial test system “RayBio Human ANGPTL4 ELISA Kit” (RayBiotech, USA) in blood serum. Levels of ESR, CRP, RF, antibodies to cyclic citrullinated peptide (anti-CCP) and modified vimentin (anti-MCV) in the ELISA test were determined for all patients with RA.

Results: The level of ANGPTL4 in the blood serum of patients with RA was significantly higher than in healthy people (p < 0.001) and patients with other RD (p = 0.012 compared with OA; p = 0.046 with PsA; p = 0.008 with AS). ANGPTL4 indices in patients with RA correlated with the age of onset of RA (r = -0.658, p < 0.001), disease activity according to DAS-28 (r = 0.449, p = 0.001), level of education (r = 0.235, p = 0.029), dose of glucocorticoid hormones (r = 0.321, p = 0.009) and methotrexate (r = -0.496, p = 0.05), the presence of osteopenia (r = 0.44), signs of kidney damage - proteinuria (r = 0.309, p = 0.047) and hypoaalbuminemia (r = 0.386, p = 0.022), as well as with CRP levels (r = 0.488, p = 0.003), ESR (r = 0.458, p = 0.002), serum vitamin D (r = -0.417) and urinary calcium when recalculated to creatinine (r = 0.797, p = 0.032).

Conclusion: Patients with RA showed a high frequency of insulin resistance (according to the HOMA-IR index) (1.27 [0.84-1.62] in patients with RA; 0.76 [0.44-1.02] in healthy individuals; p < 0.001) and the presence of coronary heart disease, as well as a positive correlation between disease activity (according to DAS-28) and insulin resistance (according to the HOMA-IR index) (p = 0.033).

Conclusion: ANGPTL4 acts as an inhibitor of low density lipoprotein lipase. His contribution to the development of dyslipidemia in RA can be demonstrated from the results we obtained when comparing groups of patients with / without signs of metabolic syndrome (MS). A positive correlation between ANGPTL4 and triglyceride levels (r = 0.42, p = 0.018) was found. An increase in the level of ANGPTL4 in blood serum of patients with RA with MS (p = 0.027 compared with RA without MS) can predict the development of cardiac pathology in this group of patients.

Disclosure of Interests: None declared

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AB0084 TNF RECEPTORS PROFILE CHANGES ON CYTOTOXIC T CELLS SUBSETS IN RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH EFFECTIVE TREATMENT

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Background: Previous studies of co-expression profile of receptors to tumor necrosis factor alpha (TNF) in rheumatoid arthritis (RA) have revealed a number of indicators associated with diseases activity with 93% sensitivity and 90% specificity. However, the ratio of receptors to cytokines remains poorly understood. However, the question of therapy effect and its effectiveness in various alteration of cytokine receptors balance remains under investigated.

Objectives: To evaluate the dynamics of co-expression and quantitative expression of type 1 and 2 receptors for TNF in the subpopulations of CD3+CD8+ cells associated with changes in disease severity before and after effective basic therapy.

Disclosure of Interests: None declared

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