RA and DAS28-CRP (p= 0.0104), Fig. 2. No significant correlation was seen between sPD-L1, birth weight and preterm delivery. For sPD-1 we focused on 3rd trimester and postpartum, however, there was no difference between healthy controls and RA patients and no correlation with disease activity or pregnancy outcome.

Conclusion: In healthy pregnancy, we observed an increase of sPD-L1, which decreases after delivery. This supports the hypothesis, that PD-1 pathway may be involved in shaping the physiological fetal-maternal tolerance. In RA higher sPD-L1 values are measured already in non-pregnant patients compared to healthy controls and there is no physiological decrease post-partum. Intriguing, sPD-L1 correlates positively with RA disease activity, reflecting a possible functional antagonist towards the inhibitory function of membrane bound PD-L1 molecules. However, the detailed function of sPD-L1 need to be further delineated. Nevertheless, sPD-L1 may have the potential to serve as prognostic marker for flares in RA pregnancy. Regarding the rather rarely observed adverse pregnancy outcome, larger cohorts need to be investigated.

References:

Fig 1 sPD-L1 in pregnant healthy donors and RA patients compared with controls (non-pregnant healthy donors and RA patients). Control = non pregnant; 1.TT = 1st trimester; 2.TT = 2nd trimester; 3.TT = 3rd trimester; pp =postpartum. * p < 0.05; ** p ≤ 0.01

Fig 2. sPD-L1 correlates positively with DAS28-CRP in RA pregnancy and postpartum.

Disclosure of Interests: Ana-Luisa Stefanski: None declared, Klara Eriksson: None declared, Astrid Zbinden: None declared, Peter Villiger Consultant of: MSD, Abbvie, Roche, Pfizer, Sanofi, Speakers bureau: Roche, MSD, Pfizer, Frauke Förger Grant/research support from: Unrestricted grant from UCB, Consultant of: UCB, GSK, Roche, Speakers bureau: UCB, GSK

DOI: 10.1136/annrheumdis-2020-eular.2889
Background: The investigation of anti-inflammatory and immunosuppressive functions of kynurenic acid (KYNA) is now in focus. Previously, we demonstrated the opposite effects of KYNA and different KYNA analogs on tumor necrosis factor (TNF-α) production and tumor necrosis factor-stimulated gene-6 (TSG-6) expression in U-937 monocytic cells. The potential effect of KYNA analogs on further immune mediators including alarmins (S100A12=EN-RAGE and S100A9=calprotectin) and on human neutrophil peptide 1-3 (defensin) production has not been investigated.

Objectives: Therefore, in the present study, we compared the newly synthesized KYNA analog on the TNF-α, alarmins and α-defensin production, correlation with the effects on TSG-6 expression in rheumatoid arthritis (RA).

Methods: 93 RA patients were involved and divided subgroups based on DAS28 activity score. Peripheral blood mononuclear cells (PBMC) was isolated from RA patients and healthy controls. As cytokine inducer heat inactivated Staphylococcus aureus (SA1) were used. In parallel in vitro experiments, the SA1 induced PBMCs were pretreated with a newly synthesized KYNA analog (compound S2R-72 was synthesized by direct amidation of KYNA). The concentrations of the above mentioned inflammatory mediators in the supernatants were quantified by ELISA kits and the TSG-6 expression was also determined by RTqPCR method.

Results: The SA1 induced TNF-α, EN-RAGE, calprotectin and α-defensin production was significantly higher in RA patients’ group than in healthy controls. KYNA analog attenuated the SA1 induced TNF-α, EN-RAGE, calprotectin and α-defensin production, and increased TSG-6 production and TSG-6 mRNA expression in PBMC cells from RA patients. The SA1 induced TNF-α and TSG-6 production correlated with the DAS28 activity score. The TNF-α inhibitor effect of the KYNA analog correlated inversely with the TSG-6 stimulatory effect in all subgroups of RA patients based on DAS28 activity score.

Conclusion: TSG-6 expression could participate in the suppression of inflammatory cytokines, such as TNF-α, EN-RAGE, calprotectin and α-defensin. We suppose that the elevation of the TSG-6 expression by KYNA and especially by new KYNA analogs might be one of the mechanisms that are responsible for their suppressive effect on TNF-α production as a feedback mechanism in RA. KYNA and KYNA analogs have an important role in influencing TSG-6 expression, and there is a possible benefit with potential therapeutic consequence of targeting TSG-6 expression by kynurenes in inflammatory conditions in RA.

Acknowledgments: This work was supported by GINOP 2.3.2-15.15-00034

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.2379

AB0109

THE ROLE OF CD70 IN THE DEVELOPMENT OF RHEUMATOID ARTHRITIS

S. J. Yeo1, S. W. Kang1, J. Kim1, I. S. Yoo1, C. K. Park1, H. R. Lee1, Changnam National University Hospital, Daejeon, Korea, Rep. of (South Korea)

Background: Rheumatoid arthritis (RA) is a progressive, chronic inflammatory autoimmune disease. Pro-inflammatory molecules, activated lymphocytes, and the migration of inflammatory cells are important in the development of RA. There are many unknown causes of RA. And there are many patients who are refractory to treatment with known disease-modifying anti-rheumatic drugs. So, unknown cause of RA needs to be elucidated.

CD70 is a member of the tumor necrosis factor (TNF) superfamily and a ligand for CD27. The interaction of CD70 with its receptor CD27 promotes expansion and differentiation of memory and effector T cells as well as B-cell expansion and plasma cell differentiation. Hypoxia is an important micro-environmental factor in RA synovium. Hypoxia induces activation of hypoxia inducible factor (HIF). The expression of HIF-2α is up-regulated in human RA synovium. Reactive oxygen species (ROS) has been implicated in the pathophysiology of RA. CD70 expression was higher in RA synovium than in OA synovium and in CD70 knockout mice synovium.

Objectives: In this study, we tried to examine the presence of CD70 in RA synovium and investigate the role of CD70 in the development of RA associated with hypoxia and ROS.

Methods: Flow cytometry was performed to examine the expression of CD70 on mononuclear cells (MNCs) and CD70 in synovial fluid (SF). Western blot analysis was performed to examine the protein expression of CD70 in MNCs and in SF. Cell proliferation and cell survival were analyzed by cell counting and cell viability assays. CD70 knockdown and CD70 overexpression experiments were performed using siRNA and lentivector. In vivo studies were performed using mouse models of RA.

Results: CD70 mRNA is up-regulated in RA synovium and in CD70 knockdown mice synovium. Protein expression of CD70 in MNCs and in SF was higher in RA synovium than in OA synovium. In vitro experiments, CD70 knockdown and CD70 overexpression experiments were performed using siRNA and lentivector. In vivo studies were performed using mouse models of RA.

Conclusions: CD70 is a marker for RA synovium and a potential therapeutic target. The presence of CD70 in RA synovium and the role of CD70 in the development of RA associated with hypoxia and ROS.