Conclusions Our study reveals a novel, protective effect of TGF- β that could help preserve cartilage homeostasis under inflammatory conditions by dampening IL-6 signaling via IL-6R down regulation. In arthritic diseases, the presence of soluble IL-6R might bypass this protective TGF- β effect and contribute to cartilage damage.

Disclosure of Interest None declared

P079

IS IGM RHEUMATOID FACTOR PRESENT ON CIRCULATING EXTRACELLULAR VESICLES OF RHEUMATOID ARTHRITIS PATIENTS A POTENTIAL BIOMARKER FOR DISEASE SEVERITY?

¹O Arntz, ¹B Pieters, ²R Thurlings, ¹PVD Kraan, ¹FVD Loo*. ¹Experimental Rheumatology, Dept. of Rheumatology; ²Rheumatology, Radboud university medical center, Nijmegen, Netherlands

10.1136/annrheumdis-2018-EWRR2019.68

Career situation of first and presenting author Student for a master or a PhD.

Introduction Rheumatoid factor (RF) are autoantibodies and measured in serum of rheumatoid arthritis patients (RA) to diagnose the disease. High serum RF levels are also predictors of more severe disease forms although the functional role of RF is still unclear.¹ Most research on RA has been focused on cytokines as main effectors in the disease process but cell-cell communication involves a much broader scope of responses such as via the release of extracellular vesicles (EVs).² EVs are small particles of around 100 nm and released by cells. They mediate intercellular communication by exchange their content (RNA, miRNA and proteins).

Objectives As EVs are communicators that carry a multitude of signals and can be derived from all cells including B-cells we set out to determine whether RF is detectable on circulating EVs in RA patients and if this relates to parameters of disease activity.

Methods EVs were isolated from platelet-free plasma of 41 RA patients by size exclusion chromatography. We quantified the particle and protein concentration, using NanoSight particle tracking analysis and micro-BCA. Tender (TJC) and swollen joints (SJC) were assessed by physicians and the global patient visual analogue score (VAS) was determined by the patient. IgM-RF, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were determined by standard laboratory blood tests in our hospital. Disease activity score (DAS28) was calculated.

Results In plasma of 28 out of 41 RA patients RF was detectable, and in 13 out of these 28 RA +RF was also detected on their isolated pEVs (RF⁺pEVs). No statistical differences were found on particle size, protein content per particle and amount of particles of pEVs between seronegative (RA-) and seropositive (RA+) patients (116 nm, 39fg, 5.4×10^{10} and 114 nm, 58fg, 1.8×10^{10} , respectively). Comparing disease parameters no differences were found between RA+ and RA- patients, except for increased ESR levels in RA+ patients. However, RA+ patients having circulating RF⁺pEVs showed significant higher CRP and ESR levels and VAS and DAS28 scores as compared to RA+ patients without circulating RF⁺pEVs while no differences were found on TJC and SJC.

Conclusions This study shows for the first time the presence of RF on pEVs in a subset of RA+ patients and this could be a plasma marker to distinguish RA patients with a more

severe disease. We found that RF+ EVs is not a reflection of the number of affected joints but might be more indicative for the underlying pathophysiology of RA.

REFERENCES

1. Gonzalez, A. *The Journal of Rheumatology* 2008.
2. György, B. *Cellular and Molecular Life Sciences* 2011.

Disclosure of Interest None declared.

P080

THE EFFECT OF ACTIVIN A AND FOLLISTATIN ON THE INTERACTION OF ENDOTHELIAL CELLS AND RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

¹I Aykara*, ¹M Diller, ²S Rehart, ¹U Müller-Ladner, ¹E Neumann. ¹Dept. of Rheumatology and Clinical Immunology, Campus Kerckhoff, Justus-Liebig-University Giessen, Bad Nauheim; ²Dept. of Orthopaedics and Trauma Surgery, Agaplesion Markus Hospital, Frankfurt, Germany

10.1136/annrheumdis-2018-EWRR2019.69

Career situation of first and presenting author Student for a master or a PhD.

Introduction The autoregulatory cycle of activin A and its antagonist follistatin is well known in the hypothalamic-pituitary-gonadal axis, but activins also play an important role in autoimmune diseases, such as rheumatoid arthritis (RA). Due to inflammation, activin A is released, then inducing its antagonist follistatin. This negative feedback mechanism has been primarily described in hepatocytes, but is inactive in synovial fibroblasts from patients with rheumatoid arthritis (RASf). Synovial fibroblasts are mediators of cartilage destruction in RA. In inflamed synovium, there is an interaction of RASf with endothelial cells. Due to tissue hyperplasia and inflammation, neoangiogenesis, mediated in part by local fibroblasts, is increased in RA synovium. The effect of activin and follistatin on the interaction of RASf and endothelial cells is still unknown.

Objectives This study focuses on the effect of the activin A and follistatin on the interaction of RASf and endothelial cells.

Methods RASf were isolated from synovial tissue of patients with RA undergoing joint replacement surgery. Endothelial cells (HUVEC) were commercially obtained. RASf and HUVEC were stimulated in mono-, or coculture with activin A (15 ng/ml), follistatin (500 ng/ml) or IL-1 β (1 ng/ml). After 18 hour the supernatants were collected and the concentrations of activin A, VEGF and IL-6 were measured by ELISA.

Results IL-1 β induced activin A release in RASf and HUVECs alone as well as in direct coculture. The stimulation with follistatin and IL-1 β at the same time reduced the activin A concentration in HUVECs as well as in cocultures in comparison to stimulation with IL-1 β alone ($p < 0.05$; $n = 4$). In monocultures of RASf this reduction could not be detected.

With respect to HUVECs, a significant reduction ($p < 0.05$) of the proinflammatory cytokine IL-6 after stimulation with activin A and IL-1 β in comparison to the stimulation with IL-1 β alone could be observed.

The release of VEGF, which plays an important role in inflammation-induced neoangiogenesis, was induced in RASf with IL-1 β (89%), activin A (55%), activin A and IL-1 β (148%), follistatin and IL-1 β (84%). In coculture with HUVECs, the induction was less pronounced as in