adiponectin. We also investigated whether these biomarkers correlated with various demographic, clinical and laboratory markers.

Methods We treated 37 RA patients with either etanercept (ETN) or certolizumab pegol (CZP) in a 12 month follow-up study. Assessments were performed at baseline, and 3, 6 and 12 months after treatment initiation. Serum chemerin and adiponectin concentrations were measured by commercially available ELISA kits (R and D System, MN and USA). PON1 and arylesterase activities were measured by spectrophotometry. In addition, age, disease duration, disease activity (DAS28), CRP, anti-CCP, IgM rheumatoid factor and plasma lipid levels were also assessed. Arterial flow-mediated vasodilation (FMD), carotid intima-media thickness (cIMT) and arterial pulse-wave velocity (PWV) were assessed by ultrasound.

Results Anti-TNF treatment resulted in a significant decrease in the levels of chemerin ($p<0.001$) and adiponectin ($p<0.007$) after 12 months. There were no significant changes in the levels of other metabolic biomarkers. We found the following correlations between the baseline values: the PON1 levels correlated with the age of patients ($R=0.466$, $p=0.004$). The adiponectin correlated with the disease activity ($R=0.385$, $p=0.030$), HDL-C ($R=0.417$, $p=0.012$) and the triglyceride levels ($R=0.481$, $p=0.003$). The total cholesterol correlated with the PWV ($R=0.449$, $p=0.021$) and the levels of the LDL-C ($R=0.911$, $p<0.001$). The baseline triglyceride correlated with the IgM rheumatoid factor ($R=0.343$, $p=0.021$); and the levels of LDL-C correlated with the PWV values ($R=0.444$, $p=0.023$).

Conclusions Metabolic factors, such as certain adipokines, PON1 and arylesterase may play a role in oxidative stress and atherosclerosis associated with RA. Anti-TNF treatment may affect adipokine levels.

Acknowledgements The work is supported by the GINOP-2.3.2-15-2016- 00015/I-KOM TEAMING project.

Disclosure of interest None declared

P076

A BIOASSAY TO MEASURE TGF β ACTIVITY REVEALS DECREASED TGF β ACTIVITY IN SYSTEMIC SCLEROSIS SERUM

¹A van Caam*, ¹E Vitters, ²F van den Hoogen, ²M Vonk, ¹P van der Kraan. ¹Experimental Rheumatology; ²Rheumatology, Radboudumc, Nijmegen, Netherlands

10.1136/annrheumdis-2018-EWRR2018.93

Introduction Systemic sclerosis (SSc) is a severe disease characterised by auto-immunity, vasculopathy and excessive fibrosis of connective tissues. The pathophysiology of SSc is still poorly understood, but its symptoms imply a role for dysregulated transforming growth factor β (TGF β) signalling because this cytokine is known to regulate vascular and connective tissue biology. TGF β circulates in blood in an inactive latent form bound to latency associated peptide and latent TGF β binding proteins. This latent TGF β has to be activated before it can become bioactive. With the use of a bioassay TGF β 's bioactivity can be measured in complex mixtures like serum. This is not possible with an ELISA because this technique does not take (cellular) activation processes into account.

Objectives To determine the bioactivity of TGF β in SSc serum compared to that of healthy control serum.

Methods Serum was collected of 10 SSc patients and 10 age and sex matched healthy controls. Primary human fibroblasts

of 3 donors were transduced with CAGA₁₂-luc which produces luciferase in response to TGF β /Smad3 or BRE-luc which produces luciferase in response to BMP/Smad1/5. These cells were treated with 10% serum for 16 hour and luciferase activity was measured. To activate all TGF β , sera were treated with 4M HCl for 1 hour at RT, after which pH was normalised with 4M NaOH. Controls were treated with HCl and NaOH simultaneously. To verify that TGF β signalling was measured in this reporter assay, sera were treated with anti-TGF β 1/2/3 for 1 hour at RT before use.

Results Control sera significantly induced reporter activity by 4.5-fold. However, SSc sera only induced a 2.5-fold increase in luciferase activity, indicating significantly lower bioactivity of TGF β ($p<0.0001$). This difference was not due to a difference in total TGF β levels; after activation of all TGF β both HC and SSc sera induced a similar 6-fold increase in signal strength. These data show that in HC sera approximately 75% of all TGF β is bioactive compared to only 42% in SSc. Addition of anti-TGF β 1/2/3 inhibited all CAGA₁₂-luc reporter activity ($p<0.0001$) of both HC and SSc serum, and of both acidified and not acidified sera ($p<0.0001$), showing that our bioassay is indeed TGF β -dependent. To investigate if reduced bioactivity is a more general phenomenon we measured BMP activity. BMP proteins are structurally closely related to TGF β and also circulate in inactive form. Both HC and SSc sera induced a similar 8-fold increase in BRE-luc activity, and this activity was increased to a 16-fold induction after acidification for both groups. BMPs in SSc sera are thus not less bioactive. This illustrates the uniqueness of our observation on TGF β bioactivity.

Conclusions TGF β in SSc serum is less bioactive than in control serum whereas BMPs are not less bioactive.

Disclosure of interest None declared

P077

EFFECTS OF IL-17 AND THE HEPATOCYTE-MONONUCLEAR CELL INTERACTIONS IN THE HEPATIC INFLAMMATORY RESPONSE

¹A Beringer*, ¹ND Thiam, ²J Molle, ²B Bartosch, ¹P Miossec. ¹Immunogenomics and Inflammation Research Unit EA4130, University of Lyon; ²Inserm U1052, Cancer Research Centre, Lyon, France

10.1136/annrheumdis-2018-EWRR2018.94

Introduction Interleukin-17A (IL-17), tumour necrosis factor- α (TNF α) and IL-6 are pro-inflammatory cytokines involved in many autoimmune and inflammatory diseases including rheumatoid arthritis. Because most acute-phase proteins are produced by the liver, the hepatic response plays an important role in systemic inflammation. By producing chemokines such as CCL-20 that attract Th17 cells, hepatocytes can recruit mononuclear cells in liver, which leads to chronic hepatitis.

Objectives To determine the effect of the IL-17/TNF α combination and the contribution of hepatocyte-peripheral blood mononuclear cell (PBMC) interactions in the hepatic inflammatory response.

Methods Human HepaRG cell line and primary human hepatocytes (PHH) were cultured with or without IL-6, anti-IL-6 receptor (anti-IL-6R) antibody, IL-17 and/or TNF α . For co-cultures, PBMC from healthy donors activated or not with phytohemagglutinin (PHA) were added on hepatocytes at a 5:1 ratio. Transwell system was used to study the contribution of the direct cell-cell contact. Cytokine expression and production were quantified by qRT-PCR and ELISA respectively and