INTERACTIONS Hôte Greffon T Tumeur, Besançon, France

REFERENCES:
2. Venclovecský J., et al. Xanthinoxidase and xanthine dehydrogenase activities were measured in lysed red blood cells by spectrophotometric method as previously described [3]. The changes of these enzymes activities were studied in RA patients before and after the injection of glucocorticoids. Statistical comparison tests were selected in according to common guidelines, differences were considered significant when p<0.05. Central tendencies were expressed as means±SEM.

Results: Mean age of patients in methylprednisolone group was 41.8±1.05 years, and mean RA duration (± SEM) was 7.9±0.21 years. Mean age of patients in diprospar group was 40.9±1.07 years, and mean RA duration was 8.0±0.33 years. Significant decreases of XO activity and increase of XDG activity were observed in enzymatic activity did not reach the level of healthy controls. As described previously, decreased XO activity and increased XDG activity were observed in plasma of RA patients just after the injection of the average therapeutic doses of glucocorticoids, as well as in lysed lymphocytes just after the injection of methylprednisolone [4].

Conclusion: Treatment with methylprednisolone and betamethasone can affect the balance of XO/XD activity and increase the antioxidant potential of the blood. This effect can exert beneficial influence on autoimmunity inflammatio in RA.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3207

TIME COURSE OF INTESTINAL PERMEABILITY AND BACTERIAL TRANSLLOCATION IN THE MODEL OF ADJUVANT-INDUCED ARTHRITIS

S. Hecquet1, P. Totoson2, H. Martin2, C. Peyronne1, M. Tournier1, P. Saas2, J. P. Pais-De-Barros4, D. Wendling1, C. Demougeot5, F. Verhoeven1, J. Centre hopitalier régional universitaire de Besançon, Rheumatology, Besançon, France; 2EPITEP PEPITE LAB, Physiology, Besançon, France; 3UMR 1098, Interactions Hôte Greffon Tumeur, Besançon, France; 4UMR 1231, Plateforme de lipodépistic, Djyon, France

Background: Intestinal inflammation, dysbiosis, intestinal permeability (IP) and bacterial translocation (BT) have been identified in patients with spondyloarthritis but the time at which they appear and their contribution to the pathogenesis of the disease is still a matter of debate.

Objectives: To investigate the time-course of intestinal inflammation, IP and BT in a rat model of reactive arthritis, a subgroup of SpA, the adjuvant-induced arthritis model.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by an injection at the base of the tail of Mycobacterium butyrycinum with incomplete Freund’s adjuvant (Day (D) 0). Control rats received saline using the same procedure. Body weights and a clinical arthritis score were daily assessed. A group of AIA and control rats (n=15 per group) were euthanized at different times of arthritis: D4 for the pre-arthritic phase (AIA-preclinical), D11 for the onset of arthritis (AIA-onset) and D28 for the acute phase (AIA-acute). In each group (AIA and control, n=15 per group), IP was assessed by measuring plasma levels of zonulin (ELISA) and ileal mRNA expression of zonulin and occludin (RT-qPCR), BT was studied by measuring bacterial endotoxins (or LPS, by LCM2 method), soluble CD-14 (sCD14, ELISA) and ileal mRNA expression of TLR-4, and intestinal inflammation was assessed by measuring ileal mRNA expression of IL-8, IL-33, IL-17, IL-23p19 and TNF-α (RT-qPCR). Joint damage was assessed by the determination of a clinical and radiographic score of hind paws.

Results: Body weights of AIA rats decreased from D4 to D28 as compared to controls, in parallel to the development of a severe clinical and radiographic arthritis disease from D11 and D28. Compared to control rats, AIA induced an increase in plasma zonulin levels at D4, D11 but not at D28. Ileal mRNA zonulin overexpression occurred at D11 while occludin was unchanged. As early as Day 4 (preclinical phase), mRNAs of IL-8, IL-33 and IL-17 were overexpressed in ileum from AIA. At Day 11 (onset), overexpression of IL-8 persisted and mRNAs of TNF-α and IL-23p19 increased in AIA. Neither LPS levels nor ileal mRNA expression of TLR-4 were changed by arthritis whatever the phase of arthritis. By contrast, blood levels of sCD-14 was significantly increased in the AIA group at all stages of arthritis. No correlation was found between clinical and radiographic arthritis scores and zonulin or LPS levels. Conversely, a negative correlation was observed between intestinal IL-6 mRNA expression and arthritis score (r=-0.3, p<0.02).

Conclusion: In an animal model of SpA, intestinal inflammation and increased intestinal permeability occur prior to joint inflammation, suggesting a role of these disorders in the pathogenesis of this disease.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3168

DIFFICULT-TO-TREAT RHEUMATOID ARTHRITIS: A BIOMARKER SCREENING PILOT STUDY

J. Baloun1, A. Pekacova2,3, H. Manni1,3, J. Venclovecský1,2, K. Pevelka1,2, L. Senoš3,1, Institute of Rheumatology, Department of Rheumatology, Prague, Czech Republic; 1Faculty of Medicine, Charles University, Department of Rheumatology, Prague, Czech Republic; 2Institute of Rheumatology, Department of Experimental Rheumatology, Prague, Czech Republic

Background: Despite modern therapeutic approaches, many patients with rheumatoid arthritis (RA) remain symptomatic after several cycles of treatment and may become so called Difficult-To-Treat (D2T). D2T RA is a multifactorial condition in which different factors may be major determinants of the persistence of signs and symptoms, which is seldom caused by drug resistance only. Discovering new biomarkers is necessary to develop tailored therapies that will be effective in an individual patient at each stage of the disease.

Objectives: The primary aim of this pilot study was to validate a target proteomic technique for the proteome profiling of the two cohorts of RA patients and controls. Moreover, we searched for potential plasma biomarker(s) predicting D2T RA.

Methods: Seven RA patients with persistent remission on biological therapy in two consecutive examinations 12 wks apart (mean age 59.6±14 yrs), seven D2T RA patients fulfilling proposed EULAR definition of D2T RA1 (mean age 59.3±13 yrs), and six healthy controls (mean age 58.8±15 yrs) were included in this study. All subjects were females and their samples were collected before starting biological therapy. We employed differentially expressed bands with nano-flow UHPLC Dionex Ultimate 3000. Prior to quantification, 125 plasma samples were modified by PepTiquant Plus Human kit to increase the sensitivity. Data were analysed by ANOVA and Tukey’s posthoc test with false-discovery-rate adjustment.

Results: The target proteome profiling reliably quantified 92 from 125 labelled proteins. Our follow-up statistical analysis revealed ten plasma proteins, which significantly differed among groups. Notably, we found significantly different plasma levels of paraoxonase/arylesterase 1 (PON1), an esterase with an anti-oxidant characteristic preventing lipid peroxidation2, between RA patients and controls and between RA patients with persistent remission and D2T RA patients.