Results: Naïve SKG ileum displayed dysbiosis with increased expression of ER stress markers Grp78, xBP1, CHOP and reduced mucin staining. After curdian treatment, goblet cell numbers were decreased and I24 mRNA was increased compared to BALB/c controls. By IF, I24 was localized to the goblet cells of the ileum in SKG and BALB/c mice and 2 weeks post curdian, ileal goblet cell number was correlated with IL-24 staining intensity. In MUC2hi LS-174T but not MUC2low mRNA was increased and active caspase 3 expression.

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Results: Despite goblet cell IL-24 over-expression in dysbiotic naïve SKG ileum, goblet cell loss due to stress associated with increased mucus production also depletes IL-24. In an in vitro model of goblet cell stress, IL-24 mitigates ER stress-induced apoptosis, suggesting that IL-24 production in SKG ileum is insufficient to prevent the disease cascade that commences with goblet cell apoptosis and epithelial barrier breakdown.

Conclusion: Despite goblet cell IL-24 over-expression in dysbiotic naïve SKG ileum, goblet cell loss due to stress associated with increased mucus production also depletes IL-24.

Arias de la Rosa1, M. L. Ladehesa Pineda1, C. López-Medina2, M. Ruiz-Ponce1, L. Cuesta López2, M. Á. Puche Larrubia1, M. D. C. Abalos-Aguilera1, Contreras1, E. Collantes Estevez2, N. Barbarroja Puerto2.

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POS0432

CHARACTERIZATION OF THE CARDIOVASCULAR DISEASE PROTEIN EPISTEMIC PROFILE IN SPONDYLOARTHRITIS PATIENTS: POTENTIAL BIOMARKERS FOR PERSISTENT INFLAMMATION

Keywords: Biomarkers, Cardiovascular disease, Spondyloarthritides

I. Arias de la Rosa1, M. L. Ladehesa Pineda1, C. López-Medina2, M. Ruiz-Ponce1, L. Cuesta López2, M. Á. Puche Larrubia1, M. D. C. Abalos-Aguilera1, Contreras1, E. Collantes Estevez2, N. Barbarroja Puerto2.

Methods: A cross-sectional study including 120 patients with SpA and 30 age-sex-matched healthy donors (HDs) was carried out. Clinical and laboratory parameters and CVD risk factors were recorded. To measure the presence of persistent inflammation, levels of c-reactive protein (CRP) and Ankylosing Spondylitis Disease Activity Score (ASDAS) were calculated.

Background: Patients with Spondyloarthritides (SpA) have an increased risk of cardiovascular disease. Taking into account the strong relationship between inflammation and CVD, there is an urgent need to identify different molecular drivers of CVD signs and their association with inflammation.

Conclusion: Persistent inflammation, levels of c-reactive protein (CRP) were collected retrospectively for 5 years previous to the study, a patient was considered to have persistent inflammation if it increased at least 50% during the previous 5 years. Levels of 92 proteins with a recognized role in CVD were analyzed in the plasma using proximity extension assay (PEA) technology (Olink Target 96 CVD III panel, Cobiotic Biosciences).

Results: SpA patients showed higher rates of CVD comorbidities compared to HDs. Plasma levels of TNF-R1, RARRES-2, CH3L1, GYPYRL-1, CTSD, IL2RA, IL12RA, TIMP-4, CTSB, GDF-15, MMP-9, and PDG-F-A were significantly increased in SpA compared to HDs. Specifically, these proteins are also related to biological processes such as neutrophil degranulation, immune response, cell activation, atherosclerosis, apoptosis, and inflammatory response. Besides, a significant alteration of these CVD-related proteins in SpA was also associated with the presence of arterial hypertension, insulin resistance, obesity, hyperuricemia, and high levels of acute phase reactants. 36% of SpA patients displayed persistence of inflammation. Interestingly, SpA patients with persistent inflammation showed higher levels of ankylosing spondylitis disease activity (ASDAS) score, CRP, glucose, complement component 3, and lower levels of HDL-cholesteral and apolipoprotein A compared to SpA patients with non-persistent inflammation, suggesting the relationship of inflammation with metabolic alterations. In addition, 8 out of 12 CVD-related proteins altered in SpA patients were specifically changed in patients with persistent inflammation: MMP-9, RARRES-2, GYPYRL-1, IL2RA, TNF-R1, PDDGF-A, IL-2RA and GDF-15, highlighting levels of MMP-9 protein as a potential biomarker for persistent inflammation in SpA (AUC=0.796 p<0.0001).

Conclusion: 1) SpA patients show an altered CVD proteome profile which is strongly associated with CVD risk factors and clinical inflammatory markers, 2) SpA patients with persistent inflammation display a deeper alteration in their plasma CVD protein pattern suggesting the link between subclinical CVD risk and the chronic inflammatory, and 3) this study identifies novel potential biomarkers to distinguish SpA patients with persistent inflammation. Funded by ISCIII (PI20/00079, PMP21/00119, and RICOR-RD21/0002/0033) co-financed by ERDF.

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POS0433

RELATIONSHIP BETWEEN MRNA-1-3P, INTERLEUKIN-17 AND TUMOR NECROSIS FACTOR IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Keywords: Spondyloarthritidis, Genetics/Epigénetics, Biomarkers

A. Pekacova1,2, J. Baoulin1, K. Bubova1,2, M. Gregova1,2, S. Forejtova1,2, J. Hornikova1,2, M. Husakova1,2, K. Mintalova1, V. Cervenak1, M. Tomcik1,2, J. Vantovska1, K. Pavelka1,2, L. Senohlava1,2, J. Cernographic, O. Vronskay, Kopek, Rep. Experimental Rheumatology, Prague, Czech Republic, 2 First Faculty of Medicine Charles University, Prague, Czech Republic, 3 St Ave University Hospital and Faculty of Medicine, Masaryk University, Department of Imaging, Brno, Czech Republic.

Background: microRNAs (miRNAs) are small non-coding RNAs that can regulate gene expression and mirror the patient's health condition. miRNAs deregulation is considered a crucial factor in the development and progression of various diseases, including axial spondyloarthritis (axSpA) [1].

Objectives: The aim of the study was to profile the miRNNome of peripheral blood mononuclear cells (PBMCs), to identify specific miRNAs and their association with several cytokines, axSpA disease activity and spinal impairment.

Methods: Massive parallel sequencing (MPS, illumina) was performed for miRNAs profiling in 96 subjects (38 patients with non-radiographic (nr-) axSpA, 38 patients with radiographic (r-) axSpA and 20 healthy controls (HC)). The expression of candidate miRNAs was validated using the qRT-PCR system (SmartChip) on a new cohort of 47 patients with nr-axSpA, 44 patients with r-axSpA and 50 HC. Disease activity was determined using C-reactive protein (CRP) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Radiographs of the cervical and lumbar spine were assessed by two independent blinded readers using modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). We employed DESeq2 and general linear modelling with a negative binomial assumption (GLM-NB) to evaluate the association of candidate miRNAs to the radiographic form, ASDAS and Oswestry Linear modelling was used to determine the association between miRNAs and laboratory/cellular parameters adjusted for CRP, age and sex.

Results: MPS detected 432 miRNAs; however, only 90 miRNAs passed through the selection criteria (p<0.05, BaseMean=10, the difference in log2FC<0.5). We selected 45 miRNAs for validation based on the selection criteria and the literature. We validated miR-1-3p (p=0.006, FC=-1.757) to be upregulated and miR-1248 (p=0.002, FC=1.125) and miR-1246 (p=0.002, FC = -1.125) to be downregulated in patients with axSpA compared to HC. In addition, the expression of miR-1-3p correlated with the plasma levels of IL-17 (p=0.016, r=0.25) and TNF (p=0.028, r=0.22), but not with the gene expression of IL-17 or TNF in PBMCs. miR-1-3p (p=0.039, p=0.665) as well as miR-1248 (p<0.001, p=0.207) correlated with the IL-8 gene expression in PBMCs. None of the miRNAs distinguished between radiographic and non-radiographic disease or correlated with disease activity or radiographic spinal impairment.

Conclusion: This cross-sectional study failed to demonstrate association between cellular miRNAs, disease activity or spinal impairment, but the association between miR-1-3p, IL-17 and TNF may suggest its role in the pathogenesis of axSpA.


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POS0434

CCL20 INHIBITION AMELIORATES PERIPHERAL ARTHRITIS IN ANKYLOSING SPONDYLITIS

Keywords: Animal models, Adaptive immunity, Spondyloarthritides

Y W. Park1, H. J. Kim1, Y. J. Lee2,3, M. J. Kim1, H. I. Lee1, S. C. Shim1, S. Jo5, T. H. Kim5, E. J. Won7, T. J. Kim1, 1Chonnam National University Medical School and Hospital, Department of Rheumatology, Gwangju, Korea, Rep. of (South Korea), 2Chonnam National University Medical School and Hospital, Department of Pathology, Gwangju, Korea, Rep. of (South Korea), 3Chonnam University College of Medicine, Gwangju, Korea, Rep. of (South Korea), 4Graduate School of Chonnam National University, Department of Biomedical Sciences, Gwangju, Korea, Rep. of (South Korea), 5Daedeo