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 Il24 mRNA was increased compared to BALB/c controls. By IF, IL-24 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 MUC2 hi LS-174T but not MUC2 low compared to BALB/c controls. By IF, IL-24 localized to the goblet cells of the ileum mRNA was increased Il24, Grp78, sXBP1 and active caspase 3 expression.

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

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**POS0432**

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

**Keywords:** Biomarkers, Cardiovascular disease, Spondyloarthritis

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Background: patients with Spondyloarthritis (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.

Objectives: to investigate the alteration of CVD-related proteins in the plasma of SpA patients, their association with clinical features, and to evaluate their potential role as biomarkers for the identification of persistent inflammation.

Methods: a cross-sectional study including 120 patients with SpA and 30 age- and 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) were collected retrospectively for 5 years prior to the study, a patient was considered to have persistent inflammation if the increased CRP levels were at least 50% of the measured levels 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, Cobiomic Biosciences).

Results: SpA patients showed higher rates of CVD comorbidities compared to HDs. Plasma levels of TNF-R1, RARRES-2, CHIS1L, PGLYRP-1, CTSD, UPAR, IL2RAA, TIMP-4, CTSB, GDF-15, MMP-9, and PDDG-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, arteriosclerosis, 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-cholesterol 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 significantly 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=0.025, 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, |r|=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 impingement, 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, Spondyloarthritis

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Background: Ankylosing spondylitis (AS) is a rheumatic disease characterized by chronic inflammation. Several lines of evidence implicate interleukin (IL)-17A-secerting T helper (Th)17 cells in AS pathogenesis. One of the receptors of Th17 cell, C-C motif chemokine ligand 20 (CCL20) is known to attract C-C chemokine receptor 6 (CCR6) expressing cells to the site of inflammation. However, the role and mechanisms of CCL20 in AS are not well understood.

Objectives: Therefore, this study aimed to evaluate the function of CCL20 in patients with AS.

Methods: Peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry and enzyme-linked immunosorbent assay (ELISA). To determine the direct effect of cell migration in the presence of CCL20, a transwell migration assay was performed. In in vivo experiments, SKG mice were treated with either CCL20 blocking antibody or isotype control antibody. Clinical signs of mice were monitored twice a week and scored by two independent observers. At the experimental endpoint, specimens of the ankle was obtained from mice. Two blinded readers then performed pathological scoring for arthritis using immunohistochemistry.

Results: IL-17A producing cells were significantly higher expressed in SFMCs of AS patients than in PBMCs of AS or healthy controls. CCL20-positive cells showed significantly increased IL-17A production than CCL20-negative cells. To confirm the relationship between CCL20 and IL-17A production, IL-17A expression was observed with either CCL20 agonist or antagonist. Treatment with CCL20 agonist showed an increase in IL-17A in PBMCs from AS patients. Meanwhile decreasing IL-17A level was observed in SFMCs from AS patients when treated with CCL20 inhibitors. In cell migration assay experiments, cell migration increased when CCL20 was added to the CD4-positive cells. In an in vivo model, CCL20 inhibitors significantly suppressed arthritis symptoms (Figure 1). In histologic evaluation showed that mice treated with CCL20 inhibitor had lower arthritis scores than isotype-treated control mice.

Conclusion: This study demonstrates CCL20 blockade improved joint inflammation in AS. Therefore, CCL20-target therapy could be a promising treatment for AS.