Conclusion: anti-PC IgG1 is negatively associated with disease activity and atherosclerosis in SLE. One potential underlying mechanism could be increased phagocytosis and clearance of dead cells. Our findings raise the possibility of prevention and/or treatment of SLE (and atherosclerosis) to raise anti-PC levels, by passive or active immunization.

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THU0217

SERUM THYMIC STROMAL LYMPHOPOIETIN (TSLP) AS A BIOMARKER OF B-CELL LYMPHOPROLIFERATION IN SJÖGREN'S SYNDROME

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Background: Thymic stromal lymphopoietin (TSLP) has been demonstrated to be expressed on salivary glands (SG) biopsies of patients with primary Sjögren's syndrome (pSS), mainly in more advanced degrees of lymphoproliferation and in B-cell MALT lymphoma tissues in pSS (1).

Objectives: To study serum TSLP in a larger number of pSS patients, to confirm its correlation with the already studied tissue expression, and then to investigate a possible role of TSLP not only as a tissue biomarker, but also as a peripheral blood biomarker.

Methods: Serum TSLP levels were assessed by ELISA in sera collected from ninety-one anti-SSA-positive pSS patients (females n=86, 94.5%; mean age 57.2 years, range 25-80), fulfilling the 2016 ACR-EULAR pSS classification criteria, 80 matched healthy blood donors (HBDs) and 21 patients with non-autoimmune sicca syndrome (nSS).

pSS patients were then stratified according to the degree of lymphoproliferation (2), well previously defined by tissue studies in the same patients, as follows: pSS fully benign (fbSS), pSS with myoepithelial sialadenitis (MESA), and pSS B-cell MALT lymphoma (NHL); the difference in serum TSLP levels was studied between these three subgroups.

In addition, prospective serum samples, collected both at the time of MESA diagnosis and later at the time of NHL development in the same patient, were studied in 3 cases.

All the pSS patients were naïve to immunosuppressants, biotechnological drugs, chemotherapies, and were not receiving steroids at the time of sample collection.

The most relevant features of pSS linked to a heavier mucosa-associated lymphoid tissue (MALT) involvement and lymphoproliferation, i.e. persistent parotid swelling and mixed cryoglobulinemia, were recorded, as well as the pathologic evidence of ectopic germinal centres (GCs) in SG biopsy. EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) was calculated for all the pSS patients.

Results: Serum TSLP was significantly higher in pSS (mean 47.19 pg/mL, range 0-324.89) compared to nSS (mean 2.74 pg/mL, range 0-15.9) ($p<0.0001$) and to HBDs controls (mean 0.59 pg/mL, range 0-11.09: very low levels being detected only in 4/80) ($p<0.0001$). The significance was the same ($p<0.0001$) also after excluding NHL pSS patients. Serum TSLP showed a progressive, significant increase from patients with fbSS (n=65; mean 26.54 pg/mL; range 0-75.11) to MESA (n=14; mean 69.72 pg/mL; range 20.62-140.8) (MESA vs fbSS $p<0.0001$) and finally to NHL (n=12; mean 151.96 pg/mL; range 58.16-324.89) (NHL vs fbSS $p<0.0001$; NHL vs MESA $p=0.009$).

In prospective sera, TSLP levels significantly increased in all the 3 pSS patients from MESA to NHL.

pSS patients showing a heavier involvement of MALT, i.e. with persistent parotid swelling, mixed cryoglobulinemia, or GCs in SG biopsy, showed

significantly higher TSLP serum levels compared to pSS patients without this heavier MALT involvement.

A significant correlation between higher TSLP serum levels and increasing ESSDAI was finally found ($p<0.0001$).

Conclusion: Serum TSLP could represent a novel biomarker of pSS-related B-cell lymphoproliferation, characterized by a heavier MALT involvement. The validation of the present monocentric results is currently ongoing within the EU HarmonicSS Project.

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THU0218

IDENTIFICATION, VERIFICATION AND VALIDATION OF NEW BIOMARKER CANDIDATES FOR MONITORING ACTIVITY IN PSORIATIC ARTHRITIS AND OTHER IMMUNE-MEDIATED INFLAMMATORY DISEASES (IMIDS)

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Background: Immune-Mediated Inflammatory Diseases (IMIDs) are a group of conditions/diseases characterized by common pathways leading to inflammation, which may result from a dysregulation of the normal immune response. The activity of these diseases is usually measured by the assessment of clinical symptoms.

Objectives: To apply a three-stage proteomic strategy to find plasma biomarkers useful to monitor disease activity in patients with three different IMIDs: rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).

Methods: A three-stage proteomic strategy was conducted: **1) Discovery stage:** a random selection of 80 plasma samples from patients with different RA activities according to the DAS28, which were classified as low activity (LA, n=40) and high activity (HA, n=40). The analysis was conducted by shotgun mass spectrometry (MS) applying an iTRAQ 8-plex strategy, by nanoLC-MS/MS using three different MS instruments. **2) Verification stage:** a targeted proteomics strategy was used to verify the candidate biomarkers from the screening, using the same 80 samples of this first stage. This analysis was performed by Multiple Reaction Monitoring (MRM) with the aid of synthetic heavy-labelled peptides, by nanoLC-MS/MS in an ESI-QTRAP 5500. **3) Validation stage:** ELISA experiments were performed to confirm the previous results on an independent set of plasma samples from patients with RA (n=170), PsA (n=80) and SLE (n=80).

Results: **1) Discovery stage:** The MS analysis led to the identification of 186 proteins. A panel of 9 proteins was identified as candidate biomarkers for disease activity monitoring in RA. Most of these proteins are related with the pathogenic process and the effects caused by this type of disease (inflammation and immune disorder in joints). **2) Verification stage:** four from the 9 proteins (SAA1, AACT, HPT, A1AG1) were found to be quantitatively altered between patients with extreme disease activities ($p<0.05$). All these proteins were up-regulated in patients with HA. **3) Validation stage:** as shown in the top row of the Figure, serum amyloid 1 (SAA1), alpha-1-antichymotrypsin (AACT) and haptoglobin (HPT) are higher in the three IMIDs compared to healthy controls, being the highest in RA. Regarding their levels in patients with different disease activities, they are all increased in the plasma of HA individuals compared to LA (bottom row). Interestingly, the levels of these 3 proteins are associated with the activity of PsA: HPT ($p<0.0001$), SAA ($p=0.0209$) and AACT ($p=0.0418$), showing a potential utility for the molecular monitoring of this disease.

Conclusion: Using a three-stage proteomic strategy, we have identified HPT, SAA1 and AACT as protein biomarker candidates for monitoring PsA activity.

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