early stage of RA, and *S100A12* was correlated to ESR, an inflammatory marker (Spear r = 0.21; $P < 0.05$).

Conclusion: We confirmed the previously described up-regulation of *S100A4* and *S100A12*, and also newly found up-regulation of *S100A5, S100A6, S100A9*, and *S100A11* in RA patients' peripheral blood. Correlation of *S100A6 /S100A9* expression levels and serum MMP3 levels; *S10012* expression levels and ESR suggested their roles in inflammatory conditions in RA.

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Proteomic Characterization of Plasma Microparticles in Autoimmune Diseases. Christoffer T. Nielsen[1], Ole Østergaard[1], Line V. Iversen[1], Søren Jacobsen[2] and Niels H.H. Heegaard[1]. [1]Statens Serum Institut, Copenhagen S, Denmark, [2]Rigshospitalet - 4242, Copenhagen, Denmark

Background/Purpose: Circulating cell-derived microparticles (MPs) are a heterogenous population of submicron membraneous vesicles shedded from the cell-surface involved in cell-cell communication and immune regulation. We explored differences on the proteome level between MPs isolated from well-characterized patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), systemic sclerosis (SSc), and from healthy controls (HCs).

Methods: 12 SLE (6 active, 6 in remission), 6 RA (3 active, 3 in remission) and 6 SSc (3 with limited and 3 diffuse cutaneous SSc) patients were compared with 12 age- and gender-matched healthy controls. MPs from platelet-poor plasma were purified using centrifugation followed by tryptic digestion and analysis with liquid chromatography tandem mass spectrometry (LC-MS/MS) on an Orbitrap mass spectrometer. MP proteins were identified and spectral counts (SCs) were used as a semiquantitative measure of the abundance of each identified protein. Two independent statistical models, hierarchical clustering and principal component analysis (PCA) were applied to all the identified MP proteins and their associated SC values to search for disease classifiers.

Results: We identified a total of 343 unique protein entities in MPs. Of the, 143 were either membrane proteins or proteins otherwise associated with the cell membrane according to gene ontology analysis. 131 proteins represented extracellular proteins and included plasma proteins such as immunoglobulins, and other well-known opsonizing proteins including serum amyloid P component and C1q. Using both hierarchical clustering analysis and PCA, we were able to separate the different disease groups and identify several MP-associated disease classifying proteins as shown in Figure 1. Very high levels of MP-associated C1q and many forms of IgG and also galectin-3-binding protein, a protein mediating adhesion and sensing intracellular changes, were associated with MPs from the SLE group. Cytoskeletal proteins (multimerin-1 and myosin-9) and integrins (integrin-beta-3 and integrin alpha-IIb) were present in higher levels in the MPs from RA patients and HCs.

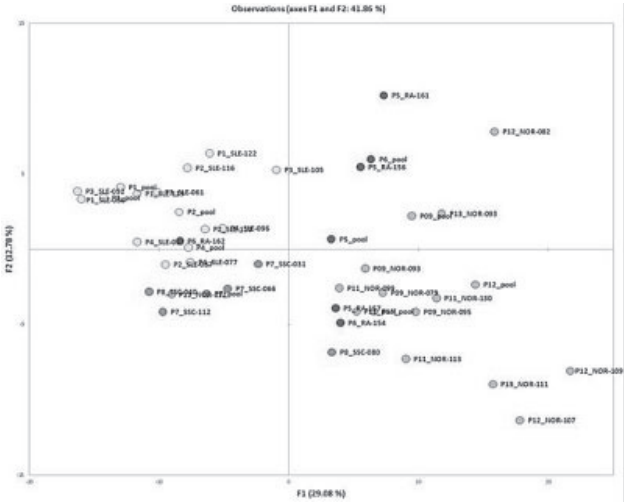

Figure 1.

Conclusion: Proteome analysis of plasma MPs in different autoimmune diseases reveals differentiating protein patterns with potential for biomarkers and supports MPs putative role in intercellular signalling and immune regulation.

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Feasibility of a Molecular Diagnosis of Arthritis Based on the Identification of Specific Transcriptomic Profiles in Knee Synovial Biopsies. Isabelle Focant[1], Daniel Hernandez-Lobato[2], Julie Ducreux[1], Patrick Durez[1], Adrien Nzeusseu Toukap[1], Dirk Elewaut[3], Frédéric. A. Houssiau[1], Pierre Dupont[2] and Bernard Lauwerys[1]. [1]Université catholique de Louvain, Brussels, Belgium, [2]Université catholique de Louvain, Louvain-La-Neuve, Belgium, [3]Gent University Hospital, Ghent, Belgium

Background/Purpose: Early diagnosis of arthritis is an "unmet medical need" in the field of rheumatology, as borne out by the number of publications addressing the issue. In particular, the delay in making a diagnosis of rheumatoid arthritis and initiating adequate therapy is associated with poor clinical, radiological and functional outcomes. In previous experiments, we performed transcriptomic studies on synovial biopsies from patients with arthritis using high-density oligonucleotide-spotted microarrays, and found that synovial gene expression profiles were significantly different according to the underlying disorder. Here, we wanted to explore whether these findings could translate into a useful diagnostic procedure.

Methods: Synovial biopsies were obtained from the knee of patients with a definite diagnosis of rheumatoid arthritis (1987 ACR criteria), seronegative arthritis or osteoarthritis (n=40), and from patients with undifferentiated arthritis (n=20). During each procedure, 6 to 8 biopsy fragments were stored overnight in RNALater at 4°, and next frozen at −80°. Biotinylated cDNA was synthesized and hybridized on customized low-density arrays, spotted with 100 diagnostic probes, house keeping genes and internal standards, in triplicates. Finally, the slides were scanned and the probe intensity data were collected for each sample. We performed the analyses by partitioning the microarray data into a training set and a testing set. The diagnosis of the samples in the testing set was generated using a nearest neighbor classification method, based on the Pearson correlation distance.

Results: In a first step of experiments, we looked whether the molecular diagnosis generated by the interpretation of the low-density microarray data matched the clinical diagnosis for the samples obtained from patients with a known diagnosis. We found that a right diagnosis was obtained in 73% of the samples. Because therapy can affect the gene expression profiles in the synovium and blur their diagnostic performances, we next restricted these analyses to the samples obtained from untreated patients. Doing this, we saw a slight improvement in the percentage of right molecular diagnoses, up to 75% of the cases. Next, we wondered whether addition of selected clinical symptoms could increase the accuracy of our model. Algorithms were developed that combine low-density array data and one or several relevant symptoms. Strikingly, the accuracy of the algorithm combining low-density expression data and 3 symptoms (presence of psoriasis, arthritis of the hands, presence of rheumatoid factors) was 92%. Finally, we performed the same analyses in 20 synovial samples obtained from UA patients. The combination of expression and clinical data resulted in a molecular diagnosis, which was confirmed in the 8 patients in whom a clinical diagnosis was made during the follow-up period after the biopsy.

Conclusion: Taken together, our data indicate that a diagnosis can be made in patients with UA based on the combination of gene expression data and selected clinical symptoms. As such, these results are particularly relevant from a clinical point of view, and open the perspective of valorization into a diagnostic test.

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Selective Inhibition of Epigenetic Factors Provide Potential New Tools for Arthritis Therapy. Timea Besenyei, Júlia Kurkó, Katalin Mikecz, Tibor T. Glant and Tibor A. Rauch. Rush University Medical Center, Chicago, IL

Background/Purpose: Rheumatoid arthritis (RA) is a degenerative inflammatory autoimmune disease that affects more than 1% of the human population. Currently, there is no ideal therapy for RA, but various types of treatments can provide alleviation of symptoms and modify disease progression. RA is considered to be a polygenic disease with strong immunogenetic components, because various immune cells (B and T lymphocytes, macrophages, dendritic cells) are involved. Besides of recently mapped genes, environmental factors can also contribute to the etiology of RA and increasing number of data proves that epigenetic factors are involved in autoimmune diseases. Therefore, enzymes that play roles in chromatin modification are plausible targets of RA therapy.

Methods: Applying specific *PCR arrays* we investigated the expression profile of 84 genes encoding key enzymes known to be specific modifiers of chromatin. Total RNA was isolated from lymphocytes from a murine model (proteoglycan-induced arthritis, **PGIA**) of RA and from mononuclear cells separated from RA patients and healthy controls.