collectively suggest that the loss of ATM activation in monocytes may contribute to the disease process of SSc, and is possibly due to DNA damage and oxidative stress.

REFERENCES:

Disclosure of Interest: None declared

AB0192 DISCOVERY OF POTENTIAL SKIN BIOPSY BIOMARKERS FOR SYSTEMIC SCLEROSIS BY HIGH-THROUGHPUT PROTEOMIC APPROACHES

P. Chante1, P. Nicolau2, K. Sokratous3, G. Spyrou4, A. Oulas5, C. Galant6, F. Houssiau7, B. Lawreny7, K. Christodoulou7, 1Neurogenetics Department, Cyprus School of Molecular Medicine, Nicosia, Cyprus; 2Neurogenetics Department, 3Bioinformatics Department, Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus; 4Department of Pathology, Université catholique de Louvain; 5Rheumatology Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium

Background: Systemic Sclerosis (SSc) is an autoimmune connective tissue rheumatic disease characterised by three main hallmarks; vasculopathy, immune system abnormalities and fibrosis. It is considered a multisystemic and heterogeneous disease as many organs of the body may be affected and symptoms vary among patients. Up to date, SSc is untreated and its etiology and pathogenesis remain unclear. Early prognosis and diagnosis of the disease are challenging.

Objectives: The aim of this study was to analyse the proteomic profile of SSc patients in order to gain insights into the mechanisms implicated in disease pathology and also discover new biomarkers that would facilitate early diagnosis, more accurate diagnosis and therapeutic targeting of SSc.

Methods: Human biopsies were obtained from ten affected and three non-affected skin areas of SSc patients and have been classified based on histological criteria. Biopsies were cryo-pulverised and proteins were extracted, purified, reduced, alkylated and digested by trypsin. Purified peptides were analysed on a Waters Synapt G2Si HDMS instrument operated in ion mobility mode using a UDMA² approach. Data were processed by the Progenesis Qtof and functional annotation analysis was carried out using multiple bioinformatics resources.

Results: Proteomic analysis led to the identification and quantification of approximately 1500 non-redundant proteins per sample. About 400 of these proteins, including interferons and interleukins, are differentially expressed between affected and non-affected samples. Functional annotation analysis of these proteins showed that they are involved in multiple pathways including, antigen processing and presentation, complement, ubiquitin mediated proteolysis and Notch signalling, which are known to be associated with autoimmune diseases and fibrosis.

Conclusions: Using a Mass Spectrometry-based proteomic approach for the identification of SSc human skin biopsies, we identified a number of proteins that might be involved in the development and pathogenesis of SSc. Interestingly, some of these proteins are differentially expressed in specific histological groups and thus could be considered as potential biomarkers for specific SSc stages.

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AB0193 SEMAPHORIN4A INDUCES TH17 CYTOKINE PRODUCTION IN SYSTEMIC SCLEROSIS

S. García Pérez, T. Carvalheiro, A.J. Affandi, B. Malvar Fernandez, I. Dullermont, M. Coissu, W. Murat, K.A. Reedquist, T.R. Radstake. Laboratory for Translational Immunology (LTI) and Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands

Background: Systemic sclerosis (SSc) is an autoimmune disease characterised by inflammation, vascular injury and excessive fibrosis in different organs. Different studies have shown that Th17 cells and Th17 cytokines (IL-17, IL-21 and IL-22) play a key role in the pathogenesis of the disease. Semaphorin 4A (Sem4A) is a transmembrane protein that belongs to a large family of proteins initially described as ligands essential for neuronal development. Further studies have shown that they also play a role in other biological processes including the control of immune responses. Importantly, Sem4A has a critical role in the skewing of CD4+ T cells towards a Th17 phenotype. However, its role in SSc is not yet clear.

Objectives: The aim of this study was to analyse the potential role of Sem4A as a regulator of Th17 skewing in SSc.

Methods: Plasma levels of Sem4A were measured by ELISA. Expression of Sem4A and its receptors PlexinB2, PlexinD1 and neuropilin-1 (NRP-1) was determined by q(quantitative)PCR, western blot and flow cytometry in monocytes and CD4+ T cells of healthy donors (HD) and SSc patients. Monocytes were stimulated with Poly IC (5 µg/ml) and Sema4A expression

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