**PS1:4** SEARCHING BIOMARKERS IN LUPUS NEPHRITIS BY PROTEOMICS


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**Introduction**
Lupus nephropathy (NL) is an important cause of morbidity and mortality in patients with SLE. The objective of the renal biopsy is to determine the type of glomerulonephritis that the patient presents to be treated. A proteomics study is proposed to determine biomarkers that help us to differentiate patients diagnosed with SLE with and without renal involvement.

**Objective**
To determine if there are a different pattern of proteins between patients diagnosed with SLE with and without renal involvement.

**Methods**
We selected 12 patients diagnosed with SLE with renal involvement and 14 patients diagnosed with SLE without renal involvement. A 24 hour urine sample was obtained for analysis.

**Results**
A total of 292 proteins (identified with at least two peptides with a FDR<1%) were quantified and further considered in the analysis. The Principal Components Analysis (PCA) reflected the differential presence of 142 proteins (p<0.01). Of these, 130 were less abundant in the urine of the patients with renal damage, whereas 17 showed the opposite pattern, being more abundant in the patients with affected renal function. Consistent with the nature of the sample, the Gene Ontology (GO analysis) of the whole list of identified proteins revealed the presence of extracellular (277 proteins, p=2.25E-171) and secretion-related proteins (49 proteins, p=1.1E-09), among others. Proteins related to defensive processes were prominent among them. Interestingly, the subset of proteins whose abundance increases upon renal damage is comprised of typical highly-abundant serum proteins. These proteins render a large number of peptides, suggesting they are very abundant. On the other hand, a large number of proteins became significantly less abundant upon renal damage. The presence of highly abundant serum proteins in the urine of patients with compromised renal function may explain this phenomenon, since this will provoke a dramatic reduction in the relative abundance of the proteins already present in their urine.

**Conclusion**
A different protein pattern is observed between the two groups of patients, so in a more detailed study we can indicate if some of these can serve as prognostic markers for this type of patients.

**PS1:5** INTERFERON SIGNATURE IS INCREASED IN INCOMPLETE SLE AND CORRELATES WITH MXA AND IP-10 LEVELS

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**Introduction**
Most SLE patients have increased expression of type-I interferon (IFN)-regulated genes, the so-called IFN-signature. IFN-regulated genes are subdivided in 3 modules (M1.2, M3.4 and M5.12). Module 1.2 is associated with disease presence and the latter two seem to be sequentially activated and to correspond with active disease.
Furthermore, IFN-related mediators might be more easily applicable biomarkers of IFN upregulation.\(^4\)

**Material and methods** Twenty-three iSLE patients (ANA titer ≥1:80, symptoms <5 years, ≥1 objectified clinical ACR criterium), 25 quiescent SLE patients (fulfilling ACR criteria, SLEDAI ≤4) and 11 healthy controls were included.

The IFN score was determined in monocytes, based on 14 IFN-related transcripts, representing all three IFN-modules. (M1.2: CXCL10, IFI44L, IFIT3, LY6E, MX1 and SERPING1. M3.4: AIM2, IFITM1, IRF7 and STAT1. M5.12: C1QA, C5L2, IFI16 and IRF9). IFN-scores >95 th percentile of controls were defined as positive.

Levels of IFN-related mediators, including IFN-γ induced protein 10 (IP-10), monocyte chemo-attractant protein (MCP-1), and Myxovirus-resistance protein A (MxA) were measured using ELISA.

**Results** IFN-score was increased in 52% of iSLE patients and 48% of SLE patients. Of iSLE patients, 52%, 52% and 48% respectively had upregulation of M1.2, M 3.4 and M5.12 (see figure 1). In SLE patients, respectively 52%, 44% and 40% were upregulated. M3.4 and M5.12 were only upregulated if M1.2 was activated.

Both MxA and IP-10 were increased in iSLE (median 120 ng/ml and 76 pg/ml, respectively) compared with controls (median 82 pg/ml and 23 pg/ml, respectively). MxA and IP-10 did not correlate in iSLE. In SLE, MxA was increased (median 111 ng/ml), while IP-10 was not. MCP-1 levels were not significantly different between the groups.

Levels of MxA correlated with IFN-score in both iSLE (r=0.49, p=0.0171) and SLE (r=0.70, p<0.0001). Levels of IP-10 correlated with IFN-score based on the 14 genes in SLE but not iSLE.

**Conclusion** IFN-signature is present in 52% of iSLE patients and correlates with MxA. We hypothesise that these patients might be at risk for disease progression. Longitudinal data however should be awaited. Interestingly, MxA levels correlated strongly with IFN-score and thus could be a suitable and easily applicable surrogate marker.