Conclusion: The group of patients undergoing CYC high dose induction therapy achieved higher frequency of remission than the group with low dose of CYC after the induction therapy period. We did not found any predictor of renal remission.

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Abstract Number: 2816

Broad Autoantibody Profiling in Ethnically Diverse SLE Cohorts Reveals a Set of Conserved Autoantibodies That Are Correlated to a Type I Interferon Signature

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SESSION INFORMATION

Session Date: Tuesday, November 15, 2016

Session Title: Systemic Lupus Erythematosus – Clinical Aspects and Treatment - Poster III: Biomarkers and Nephritis

Session Type: ACR Poster Session C

Session Time: 9:00AM-11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with a wide range of clinical manifestations. Production of autoantibodies is a hallmark of SLE and has been shown to contribute to disease pathogenesis as well as specific clinical manifestations such as nephritis. Despite the importance of autoantibodies in SLE, only a limited number of autoantibodies have been characterized and are utilized as lupus biomarkers, and many of these are not specific for lupus. We sought to address the question of whether broad autoantibody specificity profiling could identify novel and more specific autoantibodies to identify SLE patients, and if certain autoantibody specificities were enriched in patients exhibiting an interferon-I (IFN-I) signature.

Methods: To address this question, we carried out an unbiased analysis using the ProtoArray® platform (detection of >9400 autoantibodies), comparing five racially and ethnically diverse cohorts containing patients of African American, European, and Chinese descent (total of 131 healthy and 193 SLE patients).

Results: Each cohort had a group of SLE patients exhibiting very high autoantibody signals, a group that had moderate signal, and a group that had low signal against most of the 9400 autoantigens. The majority of healthy patients had very low autoantibody signals. Furthermore, we identified a core set of 17 autoantibodies that were significantly upregulated (FC>2, FDR<0.01) in SLE patients compared to healthy patients across all five cohorts. The levels of these core autoantibodies remained longitudinally stable over a 12-week period. We also demonstrated that the expression of these 17 autoantibodies correlated with levels of an interferon (IFN) signature present in whole blood from these patients.

Conclusion: Despite the diverse set of patients in our study, we were able to identify a small set of core autoantibodies that were commonly upregulated in SLE patients in all five cohorts. Importantly, we demonstrate that autoantibodies could be vital in patient stratification or as a biomarker of SLE, as our study reveals that levels of autoantibodies are potentially linked with IFN-I gene signatures.

Disclosure: T. Sato, Janssen Research and Development, LLC, 3; **M. Cesaroni**, Janssen Research and Development, LLC, 3; **J. Schreiter**, Janssen Research and Development, LLC., 3,Janssen Research and Development, LLC., 1; **J. Jordan**, Janssen Research and Development, LLC., 3; **M. Chevrier**, Janssen Research and Development, LLC., 1,Janssen Research and Development, LLC., 3; **J. Benson**, Janssen Research and Development, LLC., 3,Janssen Research and Development, LLC., 1.

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Abstract Number: 2817

Identification of Subsets of Systemic Lupus Erythematosus Patients By Principal

Component Analysis and Urine Biomarkers

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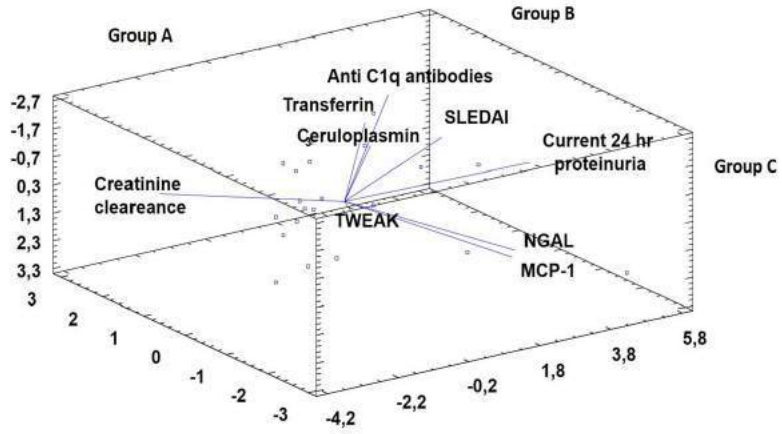
Background/Purpose: Systemic lupus erythematosus (SLE) is clinically heterogeneous disease, with a considerably variability of disease expression among patients. There have been several attempts to classify subsets or cluster of SLE patients according genes, clinical characteristics and autoantibodies. However, information about classification of SLE patients based on urinary biomarkers is scarce. We investigated whether subdivision of SLE is possible using a panel of urine biomarkers by principal component analysis (PCA).

Methods: We included in 100 consecutive SLE patients (ACR criteria 1997) from a tertiary University Hospital. We measured urinary levels of 5 different biomarkers: monocyte chemoattractant protein 1 (MCP-1), neutrophil gelatinase-associated lipocalin (NGAL), TWEAK, Ceruloplasmin (CP), and Transferrin (TF) using a commercial ELISA kits (R&D system and Assaypro, USA). In addition, serum anti C1q antibodies were measured by ELISA (Inova, USA). SLE activity was measured with SLEDAI. The PCA was performed by Statgraphics Centurion XVI.I for Windows (Statgraphics Corp., Rockville, USA). The PCA allowed simultaneous analysis of the relationship between 5 different urine biomarkers, as well as different clinical features and anti C1q antibodies. Creatinine clearance was considered as anchor factor of the PCA.

Results: 100 SLE patients were recruited (88% female) with median age of 33.6 ± 12.4 years and median disease duration of 11.5 ± 14.8 years. Hematologic disease (89%), arthritis (83%), cutaneous involvement (82%), and renal disease (66%) were among most common manifestations. Three components achieved an eigenvalue greater than 1.0. PCA revealed that the first 3 components accounted separately for a variability of 72%. According with those components we identified 3 subsets: Group A) patients with normal renal function and moderate disease activity, group B) patients with high disease activity and high levels of anti C1q, TF and CP and group C) patients with active lupus nephritis with high levels of 24 hours proteinuria, MCP-1, NGAL and TWEAK (Figure). Patients from Group B were older, had a shorter disease duration and higher SLEDAI scores than the other 2 groups.

Conclusion: We identified 3 different subgroups of SLE patients by PCA approach using urine biomarkers and serum Anti C1q antibodies. Whether these subgroups represent a different clinical outcome or a worst prognosis requires further analysis.

Biplot showing the first three loadings from a PCA



Clinical and biomarkers characteristics among different components

	Group A N=11	Group B N=8	Group C N=4	P value 1 vs 2	P value 2 vs 3	P value 1 vs 3
Current age (years ± SD)	29.5 ± 10.7	35.6 ± 10.0	28.5 ± 5.9	NS	NS	NS
Sex (Female), %	100	87	100	NS	NS	NS
Mean disease duration (years ± SD)	8.0 ± 4.35	2.33 ± 2.51	5.0 ± 1.0	0.038	NS	NS
Renal involvement	72	87	100	NS	NS	NS
Creatinine clearance	103.0 ± 35	100.7 ± 32.0	47.5 ± 12	NS	<0.001	<0.001
SLEDAI	6.45 ± 6.54	17.37 ± 6.11	16.0 ± 9.62	0.002	NS	NS
Proteinuria	716.0 ± 715.1	2592.8 ± 1802	6972 ± 2942	0.01	0.05	<0.001
MCP-1	666.6 ± 747	814.0 ± 328.8	2330.2 ± 2867.1	NS	NS	NS
NGAL	29.3 ± 34.3	49.5 ± 42.0	149.9 ± 72.1	NS	NS	0.039
CP	2571.1 ± 1299.3	4070.2 ± 274	3464. 4 ± 698.1	0.007	NS	NS
TF	1462.3 ± 532.9	1835.2 ± 40.8	1685.5 ± 131.4	0.043	NS	NS
TWEAK	1183.3 ± 841.6	2054.5 ± 1580.0	1598.0 ± 1081	NS	NS	NS
Anti C1q	50.9 ± 51.7	116.5 ± 78.3	103.2 ± 82.9	NS	NS	NS

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Abstract Number: 2818

High Sensitivity Multiplex ELISA Reveals Cytokine Expression Heterogeneity in Active SLE

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Background/Purpose: Patients with SLE have a broad clinical and immunological phenotype in which multiple immune pathways may be sequentially or simultaneously activated. No reliable biomarkers exist to identify active disease across the spectrum of lupus patients. Cytokine expression in serum is often at low levels and therefore traditional ELISA methods have inadequate sensitivity. Custom high sensitivity Multiplex arrays offer the opportunity to measure multiple cytokines within a single serum sample. We aimed to investigate the association between cytokine expression and disease activity in patients with established SLE and determine whether clusters of patients could be identified.