

Furthermore, IFN-related mediators might be more easily applicable biomarkers of IFN upregulation.⁴

Material and methods Twenty-three iSLE patients (ANA titer $\geq 1:80$, 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, CSCL2, 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.

PS1:6

DIFFERENTIAL DIAGNOSIS OF AUTOIMMUNE DISEASES, OUTLIER DETECTION PLUS SUBGROUPING IN CLINICAL TRIALS BY HIGH CONTENT AUTOANTIBODY PROFILING

P Schulz-Knappe, P Budde, H-D Zucht. *Protagen AG, Dortmund, Germany*

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Purpose Early diagnosis as well as initiation of successful treatment are two big challenges in the management of patients with autoimmune diseases (AID). Overlap of a plethora of clinical symptoms, ranging from multi-organ involvement, fatigue, inflammation to CNS-involvement make differential diagnosis quite challenging. Especially in early disease these signs are difficult to quantify, hence the lag time from start of disease until clinical diagnosis may be delayed, sometimes for years. With the growing interest in conducting clinical trials in AID, there is a need for new biomarkers that can be used to diagnose individual AIDs to reduce the inclusion of patients not carrying the intended disease, and identify clinical subsets, predict treatment outcome and assess disease activity.

Methods The autoantibody reactivity pattern in serum of AID patients was analysed using a Luminex bead-based antigen array (SeroTag) and 1,600–8000 selected human protein antigens. We screened over 3000 serum samples from Sjögren's Syndrome ($n=350$), SLE ($n\geq 1000$), SSc ($n\geq 250$), RA ($n\geq 1000$), and several other AIDs and over 1000 healthy individuals to confirm known and to discover novel autoantibodies, create reduced autoantibody panels for differential diagnosis and disease subgrouping.

Results Apart from clear confirmation of the known benchmark autoantigens known for many years we have discovered over 80 novel autoantibodies, which were detected in frequencies of 10 to $> 25\%$ in selected AIDs. Some novel autoantibodies are specific for certain diseases, such as the major vault protein in SLE or BICD2 in SSc. Others are present in several diseases, indicating overlap syndromes. Multiplex panels of 50–100 AABs were generated and tested to allow for a subgroup definition of Sjögren's, SLE, and for clear segregation of SjS/SLE overlap syndrome patients. As well, subgrouping of SSc and early RA patients was achieved.

Conclusions A set of 100–150 autoantigens, half of them well established, the other half novel, succeed in differential diagnosis of AID, in some diseases already at early disease stage. This panel has been used in several drug trials to subgroup SLE, Sjögren's or RA into subgroups. Especially in SLE, outliers in the range of 10%–15% of the trial population were seen which can be used to curate a trial population, eventually to arrive at a more precise assessment of trials primary objectives.

PS1:7

ANTINUCLEAR ANTIBODY (ANA) AND ANTINEUTROPHIL CYTOPLASMIC ANTIBODY TESTING IN A TERTIARY HEALTH CENTRE IN SHERBROOKE: AN ASSESSMENT OF THE ADHERENCE TO THE GUIDELINES AND THE IMPACTS ON THE DIAGNOSIS AND HEALTH CARE SYSTEM

M Parfenova. *Sherbrooke University, Sherbrooke, Canada*

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Objectives To describe antinuclear antibodies (ANA) and subserology ordering practices and to determine if its' indications meet the recommendations for ANA testing at the Sherbrooke University Health Centre, in Canada. To describe antineutrophil cytoplasmic antibodies (ANCA) practices and determine if they meet the 1999 guidelines proposed for ANCA testing, at the same centre.

Methods We identified the indications for the ANA and subserologies panel (Anti-SSA, anti-SSB, Anti-Jo1, Anti-Scl-70, Anti-Sm, Anti-U1 RNP) between 2012 and 2014 and compared to the guidelines for ANA testing. Moreover, the indications for ANCA tests were assessed and compared to the 1999 guidelines for the appropriate testing of ANCA. Variables included gender, age, ANA titer, subserologies panel, indication of ANA, ANCA, subtypes MPO and PR3, indication for ANCA, medical specialty, setting of the order and the final diagnosis.

Results There were a total of 268 ANA tests included. In 35.8% of cases ($n=96$), ANA was ordered as per recommendations versus 63.8% of cases ($n=171$) without indications. There were 104 subserologies ordered and 55.8% were

ordered at the same time as the ANA, against the Choosing Wisely recommendation of 2013. There were only 22% of ANA that were required for a diagnosis. The 3 specialties who ordered ANA the most were rheumatology, gastroenterology and the internal medicine (in descending order). The cost for the ANA that were not indicated is more than a thousand dollars. A total of 135 ANCA tests were included. There were 55.6% of ANCA that were ordered in line with the recommendations. However, 50.3% of ANCA were not required for the final diagnosis. Clinical remission of subjects with ANCA was predicted in 100% of cases, even before ordering the ANCA test for follow-up (negative predictive value).

Conclusion These results show that the rate of ANA and ANCA tests ordered in line with the recommendations remains low. In the majority of cases, the two antibodies are not required for the final diagnosis. These orders have an important cost for the hospital that can be lowered by providing more education for professionals on avoiding unnecessary tests.

PS1:8 ANTI-RO FALSE-NEGATIVES DETECTION THROUGH ANTI-RO52 KDA AND ANTI-RO60 KDA ANALYSIS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

¹E Grau, ¹I Chalmeta Verdejo, ¹E Labrador Sanchez, ²M Fernandez Matilla, ¹FM Ortiz Sanjuan, ¹CM Feced Olmos, ²N Fernandez-Llanio Cornella, ¹K Arevalo Ruales, ¹R Negueroles Albuixech, ¹J Ivorra Cortes, ¹JJ Frago Gil, ¹I Martinez Cordellat, ¹R Gonzalez Mazario, ¹L Gonzalez Puig, ¹C Alcañiz Escandell, ¹C Najera Herranz, ¹I Canovas Olmos, ¹E Vicens Bernabeu, ¹JE Oller Rodriguez, ¹M de la Rubia Navarro, ²JA Castellano Cuesta, ³V Fornes Ferrer, ³D Hervas Marin, ⁴D Gimenez-Romero, ¹JA Roman Ivorra. ¹Rheumatology Department. HUP La Fe, Valencia, Spain; ²Rheumatology Section. Hospital Amai de Vilanova, Valencia, Spain; ³Biostatistics Unit. IIS La Fe, Valencia, Spain; ⁴Physical-Chemistry Department, UV, Valencia, Spain

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Purpose The aim of the present study is to identify false-negatives for anti-Ro by analysing both 52 KDa and 60 KDa subunits separately, as well as to characterise if there are clinical or molecular differences in this subgroup of patients compared to anti-Ro negative cases.

Methods A cross-sectional, observational study of patients diagnosed of SLE according to SLICC 2012 criteria was performed. In these patients a complete blood-test was made, and clinical data by personal interview was collected. INF1A, Anti-Ro, anti-Ro52KDa and anti-Ro60KDa levels were

measured by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.

Results We selected 69 SLE patients with negative results for anti-Ro (2.34 ± 4.17 U/mL) out of 142 total SLE patients. A total of 51 patients were negative for both anti-Ro subunits and 18 cases presented positive results (up to 20 pg/mL) for at least one of them (See table 1).

The subgroup of patients that exhibit simultaneously high levels of anti-Ro52KDa and anti-Ro60KDa have higher clinical activity compared to negative anti-Ro cases (75% of active patients against 41.2% in anti-Ro negative patients). However, no differences in the accumulated damage evaluated by SLICC score between negative anti-Ro cases and patients with at least one positive subunit were observed.

We analyse serum levels of INF1A cytokine in the four groups of patients, and anti-Ro and subunits negative cases showed significant lower INF1A levels than the other patients (8.26 ± 14.87 pg/mL and 26.62 ± 40.71 pg/mL respectively; $p=0.04$). In addition, patients with high levels of anti-Ro52KDa subunit are those with the highest INF1A levels (anti-Ro 52+/anti-Ro60- 23.5 ± 47.6 pg/mL of INF1A; anti-Ro 52+/anti-Ro60 $+36.4 \pm 37.9$ pg/mL of INF1A).

Conclusion In our anti-Ro seronegative patients, a 26% of false-negative cases were detected. These cases with high levels of almost one anti-Ro subunit showed significantly higher levels of INF1A in contrast to negative cases, supporting the fact that they are indeed a different group from the negative cases. Moreover, the high INF1A levels could be the reason of the observed differences in the clinical activity measured by SLE-DAI score in both groups.

PS1:9 B CELL SUBPOPULATIONS IN LUPUS NEPHRITIS PATIENTS: CORRELATIONS WITH DISEASE ONSET AND OUTCOMES

¹V Varriano, ¹L Petricca, ²S Costanzi, ¹M Gigante, ¹A Paglionico, ¹G Tanti, ²G Vischini, ¹G Ferraccioli, ¹E Gremese. ¹Division of Rheumatology, Institute of Rheumatology and Affine Sciences, Catholic University of Rome, Italy; ²Division of Nephrology, Catholic University of Rome, Italy

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Purpose The relationship between B cells subsets distribution, clinical and laboratory parameters, therapeutic response and prognosis in lupus nephritis (LN) is still underestimated. The

Abstract PS1:8 Table 1

	NEGATIVES N=51	Anti-RO52KDa POSITIVES N=8	Anti-RO60KDa POSITIVES N=2	Anti-RO52KDa/ Anti-RO60KDa POSITIVES N=8
Anti-RO [U/mL] Mean (DS)	1.92 (3.11)	1.65 (3.2)	0.5 (0.71)	6.15 (8.37)
Anti-RO52 KDa [pg/mL] Mean (DS)	1.26 (1.89)	147.24 (74.25)	1.05 (0.89)	196.82 (50.06)
Anti-RO 60 KDa [pg/mL] Mean (DS)	1.73 (2.71)	6.3 (7.01)	120.96 (111.78)	145.22 (76.69)