

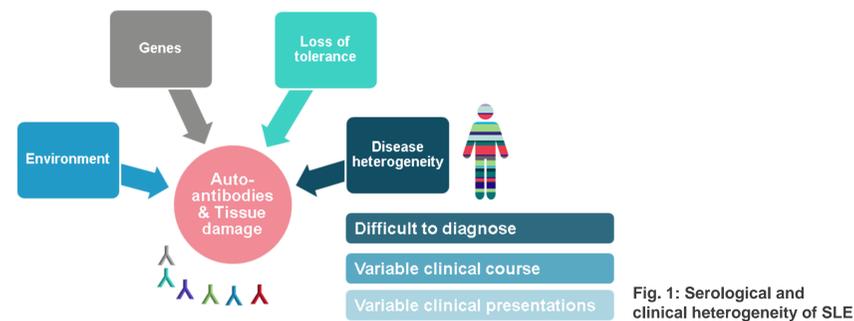
Identification of homogeneous systemic lupus erythematosus (SLE) patient groups using clustered autoantibody reactivities

P. Budde¹, H.-D. Zucht¹, D. Chamrad¹, A. Telaar¹, L. Schlieker¹, S. Vordenbäumen², P. Schulz-Knappe¹, M. Schneider²
¹Protagen AG, Dortmund, ²Rheumatology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany

ACR2015 #1862 

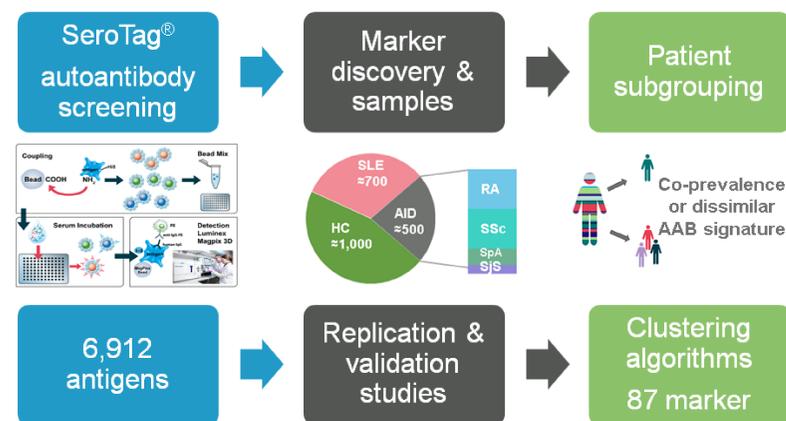
Introduction

- The heterogeneity amongst SLE patients is a major obstacle for predicting disease manifestations and for developing effective therapies.
- There is a clear need for diagnostic biomarkers that enable precise disease characterisation, patient stratification and response prediction.
- Characterization of the autoantibody repertoire in SLE might yield novel biomarkers supporting a personalized disease management approach.



Methods

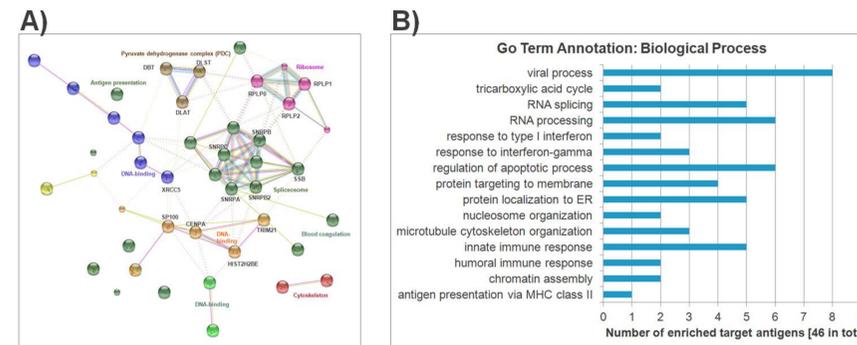
We previously reported the discovery and validation of novel SLE-associated autoantibodies (AAB) using the bead-based Luminex[®] xMAP[®] platform SeroTag[®] [1]. In the current version, SeroTag enables to detect antibodies against 6,912 antigens (well-described and novel) in parallel with small sample volume requirements (25 µl per sample and screen). During discovery and validation studies, AAB reactivity was thoroughly analyzed in 700 SLE, 1,000 healthy control (HC), and 500 autoimmune disease samples (AID) (Fig. 2).



Results

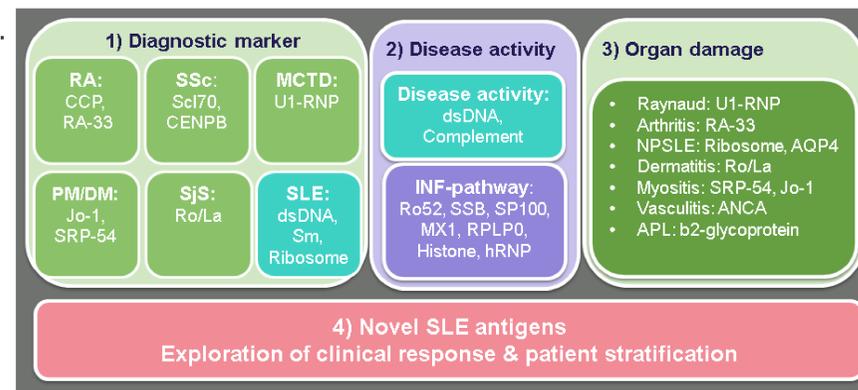
Pathway Analysis

Analysis of the identified antigens using the Gene Ontology (GO) Database and STRING (Search Tool for the Retrieval of Interacting Genes/Proteins), revealed that new autoantibodies were found that target proteins involved in apoptotic and immune processes or are encoded by type I interferon response genes (Fig. 3).



NavigAID SLE Assay

A typical feature of SLE is the production of a broad and heterogeneous group of autoantibodies. Despite efforts to link individual autoantibody reactivities to distinct clinical features, the co-prevalence of AABs in SLE patients has rarely been analyzed. Based on our discovery and validation efforts we designed an SLE stratification assay, which includes new and diagnostic antigens (Fig. 4).



Autoantibody Reactivity Signatures

The SLE stratification assay was applied to measure the total number and co-prevalence of autoantibodies in each SLE patient. Fig. 5A shows a contingency heatmap of SLE serum samples in which the total number of AABs present in each sample is shown as a color gradient (from green to red up to 60 AAB). Furthermore, similarities (co-prevalence) and dissimilarities are revealed by plotting two samples against each other. The analysis of the AAB reactivity yields at least four different reactivity groups (C1-C4) including patients: C1: a higher disease activity score, broad and homogeneous AAB reactivity; C2: with broad, but heterogeneous AAB reactivity; C3: who have few AABs and C4: with unusual AAB pattern.

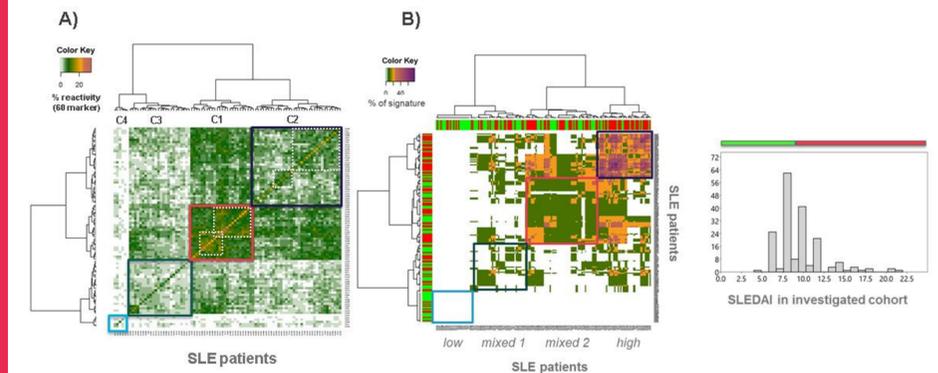


Fig. 5B shows the analysis of ten AABs targeting proteins known to be involved in the INF-type I response pathway. Specific clinical features including more severe disease activity (Systemic Lupus Erythematosus Disease Activity Index, SLEDAI) are associated with high AAB signature reactivity.

Conclusions

The multiplexed analysis of AABs in SLE enables defining an AAB reactivity score and SLE patient clusters. This might support the stratification of SLE patients into more homogenous subgroups in clinical studies thereby increasing the probability of successful drug development.

[1] Budde, P., S. Vordenbäumen, et al. (2015). "SAT0626 Discovery and Validation of New Autoantibody Biomarker in Systemic Lupus erythematosus." Ann Rheum Dis 74(Suppl 2): 888