Discovery and Validation of New Autoantibody Biomarker in Systemic Lupus Erythematosus

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Introduction

• The extreme heterogeneity amongst SLE patients is a major obstacle for predicting disease manifestations and for developing effective therapies.
• In order for this to happen, 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

To identify relevant autoantigens in autoimmune diseases, we developed a bead-based array platform using the Luminex® xMAP® technology. In the current version, SeroTag® enables to detect antibodies against 6,912 autoantigens (well-described and novel) in parallel with small sample volume requirements (25 µl per sample and screen).

Results

We previously reported the parallel profiling of autoantibodies targeting well-described and novel antigens in four autoimmune diseases using a bead-based Luminex platform [1]. IgG autoantibody reactivity was observed against 166 antigens targeting well-described and novel antigens. The selected antigens were re-arrayed to construct targeted arrays for marker validation in a new SLE cohort (SLE II). Consistent autoantibody reactivity against 46 antigens was found (p-value <0.05 and Cohen’s d effect size >0.3). Fig. 3 shows the study design and a graph of the p-values and frequency of autoantibodies in SLE II samples. Marker with an observed frequency >10 % in SLE patients were selected for further investigations.

To gain more detailed information on target antigens, we employed the Gene Ontology (GO) Database and STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) to retrieve and visualize protein-protein interaction, molecular function and pathway representation. Fig. 5 shows all antigens, which are represented by nodes in the resulting graph.

Conclusions

Using a multiplex platform we have discovered novel SLE-associated antigens. The reproducibility of the autoantibody reactivity was verified and validated in new SLE samples applying a stepwise marker refinement approach. This approach yielded novel markers combinations, which may improve the diagnostic sensitivity and specificity.