Mining for common reactivity patterns of human autoantibodies against endogenous protein targets using clustered autoantibody reactivities

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Autoimmune diseases arise from an abnormal immune response of the body against self-proteins leading to tissue and organ damage. The excessive production of harmful autoantibodies (AAB) is a hallmark of autoimmune diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and Sjogren's syndrome (SjS). Also in cancer research, it has been recently shown that AABs are useful to characterize patients.

The characterization of patient subgroups by means of stratification is essential for the efficient development of therapies, but often difficult due to the lack of appropriate biomarkers. Personalized or precision medicine approaches rely on appropriate multivariate multiplexing technology and data analysis. AABs serve as diagnostic markers for various autoimmune diseases, but the co-occurrence of AABs has rarely been analyzed and is difficult to comprehend. Detecting a broad set of AABs helps to investigate the similarity between patients. A multiplex signature enables clustering for the investigation of relationships and patterns, which can be related to relevant clinical variables.

Here, we illustrate Luminex bead-based AAB assays using a set of 96 biomarker targets and their utility to characterize SLE and SSc as well as cancer study groups.

Data analysis is based on bi-clustering algorithms and a prevalence and signature analysis of the markers. Cluster analysis was also performed using transformed data sets (qualitative) to investigate and visualize characteristic marker prevalence and co-prevalence patterns.

Based on the individual marker pattern, patients can often be stratified belonging to different study subgroups. For example, for SLE we show that different reactivity groups exist including patients with different disease activity scores and organ damage patterns.

We conclude that the approach of a comprehensive prevalence and signature analysis and a vivid data visualization is useful for any multiplex omics assay.