Introduction

Systemic sclerosis (SSc) is a remarkably heterogeneous autoimmune disease, for which effective disease-modifying therapies are still lacking. The most widely used classification divides SSc into two major subsets, diffuse cutaneous (dcSSc) and limited (lcSSc) SSc by the extent and severity of skin fibrosis. However, not all patients fit into these subsets. We explored whether autoantibodies (AAB) against a multitude of autoantigens can be reliably assayed by the Luminex platform widely used and accepted by FDA, EMA.

Methods

Novel SSc-associated autoantigens were discovered by high-content autoantibody profiling using the bead-based Luminex xMAP platform SeroTag®. To analyze the inter-patient similarity of AAB reactivity, the total number of AABs reactive in each patient was calculated and referenced to the frequency >15% were identified in SeroTag assay and explored its utility for subclassification.

Results

NavigAID SSc Assay

A Luminex bead-based assay and two SSc-specific antigens with 12 novel antigens including BICD2, JMJ3D/KDM6B, and PPP1R2. Clinical associations of anti-BICD2 in 502 samples from SSc patients enrolled in the Canadian Scleroderma Research Group (CSRG) cohort will be presented at EULAR 2017 poster SAT0372.

Autoantibody Reactivity Signatures

Based on their AAB reactivity pattern, the SSc sample cohort can be decomposed into four main clusters:

- Cluster blue (n=21): 90% of all samples were lcSSc, characterized by an extended AAB repertoire (including CENPB, BICD2, KDM6B and PPP1R2), MRSS below the average and longer disease duration.
- Cluster black (n=10): 70% were lcSSc, 20% dcSSc, and 10% SSc-overlap characterized by MRSS below the average, 40% of patients were PPP1R2 positive.
- Cluster grey (n=32): 53% were lcSSc, 28% dcSSc, and 19% SSc-overlap. 34% of patients had MRSS below the average and few AABs.
- Cluster red (n=28): 71% were dcSSc, 35% lcSSc, and 4% SSc-overlap. 86% of patients had an MRSS above the average and all had Sc170 AAB.

Conclusions

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

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