Introduction

- Primary Sjögren’s syndrome (pSS) is a chronic autoimmune disease affecting salivary and lacrimal glands and associated with multi-organ involvement and lymphoma.
- Current diagnostic criteria for pSS utilize anti-Ro/SSA and anti-La/SSB autoantibodies as diagnostic markers.
- However, several studies have found the existence of many patients with pSS lacking these markers, but suggested the existence of additional autoantibodies in pSS.
- With the growing interest in conducting clinical trials in primary Sjögren’s syndrome (pSS), there is a need for new biomarkers that can be used to diagnose pSS, identify clinical subsets of pSS, predict treatment outcome and allow for assessment of disease activity.

Objectives

- The current study was undertaken to identify novel autoantigens in pSS with a special focus on proteins and cytokines (BAFF, TNFα, IL1, IL6, IL12), which are upregulated in salivary gland tissue and saliva of pSS patients.
- We designed a targeted screen comprising 1,596 antigens which are directly relevant to Sjögren’s syndrome associated processes such as cytokines, chemokines, salivary gland proteins, proteins involved in apoptosis as well as diagnostic antigens.

Methods

Autoantibody screening was performed using Protagen SeroTag approach and 1,596 selected human protein antigens from our hPexTag protein library of 8,000 recombinant proteins.

Samples included in this study are shown in Fig. 3a. Supporting information on autoantibody reactivity in other diseases from over 14,000 patient samples is available through our autoantibody reactivity data (3b).

Results

In order to rank relevant autoantibody specificities in a list of interest, we used a set of complementing statistical tests. We choose to complement the Wilcoxon rank sum test with two additional methods (SAMR, and a 90th quantile comparison). SAMR thresholds were set to SAMR delta value of 2.4, which corresponds to local FDR of 20%. In total, 27 candidate antigens were found with different specificities for all SjS or pSS (Fig. 4).

Conclusions

Apart from clear confirmation of the benchmark autoantibodies known for many years we have discovered a small set of additional, novel autoantibodies with prevalences from 8 to >20% in primary Sjögren’s syndrome. Accumulation of autoantibody reactivities allows for a first subgroup definition of Sjörgens, and for clear segregation of SjS/SLE overlap syndrome patients.