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Figure 1. IL-40 overexpression in pSS and pSS-associated lymphoma **A**, Salivary gland biopsies stained for IL-40 showing a marked increase in IL-40 expression in presence of higher focus score. **B**, Parotid gland specimens of pSS-associated lymphoma showing intense staining for IL-40.

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POS0178

GENE SIGNATURE FINGERPRINTS DIVIDE SLE PATIENTS IN SUBGROUPS WITH COMPARABLE BIOLOGICAL DISEASE PROFILES: A MULTICENTRE LONGITUDINAL STUDY

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Background: Even in the hands of experienced clinicians, clinical phenotyping and predicting treatment responses in Systemic Lupus Erythematosus (SLE) patients remains challenging. Therefore, the identification of biomarkers that can help physicians to divide patients into subgroups based upon aberrantly activated pathways is relevant and might guide future treatment strategies. Extensive blood transcriptional profiling has identified various gene modules that seem promising for stratification of SLE patients into subgroups (1). However, the feasibility to implement these complicated and expensive tests for use in the daily practice of routine clinical laboratories is challenging if not impossible.

Objectives: The aim of this study was to develop gene signatures that stratify patients into groups with comparable disease profiles and are feasible to perform in routine clinical laboratories.

Methods: To identify coordinated expression of a set of genes and reduce data complexity, genes from 4 previously described modules (Interferon M1.2, Interferon M5.12, Neutrophil- and Plasmablast (PB)(1)) were measured using real-time quantitative PCR expression on whole blood RNA samples. Subsequently, a principle component analysis was used to select 2-5 indicator genes, that represent a specific signature. Expression levels of these genes were measured in healthy donors (n=42) and samples from two independent childhood-onset SLE cohorts (n=51 and n=20). Scores higher than the mean + 2 S.D. score of healthy controls were defined as high gene signature scores. Based on their expression levels, gene signatures were divided over 14 clusters. Associated clusters were subsequently grouped into three gene fingerprints termed 1) all-signatures-low,

2) only high IFN (M1.2 and/or M5.12) and 3) high PB and/or Neutrophil. Disease activity was measured by the SELENA-SLEDAI score.

Results: All four gene signatures were higher expressed in patients compared to healthy controls and showed a significant correlation with the SLEDAI. The PB signature showed the highest association with disease activity (r= 0.6512, P<0.0001). In longitudinally collected samples, the PB signature was reduced in patients who were on treatment and showed a significant trend with the SLEDAI. When patients were divided into the described gene fingerprints, the highest SLEDAI scores (median score=8) were observed in the high PB-Neutrophil group. The lowest disease activity (median score =2) was observed in the all-signatures-low group. The same distribution was seen when samples from a second time point were divided based on this stratification method and this was also reproduced in samples from an independent SLE cohort (figure 1).

Conclusion: Various gene signatures are associated with disease activity, which underlines the involvement of different pathophysiological mechanisms in SLE. Combining these signatures into gene fingerprints can help to stratify patients into comparable groups and guide individualized treatment choices for patients in the future.

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Figure 1. SELENA-SLEDAI scores based on gene fingerprint distribution. Blue indicates time point one of cohort 1 (n=51); pink indicates time point two of cohort 1 (n=45); red indicates time point one of the replication cohort (n=20)

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POS0179

EXPLORING THE EFFECTS OF A TWO-SCORE INTERFERON SIGNATURE AND RESPONSES TO INTERFERON STIMULUS

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Background: IFN Scores are increasingly important as biomarkers to stratify RMDs and select patients for interferon targeted therapies. Several studies have previously demonstrated that different sets of interferon stimulated genes (ISGs) have different clinical associations. We validated a 2-score system of ISGs expression consisting of Score A (a set of ISGs included in most interferon signature assays) and Score B (a set of less commonly