Disclosure of Interests: Chiara Rizzo: None declared, Marianna Lo Pizzo: None declared, Leila Mohammadianzad: None declared, Vincenzo Luca Lentini: None declared, Diana Di Libertro: None declared, Giulia Grasso: None declared, Piero Rucetti Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, Robert Bosch Hospital; Gaëtan Giacomelli Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, Francisc esco ciccia Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly, Giuliana Gug nino Consultant of: Pfizer, Novartis, Celgene, Abbvie, Roche, Lilly.

Disclosure of Interests: None declared.

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Figure 1. IL-40 overexpression in pSS and pSS-associated lymphoma A. Salivary gland bi opsies 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 stain ing for IL-40.

Figure 1. SELENA-SLEDAI based on 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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2. Interferon 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 SLE-DAI. 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 score³) were observed in the high PB-Neutrophil group. The lowest disease activity (median score³) 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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measured ISGs). Score B consistently demonstrated stronger clinical associations in studies of diagnosis, prediction of progression to SLE in At-Risk individuals, response to rituximab and imaging-proven synovitis. Previous literature suggested that subsets of ISGs were explained by different interferon subtypes.

**Objectives:** To understand the determinants of IFN Score A and IFN Score B.

**Methods:** PBMCs and whole blood Tempus from 4 different healthy donors were stimulated with various cytokines and IFNs at 6- and 24-hour time points. RNA from both sample types were extracted and the expression of 26 interferon stimulated genes were measured using TaqMan and normalised to house-keeping gene PPIA. IFN Scores A and B were calculated as previously described [1]. To compare relative increase in expression with each condition, we calculated delta Ct fold change relative to non-stimulated. To represent greater expression as numerically higher positive values, relative expression was calculated as (fold change*-100) +100. Independent T-test calculated the significant differences between each condition compared to IFN α stimulation.

**Results:** Table 1 shows differences between each condition compared with IFN α at the 6-hour time point. In both sample types, all conditions excluding IFN β stimulation were shown to induce significantly lower expression of both scores compared to IFN α (p < 0.01). At 6 and 24 hours, IFN α and IFN β showed a strong induction of IFN score A and B. At 6 hours, IFN α, γ, κ, and λ induced IFN score A and B but weaker than IFN α and β which was shown in both sample types. We did not observe a difference between the expression of these two scores according to interferon subtype. Other cytokines (TNF, IL-1 and IL-6) weakly induced expression of Score A and B. For IL-10 there was a possible discordant effect with increase in expression of Score B, but decreased expression of Score A, however these changes were small in magnitude.

**Table 1.**

<table>
<thead>
<tr>
<th>Condition</th>
<th>IFN Score A</th>
<th>IFN Score B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean relative expression vs. non-stimulated (vs IFN α)</td>
<td>P value</td>
<td>Mean relative expression vs. non-stimulated (vs IFN α)</td>
</tr>
<tr>
<td>PBMC</td>
<td>103.4</td>
<td>-</td>
</tr>
<tr>
<td>IFN α</td>
<td>97.1</td>
<td>0.373</td>
</tr>
<tr>
<td>IFN β</td>
<td>37.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IFN γ</td>
<td>16.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IFN κ</td>
<td>24.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IFN λ</td>
<td>9.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-1</td>
<td>4.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-6</td>
<td>-15.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TNF α</td>
<td>9.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>116.7</td>
<td>-</td>
</tr>
<tr>
<td>IFN α</td>
<td>116.6</td>
<td>0.997</td>
</tr>
<tr>
<td>IFN β</td>
<td>23.0</td>
<td>0.001</td>
</tr>
<tr>
<td>IFN γ</td>
<td>23.0</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** We found a difference in the induction of ISG expression between subtypes of Type I interferon, as well as other interferons and cytokines. However, the relative expression of IFN Score A and IFN Score B is not easily explained by the subtypes of interferon. We have also previously shown that these scores are both similarly expressed comparing different cell subsets. The explanation for the coordinated expression of these ISGs is therefore unclear and future work will explore the scores with a combination of conditions.

**REFERENCES:**


**Disclosure of Interests:** Zoe Wigston: None declared, Agata Burska: None declared, Miriam Wittmann Consultant of: Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Edward Vital Speakers bureau: Becton Dickinson and Co.

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