compared with healthy controls, but no significant difference in expression according to genotype at 6q23 markers was previously shown to associate with RA and SLE.

**Rheumatology key message**

- Expression of TNFAIP3 is increased in RA but does not differ according to genotype at 6q23.

**Disclosure statement:** The authors have declared no conflicts of interest.

**Table 1** Normalized TNFAIP3 expression according to genotype at 6q23 polymorphisms in RA patients and healthy controls

<table>
<thead>
<tr>
<th>SNP</th>
<th>Genotype</th>
<th>RA patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs6920220</td>
<td>G/G</td>
<td>0.106 (0.526)</td>
<td>0.049 (0.036)</td>
</tr>
<tr>
<td></td>
<td>G/A</td>
<td>0.111 (0.518)</td>
<td>0.045 (0.029)</td>
</tr>
<tr>
<td></td>
<td>A/A</td>
<td>0.223 (0.624)</td>
<td>0.053 (0.041)</td>
</tr>
<tr>
<td>rs13207033</td>
<td>G/G</td>
<td>0.096 (0.479)</td>
<td>0.048 (0.040)</td>
</tr>
<tr>
<td></td>
<td>G/A</td>
<td>0.138 (0.546)</td>
<td>0.049 (0.032)</td>
</tr>
<tr>
<td></td>
<td>A/A</td>
<td>0.123 (0.159)</td>
<td>0.043 (0.022)</td>
</tr>
<tr>
<td>rs5029937</td>
<td>G/G</td>
<td>0.100 (0.467)</td>
<td>0.050 (0.036)</td>
</tr>
<tr>
<td></td>
<td>G/T</td>
<td>0.069 (0.428)</td>
<td>0.035 (0.013)</td>
</tr>
<tr>
<td></td>
<td>T/T</td>
<td>0.112 (0.541)</td>
<td>0.050 (0.035)</td>
</tr>
<tr>
<td>rs7749323</td>
<td>G/G</td>
<td>0.112 (0.541)</td>
<td>0.050 (0.035)</td>
</tr>
<tr>
<td></td>
<td>G/A</td>
<td>0.077 (0.428)</td>
<td>0.032 (0.016)</td>
</tr>
<tr>
<td></td>
<td>A/A</td>
<td>0.077 (0.428)</td>
<td>0.032 (0.016)</td>
</tr>
</tbody>
</table>

Pc: Bonferroni-corrected $P$-value.

References

hnRNP F was strongly associated with CTD in general and SSc in particular. hnRNPs are a family of ~30 proteins that associate with RNA polymerase II transcripts. They are involved in many cellular functions, such as mRNA trafficking, splicing, telomere length control, mRNA stability, transcription and polyadenylation [2].

In the present communication, we provide evidence that there are patients with a systemic rheumatic disease who have antibodies to hnRNPs but not to ENAs or dsDNA.

The study population has been described previously [3] and included 236 patients with a systemic rheumatic disease, including PM/DM (n = 28), MCTD (n = 13), SLE (n = 80), SSc (n = 69), primary SS (n = 36) and cutaneous lupus (n = 10). All samples included in this study were obtained from patients visiting a systemic disease clinic, and had a diagnosis assigned as a result of that visit. None of the patients had received any immunosuppressive medication. Additionally, 392 control sera (139 patients with chronic fatigue syndrome, 119 healthy blood donors and 134 patients visiting the rheumatology clinic for the first time and for whom systemic rheumatic disease was excluded (diseased controls]) were included. The study was approved by the ethics committee of the University Hospitals Leuven.

All sera were tested for the presence of antibodies to dsDNA, SSA/Ro52, SSA/Ro60, SSB/La, RNP-70, RNP-A, RNP-C, Sm, centromere B, Jo-1, Sci-70, Rib-P, fibrillarin, RNA Pol III, PM-Sci, PCNA and Mi-2 by automated CTD Screen (Phadia, Freiburg, Germany) [3]. All sera were tested for the presence of antibodies to hnRNP B1, hnRNP E1 and hnRNP F by ELISA (as described in ref. [1]).

Four of 36 SS patients tested negative for anti-ENA and anti-dsDNA antibodies (CTD screen assay). One of them had antibodies to hnRNP E, and one had antibodies to hnRNP B, E and F. Twenty-one of 80 SLE patients tested negative for anti-ENA or anti-dsDNA antibodies. Five of these patients had antibodies to at least one hnRNP protein (three with antibodies to hnRNP B, one with antibodies to hnRNP F and one with antibodies to hnRNP B and F). Nineteen of the 69 SSc patients tested negative for anti-ENA or anti-dsDNA antibodies. Of these patients, one had antibodies to hnRNP B and E, and one had antibodies to hnRNP B and F. Seventeen of the 28 patients with inflammatory myopathy were negative for the CTD screen assay. One patient had antibodies to hnRNP B, and one patient had antibodies to hnRNP F. All 13 MCTD patients were positive for the CTD screening assay. None of the four patients with SCL who tested negative with the CTD screen assay had antibodies to at least one of the three tested hnRNPs.

In summary, 65 of 236 patients with a systemic rheumatic disease were negative for anti-ENA or anti-dsDNA antibodies. Of these, 65 CTD screen-negative patients, 11 (16.9%) had antibodies to hnRNP B1 (n = 8), hnRNP E1 (n = 3) or hnRNP F (n = 5), of whom 4 (6.15%) had antibodies to at least two of the three tested hnRNPs (BF, BF, BE and BEF). Twenty-six (6.8%) of the 381 CTD screen-negative controls had antibodies to at least one hnRNP, of whom only 1 (0.3%) had antibodies to at least two of the three tested hnRNPs (BE). The fraction of individuals who were negative for anti-ENA and anti-dsDNA antibodies but positive for anti-hnRNP antibodies was significantly higher in patients with systemic rheumatic diseases compared with the control group [for at least one anti-hnRNP antibody: 11 of 65 screen-negative patients with CTD vs 26 of 381 controls (P = 0.02, Fisher’s exact test)] [for at least two anti-hnRNP antibodies: 4 of 65 screen-negative patients with CTD vs 1 of 381 controls (P = 0.0037, Fisher’s exact test)].

In conclusion, we identified patients with systemic rheumatic disease who do not have antibodies to the classical ENAs or dsDNA, but have the combined presence of antibodies to hnRNP B1, E1 or F. Such a combined presence of antibodies to hnRNP B1, E1 or F is seldom in control individuals.

Rheumatology key message

- Patients with systemic rheumatic diseases have antibodies to hnRNPs.

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