Fish oil use is widespread in the community with higher levels amongst those with doctor-diagnosed arthritis. However, in the majority of people with arthritis, fish oil was not taken at analgesic/anti-inflammatory doses. This is especially important in patients with RA as symptomatic benefits are seen with doses between 2.6 g and 7.1 g per day, with no effect seen at 1 g per day [9], the most common dose seen in this study. However, the effectiveness of fish oil in OA has not yet been the subject of a randomized controlled trial. The pattern of usage we observed suggested that GPs or other therapists were recommending usage of fish oil in patients with doctor-diagnosed arthritis. Fish oil has been demonstrated to reduce coronary artery disease events and reduce triglyceride levels [10]. However, in this population-based study, those at highest risk of CVD events (those with existing CVD, uncontrolled hypertension, current smokers and NSAID users) were less likely to be using fish oil. The symptomatic benefits of fish oil in arthritis have been well known for some time; however, most users are using suboptimal doses. In addition, less than one in five participants with RA were using fish oil, a proven intervention that is safe and inexpensive with favourable collateral benefits on cardiovascular risk and can reduce reliance on NSAIDs.

### Rheumatology key message

- Few RA patients use fish oil, a proven intervention with collateral benefits on cardiovascular risk.

## Acknowledgements

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### Detection of anti-PTX3 autoantibodies in systemic lupus erythematosus

**Sir,** Systemic lupus erythematosus is a multiorgan autoimmune disease characterized by the presence of autoantibodies mainly directed against components of the nucleus. The main
immunological features of SLE are the presence of autoreactive B and T lymphocytes and high titres of autoantibodies. The pathophysiology of SLE remains unknown. An excessive activation of monocytes and dendritic cells, resulting from an unabated production of type I IFN [1] and/or a deregulation of the apoptotic [2] process may contribute to the rupture of tolerance against self-antigens. A defect in apoptotic cell clearance has been associated with some autoimmune diseases, as reported in SLE patients. We have thus hypothesized that a deregulation in PTX3 production/expression may occur in SLE. As previously reported [12], we confirm that the levels of circulating PTX3 are decreased in SLE patients compared with healthy subjects (data not shown). In contrast, we report the presence of anti-PTX3 autoantibodies in SLE patients.

We have selected sera from 36 patients suffering from SLE and 40 patients suffering from RA fulfilling the ACR criteria. Clinical and biological characteristics of SLE patients are summarized in the supplementary table 1 (available as supplementary data at Rheumatology Online). Sera from 93 healthy donors (Blood Collection Center, Angers, France) were used as controls. Auto-antibodies directed against PTX3 were detected by ELISA following a standardized protocol. Elevated anti-PTX3 antibody levels were found in 50% of the patients corresponding to 42 of 83 SLE sera (30.2%; mean optical density (OD) = 5.03 ± 0.462; range 0–2.191). Anti-PTX3 antibodies were detected in 1/40 RA patients (2.5%; mean OD ± S.D. = 0.198 ± 0.168; range 0.048–0.817) and in 4/93 sera from healthy subjects (4%; mean OD ± S.D. = 0.236 ± 0.150; range 0–0.672) (Fig. 1A).

In order to discriminate between anti-PTX3 antibodies and anti-SAP antibodies have been also reported in 44% of the SLE patients and the antibody levels were correlated with SLE activity [11]. We have thus hypothesized that a deregulation in PTX3 production/expression may occur in SLE. As previously reported [12], we confirm that the levels of circulating PTX3 are decreased in SLE patients compared with healthy subjects (data not shown). In contrast, we report the presence of anti-PTX3 autoantibodies in SLE patients. We have selected sera from 36 patients suffering from SLE and 40 patients suffering from RA fulfilling the ACR criteria. Clinical and biological characteristics of SLE patients are summarized in the supplementary table 1 (available as supplementary data at Rheumatology Online). Sera from 93 healthy donors (Blood Collection Center, Angers, France) were used as controls. Auto-antibodies directed against PTX3 were detected by ELISA following a standardized protocol. Elevated anti-PTX3 antibody levels were found in 50% of the patients corresponding to 42 of 83 SLE sera (30.2%; mean optical density (OD) = 5.03 ± 0.462; range 0–2.191). Anti-PTX3 antibodies were detected in 1/40 RA patients (2.5%; mean OD ± S.D. = 0.198 ± 0.168; range 0.048–0.817) and in 4/93 sera from healthy subjects (4%; mean OD ± S.D. = 0.236 ± 0.150; range 0–0.672) (Fig. 1A).

In order to discriminate between anti-PTX3 antibodies and
anti-CRP or anti-SAP antibodies, we took advantage of the presence of the extra-Nt domain in PTX3 which is not present in SAP and CRP. Autoantibodies specific for the Nt domain of PTX3 were detected in 10 SLE sera presenting elevated anti-PTX3 antibody reactivity (S1–S10) while no immunoreactivity was observed in two SLE sera (S11 and S12) without detectable anti-PTX3 antibody (Fig. 1B). Moreover, the depletion of anti-SAP or anti-CRP antibodies of sera containing anti-PTX3 antibodies did not modulate their ability to recognize PTX3 but their ability to recognize SAP or CRP was reduced to non-significant levels.

In the group of 36 patients, we first tested 60 sera from 24 patients sampled during either inactive (SLEDAI < 6: n = 18) or active (SLEDAI ≥ 6: n = 6) phase of the disease. The mean titre of anti-PTX3 antibodies was positive only in the six patients sampled in acute phase of the disease (Fig. 1C). Further we tested 79 sera from 12 other patients. Blood samples were obtained at different stages of their disease, at the time of diagnosis, during remissions and flares. For each patient, the mean titre of anti-PTX3 antibodies was positive only in active phase of the disease (Fig. 1D).

Furthermore, we tested 86 sera from 29 patients for the concomitant presence of anti-CRP, anti-SAP and anti-PTX3 autoantibodies. Of the 15 patients with anti-PTX3 antibodies, 12 had either anti-CRP or anti-SAP antibodies. Of the 14 patients without anti-PTX3 antibodies, 11 had either anti-CRP or anti-SAP antibodies. Only three patients were anti-CRP, anti-SAP and anti-PTX-3 antibody negative.

Compared with clinical and biological markers of SLE activity (Table 1), statistical analysis showed that anti-PTX3 antibodies levels correlated with ANA, anti-dsDNA antibody, C3 and C4 level and white blood cells count. The strongest correlation coefficients between SLEDAI and biomarkers were obtained with anti-PTX3 antibodies and ANA. Interestingly, five SLE patients without anti-dsDNA antibodies presented elevated titres of anti-PTX3 antibodies. We observed that increase or decrease in anti-PTX3 antibody titres in three patients preceded the clinical flares and remissions of the disease, respectively.

In conclusion, we describe for the first time the presence of anti-PTX3 autoantibodies in SLE. The PTX3 immunoreactivity does not result from the recognition of PTX3 by anti-SAP or anti-CRP antibodies. Since PTX3 as well as CRP and SAP is implicated in the clearance of apoptotic cells, the presence of anti-PTX3 antibodies in SLE is of importance in the understanding of the pathophysiology of the disease. Correlation of anti-PTX3 antibodies titre and disease activity has to be confirmed.

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Supplementary data

Supplementary data are available at Rheumatology Online.

Rheumatology key message

- Although anti-PTX3 autoantibodies were detected in SLE patients, autoantibodies titres need to be confirmed for correlation with disease activity.

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Table 1. Correlation between anti-PTX3 autoantibody titres or SLEDAI with biological parameters

<table>
<thead>
<tr>
<th>Anti-PTX3 Abs</th>
<th>Anti-dsDNA Abs</th>
<th>ANA</th>
<th>C3</th>
<th>C4</th>
<th>White blood cell count</th>
</tr>
</thead>
<tbody>
<tr>
<td>ρ = 0.218</td>
<td>ρ = -0.424</td>
<td>ρ = -0.348</td>
<td>ρ = -0.308</td>
<td>ρ = -0.276</td>
<td></td>
</tr>
<tr>
<td>P &lt; 0.02</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.005</td>
<td></td>
</tr>
<tr>
<td>SLEDAI</td>
<td>n = 0.579</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

Non-parametric Spearman’s correlation coefficients (ρ) are calculated for all 36 patients and 139 sera. Abs: antibodies.

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