**TABLE I**

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>Female</th>
<th>Duration of RP (yr)</th>
<th>Positive ANA</th>
<th>Positive RF</th>
<th>Abnormal NCM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;4</td>
<td>4–9</td>
<td>10+</td>
<td></td>
</tr>
<tr>
<td>RP only</td>
<td>26</td>
<td>22</td>
<td>39.4 (21–74)</td>
<td>8</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Possible CTD</td>
<td>36</td>
<td>33</td>
<td>52.2 (28–79)</td>
<td>14</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 (55.6%)</td>
</tr>
<tr>
<td>Definite CTD</td>
<td>13</td>
<td>11</td>
<td>48 (28–69)</td>
<td>3</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>SSc 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 (46%)</td>
</tr>
<tr>
<td>SLE 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5 DL (46%)</td>
</tr>
<tr>
<td>RA 2 DM 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 TL (46%)</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>66</td>
<td>47</td>
<td>25</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>26 (34.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>19 (25.3%)</td>
</tr>
</tbody>
</table>

DL, dilated loops; TL, tortuous loops.

Correspondence to: J. Currey, Department of Rheumatology, Princess Alexandra Hospital, Hamstel Road, Harlow, Essex CM20 1QX.


**CD134/OX40 Expression by Synovial Fluid CD4+ T Lymphocytes in Chronic Synovitis**

Sir–Pitzalis [1] has recently reviewed the role of adhesion mechanisms in the pathogenesis of chronic synovitis. The processes leading to the accumulation of CD45R0+ T lymphocytes in synovial fluid (SF) of chronic synovitis were illustrated focusing on the selective adhesion to and migration through the endothelium by activated T cells. The main role in these mechanisms is played by LFA-1 and VLA integrins, but a proportion of the binding of T cells to endothelial cells cannot be inhibited by the addition of combinations of blocking antibodies against known adhesion molecules.

Recently, a new molecule has been demonstrated to play an important role in the process of adhesion of activated T cells to the endothelium [2], and it has been identified as the previously described OX40 antigen (now, also termed CD134), a member of the tumour necrosis factor receptor family [3–5]. Anti-OX40 antibodies inhibit the binding of phytohaemagglutinin-activated CD4+ T cells to human vascular endothelial cells, which were found to express OX40-ligand [2]. Moreover, OX40-transfected T cells were shown to bind in an OX40-system specific way to vascular endothelial cells [2].

In humans, OX40 is detectable in non-malignant tissues only on very rare lymphocytes in the T-cell compartment of lymphoid organs [6] and is virtually absent on peripheral blood resting lymphocytes [6, 7]. However, its expression can be induced upon stimulation in vitro with mitogens, mainly on CD4+ cells, but also on a small number of CD8+ cells [6, 7].

We have studied by flow cytometry the expression of OX40 using the monoclonal antibody L106 (provided by the VI International Workshop for Leucocyte Differentiation Antigens) in eight patients with rheumatoid arthritis (RA) and in six age-comparable normal individuals. On CD4+ cells purified from peripheral blood by means of immunomagnetic beads (Dynal, Oslo, Norway; purity was always >96%), only a moderate difference between the two groups was observed, as far as the number of cells co-expressing OX40 was concerned (mean ± 1 s.d. in RA 13 ± 3% vs 6 ± 2% in healthy controls; P = 0.035; Wilcoxon’s rank sum test).

However, high levels of OX40 expression were observed on CD4+ cells purified from SF of eight patients with RA (49 ± 25%; P < 0.01 vs peripheral blood CD4+ cells from healthy controls), in a patient with psoriatic arthritis (PsA) (29%), and even in two patients with osteoarthritis (OA) of the knee, from whom lymphocytic SF was aspirated (median 30%). On the other hand, only a small number of purified...
CD8+ SF lymphocytes expressed OX40 (RA: 10 ± 10%, n = 6; PsA: 9%, n = 1; OA: median = 8.5%, n = 2).

This observation suggests a possible role of OX40 in the process of migration into inflamed synovial joint by activated CD4+ T cells (worthy of future studies), but not by CD8+ cells, thus confirming the preferential expression of OX40 by CD4+ cells in rats [1], mice and humans after optimal stimulation in vitro and in vivo in patients with ongoing immune activation [7].

Moreover, these data add to those that have emerged from recent studies demonstrating on SF T cells from patients with RA (much more than in their peripheral blood) phenotypic features that can be obtained only after T-cell stimulation, such as the expression of CD69, CD70 and the down-modulation of CD27 [8, 9]. CD69, CD70 and the down-modulation of CD27 [8, 9].

Moreover, these data add to those that have emerged from recent studies demonstrating on SF T cells from patients with RA (much more than in their peripheral blood) phenotypic features that can be obtained only after T-cell stimulation, such as the expression of CD69, CD70 and the down-modulation of CD27 [8, 9]. CD69, CD70 and the down-modulation of CD27 [8, 9].

Finally, considering that OX40 can enhance the proliferation and immunoglobulin secretion by activated B cells expressing OX40-ligand [11, 12], this molecule might contribute to the pathogenesis of rheumatoid synovitis, also having a role in the potent helper effect for B cells provided by CD4+ memory cells within the rheumatoid synovium [13].

D. Brugnoni, A. Bettinardi, F. Malacarne, P. Airò, R. Cattaneo
Servizio di Immunologia Clinica, Spedali Civili di Brescia, Italy
Accepted 10 November 1997
Correspondence to: P. Airò, Servizio di Immunologia Clinica, Spedali Civili, P.le Spedali Civili, 25123 Brescia, Italy.

1. Brugnoni D, Airò R, Cattaneo R. CD70 (CD27 ligand) expres-