Human T-Cell Leukemia Virus Type I Tax Induces Intracellular Adhesion Molecule-1 Expression in T Cells

To the Editor:

Human T-cell leukemia virus type I (HTLV-I) is the etiologic agent associated with adult T-cell leukemia (ATL) as well as the neurologic disease tropical spastic paraparesis/HTLV-I-associated myelopathy (TSPmAM). Tax is a 40-kD viral protein, encoded by the pX region of the HTLV-I genome, that induces viral transcription and also transactivates a number of cellular genes such as interleukin-2 (IL-2) and the IL-2 receptor.1

Intracellular adhesion molecule-1 (ICAM-1) is a sialylated glycoprotein that binds to the leukocyte integrins LFA-1 (CD11a/CD18) and Mac-1 (CD11b/CD18) to support cell-cell adhesion and induction and effector functions in the immune response.2 4 Analysis of leukemic cells from patients with ATL and HTLV-I-transformed cell lines has shown that ICAM-1 is highly expressed on these cells.5 Furthermore, Lal et al extensively report that serum ICAM-1 level is significantly increased in patients with ATL and TSPmAM. However, the molecular mechanism of induction of ICAM-1 in HTLV-I-infected T cells is not known at present. Therefore, it was of interest to determine whether tax could induce ICAM-1 expression.

In this study, we examined the effect of tax on expression of ICAM-1 by using JPX-9, a Jurkat clone stably transfected with a heavy-metal-inducible tax expression plasmid (kindly provided by Dr M. Nakamura, Tohoku University, Sendai, Japan).7 The levels of expression of ICAM-1 were compared before and after induction of tax. JPX-9 cells were treated with CdCl2 and expression of ICAM-1 was examined by flow cytometry. As shown in Table 1 and Fig 1, enhanced expression of ICAM-1 on these transfected cells was observed, whereas in parental Jurkat cells expression of ICAM-1 was not enhanced after treatment with CdCl2. These results suggest that ICAM-1, which is essential for leukocyte migration and homing processes, is activated directly or indirectly by tax.

Several tax-responsive elements have been found that confer tax responsiveness to promoters. For example, the nuclear factor (NF)-κ B element and the cyclic adenosine monophosphate-responsive element are common tax-responsive elements in several genes.1 Interestingly, the ICAM-1 promoter contains NF-κ B sequences.8 Therefore, it is possible that enhanced expression of ICAM-1 is mediated by NF-κ B. However, further studies are required to investigate the role of tax on ICAM-1 gene activation. These results indicate that tax-induced ICAM-1 expression may play a significant biologic role in the cell attachment to vascular endothelium, resulting in infiltration of ATL cells into various tissues such as skin, liver, spleen, and lymph node, one peculiar clinical manifestation of ATL.

Table 1. Kinetics of Induction of ICAM-1 Expression by tax in JPX-9 Cells

<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Incubation Time (hrs)</th>
<th>CdCl2 (-)</th>
<th>CdCl2 (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JPX-9</td>
<td>0</td>
<td>4.9</td>
<td>22.5</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>6.5</td>
<td>49.5</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>3.0</td>
<td>72.3</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>6.6</td>
<td>7.3</td>
</tr>
<tr>
<td>Jurkat</td>
<td>0</td>
<td>7.2</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>7.2</td>
<td>8.7</td>
</tr>
</tbody>
</table>

Flow cytometric analysis of expression of ICAM-1 after induction of tax in JPX-9. JPX-9 and parental Jurkat cells were incubated in the presence (+) or absence (−) of 20 μmol/L CdCl2 for 72 hours. Cells were analyzed for surface expression of ICAM-1 by flow cytometry. Cytofluorograms of anti-ICAM-1-stained cells (−) are superimposed over cytofluorograms of control cells (+). The vertical axes denote the relative cell number, and the horizontal axes show the fluorescence intensity on logarithmic amplification.
or in the abnormal localization of activated or HTLV-I-infected T cells to the central nervous system of patients with TSP/HAM.

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REFERENCES

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