Biological characteristics of CD7 positive acute myelogenous leukaemia

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CD7 has been recognized as one of the early T-cell antigens, and is usually expressed on immature T-cells and prothymocytes (Palmer et al., 1986; Sutherland et al., 1984). Recent reports have shown that leukaemic blasts in the minority of acute myelogenous leukaemia (AML) cases expressed CD7 (Lo Coco et al., 1988; Liu et al., 1990). One possible explanation for this observation is that the expression of CD7 and myeloid antigens in AML reflects the involvement of a minor normal counterpart of early haematopoietic progenitors. Alternatively, CD7 is aberrantly expressed in some CD7 and myeloid antigens in AML reflects the involvement of a minor normal counterpart of early haematopoietic progenitors. Alternatively, CD7 is aberrantly expressed in some AML cases. The proliferative responses to stimulation by various growth factors. Among interleukin-3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-CSF), and granulocyte-colony-stimulating factor (G-CSF), IL-3 showed the strongest stimulatory effect on DNA synthesis and leukaemic blast colony formation in 8/9 and 6/22 AML cases examined, respectively. On the other hand, the strongest stimulatory effect exerted by IL-1 was on blast colony formation observed in only six out of the five AML cases examined. Furthermore, CD7+ AML blasts could proliferate in response to stem cell factor (SCF). SCF alone showed stimulatory effects on blast colony formation in 7/8 cases, and in 5/7 SCF responding cases, stimulatory effects of SCF were more potent than those of IL-3. In addition, SCF enhanced blast colony formation synergistically with IL-3 in four of these seven cases. These data suggest that progenitor cells of CD7+ AML possess the biological properties characteristic of immature haematopoietic stem cells.

The leukaemic blasts were cryopreserved in Iscove's modified Dulbecco's medium containing 10% fetal calf serum and 40% dimethyl sulfoxide (DMSO) until use for experiments with SCF. Immunofluorescence analysis. Leukaemic blasts were phenotypically studied with a direct murine immunofluorescence technique. For immunofluorescence assays, mouse IgG1 conjugated to fluorescein isothiocyanate (FITC) or mouse IgG1 conjugated to phycoerythrin (PE) was used as a negative control. The FITC- or PE-conjugated antibodies used were as follows: CD2 (T11), CD3 (leu 4a), CD4 (leu 6a), CD7 (leu 7a), CD8 (leu 2a), anti-HLA-DR and CD14 (B8-1) were obtained from Becton Dickinson Monoclonal Center (Mountain View, Calif., U.S.A). CD34 (3G8), CD10 (B1) and CD11b (M1) were obtained from Coulter Immunology (Hialeah, Fla., U.S.A.). The immunofluorescence positivity was determined with a FACScan flow cytometer (Becton Dickinson) and leukaemic blasts were judged as positive for each marker when more than 20% of the blasts showed fluorescent staining.

In normal haematopoiesis it has been demonstrated that a minor normal counterpart of early haematopoietic progenitors. Alternatively, CD7 is aberrantly expressed in some AML cases. These data suggest that progenitor cells of CD7+ AML possess the biological properties characteristic of immature haematopoietic stem cells.

### Materials and Methods

AML blast cells. Between 1986 and 1988, 89 consecutive cases of de novo AML patients were admitted to our institution. The diagnosis was made according to the revised criteria of the French-American-British group (Heimert et al., 1988) based on the morphological and cytochemical examination. Peripheral blood mononuclear cells (PBMCs) were obtained by Ficoll-Hypaque density-gradient centrifugation. Adherent cells were removed by incubating the cell suspension (2 x 10^6/ml) in 1 ml of a plastic tissue culture flask. All samples contained more than 85% blasts. These fresh non-adherent AML blasts were used for the following experiments. The leukaemic blasts were cryopreserved in Iscove's modified Dulbecco's medium containing 10% fetal calf serum and 4% dimethyl sulfoxide (DMSO) until use for experiments with SCF. The proliferative responses to stimulation by various growth factors. Among interleukin-3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-CSF), and granulocyte-colony-stimulating factor (G-CSF), IL-3 showed the strongest stimulatory effect on DNA synthesis and leukaemic blast colony formation in 8/9 and 6/22 AML cases examined, respectively. On the other hand, the strongest stimulatory effect exerted by IL-1 was on blast colony formation observed in only six out of the five AML cases examined. Furthermore, CD7+ AML blasts could proliferate in response to stem cell factor (SCF). SCF alone showed stimulatory effects on blast colony formation in 7/8 cases, and in 5/7 SCF responding cases, stimulatory effects of SCF were more potent than those of IL-3. In addition, SCF enhanced blast colony formation synergistically with IL-3 in four of these seven cases. These data suggest that progenitor cells of CD7+ AML possess the biological properties characteristic of immature haematopoietic stem cells.
lymphoid (CD10). (HL or CD20) non mature T lymphoid (CD3, CD4 or CD8) antigens were detected in any of the nine cases. With respect to CD10, CD20, and CD7 cases diagnosed at CD7 lymphoid (CD3, CD4 or CD8) antigens were detected in any of the nine cases. With respect to CD7, CD20 and CD34+, 46 cases were diagnosed at CD7 lymphoid (CD3, CD4 or CD8) antigens were detected in any of the nine cases.

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the CD7 expression on myeloid leukemic blasts might reflect the cell immaturity: leukemic transformation would occur in a subset of CD7+ myeloid progenitors because of the high incidence of CD7+ AML in less differentiated subgroup of AML such as M0 or M1, and because of the rare occurrence of clonal rearrangement of the TcR-β gene in the TcR-γ gene. Similarly, in our study, the incidence of CD7+ AML was also high in M1 and neither the TcR-β nor the TcR-γ gene incidence of CD34 expression in CD17-AML and the tendency of high proportion of CD37 positivity associated with high percentages of CD34+ blasts. These data suggest the possibility that the leukemic transformation may occur at a stage of CD37-/CD34+ or more immature haematopoietic progenitors. Based on these biological characteristics of CD7+ AML blasts, we deduce that the CD7 expression in AML could be ascribed to the involvement of leukemic progenitors at an early stage of myeloid or myeloid/lymphoid differentiation rather than to the aberrant expression of leukemic progenitors due to the leukemic transformation.

**ACKNOWLEDGMENTS**

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**REFERENCES**


**Table IV. Effects of IL-3, GM-CSF and G-CSF on colony formation.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>EAF</th>
<th>CD7</th>
<th>CD34</th>
<th>Control</th>
<th>IL-3</th>
<th>GM-CSF</th>
<th>G-CSF</th>
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<tr>
<td>1</td>
<td>M1</td>
<td>++</td>
<td>++</td>
<td>9±1</td>
<td>186±25</td>
<td>24±2</td>
<td>58±1</td>
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<tr>
<td>2</td>
<td>M1</td>
<td>++</td>
<td>++</td>
<td>0</td>
<td>896±53</td>
<td>12±21</td>
<td>59±1</td>
</tr>
<tr>
<td>3</td>
<td>M1</td>
<td>++</td>
<td>++</td>
<td>25±5</td>
<td>109±7</td>
<td>28±39</td>
<td>10±3</td>
</tr>
<tr>
<td>4</td>
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<td>++</td>
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<td>187±16</td>
<td>20±4</td>
<td>130±11</td>
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<tr>
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<td>M1</td>
<td>++</td>
<td>+</td>
<td>15±4</td>
<td>18±6</td>
<td>14±7</td>
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<tr>
<td>6</td>
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<td>45±8</td>
<td>23±7</td>
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<td>6±1</td>
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<tr>
<td>7</td>
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<td>85±6</td>
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<td>8</td>
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<td>8.2±2</td>
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<tr>
<td>9</td>
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<td>+</td>
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<td>18±6</td>
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</tr>
<tr>
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<td>51±6</td>
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</tr>
<tr>
<td>13</td>
<td>M1</td>
<td>++</td>
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<tr>
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<td>++</td>
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</tr>
<tr>
<td>15</td>
<td>M1</td>
<td>++</td>
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<tr>
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</tr>
<tr>
<td>18</td>
<td>M2</td>
<td>++</td>
<td>+</td>
<td>23±4</td>
<td>12±6</td>
<td>47±10</td>
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</table>

*Significant enhancement of blast colony formation compared to the cultures in the presence of growth factors (P<0.05).*

**Table V. Effects of IL-3, GM-CSF and G-CSF on DNA synthesis of CD7+ AML blasts.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>IL-3</th>
<th>GM-CSF</th>
<th>G-CSF</th>
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<tr>
<td>1</td>
<td>1224±409</td>
<td>42185±(16±976)</td>
<td>150±89</td>
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<td>2</td>
<td>1018±12</td>
<td>11570±14±318</td>
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<tr>
<td>3</td>
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<td>4</td>
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<td>150±89</td>
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*Significant enhancement of 3H-TdR incorporation of leukemic blasts compared to the cultures with growth factors (P<0.05).*


