Differential Expression of CD54/Intercellular Adhesion Molecule-1 in Myeloid Leukemias and in Lymphoproliferative Disorders

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Indirect immunofluorescence staining with monoclonal antibody (MoAb) CL203.4 of malignant cells from 269 patients with hematologic malignancies showed a heterogeneous expression of CD54/intercellular adhesion molecule-1 (ICAM-1). This marker was expressed by malignant cells of 57 out of 118 patients with myeloid malignancies and 69 out of 135 with B-lymphoid malignancies. On the other hand, CD54 was not detected on malignant cells of 16 patients with T-lymphoid malignancies. In myeloid malignancies, CD54 is preferentially expressed by "stem cell-derived" malignancies, being detectable on blast cells from almost all patients affected by chronic myelogenous leukemia in blast phase or myelodysplastic syndromes and by only 34% of patients with de novo acute myeloid leukemia (AML). The expression of CD54 did not correlate with any specific myeloid FAB subtype, although three cases of highly undifferentiated AML (FAB MO) displayed maximal levels of the antigen. The expression of CD54 in AML was significantly associated with that of CD34 and HLA-DR antigens. In B-lymphoid malignancies, CD54 expression appears to correlate with the differentiation stage of malignant cells, since B-origin acute lymphoblastic leukaemias and conventional B-chronic lymphocytic leukaemias (B-CLL; i.e., "dim Slg" CLl) expressed lower levels of CD54 than more mature lymphoproliferative disorders ("bright Slg" CLL, prolymphocytic leukaemias, and lymphoplasmacytic tumors). "High-grade" B-cell non-Hodgkin's lymphomas (B-NHL) express in general a higher level of CD54 than "low-grade" ones. This finding in conjunction with the expression of CD54 in all 17 patients with "bright Slg" CLL investigated (characterized by marked organomegaly and poor prognosis) suggest that the differential expression of CD54 in lymphoproliferative disorders may also relate to their degree of malignancy.

CD54/INTERCELLULAR adhesion molecule-1 (ICAM-1) is a glycoprotein with an apparent molecular weight ranging between 80 and 114 Kd. Through the binding to its physiologic ligand, the leukocyte function-associated antigen-1 (LFA-1/CD11a), CD54 plays a crucial role in cell-cell and cell-stroma interactions, which are important for the initiation of the immune response,17 inflammatory processes,18 and cellular interactions with vessel endothelium.3

The role of CD54 in cell-cell interactions has stimulated interest in the characterization of its tissue distribution and of changes in its expression associated with malignant transformation of cells. Extensive immunohistochemical analysis of normal tissues has shown that CD54 has a restricted distribution, since it is detected only on endothelial cells and on lymphoid and splenic follicles.1,3 Immunohistochemical staining of a large number of solid tumors of various embryologic origin has found CD54 in a high percentage of melanoma lesions with a significantly higher expression in metastatic than in primary lesions.5 On the other hand, the distribution of CD54 on hematopoietic cells has been investigated only in a limited number of samples.1011 The expression of CD54 has been found to be a differentiation-dependent phenomenon in certain lineages; CD54 is expressed on bone-marrow progenitors and is lost at the stage of erythroblasts in the erythroid lineage and at the stage of myelocytes in the granulocyte lineage.11 In the monocytic lineage CD54 is retained throughout the differentiation stages, being strongly expressed on mature monocytes.7 Mature B cells express CD54.12 Terminally differentiated T cells lack CD54 but acquire it following activation with mitogens or antigens.5,6,7

Leukemic cells greatly facilitate the analysis of the relationship of surface-marker expression with cell differentiation, since they may represent the clonal expansion of cells reflecting the phenotype of normal blood-cell precursors at various steps of differentiation. Therefore in the present study we have investigated the distribution of CD54 on various types of myeloid and lymphoid leukemic cells to further assess the relationship between CD54 expression and stages of blood-cell differentiation. Furthermore, we have correlated the expression of CD54 with that of other cell-surface markers to evaluate the usefulness of CD54 to phenotype leukemic cells. Lastly, we have correlated the expression of CD54 with clinical parameters of malignancy, since the expression of this molecule in primary melanoma lesions is associated with a poor clinical course of the disease.913

MATERIAL AND METHODS

Patients. All the patients included in this study except 14 with myelodysplastic syndrome (MDS) had more than 80% of leukemic cells in peripheral blood (PB). Acute lymphocytic leukemias (ALL; L1-L3), acute myeloid leukemias (AML; M0-M7), and MDS were diagnosed by cell morphology and enzyme cytochemistry and classified according to the French-American-British (FAB) criteria14;

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chronic lymphoproliferative disorders were diagnosed by morphologic, cytochemistry, immunophenotype, and clinical parameters; non-Hodgkin’s lymphomas (NHL) were diagnosed by histopathologic examination of lymph-node sections and classified according to the International Working Formulation (WF). Lineage assignment and immunologic subclassification of various disorders were determined by flow cytometric analysis of cells stained with monoclonal antibodies (MoAb) and/or in situ immunohistochemistry of tissue sections.

**Cells and tissues.** Peripheral blood and bone marrow aspirates were collected in heparin before chemotherapy. Leukemic cells were isolated by centrifugation on a Ficoll-Hypaque (Pharmacia, Fine Chemicals AB, Uppsala, Sweden) gradient. Lymph nodes were processed within 15 minutes following surgical removal. Each specimen was divided into two parts. One half was fixed in Bouin’s solution, embedded in paraffin, and processed for routine histopathology. The other half of the specimen was snap frozen in liquid nitrogen and stored at -80°C until use. Four-micrometer thick cryostat sections were dried, fixed in absolute acetone for 1 minute, and used as substrates in immunoperoxidase.

**MoAb and conventional antisera.** The anti-CD54 MoAb CL203.4 was developed and characterized as described. The anti-CD1a MoAb OKT6, the anti-CD2 MoAb OKT11, the anti-CD4 MoAb OKT4, the anti-CD8 MoAb OKT8, the anti-CD3 MoAb OKT10, and the anti-CD24 MoAb OKB2 were purchased from Ortho Diagnostics (Raritan, NJ); the anti-CD3 MoAb Leu-4, the anti-CD5 MoAb Leu-1, the anti-CD7 MoAb Leu-9, the anti-CD11c MoAb Leu-M5, the anti-CD34 MoAb HPCA1, and the anti-CD54 MoAb CL203.4 were purchased from Becton Dickinson Immunocytometry System (Mountain View, CA); the anti-CD19 MoAb B4, the anti-CD20 MoAb B1, the anti-CD21 MoAb B2, the anti-CD23 MoAb B6, the anti-CD11b MoAb M01, the anti-CD13 MoAb M7, the anti-CD14 MoAb M4 and M02, the anti-CD33 MoAb M9, and the anti-CD10 MoAb J5 were purchased from Coulter Immunology (Hialeah, FL); the anti-FMC7 MoAb TEC-B cells 2 was purchased from Technogenetics (Milan, Italy).

Affinity-purified rabbit antitissue IgG + IgM (H + L) antibodies were purchased from Jackson Immunoresearch Laboratories Inc, (West Grove, PA). Fluorescein isothiocyanate-conjugated (FITC) F(ab’), fragments of goat antibodies specific for human κ light chain and λ light chain were purchased from Kallestad (Austin, TX). FITC F(ab’)2 fragments of goat antitissue IgG (H + L) antibodies were purchased from Technogenetics.

Reagents for indirect immunoperoxidase (ABC Kit) were purchased from Vector Laboratories (Burlingame, CA).

**Serologic assays.** In direct immunofluorescence (IF) Preincubating for 30 minutes at 4°C with occasional gentle shaking, 100 μL of a cell suspension (5 × 10^6/mL Hanks’ balanced salt solution supplemented with 10% rabbit serum and 0.01% sodium azide [HBSS-RS-AZ]) were incubated with 10 μL of FITC anti-human κ light chain and λ light chain xenon antibodies for 30 minutes at 4°C. In indirect immunofluorescence (IF) following a preincubation for 30 minutes at 4°C with occasional gentle shaking, 100 μL of a cell suspension (5 × 10^6/mL HBSS-RS-AZ) were incubated with an excess of MoAb for 30 minutes at 4°C. Then cells were washed three times with phosphate buffered saline (PBS), pH 7.4, supplemented with 0.1% bovine serum albumin (BSA) and 0.01% sodium azide (PBS-BSA-AZ) and incubated for an additional 30 minutes at 4°C with FITC F(ab’)2 fragments of antitissue IgG xenon antibodies. Negative controls were performed by incubating cells with isotype-matched control murine Ig. At the end of the incubation, cells were washed three times with PBS-BSA-AZ, fixed in 0.5% paraformaldehyde in PBS, and analyzed with a FACStar flow cytometer (Becton Dickinson); 1 × 10^6 (volume gated) viable cells were collected in a list-mode fashion for data analysis. Forward and 90° scatter gating were used to select the leukemic cell population during flow-cytometric analysis. AML and MDS samples were analyzed using scatter gates set around blast cells. A sample was classified positive when the percentage of stained cells was at least 35% when incubated with anti HLA-DR MoAb and at least 20% when incubated with MoAb to all other markers tested.

Indirect immunoperoxidase staining of frozen tissues was performed using the ABC method as previously described.

**Radiolabeling of cells, indirect immunoprecipitation, and SDS-PAGE.** They were performed as described elsewhere. Briefly, cells were labeled with ^125I (Amersham International, Amersham, UK) using the lactoperoxidase method. Then cells were solubilized by incubation for 30 min at 4°C in lysis buffer containing 1% NP40, 10 mmol/L Tris-HCl (pH 8.2), 0.5 mol/L NaCl, 1 mmol/L EDTA, 1 mg/mL BSA, and 1 mmol/L PMSF and incubated for 12 hours with MoAb CL203.4 bound to Protein A-Sepharose (Pharmacia) precoated with rabbit antitissue Ig antibodies (H + L). One-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed on 10% polyacrylamide slab gels under reducing conditions using the buffer system described by Laemmli. Gels were processed for autoradiography using a Kodak XAR-5 film (Eastman Kodak Company, Rochester, NY).

**RESULTS**

Cytfluorographic analysis of leukemic cells stained with anti-CD54 MoAb CL203.4 showed that this antigen is expressed, although with different frequency, in various subtypes of myeloid leukemias and of B-lymphoid leukemias and lymphomas but is not detectable in T-cell malignancies.

**CD54 expression by leukemic cells of the myeloid lineage.** CD54 was found on blast cells from almost all the patients investigated with MDS (refractory anemia with excess blasts in transformation, RAEB-T) or leukemic evolution of a preceding MDS or with chronic myelogenous leukemia in blastic phase (CML-bp) with a myeloid phenotype. On the other hand, CD54 was detected in only 34% of patients with de novo AML (Table 1). In this latter group the mean percentage of leukemic cells stained with MoAb CL203.4 was significantly lower (P < .001) than in the other two types of malignancies (Fig 1). Furthermore, cytofluorographic analysis of gated monocytes in two cases of chronic myelomonocytic leukemia (CML-L) in preleukemic phase showed a high percentage of positive cells (Table 1, Fig 1).

Although not closely correlated with any FAB subtype, CD54 expression was higher in undifferentiated than in differentiated types of AML (Table 1). In fact, CD54 was expressed in the three most immature AML cases studied (FAB MO, HLA-DR+, CD34+, CD13+, CD33-) but only in about 25% of each of the other FAB subtypes investigated (Table 1). Furthermore, the percentage of leukemic cells expressing CD54 was at most 73 in the latter subtypes but was at least 80 in the three most undifferentiated cases (Table 1).

Using the Pearson’s correlation test, expression of CD54 in AML samples was compared to that of the other antigens tested for immunophenotypic analysis of leukemic cells. CD54 expression was found to directly correlate with that of
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Table 1. CDW Expression in Myeloid Malignancies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. Positive/No. Tested</th>
<th>% Stained Cells (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>30/88</td>
<td>20-90</td>
</tr>
<tr>
<td>FAB* M0</td>
<td>3/2</td>
<td>80-90</td>
</tr>
<tr>
<td>FAB M1</td>
<td>4/18</td>
<td>21-49</td>
</tr>
<tr>
<td>FAB M2</td>
<td>5/19</td>
<td>23-44</td>
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<tr>
<td>FAB M3</td>
<td>1/4</td>
<td>27</td>
</tr>
<tr>
<td>FAB M4</td>
<td>6/25</td>
<td>22-73</td>
</tr>
<tr>
<td>FAB M5</td>
<td>2/8</td>
<td>20-67</td>
</tr>
<tr>
<td>FAB M6</td>
<td>2/2</td>
<td>47-60</td>
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<tr>
<td>MDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAEB-T</td>
<td>5/5</td>
<td>22-37</td>
</tr>
<tr>
<td>CMML</td>
<td>2/2</td>
<td>52-78</td>
</tr>
<tr>
<td>CMML-M4</td>
<td>7/7</td>
<td>30-82</td>
</tr>
<tr>
<td>CML-bp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myeloid</td>
<td>8/11</td>
<td>28-48</td>
</tr>
<tr>
<td>Lymphoid</td>
<td>5/5</td>
<td>32-66</td>
</tr>
</tbody>
</table>

Malignant cells were sequentially incubated with anti-CD54 MoAb CL203.4 and with FITC-antimouse Ig xenoantibodies. Then cells were analyzed in flow cytometry. A sample was classified positive when at least 20% of malignant cells were stained by MoAb CL203.4.

Abbreviations: AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; RAEB-T, refractory anemia with excess blast in transformation; CMML, chronic myelomonocytic leukemia; CMML-M4, chronic myelomonocytic leukemia evolved into FAB M4 AML; CML-bp, chronic myelogenous leukemia in blastic phase; FAB, French-American-English classification.

*Leukemic cells were morphologically and cytochemically classified by two investigators according to revised FAB criteria; nine cases of AML investigated were excluded from the analysis because of discrepancy in FAB assignment.

CD54 expression by malignant cells of the lymphoid lineage. Expression of CD54 in B-lineage ALL is heterogeneous. Seven out of 18 samples reacted with the MoAb CL203.4; the percentage of positive cells ranged between 24 and 89 (Table 2). The mean percentage of leukemic cells reacting with MoAb CL203.4 was significantly lower than that of CML in blast phase with a lymphoid phenotype (MPOX-, TdT+, CD19+, CD20+, CD24+, CD13-, CD33-; Fig 1). No statistically significant association was found between the expression of CD54 and that of the markers specific for stages of B-cell differentiation investigated. Specifically, CD54 was detected in 5 of 14 CD10+ ALL and in 2 of 4 CD10− ALL. Furthermore, a high level of CD54 was found on malignant cells in a single case of FAB L3 Burkitt's type ALL (SM Ig+).

In B NHL with a peripheral leukemic picture, the expression of CD54 was higher in high-grade (H, I, and J groups according to the WF classification) than in low-grade (A, B, and C groups according to the WF classification) lymphomas. Specifically, CD54 was expressed by all 5 high-grade B-NHL investigated but only 11 out of the 20 low-grade B-NHL analyzed (Table 2). Furthermore, the mean percentage of malignant cells stained by anti-CD54 MoAb CL203.4 was 65 in high-grade B-NHL but only 37 in the low-grade ones (Fig 1). Similar results were derived from the immunohistochemical staining with MoAb CL203.4 of frozen sections of lymph nodes from patients with B-NHL. CD54 was found on malignant cells from all 7 patients with intermedi-
Table 2. CD54 Expression in Lymphoid Malignancies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. Positive/No. Studied (%)</th>
<th>% Stained Cells (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-lineage ALL</td>
<td>7/18</td>
<td>24-89</td>
</tr>
<tr>
<td>B-CLL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dim Slg</td>
<td>17/61</td>
<td>22-50</td>
</tr>
<tr>
<td>Bright Slg</td>
<td>17/17</td>
<td>33-96</td>
</tr>
<tr>
<td>B-PLL</td>
<td>3/3</td>
<td>48-73</td>
</tr>
<tr>
<td>B-NHL*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-grade</td>
<td>5/5</td>
<td>52-73</td>
</tr>
<tr>
<td>Low-grade</td>
<td>11/20</td>
<td>28-90</td>
</tr>
<tr>
<td>HCL</td>
<td>1/3</td>
<td>—</td>
</tr>
<tr>
<td>MM</td>
<td>4/4</td>
<td>43-73</td>
</tr>
<tr>
<td>LPL</td>
<td>4/4</td>
<td>36-82</td>
</tr>
<tr>
<td>T-ALL†</td>
<td>0/12</td>
<td>—</td>
</tr>
<tr>
<td>T-LPD‡</td>
<td>0/4</td>
<td>—</td>
</tr>
</tbody>
</table>

Malignant cells were sequentially incubated with anti-CD54 MoAb CL203.4 and with FITC-anti-mouse Ig xenoantibodies. Then cells were analyzed in flow cytometry. A sample was classified positive when at least 20% of malignant cells were stained by MoAb CL203.4.

Abbreviations: ALL, acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; PLL, prolymphocytic leukemia; NHL, non-Hodgkin lymphoma; HCL, hairy cell leukemia; MM, multiple myeloma; LPL, lymphoplasmacytoid lymphoma; LPD, lymphoproliferative disorder.

*Classified according to the International Working Formulation (WF).
†This group includes three cases of lymphoblastic T-cell lymphomas in leukemic phase.
‡This group includes one case of mycosis fungoides and three cases of T-CLL.

CD54 was found on leukemic cells in 34 out of 78 patients with chronic lymphocytic leukemia (B-CLL; Table 2). Morphology, cytochemistry, immunophenotypic characteristics, and clinical parameters ruled out an alternative diagnosis of prolymphocytic leukemia (PLL), hairy cell leukemia (HCL), or low-grade B-NHL. Three lines of evidence indicate that the expression of CD54 was significantly lower in dim Slg B-CLL than in bright Slg B-CLL. The latter were also characterized by the expression of the FMC7 molecule, the lack of CD23 (Fig 3), and the heterogeneous expression of...
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Fig 3. Differential expression of CD54 in dim S Ig and bright S Ig B-CLL. Leukemic cells from 61 patients with dim S Ig B-CLL (■) and from 17 patients with bright S Ig B-CLL (□) were incubated with either anti-CD54 MoAb CL203.4, anti-CD23 MoAb B6, or anti-FMC7 MoAb TEC-B cells 2. Then cells were stained with FITC-antimouse Ig xenoantibodies and analyzed in flow cytometry. Results are expressed as mean ± SD of the percentage of stained cells. S Ig intensity was evaluated in flow cytometry after staining of leukemic cells with FITC Fab'1, fragments of goat antibodies specific for human α light chain and λ light chain.

CD54 was found in all 17 samples with a bright S Ig staining and in only 17 out of the 61 with a dim S Ig staining (P < .0001; Table 2). Second, the mean percentage of leukemic cells stained by MoAb CL203.4 in the bright S Ig group was significantly (P < .0001) higher than that in the dim S Ig group (Fig 1). Third, the mean fluorescence intensity of the leukemic cell population stained by MoAb CL203.4 was higher in the bright S Ig group than in the dim S Ig group (data not shown).

CD54 was found in the three cases of clinically and immunologically proven PLL; the percentage of leukemic cells stained by MoAb CL203.4 ranged between 48 and 73 (Table 2).

CD54 was found in 82% of the 11 investigated cases of B-cell neoplasms of the preplasmacytic and plasmacytic differentiation area. Malignant cells in 1 of 3 HCL, in the four lymphoplasmacytic lymphomas (LPL), and in the four multiple myelomas (MM) in leukemic phase investigated expressed high level of CD54 (Table 2). It is noteworthy that in MM the mean percentage of reactivity of plasma cells with MoAb CL203.4 was 60 (Fig 1).

CD54 was not detected on malignant T cells (Table 2). Less than 5% of malignant T cells were stained by MoAb CL203.4 in nine patients with T-ALL, three with lymphoblastic T-cell lymphoma, two with CD4+ T-CLL, one with CD8+ T-CLL, and one with mycosis fungoides (Fig 1).

Molecular profile of CD54 expressed by leukemic cells. To analyze the structural profile of CD54 expressed by leukemic cells, the component immunoprecipitated by MoAb CL203.4 from 125I-labeled leukemic cells from one patient with AML, MO-FAB; from one with low-grade B-NHL, and from one with CMML-M4 was analyzed by SDS-PAGE. One component with the apparent molecular weight of 85 Kd was detected (Fig 4).

DISCUSSION

IIF staining with the anti-CD54 MoAb CL203.4 of malignant cells from a large number of patients with hematopoietic malignancies showed that CD54 is expressed on myeloid and B-lymphoid malignant cells but is not detectable on T-lymphoid malignant cells. The latter included stages of T-cell maturation ranging from "pre-thymic" T-ALL to mature "helper" or "suppressor" T-cell leukemias. It should be noted, however, that adult T-cell leukemias (ATL) could not be included in the present study.
since samples from patients with this malignancy were not available. These neoplastic cells are, however, of particular interest, since their antigenic phenotype resembles that of activated normal T cells that have been shown to express CD54. Furthermore, in preliminary experiments, T-ALL cells have acquired CD54 following in vitro incubation with 5-Azacytidine, PHA, or TPA.

One of us has recently shown that normal bone marrow progenitors such as burst-forming unit–E (BFU-E), colony-forming unit–E (CFU-E), and CFU-GM express CD54 and that maturation of cells of the erythroid and myeloid lineage is associated with loss of CD54. The detection of CD54 on early blood-cell precursors and/or hematopoietic stem cells is in agreement with the bright staining by MoAb CL203.4 of malignant cells in clonal leukemias arising from pluripotent progenitors (CML, MDS, and their leukemic evolutions). Blast cells from almost all our RAEB-T, myelomonocytic evolutions of a preceding CML (CML-M4), and CML-bp cases display, in fact, a very high level of CD54. Conversely, CD54 was found to be expressed by only 34% of the de novo AML samples analyzed. If such differential expression is confirmed on a larger number of samples, then CD54 might represent a potentially useful marker to discriminate secondary (ie, those arising from a preceding MDS) from de novo AML. Moreover, it will be of interest to verify whether CD54 expression in AML could identify a subset of patients characterized by a distinct clinical outcome. On a biological ground, such cases might be closely related to leukemic phases of MDS, in which we demonstrated a strong and constant CD54 expression.

In CD54+ de novo AML cases, the percentage of CD54 expressing leukemic cells was variable and did not generally correlate with the total number of blasts in each sample (data not shown). The detection of CD54 on only a fraction of leukemic blasts in positive samples may be viewed as a form of “subpopulation heterogeneity,” a phenomenon already reported for other antigens in AML. CD54 positive blast cells could take a “growth advantage” from a preferential interaction with T lymphocytes, monocytes, natural killer (NK), and stromal cells, which actively produce colony-stimulating factors and other cytokines and which express high amounts of the CD54 ligand, LFA-1 (CD11a).

In AML blasts, CD54 expression is significantly associated with that of CD34 and HLA-DR antigens, which are generally considered as differentiation-linked molecules. The association between CD54 and HLA-DR antigen expression in AML is noteworthy, since both molecules share several properties in terms of susceptibility to modulation by mitogens and cytokines and functional role in cell–cell interactions. Similarly, the association between CD54 and CD34 expression is of great interest, since the latter antigen is considered the earliest surface marker of hematopoietic stem cells.

In B-lymphoid malignancies, CD54 expression appears to be related to differentiation of neoplastic cells as defined by Foon and Todd. CD54 expression is low on acute leukemia and “dim SIg” CLL but is high on malignant cells arising from more mature compartments as in some NHL, PLL, “variant” CLL, and neoplasms of preplasmacytic and plasmacytic differentiation area, including multiple myeloma.

CD54 expression in B-CLL is heterogeneous. If B-CLL cases are divided on the basis of SIg intensity, CD54 positive samples are mainly restricted to “bright” SIg subsets (FMC7+). Furthermore, CD54 expression is inversely correlated with CD23 expression. Interestingly, both SIg brightness and lack of CD23 expression have been associated with poor clinical prognosis in B-CLL.

CD54 was also more expressed in high-grade than in low-grade B-NHL. The association of CD54 expression with a more aggressive clinical course of “bright SIg” B-CLL and intermediate or high-grade B-NHL is reminiscent of the association of CD54 expression in primary melanoma lesions with poor prognosis of the disease. Both findings are surprising, since CD54 facilitates the interactions between target cells and cytotoxic T cells and since the low expression of CD54 by some Burkitt’s lymphoma cell lines has been suggested to be a mechanism for their escape from immune destruction. The association between CD54 expression and poor prognosis in “bright SIg” B-CLL and high-grade B-NHL argues against a major role of this molecule in immune, cell-mediated destruction of leukemic cells in the course of the disease.

Some of the data reported in this article show discrepancies with previous observations on CD54 distribution on lymphohematopoietic cells. In our study we found that CD54 is expressed on malignant cells of about one third of the 88 patients with AML investigated. This frequency is markedly lower than that recently reported by Boyd et al, who found CD54 on malignant cells of 30 out of the 34 patients with AML tested. This discrepancy may reflect differences in the affinity and specificity of the anti-CD54 MoAb used, in the AML cytotypes studied, and/or in the cut-off values established to identify positive cases. The cut-off value used by Boyd et al is not indicated in their publication; we used a cut-off point of 20% stained cells, since this criterion is widely used for leukemia typing with MoAb in flow cytometry. These reasons, in addition to different criteria used to classify the patients, may account also for the conflicting results obtained by us and by Stauder et al about the distribution of CD54 in low- and intermediate- or high-grade B-NHL. The latter investigators, who reported no difference between the two groups of B-NHL, classified their patients according to the Kiel criteria. It is therefore likely that a number of lymphoma cases of intermediate grade according to the WF classification might have been included in their low-grade group.

The mechanism(s) underlying the differential expression of CD54 in various types of leukemias have not been investigated in the present study. These analyses will be greatly facilitated by the availability of recombinant DNA probes for this molecule. Experiments along this line are in progress in our laboratory.

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