Hematopathology / PAX5, OCT-2, and BOB.1 Expression in AML

Expression of the B Cell–Associated Transcription Factors PAX5, OCT-2, and BOB.1 in Acute Myeloid Leukemia

Associations With B-Cell Antigen Expression and Myelomonocytic Maturation

Sarah E. Gibson, MD,1 Henry Y. Dong, MD, PhD,2 Anjali S. Advani, MD,3 and Eric D. Hsi, MD1

Key Words: Acute myeloid leukemia; AML; PAX5; OCT-2; BOB.1

DOI: 10.1309/UJUL60UPUP3YJE93

Abstract

The aberrant expression of the B-cell transcription factor PAX5 has been described in a subset of acute myeloid leukemia (AML) with t(8;21)(q22;q22) in association with B-cell antigen expression. However, the expression of other B cell–associated transcription factors, particularly OCT-2 and its B cell–specific coactivator BOB.1, has not been described in AML. In this study, expression of PAX5, OCT-2 and BOB.1 was evaluated by immunohistochemical staining of bone marrow samples from 83 cases of AML. The expression patterns were correlated with t(8;21)(q22;q22), B cell–associated antigen expression, and AML subtype. We confirmed the expression of PAX5 in AML with t(8;21)(q22;q22), but also demonstrated its expression in cases that express B-cell antigens but lack this translocation. Although OCT-2 and BOB.1 were not associated with PAX5 expression, we report expression of OCT-2 in AML with myelomonocytic/monocytic maturation and BOB.1 in normal hematopoietic elements.

PAX5, a member of the PAX gene family of transcription factors, is a B-cell lineage transcription factor that is expressed in developing B cells, neural tissue, and testis.1 Also known as the B cell–specific activator protein, or BSAP, PAX5 has a major role in the commitment of bone marrow progenitor cells to the B-lymphoid lineage and continues to be expressed throughout B-cell development until it is down-regulated with plasma cell differentiation.2-5 In its control of B-cell commitment, PAX5 activates the expression of B cell–specific genes such as CD19, CD79a, blk, and Igα.6-9 At the same time, it represses the transcription of genes specific to other hematopoietic lineages, including myeloperoxidase, and macrophage colony-stimulating factor receptor.2,8,10 The expression of CD19 in particular seems to be entirely dependent on the presence of PAX5 in normal B cells.7 It has also been hypothesized that PAX5 mediates the balance between B-cell proliferation and immunoglobulin secretion.11,12

Alterations of the PAX5 gene, including reciprocal chromosomal translocations and hypermutation, have been described in B-cell malignancies.13-16 In addition, immunohistochemical studies have shown expression of PAX5 in B-cell leukemias and lymphomas, including classical Hodgkin lymphoma.17-20 In addition to B-cell leukemia/lymphoma, PAX5 expression has been identified in a subset of acute myeloid leukemias (AMLs), specifically in more than 30% of AMLs with t(8;21)(q22;q22).21 PAX5 seems to correlate with CD19 and CD79a expression in this subset of leukemia.21 During a search of CD19+ non–B-cell hematopoietic neoplasms, Dong22 found that expression of CD19 in AML and T-cell lymphoma/leukemia was closely associated with PAX5 expression. Although the initial 5 cases of PAX5+ and CD19+ AML were associated with t(8;21)(q22;q22), 3 cases of CD19+ AML...
without t(8;21)(q22;q22) were subsequently found to have strong PAX5 expression (H.Y.D., unpublished data, February 2006). It is thought that PAX5 is responsible for the aberrant CD19 expression in these cases of AML given the role of PAX5 in regulating CD19 expression.

Although PAX5 has been identified in t(8;21)(q22;q22) AML, the expression of other B-cell transcription factors, specifically OCT-2 and its coactivator BOB.1, has not been described in AML. OCT-2 is an octamer motif-binding transcription factor, which has been identified in B lymphocytes and neuronal cells. OCT-2 interacts with its B lymphocyte–specific coactivator, BOB.1, to activate immunoglobulin gene transcription. BOB.1 seems to have an important role in the antigen-dependent stages of B-cell development, where it has been shown to mediate germinal center formation. Its absence in BOB.1−/− mice is associated with the failure of germinal center development and the impaired production of transitional B cells and maturation of recirculating B cells.

Although OCT-2 and BOB.1 expression is down-regulated in the Reed-Sternberg cells of classical Hodgkin lymphoma, it is expressed in most cases of lymphocyte predominant Hodgkin lymphoma and other B-cell non-Hodgkin lymphomas. The overexpression of BOB.1 has also been described in germinal center–derived lymphomas and T-cell lymphomas.

Because the B-cell transcription factor PAX5 has been identified in a subset of AML with t(8;21)(q22;q22) and aberrant B-cell antigen expression, we hypothesized that other B-cell transcription factors, specifically OCT-2 and BOB.1, may be expressed in these cases. In this study, the expression of PAX5, OCT-2, and BOB.1 was evaluated by immunohistochemical staining of bone marrow samples from 83 cases of AML. The expression patterns were correlated with t(8;21)(q22;q22), B-cell–associated antigen expression, and AML subtype. We confirmed the expression of PAX5 in AML with t(8;21)(q22;q22), but also demonstrated its expression in cases lacking this translocation. Although OCT-2 and BOB.1 were not associated with PAX5 expression, we report expression of OCT-2 in AML with myelomonocytic/myocytic maturation and BOB.1 in normal hematopoietic elements.

### Materials and Methods

#### Samples

Approval for the study was obtained from the Cleveland Clinic Institutional Review Board (Cleveland, OH). Paraffin blocks from 16 consecutive cases of newly diagnosed AML with t(8;21)(q22;q22) identified between November 1999 and October 2004, 67 cases of newly diagnosed AML without t(8;21)(q22;q22) identified during 27 consecutive months, and 5 normal bone marrow samples were obtained. The leukemia samples included 16 AMLs with t(8;21)(q22;q22), 13 AMLs with maturation, 12 acute myelomonocytic leukemias, 11 AMLs without maturation, 7 AMLs with 11q23 abnormalities, 5 AMLs with multilineage dysplasia, 4 minimally differentiated AMLs, 3 acute promyelocytic leukemias with t(15;17), 3 acute monoblastic leukemias, 3 acute monocytic leukemias, 3 acute erythroid leukemias, 2 acute megakaryoblastic leukemias, and 1 AML with inv(16)(p13;q22). The bone marrow samples examined were B-5-fixed core biopsy specimens or formalin-fixed clot tissue blocks.

#### Tissue Microarray

Histologic slides were reviewed, and separate tissue microarrays were constructed from the B-5-fixed bone marrow core biopsy specimens and from the formalin-fixed bone marrow clot tissue blocks obtained (Beecher Instruments, Sun Prairie, WI). The bone marrow was sampled using 1.0-mm-diameter tissue cores selected from areas of the tissue with the highest concentration of blasts. The cores were arrayed in duplicate in the majority of samples, with a few samples having only 1 core.

#### Immunohistochemical Staining

Immunohistochemical staining was performed using automated immunohistochemical stainers (Ventana Benchmark, Ventana Medical Systems, Tucson, AZ) and antibodies to PAX5 (clone 24, dilution 1:20; BD Transduction Laboratories, San Jose, CA), OCT-2 (polyclonal, dilution 1:200; Santa Cruz Biotechnology, Santa Cruz, CA), BOB.1 (polyclonal, dilution 1:50; Santa Cruz Biotechnology), CD22 (clone FPC1, dilution 1:10; NeoMarkers, Fremont, CA), and CD79a (clone JCB117, dilution 1:20; DAKO, Carpinteria, CA). Protein-matched negative control experiments for PAX5 (mouse IgG1, DAKO), OCT-2, and BOB.1 (rabbit immunoglobulin fraction, DAKO) were also performed. In addition, all identified PAX5+ cases underwent double-labeling immunohistochemical staining with PAX5 and CD3 (polyclonal, dilution 1:600; Cell Marque, Hot Springs, AR), CD20 (clone L26, dilution 1:400; DAKO), and CD34 (clone QBEnd/10, Ventana Medical Systems), myeloperoxidase (polyclonal, Ventana Medical Systems), muramidase (polyclonal, dilution 1:100; DAKO), or hemoglobin A (polyclonal, dilution 1:50; Novocastra, Newcastle upon Tyne, England) to confirm that the PAX5+ cells were leukemic blasts and not other hematopoietic elements. Heat-induced epitope retrieval was performed using CC1 solution (Ventana Medical Systems) for PAX5, OCT-2, BOB.1, CD22 (B-5-fixed tissue samples), CD79a, CD3, and CD20. CC2 solution (Ventana Medical Systems) was used for epitope retrieval of CD22 on formalin-fixed tissue samples.

AML and normal bone marrow samples were reviewed for expression of these proteins in myeloid blasts. The pattern of staining was classified as positive (staining in >10% of...
blasts) or negative. The expression of PAX5, OCT-2, and BOB.1 was characterized by nuclear staining, and CD22 and CD79a expression was characterized by cytoplasmic staining.

Flow Cytometry, Cytogenetic, and Fluorescence In Situ Hybridization Studies

Routine flow cytometry was performed on all AML cases. B-cell antigen expression was determined by evaluating gated blasts for the coexpression of myeloid markers (CD13 and CD33) with B-cell antigens (CD19 and CD20). Cases were judged positive for CD19 or CD20 if greater than 20% of the blasts were positive relative to an autofluorescent control. Cytogenetic studies were available for 82 of 83 AML cases as part of the routine diagnostic workup. In addition, fluorescence in situ hybridization (FISH) for AML1/ETO (Vysis, Des Plaines, IL) was performed on 4 of 5 cases of CD19+ AML without previous cytogenetic evidence of t(8;21)(q22;q22) at the Cleveland Clinic. FISH was not performed on the fifth case owing to lack of available tissue.

Results

PAX5 Expression in Normal Bone Marrow Samples

In the 5 normal bone marrow samples, there was strong nuclear expression of PAX5 in lymphoid cells. Double immunohistochemical staining for PAX5 and CD20 and CD79a confirmed that these cells represented B-lineage cells. Rare PAX5+ cells were negative for CD20 or CD79a. However, all PAX5+ cells were negative for CD3. The identity of these cells is uncertain. They may represent very early hematogones with CD79a expression below the limit of detection of our immunostain or, perhaps, nonlymphoid cells.

PAX5 Expression in AML

PAX5 expression was identified in 10 cases of AML. Although PAX5 positivity was defined as nuclear staining in more than 10% of myeloid blasts, nuclear staining for PAX5 was identified in 20% to 90% of myeloid blasts in the majority of positive cases (n = 9). The nuclear staining for PAX5 in myeloid blasts was usually weaker than staining in residual B lymphocytes. An isotype control, using an equal concentration of mouse IgG1, was negative in all PAX5+ cases. To confirm that PAX5 staining was present in myeloid blasts, double-labeling immunohistochemical staining was performed with PAX5 and CD3, CD20, CD34, myeloperoxidase, and hemoglobin A. Of 10 PAX5+ cases, 9 were positive for CD34 and myeloperoxidase. The 10th PAX5+ case, an acute monoblastic leukemia, was negative for CD34 and myeloperoxidase. However, the blasts were positive for muramidase, confirming monocytic differentiation. All PAX5+ myeloid blasts were negative for CD3, CD20, and hemoglobin A.

Of the 16 cases of AML with t(8;21)(q22;q22) confirmed by cytogenetic or FISH studies, 7 were PAX5+.

Although CD19 was expressed in all 7 of the t(8;21)(q22;q22) AML cases, PAX5 expression was not identified in maturing myeloid, erythroid, or megakaryocytic cells. Plasma cells were consistently negative for PAX5 expression.

**Image 1** PAX5 expression in normal bone marrow. A, PAX5 nuclear expression in B lymphocytes is shown with a double stain for CD79a (arrow) (original magnification ×1,000). Rare PAX5+ cells are negative for CD79a and are of uncertain lineage. These cells may represent early hematogones or other nonlymphoid hematopoietic cells. Plasma cells are consistently negative for PAX5 (arrowhead). B, A double stain for PAX5 and CD3 shows that the PAX5+ cells are not T lymphocytes (arrowhead) (original magnification ×1,000). CD3+ cells are consistently negative for PAX5 (arrow).
PAX5+ cases, CD20 expression was not identified. CD79a and CD22 expression was evaluated in all 7 t(8;21)(q22;q22) PAX5+ cases. CD79a expression was identified in 1 case, whereas CD22 was expressed in none. Of the 9 t(8;21)(q22;q22) cases without PAX5 expression, 7 expressed CD19, 1 expressed CD79a, and none expressed CD22.

Of the 67 cases of AML without t(8;21)(q22;q22), 3 expressed PAX5 (Table 1). Thus, as previously reported, PAX5 expression was highly correlated with t(8;21)(q22;q22) (P = .0002 and P < .0001, respectively; Fisher exact test).21 These 3 cases included 1 case of AML minimally differentiated, 1 AML without maturation, and 1 case of AML with an 11q23 abnormality. Expression of CD19 was detected in 2 of these cases. The third case had t(11;19)(q23;p13.1) and CD20 expression without CD19 expression. Of note, 6 additional cases of AML with 11q23 abnormalities were included in this cohort, none of which expressed PAX5. Thus, if there is an association between PAX5 expression and this genetic abnormality, it is not a strong one. CD79a and CD22 expression was evaluated in all of the non-t(8;21)(q22;q22) cases and was not identified. There was a significant association between PAX5 expression and CD19 expression in the entire cohort of cases.

<table>
<thead>
<tr>
<th>Leukemia Diagnosis</th>
<th>No. of Cases</th>
<th>PAX5</th>
<th>OCT-2</th>
<th>BOB.1</th>
<th>CD19</th>
<th>CD20</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML with t(8;21)(q22;q22)</td>
<td>16</td>
<td>7 (44)†</td>
<td>3 (19)</td>
<td>6 (38)</td>
<td>14 (88)‡</td>
<td>0 (0)</td>
</tr>
<tr>
<td>inv(16)(p13;q22)</td>
<td>1</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>t(15;17)(q22;q12)</td>
<td>3</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>t(11)(q23) abnormalities‡</td>
<td>7</td>
<td>1 (14)</td>
<td>4 (57)</td>
<td>4 (57)</td>
<td>0 (0)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Multilineage dysplasia</td>
<td>5</td>
<td>0 (0)</td>
<td>1 (20)</td>
<td>2 (40)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AML, minimally differentiated</td>
<td>4</td>
<td>1 (25)</td>
<td>2 (50)</td>
<td>2 (50)</td>
<td>2 (50)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>AML without maturation</td>
<td>11</td>
<td>1 (9)</td>
<td>2 (18)</td>
<td>6 (55)</td>
<td>1 (9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AML with maturation</td>
<td>13</td>
<td>0 (0)</td>
<td>1 (8)</td>
<td>5 (39)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Acute myelomonocytic</td>
<td>12</td>
<td>0 (0)</td>
<td>9 (75)</td>
<td>7 (58)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Acute monocytic/monocytic</td>
<td>6</td>
<td>0 (0)</td>
<td>2 (33)</td>
<td>3 (50)</td>
<td>0 (0)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Acute erythroid</td>
<td>3</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (33)</td>
<td>1 (33)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>Acute megakaryoblastic</td>
<td>2</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (50)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>10 (12)</td>
<td>25 (30)</td>
<td>40 (48)</td>
<td>19 (23)</td>
<td>6 (7)</td>
</tr>
</tbody>
</table>

AML, acute myeloid leukemia.
† Data are given as number (percentage).
‡ All cases had myelomonocytic/monocytic differentiation.

AML, acute myeloid leukemia with t(8;21)(q22;q22). A, The bone marrow core biopsy specimen is characterized by increased blasts, accounting for approximately 70% of total cellularity (H&E, original magnification ×400). B, Approximately 50% of myeloid blasts exhibit nuclear staining for PAX5. At higher magnification, the myeloid blasts have weaker expression of PAX5 than residual B cells (original magnification ×1,000).
(P < .0001; Fisher exact test). Even when cases of t(8;21)(q22;q22) AML were excluded, there was still a significant association between PAX5 and CD19 expression (P = .01; Fisher exact test).

OCT-2 and BOB.1 Expression in Normal Bone Marrow Samples

Although OCT-2 expression was not identified in the hematopoietic cells of normal bone marrow samples, BOB.1 expression was identified in a small subset (range, 10%-30%) of differentiated myeloid, erythroid, and megakaryocytic cells in all 5 normal bone marrow samples examined. However, the intensity of staining was weaker than that seen in lymphocytes. Double immunohistochemical staining for BOB.1 and myeloperoxidase or hemoglobin A confirmed this observation Image 4.

OCT-2 and BOB.1 Expression in AML

Expression of OCT-2 and BOB.1 was identified in 25 (30%) and 40 (48%) cases of AML, respectively (Table 1). Although expression of OCT-2 and BOB.1 was defined as nuclear staining in more than 10% of myeloid blasts, nuclear staining for these proteins was identified in 20% to 90% of myeloid blasts in all positive cases (OCT-2, n = 25; BOB.1, n = 40) Image 5. A negative control sample stained appropriately in all OCT-2+ and BOB.1+ cases. Expression of OCT-2 and BOB.1 was not significantly associated with t(8;21)(q22;q22) AML (P = .2 and P = .3, respectively; Fisher exact test). Neither OCT-2 nor BOB.1 expression correlated with PAX5 expression (P = .7 and P = .1, respectively; Fisher exact test). Although PAX5 expression was strongly associated with CD19 expression, there was no statistically significant association between OCT-2 or BOB.1 expression and the B-cell antigens CD19, CD20, CD22, and CD79a Table 3.

Interestingly, OCT-2 expression was highly associated with myelomonocytic/monocytic differentiation. Of the 25 cases with myelomonocytic/monocytic differentiation, which includes 7 cases with 11q23 abnormalities, OCT-2 expression was identified in 15 (60%) of 25 cases but in only 10 (17%) of 58 AML cases without monocytic differentiation (P = .0002; Fisher exact test). BOB.1 showed no such association (P = .2;
Image 4: BOB.1 expression in normal bone marrow. A, BOB.1 nuclear expression in myeloid cells is shown with a double stain for myeloperoxidase (arrow) (original magnification ×1,000). Nuclear staining is also identified in megakaryocytes. The majority of erythroid cells are negative for BOB.1 (arrowhead). B, A double stain with BOB.1 and hemoglobin A shows a rare positive erythroid precursor (arrow) (original magnification ×1,000).

Image 5: Acute monoblastic leukemia. A, The bone marrow core biopsy is characterized by increased blasts accounting for approximately 70% of the total cellularity (H&E, original magnification ×400). B, Approximately 70% of blasts exhibit nuclear staining for OCT-2 (original magnification ×1,000). C, The nuclear expression of BOB.1 was identified in approximately 80% of blasts (original magnification ×1,000).
Fisher exact test) Table 4. Coexpression of OCT-2 and BOB.1 was also associated with myelomonocytic/monocytic differentiation \((P = .001; \text{Fisher exact test})\). However, this is probably due to the strong association of OCT-2.

**Discussion**

This study demonstrated that the B-cell transcription factors PAX5 and OCT-2 and the coactivator BOB.1 may be expressed in AMLs with and without associated cytogenetic abnormalities. Similar to a study by Tiacci et al.\(^\text{21}\) we identified PAX5 in a subset of AMLs with t(8;21)(q22;q22). However, PAX5 expression was also seen in 3 cases of AML without t(8;21)(q22;q22), a finding not reported in the previous study. Of these 3 PAX5+ cases, 2 were associated with CD19 expression, the transcription of which has been shown to be controlled by PAX5.\(^\text{6}\) AML1 has been shown to bind via its Runt domain to PAX5, which in turn activates the blk gene promoter during B-cell differentiation.\(^\text{34}\) Thus, it has been proposed that the fusion gene AML1-ETO found in t(8;21)(q22;q22) AML interacts similarly with PAX5 to activate transcription of CD19 and, potentially, CD79a.\(^\text{21}\)

The identification of 2 cases of non-t(8;21)(q22;q22) AML with PAX5 and CD19 expression in the present study suggests other mechanisms must be at play. Indeed, 3 additional PAX5+/CD19+ cases lacking t(8;21)(q22;q22) have been identified by one of us (H.Y.D.; data not shown). Furthermore, 10 cases of AML in this series expressed CD19 in the absence of PAX5. Thus, it is likely that CD19 expression in AML is not entirely controlled by PAX5, and it would be worthwhile to investigate the expression of other B-cell–associated transcription factors. Two such candidates could include PU.1 and E2A; however, these transcription factors also seem to have functions in nonlymphoid cells.\(^\text{35,36}\)

In the study by Tiacci et al.,\(^\text{21}\) PAX5 expression in t(8;21)(q22;q22) AML was associated with the expression of both CD19 and CD79a. Although PAX5 was also associated with CD19 expression in our series, there was no association with CD79a expression. The reason for this apparent discrepancy is uncertain. It is possible that the sensitivity of our immunostain is less than that of Tiacci et al.\(^\text{21}\) However, it is noteworthy that CD79a was not found to be expressed in 39 AML-M2 cases in 2 previous studies.\(^\text{37,38}\)

The expression of OCT-2 and BOB.1 has not been previously described in AML. In this study, expression of OCT-2 and BOB.1 was identified in 30% and 48% of AML cases, respectively. Expression was not associated with B-cell antigen expression or PAX5 expression. These findings suggest that the mechanism underlying OCT-2 and BOB.1 expression in AML is unrelated to PAX5 and that OCT-2 and BOB.1 are incapable of effecting B-cell differentiation in this cell type. OCT-2 was, however, associated with myelomonocytic/monocytic differentiation in AML. Despite the accepted role of OCT-2 as a B-cell transcription factor, OCT-2 has been previously described in murine and human monocytes by electrophoretic mobility shift assays.\(^\text{39-41}\) It has, in fact, been reported to be induced on monocytic differentiation of myeloid cell lines and can regulate CD11c expression.\(^\text{40}\) Thus, our finding of OCT-2 expression in these leukemias may reflect its normal physiologic functions. Owing to its expression in other types of AML, OCT-2 cannot be recommended as a specific marker of myelomonocytic or monocytic differentiation.

Previous studies have shown that B-cell precursors have the ability to undergo myeloid differentiation into mature

| Table 3 |
| Expression of B-Cell Antigens in OCT-2+ or BOB.1+ Acute Myeloid Leukemia* |

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>CD19</th>
<th>CD20</th>
<th>CD22</th>
<th>CD79a</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCT-2+</td>
<td>25</td>
<td>4 (16)</td>
<td>3 (12)</td>
<td>0</td>
</tr>
<tr>
<td>OCT-2−</td>
<td>58</td>
<td>15 (26)</td>
<td>3 (5)</td>
<td>0</td>
</tr>
<tr>
<td>BOB.1+</td>
<td>40</td>
<td>7 (18)</td>
<td>4 (10)</td>
<td>0</td>
</tr>
<tr>
<td>BOB.1−</td>
<td>43</td>
<td>12 (28)</td>
<td>2 (5)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Data are given as number (percentage).

| Table 4 |
| Expression of B Cell–Associated Transcription Factors in Myelomonocytic/Monocytic AML* |

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>PAX5</th>
<th>OCT-2</th>
<th>BOB.1</th>
<th>OCT-2/BOB.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelomonocytic/ monocytic AML</td>
<td>25</td>
<td>1 (4)</td>
<td>15 (60)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Non–myelomonocytic/monocytic AML</td>
<td>58</td>
<td>9 (16)</td>
<td>10 (17)</td>
<td>26 (45)</td>
</tr>
</tbody>
</table>

* Data are given as number (percentage).

AML, acute myeloid leukemia.
macrophages spontaneously and following exposure to various cytokines, drugs, and retroviral infections. In addition, it has been shown that the enforced expression of the myeloid-associated transcription factors C/EBPα and C/EBPβ in differentiated B cells leads to rapid macrophage differentiation, whereas the expression of the E12 transcription factor in a macrophage cell line leads to the induction of B-lineage genes, including EBF, IL7Rα, λ5, and Rag-1. These observations suggest that there may be a close relationship between B-cell and monocyte/macrophage differentiation. The identification of a bipotential B-macrophage progenitor cell population accounting for approximately 0.02% of bone marrow cells in adult mice lends support to this hypothesis. The expression of OCT-2 in AMLs with a monocytic component may reflect a bipotential myeloid/B-cell progenitor, which has been identified in multilineage progenitor assays.

BOB.1 expression was identified in a subset of myeloid, erythroid, and megakaryocytic cells in normal bone marrow samples. In addition, it was expressed in almost half of AMLs tested without apparent predilection for particular subtypes. Interestingly, BOB.1 expression was not identified by Northern blot analysis in the human promyelocytic cell line HL-60, promonocytic line U937, or monocytic line Mono Mac 6. However, it is possible that more sensitive amplification-based techniques would detect BOB.1 RNA. Furthermore, protein expression does not always correlate with messenger RNA levels. Although immunohistochemical staining has revealed BOB.1 expression in a subset of CD3+ T cells and T-cell lymphomas, to our knowledge, similar studies of myeloid, erythroid, and megakaryocytic cells in normal bone marrow samples have not been reported in the literature.

This study demonstrates that the B-cell transcription factors PAX5 and OCT-2 and the coactivator BOB.1 are expressed in AML with and without associated cytogenetic abnormalities. Although PAX5 was associated with t(8;21)(q22;q22) AML and CD19 expression, it was not associated with OCT-2 or BOB.1 expression. However, OCT-2 was associated with myelomonocytic/monocytic differentiation. In addition, the expression of BOB.1 was identified in a subset of differentiated myeloid, erythroid, and megakaryocytic cells in normal bone marrow samples. Although the significance of this finding is unknown, it seems that BOB.1 may be more widely expressed than previously thought. The mechanisms underlying the expression of these transcription factors and their consequences in AML require further study.

References


From the Departments of 1Clinical Pathology and 2Hematology and Medical Oncology, Cleveland Clinic, Cleveland, OH; and 3Genzyme Genetics, New York, NY.

Address reprint requests to Dr Hsi: Dept of Clinical Pathology, Cleveland Clinic, 9500 Euclid Ave, L11, Cleveland, OH 44195.

© American Society for Clinical Pathology

Hematopathology / ORIGINAL ARTICLE

Am J Clin Pathol 2006;126:916-924
DOI: 10.1093/ajcp/puj027


