# Chromosome Aberrations in CD34-Positive Acute Myeloid Leukemia

## Correlation with Clinicopathologic Features

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**ABSTRACT:** *Morphologic, immunologic, and cytogenetic features were studied in 30 newly diagnosed patients with CD34-positive (CD34+) de novo acute myeloid leukemia (AML) in comparison with 30 patients with CD34-negative (CD34−) AML. Karyotype at diagnosis was abnormal in 25/30 CD34+ AML patients, of which nine had major karyotype aberrations (MAKA). Clonal chromosome changes were detected in 9/30 patients with CD34− AML. The most frequent chromosome aberration in CD34+ patients was −5/5q−, an aberration showing a strong association with the M2 FAB subtype of AML. Other recurring chromosome changes involved chromosome 16q (four cases) and chromosome 17p (three cases). Total or partial monosomy 7q was detected in three cases. Among CD34− AML, two patients had the classical t(15;17) and two had structural aberrations of 6q. Among patients with CD34+ AML, nine had MAKA in association with trilineage myelodysplasia (TMDS). TMDS was infrequent in CD34+ AML without MAKA and in CD34− AML. Complete remission (CR) was achieved in 8/30 CD34+ AML (26%), as compared with 22/30 CD34− AML (73%), and median survival was 2 months in the former group and 8 months in the latter. No patient with CD34+ AML and MAKA achieved CR, whereas 8/21 CD34+ AML without complex chromosome changes or with normal karyotype achieved CR.*

*In conclusion, a distinct cytogenetic profile may be associated with CD34+ AML. Cytogenetic findings in CD34+ AML may be clinically relevant in that they may disclose a subset of patients with MAKA with a low CR rate.*

## INTRODUCTION

The CD34 monoclonal antibody detects a 110–115 kD membrane glycoprotein present on 1–2% of normal bone marrow cells, including unipotent and multipotent progenitors [1, 2]. CD34 expression is higher on early progenitor cells and tends to decrease progressively with maturation [3].

In order to better understand the clinico-biologic significance of CD34 positivity in acute leukemia, growing attention has been devoted over the last 5 years to the presence of CD34+ blast cells in acute myeloid leukemia (AML), highlighting some important cytogenetic and clinical correlations in this immunologic subset of AML [4–6].

This stage-specific marker was found in 40–50% of AML cases, possibly identifying a subset of patients with a low remission induction rate. Patients with CD34+ AML have been frequently shown to fall within the M1-M2 category of the FAB classification and to carry clonal abnormalities involving the long arm of chromosome 7 [4, 5].

To further analyze the cytogenetic and clinicopathologic features of CD34+ AML, we performed morphologic, immunologic, and cytogenetic (MIC) studies in 60 newly diagnosed adult AML patients, 30 of whom expressed the CD34 antigen in more than 20% blast cells.

## PATIENTS AND METHODS

Sixty patients with de novo AML, seen at our Institution between January 1988 and July 1992, are included in the present report. Bone marrow (BM) smears were available for review in all cases. Immunologic and cytogenetic analysis were performed successfully at diagnosis. The patients were divided into two groups according to the positivity or negativity for the CD34 stem cell marker.

### Cytologic Studies

*Morphology:* Patients were classified according to the FAB criteria [7]. Bone marrow smears were reviewed to assess the presence of myelodysplastic features. According to previously

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proposed criteria [8, 9], trilineage myelodysplasia (TMDS) was defined by the presence of more than 25% dysplastic erythroblasts and more than 50% abnormal granulocytes and megakaryocytes.

*Immunophenotyping:* BM cytospin preparations and/or peripheral blood smears were stained by an immunocytochemical method using alkaline phosphatase–anti-alkaline phosphatase (APAAP) complexes [10]. To minimize Fc nonspecific binding, the slides were pre-incubated with rabbit serum (Dakopatts, Copenhagen, Denmark). Reactivity was tested to a panel of monoclonal antibodies purchased from various firms: stem cell marker: HPCA-1 (CD34); myeloid-associated markers: LeuM1 (CD15) (Becton-Dickinson, Mountain View, CA); My9 (CD33), My7 (CD13), My4 (CD14) (Coulter Inc., Hialeah, FL), GpIIb/IIIA (CD41a) (Dakopatts, Copenhagen, Denmark); lymphoid-associated markers: Leu12 (CD19) (Becton-Dickinson), OKBCalla (CD10), OKT16 (CD7), OKT11 (CD2) (Ortho Diagnostic System Inc., Raritan, NJ).

### Cytogenetic Studies

Chromosome analysis was performed at initial presentation in all patients. BM samples were cultured for 24 and 48 hours without mitogens. Synchronization with methotrexate and thymidine was performed. Metaphases were G-banded with Wright stain [10]. Chromosome aberrations were described according to the International System for Human Cytogenetic Nomenclature (ISCN) [11]. The presence of three or more events of translocation or non-disjunction in the same clone was defined as "major karyotype aberration" (MAKA). Minor karyotype aberration (MIKA) was defined by one or two such events [12].

### Clinical Studies

Salient clinical features at presentation, outcome of remission induction therapy, and survival were analyzed in all patients.

## RESULTS

Thirty patients (50%) had more than 20% blast cells expressing the CD34 antigen. Positivity for the anti-CD34 monoclonal antibody was less than 3% in the blast cells of 30 patients, here referred to as CD34 - .

### Cytologic Studies

FAB subtypes in CD34 + and CD34 - are detailed in Table 1. The M2 FAB subtype was found more frequently among CD34 + patients (12/30) than among CD34 - patients (2/30). Conversely, the M5 FAB subtype was found in 4/30 CD34 + patients versus 11/30 CD34 - patients.

Morphologic abnormalities affecting multiple cell lineages, fulfilling the stringent criteria for the diagnosis of AML with TMDS, were present in 12 patients with CD34 + AML and were not assessable in 10 patients because of an overwhelming blast infiltrate. In eight patients with CD34 +, AML dysplastic features were present only in the erythroid and/or granulocytic series.

In patients with CD34 - AML, morphologic abnormalities of the non-blast cell population were mostly confined to the granulocytic lineage (seven patients), whereas myelodysplasia affecting more than one cell lineage was seen in five patients, none of whom fulfilled the cytologic criteria for the diagnosis of AML with TMDS. TMDS was not assessable in 18 patients because of an overwhelming blast infiltrate.

**Table 1** Clinical features at presentation, FAB subtypes, response to chemotherapy and survival in patients with AML CD34 + and CD34 - [a]

| | CD34 + | CD34 - |
|---|---|---|
| Age (yr) | 64 (24–81) | 63 (14–75) |
| Hemoglobin value (g/dl) | 8.6 (5–10.5) | 9.2 (5.6–13) |
| Leukocyte count ( $\times 10^9$/L) | 8. (1–83) | 25. (1–249) |
| Platelet count ( $\times 10^9$/L) | 90. (18–488) | 80. (26–240) |
| FAB subtypes[b] | M1 (3), M2 (12) M4 (7), M5 (4), M6 (2), M7 (2) | M1 (2), M2 (2) M3 (4), M4 (11) M5 (11) |
| CR (%) | 33 | 73 |
| Survival (mo) | 2 | 8 |

[a] The results are reported as median value; variation ranges are given in parentheses.

[b] Number of cases in each FAB category.

*Abbreviations:* FAB, French-American-British; AML, acute myeloid leukemia; CR, complete remission rate.

*Immunophenotyping:* All cases expressed at least one myeloid-associated antigen (CD33, CD13, CD15, CD14, glycophorin, and CD41a).

CD34 expression was negatively correlated with the CD14 and CD15 positivity, the latter two myelomonocytic antigens having been found more frequently in CD34 - AML, as reported in Figure 1, where immunophenotypic data are summarized.

Unequivocal positivity for the CD41a platelet antigen was found in a minority of cells (5–10%) in six patients with CD34 + AML and in one patient with CD34 - AML.

Inappropriate expression of lymphoid-associated antigens was detected in six patients with CD34 + AML, two of whom expressed the CD19 antigen, two the CD10, one the CD2, and one the CD7. Positivity for CD7 was found in one patient with CD34 - AML.

### Cytogenetic Studies

Results of chromosome investigations are detailed in Tables 2 and 3.

Karyotype at diagnosis was abnormal in 25/30 patients with CD34 + AML, nine of whom had MAKA. The most frequent aberrations involved the long arm of chromosome 5. Total or partial monosomy 5q plus additional aberrations were detected in eight patients with AML-M2, whereas one patient with AML-M4 had a 5q translocation as the sole aberration. In five cases the abnormal 5q chromosome was found in the context of complex karyotypes.

Other recurring chromosome aberrations in this group of patients were deletions or translocations of 16q22 (four patients), and deletions or translocations of 17p and -7/7q - (three patients). Trisomy 11q, del(11)(q13q23), and monosomy 17 were found in two patients each.

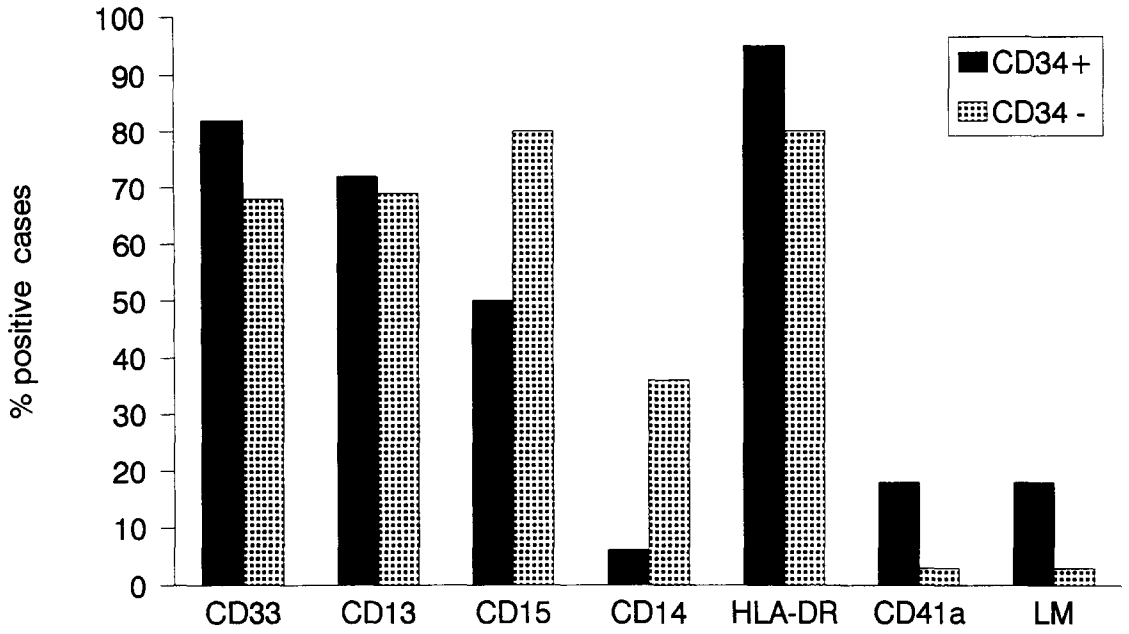


**Figure 1** Percentage of AML cases showing more than 20% positivity for immunologic markers (CD34+ cases: dark columns; CD34- cases: dotted columns) (LM: lymphoid-associated markers).

**Table 2** Clonal chromosome aberrations in 25 patients with CD34+ AML

| Patient no. | Age (yr) | FAB subtype | Modal Karyotype | Abnormal cells/ normal cells |
|---|---|---|---|---|
| 1 | 67 | M4 | 46,XX,der(1)add(1)(q32)i(1)(q10)46,idem,i(11)(q10) | 8/3 |
| 2 | 51 | M4 | 45,XX, - 5,der(22)t(22;?)(q11;?) | 6/6 |
| 3 | 61 | M4 | 47,XY, + 8 | 5/5 |
| 4 | 54 | M2 | 46,XX,t(5;10)(q12;q26) | 8/2 |
| 5 | 33 | M6 | 49,XY, + 11,der(13)t(13;?)(p11;?), + mar1, + mar2/ 50,idem, + mar3 | 9/7 |
| 6 | 26 | M2 | 47,XX,t(8;21)(q22;q22),del(15)(q15) | 7/3 |
| 7 | 40 | M6 | 45,XY, - 8,der(13)t(13;?)(q14;?),del(20)(q11q13) | 12/5 |
| 8 | 24 | M1 | 46,XY,del(3)(q21q26),dup(17)(q12q14) | 12/4 |
| 9 | 31 | M4 | 46,XX,t(9;11)(p22;q23) | 8/4 |
| 10 | 55 | M2 | 44,XX,del(5)(q13q33),del(16)(q22),der(17) t(17;?)(p12;?), - 18,der(20)t(20;?)(p11;?), - 21/45,idem, + mar | 10/0 |
| 11 | 71 | M2 | 46,XX, - 4,del(5)(q21q32), + 10, - 14,del(17)(p11), + mar | 8/3 |
| 12 | 47 | M4 | 47,XX, + 11 | 6/4 |
| 13 | 64 | M2 | 46,XX,del(6)(q22)/47,idem, + 22 | 10/0 |
| 14 | 50 | M4 | 44,XY,der(6)t(6;7)(p23;p14), - 7,der(16)t(11;16) (q13;q22), - 19/45,idem, + mar1 | 10/0 |
| 15 | 61 | M2 | 43,XY, - 3, - 5,add(15)(q22), - 17 | 8/2 |
| 16 | 72 | M2 | 43,XY, - 5,del(11)(q23),t(12;13;15) (q13;q13;p11),del(16)(q22),der(17)t(17;?) (p12;?), - 18, - 21 | 10/0 |
| 17 | 69 | M2 | 47,XY, + mar(E-size) | 10/0 |
| 18 | 61 | M2 | 45,XY, - 5,i(17q) | 7/3 |
| 19 | 69 | M5 | 46,XY,del(11)(q13q23) | 8/4 |
| 20 | 73 | M7 | 45,XY, - 17 | 4/6 |
| 21 | 64 | M7 | 46,XY,del(7)(q22q35)/45,idem, - 9 | 12/0 |
| 22 | 69 | M4 | 46,XX,del(16)(q22) | 12/6 |
| 23 | 81 | M2 | 46,XX,del(5)(q21q31) | 10/0 |
| 24 | 68 | M2 | 44,XX,del(5)(q13q31), - 7,del(11)(q13q23), - 12 | 6/4 |
| 25 | 70 | M1 | 45,XX, - 21 | 5/5 |

*Abbreviations:* AML, acute myeloid leukemia; FAB, French-American British.

**Table 3** Clonal chromosome aberrations in 10 patients with CD34 - AML

| Patient no. | Age (yr) | FAB subtypes | Modal Karyotype | Abnormal cells/ normal cells |
|---|---|---|---|---|
| 1 | 21 | M3 | 46,XX,t(15;17)(q22;q12) | 10/0 |
| 2 | 14 | M3 | 46,XY,t(15;17)(q22;q12),47,idem, + 22 | 10/0 |
| 3 | 25 | M1 | 45,XY,inv(3)(q21q26), - 8/46,inv(3)(q21q26),del(8)(q12) | 9/2 |
| 4 | 75 | M5 | 46,XY,der(8)t(8;?)(q22;?) | 4/6 |
| 5 | 36 | M5 | 46,XX,del(6)(q12q14) | 6/4 |
| 6 | 75 | M4 | 47,XY, + 15 | 8/2 |
| 7 | 68 | M4 | 46,XY,del(5)(q14q21)/43,idem, - X, - Y, - 7 | 9/1 |
| 8 | 56 | M1 | 46,XX,del(4)(p15) | 7/3 |
| 9 | 60 | M4 | 46,del(6q) | 7/3 |

Nine of 30 patients with CD34 - AML had chromosome aberrations, one of whom had MAKA. In this group, two patients with AML-M3 had the t(15;17) and two patients had aberrations of the long arm of chromosome 6. Aberrations involving the long arm of chromosomes 3 and 5 were detected in one patient each.

### Clinical Features

Clinical data at presentation are summarized in Table 1.

Except for median white blood cell count, no important difference emerged when comparing clinical features in patients with CD34 + AML and those with CD34 - AML. The median age, hemoglobin value, and platelet count were similar. The M2 and M5 FAB subtypes were more frequently encountered in CD34 + and CD34 - patients, respectively.

All patients were treated with a standard induction regimen consisting of an anthracycline drug with cytarabine, in combination with vindesine, cytarabine and etoposide, when the FAB diagnosis was M4 or M5. Eight of 30 patients (27%) with CD34 + AML attained complete remission (CR), compared with 22/30 (73%) with CD34 - AML ($p$ = 0.0003). The overall median survival was 2 months in the CD34 + group and 8 months in the CD34 - AML.

### Cytogenetic Findings and Clinico-Cytologic Features

In patients with CD34 + AML, two subgroups of patients according to the presence or absence of MAKA could be identified.

All nine patients with MAKA had TMDS (nos. 5, 7, 10, 11, 14, 15, 16, 21, and 24 in Table 2), six of whom had a minor megakaryoblastic component (nos. 5, 10, 11, 14, 16, and 24 in Table 2), as shown by positivity for the CD41 platelet antigen.

In patients with MIKA or normal karyotype, TMDS was detected in 3/16 cases, none of whom had a minor megakaryoblastic component.

Inappropriate expression of lymphoid antigens was detected in six patients (nos. 1, 2, 6, 9, 19, and 22 in Table 2) with MIKA or normal karyotype.

A significant difference in the complete remission rate of these two subgroups was detected: none of the patients with MAKA attained a CR, whereas 8/21 (31%) patients (nos. 1, 4, 6, 8, 9, 12, 13, and 25 in Table 2) with MIKA or normal karyotype attained CR ($p$ = 0.03).

## DISCUSSION

Morphologic, immunologic, and cytogenetic studies have been shown to be valuable in defining disease subsets of AML with distinct clinicopathologic features and prognosis [13–16].

This multiparameter study of 60 newly diagnosed AML patients treated at a single institution extends previous observations on CD34 + AML [4–6], showing that a) CD34 + AML has a distinct cytogenetic profile with respect to CD34 - AML; b) within CD34 + AML, a subset of patients with distinct cytologic and clinical features can be recognized according to the cytogenetic pattern; and c) prognosis in CD34 + AML is worse than in CD34 - AML.

### Cytogenetic Profile of CD34 + AML

The frequent occurrence of aberrations involving the long arm of chromosome 7 in CD34 + AML was recognized as early as 1988 by Vaughan and colleagues [4] and later confirmed by Borowitz et al. [6], who found the -7/7q - abnormality in 8/26 CD34 + AML as compared with 1/28 CD34 - AML. Likewise, Geller et al. [6] frequently detected abnormalities of chromosome 5 and/or 7 in CD34 + AML. In these series, however, a significant fraction of patients with preceding chemotherapy of another tumor (secondary AML) or with a prior history of myelodysplasia was included.

In this study of de novo AML, the most frequent chromosome abnormality in CD34 + patients was -5/5q - (eight cases), whereas aberrations of chromosome 7 were detected in three patients. All patients with 5q abnormalities had additional chromosome changes and 5q - was never found as the sole aberration.

All eight patients with -5/5q - had features of AML-M2, while only four patients with CD34 + AML-M2 did not show chromosome 5q abnormalities, thus suggesting that the AML-M2/-5/5q - subtype may represent a previously unrecognized cytologic-cytogenetic association among CD34 + AML.

Noteworthy is the observation that our patients with AML-M2/-5/5q - showed a poor prognosis, none of them having achieved CR with a survival range of less than 1–15 months (median 1 month).

Other recurring chromosome aberrations involved the long arm of chromosome 16 with a breakpoint at band q22 and the short arm of chromosome 17 in four and three cases, respectively.

All patients with 16q22 aberrations had multiple chromosome changes, frequently trilineage myelodysplasia, and did not show abnormal eosinophils in the BM, suggesting that complex karyotypes with aberrations of 16q may be associated with a different cytologic picture, compared with that of patients carrying the inv(16)(p13q22). This finding is in keeping with a previous study showing different clinicopathologic features in myeloid neoplasias with 16q deletion versus 16q inversion [17].

Aberrations of the short arm of chromosome 17 have recently been added to the list of chromosome changes nonrandomly associated with secondary leukemia [18], a disease subset in which the involvement of chromosomes 5 and 7, as well as complex chromosome rearrangements, have been well documented.

In this series, aberrations of chromosome 5, 7, 16, and 17 occurred in the context of complex karyotypes in six cases, and were detected as single aberrations in two cases only. Thus, some cytogenetic features in CD34+ de novo AML recall those usually found in secondary AML [18–20]. Noteworthy is the fact that 25/30 CD34+ patients in this series had been professionally exposed to pesticides and organic solvents for many years, whereas such exposure was uncommon (5/30) cases) in CD34− patients [21].

Other recurring chromosome changes in CD34+ AML, i.e., trisomy 11q and del(11)(q13q23), were previously described in myelodysplasia and preleukemic syndromes [22, 23]. Most of our CD34+ patients had the features of trilineage MDS.

### Cytogenetic Patterns and Clinicopathologic Features

Patients with MAKA (i.e., three or more events of translocation or non-disjunction in the same clone) appear to represent a distinct clinicopathologic entity of CD34+ AML, as these patients frequently showed myelodypslastic features of the nonblast cell population associated with circulating megakaryoblasts. Such cytologic findings were uncommon in CD34+ patients with MIKA (one or two aberrant events in the abnormal clone) or with normal karyotype. Although the reason accounting for this difference is unknown, it is reasonable to assume that transformation may have involved an early CD34+ progenitor cell both in patients with MAKA and in patients with MIKA or normal karyotype and that limited differentiation along multilineage pathways may be maintained in the former group and abolished in the latter. Inappropriate expression of lymphoid-associated markers was only detected in CD34+ patients with MIKA or normal karyotype and was not detected in patients with MAKA and in CD34− patients.

### Clinical Outcome in CD34+ AML

Patients with CD34+ AML are less responsive to chemotherapy than patients with CD34− AML, resulting in a significantly lower CR rate and in a shorter overall survival. Noteworthy, all patients in this study were treated with the same induction regimen, followed by monthly maintenance chemotherapy, over a 2-year period.

While other clinical parameters with prognostic predictability, such as age and WBC count at presentation, could not account for this discrepancy, patients with CD34+ AML had unfavorable cytogenetic abnormalities more frequently than patients with CD34− AML. Furthermore, a particularly severe outcome was obtained in CD34+ patients with MAKA, the presence of which allowed for the identification of a subgroup of CD34+ AML resistant to induction therapy. This finding stresses the prognostic importance of karyotype findings in AML.

In conclusion, we have studied the cytogenetic and clinicopathologic features in CD34+ AML, in comparison with CD34− AML, showing that a distinct cytogentic profile may be associated with CD34+ AML. Among CD34+ AML, a strong association was found between the M2 FAB subtype and chromosome 5q aberrations. Cytogenetic findings in CD34+ AML may be clinically relevant in distinguishing CD34+ patients unlikely to achieve CR with a conventional induction regimen.

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## REFERENCES

1. Civin CI, Strauss LC, Brovall C, Fackler MJ, Schwartz JR, Shaper JH (1984): Antigenic analysis of haematopoiesis. III. A haematopoietic progenitor cell surface antigen defined by a monoclonal antibody raised against KG-1a cells. J Immunol 133:157–165.
2. Tindle RW, Nichols RAB, Chan L, Campana D, Catovsky D, Birniet GD (1985): A novel monoclonal antibody BI-3C5 recognises myeloblasts and non-B non-T lymphoblasts in acute leukemias and CGL blast crises, and reacts with immature cells in normal bone marrow. Leuk Res 9:1–9.
3. Katz FE, Tindle RW, Sutherlands DR, Greaves MF (1985): Identification of a membrane glycoprotein associated with haematopoietic progenitor cells. Leuk Res 9:191–198.
4. Vaughan WP, Civin CI, Weisenburger DD, Karp JE, Graham ML, Sanger WG, Grierson HL, Joshi SS, Burke PJ (1988): Acute leukemia expressing the normal human hematopoietic stem cell membrane glycoprotein CD34 (My10) Leukemia 2:661–666.
5. Borowitz MJ, Gockerman JO, Moore JO, Civin CI, Page SO, Robertson J, Bigner SH (1989): Clinicopathologic and cytogenetic features of CD34 (My10) positive acute nonlymphocytic leukemia. Am J Clin Pathol 91:265–270.
6. Geller RB, Zahurak M, Hurwitz CA, Burke PJ, Karp JE, Piantadosi S, Civin CI (1990): Prognostic importance of immunophenotyping in adults with acute myelocytic leukemia: the significance of stem cell glycoprotein CD34 (My10). Br J Haematol 76:340–347.
7. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnick HR, Sultan C (1985): Proposed revised criteria for the classification of acute myeloid leukemia: a report of the French-American-British Cooperative Group. Ann Intern Med 103: 460–462.
8. Brito-Babapulle F, Catovsky D, Galton DAG (1987): Clinical and laboratory features of de novo acute myeloid leukemia with trilineage myelodysplasia. Br J Haematol 66:445–450.
9. Cuneo A, Mecucci C, Kerim S, Vandenberghe E, Dal Cin P, Van Horsoven A, Rodhain J, Bosly A, Michaux JL, Martiat P, Boogaerts M, Carli MG, Castoldi GL, Van Den Berghe H (1989): Multipotent stem cell involvement in megakaryoblastic leukemia:

cytological and cytogenetic evidence in 15 patients. Blood 74:1781–1790.

10. Cordel JL, Falini B, Erber WN, Glosh AK, Abdulaziz Z, McDonald S (1984): Immunoenzymatic labeling of monoclonal antibodies using immune complexes of alkaline phosphatase and monoclonal anti alkaline phosphatase (APAAP complexes). J Histochem Cytochem 32:219–229.
11. de la Maza M, Sanchez O (1976): Simultaneous G and C banding of human chromosomes. J Med Genet 13:235–243.
12. ISCN: Guidelines for cancer cytogenetics, supplement to an international system for human cytogenetic nomenclature (1991). In: Mitelman F, ed. Basel: S. Karger 1–54.
13. Sandberg AA (1980): The Chromosomes of Human Cancer and Leukemia. New York, Elsevier North Holland.
14. Second MIC Co-operative Study Group (1988): Morphologic, immunologic citogenetic (MIC) working classification of acute myeloid leukemias. Cancer Genet Cytogenet 30:1–15.
15. Cuneo A, Van Orshoven A, Michaux JL, Boogaerts M, Louwagie A, Doyenne CH, Dal Cin P, Fagioli F, Castoldi GL, Van den Berghe H (1990): Morphologic, immunologic and cytogenetic studies in erythroleukemia: evidence for multilineage involvement and identification of two distinct cytogenetic-clinicopathological types. Br J Haematol 75:346–354.
16. Sandberg AA (1990): The Chromosomes of Human Cancer and Leukemia, 2nd Ed. New York, Elsevier North Holland, pp. 408–410.
17. Ohyashiki K, Ohyashiki JH, Kondo M, Ito H, Toyama K (1988): Chromosome change at 16q22 in nonlymphocytic leukemia: clinical implication on leukemia patients with inv(16) versus del(16). Leukemia 2:35–40.
18. Pedersen-Bjergaard J, Philip P, Larsen SO, Jensen G, Byrsting K (1990): Chromosome aberrations and prognostic factors in therapy-related myelodysplasia and acute nonlymphocytic leukemia. Blood 76:1083–1091.
19. Whang-Peng J, Young RC, Lee EC, Longo DL, Schecter GP, De Vita VT (1988): Cytogenetic studies in patients with secondary leukemia/dysmyelopoietic syndrome after different treatment modalities. Blood 71:403–414.
20. Iurlo A, Mecucci C, Van Orshoven A, Michaux JL, Boogaerts M, Noens L, Bosly A, Louwagie A, Van den Berghe H (1989): Cytogenetic and clinical investigations in 76 cases with therapy-related leukemia and myelodysplastic syndrome. Cancer Genet Cytogenet 43:227–241.
21. Fagioli F, Cuneo A, Piva N, Carli MG, Previati R, Balboni M, Tomasi P, Cariani D, Scapoli GI, Castoldi GL (1992): Distinct cytogenetic and clinicopathological features in acute myeloid leukemia after occupational exposure to pesticides and organic solvents. Cancer 70:77–85.
22. Takasaki N, Kaneko Y, Sakurakai M (1988): Trisomy 11 in chronic myelomonocytic leukemia: report of two cases and review of the literature. Cancer Genet Cytogenet 30:109–117.
23. Mecucci C, Van Orshoven A, Vermaelen K, Michaux JL, Tricot G, Louwagie A (1987): 11q – chromosome is associated with abnormal iron stores in myelodysplastic syndromes. Cancer Genet Cytogenet 27:39–44.