Cytogenetic Studies in Acute Myelocytic Leukemia with Special Emphasis on the Occurrence of Ph¹ Chromosome

By J. WHANG-PENG, E. S. HENDERSON, T. KNUTSEN, E. J. FREIREICH
AND J. J. GART

Cytogenetic studies were carried out on 103 unselected patients with acute myelogenous leukemia (AML) at the Clinical Center of the National Institutes of Health. Seventy-three patients (70.9%) had a normal karyotype and 30 patients (29.1%) were aneuploid. No unique chromosomal abnormalities were found in patients with aneuploidy; however, there was a significantly higher incidence of G group involvement. Four cases had a history of radiation exposure; three of these four patients had a normal karyotype and one had one Ph¹ chromosome in her bone marrow cells. Another patient with no history of radiation also had one Ph¹ chromosome in his marrow cells. Reclassification of AML patients with Ph¹ chromosomes as a rare entity of blast crisis in chronic myelogenous leukemia (CML) rather than as AML's is proposed. Two patients exhibited the 45 chromosome syndrome before the diagnosis of AML was made. The normal and aneuploid groups had about the same median survival time and same median date from diagnosis to chromosome study; however, none of the patients in the aneuploid group lived longer than 26 months after the date of diagnosis, while seven patients (nearly 10%) in the normal group did so, one living over 112 months.

THE RESULTS OF CHROMOSOMAL STUDIES in acute myelogenous leukemia have been reported by many investigators. Aneuploidy, including both hypodiploidy and hyperdiploidy, has been found in 40-50 per cent of the cases. No consistent chromosome changes were found, and no one chromosome group was especially involved. A few of the cases were reported to have the Ph¹ chromosome. We report here an additional 103 patients with acute myelogenous leukemia for further observation and study into questions concerning this disease.

MATERIALS AND METHODS

Cytogenetic studies were performed on the bone marrow and peripheral blood of 103 unselected patients with acute myelogenous leukemia (AML) who were diagnosed and
treated at the National Cancer Institute, the National Institutes of Health, from January
1961 to December 1969. The patients ranged in age from 7 months to 75 years; 10 of them
were under the age of 10 years and 11 of them were over the age of 60. The duration of
the disease was calculated from the time of diagnosis. The chromosome preparations from
bone marrow were made according to the direct air-dry method as described by Tjio and
Whang.\textsuperscript{12} Cells from peripheral blood were cultured according to the method of Moorhead
et al.\textsuperscript{13} In most cases cytogenetic studies were performed several times throughout the
course of the disease.

**Results**

Patients with AML were divided into groups according to the initial bone
marrow cytogenetic findings (Table 1). Seventy-three patients (70.9\%) had
a normal karyotype on the first bone marrow study. One patient who had a
normal karyotype on the first bone marrow study became aneuploid after 16
months, with 45 chromosomes in 10 per cent of his cells, including one extra
chromosome in group D and a deficiency of two chromosomes in group G.
Three patients with a history of radiation had normal karyotypes on repeated
chromosome studies. The first of these had X-ray treatment for ankylosing
spondylitis 18 years prior to the onset of his leukemia; the second had 6000 R
for cancer of the pharynx 22 months prior to onset; and the third patient had
radium insertion for cancer of the cervix 2 years prior to onset. They lived
1 month, 22 months, and 7 months, respectively, after the diagnosis of
leukemia was made. One patient with mental retardation had a normal
karyotype; he is still alive 64 months after the diagnosis was made.

Thirty patients (29.1\%) were aneuploid. For technical reasons detailed
analyses of the chromosomes could be performed in only 14 of these patients,
the results of which are shown in Tables 2 and 3. The distribution of the
chromosome abnormalities over the chromosome numbers was analyzed. The
theoretical probability, $P_i$, is computed under the hypothesis of a completely

<table>
<thead>
<tr>
<th>Status</th>
<th>Number of Patients</th>
<th>Male:Female</th>
<th>Survival</th>
<th>Diagnosis to Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cytogenetic abnormalities*</td>
<td>73 (70.9%)</td>
<td>48:25</td>
<td>9–10 months</td>
<td>3 weeks (1 day → 3 years)</td>
</tr>
<tr>
<td>No History of radiation</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of radiation</td>
<td>3</td>
<td>112 mos. +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mentally retarded</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With cytogenetic abnormalities †</td>
<td>30 (29.1%)</td>
<td>13:17</td>
<td>9 months</td>
<td>2 weeks (1 day → 9 months)</td>
</tr>
<tr>
<td>45 chromosomes (missing 1 chromosome in C group)</td>
<td>4</td>
<td></td>
<td>6 days → 28 months</td>
<td></td>
</tr>
<tr>
<td>Aneuploid with definite cell line</td>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneuploid with uncertain cell line</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ph1-positive received $^{32}$P</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No history of radiation</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* One patient changed from normal to aneuploid.
† One patient changed from aneuploid to normal.
<table>
<thead>
<tr>
<th>Type</th>
<th>Name</th>
<th>Chromosome No. and Percentage*</th>
<th>Deviations from Normal in Chromosome Groups †</th>
<th>No. of Metaphases Analyzed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1   2  3  4-5 6-X-12 13-15 16-18 19-20 21-23 Y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypo</td>
<td>H.M.</td>
<td>43 + minute (100%)</td>
<td>-2  -1 -1</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>N § + Hypo</td>
<td>T.W.</td>
<td>46N (2%)</td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>M.I.</td>
<td>46N (10%)</td>
<td>-1  +1 +1</td>
<td>20</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>45 (90%)</td>
<td></td>
<td></td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Pseudo</td>
<td></td>
<td>+ Hypo</td>
<td>P.E.</td>
<td>46 (36%)</td>
<td>-1  +1 +1</td>
</tr>
<tr>
<td></td>
<td>45 (57%)</td>
<td></td>
<td></td>
<td>5</td>
<td>19</td>
</tr>
<tr>
<td>Pseudo</td>
<td>S.P.</td>
<td>46 (100%)</td>
<td>-2  +1 +2</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>F.H.</td>
<td>46 (100%)</td>
<td></td>
<td>-1  +1 +1</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>N + Pseudo</td>
<td>O.R.</td>
<td>46N (80%)</td>
<td></td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>Hyper †</td>
<td>O.S.</td>
<td>49 (91%)</td>
<td></td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>N + Hyper</td>
<td>S.G.</td>
<td>46N (9%)</td>
<td></td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>B.Y.</td>
<td>46N (9%)</td>
<td></td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>49 (92%)</td>
<td></td>
<td>+2  -1</td>
<td>30</td>
<td>92</td>
</tr>
<tr>
<td>R.A.</td>
<td>46N (82%)</td>
<td></td>
<td></td>
<td>10</td>
<td>41</td>
</tr>
<tr>
<td>O.A.</td>
<td>46N (6%)</td>
<td></td>
<td></td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>47 (48%)</td>
<td></td>
<td>+1  +1</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>48 (46%)</td>
<td></td>
<td></td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>B.J.</td>
<td>46N (6%)</td>
<td></td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>47 (80%)</td>
<td></td>
<td>+1  +1</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>48 (14%)</td>
<td></td>
<td></td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>N + Hyper + Hypo</td>
<td>B.A.</td>
<td>45 + minute (13%)</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>46N (32%)</td>
<td></td>
<td></td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>47 (15%)</td>
<td></td>
<td></td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>48 (13%)</td>
<td></td>
<td></td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>49 (13%)</td>
<td></td>
<td></td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>

* For cell lines with two or more analyzable metaphases.
† Denver nomenclature.
‖ Hypo, hypodiploid.
§ N, normal.

Pseudo, pseudodiploid.
Hyper, hyperdiploid.
** One large submetacentric chromosome.
Table 3.—Comparison of Expected and Observed Incidence of Abnormalities per Chromosome Group

<table>
<thead>
<tr>
<th>No.</th>
<th>Chromosome</th>
<th>Random Probability of Gain or Loss of Chromosome (Pi)</th>
<th>Observed Distribution</th>
<th>Expected Distribution (34Pi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>2/46</td>
<td>0</td>
<td>1.48</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2/46</td>
<td>1</td>
<td>1.48</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2/46</td>
<td>1</td>
<td>1.48</td>
</tr>
<tr>
<td>4</td>
<td>4-5</td>
<td>4/46</td>
<td>2</td>
<td>2.96</td>
</tr>
<tr>
<td>5</td>
<td>6-12</td>
<td>14/46</td>
<td>9</td>
<td>10.35</td>
</tr>
<tr>
<td>6</td>
<td>13-15</td>
<td>6/46</td>
<td>6</td>
<td>4.43</td>
</tr>
<tr>
<td>7</td>
<td>16-18</td>
<td>6/46</td>
<td>5</td>
<td>4.43</td>
</tr>
<tr>
<td>8</td>
<td>19-20</td>
<td>4/46</td>
<td>2</td>
<td>2.96</td>
</tr>
<tr>
<td>9</td>
<td>21-22*</td>
<td>4/46</td>
<td>8</td>
<td>2.96</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>2/46</td>
<td>0</td>
<td>1.48</td>
</tr>
<tr>
<td>Totals</td>
<td></td>
<td>1</td>
<td>34</td>
<td>34.01</td>
</tr>
</tbody>
</table>

* p = 0.002.

random distribution of the 34 abnormalities over the 10 chromosome groups. The chi-square goodness of fit test of the hypothesis yields \( \chi^2 = 13.28 \) with nine degrees of freedom for which \( p = 0.15 \); i.e., there is not sufficient evidence to reject the random distribution hypothesis from this statistical test. However, we note in Table 3 that the number of abnormalities in chromosome numbers 21-22 is considerably more than its expected value, 8 versus 2.96. The chi-square for this deviation alone is

\[
\chi^2 = \frac{(8 - 2.96)^2}{(34 \cdot 4 \cdot 42)/(46)^2} = 9.41
\]

with one degree of freedom, for which \( p = 0.002 \), that is, the number of abnormalities at this location significantly exceeds the expected number under the random assumption. Three of these 14 patients had marker chromosomes: one had a long submetacentric chromosome and each of the other two had a minute chromosome morphologically distinguishable from the Ph1 chromosome. The remaining patients exhibited additions or deletions in the chromosome number scattered through the various groups.

Four patients had cell lines with 45 chromosomes with one missing chromosome in group C; in two of the patients, the 45 chromosome syndrome was first noted during work-up for refractory anemia, before a clinical and morphologic diagnosis of AML could be made. In the other two, the 45 chromosome line was noted on the onset of AML. Chromosome studies carried out on the peripheral bloods of these four patients failed in each case to demonstrate a genetic chromosomal abnormality.

Two patients had the Ph1 chromosome in their bone marrow. One was a 9-year-old boy who, on the first marrow studied, had a Ph1 chromosome in 50 per cent of his cells. The Ph1 chromosome was present in cells with 46, 65, 66, 67, 68, 69, and 70 chromosomes. On achieving remission, the percentage of hyperdiploid cells decreased, but the percentage of Ph1-positive 46 chromosome cells continued to increase steadily unrelated to the clinical state of the patient. Cytogenetic studies on serial bone marrows were performed a total of 28 times during both remission and relapse. Just prior to the patient's
death, 2 years after diagnosis, the percentage of Ph₁ positive cells reached
100 per cent and 74 per cent of these were aneuploid with chromosome
numbers ranging from 65 to 70. The second Ph₁-positive case was a 67-year-
old female who had been treated for polycythemia vera with ³²P (3 mCi) for
3 years prior to the diagnosis of AML. Eighty per cent of her marrow cells
had 48 chromosomes with one Ph₁ chromosome and one extra chromosome
in both groups C and D; the remaining 20 per cent had 46 chromosomes with
one Ph₁ chromosome. No chromosome studies had been done before treatment
with ³²P.

In 10 patients with cytogenetic abnormalities it was not possible to deter-
mine definite aneuploid cell lines. The reason for this was either the small
numbers of aneuploid cells or poor preparations not suitable for analysis. One
of these patients had an abnormal cell line in which it was possible to definitely
count 47 chromosomes, but these cells could not be analyzed in detail, and
when a 26-month followup marrow was done, this cell line had disappeared
and been replaced by a normal one.

The median survival for patients of the aneuploid group was 9 months (6
days to 26 months) and 9-10 months for the normal karyotype group (3 days
to 112 months).

DISCUSSION

Aneuploidy in AML has been reported by different investigators. In a large
series reported by Sandberg et al.,⁷ 50 per cent of the cases were found to be
aneuploid; the karyotype showed a remarkable variability from case to case,
and, except for a small number of cases with group C trisomy, no consistent
or characteristic chromosomal changes were found in acute leukemia. Fitz-
gerald et al.³ found that the chromosomal abnormalities in AML patients
consisted of both numerical and structural changes, and repeated studies
showed that the abnormalities persisted regardless of the stage of the disease.

In reviewing our data we found aneuploid cell lines in slightly less than
30 per cent of the cases. As in other reviews, no chromosome group was con-
sistently involved, the greatest number of patients showing changes within
group C, group D, or group G. Analysis of the data in terms of risk per
chromosome, assuming the possibility of chromosome addition or deletion to
be normally the same for each individual chromosome, revealed a significantly
higher rate of abnormality for group G. These results closely reproduce the
finding previously reported for patients with acute lymphocytic leukemia
(ALL).¹⁴ The observation that group G is also involved in abnormalities in
CML (Ph₁ chromosome)¹⁵ and Down's syndrome (trisomy 21-22)¹⁶ leads us
to suspect that at least some genes concerned with the control of replication
and/or differentiation of white blood cells are located in the group G
chromosomes. There was no difference in median survival of patients with
normal or aneuploid malignant cell lines, nor was there any difference in
the duration of time from diagnosis to the initial marrow study. However,
the longest surviving patients were in the group with normal karyotypes.

Aneuploidy in the C group of chromosomes in preleukemia patients has
been reported by several investigators.¹⁷-²⁰ Rowley et al.²¹ reported three
cases. The first case had aplastic anemia and a 45 chromosome cell line with one chromosome missing in the C group. The second had idiopathic sideroachrestic anemia; most of his marrow cells had 47 chromosomes with one extra chromosome in group C. The third patient had idiopathic thrombocytopenia with a minority cell line of 48 chromosomes in which there were two extra chromosomes in the C group. Freireich et al. reported three cases of refractory anemia, granulocytic hyperplasia, and low or absent leukocyte alkaline phosphatase which on bone marrow cytogenetic studies were missing one chromosome in the C group. Each of these patients subsequently died of acute myelocytic leukemia. Three out of 10 cases of preleukemia reported by Nowell et al. had one chromosome missing in the C group as well as some other chromosomal abnormalities. He proposed that a positive marrow chromosome study (i.e., a cytogenetically abnormal one) in a nonirradiated patient with preleukemic symptoms suggests that a leukemic phase is imminent, whereas a negative study may indicate a protracted nonleukemic course.

There was only one case which changed from an originally normal karyotype to one with a minor aneuploid cell line. This probably represents selective growth of abnormal cells during the progress of the disease. In another case, an originally aneuploid cell line disappeared during remission; a followup marrow after relapse was obtained during daunomycin treatment, but because of the high percentage of chromosomal aberrations resulting from the drug, no detailed analysis could be made. It is possible that the aneuploid cells were more sensitive to the treatment and so were no longer in the marrow.

The Ph\textsuperscript{1} chromosome, which is found in 90 per cent of all CML patients, is the only consistent chromosome abnormality found in neoplastic disease. Except for a few cases of AML\textsuperscript{4,8-11} and a few cases in which a small Y chromosome perhaps is easily misdiagnosed as a Ph\textsuperscript{1} chromosome,\textsuperscript{22-23} this chromosome abnormality has been strictly confined to CML.

The six documented cases of acute myelocytic leukemia with Ph\textsuperscript{1} chromosomes are summarized in Table 4. Two of these were seen at the National Cancer Institute during 1969 and therefore are not included in the 103 patients reviewed earlier in this report. In each instance, the initial diagnosis of AML was firmly established on clinical and morphological grounds, although in two patients (NCI case No. 4 and the case of Mastrangelo et al.) followup studies of peripheral blood and bone marrow after therapy suggested chronic myelocytic leukemia. In one case previously reported by Hollan and co-workers,\textsuperscript{24} AML was preceded by polycythemia rubra vera and \textsuperscript{32}P therapy, and the clinical course was complicated by coexistent acquired autoimmune hemolytic anemia and bronchogenic carcinoma. A history of radiation and Ph\textsuperscript{1} chromosome has been reported in several other cases.\textsuperscript{25,26} The prediagnosis history in the other patients was entirely consistent with that reported for AML in large series.\textsuperscript{27,28} Similarly, the initial physical examinations and hematological studies suggested acute rather than chronic leukemia, the peripheral leukocyte count being markedly elevated in only one case, and splenomegaly being slight or absent. Presenting thrombocytopenia was noted in all but one instance, a rare occurrence with CML.\textsuperscript{29}

A high incidence of aneuploidy in addition to the Ph\textsuperscript{1} chromosome has
### Table 4.—Summary of AML Cases with Ph¹ Chromosome

<table>
<thead>
<tr>
<th>Cases</th>
<th>Age</th>
<th>Sex</th>
<th>Chromosome No.</th>
<th>Per Cent Ph¹</th>
<th>No. Ph¹/Cell</th>
<th>Duration (Months)</th>
<th>LAP</th>
<th>HGB¹</th>
<th>WBC¹</th>
<th>Initial Size</th>
<th>Response to Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCI No. 1</td>
<td>9</td>
<td>M</td>
<td>46,65,66,67,68,69,70</td>
<td>50–26–100</td>
<td>1</td>
<td>1.5</td>
<td>24</td>
<td>Normal</td>
<td>7.5</td>
<td>10,300</td>
<td>258,000</td>
</tr>
<tr>
<td>NCI No. 2</td>
<td>88</td>
<td>F</td>
<td>46,47,48,49</td>
<td>100</td>
<td>1</td>
<td>24</td>
<td>3</td>
<td>Normal</td>
<td>13.1</td>
<td>17,000</td>
<td>37,000</td>
</tr>
<tr>
<td>NCI No. 3 §</td>
<td>3</td>
<td>M</td>
<td>46</td>
<td>83</td>
<td>1</td>
<td>0.25</td>
<td>4+</td>
<td>High</td>
<td>10.1</td>
<td>5100</td>
<td>15,000</td>
</tr>
<tr>
<td>NCI No. 4 §</td>
<td>46</td>
<td>F</td>
<td>46 (2 large D group, Fig. 1)</td>
<td>74–100</td>
<td>1</td>
<td>2</td>
<td>4+</td>
<td>Very high</td>
<td>9.5</td>
<td>13,000</td>
<td>130,000</td>
</tr>
<tr>
<td>Kiosoglou et al. §</td>
<td>65</td>
<td>F</td>
<td>39–46</td>
<td>100</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>7.5</td>
<td>9700</td>
<td>80,660</td>
<td>0</td>
</tr>
<tr>
<td>Mastrangelo et al. §</td>
<td>5</td>
<td>M</td>
<td>46–46,48</td>
<td>57–20–88–22–100</td>
<td>0.25</td>
<td>21</td>
<td>8.3</td>
<td>3400</td>
<td>1+</td>
<td>2 cm.</td>
<td>+</td>
</tr>
</tbody>
</table>

* Months from onset of first symptoms of hematopoietic illness to the date of diagnosis of acute leukemia.

† LAP, leukocyte alkaline phosphatase.

‡ Hemoglobin in grams per 100 ml, WBC and platelets per cubic mm., liver and spleen size in centimeters below the costal margin, lymph nodes 1+ < 2 cm. enlargement in normal and lymph node areas, 2+ 2–4 cm. enlargement in normal lymph node-bearing sites.

§ Patients seen during 1969 and therefore not included in Table 1.

¶ Severely decreased.
Fig. 1.—Metaphase and karyotype of bone marrow cell from NCI patient No. 4 who had a Ph¹ chromosome, two extra large acrocentric chromosomes, and one missing chromosome in group 4-5 and group 13-15.
been found in the blast crisis stage of CML.4,31 Four of the six patients with AML plus Ph1 showed aneuploidy, but this is not inconsistent with the findings of our 101 AML patients who did not exhibit a Ph1 marker chromosome.

Nicoara et al.32 proposed a reclassification of Ph1-positive polycythemia into a group transitional between polycythemia and CML. For the time being a similar subclassification for AML with the Ph1 chromosome would be appropriate. It must be recognized that this leaves unanswered the question of whether these cases are primary AML more or less independently associated with a Ph1 chromosome, or alternatively, whether they represent instances of CML in which a myeloblastic cell line appeared early before the typical stigmata of CML had developed. In each instance in which followup cytogenetic studies could be followed there has been progressive replacement of the marrow with Ph1+ cells. However, in two instances (NCI case No. 1 and the case of Mastrangelo et al.) successful remission induction temporarily reduced the percentage of abnormal metaphases.

It has been suggested that CML cell lines, in common with other species of genetically aberrant cells,33 are more likely to spawn clones of malignant myeloblasts. If such a phenomenon were a random event, it would be surprising if acute myeloblastic leukemia were not occasionally seen early in the course of the underlying myeloproliferative disorder. Furthermore, the increased resistance to therapy of AML occurring after a long history of CML, polycythemia rubra vera, or other preacute leukemia marrow diseases has been postulated by some to reflect a progressive reduction of normal hematopoietic stem cells militating against recovery of normal marrow function despite successful destruction of the abnormal myeloblastic infiltrate.34 While the cases reported to date do not establish such a pathologic progression, they are consistent with it. For the present it would be of value to identify and follow as many patients with clinical AML associated with the Ph1 chromosome as possible, to assess their response to therapy and their clinical course, especially the sequential incidence of Ph1 metaphases in the marrow and the possible development of the diagnostic features of CML in patients with extended survival.

REFERENCES

8. Hardisty, R. M., Speed, D., and Till,


Cytogenetic Studies in Acute Myelocytic Leukemia with Special Emphasis on the Occurrence of Ph Chromosome

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