Identification of the Philadelphia (Ph-1) Chromosome

By FELIX PRIETO, JOSE EGOCZUE, GERONIMO FORTEZA AND FELIX MARCO

Since its discovery by Nowell and Hungerford in 1960, attempts have been made to identify the Philadelphia (Ph-1) chromosome characteristic of some types of chronic myelogenous leukemia (CML). The most widely accepted explanation considers the Ph-1 chromosome to be a deletion of a member of the G group, although a more complex rearrangement, e.g., a translocation, cannot be excluded.

Decreased values of leukocyte alkaline phosphatase in CML suggest that the Ph-1 chromosome may be a G-21, since increased alkaline phosphatase values are found in trisomy 21. However, this simple gene–dose relationship is not consistent with other observations, such as decreased alkaline phosphatase values in CML patients without the Ph-1 chromosome in their complements, and the normal values of galactose-1-phosphate uridyl transferase—an enzyme also elevated in mongolism—found in CML.

In spite of the characteristic DNA replication patterns of pairs 21 and 22, autoradiographic studies are of little value in identifying the Ph-1 chromosome, which does not always show a single replication pattern.

This paper describes a case of CML in which a marker G converted into the Ph-1 chromosome and enabled us to identify it.

Materials and Methods

A 34-year-old Caucasian female, previously treated with Busulfan (Myleran) for one year for “leukemia,” was referred to one of us (F.M.) for further diagnosis and to our laboratory for chromosomal studies. The diagnosis was CML, and direct bone marrow preparations were made according to a standard method. Four weeks later, during a remission of the disease, blood was obtained for chromosomal studies. H3-thymidine was added to the blood cultures for the last six hours of incubation for autoradiographic studies. Because of the favorable course of her disease, the patient has not been treated since the diagnosis was made about seven months ago.
RESULTS

Analysis of 38 bone marrow metaphases showed the karyotype characteristic of CML, 46 XX (Cq-), and a Ph-1 chromosome with extremely large satellites (Figs. 1, 2). The possibility that the Ph-1 had originated from a marker G was explored. Blood cultures resulted in a normal karyotype with enlarged satellites in one of the G-group chromosomes (Figs. 3, 4).

Autoradiographic studies (Fig. 4) revealed the characteristic labeling pattern described for the G group: in 26 of 35 cells analyzed (Fig. 4), two G chromosomes, including the one with enlarged satellites, replicated their DNA earlier than the other two. Nine metaphases showed different labeling patterns in their G-group chromosomes (Table 1).

Table 1.—No. of Heavily-vs.-Lightly-Labeled G Chromosomes

<table>
<thead>
<tr>
<th>No. of cells</th>
<th>4-0</th>
<th>3-1</th>
<th>2-2</th>
<th>1-3</th>
<th>0-4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cells</td>
<td>1</td>
<td>2</td>
<td>26</td>
<td>3</td>
<td>3</td>
<td>35</td>
</tr>
</tbody>
</table>
The most common pattern of replication, two early and two late replicating G’s, is consistent with the replication pattern described for the G group.

**DISCUSSION**

The presence in the cells of a CML patient of a marker G, which later converted into the Ph-1 chromosome, enabled us to identify the chromosome...
Fig. 5.—C chromosomes from three cells with trisomy 21; three chromosomes (left) late replicating, two (right) early replicating.

from which the Ph-1 originated as a member of the early replicating G-22 pair. Existing evidence suggests that the chromosome present in triplicate in mongolism is late replicating (Fig. 5), and that the extra chromosome of the so-called trisomy 22 is early replicating, although this autoradiographic distinction is not firmly established as yet. On this basis, however, the question on whether one of the autosomes present in triplicate in trisomics is always delayed in its DNA synthesis does not seem valid. The present evidence suggests that, at least in our case, the Ph-1 chromosome is a member of the G pair not involved in trisomy 21. Thus, since G-21 trisomy is the accepted nomenclature for the chromosomal defect associated with Down's syndrome, the Ph-1 chromosome should be considered a deletion (or trans-location) of G-22.

SUMMARY

The presence of a marker G, which later converted into the Ph-1 chromosome, in a female patient with chronic myelogenous leukemia, permitted identification of the G chromosome from which the Ph-1 originated as a member of the early replicating, G-22 pair.

REFERENCES


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