To the Editor:

Scarpa et al1 assert that the variant t(8;14) translocations, t(2;8) and t(8;22), have only been identified in cases of Burkitt's lymphoma (BL) and Burkitt's-type leukemia (L3) to the exclusion of other types of non-Hodgkin's lymphoma (NHL). We are aware of at least three reported exceptions to this statement, including a case of chronic lymphocytic leukemia with the t(2;8), a case of follicular lymphoma with the t(2;8), and a diffuse large cell lymphoma (DLCL) with a t(8;22) previously reported by our group.4 We have recently reported three additional cases of DLCL with the t(8;22). The cytogenetic data on our four cases of DLCL with the t(8;22) are presented in Table 1. In two of our four cases, we were able to examine the configuration of the MYC gene. One of the two cases showed evidence of point mutation at the 3' end of the first exon, which is similar to the results obtained by Scarpa et al. As expected, neither case showed a rearrangement within the MYC gene. Additional work is needed to understand the state of the MYC gene in cases of non-Burkitt's NHL. Specifically, it will be important to determine whether the clinical and pathologic differences between BL and non-Burkitt's NHL correspond to differences in the molecular structure of the t(8;14) and whether within a given pathologic subtype of non-Burkitt's NHL, t(8;14) translocations with different molecular structures represent distinct clinical or morphologic subsets.

MARC LADANYI
KENNETH OFFIT
R.S.K. CHAGANTI
Memorial Sloan-Kettering Cancer Center
New York, NY

Table 1. Clinical, Pathologic, and Cytogenetic Data on Four DLCL With the t(8;22)

<table>
<thead>
<tr>
<th>UTN</th>
<th>Age/Sex</th>
<th>Path</th>
<th>Site</th>
<th>Surface Ig</th>
<th>Therapy</th>
<th>No.</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>143</td>
<td>58/F</td>
<td>IMB-D</td>
<td>LN</td>
<td>IgG-κ</td>
<td>Post</td>
<td>27</td>
<td>48, X, -X, +7, +8, t(8;22)(q24;q11), t(14;18)(q22;q21), del(1)(q22→ter), +der(1)(qter→q21::?), del(9)(qter→p24::9q13→ter)</td>
</tr>
<tr>
<td>405</td>
<td>29/F</td>
<td>IMB-D</td>
<td>LN</td>
<td>IgG-λ</td>
<td>Pre</td>
<td>3</td>
<td>46, XX</td>
</tr>
<tr>
<td>448</td>
<td>78/M</td>
<td>LNCC-D</td>
<td>Bowel</td>
<td>IgA-λ</td>
<td>Pre</td>
<td>21</td>
<td>48, XY, +12, -17, t(8;22)(q24;q11), dup(7)(q11→q31), +random mars</td>
</tr>
<tr>
<td>540</td>
<td>74/F</td>
<td>IMB-D</td>
<td>LN</td>
<td>ND</td>
<td>Pre</td>
<td>6</td>
<td>46, XX</td>
</tr>
</tbody>
</table>

Abbreviations: UTN, unique tumor number; LN, lymph node; IMB-D, immunoblastic diffuse; LNCC-D, large noncleaved cell diffuse; Pre, studies performed on pretreatment material; Post, studies performed posttreatment material; ND, not done.
REFERENCES


RESPONSE

We are grateful to Dr Ladanyi et al for pointing out the existence of rare cases of non-Burkitt's non-Hodgkin's lymphomas with the translocations t(2;8) and t(8;22). We found their letter of the utmost interest because it summarizes data that are often difficult to extrapolate from the large literature existing in the field. In fact, even if we are aware of the study of Ladanyi et al, published while our report was under review, we actually overlooked the existence of the other three reported exceptions.

In addition, our assertion that reads "... the molecular anatomy of the t(8;14) found in diffuse large cell lymphomas (DLCL) remains unexplored" should also be restated in the light of the recent report by Ladanyi et al, which is the first study addressing the issue of the molecular configuration of translocations involving band 8q24 in DLCL. In this regard, we would like to complement the discussion about c-myc gene involvement in mediastinal large cell lymphomas of young adults (MLCL). In their study of 124 DLCLs, Ladanyi et al found that 18.5% of cases had a translocation involving 8q24, in the form of t(8;14), t(8;22) or other types of t(8;24) in 17, 4, and 2 cases, respectively. However, only 6 of 15 cases (40%) with a t(8;24) showed a c-myc molecular abnormality (a major rearrangement in four cases; mutations at the 3' end of the first exon in two cases with unrearranged c-myc), whereas none of the 81 DLCLs without 8q24 involvement had any molecularly detectable c-myc anomaly. Three considerations can be drawn from these data. First, the breakpoint in the majority of DLCL cases (11 of 15, 73%) with a t(8;24) lies outside the c-myc locus, as in t(8;14) of endemic Burkitt's lymphoma and in the variant t(2;8) and t(8;22) translocations, whereas the remaining cases (4 of 15, 27%) show the truncation of c-myc, as observed in the t(8;14) of sporadic Burkitt's and acquired immunodeficiency syndrome-associated lymphomas. Second, the molecular detection of either c-myc major rearrangements or mutations at the 3' end of the first exon is specific for the existence of a translocation involving band 8q24. Third, the molecular detection rate of t(8;24) in which the breakpoint lies outside c-myc locus is quite low (2 of 11 cases with unrearranged c-myc).

Since our last report, we were able to collect 10 additional cases of MLCL and study their c-myc gene configuration (Scarpa et al, in preparation). We found two further cases showing mutations at the 3' end of the first exon in unrearranged c-myc loci. In summary, molecular abnormalities characteristic of translocated c-myc genes are present in 5 of 16 (31%) of our MLCL cases, including four in which the breakpoint lies outside the c-myc locus. These data, together with the observation that the molecular detection rate of t(8;24) in DLCLs is far below the actual occurrence of such translocations, suggest that a larger number of MLCLs may harbor a t(8;24) not detectable with our molecular analysis. We hope that other scientists, in addition to Ladanyi et al, who have cytogenetic recordings may be moved to search their files for the information regarding this particular group of lymphomas.

We agree with Ladanyi et al about the importance of determining whether the different molecular configurations of c-myc in t(8;14) or in other t(8q24) translocations are associated to distinct clinical or morphologic subsets of DLCL. However, what is known is the existence of clinical differences, in addition to pathogenetic and molecular ones, between the endemic (eBL) and the sporadic forms (sBL) of Burkitt's lymphoma. Among these, bone marrow localizations are virtually absent in eBL (even after many relapses), whereas are frequent in sBL. The kidney is involved in over 50% of eBL cases (virtually 100% of the autopic cases). In this regard, it is worth noting that in our cases of MLCL, bone marrow involvement has never been detected (0 of 21 cases) and the kidney, which is rarely involved in adult non-Hodgkin's lymphoma, has been found involved in 75% (6 of 8) of our MLCL cases with a clinical stage IV. It will be of the utmost interest to determine whether there are differences in the clinical behavior and spreading attitude between DLCL with and those without a t(8q24) translocation.

ALDO SCARPA
PAOLA CAPELLI
MARCO CHILOSI
FABIO MENESTRINA
LUCIANO FIORE DONATI
Istituto di Anatomia Patologica
Università di Verona
Verona, Italy

REFERENCES


Variant t(8;14) translocations in non-Burkitt's non-Hodgkin's lymphomas [letter; comment]

M Ladanyi, K Offit and RS Chaganti