CORRESPONDENCE

ABSENCE OF LOSS OF HETEROZYGOSITY OF THE IRF1 GENE IN SOME PATIENTS WITH A 5Q31 DELETION

To the Editor:

Loss of chromosome 5 or a deletion of its long arm (5q) is the most frequent recurring cytogenetic abnormality in myelodysplastic syndromes (MDS). By comparing the position of the breakpoints in 135 patients with interstitial deletions, Le Beau et al.1 have identified a commonly deleted segment at 5q31. This segment of the genome has been termed the critical region and could harbor a gene that is important in the development of these myeloid disorders. Several genes encoding, for instance, hematopoietic growth factors and proteins involved in transcriptional regulation have been assigned to this region. Of them, IRF1 (interferon regulatory factor 1) has recently been implicated as the long-sought tumor-suppressor gene, because it was reported to be consistently deleted at one or both alleles in 11 cases of acute myeloid leukemia (AML) and MDS with deletions of the long arm of chromosome 5. However, Boulwood et al.2 recently showed that 2 of 14 MDS and AML patients with deletions involving 5q31 had retained both copies of the IRF1 gene. This was demonstrated by gene dose experiments and was confirmed by fluorescent in situ hybridization analysis using a large genomic probe. We report here 2 additional patients who have both IRF1 alleles despite the presence of 5q31 deletions. In a previous study, six highly polymorphic minisatelites and microsatellites located at or near the common deleted segment were used to detect loss of heterozygosity (LOH) by polymerase chain reaction in purified peripheral blood cells from 10 patients with a 5q deletion. It was shown that the allelic losses occurred in polymorphonuclear cells and monocytes, but not in lymphocytes.3 Using a recently identified GT repeat in the IRF1 gene,4 LOH was analyzed in the same patients. Five of them proved to be informative for the IRF1 repeat as tested on T-lymphocyte samples (Table 1). In 3 patients, LOH could be detected in cells of myeloid origin, whereas 2 patients (UPN 01 and 09) remained heterozygous for this marker (Fig 1).

In conclusion, we provide further evidence that IRF1 is not consistently lost in every patient with a 5q31 deletion. However, these findings do not exclude IRF1 from being the responsible tumor-suppressor, because inactivation of both alleles could still have occurred by 2 independent (point) mutations. Detailed characterization of the IRF1 coding regions in these patients by, for instance, single-strand conformation polymorphism-based screening methods and sequence analysis should provide insight into the potential role of the IRF1 gene.

Table 1. Analysis of LOH of the IRF1 Repeat

<table>
<thead>
<tr>
<th>UPN*</th>
<th>5q Deletion</th>
<th>PMN</th>
<th>Mo</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>q22-q31</td>
<td></td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>06</td>
<td>q13-q33</td>
<td></td>
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<tr>
<td>08</td>
<td>q13-q31</td>
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<tr>
<td>09</td>
<td>q13-q31</td>
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<tr>
<td>10</td>
<td>q13-qter</td>
<td></td>
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</tbody>
</table>

Abbreviations: PMN, polymorphonuclear cells; Mo, monocytes; T, T lymphocytes; NA, not available.

* Numbering of the patients according to Kroef et al.4 (Table 1).
† Presence of (+) or absence of (−) allelic losses in purified cells in peripheral blood from patients informative for the IRF1 repeat.

Fig 1. Examples of LOH analysis of the IRF1 repeat. In UPN 08 LOH was observed, whereas heterozygosity was retained in UPN 09. Abbreviations: PMN, polymorphonuclear cells; Mo, monocytes; T, T lymphocytes.

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REFERENCES


Absence of loss of heterozygosity of the IRF1 gene in some patients with a 5q31 deletion [letter]

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