CONCISE REPORT

Interleukin-5 Is at 5q31 and Is Deleted in the 5q- Syndrome

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Human interleukin-5 (IL-5) is a selective eosinophilopoietic and eosinophil-activating growth hormone. By in situ hybridization this gene is mapped to chromosome 5q23.3 to 5q32. It is shown to be deleted in two patients with the 5q- syndrome and in one patient previously diagnosed with myelodysplasia whose condition had progressed to acute myeloblastic leukemia. The clustering of other genes involved in hematopoiesis (IL-3, granulocyte-macrophage colony-stimulating factor, feline sarcoma viral oncogene homolog, colony-stimulating factor 1) to the same region as IL-5 suggests a nonrandom localization and raises interesting questions concerning the evolution and regulation of these genes.

C-DNA clones for IL-5 have been isolated and the structure of the human IL-5 gene determined. We have used the human IL-5 gene for in situ hybridization to map the gene and, having mapped it to the long arm of chromosome 5, have shown that it is on the segment of this chromosome deleted in the 5q- syndrome.

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Submitted August 26, 1987; accepted December 17, 1987.

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MATERIALS AND METHODS

The Probe. The probe was a 3.2-kilobase (kb) BamHI genomic DNA fragment that carries the complete human IL-5 gene.1

Patients. Patient 1, a female aged 83 years, had myelodysplasia and a del(5)(q13q31) as the only chromosome abnormality in her bone marrow cells. Patient 2, a male aged 65 years with myelodysplasia, exhibited a hypodiploid complex karyotype including del(5)(q14q31). Patient 3 was a male aged 69 years with acute myeloblastic leukemia after a myelodysplastic syndrome who had two abnormal clones in the marrow, one containing a del(5)(q15q33) only and the other being hypodiploid with numerical and structural abnormalities additional to the 5q-

In situ hybridization. The probe was labeled to a specific activity of 2.8 x 107 cpm/μg with three tritiated nucleotides and hybridized in situ at a concentration of 0.4 μg/mL to chromosomes from two chromosomally normal males.4 The slides were dipped in Kodak NTB-2 nuclear research emulsion diluted 2:1 with water, exposed for 14 days, and developed in Kodak D19, followed by counterstaining with DAPI.

Fig 1. Distribution of silver grains scored over all chromosomes in 25 metaphases after in situ hybridization.
expression of the gene encoding Clutterbuck EJ, Sanderson CI, Young IG: Molecular cloning and Severinson E, Honjo T: Cloning of cDNA for human T-cell replac-


Fig 2. Distribution of silver grains on the long arm of chromosome 5 from 42 metaphases showing signal in this region.

exposed for 21 days, developed, and banded. The slides from the patients were G-banded and prephotographed before hybridization and development, which were under the same conditions as those from the normal individuals.

RESULTS

Twenty-five metaphases from one normal male showed 30 silver grains over the area 5q22 to 5qter (18.2% of signal) and 135 grains over other chromosomal regions (Fig 1). The distribution of the silver grains from the 17 of these 25 metaphases that had signal on 5q and an additional 25 metaphases with silver grains on this chromosome arm are shown in Fig 2. These data assign the gene for IL-5 to the region 5q23.3 to 5q32, but most probably in 5q31. This finding was confirmed on metaphases from a different normal male (data not shown).

The results of the hybridization to the three patients are shown in Table 1. These clearly indicate that the IL-5 locus has been lost from the deleted chromosome.

Table 1. Numbers of Silver Grains Scored in Patients With del(5q)

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Deletion</th>
<th>Metaphases Scored</th>
<th>No. of Silver Grains Over</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5q</td>
<td>5q</td>
</tr>
<tr>
<td>1</td>
<td>q13q31</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>q14q31</td>
<td>37</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>q15q33</td>
<td>40</td>
<td>16</td>
</tr>
</tbody>
</table>

DISCUSSION

A number of genes regulating hematopoiesis have been mapped to the long arm of chromosome 5 (colony-stimulating factor 1 to 5q33.1, granulocyte-macrophage colony-stimulating factor to 5q23-31, and feline sarcoma viral oncogene homolog to 5q33.2 to 533.3) and have been shown to be on the deleted segment of chromosome 5 in the myeloid disorders with the 5q- syndrome. The present study identifies another hematopoietic growth factor gene with a possible role in the 5q- syndrome. With more detailed studies it may be possible to relate the clinical features of 5q-patients to the deletion of specific genes in this region and to address the question of possible mutations in the corresponding genes on the homologous chromosome.

There is no striking sequence homology between the genes for IL-3 and GM-CSF, which are tandemly arranged on 5q and are only 9 kb apart. There is, however, some sequence homology between IL-3 and IL-5, and it has been further suggested that other lymphokines that share sequence homology with IL-3 and GM-CSF may be distantly related members of a gene family.

Other genes such as platelet-derived growth factor receptor, β2-adrenergic receptor, and endothelial cell growth factor have also been mapped to the 5q area and are probably removed in the 5q deletion, although this has not been formally demonstrated. It is interesting to note that the three human eosinophil growth factor genes so far mapped, GM-CSF, IL-3, and now IL-5, appear very close to each other on the long arm of chromosome 5. In contrast, we have shown that the neutrophil-selective CSF gene G-CSF is located on chromosome 17. The significance of the clustering of the genes for the eosinophil growth regulators in terms of gene regulation remains to be established.

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