Table 2. β-globin gene alleles and haplotypes detected in 58 Albanian patients; populations in which the alleles have been reported.

<table>
<thead>
<tr>
<th>Alleles</th>
<th>Haplotypes</th>
<th>Chromosomes</th>
<th>Populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVS-I-110 (G→A)</td>
<td>I</td>
<td>42</td>
<td>Mediterranean</td>
</tr>
<tr>
<td>Codon 39 (C→T)</td>
<td>II</td>
<td>17</td>
<td>Mediterranean</td>
</tr>
<tr>
<td>IVS-6 (T→C)</td>
<td>M</td>
<td>12</td>
<td>Mediterranean</td>
</tr>
<tr>
<td>Codon 44 (C)</td>
<td>I</td>
<td>4</td>
<td>Kurdish, Jewish (30%), Mediterranean</td>
</tr>
<tr>
<td>IVS-1 (G→A)</td>
<td>V</td>
<td>3</td>
<td>Mediterranean</td>
</tr>
<tr>
<td>IVS-II-1 (G→A)</td>
<td>III</td>
<td>2</td>
<td>Mediterranean</td>
</tr>
<tr>
<td>Poly A (ATT/AA→ATT/AA)</td>
<td>I</td>
<td>1</td>
<td>Druze and Yemenite Jews, Balkan, Yugoslavian (4%), Turkish</td>
</tr>
<tr>
<td>IVS-II-745 (C→G)</td>
<td>VI</td>
<td>1</td>
<td>Mediterranean, Turkish, Egyptian</td>
</tr>
<tr>
<td>Codon 5 (CT)</td>
<td>V</td>
<td>1</td>
<td>Mediterranean, Bulgarian (5%), Turkish, Albanian, Croatian, United Arab Emirates</td>
</tr>
<tr>
<td>Codon 82-83 (-G)</td>
<td>II</td>
<td>1</td>
<td>Jordanian, Czecho-Slovakian, Balkan</td>
</tr>
<tr>
<td>Codon 37 (G→A)</td>
<td>I</td>
<td>1</td>
<td>Jordanian (9%), Israeli Arab (5%), Saudi Arabian, Egyptian, Turkish, Iberian</td>
</tr>
<tr>
<td>β¹</td>
<td>Benin type</td>
<td>24</td>
<td>Mediterranean, Central West Africa</td>
</tr>
<tr>
<td>β²</td>
<td>Benin type</td>
<td>2</td>
<td>Mediterranean, Central West Africa</td>
</tr>
<tr>
<td>β²</td>
<td></td>
<td>1</td>
<td>Mediterranean, Indian Asian</td>
</tr>
</tbody>
</table>

Total of chromosomes 114

RFLP haplotype analysis was carried out as previously reported. The RFLPs analyzed were Hind III/γ, Hind III/γ, Hind III/γ, γ, Ava III/β and Bam HI/3′β. The haplotypes were classified according to Orkin. In italics: populations in which the haplotypes have not yet been characterized.

37(G→A), codon 82-83 (G→I).

All the β-thal and the HB variant alleles were found to be associated with the same haplotypes described in other populations (Table 2). This indicates that mutations did not have an independent origin and suggests that the origin and spread of β-thal mutations and HB variants in Albania is in keeping with the historical relationships between Albania and neighboring or more distant populations (Greeks, Romans, Slavs and Arabs) and that Albania has experienced a discrete genetic flow.

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Key words: β-thalassemia, HB variants, α-globin Albania.

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References


Late response to donor lymphocyte infusions in patients with chronic myeloid leukemia relapsing after allogeneic stem cell transplantation

Donor lymphocyte infusions were given to 13 consecutive chronic myeloid leukemia patients in relapse after allogeneic stem cell transplantation. Of the 13 patients, 11 achieved a cytogenetic remission and 2 a cytogenetic remission. The median response duration is 16 months (range 1-36), respectively. After a median follow-up of 24 months, no patient shows evidence of relapse.


Thirteen consecutive chronic myeloid leukemia (CML) patients relapsing after allogeneic stem cell transplant (allo-SCT) from an HLA-identical sibling were treated with donor lymphocyte infu-
After the start of IFN-interferon (IFN) 5th patient either after 9 months of the LDL or after 8 months and 14 months, respectively. No response was observed in the lymphocyte (HDL) infusion, obtaining molecular remission at 5 did not respond at 3 and 16 months, and received a high dose molecular remission, at 3 and 6 months, respectively. Two patients (1 hematologic relapse and 1 cytogenetic relapse) achieved a molecular remission more than 1 year after DLI. After a median (range) can be seen, several patients achieved a cytogenetic or molecular response after DLI. As can be seen, these patients had a median time of 5 months to obtain a cytogenetic and molecular response, with a significant number of patients responding more than one year after DLI. This is much longer than usually waited before a second infusion, with a higher lymphocyte dose, as given.4 These results seem to indicate the importance of allowing an interval of at least 6 months between increasing doses of donor lymphocytes in order to assess the response to a particular lymphocyte dose better. Regular follow-up with quantitative reverse transcriptase polymerase chain reaction (RT-PCR) for BCR-ABL transcripts would help to identify late responders.

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Key words: donor lymphocyte infusions, chronic myeloid leukemia, relapse, allogeneic stem cell transplantation.

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References

Figure 1. Time to achieve a hematologic, cytogenetic, or molecular response after DLI.
NFκB activity consistently showed higher mRNA levels of NFκB-regulated genes in MDS compared with normal donors. However, as shown in Figure 1, there were no significant differences in Stat activation. Another transcript factor associated with NFκB activity), and from a normal donor (C5) was obtained and analyzed for the expression of a number of NFκB target genes by semiquantitative RT-PCR. (B) Bone marrow cells of MDS patients and normal donors (controls). Formation of protein-DNA complexes was determined by EMSA using radiolabeled probes that contained consensus sites for Stat3, Stat5, and NFκB. Nuclear extracts from sample 11 were pre-incubated with antibodies specific for p50, p65, p52, c-Rel, and RelB. We describe a significant increase in the DNA binding activity of nuclear factor-κB (NFκB) in bone marrow cells from patients with myelodysplastic syndrome (MDS) compared with normal donor cells. Furthermore, MDS samples with increased NFκB activity consistently showed higher mRNA levels of NFκB-regulated cytokines.

Increased intramedullary apoptotic death of hematopoietic cells is believed to contribute to the ineffective hematopoiesis in myelodysplastic syndromes (MDS), a myeloid hemopathy with a tendency to evolve to acute leukemia. However, the underlying molecular mechanisms that are responsible for this alteration remain elusive.

A deregulated expression of Bcl-2 and Bcl-xL has been associated with disease progression in MDS. As these antiapoptotic genes are transcriptionally regulated by Stat3 and Stat5 in different cell systems, we first analyzed the DNA binding activity of these Stat proteins in bone marrow from 14 patients with MDS and 6 normal donors. However, as shown in Figure 1, there were no significant differences in Stat activation. Another transcription factor associated with Bcl-2 family members (Bcl-xL, Bcl-2, A1) is NFκB. We, therefore, analyzed the activity of NFκB present in 17 MDS bone marrow samples (refractory anemia, n=5; refractory anemia with ring sideroblasts, n=5; refractory anemia with excess blasts, n=3; refractory anemia with excess blasts in transformation, n=2; chronic myelomonocytic leukemia, n=2), and found that at least six of them, including 4 refractory anemia samples (3, 11, 14, and 17), 1 refractory anemia with ring sideroblasts (sample #4), and 1 refractory anemia with excess of blasts (sample #7) showed a significant increase in the signal given by the NFκB-DNA complex, as assessed by electrophoresis onto a 2% agarose gel and stained with ethidium bromide. 18S rRNA was used as an amplification control. Each amplification was repeated at least three times, and similar results were obtained.