anomalies (for review see Willig et al3). Ribosomal protein S19 (RPS19) was identified as a candidate gene for DBA and mutations in this gene have been described in 25% of DBA patients.2,3 However, the mechanism by which mutations in RPS19 can lead to DBA remains unclear.

RPS19 is a structural component of a small ribosomal subunit and is known to have two other functions. First, RPS19 homodimers are released by apoptotic cells and act as a chemotactic factor for monocytes during macrophage-dependent apoptotic cell clearance.4 Second, RPS19, together with ribosomal proteins S3a, S13, S16, and S24, participates in the binding of eukaryotic initiation factor 2 (eIF-2) to ribosomes.5 eIF-2 plays a central role in the initiation of translation, and its function is controlled in an erythroid-specific manner by heme-regulated kinase.6 To investigate the possibility that DBA phenotype might result from mutations in ribosomal proteins involved in eIF-2 binding, we sequenced cDNAs for RPS3a, S13, S16, and S24 in 14 patients from the Czech National DBA Registry. Five of these patients have been previously shown to carry a mutation in the RPS19 gene.7

After obtaining informed consent, total RNA was isolated from peripheral blood mononuclear cells, and reverse transcription was performed using an oligo(dT) primer. Primers specific for full-length coding regions of RPS3a, S13, S16, and S24 were used for PCR amplification. PCR products were sequenced on an automated genetizer, and resulting sequences were evaluated for the presence of mutations.

In all DBA patients tested, no mutations in RPS3a, S13, S16, and S24 were found on the cDNA level. We therefore conclude that these four of the five ribosomal proteins important for eIF-2 binding to ribosomes are not involved in DBA pathogenesis.

To the editor:

Increased frequency of HLA-DRB1*1302 haplotype in patients with nonimmune chronic idiopathic neutropenia of adults

Nonimmune chronic idiopathic neutropenia of adults (NI-CINA) is a frequently seen granulocytic disorder characterized by the “unexplained” persistent decrease of the number of circulating neutrophils below the lower limit of the normal distribution in a given ethnic population.1,2 The diagnostic criteria allowing the identification of the condition among other types of chronic neutropenia are presented elsewhere.1,5 The cause of the disorder and the underlying mechanisms leading to neutropenia in the affected subjects are unknown, but recent studies in our laboratory provided strong evidence for the existence of an unrecognized low-grade chronic inflammatory process in these patients, which may be involved in the pathogenesis of NI-CINA by increasing the production of a variety of proinflammatory cytokines and chemokines3 and therefore affecting both neutrophil production in bone marrow4 and neutrophil extravasation in the periphery.5 Here, we describe a predisposition of HLA-DRB1*1302 haplotype–carrying individuals to develop NI-CINA.

The study was carried out on 56 NI-CINA patients and 39 healthy volunteers, all residents of the island of Crete. Venous blood was collected into vacutainer tubes containing ethylenediaminetetraacetic acid (EDTA) as anticoagulant and used as a DNA source. DNA extraction was carried out by salting-out technique. For the typing of HLA alleles, polymerase chain reaction (PCR) was utilized. HLA-A, -B, and -C alleles were typed using PCR-sequence specific primers (PCR-SSP) with primer sets provided by PelFreez Clinical systems (Brown Deer, WI). HLA-DRB1 alleles were typed using the ELPHA high resolution hybridization system provided by Biotest AG (Dreieich, Germany). HLA-DQB1 and DPB1 alleles were typed using the

Table 1. Frequency of selected HLA-DRB1 haplotypes in the NI-CINA patients

<table>
<thead>
<tr>
<th>Haplotype</th>
<th>Patients (%)</th>
<th>Healthy controls (%)</th>
<th>x2-value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-DRB1*0101</td>
<td>4 (7.14)</td>
<td>2 (5.13)</td>
<td>0.9748</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*0301</td>
<td>3 (5.36)</td>
<td>1 (2.56)</td>
<td>0.8827</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*0701</td>
<td>12 (21.43)</td>
<td>6 (15.38)</td>
<td>0.6359</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1101</td>
<td>2 (3.57)</td>
<td>3 (7.69)</td>
<td>0.6761</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1110</td>
<td>10 (17.66)</td>
<td>12 (30.77)</td>
<td>0.2223</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1114</td>
<td>21 (37.5)</td>
<td>15 (38.46)</td>
<td>0.9045</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1201</td>
<td>2 (3.57)</td>
<td>2 (5.13)</td>
<td>0.8827</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1301</td>
<td>3 (5.36)</td>
<td>5 (12.82)</td>
<td>0.3612</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1302</td>
<td>12 (21.43)</td>
<td>1 (2.56)</td>
<td>5.4210</td>
<td>P = .0199</td>
</tr>
<tr>
<td>HLA-DRB1*1401</td>
<td>5 (8.93)</td>
<td>6 (15.38)</td>
<td>0.5212</td>
<td>ns</td>
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<tr>
<td>HLA-DRB1*1501</td>
<td>3 (5.36)</td>
<td>4 (10.26)</td>
<td>0.6171</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1502</td>
<td>4 (7.14)</td>
<td>3 (7.69)</td>
<td>0.7655</td>
<td>ns</td>
</tr>
<tr>
<td>HLA-DRB1*1601</td>
<td>10 (17.66)</td>
<td>3 (7.69)</td>
<td>0.2650</td>
<td>ns</td>
</tr>
</tbody>
</table>

†Yates continuity-corrected chi-square test. Statistically significant at P ≤ .05. ns, nonsignificant difference.
‡Proportions of haplotype-carrying subjects are in parentheses.

References

Innomipad reverse slot blot hybridization system provided by Murex (Immunogenetics, Zwindezech, Belgium). Results were analyzed with the Yates continuity-corrected chi-square test using the GraphPad program.

We found that the frequency of the HLA-DRB1*1302 haplotype was 21.43% in the group of patients compared to 2.56% in the controls (P = .0199) (Table 1). The relative risk for the carriers was 8.36. The frequencies of all other HLA haplotypes did not differ significantly between patients and control subjects.

The clinical and biologic significance of our finding is unknown, but it seems possible that the frequency of the HLA-DRB1*1302 haplotype may have a role in the development of the aforementioned unrecognized low-grade chronic inflammation. Associations of HLA haplotypes with chronic inflammatory processes have already been well documented in a variety of clinical disorders.8 We believe that the increased frequency of the HLA-DRB1*1302 haplotype in NCI-CINA patients may indicate the possible genetic basis in the development of such an inflammation, and thus it may predispose the haplotype-carrying subjects to develop the disorder.

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To the editor:

CD15-expressing phagocytic plasma cells in a patient with multiple myeloma

In mammals there are 2 cell types that can phagocytize: macrophages and neutrophils. Malignant cytophagocytosis is a fulminating disease characterized by phagocytosis of bone marrow cellular elements mainly by marrow macrophages (histiocytes) or rarely by other cells (eg, myeloid blasts). Cytophagocytosis by plasma cells in multiple myeloma is an extremely rare condition. Plasma cells are antibody-producing cells and have no phagocytic function. There are only a few reports describing phagocytic plasma cells in patients with multiple myeloma.1-4 None of these reports could explain the mechanism or the clinical importance of phagocytosis by plasma cells. Here we report a myeloma patient with phagocytic myeloma cells expressing CD15 on their surfaces.

A 52-year-old female patient was admitted to our hospital with complaints of weakness and fatigue. Her medical history was unremarkable. Findings from a physical examination were normal, except that there was pallor. Laboratory findings were as follows: erythrocyte sedimentation rate was 120 mm/h; hemoglobin, 8.9 g/dL; white blood cell count, 3.8 × 10⁹/L; neutrophil count, 1.3 × 10⁹/L; and platelet count, 138 × 10⁹/L. Rouleaux formation was seen on peripheral blood smear. Blood urea nitrogen, uric acid, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase levels were normal. Serum protein electrophoresis showed a monoclonal band (4.22 g/dL) in the gamma region. Serum immunoelectrophoresis revealed an abnormal immunoprecipitin with IgG-kappa specificity. Beta-2 microglobulin level was 6478 ng/mL (normal range, 1.3-1.9 mg/dL). Results of x-ray studies of the extremities, skull, ribs, pelvis, and long bones were normal. Bone marrow aspiration showed normal maturation of the granulocytic, erythrocytic, and megakaryocytic series. The myeloid/erythroid ratio was 2:1. Plasma cells represented 22% of the nucleated cells of bone marrow, and binucleated and atypical plasma cells were seen. In one-third of plasma cells, phagocytosis of mainly erythrocytes and platelets (and rarely, neutrophils, myelocytes, and lymphocytes) was seen (Figure 1). Diffuse plasma-cell infiltration with prominent kappa

Figure 1. Phagocytic plasma cells. May-Grünwald-Giemsa stain (original magnification × 1000).

References

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Increased frequency of HLA-DRB1*1302 haplotype in patients with nonimmune chronic idiopathic neutropenia of adults

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