Abstract detail

Reference	Haematologica 2009; 94[suppl.2]:593 abs. 1529
Title	_TNFRSF13B GENE EXPRESSION AND MOLECULAR ANALYSIS IN B-CELL CHRONIC LYMPHOPROLIFERATIVE DISORDERS
Authors	_M. Speletas,1 A. Mamara,1 F. Kalala,1 K. Liadaki,1 N. Papadoulis,2 A. Kioumi,3 N. Giannakoulas,1 S. Lafioniatis,4 K. Loukidis,3 P. Matsouka,1 Z. Kartasis5, A. Germenis1
Abstract	_Background. Mutations in the TNFRSF13B gene, encoding TACI, a tumor necrosis factor (TNF) superfamily member, have recently been implicated in the pathogenesis of common variable immunodeficiency. Expression of this gene, yet of unknown significance, has been detected in malignant lymphocytes of patients with chronic lymphoproliferative disorders (LPDs). Aims. Since certain genotypes of other TNF superfamily members have been implicated as contributing to the enhanced survival potential of malignant lymphocytes, this study was scheduled to investigate in LPDs the mutational status of the TNFRSF13B gene and its expression, in relation to the disease phenotype. Materials and Design and Methods: One-hundred and forty-five patients (M/F: 78/67, mean age: 67.9 years, range: 41-87) with LPDs (108 with B-cell chronic lymphocytic leukemia, B-CLL; 29 with low-grade non-Hodgkin lymphomas (NHL); 3 with diffuse large B-cell lymphoma, DLBCL; 5 with hairy cell leukemia, HCL) were enrolled in the study. Diagnoses were made by standard criteria. The expression levels of TACI were estimated by flow cytometry using an anti-CD267 monoclonal antibody (Abcam, clone: 1a1) in 102 LPD patients (81 with B-CLL and 21 with low-grade NHL). The two most common polymorphisms of TNFRSF13B (V220A and P251L) were detected by PCR-RFLP, using DNA extracted from peripheral blood or bone marrow

DNA extracted from peripheral blood or bone marrow. Thirty-seven individuals (M/F:19/18, mean age: 64.8 years, range: 47-87), free of disease, were also analyzed for TACI expression and TNFRSF13B polymorphisms and were considered as normal controls. Statistical analysis was performed using the SPSS statistical software. Results: Patients with B-CLL displayed significantly lower expression levels of TACI (mean±STDEV: 16.2±21.3%) compared to both patients with low-grade NHL (43.2±27.6%) and normal controls (40.6±20.6%) ($p<0.001$ and $p<0.001$, respectively). Moreover, the presence of TNFRSF13B-P251L was associated with a 2.8-fold increased probability for LPD development (allele frequencies 17.2% vs 6.8%, 95%CI: 1.05-7.87, $p=0.039$), while the allele frequency of TNFRSF13B-V220A did not significantly differ between patients and controls (3.1% vs 5.4%, $p=0.338$). Finally, no correlation of TACI expression or the presence of TNFRSF13B polymorphisms with autoimmune manifestations, the presence of hypogammaglobulinemia, or monoclonal gammapathy was observed. Conclusions. A positive association of TACI expression and TNFRSF13B-P251L polymorphism with LPD phenotype was observed and considering the development of new anti-TACI treatments, our findings might have significant therapeutic consequences.