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Original article

Genetic Variability of Tumor Necrosis Factor Receptors Type I and II in Lymphoproliferative Diseases in the Serbian Population –

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SUMMARY

TNF-alpha and LT-alpha are involved in the pathogenesis of established lymphoproliferative diseases. Both molecules bind to TNFRI and TNFRII. TNFRI is the major mediator of the TNF pro-apoptotic and proliferative effects and TNFRII might enhance these effects. TNF receptors I and II are normally present on hematopoetic cells. TNFR II is characteristic only on immune cells, especially on peripheral leukocytes. Neoplastic B cells and activated B lymphocytes have increased expression of surface TNFR I. In this study, we have analyzed polymorphisms in the TNFRI gene (TNFRI+36A/G SNP) and polymorphism in the TNFRII gene (TNFRII + 676 T/G). All these polymorphisms were studied in patients with chronic lymphocytic leukemia (CLL), patients with non-Hodkin's lymphoma (NHL) and in healthy controls. The present study was undertaken to investigate the genetic association of these polymorphisms with lymproproliferative disease development.

A total of 68 patients (49-CLL, 19-HNL) were diagnosed at the Clinic of Hematology, Clinical centre Niš, Serbia, using clinical findings and conventional morphological, cytochemical and immunological tests. Genomic DNA was isolated from isolated lymphocytes by proteinase K/phenol/chloroform method, and genotyped for TNFR I (A36G) and TNFR II (T676G) using the PCR-RFLP method.

No significant differences in allele frequencies of TNFR1 polymorphism were found between the patients with lymphoproliferative disease and healthy individuals. In a group of healthy individuals, the study has revealed for the first time significantly higher TNFRI G/G genotype compared to the patients with lymphoproliferative disease ($\chi^2 2 = 5.66$; $p = 0.017$). Also, we reported the implication of TNFRII T allele in NHL pathogenesis, respectively ($\chi^2 2 = 10.77$; $p = 0.001$; Mantel-Haenszel: $\chi^2 2 = 10.64$; $p = 0.0011$).

Our data showed that TNFRII T676G polymorphisms have an important role in NHL pathogenesis but not in CLL patients. A/A polymorphism in TNFRI was not associated with CLL and NHL patients in the Serbian population. Investigated polymorphisms on TNFR genes in leukemic cells of CLL and NHL patients have not showed a correlation with increased proliferation of B lymphocytes and increased expression of TNF R II on B CLL lymphocytes.

Key words: **TNFR, CLL, NHL, genetic polymorphism**

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