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SHORT COMMUNICATION

Expression of Bcl2L12 in chronic lymphocytic leukemia patients: association with clinical and molecular prognostic markers

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Abstract Dysregulation of apoptosis is a distinctive feature of chronic lymphocytic leukemia (CLL), although a unique mechanism underlying apoptosis resistance of CLL B lymphocytes has not been identified yet. Aberrant expression as well as genetic and epigenetic alterations of numerous genes involved in different pathways of apoptosis regulation has been described in CLL. Here, we report the expression analysis of Bcl2L12 (Bcl2-like 12), a novel apoptotic gene belonging to Bcl2 family, in 58 Serbian CLL patients. Quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR) analysis revealed a significant overexpression of Bcl2L12 mRNA in CLL samples compared to non-leukemic samples, implying its role in the pathogenesis of the disease. Receiver operating characteristic (ROC) analysis showed that Bcl2L12 expression efficiently discriminates CLL cases from healthy controls. However, relatively homogenous Bcl2L12 mRNA expression among patients did not reflect their clinical characteristics (with the exception of lactate dehydrogenase status and time from diagnosis to treatment) and failed to show association with the most informative prognostic markers, namely the mutational status of rearranged immunoglobulin heavy chain variable region genes, CD38 and lipoprotein lipase gene (LPL) expression.

Keywords Chronic lymphocytic leukemia · Bcl2L12 · IGHV mutational status · CD38 · LPL · Expression analysis

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Introduction

Chronic lymphocytic leukemia (CLL), the most common type of adult leukemia in Western countries, manifests as monoclonal expansion of small, mature $CD5^+$ $CD19^+$ $CD23^+$ $sIgM^{low}$ B lymphocytes. Since circulating CLL cells are arrested in G_0/G_1 phase of the cell cycle, their gradual accumulation in blood, bone marrow and secondary lymphoid organs is being attributed primarily to impaired apoptosis, although recent studies identified substantial levels of cell turnover within the leukemic clone [1, 2]. Resistance to apoptosis results from microenvironmental survival signals [3], as well as from inherent dysregulation of apoptotic machinery in CLL cells [4–7]. Genetic alterations and aberrant expression of Bcl2-family proteins have been described in CLL, such as overexpression of Bcl2, $BclX_L$ and Mcl1, and increased Bcl2/Bax ratio [8–12]. However, these alterations could not be consistently associated with the disease stage, clinical progression and response to treatment.

Bcl2L12 (Bcl2-like 12) is a novel member of Bcl2-family of apoptosis regulators, whose pro- or anti-apoptotic

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