

BCL2 expression in chronic lymphocytic leukemia (CLL): lack of association with the *BCL2*-938A>C promoter single nucleotide polymorphism (SNP).

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High-level expression of BCL2 comparable to that seen in follicular lymphoma with t(14;18)(q32;q21) is seen in about 80% of CLL in the absence of *BCL2* chromosomal translocation. Various mechanisms have been proposed, including promoter hypomethylation, loss of miRNA expression and high-level expression of nucleolin. *BCL2* transcription is controlled by two major promoters, P1 and P2. A SNP (-938C>A) within an inhibitory region of the *BCL2* promoter has been reported to regulate BCL2 protein expression and to be associated with several adverse prognostic factors in CLL (Nuckel et al Blood. 2007;109:290). We assessed the frequency of this SNP in 276 CLL attending a single centre. 97 were A/A genotype, 127 were A/C and 52 C/C, comparable to the frequencies seen in the previous study. However, in contrast to the previous report, we found no association of this SNP with either BCL2 protein levels or with clinical or laboratory parameters including clinical stage, time to progression or *IGHV* mutations or cytogenetic abnormalities. Of 100 cases investigated by quantitative western blot, BCL2 protein levels remained constant within individual cases at multiple time points. The 19 cases showing the lowest levels of BCL2 protein expression were studied further to assess whether this group was distinct. CLL expressing lower amounts of BCL2 were biologically and clinically heterogeneous. Five cases nevertheless exhibited high-level *BCL2* RNA expression indicating translational control. Four cases were rapidly progressive and exhibited fludarabine-resistance. BCL2 protein levels in CLL reflect a complex interplay of transcriptional and post-transcriptional controls, but are not associated with the promoter SNP.