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DEREGULATION OF NOTCH2 SIGNALING IN B-CLL

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The overexpression of the transmembrane glycoprotein CD23 is one of the major characteristics of B-CLL cells. Besides the prognostic potential of its soluble cleavage product, sCD23, selective expression of the CD23a isoform is concurrent to a state of B-CLL cell survival, thereby providing a link between CD23a and the malfunction of apoptosis characteristic for this neoplastic B-cell type.
By electrophoretic mobility shift assays, we identified a transcription factor complex (C1) which binds sequence specific to one known and four newly identified putative CBF1 recognition sites in the *CD23a* core promoter region. The significance of this complex was underlined by the fact, that in B-cell samples the intensity of C1 correlated with their respective levels of *CD23a* transcription. Furthermore, using Epstein Barr virus (EBV) infected B-cells as a model for CBF1 mediated *CD23a* expression, C1 was found to be EBV inducible. Supershift assays revealed that the nuclear form of Notch2 is a component of C1 in B-CLL cells, supporting a model in which NotchIC activates transcription by binding to CBF1 tethered to DNA. Finally, RT-PCR analysis indicates that the Notch2 oncogene is overexpressed in B-CLL cells. These data suggest that deregulation of Notch2 signaling, which is known to inhibit differentiation and apoptosis, plays a pivotal role in the upregulation of the CD23 gene in B-CLL cells.