Dysregulation of apoptosis in Waldenström's macroglobulinaemia does not involve NFkB activation.

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Low-grade lymphoproliferative disorders are characterized by defective apoptosis leading to the accumulation of slowly dividing neoplastic lymphocytes. Constitutive activation of NFkB, has been demonstrated to play a key role in apoptosis inhibition in lymphomas, in particular extranodal marginal zone lymphoma, where the t(11;18) and t(1;14) chromosomal translocations activate NFkB through the activation of I kappa kinase. This results in the nuclear translocation of both NFkB and Bcl-10.

We postulated that Waldenström's macroglobulinaemia (WM), a lymphoproliferative disorder in which Bcl-2 is universally expressed, might also have NFkB activation as a central anti-apoptotic mechanism. We therefore used immunohistochemistry (ABC technique) to determine the expression and cellular localization of two major NFkB subunits (p50 and p65) as well as Bcl-10. Immunostaining for the c-rel NFkB subunit is ongoing. Resin-embedded bone marrow trephine biopsies were obtained from 20 patients with WM and Bcl-2 expression was demonstrated in each case. p50 and p65 expression was demonstrated in each of the 20 cases examined but staining appeared to be exclusively cytoplasmic. Nuclear expression of NFkB subunits was not seen in any of the cases examined. Similarly, 17 of 20 cases demonstrated positive staining for Bcl-10 but again the staining appeared to be exclusively cytoplasmic. 3 cases were Bcl-10 negative.

The absence of nuclear NFkB suggests that its activation is not a feature of WM and that alternative mechanisms of apoptosis inhibition exist in this disorder. This also suggests that novel therapeutic strategies involving proteasome inhibitors may not be appropriate in WM.