Immunotoxin BL22 induces apoptosis in mantle cell lymphoma (MCL) cells dependent on Bcl-2 expression.

Abstract:
Mantle cell lymphoma (MCL) is an incurable mature B cell proliferation, combining the unfavourable clinical features of aggressive and indolent lymphomas. The blastic variant of MCL has an even worse prognosis and new treatment options are clearly needed. We analysed the effects of BL22, an immunotoxin composed of the Fv portion of an anti-CD22 antibody fused to a 38-kDa Pseudomonas exotoxin-A fragment on four MCL cell lines as well as on primary cells of four MCL patients. Apoptosis induction by BL22 was much more pronounced in MCL cell lines with low Bcl-2 expression (NCEB-1, JeKo-1 and JVM-2) compared to Granta-519 cells with high Bcl-2 expression. While the expression of the antiapoptotic protein Mcl-1 declined (NCEB-1, Granta-519), Bcl-2 levels remained unchanged in Granta-519 cells. However transfection of BCL2 cDNA into NCEB-1, JeKo-1 and JVM-2 cells significantly reduced BL22-mediated toxicity. Accordingly we examined the effects of Bcl-2 inactivation in Granta-519 cells using siRNA. Indeed, apoptosis induction was strongly enhanced in Granta-519 cells with silenced Bcl-2. Our results were confirmed in freshly isolated MCL-cells from patients with leukaemic MCL. We conclude that Bcl-2 expression is important for mediating resistance against the immunotoxin BL22 in MCL cells.