



Type I interferon (IFN-alpha/beta) rescues B-lymphocytes from apoptosis via PI3Kdelta/Akt, Rho-A, NFkappaB and Bcl-2/Bcl(XL).

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Abstract:

Although IFN-alpha was reported to promote the survival of peripheral B-lymphocytes via the PI3-kinase-Akt pathway, the triggered signalling pathways involved in the protection of B cell from apoptosis need to be clarified. Using flow cytometry and western blot analysis, we have found that type 1 IFNs (IFN-alpha/beta) protect human B cells in culture from spontaneous apoptosis and from apoptosis mediated by anti-CD95 agonist, in a dose- and time-dependant manner. IFN-alpha/beta-mediated anti-apoptotic effect on human B cells was totally abrogated by blockade of IFNR1 chain. Our data indicate that PI3Kdelta, Rho-A, NFkappaB and Bcl-2/Bcl(XL) are active downstream of IFN receptors and are the major effectors of IFN-alpha/beta-rescued B cells from apoptosis. Furthermore, immunohistochemical results show marked reduction in numbers of CD20 positive B cell in both spleen and Peyer's patches from mice treated with anti-IFNR1 blocking antibody compared with control group. Moreover, ultrastructural observations of these organs show an obvious increase in apoptotic cells from mice treated with anti-IFNR1 blocking antibody. Our results provide more details about the triggered signalling pathways and the phosphorylation cascade which are involved in the protection of B cell from apoptosis after treatment with IFN-alpha/beta. Copyright 2010 Elsevier Inc. All rights reserved.

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