Blocking type I interferon (IFN) signaling impairs antigen responsiveness of circulating lymphocytes and alters their homing to lymphoid organs: protective role of type I IFN.

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Abstract:

BACKGROUND: We recently demonstrated that type I Interferon (IFN) rescues in vitro, human B-lymphocytes from apoptosis via PI3K□/Akt, Rho-A, NF□B and Bcl-2/BclXL. In the present study we extended our work to clarify, in vivo, the role of type I IFN signalling on the circulating and lymphoid organs homing lymphocytes. METHODOLOGY: Two groups of mice 13 in each were set: type I IFN signalling blocked mice injected with anti-IFNAR1 antagonist antibody (10 mg/kg body weight) once/day for up to 20 days, and control group were injected with vehicle alone. RESULTS: Flow cytometry analysis to monitor the blood lymphocyte phenotype and proliferation have shown a significant decrease in CD45R/B220(+) [corrected] B cells, CD4(+) and CD8(+) T cells in treated animals. Furthermore, the proliferative capacities of these lymphocyte subsets were significantly decreased in treated animals compared to those of control mice. Marked reduction in the plasma levels of IL-2 and IL-7 (cytokines important for the development of T and B cells) but not of IL-6 or IL-10 was observed in treated mice and this may a cause for emergence decrease in B and T cell numbers. Immunohistochemical studies have further shown a marked reduction in the numbers of CD20(+) B cells in spleen and Peyer's patches and CD3(+) T cells in thymus of treated animals. Moreover, electron microscopy examinations have revealed a loss of lymphocytes with characteristic features of apoptosis. CONCLUSION: Our data confirmed that the in vivo inhibition of type I IFN signaling induce decrease in the numbers and defective functions of circulating and lymphoid organs homing lymphocytes providing a strong evidence for the protective effects of type 1 IFNs (IFN-□/□) on B and T lymphocytes. Copyright © 2010 S. Karger AG, Basel.

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