Effects of interferon gamma on native human acute myelogenous leukaemia cells

Journal	Cancer Immunology, Immunotherapy
Publisher	Springer Berlin / Heidelberg
ISSN	0340-7004 (Print) 1432-0851 (Online)
Subject	Medicine
Issue	Volume 56, Number 1 / January, 2007
Category	Original Article
DOI	10.1007/s00262-006-0159-1
Pages	13-24
SpringerLink Date	Thursday, April 13, 2006

Elisabeth Ersvaer[1], Jørn Skavland[1], Elling Ulvestad[2], Bjørn Tore Gjertsen[1] and Øystein Bruserud[1]

(1) Institute of Medicine, Section for Hematology, The University of Bergen and Haukeland University Hospital, Bergen, Norway

(2) Department of Microbiology and Immunology, The Gade Institute, Haukeland University Hospital and The University of Bergen, Bergen, Norway

Received: 21 December 2005 **Accepted:** 14 March 2006 **Published online:** 13 April 2006

Abstract T cell targeting immunotherapy is now considered a possible strategy in acute myelogenous leukaemia (AML), and IFNγ release may then contribute to the antileukaemic effects. We investigated the effects of IFNγ on native human AML cells. Normal T cells could be activated to release IFNγ in the presence of AML cells. Furthermore, high levels of CD119 (IFNγ receptor α chain) expression were observed for all 39 patients examined. Receptor expression was decreased after exposure to exogenous IFNγ, and receptor ligation caused Stat1 phosphorylation but no phosphorylation of the alternative messengers Erk1/2. The effect of exogenous IFNγ on AML blast proliferation was dependent on the local cytokine network and IFNγ (1) inhibited proliferation in the presence of exogenous IL1β, GM-CSF, G-CSF and SCF; (2) had divergent effects in the presence of IL3 and Flt3 (65 patients examined); (3) inhibited proliferation in the presence of endothelial cells but had divergent effects in the presence of fibroblasts, osteoblasts and normal stromal cells (65 patients examined). IFNγ increased stress-induced (spontaneous) in vitro apoptosis as well as cytarabine-induced apoptosis only for a subset of patients. Furthermore, IFNγ decreased the release of proangiogenic CXCL8 and increased the release of antiangiogenic CXCL9–11. We conclude that IFNγ can be released in the presence of native human AML cells and affect AML cell proliferation, regulation of apoptosis and the balance between pro- and antiangiogenic chemokine release.

Keywords Acute myeloid leukaemia - Interferon gamma - Cytokines - Apoptosis - Proliferation