Role of NF-κB in regulation of apoptosis of erythroid progenitor cells

N. Sae-ung 1,2,3, T. Matsushima 1, I. Choi 1, Y. Abe 1, P. Winichagoon 3, S. Fucharoen 3, H. Nawata 1, K. Muta 1

1 Department of Medicine and Bioregulatory Science, Graduate School of Medical Science, Kyushu University, Fukuoka, Japan
2 Faculty of Medical Technology, Mahidol University, Bangkok, Thailand
3 Thalassemia Research Center, Institute of Science and Technology for Research and Development, Mahidol University, Salaya Campus, Nakornpathom, Thailand

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ABSTRACT

Abstract: Erythropoietin (EPO) and interferon-γ (IFN-γ) added to human erythroid progenitor cells purified from peripheral blood (erythroid colony-forming cells; ECFC) significantly reduces apoptosis as assessed by flow cytometry (FCM) using annexin V. To clarify the role of NF-κB in the regulation of the apoptosis of erythroid progenitor cells, cyclosporin A (CsA), which blocks dissociation of the NF-κB complex, was added to serum-free cultures of ECFC. CsA induced the apoptosis of ECFCs in the presence of EPO or IFN-γ, but at different magnitudes. In the presence of a relatively low concentration of CsA (10 μM), apoptosis was induced only in cultures with EPO. The direct involvement of NF-κB was then assessed by Western blotting and confocal microscopy. In the presence of EPO, NF-κB was abundant both in the cytoplasm and in the nucleus, and nuclear expression was diminished after adding CsA. In contrast, NF-κB was undetectable in the nucleus in the presence of IFN-γ. The effect of CsA on mitochondrial function was investigated by determining the ΔΨm and reactive oxygen species production. CsA disturbed the transmembrane potential in the presence of either EPO or IFN-γ, although the viability of the cells was maintained in the presence of IFN-γ plus CsA. These results indicate that IFN-γ reduced the apoptosis of erythroid progenitor cells through a unique signaling pathway that is independent of NF-κB translocation, and which is not mediated by modulating mitochondrial function, whereas EPO reduced apoptosis through NF-κB translocation to the nucleus.

KEYWORDS: apoptosis • NF-κB • erythroid progenitor cell

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