[S15-5] [11/29/2005(Tues) 16:30-17:00/ Annex Banquet]

Heme Oxygenase-1 Induction by YS 51, An Analogue of Higenamine, Inhibits Nitric Oxide-Induced Apoptosis of ROS 17/2.8 cells

Kichurl Chang

Department of Pharmacology, College of Medicine, Gyeogsang national University, Korea

Anti-apoptotic mechanism of action of YS 51, a synthetic isoquinoline alkaloid, was investigated in osteoblast cells, ROS 17/2.8, when activated with three combination (cytokine mixture, CM) of IFN-g (10 U/ ml), TNF-a (10 U/ ml) and LPS (1 mg/ ml). ROS 17/2.8 cells were treated with CM in the presence or absence of YS 51, where Western blot analysis was performed to quantify expression of inducible nitric oxide synthase (iNOS) and heme oxygenase-1 (HO-1). Effect of YS 51 against NO-mediated apoptosis was analyzed by DNA-strand break experiment. Co- or pre-treatment of YS 51 with CM significantly reduced not only NO production but also iNOS expression. YS 51 increased HO-1 expression and activity in a concentration-dependent manner, which was related with inhibition of the activation and translocation of NF-kB to the nucleus by suppressing the degradation of its inhibitory protein IkBa in the cytoplasm. The effects on inhibition of NF-kB activation, on alkaline phosphatase activity, and on apoptosis by YS 51 were antagonized by ZnPPIX. Taken together, our results indicate that YS 51 inhibits NO-mediated apoptosis of osteoblast cells, ROS 17/2.8, by inducing HO-1 expression. It may be beneficial in NO-mediated inflammatory conditions such as rheumatoid arthritis or osteoporosis.