VI Seminario Nazionale per Dottorandi in Farmacologia e Scienze Affini
Siena, Certosa di Pontignano, 23 - 26 Settembre 2002

ANTIOXIDANTS MODULATION OF CYCLOOXYGENASE-2 IN HUMAN BRONCHIAL SMOOTH MUSCLE CELLS

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We studied the effect of changes in red-ox status on the expression and the activity of the cyclooxygenase in human bronchial smooth muscle cells (HBSMC) obtained from segments of human bronchi. Treatment with both Vitamin C (Vit C) and Lipoic Acid (LA) (1 mM) coadministered with IL-1b (100 U/ml), resulted in enhanced expression of COX-2 protein and mRNA determined by Western and Northern blot analysis, when compared to treatment with the cytokine alone. COX-2 protein overexpression was concentration-dependent (10-1000 µM), while none of the conditions used affected the expression of the constitutive cyclooxygenase (COX-1). Concomitant treatment with actinomycin D (5 µg/ml) and Vit C or LA after the cytokine, totally abolished the induced up-regulation, suggesting that COX-2 is trascriptionally activated under these condition. Quantitative analysis of PGE2, the main COX metabolite in HBSMC, performed with an enzyme-immunoassay (EIA), showed that treatment with Vit C enhances the production of PGE2 (997±397 pg/ml) when compared with IL-1b *per se* (277.3±49.3 pg/ml), while LA completely abolishes its synthesis (69.3±32.1 pg/ml). Depletion of endogenous GSH using BSO and DEM restored PGE2 production, suggesting that changes in GSH as a reflex of changes in the red-ox status, are underlying the discrepancy between COX-2 expression and PGE2 production observed upon LA treatment.