

EFFECTS OF SIMVASTATIN AND BETAMETHASONE ON HYDROGEN PEROXIDE INDUCED MAPK ACTIVATION, IL-8 PRODUCTION AND CELL PROLIFERATION IN PRIMARY CULTURES OF HUMAN SQUAMOUS LUNG CANCER CELLS

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The airway epithelium is continuously exposed to inhaled oxidants, such as airborne pollutants and cigarette smoke, which exerting proinflammatory and cytotoxic effects, could be able to induce cancer development. The aim of our study was to investigate, in primary cultures of human squamous lung cancer cells (Calu-1), the signal transduction pathways activated by increasing concentrations (0.25, 0.5, and 1 mM) of hydrogen peroxide (H₂O₂), as well as their effects on both cell proliferation and viability with and without pre-treatment by betamethasone (200 nM) and simvastatin (1, 15, 30 µM). The reported results show that H₂O₂ elicited, in a concentration-dependent fashion, a remarkable increase in phosphorylation-dependent activation of mitogen-activated protein kinases (MAPKs), associated with a significant induction of IL-8 synthesis and a dramatically enhanced cell death. Pre-treatment of Calu-1 with betamethasone and simvastatin were able to significantly inhibit the effects of H₂O₂ on IL-8 secretion, and to effectively prevent cell proliferation. Therefore, these findings suggest that MAPKs play a key role as molecular transducers of the lung injury triggered by oxidative stress, as well as potential pharmacologic targets for indirect antioxidant intervention.