Effects of simvastatin in adenocarcinoma lung cancer cells exposed to hydrogen peroxide

L. Gallelli[1],D. Falcone[1], G. Pelaia[2], M. Scaramuzzino[1], R. Maselli, R. Savino[1], G. De Sarro[1]

[1]Dept. of Health Science, School of Medicine, University of Catanzaro
[2]Dept. of Medical and Surgical Sciences, School of Medicine, University of Catanzaro

Lung cancer is characterized by a high mortality rate probably attributable to early metastasis. Oxidative stress is involved in development and progression of lung cancer, via cellular and molecular mechanisms which at least in part overlap with proinflammatory pathways. Moreover, statins can act as anti-oxidants, and these pharmacologic properties may contribute to their potential anti-cancer activity. Therefore, the aim of this study was to evaluate, in a lung adenocarcinoma cell line (GLC-82), the effects of a 24-hour pretreatment with simvastatin on hydrogen peroxide (H2O2)-induced changes in cell viability, ERK phosphorylation, matrix metalloproteinase (MMP) expression, innate immunity signaling, NF-kB activation and IL-8 secretion. Cell counting was performed after trypan blue staining, Western blotting was used to analyze both whole cell and nuclear extracts, and IL-8 release into cell culture supernatants was assessed by ELISA. Our results show that simvastatin (30 μM) was able to significantly ($P < 0.01$) inhibit the proliferative action of H2O2 (0.5 mM) and its stimulatory effects on ERK1/2 phosphorylation, NF-kB activation and IL-8 production. Furthermore, simvastatin prevented H2O2-mediated induction of the cellular expression of MMP-2 and MMP-9, as well as of several components of the signaling complex activated by innate immune responses, including MyD88, TRAF2, TRAF6 and TRADD. In conclusion, these findings suggest that simvastatin could play a role in prevention and treatment of lung cancer via modulation of important proinflammatory and tumorigenic events, promoted by oxidative stress and involved in cell proliferation and metastatic invasion.