Down-regulation of Fatty Acid Synthase Is Associated with Decreased Akt Activation in Lovastatin Induced Apoptosis Cells

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摘要.

Abstract

Increased fatty acid synthase (FAS) protein expression is coordinated with cancer development. FAS inhibitors become a focus of anticancer drug development. Lovastatin, one of the active ingredients in red yeast rice, is a product of Monascus purpureus. Lovastatin has been shown to inhibit proliferation and to induce apoptosis in a variety of tumor cells. This report shows that chemopreventive effects of lovastatin may be through the down regulation of FAS. Lovastatin exhibited significant apoptosis-inducing activity in HL-60 cells, as observed by flow cytometry (with 49.83% in sub-G1 peak compared to the control, 10.43%), blebbing cell membrane morphology, and nuclear condensation. Cellular triglyceride, cholesterol, and free fatty acid in HepG2 cells were reduced to 79%, 81%, and 75%, respectively, upon lovastatin treatment (50 μM) for 4 h. The relative levels of FAS protein after treatment with 0, 10, 20, and 50 μM lovastatin were 1.00, 0.89, 0.72, and 0.31, respectively. Phosphorylated Akt was reduced in a dose-dependent manner. Reverse transcription PCR analysis showed that lovastatin upregulated PPAR-γ and inhibited SREBP-1 mRNA expression in HepG2 cells. Our current results implicate that lovastatin inhibiting FAS expression is associated with the decreased Akt activation.