HMG-CoA reductase inhibitor cerivastatin inhibits interleukin-6 expression and secretion in human adipocytes.

Abstract: Human adipose tissue is a main contributor to plasma levels of pro-inflammatory cytokine IL-6. How IL-6 expression is regulated in adipocytes remains unclear. In the current study, we investigated the effect of the HMG-CoA reductase inhibitor, cerivastatin, on the production of IL-6 from cultured human adipocytes. Cerivastatin reduced both IL-6 mRNA and secretion in a dose- and time-dependent manner. The inhibitory effect on IL-6 mRNA was prevented by the intermediates of the cholesterol synthesis pathway, mevalonate and geranyl-geranyl-phyrophosphate (GGPP) but not by farnesyl-pyrophosphate. This suggests the involvement of geranylgeranyl-modified intermediates in the effect of cerivastatin on IL-6. Moreover, cerivastatin induced an inactivation of the phosphorylation of the p65 subunit of NFkappaB which was prevented by GGPP. Our data suggest that cerivastatin exerts an anti-inflammatory effect by down-regulating IL-6 levels in adipocytes, which seems to be mediated by reduced production of GGPP and interference with the NFkappaB pathway.