

Dramatic synergistic anticancer effect of clinically achievable doses of lovastatin and troglitazone

賴基銘

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摘要

Abstract

Lovastatin (an HMG-CoA reductase inhibitor) and troglitazone (a PPAR- agonist) have been intensively studied prospectively for their application in cancer treatment. However, clinical trials of lovastatin or troglitazone in cancer treatment resulted in only limited responses. To improve their efficacy, lovastatin and troglitazone have, respectively, been tried to combine with other anticancer agents with varied outcomes. In our study, we found a dramatic synergism between lovastatin and troglitazone in anticancer at clinically achievable concentrations. This synergism was found in far majority of cell lines tested including DBTRG 05 MG (glioblastoma) and CL1-0 (lung). This amazing synergism was accompanied by synergistic modulation of E2F-1 and p27Kip1, which were reported to mediate the anticancer activities of lovastatin and troglitazone, respectively, and other cell cycle regulating proteins such as CDK2, cyclin A and RB phosphorylation status. With this dramatic combination effect of lovastatin and troglitazone, a promising regimen of cancer therapy may be materialized in the future. © 2005 Wiley-Liss, Inc.