題名:Small molecule c-Myc inhibitor; 10058-F4; inhibits proliferation and downregulates human telomerase reverse transcriptase and enhances chemosensitivity in human hepatocellular carcinoma

作者:劉興璟
Lin CP; Liu JD; Chow JM; Liu CR; Liu HE;
貢獻者:臨床醫學研究所

上傳時間:2009-08-21T08:58:56Z

摘要:c-Myc oncogene is critical for the development of hepatocellular carcinoma. Given the successful use of small-molecule inhibitors on cancers, targeting c-Myc with small-molecule inhibitors represents a promising approach. The potential of using small-molecule c-Myc inhibitor, 10058-F4, was evaluated on hepatocellular carcinoma cell lines, HepG2 and Hep3B cells. HepG2 cells were more sensitive to 10058-F4 than Hep3B cells, as demonstrated by reduced cell viability, marked morphological changes and decreased c-Myc levels. 10058-F4 arrested the cell cycle (at G0/G1 phase) and induced apoptosis upon extended treatment. These observations might be attributable to the increased cyclin-dependent kinase inhibitor, p21, and decreased cyclin D3 levels. Besides, 10058-F4 also significantly decreased the alpha-fetoprotein levels, an indicator for hepatocellular carcinoma differentiation. We further found that 10058-F4 inhibited the transactivation of human telomerase reverse transcriptase, downregulated human telomerase reverse transcriptase expression and abrogated telomerase activity. In addition, pretreatment with 10058-F4 increased the chemosensitivity of HepG2 cells to low-dose doxorubicin, 5-fluorouracil and cisplatin. Therefore, small-molecule c-Myc inhibitors might represent a novel agent, alone or in combination with conventional chemotherapeutic agents, for anti-hepatocellular carcinoma therapy.