Abstract

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Sulfasalazine synergistically enhances the inhibitory effects of imatinib against hepatocellular carcinoma (HCC) cells by targeting NF?B, BCR/ABL, and PI3K/AKT signaling pathway?related proteins

Hepatocellular carcinoma (HCC) is the third leading cause of cancer?related fatalities worldwide. Identification of second?line therapies for patients with progressive HCC is urgently required as the use of sorafenib and/or regorafenib remains unsatisfactory. Imatinib, a small?molecule kinase inhibitor, is used to treat certain types of cancer, and nuclear factor ?B (NF?B) is a positive regulator of cancer cell expansion. The combined use of tyrosine kinase and NF?B inhibitors may have potential for treating HCC. The aim of this work was to assess the potential anticarcinogenic effects of imatinib and sulfasalazine alone in combination on the human HCC cell lines, HEPG2 and Huh?7. Both drugs were shown to affect the phosphoinositide 3?kinase/protein kinase B (PI3K/AKT), signal transducer and activator of translation (p?STAT?3), breakpoint cluster region protein/Abelson proto?oncogene (BCR/ABL), and NF?B pathways. At the transcriptional level, imatinib and sulfasalazine were found to synergistically down?regulate c?MET gene expression. When compared to the activities of either medication alone, combined use of imatinib and sulfasalazine enhanced inhibition of HCC cell proliferation and extended induction of apoptosis. In summary, the presented data suggest that sulfasalazine synergistically potentiated the antitumor effects of imatinib.