Poster

Regulation of apoptosis and cell proliferation by Sorafenib in Hepatocellular carcinoma

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ABSTRACT

Motivation: Hepatocellular carcinoma (HCC), which represents more than 90% of primary liver cancers, is the sixth most common type of cancer with 749.000 new cases each year and the third cause of death associated with cancer. At early stages of HCC, the tumor might be cured by treatments as resection, ablation or liver transplantation. However, there are no effective therapies for patients with advanced HCC, who represents two thirds of diagnosed patients. In this context, Sorafenib, an oral multikinase inhibitor of some targets like Raf, VEGFR and PDGFR, among others, is the only therapeutic option in advanced HCC. Sorafenib has important actions inhibiting the cell proliferation and apoptosis in tumor hepatocytes, developing limited side effects but, more fundamentally, disease stabilization and increasing the survival rate to 9.2 months. The importance of this work is based on the lack of curative therapies in advanced HCC. Bearing in mind that illness is a major global health problem, is really important to carry out researches for finding new mechanisms, other targets and improvements of this drug in order to enhance the therapeutic options of patients, especially who suffer advanced HCC.

Results: On the one hand, we find that Sorafenib decreases the Mcl-1 expression and increases the pMcl-1 (pSer159 + pThr193) leading to an increment of intrinsic apoptosis. In this context, not only does Sorafenib promote the activity of caspase-3 and caspasa-9, but also alters mitochondrial membrane potential in different HCC cell lines. On the other hand, Sorafenib decreases the cell proliferation. Taking into account all these results, Sorafenib has a relevant anti-tumor activity in in vitro studies.

Conclusions: Sorafenib has an anti-tumor activity by activating cell death and blocking cell proliferation. The promotion of intrinsic apoptosis is due to the activation of caspase-3 and caspase-9 as well as inhibition the anti-apoptotic action of Mcl-1 and changes in the mitochondrial membrane potential.

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