

2nd International Conference on

Hepatology

May 09-11, 2016 Chicago, USA

PTPN13 causes apoptosis-dependent resistance to 5-FU in hepatocellular carcinoma

Zhiyu Xiao

Sun Yat-sen University, China

Drug resistance is a major factor contributing to the extremely poor prognosis of patients suffering from advanced-staged hepatocellular carcinoma (HCC). 5-Fluorouracil (5-FU) is the most commonly used chemotherapeutic agent against HCC. Here, we found that protein tyrosine phosphatase, non-receptor type 13 (PTPN13, also known as FAP-1) was expressed at high levels in HCC patients who developed recurrence after chemotherapy and that changes in PTPN13 expression before and after chemotherapy were inversely correlated with recurrence time. In parental cells, after treatment with 5-FU, upregulation of total and surface Fas, downregulation of PTPN13 and activation of apoptosis were observed, while in 5-FU resistant cells, upregulation of PTPN13 resulted in resistance to apoptosis. After stable knockdown of PTPN13 in 5-FU resistant cells, improved chemotherapeutic efficiency was detected both *in vitro* and *in vivo*. More importantly, we provide evidence that miR-200c is upstream of PTPN13 using bioinformatics methods confirmed by luciferase reporter assays. We also demonstrate that miR-200c sensitizes 5-FU resistant cells to apoptosis. Moreover, resistance to 5-FU-induced apoptosis was effectively overcome by the addition of the apoptosis activator procaspase-activating compound 1 (PAC-1). 5-FU and PAC-1 synergistically inhibited HCC cell proliferation measured using *in vitro*, *ex vivo* and *in vivo* models. In conclusion, the upregulation of PTPN13 is one of the mechanisms that mediate 5-FU resistance in HCC. Combining 5-FU with the apoptotic pathway activator PAC-1 can overcome this resistance, suggesting that this combination may be a novel approach for the treatment of chemoresistant HCC.

Biography

Zhiyu Xiao has completed his PhD from Sun Yat-sen University School of Medicine in 2011. He is now an Associate Professor of Sun Yat-sen Memorial Hospital. He has been engaged in the clinical and basic research of hepatocellular carcinoma for many years. He has published several papers in reputed journals.

xzysurgeon@163.com

Notes: