ZBP-89 enhances the killing/toxic effects of anti-tumor agents on hepatocellular carcinoma via multiple channels

George G Chen, Cai Guo Ye, Chris ZY Zhang, Rocky LK Ho and Paul BS Lai
Chinese University of Hong Kong, Hong Kong

ZBP-89 is able to regulate a number of gene expressions via binding to GC-rich sequences of the gene promoter region. To explore the possibility of ZBP-89 in the induction of cell death in hepatocellular carcinoma (HCC), we tested the killing/toxic effects of ZBP-89 in cultured HCC cells and a HCC xenograft mouse model. Tumor cell death was determined by MTT assay and TUNEL method. Protein expression was determined by Western blot. The xenograft tumor model was generated by injecting HCC cells into the left axilla of nude mice. Our results showed that ZBP-89 was able to induce apoptosis in HCC cells and enhance HCC cells to other anti-HCC treatments such as HDACis both in vitro and in vivo. Mechanically, the killing effect of ZBP-89 was via multiple channels. 1). It can bind to the promoter region of pro-apoptotic Bak to increase its expression. 2). ZBP-89 can interact with some p53 mutants to re-install the normal function of p53. 3). ZBP-89 can participate in gene methylation by maintaining histone H3 and H4 acetylation, leading to the demethylation of CpG island in the some promoters of pro-apoptotic genes. 4). ZBP-89 may also interact with other transcriptional factors such as SP-1 to promote the expression of pro-apoptotic molecules and suppress the expression of anti-apoptotic molecules. Collectively, our data demonstrate that ZBP-89 is able to enhance the killing/toxic effects of anti-HCC agents via multiple mechanisms, leading to the inhibition of HCC growth in vitro and in vivo.

Biography

George G Chen had medical training in China and PhD and postdoctoral training in United Kingdom. Currently he is a Professor at Department of Surgery, Faculty of Medicine, the Chinese University of Hong Kong, and he is also the Director of Surgical Laboratories at the same institute. He has published more than 150 papers in peer-reviewed journals and served several journals as a board member.

gchen@cuhk.edu.hk