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Suppression of lncRNA MALAT1 by betulinic acid inhibits hepatocellular carcinoma progression by targeting IAPs via miR-22-3p

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Betulinic acid (BA) is a natural product extracted from a broad range of medicinal and edible herbal plants. Previous studies showed that BA induces cell death in tumours derived from multiple tissues, however the underlying mechanism remains obscure. The present study aimed to study the effects of BA on autophagy and apoptosis of hepatocellular carcinoma (HCC). Human HCC cell lines and orthotopic HCC implanted mice were employed to examine the BA-induced tumor suppression; RT2 lncRNA PCR array and database analysis were used to explore the possible mechanisms; validation of pathways was performed using siRNA and miRNA inhibitors. The results indicated that BA regulated autophagy and induced apoptosis in HCC. The degradation of inhibitor of apoptosis proteins (IAPs), the conversion of LC3-I to LC3-II, as well as p62 accumulation were enhanced by BA, thereby suggesting that the down-regulation of IAPs and autophagic cell death are induced by BA. The addition of autophagy and lysosomal inhibitors indicated that BA induced autophagy-independent apoptosis via degradation of IAPs. Moreover, RT2 lncRNA PCR array and database analysis suggested that BA downregulated the levels of lncRNA MALAT1, which is considered to be an oncogene. Further investigations demonstrated that lncRNA MALAT1 functioned as a ceRNA (competing endogenous RNA) to contribute to BA-mediated degradation of IAPs by sponging miR-22-3p. Therefore, BA could be developed as a potential anti-cancer agent for HCC.

Keywords: Hepatocellular carcinoma; Betulinic acid; Cell Death; Apoptosis; lncRNA; Autophagy

Biography:

Feiyu Chen is now the final year of PhD candidature at the School of Chinese Medicine, the University of Hong Kong. My work mainly focuses on the pharmacology of Chinese Medicine in hepatocellular carcinoma. Her 7 articles & interview papers published, which are 2 research articles (Clinical and Translatinal Medicine IF7.9, Frontiers in Pharmacology IF4.4); 3 review articles (Cancer Biology & Therapy IF: 3.38, Frontiers in Pharmacology IF4.4,Cancers IF6.1); 2 chapters for online open access books. And she have 2 articles that are under peer-review process.

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