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Combined use of zoledronic acid augments ursolic acid-induced apoptosis in human osteosarcoma cells through enhanced oxidative stress and autophagy

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Ursolic Acid (UA), a naturally occurring pentacyclic triterpene acid found in many medicinal herbs and edible plants, triggers apoptosis in several tumor cell lines but not in human bone cancer cells. Most recently, we have demonstrated that UA exposure reduces the viability of human osteosarcoma MG-63 cells through enhanced oxidative stress and apoptosis. Interestingly, an inhibitor of osteoclast-mediated bone resorption, Zoledronic Acid (ZOL), also a third-generation nitrogen-containing bisphosphonate, is effective in the treatment of bone metastases in patients with various solid tumors. In this present study, we found that UA combined with ZOL to significantly suppress cell viability, colony formation, and induce apoptosis in two lines of human osteosarcoma cells. The pre-treatment of the antioxidant had reversed the oxidative stress and cell viability inhibition in the combined treatment, indicating that oxidative stress is important in the combined anti-tumor effects. Moreover, we demonstrated that ZOL combined with UA significantly induced autophagy and co-administration of autophagy inhibitor reduces the growth inhibitory effect of combined treatment. Collectively, these data shed light on the pathways involved in the combined effects of ZOL and UA that might serve as a potential therapy against osteosarcoma.

Biography

Chia-Chieh Wu is currently pursuing his PhD degree at the Institute of Biomedical Sciences, National Chung Hsing University in Taiwan.

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