

3RD GLOBAL SUMMIT ON

HERBALS & TRADITIONAL MEDICINE

OCTOBER 18-20, 2017 OSAKA, JAPAN

Garcinol sensitizes breast cancer cells to Taxol through suppression of Caspase-3/iPLA₂ and NF- B/ Twist1 signaling pathways in mouse 4T1 breast tumor Model

Yi-Shiou Chiou

National Taiwan University of Food Science, Taiwan

Breast cancer is a significant threat to women's health and has high incidence and mortality. Metastasis in breast cancer patients is a major cause of cancer deaths among women worldwide. Clinical experience suggests that patients with metastatic Triple-Negative Breast Cancer (TNBC) relapse quickly and often have chemotherapy resistance. Taxol (paclitaxel) is an effective chemotherapeutic agent for treating metastatic breast cancer, but Taxol at high doses can cause adverse effects and recurrent resistance. Thus, select synergistic combination therapy is recommended, which is safer and has a more significant response rate than monotherapy. In this study, our strategy is to combine a low dose of Taxol (5 mg/kg, i.p.) and garcinol (1 mg/kg, i.g.) to investigate the synergistic antitumor and anti-metastasis effects and to determine the underlying mechanisms of these effects *in vivo*. For the *in vivo* study, metastasis-specific mouse mammary carcinoma 4T1 cells were inoculated in Balb/c mice to establish an orthotopic primary tumor and spontaneous metastasis model. Tumor growth and metastases were monitored. The mechanisms of synergistic efficacies were evaluated at different signaling, including proliferation, survival, and Epithelial-Mesenchymal Transition (EMT)-regulated metastatic propensity. We demonstrated that garcinol combined with Taxol significantly increased therapeutic efficacy when compared with either treatment alone. The synergistic antitumor and anti-metastasis effects were enhanced primarily through induction of Taxol-stimulated G2/M phase arrest and inhibition of caspase-3/cytosolic Ca²⁺-independent phospholipase A₂ (iPLA₂) and nuclear factor-κB (NF- B)/Twist-related protein 1 (Twist1) drive downstream events including tumor cell repopulation, survival, inflammation, angiogenesis, invasion, and EMT. Our current findings provide the first experimental evidence that a combination of a low dose of Taxol and garcinol is a promising therapeutic strategy for controlling advanced or metastatic breast cancer. Finally, our results also point to the role of NF- B/Twist1 and caspase-3/iPLA₂ signaling pathways might be as a biomarker to predict tumor response to treatment.

Biography

Yi-Shiou Chiou has completed her PhD at the age of 34 years from National Cheng Kung University and postdoctoral studies from National Taiwan University of Food Science and Technology. She has been working with various *in vitro* and *in vivo* models realizing basic theories and mechanisms underlining relationship between bioactive nutraceuticals and chemoprevention. She is very active to participate in various national and international academic conferences. She has also published more than 20 papers in reputed journals and receive many positive comments from experts in related field.

chiouyishiou@gmail.com

Notes: