

Ácido ursólico inibe a proliferação das células do câncer de ovário via transição epitelio-mesenquimal – EMT

Ursolic acid inhibits the proliferation of human ovarian cancer stem-like cells through epithelial-mesenchymal transition.

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Abstract

Ovarian cancer is the most frequent cause of cancer-related death among all gynecological cancers. Increasing evidence suggests that human ovarian cancer stem-like cells could be enriched under serum-free culture conditions. In the present study, SKOV3 ovarian epithelial cancer cells were cultured for sphere cells. Ursolic acid (UA) with triterpenoid compounds exist widely in food, medicinal herbs and other plants. Evidence shows that UA has anticancer activities in human ovarian cancer cells, but the role of UA in ovarian cancer stem cells (CSCs) remains unknown. The aim of the present study was to investigate the anticancer effects of UA in combination with cisplatin in ovarian CSCs (in vitro and in vivo), along with the molecular mechanism of action. Treatment with UA at various concentrations was examined in combination with cisplatin in human ovarian CSCs. MTT assay and flow cytometry were used for cell viability and apoptosis analysis, and qRT-PCR for stem cell markers and epithelial-mesenchymal transition (EMT) markers for mRNA expression. Transwell assay was employed to observe the migration and invasion of SKOV3 cells and SKOV3 sphere cells after treatment. Moreover, athymic BALB/c-*nu* nude mice were injected with SKOV3 sphere cells to obtain a xenograft model for in vivo studies. The results showed that CSCs possessed mesenchymal characteristics and EMT ability, and the growth of SKOV3 and sphere cells was significantly inhibited by UA. Transplanted tumors were significantly reduced after injection of UA and UA plus cisplatin. Furthermore, we found that UA could play a role in enhancing the sensitivity of CSCs to cisplatin resistance. Our findings suggested that UA is involved in EMT mechanism to affect the proliferation and apoptosis of human ovarian cancer stem-like cells and it is a potent anti-ovarian cancer agent.

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