Poster

[P26-9] P26-9: Oncologic drugs (5): Pharmacokinetics, TDM practice

Chair: Kiyoshi Mihara, Japan

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[P26-9-6] A-mangostin induces apoptosis and enhances cisplatin sensitivity in human cerivcal cancer stem cell

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Keywords: a-mangostin, cervical cancer stem cells, cisplatin, apoptosis

Background

Cervical cancer is one of the most common female malignancies, and cisplatin-based chemotherapy is routinely utilized in locally advanced cervical cancer patients. a-mangostin is a dietary xanthone that has been shown to have anti-cancer and anti-proliferative properties in various types of human cancer cells. We evaluated the anti-tumor effect of a-mangostin on cervical cancer stem cells (CSCs), both alone and in combination with cisplatin.

Methods

Two human cervical CSCs cells, SiHa and HeLa, were used as model systems to investigate the anti-tumor effect of a-mangostin combined with cisplatin. Cell viability was examined and analyzed by MTT assay. Flow cytometry was also used to measure the levels of ALDH1 population, CD49f positivity, apoptosis and mitochondrial membrane potential (Ψm). Immunoblotting assays were used to examine the effect of a-mangostin combination with cisplatin on caspases expression and stemness-related transcription factors (Oct4, Nanog, and Sox2) expression. In vivo xenograft experiments to determine the effects of a-mangostin combined with cisplatin on cervical CSCs tumor growth.

Results

In this study, we found that human cervical CSCs cells with a-mangostin exposure resulted in decreased ALDH1 population, CD49f positivity, stemness-related transcription factors (Oct4, Nanog, and Sox2) and induces apoptosis of human CCSCs. Additionally, combination treatment with a-mangostin and cisplatin yielded synergistic inhibitory effects in suppressed ALDH1 population, CD49f positivity, stemness-related transcription factors (Oct4, Nanog, and Sox2), loss of MMPs and induced apoptosis of human cervical CSCs cells. Moreover, a-mangostin significantly enhanced the anti-tumor effects of cisplatin in human cervical CSCs cells in vitro and in vivo.

Conclusions

Based on our findings, a-mangostin is a promising flavonoid compound targeting the cisplatin- sensitivity cervical cancer stems cells and regulating their stemness, which will be applied as a potential candidate for the development of a cisplatin- sensitivity cervical CSCs agent and combination therapy of human cervical CSCs.