Abstract

Targeting of cancer cells and cancer stem cells in ovarian cancer

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Ovarian cancer ranks fifth in cancer-related deaths in women in the United States, and it is also the leading cause of death among gynecologic cancers. Since a majority of cases are diagnosed in the more progressive stages, treatment options are limited and have not been sufficient. They include cytoreductive surgery followed by chemotherapy with platinum derivatives, including carboplatin or paclitaxel. After the initial treatment however 70% of women will relapse and experience recurrent cancer. This is accredited to the resistance of the ovarian cancer stem cells. Therefore, our goal is to develop a combination therapy that will target both the cancer cells as well as the cancer stem cells. In our experiments, we have observed that Withaferin A (WFA) in combination with Cisplatin has a synergistic effect on the inhibition of cell proliferation. Withaferin A is a natural product isolated from *Withania somnifera* commonly used as an over-the-counter dietary supplement but more recently has been used to inhibit tumor growth. Cisplatin is a platinum-derivate chemotherapy drug, which causes severe side effects and cells eventually become resistant to it. The synergistic effect of the combination therapy would allow a reduction in dosage of Cisplatin minimizing the side effects and resistant cancer stem cells. ALDH1, CD44, CD133, PTTG, Notch1, E-Cadherin, Vimentin, Snail, and Wnt1 have been well defined cancer stem cell markers and their expression in the treatment groups will be studied to determine which are responsible for the self-renewal of cancer stem cells and also which serve as survival genes. This information will allow us to evaluate the expression of these genes and eventually control the pathways being affected. Cisplatin in combination with Withaferin A could be a novel yet effective, alternative chemotherapy treatment.