

Alterations in Stiffness of Ovarian Cancer Cells as the First Manifestation of Anti-cancer Activities of Membrane Active Compounds

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Ovarian cancer is considered as the leading neoplastic disease affecting women worldwide. Presently, ceragenins (CSA), as synthetic steroid analogs of natural antimicrobial peptides, are comprehensively tested as novel antineoplastic agents due to their high membrane-permeabilizing activity. The studies carried out so far have shown that various types of tumors are characterized by a specific cellular stiffness, and the reduction of this value and thus the greater deformability of cells significantly correlates with tumor invasiveness. Previous studies confirm that cancer cells treated with agents with antineoplastic activity are characterized by increased stiffness, which reduces their ability to metastasize. Considering the above, it is suggested that AFM analysis can be used to identify new mechanomarkers that will allow rapid assessment of the therapeutic effect of the anti-cancer drugs.

The aim of the research is to assess whether measurements of nanomechanical properties of treated cancer cells might be employed to assess the therapeutic activity of antineoplastic compounds, in a time shorter than required by existing research methods.

The anti-cancer activity of ceragenin CSA-13 against SKOV-3 ovarian cancer cells was evaluated using MTT assay. Investigation of mechanical properties of ovarian cancer cells upon treatment with ceragenin CSA-13 was carried out using an atomic force microscope (NanoWizard 4 Bioscience, Bruker / JPK, United States) in force spectroscopy mode. The level of CSA13-induced apoptosis was assessed using flow cytometry.

Conducted studies demonstrated that treatment of ovarian cancer SKOV-3 cells with CSA-13 significantly decrease their viability and metabolic activity. The cellular stiffness of treated cancer cells was noted to be increased upon 15 min treatment with membrane active compound. At the same time, CSA13-induced apoptosis was detected using flow cytometry after 8h incubation.

Ceragenin CSA-13 is characterized by strong anti-cancer activity against ovarian cancer SKOV-3 cells and possesses the potential to be used as novel antineoplastic agent in the treatment of malignancies. Investigation of cellular stiffness of treated cancer cells is a quick diagnostic method allowing for screening of anti-cancer properties of tested drugs.

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Keywords: ovarian cancer, nanotechnology, ceragenins, drug resistance

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