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Diindolylmethane selectively inhibites activity of cancer stem cells

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There is accumulating evidence to support the cancer stem cell hypothesis. Becomes more obvious that the minor population of cancer stem cells (CSCs), possessing increased tumor/ metastasis-initiating activity, and resistance to cancer chemotherapy, causes malignant growth, including development of relapses and metastases. Hence there is an urgent need to identify drugs that selectively target CSCs. We have found out for the first time that 3, 3'-diindolylmethane (DIM) - the substance of a natural origin with proved multitargeted antitumor activity, is selective and potent inhibitor of CSCs cultivated in serum-free medium as tumor spheres. Thus efficiency of DIM as inhibitor of CSCs was 10 times more than that of tranilast - an antiallergenic preparation for which ability of inhibition of CSC has been shown earlier. In several various cancer cell lines, DIM inhibited tumor sphere formation in a dose-dependent manner at the concentrations 30-300 times lower than those required for growth inhibition of parental adherent cells. Protein levels of the specific stem cell and cancer stem cell markers were declined in DIM-treated primary tumor spheres compared with untreated cells. We also found that treatment with DIM overcomes chemoresistance of CSCs to conventional cytotoxics such as paclitaxel, doxorubicin, and SN-38. Pre-reatment of tumor spheres with DIM before implantation to mice significantly retarded the growth of primary tumors and improves the survival of tumor-bearing mice in comparison with tumors formed by non-treated tumor spheres. Using innovative nanobiotechnological approaches we had been developed two drug formulations in which bioavailability of DIM is significantly increased in comparison with crystalline DIM, that will allow to realize a phenomenal antitumor therapeutic potential of the compound.

Biography

Ekaterina Muyzhnek has completed her PhD at Moscow State University (Biological faculty, biochemistry chair). She has passed away from younger to the leading research assistant, working in Russian research Institutes. Area of scientific interests made: cellular biology, molecular medicine, regulatory mechanisms of physiological processes. Now is the Director for a Science (Chief Scientific Officer) in biotechnological company "MiraxBioPharma" (Moscow, Russian Federation) where is engaged in working out and a substantiation of molecular mechanisms of action of the innovative pharmaceutical preparations developed by the company and intended for treatment and preventive maintenance of proliferative diseases of reproductive system. She is author of more than 25 publications in international and Russian journals, 5 monographies and the co-author of 1 patent.

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