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Inhibition of cancer cell proliferation and the inflammatory microenvironment by an organotin indomethacin derivative

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Inflammatory microenvironment in different types of cancer provides sustained tumor growth, invasion and metastasis. Nonsteroidal anti-inflammatory drugs as indomethacin have demonstrated chemo-preventive, anti-proliferative and cytotoxic effects in a variety of tumors. The aim of this work was to investigate the effect of an organotin derivative of indomethacin on the proliferation of breast, prostate and cervical cancer cell lines and the possible mechanisms of action involved on the inhibition of cell proliferation. Different cancer cell lines were treated with the organotin indomethacin derivative and cell proliferation was measured by quantification of DNA content, changes in the cell cycle profile and the activation of caspase 3 were evaluated by flow cytometry, tumor necrosis factor alpha and interleukin 6 (TNF-α and IL-6) gene and protein expression were evaluated by qPCR and ELISA assays respectively. Organotin derivative of indomethacin inhibited the cell proliferation of different cancer types in a concentration-dependent manner. The mechanism of action of this compound was mediated by the induction of apoptosis and the modulation of the inflammatory microenvironment through decreasing the expression of TNF-α and IL-6. We also observed that the combination of the organotin derivative with lapatinib, a target therapy for breast cancer, widely diminished the cell proliferation. Moreover, the combined treatment increased more the caspase 3 expression and diminished the ERK phosphorylation as compared with the treatments alone. Our results suggest that the use of the organotin derivatives of indomethacin alone or in combination with other drugs could be helpful in inhibiting the inflammatory microenvironment in patients with different tumors.