METHYLENE BLUE PHOTODYNAMIC THERAPY: AN EFFECTIVE CHOICE TO FIGHT AGAINST HUMAN BREAST CANCER CELLS

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Breast cancer is the main cause of mortality among women presenting high recurrence due to treatment failure. Photodynamic therapy (PDT), which cause tissue destruction by light-activation of a photosensitizer, appears as a promising treatment. However both PDT efficacy and the pathways leading to cell death remain unclear. In this work, we study both the effect of methylene blue-PDT (MB-PDT) and the involvement of cell death pathways in two (2D) and three (3D) dimension cultures of tumoral and non-tumorigenic human breast cell-lines. Cells were incubated in the absence or presence of MB and irradiated or not at 4.5J/cm². Cell death morphology was evaluated by fluorescence microscopy. Apoptosis, autophagy and necroptosis were analyzed by western blotting and/or by specific enzymatic assays. The role of these pathways was investigated using specific inhibitors, activators or gene silencing. MB-PDT significantly increased cell death in tumoral cells kept under either 2D or 3D culture (98.6±0.5%). This effect was significantly lowered in non-tumorigenic cells (52.2±3.8%). While nuclear staining showed no signs of apoptosis, in two of the cell lines caspase-activities were involved in cell death since their inhibition modified MB-PDT effect. A significant increase in LC3-II and acidic vesicle formation was observed upon MB-PDT, but depending on the cell line, autophagy displayed a cytoprotective or prodeath function. Moreover, necroptosis inhibition strongly decreased MB-PDT effect in the three cell lines studied. Finally, we showed that MB-PDT induced massive cell death in two human breast cancer cell lines in a model that recapitulates the morphology of glandular epithelium. Moreover, we demonstrated that different cell death mechanisms are being activated upon MB-PDT induction, a desired property for improving an anticancer therapy. Overall, our observations point MB-PDT as an alternative and effective therapy for breast cancer treatment, displaying minimal side effects.

Keywords: MB-PDT, breast cancer

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