Involvement of autophagy in melatonin-induced cytotoxicity in glioma-initiating cells.

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Abstract

Glioblastoma-initiating cells (GICs) represent a stem cell-like subpopulation within malignant glioblastomas responsible for tumor development, progression, therapeutic resistance, and tumor relapse. Thus, eradication of this subpopulation is essential to achieve stable, long-lasting remission. We have previously reported that melatonin decreases cell proliferation of glioblastoma cells both in vitro and in vivo and synergistically increases effectiveness of drugs in glioblastoma cells and also in GICs. In this study, we evaluated the effect of the indolamine alone in GICs and found that melatonin treatment reduces GICs proliferation and induces a decrease in self-renewal and clonogenic ability accompanied by a reduction in the expression of stem cell markers. Moreover, our results also indicate that melatonin treatment, by modulating stem cell properties, induces cell death with ultrastructural features of autophagy. Thus, data reported here reinforce the therapeutic potential of melatonin as a treatment of malignant glioblastoma both by inhibiting tumor bulk proliferation or killing GICs, and simultaneously enhancing the effect of chemotherapy.

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KEYWORDS: autophagy; cancer stem cells; differentiation; glioma; melatonin

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