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Abstract:
The search for new drugs and treatment approaches is of particular importance for glioblastomas (GBMs), as with other types of malignant gliomas, as they are lethal without the available medical care. Current anticancer cocktails have failed to prolong survival beyond 1 year, in part owing to the natural resistance of GBM cells and to the toxic side effects of the available drugs. In many organisms, cell death can be induced by cytolysins, which are proteins that can form pores in biological membranes. Perhaps by facilitating drugs to enter into the cytosol, cytolysins might be used to increase the efficacy of conventional anticancer agents. Here, the cytotoxicity of two sea anemone pore-forming cytolysins, toxin Bc2, and equinatoxin (EqTx-II) were investigated. Toxin Bc2 and EqTx-II were cytotoxic against human U87 and A172 GBM cell lines either wild type or p53 mutant, a tumor suppressor frequently mutated in malignant gliomas. Moreover, noncytotoxic concentrations of Bc2 or EqTx-II potentiated the cytotoxicity induced by low dose concentrations of all classical chemotherapeutics agents tested: cytosine arabinoside, doxorubicin, and vincristine. In comparison with the cytotoxicity induced by each of these classical anticancer drugs alone, 10-300-fold less of the therapeutic drug was needed when combined with the cytolysins. These results are promising, since lower concentrations of chemotherapeutic drugs could reduce the adverse effects of chemotherapy.

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