Cytotoxic Activity of Atroxlysin a RGD-like Protein from Peruvian *Bothrops atrox* Against Malignant Tumors

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Introduction: Tumor cells are characterized by uncontrolled growth, adjacent tissue invasion and spread of metastasis. Integrin receptors are involved in the recognition between cells and RGD sequence domain from extracellular matrix (ECM) proteins, acting on the anchorage, migration, cell proliferation and processes related to induction of angiogenesis and metastasis. Malignant tumors overexpress integrins, leading to a more aggressive profile and resistance to usual treatments, so making these receptors strategic targets for development of new antitumor agents. Disintegrins containing RGD and RGD-like sequences, isolated from snake venoms, are able to specifically binding to integrin receptors and interfere with their function. **Objectives:** This study aimed to evaluate the antitumor effect of a PIII metaloprotease isolated from peruvian *Bothrops atrox* venom (Atroxlysin III) against different tumor cell lines: glioblastoma (T98 and U87), breast (MCF7) and melanoma (UACC). **Material and Methods:** The in vitro antitumor effect was evaluated by quantitation of the metabolic cellular viability and the molecular mechanisms involved were analyzed by fluorescence studies of DNA damage and reactive oxygen species generation (ROS). **Results and Discussion:** Atroxlysin III promoted potent cytotoxic effect in all tested tumor cell lines, with IC_{50} in submicromolar range, showing its broad spectrum of action independent of the tumor lines. The Atroxlysin III cytotoxic effect showed to be more potent compared to RGD molecules already described in the literature as Echistatin, Jararhagin and Cilengitide an antineoplastic drug in clinical trial. Evaluation of DNA demonstrated that the molecule induces DNA condensation indicative of apoptosis and evaluation the ROS generation in cell lines studied demonstrated that treatment with Atroxlysin III increases ROS production when compared to the untreated control. **Conclusion:** Atroxlysin III promoted cytotoxic effect, reducing the number of viable tumor cells and inducing cell death. These results indicate Atroxlysin III as a promising molecule for the development of antitumor agents.

Key words: Atroslysin III, Snake Venom, RGD-like domain

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