Genotoxicity and Cytotoxicity by Phospholipases-A_2 on Human Breast Cancer cells: Evaluation of Cell Cycle Gene Expression

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Introduction: Currently, new anticancer therapies have been extensively investigated. In this context, natural products such as toxins from snake venom possess great potential as structural models for cancer therapy. BnSP-6 and BnSP-7 are phospholipases A_2 isolated from *Bothrops pauloensis* snake venom and their antitumor potential has been studied by our research group. **Objectives:** We investigated the citotoxicity and genotoxicity as well as, the expression of genes related to cell cycle regulation induced by BnSP-6 and BnSP-7 on human breast cancer cell line (MDA-MB-231) and non-tumorigenic breast cell line (MCF-10A) (control). **Material and Methods:** MDA-MB-231 and MCF-10A cells were treated with toxins at different concentrations for 24 h at 37 °C and the viability and genotoxicity were evaluated by methyl thiazolyl tetrazolium (MTT) and by micronucleus assays (OECD) respectively. MDA-MB-231 cells were incubated with BnSP-6 and BnSp-7 (50 µg/ml) for 24h. After that, total RNA was extracted using TRIZOL reagent and cDNAs as well as real-time PCR experiments were performed according to the manufacturer's protocol to gene expression analysis. **Results and Discussion:** BnSP-6 and BnSP-7 were more cytotoxic to MDA-MB-231 cell line than to control cell (MDF-10A). The toxins were genotoxic inducing the micronucleus formation on cells treated, furthermore, both toxins were capable to down and up-regulating some genes related of the cell cycle. **Conclusions:** These results showed that BnSP-6 e BnSp-7 are genotoxic and capable of interfering on cell cycle gene expression, decreasing MDA-MB-231 breast cancer cell line viability. Thus, this work can bring new approach for antitumor drug design.

Key words: Cell Cycle, Human Breast Cancer Cell, Snake Venom phospholipase A2.

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