Cytotoxic effects of parthenolide on lymphoid malignancies' cell lines

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Aim: The aim of this study was to evaluate the therapeutic potential of parthenolide (PRT), an NF-κB inhibitor, on acute lymphoblastic leukemia (ALL) and Burkitt Lymphoma (BL) cell lines and characterize the type of cell death induced and its molecular mechanisms.

Introduction: Playing an important role in the regulation of diverse biological processes such as cell proliferation and survival, nuclear factor kappa B (NF-κB) is closely associated with various human malignancies. Deregulated NF-κB signaling has been appointed as one important player in all stages of tumorigenesis. PRT has a dual anti-tumor effect – NF-κB pathway inhibition and oxidative stress induction – on a wide range of malignancies and could be a valid option for hematological cancer.

Methods: We used one BL (RAJ1) and five ALL (697, CEM, JURKAT, MOLT-4 and KOPN8) cell lines. Cells were incubated in absence or presence of different concentrations of PRT in single dose and daily administration. Metabolic activity was assessed by Resazurin Assay. Cell death was analyzed by Optical Microscopy and Flow Cytometry (FC) using Annexin V/7-AAD double staining and JC-1 probe. Apoptotic proteins levels (FAS, FAS-L, BCL-2, BAX and activated caspase 3), cell cycle and oxidative stress parameters (superoxide anion, peroxides and reduced glutathione through the DHE, DCFH2DA and mercury orange probes, respectively) will be evaluated by FC.

Results: Preliminary results showed that PRT reduces the metabolic activity in time, dose and cell line dependent manner, being the KOPN8 and RAJ1 cells the most sensitive and JURKAT cells the lowest. In fact, the half maximal inhibitory concentration (IC50) at 72 h was 2 μM for KOPN8 and RAJ1, 3 μM for CEM, 4 μM for 697, 6 μM for MOLT-4 and 12 μM for JURKAT. These results may be related with the cell type and genetic background. Cell death analysis suggested that PRT induced apoptosis in these cell lines. Studies on the cell cycle and oxidative stress are still underway.

Conclusion: Our results suggest that PRT is a potential new targeted therapy in lymphoid malignancies, mainly ALL and BL.

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