Negative and positive regulation of Survivin expression by anthracyclines in leukemic cell lines

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Survivin, an anti-apoptotic protein, has been related to drug resistance and poor prognosis in leukemias. To explore the relationship between Survivin and drug resistance we investigated the alteration of Survivin expression in three leukemic cell lines HL60, U937 and K562 treated with two anthracyclines, doxorubicin and idarubicin, frequently used in leukemia treatment. MTT assay was performed to determine the dose of drugs capable to induce cell death in 50% of treated cells (DL_{50}). Immunoblotting was applied to examine the changes in Survivin levels before and after cell lines incubation with drugs at DL_{50}. Among cell lines studied, HL60 was the most sensitive for both drugs tested, followed by U937 and K562. Idarubicin showed to be more potent than doxorubicin in inducing cell death. Immunobloting analysis showed that doxorubicin was capable to downregulate Survivin expression in approximately 70 % in HL60 cell line, but there were no significant differences in U937 and K562 cells. Interestingly, preliminary results showed that idarubicin increased the levels of Survivin expression in all cell lines tested. These data suggest that instead of idarubicin efficacy, it might be promoting the selection of resistance cells, calling our attention for the possibility of resistant clone selection in leukemia patients after idarubicin treatment.

Supported by: SwissBridge, CNPq, CAPES.