Title: Survivin induces chemoresistance in breast cancer cells

Abstract: <strong>Introduction</strong> Breast cancer is the second leading cause of death in women after lung cancer. Systemic chemotherapy is the most common modality for breast cancer. Adjuvant therapy has been applied as a desirable strategy to overcome the observed chemoresistance. Survivin as the smallest member of inhibitor of apoptosis protein (IAP) family is a bifunctional protein involved in cell division and caspase inhibition. This protein plays key roles in cancer initiation, tumor progression and chemoresistance to various chemotherapeutics including taxanes. Inhibition of survivin induces apoptosis and thus, sensitizes cancer cells to a number of chemotherapeutic agents. Understanding the role of survivin in chemoresistance has been facilitated by development of survivin inhibitors including deguelin. In the current study, we investigated the role of survivin in chemoresistance to both single and combined treatments of docetaxel with deguelin in MDA-MB-231 breast cancer cells. 

**Methods:** MTT assay was used to measure proliferation of the cells. The amount of apoptosis was assessed using DAPI staining. Survivin expression was investigated at two different levels, gene level by Real-time PCR and protein level by Western blot analysis, both after single and combined treatment. 

**Results:** Our findings showed an IC50 of 10 nM for docetaxel after 48 h incubation with MDA-MB-231 cells. Next, we applied IC50 concentrations of docetaxel along with variable concentrations of deguelin. Combined treatment showed a marked increase in the percentage of apoptosis. Combination therapy also decreased survivin gene expression markedly.

**Conclusion:** A better understanding of the molecular mechanisms involved in resistance to chemotherapy helps us to find better strategies for cancer therapy. Survivin is an important inducer of resistance to chemotherapy in breast cancer cells which can be considered as a potential molecule for target therapy of cancer. Our results confirm the role of adjuvant therapy in increasing the efficacy of treatment.