

Calpain-Mediated, Cisplatin-Induced Apoptosis in Breast Cancer Cells

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Abstract : Breast cancer is the most common cancer in women worldwide. Triple-Negative Breast Cancer (TNBC) is an aggressive type of breast cancer, which is defined by the absence of Estrogen (ER), Progesterone (PR) and human epidermal growth factor (Her-2) receptors. The calpain system plays an important role in many cellular processes including apoptosis, necrosis, cell signaling and proliferation. However, the role of calpain in cisplatin (CDDP)-induced apoptosis in TNBC cells is not fully understood. Here, TNBC (MDA-MB231) cells were treated with different concentration of CDDP (0, 20 & 40 μ M) and calpain activation and apoptosis were measured by western blot and Hoechst Stain respectively. In addition, calpain modulation by either activation and/or inhibition and its effect on CDDP-induced apoptosis were assessed by the same above approaches. Our findings showed that CDDP induced endoplasmic reticulum stress and thus Calcium release and subsequently activate calpain α -fodrin cleavage indicated by the increase in GRP78 and Calmodulin protein expression and respectively in MDA-MB231 cells. It also induced apoptosis as measured by Hoechst stain and caspase-12 cleavage. Calpain activation by both Cyclopiazonic acid and Thapsigargin showed similar effect and enhanced the sensitivity of these cells to CDDP treatment. On the other hand, calpain inhibition by either specific siRNA and/or exogenous inhibitor (Calpeptin) had an adverse effect where it attenuated calpain activation and thus CDDP- induced apoptosis in these cells. Altogether, these findings suggested that calpain activation play an essential role in sensitizing the TNBC cells to CDDP-induced apoptosis. This might lead to the discovery of novel treatment to over this aggressive type of breast cancer.

Keywords : calpain, cisplatin, apoptosis, breast cancer

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