

THE ROLE OF TREFOIL FACTOR FAMILY -1 (TFF1) IN ESTROGEN-PROMOTED APOPTOSIS RESISTANCE IN BREAST CANCER CELLS

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ABSTRACT

TFF1 is a secreted protein and is expressed in various types of carcinomas. The *TFF1* gene contains an estrogen responsive element in its promoter, due to which its expression could be regulated by estrogen. In addition, estrogen has demonstrated its ability to promote resistance to doxorubicin in estrogen receptor positive MCF-7 breast cancer cell line. This study aims to explain the estrogen induced resistance to chemotherapy by exploring the relationship between the estrogen-induced TFF1 and its role in inferring resistance to apoptosis. Permanent knockdown of *TFF1* gene in MCF-7 cell was generated, to test the sensitivity to doxorubicin in comparison to the parental cell in the presence or absence of 17 β -estradiol, which is a potent estrogenic agent. Flow cytometry analysis showed that, 17 β -estradiol could rescue MCF-7 cells from doxorubicin induced apoptosis ($P = 0.016$) but failed to demonstrate this effect in the *TFF1* knockdown MCF-7 cells. Trypan blue cell counting showed that, neutralizing secreted TFF1 resulted in aggravated apoptosis, much higher than just the doxorubicin treated condition ($P = 0.029$). Moreover reconstituting TFF1 in the knockdown cells refurbished its protective role ($P = 0.05$). Apoptosis protein array revealed changes in expressions of key apoptosis regulatory proteins under varying treatment conditions, particularly the anti-oxidative enzymes catalase and heme oxygenase 1 (HO-1), on the whole trying to restore homeostasis. These phenomena determine the contribution of TFF1 in estrogen-promoted resistance to apoptosis induced by doxorubicin in MCF-7 breast cancer cells. TFF1 may be a target for manipulation of chemotherapeutic resistance in breast cancer.

KEY WORDS: TFF1 / BREAST CANCER / APOPTOSIS

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