Abstract

Title: Evaluating the Chemotherapeutic Effects of the FAC Regimen in MDA MB 231 Breast Cancer Cells with Reduced Beta arrestin 2 Expression Levels

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Purpose: A long- standing issue in breast cancer therapy is the variable effectiveness of chemotherapeutics towards various types of breast cancers. In many cases, chemotherapeutics are combined to increase their effectiveness in treating hard to treat cancers. One popular regimen is the FAC regimen, which is a combination of 5-fluorouracil (F), doxorubicin (A) and cyclophosphamide (C). In this study, we explore the effectiveness of this regimen in killing MDA MB 231 breast cancer cells with decreased protein expression of beta arrestin-2, a protein that has been shown to modify doxorubicin-associated cell death.

Methods: MDA MB 231 breast cancer cells, with or without stable transfection with beta-arrestin 2 shRNA to effectively decrease beta-arrestin 2 protein expression, were treated with 5-fluorouracil (F), doxorubicin (A) or cyclophosphamide (C) or all three combined for 24-72 hours. Thereafter, the extent of cell death was evaluated using trypan blue exclusion. Changes in nuclear morphologies, as an indicator for cell death, was monitored by staining the treated cells with dapi and visualized under fluorescent microscopy.

Results: MDA MB 231 breast cancer cells without beta-arrestin 2 protein expression were more sensitive to doxorubicin, as reported previously, and the FAC regimen. This effect was also observed time-dependently and in experiments where doxorubicin concentrations were varied, from 10X less to 10X more but both 5-fluorouracil and cyclophosphamide concentrations were kept constant. Preliminarily, nuclear morphologies were similar in treated cells versus untreated cells when the cells were treated with 100X lower FAC concentrations, suggesting an increase in drug concentrations may be required to see any desired effect.

Conclusion: In this study, we analyzed the cell death of MDA MB 231 cells caused by various chemotherapeutics in order to better gauge the effectiveness of various chemotherapeutic regimens. Based on these preliminary results, the FAC regimen appears to be more effective in killing MDA MB 231 breast cancer cells without beta-arrestin 2. This may imply that beta arrestin 2 may be a biomarker to predict the effectiveness of FAC treatment, with potentially some breast cancers with lower beta arrestin 2 protein expression levels showing more sensitivity to FAC compared to those with higher beta arrestin 2 protein levels.