Title: Evaluating the Chemotherapeutic Effects of the FAC Regimen in MDA MB 231 Breast Cancer Cells with Reduced G Protein Coupled Receptor Kinase 2 Expression

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Purpose: Improving the effectiveness of chemotherapeutic regimens has been a long- standing goal in breast cancer therapy. In many cases, certain chemotherapeutic agents are combined to effectively treat certain breast cancers. For instance, 5-fluorouracil (F), doxorubicin (A) and cyclophosphamide (C) are combined together as the FAC regimen to treat various types of breast cancers. In this study, we explored the effectiveness of this regimen in killing MDA MB 231 breast cancer cells with reduced G protein coupled receptor kinases 2 (GRK2).

Methods: Triple negative MDA MB 231 breast cancer cells, with or without stable transfection with GRK2 shRNA to effectively decrease GRK2 protein expression, were treated with 5-fluorouracil (F), doxorubicin (A) or cyclophosphamide (C) or all three combined for 72 hours. Thereafter, the extent of cell death was evaluated using trypan blue exclusion. Changes in nuclear morphologies, an indicator for cell death, was performed by staining the treated cells with dapi and visualized under fluorescent microscopy.

Results: MDA MB 231 breast cancer cells without GRK2 protein expression was 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 with both 5-fluorouracil and cyclophosphamide concentrations kept constant. Preliminarily, nuclear morphologies were similar in treated cells versus untreated cells when the cells were treated with 100X lower FAC concentrations.

Conclusion: In this study, we analyzed breast cancer cell death 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 GRK2. This may imply that GRK2 may be a biomarker to predict the effectiveness of FAC treatment, with potentially some breast cancers with lower GRK2 expression levels showing more sensitivity to FAC compared to those with higher GRK2 levels. This may also mean that inhibitors towards GRK2 may be beneficial combined with this particular regimen.