

TRANSGENIC INTRODUCTION OF THE ANDROGEN RECEPTOR (AR) INTO ER-/PR-/AR- BREAST CANCER CELLS RENDERS THEM RESPONSIVE TO HORMONAL MANIPULATION

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Background: Estrogen and progesterone receptors (ER, PR) are prognostic and therapeutic tools in the management of breast. However, androgens have been shown to play an increasingly important role in breast cancer. We have demonstrated in other publications that treatment of ER-/PR-/AR+ (androgen receptor) breast cancer cells with dehydroepiandrosterone-sulfate (DHEAS) and an aromatase inhibitor (AI) results in cell death, while ER-/PR-/AR- breast cancer cells are unaffected by treatment with DHEAS/AI. We hypothesize that when ER-/PR-/AR- breast cancer cells are successfully transfected with an AR expression vector, they become hormonally sensitive and their growth is inhibited with DHEAS/AI treatment.

Methods: The ER-/PR-/AR- breast cancer cell line HCC 1806 was transfected with the pAR-IRES-EGFP androgen receptor expression vector. These cells were then treated with DHEAS/AI for 1 and 2 days. Growth inhibition was measured on each of these days by counting the number of GFP positive cells and comparing them to transfected cells treated with only an AI (control group) or to non-transfected cells treated with DHEAS/AI. Mann-Whitney U test was used to determine statistical significance.

Results: There was a 53.5% ($p = 0.001$) and 40.1% ($p = 0.006$) cell death rate seen in transfected cells treated with DHEAS/AI as compared to control for days 1 and 2 of treatment respectively. There was no difference seen between treatment groups in the non-transfected cells.

Conclusions: After the ER-/PR-/AR- breast cancer cell line HCC 1806 was successfully transfected, it became sensitized to the cytotoxic effect of DHEAS/AI treatment. Thus far chemotherapy has been the only treatment option for patients with ER-/PR-/AR+ breast cancer. However, DHEAS/AI offers the first hormone therapy option in this patient population.