

5th International Conference on Biomarkers & Clinical Research

April 15-17, 2014 St. Hilda's College - University of Oxford, UK

Discovery of novel markers and targets for therapy of breast cancer via phyto-chemoprevention

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Complementary Alternative Medicine (CAM) is increasingly being practiced worldwide due to its safety and beneficial therapeutic effects. A number of phyto-compounds have been used in CAM, individually or in combination for cancer therapy, particularly at late and desperate stages. In the present study, we hypothesized that a combination three well documented phyto-compounds (Resveratrol - RE, Indole 3 Carbinol - I3C and Quercetin - QURC) used at sub-optimal levels can induce 100% killing of breast cancer (BC) cells in-vitro without toxic effects on normal cells.

To test the hypothesis, normal breast epithelial cells (MCF-10A; Control) and also two Breast Cancer (BC) cell lines (MDA-MB-231 and MCF-7) were treated with RE, I3C, QURC both individually and in combination at sub-optimal levels. Alamar-Blue assay and Flow Cytometry revealed that the combination of RE+I3C+QURC induced 100% death of BC cell lines but not normal cells. In addition, wound healing and invasion assays revealed loss of cell migration/invasion through Matrigel. Western Blot analysis was used to examine the expression of genes associated with apoptosis (Bcl-2 family members and Survivin), cell motility (CD44) and cell proliferation, (PCNA, Rb, CDK4) in the BC cell lines. Microarray analysis revealed several differentially expressed key genes and four unique genes were highly and differentially up-regulated (ARC, GADD45B, MYLIP and CDKN1C). The present study identified RE+I3C+QURC as a powerful combination that induced 100% BC cell death and determined its underlying molecular players.

Ongoing *in vivo* experiments aim to evaluate the efficacy of this 3-SC in preventing tumor growth using xenograft mouse BC model, and further validate the functional relevance of its underlying key genes.

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