Role of Wnt Self-Renewal Pathway in Regulating Tumor Initiating Cells in Breast Cancer

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Breast cancer is the second leading cause of death in females worldwide and shows a 28% increase amongst Saudi females in current statistics. Despite many treatment options, severe relapse still occurs. This could be attributed to a sub-population of cells called Tumour Initiating Cells (TICs) or Cancer Stem Cells (CSCs). There are many attempts to implicate the Wnt self-renewal pathway in breast cancer and stem cells, but the results still need clarification. This project aims to determine inhibiting the Wnt self-renewal pathway to target and eradicate CSCs. For the experiments, flow cytometry, quantitative real-time PCR and functional assays were utilized on three breast cell lines; tumourgenic breast cancer (MDA-MB-231), non-tumourgenic (T-47D and MCF-7) and normal breast cell lines (MCF-10A and MCF-12). Specific media were used according to the cell type and the complete DMEM media were used for breast cancer cells. Complete universal media were used for normal breast cells. Different doses of the stimulators and inhibitors of the Wnt pathway were tested. The results show stimulation of Wnt enhances the function of breast CSCs in tumourgenic cell lines. The level of TCF3 and STAT3 mRNA was 54% and 20% higher in the stimulated cells as compared to control, respectively. In addition, the inhibition of Wnt reduced the self-renewal function of CSCs and decreased the level of CyclD mRNA up to 80%. Therefore, targeting these breast CSCs by Wnt inhibitors may provide a useful approach in the treatment of breast cancer to eradicate the tumour from its' roots.