Abstract

Breast cancer is the most frequent cancer type between women, which influences more than 2 million women every year. It represents 15% of total cancer deaths among women. Genomic alternations are the main cause of breast cancer transformation. The differences in gene expression patterns among breast cancer subtypes are likely to reflect basic differences in the cell biology of each type and that gives the apparent phenotypes. The imbalance between the activities of tumor suppressors and oncogenes is a common event that leads to cancer transformation. Our preliminary data shows that different p53 variants lead to differential gene expression. Thus we hypothesized that different gene alteration combinations would result in differential gene expression pattern and consequently to different phenotypes. We aimed to create different breast cancer transformation models by transforming the normal mammary epithelial cell lines, MCF10A cells, that contain different *TP53* gene variants with *HRAS G12V*. Afterwards, we tested the differences in distinct cellular phenotypes (cancer hallmarks) caused by this combination. The *HRAS* overexpression increased cell proliferation, migration, invasion and resistance to apoptosis. Moreover, *HRAS* overexpression in combination with different *TP53* mutations lead to different phenotypes and gene expression patterns. This study demonstrates a critical role of two hit system in induction of cancer transformation. Altogether, we successfully generated models for studying breast cancer transformation that might help in understanding the differential behavior of different breast cancer tumors, which could be used to improve breast cancer detection, diagnosis and treatment.