

Identification of genes involved in breast cancer and breast cancer stem cells

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Abstract: Breast cancer is the most frequent type of cancer in women. Great progress has been made in its treatment but relapse is common. One hypothesis to account for the high recurrence rates is the presence of cancer stem cells (CSCs), which have the ability to self-renew and differentiate into multiple malignant cell types. This study aimed to determine genes that are expressed in breast cancer and breast CSCs and to investigate their correlation with stemness. RNA was extracted from established breast cancer cell lines and from CSCs derived from five different breast cancer patients. DNA microarray analysis was performed and any upregulated genes were also studied in other cancer types, including colorectal and lung cancer. For genes that were expressed only in breast cancer, knockdown-based experiments were performed. Finally, the gene expression levels of stemness transcription factors were measured. The outcome of the analysis indicated a group of genes that were aberrantly expressed mainly in breast cancer cells with stemness properties. Knockdown experiments confirmed the impact of several of these on *NANOG*, *OCT3/4*, and *SOX2* transcription factors. It seems that several genes that are not directly related with hormone metabolism and basic signal transduction pathways might have an important role in relapse and disease progression and, thus, can be targeted for new treatment approaches for breast cancer.

Keywords: breast cancer, cancer stem cells, stemness, DNA microarray

Introduction

Breast cancer is the most frequent type of cancer among women, with more than 230,000 new cases diagnosed in the US in 2013. It is the leading cause of death in women worldwide, and the second highest cause in the US among all cancer types.^{1,2} The treatment of breast carcinoma mainly involves conserving surgery or mastectomy, depending on the localization of the tumor and the stage.^{3,4} Chemotherapy and/or radiation therapy, as well as hormone-dependent therapies, is also used, depending on stage, histology, and biomarkers.⁵

One of the major problems in cancer treatment is multidrug resistance, as many breast tumors either possess or develop resistance to chemotherapeutic drugs.⁶ The recurrence of breast cancer is also an important issue in the treatment, and the ability to predict a pattern for breast cancer recurrence is of high priority for many researchers.⁷ According to previously published literature and experimental data, resistance and recurrence of breast cancer could be due to the existence of cancer stem cells (CSCs), the epithelial–mesenchymal transition, and the signaling transduction pathways as well as microRNAs.^{8–11}

CSCs have the ability to self-renew and initiate differentiation into heterogenic cancer cells, which may cause metastasis and relapse.¹² In breast cancer, it has been

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