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Genetic Approaches Used To Manage Patients with Breast Cancer: Implications for Individualized Therapy and Translational Medicine

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Introduction

Breast cancer is the cancer that forms in tissues of the breast and it is one of the most common cancers in women. Treatment strategies include surgery, radiation, biological therapy, and supplemental hormone therapy, but the efficacy of these therapies need improving and tumor recurrence is still a problem. In addition, various side effects, such as anemia, toxicity are quite common in breast cancer patients [1-4]. Effective communication with patients is crucial to address concerns and symptoms, and more studies are needed to discover effective strategies to minimize these side effects [2].

Breast cancer is the most common cancer in women both in the developed and developing countries. It is estimated that more than 508 000 women died worldwide in 2011 due to breast cancer (Global Health Estimates, WHO 2013). Although breast cancer is considered to be a disease of the developed world, almost 50% of breast cancer cases and 58% of deaths occur in the developing countries (GLOBOCAN 2008). Incidence rates vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. In most of the less developed regions the incidence rates are under 40 per 100,000 (GLOBOCAN 2008). The lowest incidence rates are found in most African countries but the incidence rates are also going up.

It has been shown that the progression of primary and secondary tumors into uncontrolled proliferation plays a vital role in the pathogenesis of breast cancer [5]. Breast cancer in young women is still a big challenge to patients, families and health care providers. Although the diagnosis of breast cancer is much less common in women under the age of 40 years old, it can have a greater influence than in older counterparts, as it tends to be more aggressive and has a poorer prognosis [6-7]. With the development of high throughput screening methods, various genetic approached were developed to better management of patients with breast cancer, especially in predicting cancer recurrence and chemo-sensitivity.

Genetic Approaches used to Manage Breast Cancer

Genetic approaches have been successfully used to study many diseases. As for the breast cancer, a lot of host genes as biomarkers have been validated in the prediction of tumor recurrence. In this editorial, we first present the predictive value of 21-gene signature followed by HER2, HOXB13, IL17BR and other host genes reported rarely.

21-gene siganture

21-gene Recurrence Score (RS) is a gene expression profile assay currently endorsed for use in patients with endocrine-sensitive node-negative breast cancers. The RS has been shown to supplement current 'prognostic' and 'predictive' assessments of relapse risk and chemotherapy benefits, respectively, and lead to significant changes in oncologists' recommendation for adjuvant chemotherapy, with an overall reduction in chemotherapy utilization [8]. Following surgery, one obvious question is whether a given patient should receive chemotherapy or not. For those patients with low recurrence risk, use of chemotherapy is not only waste of money but also make them suffer from unnecessary side-effects. Genome Health developed a genetic method by examining the gene expression levels of 21-genes from surgery-resected breast cancer tissue to determine the risk of tumor recurrence in order to help doctors make sound decision. From retrospectively study, doctors make therapy decision according to 21-gene recurrence score [9], Furthermore, many patients with intermediate Recurrence Score values switched one therapy to another because chemo hormonal treatment tended to decrease following assay results [10].

HER2

Overexpression of Human Epidermal Growth Factor Receptor 2 (HER2) can lead to breast cancer. But only 15% to 20% patients with breast cancer are HER2 positive [11]. Testing status of HER2 is critical for treatment decision as to whether HER2-targeted therapy should be used. HER2 expression can be tested by Immunohistochemistry (IHC) or *In situ* Hybridization (ISH). In addition to help doctor decide whether anti-HER2 agents should be used or not, patients with HER2 positive may have a lower risk of recurrence [12].

HOXB13:IL17BR

Homeobox B13 (HOXB13) is a protein encoded by HOXB13 gene while Interleukin-17 receptor B (IL17BR) is encoded by IL17BR gene. The HOXB13/IL17BR ratio index is used as a prognostic biomarker for breast cancer. HOXB13/IL17BR (H/I) and Molecular Grade Index (MGI) have been shown to have predictive value from the retrospective study. Among the patients treated with tamoxifen, more than 50% are low risk and less than 10% have 10 years distant recurrence risk [13]. Tamoxifen can prolong the longer Distant Recurrence-Free Survival (DRFS) of patients with low levels of HOXB13 expression [14]. Another medication such as letrozole treatment can decrease the late recurrence for patients with high H/I [15].

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95-gene signature

95-gene classifier has been used as predictor for relapse in breast cancer with high accuracy, and it could separate patients into high-risk and low-risk groups. In estrogen receptor positive(ER+) patients with node negative, 10 years recurrence-free survival rates of low-risk is 93% whereas the counterpart of low-risk is 53% [16].

Ki-67

Ki-67 is a protein that is associated with cell proliferation, and it is assessed by immunohistochemistry method on formalin-fixed paraffin-embedded blocks. Recurrent patients have higher Ki67 values while overall survival is significantly lower in patients with high Ki67 values [17].

Future Direction

With traditional therapy, patients usually get adjuvant therapy after surgery for the sake of avoiding the recurrence. Many patients have low-risk of recurrence but they also have to receive such treatment. So the individualized therapy is becoming more and more important in the field of breast cancer treatment in order to recommend whether a given patient should be given chemotherapy following tumor resection. For those patients with low risk of recurrence, sparing chemotherapy can not only save cost but also avoid side effects.

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