Breast cancer: Biomarkers and disease management

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Breast cancer remains one of the top threats to the health of women. Breast cancer is considered as a heterogeneous disease comprising various types of neoplasms, which involves different profile changes in both mRNA and micro-RNA (miRNA) expression. Extensive studies on mRNA expression in breast tumor have yielded some very interesting findings, some of which have been validated and used in clinic. Recent miRNA research advances showed great potential for the development of novel biomarkers and therapeutic targets. miRNAs are a new class of small non-coding regulatory RNAs that are involved in regulating gene expression at the posttranscriptional level. It has been demonstrated that miRNA expression is frequently deregulated in breast cancer, which warrants further in-depth investigation to decipher their precise regulatory role in tumorigenesis. Recent advances in phenotyping and expression profiling of human cancers have greatly enhanced the diagnosis and biological classification of several tumors, in particular breast cancers. Carbohydrate antigen 15-3 (CA 15-3) is the most widely applied serum marker. However, the lack of sensitivity precluded its clinical use in early stage disease.

The management of breast cancer is the current lack of tumor marker with sufficient sensitivity and specificity. A growing body of evidence implicates the diagnostic potential of circulating miRNAs in cancer detection. MiR-155 plays an important role in the pathogenesis of breast cancer. However, the level of circulating miR-155 and its clinical relevance are not well established. Serum markers such as carcinoembryonic antigen (CEA) and tissue polypeptide specific antigen (TPS) are even less sensitive than CA 15-3. At least five subtypes of breast cancer have been identified on the basis of their patterns of biomarker expression. Triple-negative breast cancer, or TNBC, is defined as breast epithelial cancer cells that lack the HER-2/neu receptor, the estrogen receptor and the progesterone receptor. The value of current histological prognostic indicators in predicting the course of the disease is weak and many of the molecular mechanisms underlying breast cancer progression remain poorly understood. This deficit has led to significant interest in the quest for novel predictive markers for breast cancer. Elucidation of the molecular mechanisms involved in breast cancer has been the subject of extensive research in recent years, yet several dilemmas and major challenges still prevail in the management of breast cancer patients including unpredictable response and development of adjuvant therapies. Current challenges in the management of breast cancer include a continuing search for sensitive minimally invasive markers that can be exploited to detect early neoplastic changes thus facilitating the detection of breast cancer at an early stage, as well as for monitoring the progress of patients with breast cancer and their response to treatments. Existing biomarkers for breast cancer have many inherent deficiencies. Mammography is currently the gold standard diagnostic tool however it is not without limitations, including its use of ionizing radiation and a false positive rate of 5–10%. To date, only two markers have been established so far in the routine assessment of breast cancer: ER (for predicting response to endocrine therapies) and HER2 (for predicting response to Trastuzumab). Although these markers are currently available, ER and HER2 assessment is far from perfect. A number of circulating tumour markers (e.g., carcinoembryonic antigen [CEA] and carbohydrate antigen 15-3 [CA 15-3]) are used clinically in the management of breast cancer, but the sensitivity of these markers is low, so that they are not useful as screening tools though they have long been in clinical use as prognostic markers and to monitor for disease progression or recurrence. The ideal biomarker should be easily accessible such that it can be sampled relatively noninvasively, sensitive enough to detect early presence of tumors in almost all patients and absent or minimal in healthy tumor-free individuals.

There is also great need for the identification of sensitive, reliable and acceptable markers of response to neoadjuvant and adjuvant therapies. MRNAs have enormous potential to serve as an ideal class of cancer biomarkers for the following reasons. 1) MRNA expression is known to be aberrant in cancer. 2) MRNA expression profiles are pathognomonic or tissue-specific. 3) MRNAs are remarkably stable molecules that have been shown to be well preserved in formalin fixed, paraffin embedded tissues as well as fresh snap frozen specimens. The potential role of miRNAs in breast cancer management is, particularly in improving current prognostic tools and achieving the goal of individualized cancer treatment.