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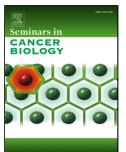
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Please cite this article as: Nicolini Andrea, Ferrari Paola, Duffy Michael J.Prognostic and Predictive Biomarkers in Breast Cancer: Past, Present and Future.*Seminars in Cancer Biology* http://dx.doi.org/10.1016/j.semcancer.2017.08.010

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Prognostic and Predictive Biomarkers in Breast Cancer: Past, Present and Future

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Abbreviations: uPA, urokinase plasminogen activator; PAI-1, plasminogen activator inhibitor 1; ctDNA, circulating tumor DNA; CTC, circulating tumor cells; PFS, progression-free survival; pCR, pathological complete response; SNVs, single nucleotide variants; CNVs; copy number variants

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Abstract

Following a diagnosis of breast cancer, the most immediate challenges in patient management are the determination of prognosis and identification of the most appropriate adjuvant systemic therapy. Determining prognosis can best be addressed with a combination of traditional clinicopathological prognostic factors, biomarkers such as HER2/*neu* and specific multigene genes tests. Amongst the best validated prognostic multigene tests are uPA/PAI1, Oncotype DX and MammaPrint. Oncotype DX and MammaPrint, may be used for predicting outcome and aiding adjunct therapy decision making in patients with ER-positive, HER2-negative breast cancers that are either lymph node-negative or node positive (1-3 metastatic nodes), while uPA/PAI-1 may be similarly used in ER-positive, lymph node-negative patients. For selecting likely response to endocrine therapy, both estrogen receptors (ER) and progesterone receptors (PR) should be measured. On the other hand, for identifying likely response to anti-HER2 therapy, determination of HER2 gene amplification or overexpression is necessary. To identify new prognostic and predictive biomarkers for breast cancer, current research is focusing on tumor and circulating DNA (ctDNA) and RNA (e.g., micro RNAs) and circulating tumor cells. A promising ctDNA biomarker is the mutational status of ER (*ESR1*) for predicting the emergence of resistance to aromatase inhibitors. Challenges for future research include the identification of biomarkers

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