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Molecular Biomarkers for Early Detection and Prognosis of Triple-Negative Breast Cancer: A Clinical Pathology Perspective

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Introduction

Triple-Negative Breast Cancer (TNBC) represents one of the most aggressive subtypes of breast malignancies, characterized by the absence of Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal Growth Factor Receptor 2 (HER2) expression. Accounting for approximately 15–20% of all breast cancers, TNBC is associated with a poor prognosis, high recurrence rates, and limited therapeutic options due to the lack of targeted therapies. Traditional histopathological assessment provides limited information on disease heterogeneity, necessitating the identification of molecular biomarkers that can improve early detection, predict therapeutic response, and refine prognosis. Recent advances in genomics, proteomics, and transcriptomics have enabled the discovery of diverse biomarkers ranging from genetic mutations and non-coding RNAs to circulating tumor DNA (ctDNA) and exosomal proteins that hold significant potential in transforming TNBC diagnosis and management [1].

Description

Molecular biomarker research in TNBC has revealed several critical genetic and epigenetic alterations driving tumor progression. Mutations in TP53, BRCA1/2, and PIK3CA are among the most prevalent, contributing to genomic instability and therapy resistance. BRCA1-deficient TNBCs, for instance, are particularly sensitive to PARP inhibitors, establishing the foundation for targeted therapeutics in this challenging subtype.

Transcriptomic studies have also highlighted differential expression of microRNAs (miRNAs) such as miR-21, miR-155, and miR-200c, which regulate Epithelial–Mesenchymal Transition (EMT) and metastatic potential. Moreover, proteomic and metabolomics profiling has identified key biomarkers like cytokeratin 5/6, EGFR, and Androgen Receptor (AR) that serve as diagnostic markers and potential therapeutic targets [2].

Importantly, these molecular insights allow for the sub classification of TNBC into basal-like, mesenchymal, and immunomodulatory subtypes each with distinct molecular signatures and clinical outcomes. In the realm of liquid biopsy, Circulating Tumor Cells (CTCs), ctDNA, and extracellular vesicles have emerged as non-invasive biomarkers for real-time monitoring of disease progression and therapeutic efficacy.

For instance, elevated plasma levels of miR-373 and exosomal protein CD44 have been linked to metastasis and poor survival outcomes. Integration of these biomarkers into clinical workflows can facilitate early diagnosis and enable personalized treatment regimens [3].

Despite these advancements, translating molecular findings into clinical practice remains challenging due to tumor heterogeneity, small sample cohorts, and lack of standardized validation protocols. Ongoing clinical trials combining multi-omics data with Artificial Intelligence (AI) analytics promise to overcome these barriers, refining prognostic accuracy and enabling dynamic disease surveillance in TNBC [4,5].

Conclusion

The identification and validation of molecular biomarkers hold immense promise for the early detection and prognosis of triple-negative breast cancer. As omics technologies and computational analytics continue to advance, biomarker-driven precision medicine is expected to revolutionize TNBC management. The integration of genomic, proteomic, and liquid biopsy data into clinical pathology will enhance diagnostic accuracy, enable real-time disease monitoring, and guide individualized therapeutic decisions. Ultimately, translating these discoveries into clinical application will improve survival outcomes and quality of life for TNBC patients worldwide.

Acknowledgement

None

Conflicts of Interest

None

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