MOLECULAR MECHANISMS AND GENETIC MUTATIONS IN BREAST CANCER DEVELOPMENT

Dallo Salva Faekovna
Assistant, Department of Oncology, Oncohematology, and Radiation Oncology, Tashkent State Medical University, Tashkent, Uzbekistan

Abstract. *Breast cancer remains one of the most prevalent and life-threatening malignancies among women worldwide. The development and progression of breast cancer are driven by complex molecular mechanisms involving genetic mutations, epigenetic alterations, and dysregulated signaling pathways. Key genetic mutations such as BRCA1, BRCA2, TP53, and HER2 play a crucial role in tumor initiation, cell proliferation, invasion, and metastasis. In addition, abnormalities in hormone receptor signaling pathways, including estrogen and progesterone receptors, significantly contribute to carcinogenesis. Recent advances in molecular biology and genomics have improved the understanding of the biological behavior of breast cancer, enabling the development of targeted therapies and personalized treatment approaches. This article reviews the major molecular mechanisms and genetic alterations involved in breast cancer development, highlighting their clinical significance and potential implications for diagnosis, prognosis, and therapy.*

Keywords. *Breast cancer; molecular mechanisms; genetic mutations; BRCA1; BRCA2; TP53; HER2; oncogenes; tumor suppressor genes; targeted therapy.*

Introduction

Breast cancer is one of the most common malignancies affecting women globally and represents a significant public health challenge. According to global cancer statistics, it accounts for a substantial proportion of cancer-related morbidity and mortality among women. Despite advances in early detection and treatment strategies, breast cancer remains a biologically heterogeneous disease characterized by diverse molecular subtypes and variable clinical outcomes.

The development of breast cancer is a multistep process involving the accumulation of genetic and epigenetic alterations that disrupt normal cellular regulatory mechanisms. These alterations affect key processes such as cell cycle control, apoptosis, DNA repair, and signal transduction. Mutations in tumor suppressor genes and oncogenes play a central role in initiating and promoting malignant transformation. Among the most extensively studied genes are BRCA1 and BRCA2, which are involved in DNA repair pathways, TP53, which regulates cell cycle arrest and apoptosis, and HER2, which promotes cell proliferation through growth factor signaling pathways.

In addition to genetic mutations, dysregulation of hormonal signaling pathways, particularly those mediated by estrogen and progesterone receptors, significantly

contributes to breast carcinogenesis. The interaction between genetic predisposition, environmental factors, and hormonal influences creates a complex molecular landscape that underlies tumor heterogeneity.

Understanding the molecular mechanisms involved in breast cancer development is essential for improving diagnostic accuracy, identifying prognostic biomarkers, and developing targeted therapeutic strategies. In recent years, advances in molecular biology, genomics, and precision medicine have provided deeper insights into the pathogenesis of breast cancer, paving the way for individualized treatment approaches.

This article aims to analyze the key molecular mechanisms and genetic mutations involved in breast cancer development and to discuss their clinical relevance in modern oncology.

Materials and Methods

This study was designed as a comprehensive narrative review aimed at analyzing the molecular mechanisms and genetic mutations involved in breast cancer development. A systematic search of scientific literature was conducted to identify relevant peer-reviewed publications addressing genetic alterations, signaling pathways, and molecular subtypes of breast cancer.

Electronic databases including PubMed, Scopus, and Web of Science were used to retrieve scientific articles. The search strategy included combinations of the following keywords: “breast cancer,” “molecular mechanisms,” “genetic mutations,” “BRCA1,” “BRCA2,” “TP53,” “HER2,” “oncogenes,” “tumor suppressor genes,” “DNA repair,” “signal transduction pathways,” and “epigenetic alterations.” Boolean operators (AND, OR) were applied to refine the search results.

Articles published in English between 2008 and 2024 were prioritized to ensure updated scientific evidence. However, earlier landmark studies were included when they provided fundamental insights into molecular carcinogenesis. Only peer-reviewed original research articles, systematic reviews, and meta-analyses were considered eligible for inclusion.

Inclusion criteria consisted of studies that:

1. investigated genetic mutations associated with breast cancer;
2. analyzed molecular signaling pathways involved in tumor progression;
3. provided clinical or experimental data supporting molecular findings.

Exclusion criteria included non-peer-reviewed sources, studies lacking methodological clarity, conference abstracts without full data, and articles unrelated to molecular or genetic mechanisms.

Selected studies were analyzed qualitatively. Data were extracted regarding gene mutations, molecular pathways, subtype classification, prognostic implications, and therapeutic relevance. The findings were synthesized to identify consistent molecular patterns contributing to breast cancer development and progression.

This methodological approach allowed for a comprehensive evaluation of current scientific knowledge on the genetic and molecular basis of breast cancer.

Discussion

The findings of this review confirm that breast cancer development is driven by a complex interplay of genetic mutations, molecular signaling dysregulation, and epigenetic modifications. The high prevalence of BRCA1 and BRCA2 mutations in hereditary breast cancer cases highlights the critical role of defective DNA repair mechanisms in tumor initiation. Loss of homologous recombination repair capacity leads to genomic instability, which serves as a fundamental hallmark of carcinogenesis. These findings also explain the clinical effectiveness of PARP inhibitors in BRCA-mutated breast cancer patients, demonstrating the direct therapeutic implications of molecular research.

Mutations in the TP53 gene were strongly associated with aggressive tumor phenotypes and poor clinical outcomes. TP53 dysfunction disrupts normal cell cycle control and apoptosis, allowing abnormal cells to evade programmed cell death. This contributes to increased tumor heterogeneity and resistance to standard chemotherapy. The strong association between TP53 mutations and triple-negative breast cancer further emphasizes the need for novel targeted treatment strategies in this subgroup.

HER2 amplification represents another crucial molecular alteration in breast cancer. Although HER2-positive tumors tend to exhibit rapid growth and higher metastatic potential, the introduction of targeted therapies such as monoclonal antibodies has significantly improved survival rates. This demonstrates how understanding oncogenic signaling pathways directly influences therapeutic innovation and patient prognosis.

Hormone receptor signaling remains a dominant factor in the majority of breast cancer cases. Estrogen receptor–positive tumors generally show better differentiation and more favorable outcomes due to responsiveness to endocrine therapy. However, endocrine resistance remains a major clinical challenge, often linked to additional molecular alterations in PI3K/AKT/mTOR pathways.

Epigenetic mechanisms, including DNA methylation and microRNA dysregulation, add another layer of complexity to breast cancer biology. Unlike genetic mutations, epigenetic changes are potentially reversible, making them promising targets for future therapeutic interventions. Growing evidence suggests that combining genetic profiling with epigenetic analysis may improve precision medicine strategies.

Overall, the heterogeneity of breast cancer underscores the necessity of molecular classification and personalized treatment approaches. Advances in next-generation sequencing and genomic profiling continue to refine our understanding of tumor biology and guide individualized therapy selection.

Conclusion

Breast cancer development is a multifactorial and genetically driven process characterized by complex molecular alterations that disrupt normal cellular regulation.

Mutations in key tumor suppressor genes such as **BRCA1, BRCA2, and TP53**, along with amplification of oncogenes like **HER2**, play a central role in tumor initiation, progression, and metastasis. Additionally, dysregulation of hormone receptor signaling and epigenetic modifications further contribute to disease heterogeneity and therapeutic resistance.

The findings emphasize that breast cancer is not a single disease but a collection of molecularly distinct subtypes, each with unique biological behavior and clinical outcomes. Understanding the underlying genetic and molecular mechanisms has significantly improved diagnostic precision, prognostic assessment, and the development of targeted therapies. The success of HER2-targeted treatments and PARP inhibitors in BRCA-mutated cancers demonstrates the practical impact of molecular research on clinical oncology.

Future advances in genomic profiling, molecular diagnostics, and precision medicine are expected to further refine individualized treatment strategies and improve survival rates. Continued investigation into molecular pathways and genetic alterations will remain essential for optimizing early detection, therapeutic innovation, and long-term patient management.

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