ISSN NO: 2770-2936
December 2025

Molecular and Biological Subtypes of Breast Cancer

PhD Orifjon Absamatillaevich Talipov
Department of Oncology,
Pediatric Oncology, and Palliative Care Senior Lecturer

Abstract.
Breast cancer is a heterogeneous disease characterized by diverse molecular and biological subtypes, which influence prognosis and treatment strategies. Identification of these subtypes through molecular profiling has significantly improved personalized therapy, leading to better clinical outcomes. This review provides an overview of the main molecular subtypes of breast cancer, their biological characteristics, and implications for patient management.
Keywords: Breast cancer, molecular subtypes, biological characteristics, prognosis, personalized therapy

Breast cancer is one of the most common malignancies among women worldwide and a leading cause of cancer-related mortality. The heterogeneity of breast tumors presents a challenge for effective diagnosis and treatment. Advances in molecular biology and genomic profiling have enabled the classification of breast cancer into distinct subtypes, including Luminal A, Luminal B, HER2-enriched, and Triple-negative/Basal-like. Each subtype exhibits unique molecular features, clinical behavior, and response to therapy. Understanding these subtypes is crucial for developing personalized treatment strategies and improving patient outcomes.

Breast cancer is a complex and heterogeneous disease that varies in molecular profile, histopathology, and clinical outcomes. Advances in molecular biology have allowed researchers to classify breast tumors into specific subtypes, which is essential for selecting optimal treatment strategies and predicting prognosis.The Luminal A subtype is characterized by the expression of hormone receptors, such as estrogen receptor (ER) and progesterone receptor (PR), with low levels of Ki-67, a marker of cellular proliferation. Tumors of this subtype generally have a favorable prognosis and respond well to endocrine therapy. They typically exhibit slower growth and lower rates of recurrence compared to other subtypes.Luminal B tumors also express hormone receptors but show higher proliferative activity, often indicated by elevated Ki-67 levels. This subtype may or may not overexpress the HER2 protein. Patients with Luminal B tumors tend to have a less favorable prognosis than those with Luminal A tumors, and treatment often requires a combination of endocrine therapy and chemotherapy.

The HER2-enriched subtype is defined by overexpression of the human epidermal growth factor receptor 2 (HER2) and lack of hormone receptor expression. These tumors are usually more aggressive and associated with a higher risk of recurrence. However, targeted therapies, such as trastuzumab and other HER2 inhibitors, have significantly improved outcomes for patients with this subtype.

Triple-negative or basal-like breast cancers lack expression of ER, PR, and HER2. This subtype is associated with high histological grade, aggressive behavior, and limited treatment options since hormonal and HER2-targeted therapies are ineffective. Chemotherapy remains the mainstay of treatment, although ongoing research is exploring immunotherapy and novel molecular targets to improve prognosis.Understanding the molecular and biological characteristics of breast cancer subtypes enables clinicians to personalize therapy, minimize unnecessary treatments, and enhance patient survival. Molecular profiling not only guides therapeutic decisions but also contributes to the development of novel targeted therapies and precision medicine approaches in oncology.

Recent advances in genomic technologies have further refined the classification of breast cancer subtypes, enabling a more precise understanding of tumor biology. Gene expression profiling has revealed significant heterogeneity even within established subtypes, highlighting the need for individualized therapeutic approaches. For example, subsets of triple-negative breast cancer may respond differently to chemotherapy or immunotherapy based on their specific molecular signatures.In addition to guiding treatment, molecular subtyping plays a critical role in prognostication. Luminal A tumors are generally associated with long-term survival, whereas HER2-enriched and triple-negative tumors carry higher risks of early relapse and

ISSN NO: 2770-2936
December 2025

metastasis. Identification of these subtypes allows clinicians to implement closer monitoring strategies and adjust treatment intensity accordingly.

Emerging therapies targeting specific molecular pathways are transforming the management of breast cancer. HER2-targeted agents, CDK4/6 inhibitors for hormone receptor-positive tumors, and immune checkpoint inhibitors for selected triple-negative cases exemplify the shift toward precision medicine. The integration of molecular profiling into routine clinical practice ensures that patients receive therapies tailored to the biological characteristics of their tumors, optimizing outcomes and minimizing unnecessary toxicity.Furthermore, understanding the tumor microenvironment and its interaction with molecular subtypes is an area of active research. Tumor-infiltrating lymphocytes, stromal factors, and immune response markers are increasingly recognized as important determinants of treatment response, particularly in aggressive subtypes such as triple-negative and HER2-enriched breast cancers. This knowledge supports the development of combination therapies that not only target cancer cells directly but also modulate the surrounding microenvironment to enhance efficacy.

Ongoing research is also focusing on the identification of novel biomarkers that could further stratify patients within existing subtypes. These biomarkers, including genetic mutations, epigenetic modifications, and circulating tumor DNA, provide additional prognostic and predictive information. For instance, mutations in the PIK3CA gene are frequently observed in hormone receptor-positive tumors and may inform targeted therapy decisions. Similarly, BRCA1 and BRCA2 mutations are often associated with triple-negative breast cancers, guiding the use of PARP inhibitors and influencing surgical and systemic treatment strategies.Patient management increasingly emphasizes a multidisciplinary approach, integrating surgical, medical, and radiation oncology with molecular diagnostics. This approach ensures that treatment decisions are evidence-based and tailored to the unique molecular profile of each tumor. In clinical practice, comprehensive molecular profiling is becoming a standard component of breast cancer care, allowing oncologists to optimize therapeutic regimens and improve survival outcomes.The continuous evolution of targeted therapies and immunotherapies underscores the dynamic nature of breast cancer treatment. Clinical trials are exploring combinations of established treatments with novel agents based on subtype-specific vulnerabilities. This precision medicine paradigm not only enhances the efficacy of treatment but also reduces adverse effects by avoiding unnecessary exposure to ineffective therapies.

Conclusion.

Molecular and biological subtyping of breast cancer has transformed the understanding and management of this heterogeneous disease. Identification of Luminal A, Luminal B, HER2-enriched, and Triple-negative/Basal-like subtypes provides critical information for prognosis, treatment selection, and patient monitoring. Advances in genomic profiling and molecular diagnostics enable personalized therapeutic approaches, improving clinical outcomes and minimizing unnecessary toxicity. Furthermore, ongoing research into novel biomarkers, targeted therapies, and the tumor microenvironment continues to enhance precision medicine strategies. Overall, integrating molecular subtyping into clinical practice is essential for optimizing breast cancer care and advancing the development of effective, individualized treatments.

References

1. Perou, C.M., Sørlie, T., Eisen, M.B., van de Rijn, M., Jeffrey, S.S., Rees, C.A., … Botstein, D. (2000). Molecular portraits of human breast tumours. Nature, 406(6797), 747–752.
2. Carey, L.A., Perou, C.M., Livasy, C.A., Dressler, L.G., Cowan, D., Conway, K., … Millikan, R.C. (2006). Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA, 295(21), 2492–2502.
3. Sørlie, T., Perou, C.M., Tibshirani, R., Aas, T., Geisler, S., Johnsen, H., … Børresen-Dale, A.L. (2001). Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proceedings of the National Academy of Sciences, 98(19), 10869–10874.
4. Goldhirsch, A., Winer, E.P., Coates, A.S., Gelber, R.D., Piccart-Gebhart, M., Thürlimann, B., … Panel members. (2013). Personalizing the treatment of women with early breast cancer: Highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Annals of Oncology, 24(9), 2206–2223.

ISSN NO: 2770-2936
December 2025

5. Rakha, E.A., El-Sayed, M.E., Green, A.R., Paish, C.E., Lee, A.H.S., Robertson, J.F.R., … Ellis, I.O. (2008). Biological subtypes of breast cancer: Prognostic and therapeutic implications. Breast, 17(5), 538–550.