

Breast Cancer: Biological Mechanism, Current Understanding, and Future Perspectives

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Key points:

- Introduction
- Epidemiology and risk factors
- Biological Mechanisms of Breast Cancer
- Classification and Molecular Subtypes
- Current Diagnostic and Therapeutic Approaches
- Challenges in Breast Cancer Management
- Future Decisions
- Conclusion

Introduction

Breast cancer is a heterogeneous disease characterized by the uncontrolled proliferation of breast epithelial cells. It is the most frequently diagnosed cancer in women and ranks second in cancer-related mortality globally. In the United States, more than 250,000 new cases of breast cancer were diagnosed in 2017.¹ Understanding the molecular and cellular mechanisms of breast cancer is vital for the development of effective targeted therapies and for reducing mortality rates.

Epidemiology And Risk Factors

.Key risk factors include:

- **Genetic predisposition:** Mutations in BRCA1, BRCA2, and other tumor suppressor genes.
- **Lifestyle factors:** Alcohol consumption, obesity, lack of physical activity, and diet.

Breast cancer refers to cancers originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk.²

Biological Mechanisms of Breast Cancer

It includes:

- Tumor Initiation
- Hormonal Influence
- Cellular Signaling Pathways

Several intracellular pathways are implicated in breast cancer:

- PI3K/AKT/mTOR pathway
- MAPK/ERK pathway
- Notch and Wnt pathways

Tumor Microenvironment

The tumor microenvironment, composed of immune cells, fibroblasts, and extracellular matrix, plays a vital role in tumor progression. Cancer-associated fibroblasts (CAFs) and tumor-associated macrophages (TAMs) contribute to immune evasion and metastasis.

Classification and Molecular Subtypes

Modern classification relies on gene expression profiling, leading to the identification of major molecular subtypes:

1. Luminal A: ER+, PR+, HER2-, low Ki-67.
2. Luminal B: ER+, PR+, HER2+/-, high Ki-67.
3. HER2-enriched: HER2+, ER-, PR-.
4. Basal-like (Triple-negative): ER-, PR-, HER2-, often aggressive and lacks targeted therapy.

This classification aids in guiding treatment strategies and predicting prognosis.

Current Diagnostic and Therapeutic Approaches

Diagnosis

- **Imaging:** Mammography, ultrasound, MRI.
- **Biopsy and Histopathology:** Essential for subtype identification.
- **Molecular testing:** Determines receptor status and genetic mutations.

Treatment Modalities

- **Surgery:** Lumpectomy or mastectomy.
- **Radiation therapy:** Post-operative or palliative.
- **Chemotherapy:** Neoadjuvant or adjuvant.
- **Hormonal therapy:** Tamoxifen, aromatase inhibitors.
- **Targeted therapy:** Trastuzumab for HER2+, CDK4/6 inhibitors for ER+.

Emerging therapies include immune checkpoint inhibitors and PARP inhibitors for BRCA-mutant cancers. There are two options for the surgical phase with similar survival rates: a lumpectomy with radiation if the tumor can be excised completely with good cosmetic results, or a mastectomy. (Kathryn P et al., 2021)³.

Challenges in Breast Cancer Management

- **Resistance to therapy:** Especially in hormone and HER2-targeted treatments.

- **Metastasis:** Particularly in triple-negative breast cancer.
- **Heterogeneity:** Intra- and inter-tumor variability limits the efficacy of universal treatment regimens.

Future Directions

Precision Medicine

Advancements in genomics and bioinformatics allow for patient-specific therapeutic strategies based on tumor molecular profiles.

Immunotherapy

Checkpoint inhibitors (e.g., PD-1/PD-L1 blockers) and cancer vaccines are under investigation. Success has been modest but promising in subgroups of patients.

Liquid Biopsy

A non-invasive method for early detection and monitoring through circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs).

Artificial Intelligence and Big Data

AI can improve diagnostic accuracy, treatment planning, and patient outcome prediction by analyzing vast datasets, including imaging and genomics.

Gene Editing

CRISPR-Cas9 technology offers potential for correcting genetic defects and studying gene function in cancer development.

Conclusion

Breast cancer continues to be a complex and evolving disease with significant global impact. Understanding the intricate biological mechanisms has led to improved diagnostic and therapeutic strategies. The future of breast cancer treatment lies in the integration of molecular science, personalized medicine, and technological innovations, aiming to transform it from a fatal disease into a manageable condition.

References

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