

The Role of Estrogen and Progesterone in Hormone Receptor-Positive Breast Cancer

Research Paper
Submitted by:

- Mariam Mohammed Basheer
- Malak HythamArafa
- Nada Mohammed Sadk
- Safya Ahmed Abdullah Algazar
- Basmalh Mutaz Bashir

Team Name:
Hormone Nexus

Team Name:
Mariam Mohammed Basheer



RCRP Competition

The Role of Estrogen and Progesterone in Hormone Receptor-Positive Breast Cancer

Research Paper Submitted by

1-Mariam Mohammed Basheer

2-Malak Hytham Arafa

3- Nada Mohammed Sadk

4- Safya Ahmed Abdullah Algazar

5 – Basmalh Mutaz Bashir

Team Name :

(Hormone Nexus)

Team Leader :Mariam Mohammed Basheer

Submission Date :17 October 2026

Abstract

Breast cancer is one of the most common cancers among women, and is defined as a disease in which abnormal and uncontrolled growth of breast cells occurs, and these cells may be transmitted to other parts of the body if the disease is not detected and treated in a timely manner. The study of biological factors associated with the growth of breast cancer is important, especially hormones such as oestrogen and progesterone, because of the growth and reproduction processes of breast cells that are regulated.

Scientific studies have shown that some breast cells, including some cancer cells, are expressed by oestrogen and progesterone receptors. When these hormones are linked to their receptors, the growth and reproduction of some breast cancer cells may be stimulated. Therefore, the presence of hormone receptors was considered an important factor that is used in the classification of some types of breast cancer and determining their response to hormone therapy.

Attention has been paid to the study of the relationship between hormones and breast cancer because of the role that estrogen and progesterone may play in regulating the growth of breast tissue. It was also explained that the relationship between hormones and the development of breast cancer is complex, and does not depend on the effect of only one hormone, but may be affected by the interaction between hormones and their receptors and various cellular and molecular factors.

Approximately 70% of breast cancers are estrogen receptor α (ER)-positive and are treated with endocrine therapy, yet acquired resistance remains a major clinical challenge. Gain-of-function mutations in ESR1, clustered in the ligand-binding domain, occur in roughly 20% of patients with metastatic ER-positive disease previously treated with endocrine agents such as aromatase inhibitors (AIs). These mutations confer ligand-independent receptor activity, allowing tumor growth despite estrogen deprivation.

Estrogen and progesterone are the two main ovarian hormones. They play important and coordinated roles in the development and function of breast tissue, particularly through their receptors, estrogen receptor (ER) and progesterone receptor (PR).

The overall findings demonstrate that hormonal therapy is an important and effective approach for treating hormone receptor-positive breast cancer, particularly because it directly targets a major pathway involved in cancer cell growth. However, the response to treatment is not the same in all patients, and some cancer cells can eventually become resistant to hormonal therapy. This resistance may result from changes in estrogen receptor activity, mutations in the ESR1 gene, or the activation of alternative signaling pathways that allow cancer cells to continue growing. As a result, newer treatment strategies have focused on combining hormonal therapy with targeted therapies, such as CDK4/6 and PI3K/AKT/mTOR inhibitors, to target cancer cells through more than one mechanism. This

approach may help overcome resistance and improve treatment response.

Research Question

How do Estrogen and Progesterone influence the development and progression of hormone receptor-positive breast cancer?

Introduction

Breast cancer is the most commonly diagnosed cancer among women worldwide and remains one of the leading causes of cancer-related death. According to GLOBOCAN 2022 estimates, it accounted for about 2.3 million new cases globally in that year. Its development is influenced by many factors, including genetic susceptibility, age, lifestyle, reproductive history, and hormonal exposure.

Among these factors, hormones play a particularly important role. Estrogen and progesterone regulate normal breast development, but through their receptors they can also stimulate the growth and survival of breast cells, which may promote malignant transformation. Approximately 70% of breast cancers are hormone receptor-positive, meaning that their growth depends at least partly on hormonal signaling. Other factors, such as insulin and growth factors, may also interact with these pathways and contribute to tumor development and progression.

Understanding hormonal mechanisms has had major clinical importance, leading to endocrine therapies such as tamoxifen and aromatase inhibitors. However, resistance to these treatments and the multifactorial nature of the disease show that hormonal pathways alone do not explain breast cancer behavior. Therefore, this review aims to summarize recent evidence (2020–2026) on the role of hormonal factors in breast cancer development, progression, and treatment response, highlighting both established mechanisms and remaining gaps in knowledge.

Methodology / Materials and Methods

This study is based on a review of scientific articles examining the role of hormonal factors in breast cancer development and progression. The research focuses on estrogen, progesterone, hormone receptors, insulin, growth factors, and hormonal changes that may be related to breast cancer.

Relevant studies published between 2020 and 2026 were searched for using PubMed and Google Scholar. Keywords such as “breast cancer,” “hormonal factors,” “estrogen,” “progesterone,” and “hormone receptors” were used to find studies related to the research topic.

The articles were reviewed to understand how hormonal factors may influence breast cancer development, tumor growth, and treatment response. The findings were compared and organized according to the main topics of the research, with attention to similarities and differences between the results of different studies.

Since this research is based on previously published studies, no laboratory experiments or new patient data were collected. The conclusions are based on the scientific findings reported in the selected articles.

Results & Analysis

The reviewed studies showed that hormonal factors play an important role in the development and progression of breast cancer. The main findings were related to estrogen, progesterone, hormone receptor status, and the influence of hormonal changes on tumor growth and treatment response.

1. The Role of Estrogen

The findings indicated that estrogen can stimulate the growth and multiplication of breast cancer cells that express estrogen receptors (ER). Prolonged exposure to estrogen throughout a woman's life may contribute to an increased risk of developing breast cancer. However, the effect of estrogen depends on several factors, including age, reproductive history, and the biological characteristics of the tumor.

2. The Role of Progesterone

The reviewed literature showed that progesterone signaling also contributes to breast tissue development and may influence breast cancer progression. Its effects are complex and depend on interactions with estrogen, progesterone receptors, and other molecular pathways. Therefore, progesterone cannot be considered an independent factor in all cases of breast cancer.

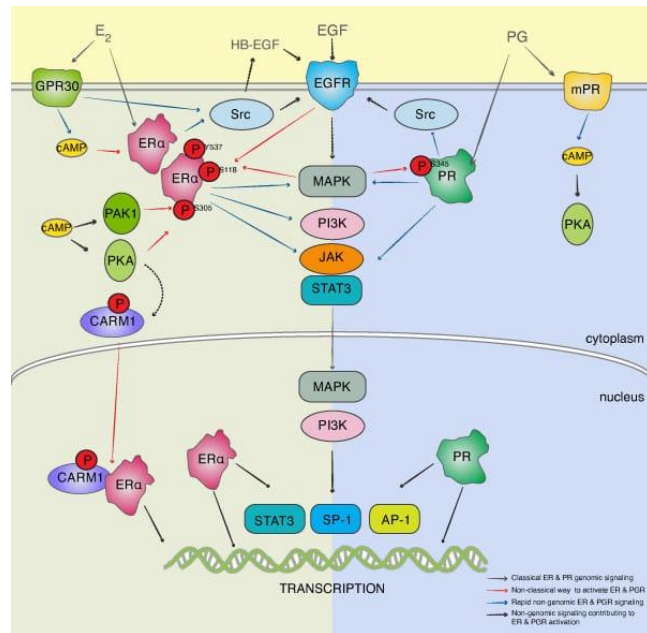


Figure 1

3. Hormone Receptor Status

The findings showed that hormone receptor status is an important factor in classifying breast cancer and selecting appropriate treatment. Tumors that express estrogen receptors (ER-positive) and/or progesterone receptors (PR-positive) may respond to hormone therapy. According to the American Cancer Society, approximately three out of four breast cancers have at least one of these hormone receptors. This highlights the importance of testing tumor tissue for hormone receptor expression during diagnosis.

4. Hormonal Therapy and Treatment Response

The reviewed studies demonstrated that hormone therapy can help treat hormone receptor-positive breast cancer by blocking hormonal signals or reducing estrogen production. However, treatment response varies among patients. Some tumors may develop resistance to hormonal treatment, emphasizing the importance of understanding the molecular mechanisms involved in tumor growth and progression.

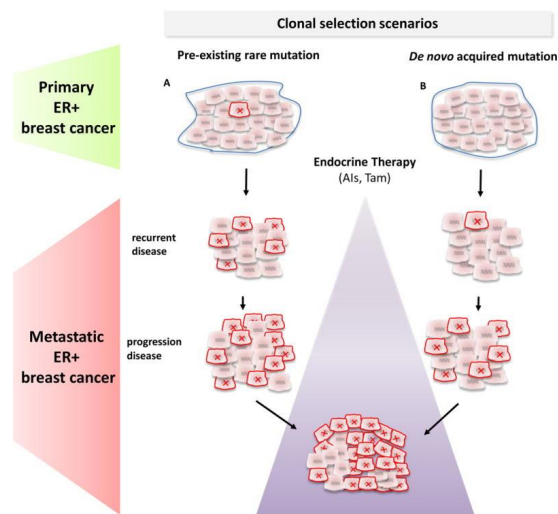


Figure 2

5. Hormonal Factors and Breast Cancer Risk

The reviewed evidence indicated that prolonged use of combined estrogen–progestin menopausal hormone therapy is associated with an increased risk of breast cancer. The degree of risk varies according to the duration of use and other individual factors. These findings suggest that hormonal exposure is an important component of breast cancer risk, although it is not the only factor responsible for disease development.

Overall, the results suggest that estrogen and progesterone signaling, hormone receptor expression, and the duration of hormonal exposure are

important factors in understanding breast cancer development and progression. Further research is needed to clarify the interactions between hormonal pathways and other biological factors and to improve individualized treatment strategies.

Discussion & Conclusion

Estrogen and progesterone play important roles in normal breast development, but their activity may also contribute to hormone receptor-positive breast cancer. By interacting with their receptors, these hormones influence breast cell growth and survival. Therefore, hormonal exposure, reproductive history, and other risk factors may affect the likelihood of developing breast cancer.

The role of hormones does not end with cancer development; hormonal signaling can also support tumor progression. This explains why endocrine therapies, such as tamoxifen and aromatase inhibitors, are used to reduce the effects of estrogen on cancer cells. However, treatment resistance shows that other biological pathways must also be considered.

Conclusion

In conclusion, estrogen and progesterone are linked to the development and progression of hormone receptor-positive breast cancer through their effects on breast cells. Understanding these hormonal mechanisms has helped guide the development of targeted treatments. However, because breast cancer is a multifactorial disease, further understanding of hormonal and other biological influences is important for improving treatment outcomes.

Recommendations

Based on current scientific evidence, several recommendations can be made to reduce breast cancer risk and improve early detection. Regular physical activity, maintaining a healthy body weight, and following a balanced diet rich in vegetables, fruits, and whole grains may contribute to reducing risk. Avoiding alcohol is also recommended because alcohol consumption is an established risk factor for breast cancer.

Public health awareness programs should educate women about breast cancer risk factors, warning signs, and the importance of seeking medical advice when unusual breast changes occur. Breastfeeding should be supported when possible, as it is associated with a lower risk of breast cancer.

Furthermore, healthcare systems should promote appropriate breast cancer screening according to age and individual risk. Women with a strong family history or known inherited genetic risk should receive individualized medical assessment. Mammography is an important tool for early detection, but it does not prevent breast cancer from developing.

Finally, further research into hormonal mechanisms, genetic susceptibility, and environmental influences is needed to improve prevention strategies and develop more effective approaches to reducing breast cancer incidence and mortality.

References

1. Anderson E. The role of oestrogen and progesterone receptors in human mammary development and tumorigenesis. *Breast Cancer Research*. 2002;4(5):197–201. Doi:10.1186/bcr452. PMID:12223124.
2. Lange CA, Yee D. Progesterone and breast cancer. *Breast Cancer Research*. 2008;4(2):151–162. Doi:10.2217/17455057.4.2.151. PMID:19072517.
3. Trabert B, Sherman ME, Kannan N, Stanczyk FZ. Progesterone and breast cancer. *Endocrine Reviews*. 2020;41(2):320–344. Doi:10.1210/endrev/bnz001. PMID:31512725.

- 4. Jeselsohn R, Buchwalter G, De Angelis C, Brown M, Schiff R. ESR1 mutations—a mechanism for acquired endocrine resistance in breast cancer. *Nature Reviews Clinical Oncology*. 2015;12(10):573–583. Doi:10.1038/nrclinonc.2015.117. PMID:26122181.**
- 5. Dustin D, Gu G, Fuqua SAW. ESR1 mutations in breast cancer. *Cancer*. 2019;125(21):3714–3728. Doi:10.1002/cncr.32345. PMID:31318440.**
- 6. Brett JO, Spring LM, Bardia A, Wander SA. ESR1 mutation as an emerging clinical biomarker in metastatic hormone receptor-positive breast cancer. *Breast Cancer Research*. 2021;23(1):85. Doi:10.1186/s13058-021-01462-3. PMID:34392831.**
- 7. American Cancer Society. Breast Cancer Hormone Receptor Status. American Cancer Society.**
- 8. National Cancer Institute. Breast Cancer Biomarker Tests. National Cancer Institute, National Institutes of Health.**