

# Estrogen and Other Hormones and Factors Receptor Status

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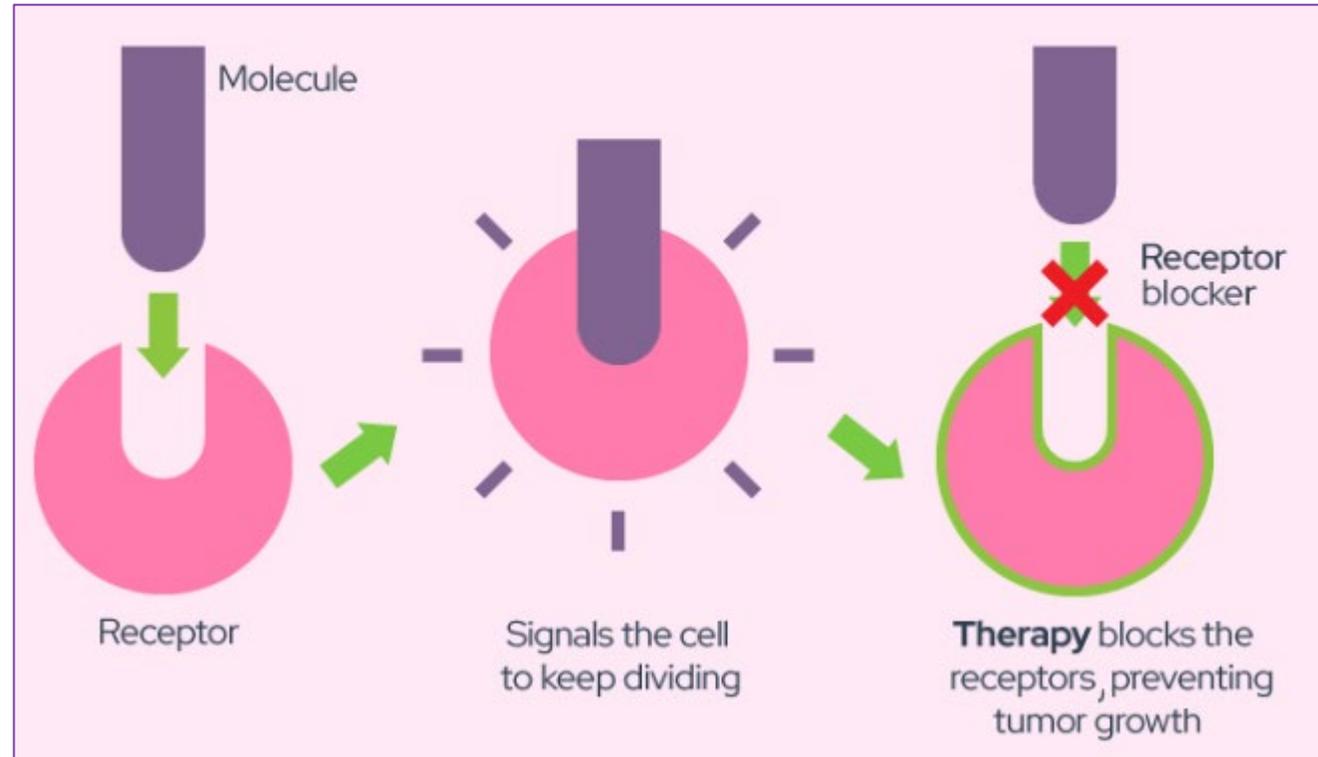
# Clinical Biomarkers in Breast Cancer

- Clinical biomarkers are major factors in workup and treatment of breast cancer
- There are three key biomarkers for breast cancer:
  - ① estrogen receptor (ER)
  - ② progesterone receptor (PR)
  - ③ human epidermal growth factor receptor (HER2)
- The biomarkers can be positive + or negative –



# Receptor Basics

- Receptors are proteins, typically found on a cell surface
- A specific molecule, eg, a hormone, can bind with the receptor
- In cancer, binding signals the cell to keep dividing



- Treatment with a receptor blocker prevents continued cell division

# Estrogen and Progesterone Receptors

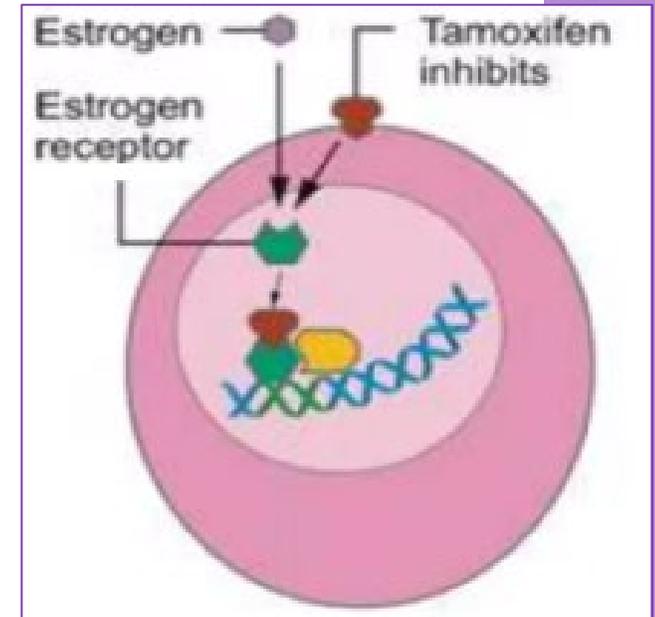
Estrogen and progesterone are hormones. Breast cancer treatment options vary by receptor status.

## Hormone receptor positive [ER+, PR+] [HR+]

- Hormone/endocrine therapy can be effective, via several mechanisms:
  - ✓ block the hormone receptor, eg, tamoxifen
  - ✓ reduce the hormone level, eg, aromatase inhibitors
  - ✓ degrade the hormone receptor, eg, fulvestrant

## Hormone receptor negative [ER-, PR-] [HR-]

- Hormone/endocrine therapy is rarely effective when hormone receptor status is negative



# HER2

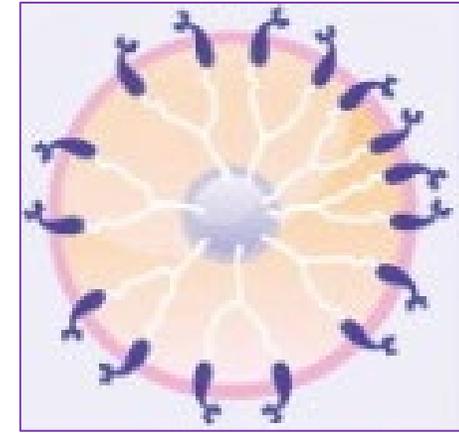
Human epidermal growth factor 2 receptor is a protein normally found on breast cells and is involved with normal cell growth.

## HER2 positive [HER2+]

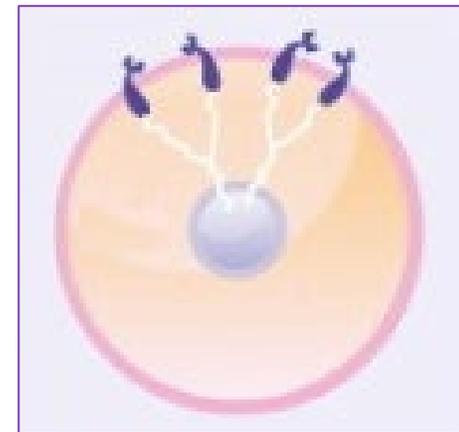
- HER2 can become overexpressed and then behave aggressively
  - ✓ certain drugs target the HER2 protein, eg, trastuzumab (Herceptin)

## HER2 negative [HER2-]

- These drugs are generally ineffective when HER2 is not overexpressed



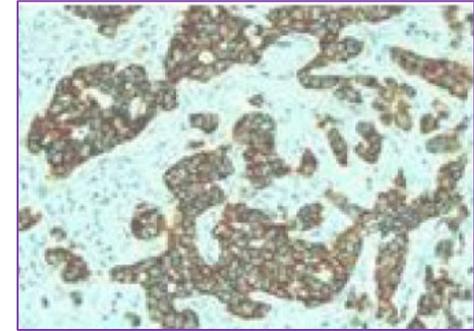
HER2+



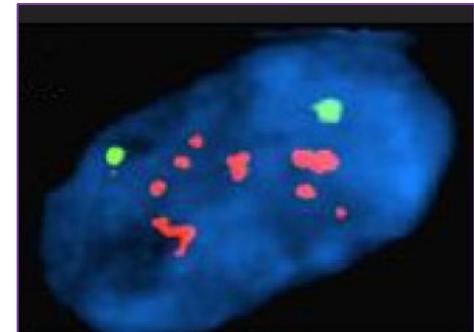
HER2-

# Breast Cancer Diagnosis

- Standard of care is to examine excised breast tissue (biopsy, other surgery) for the status of all three receptors
  - ✓ immunohistochemistry (IHC) staining
  - ✓ fluorescence in situ hybridization (FISH)
- Each receptor is identified separately on pathological reports
- The status for each receptor is independent of the receptor status for the others



IHC staining



FISH

# Impact of Receptor Status

ER, PR, and HER2 status determine the management of breast cancer to a significant extent.

- All three are key factors in medical decision-making related to:
  - ✓ deciding which treatment options to pursue
  - ✓ predicting treatment response
  - ✓ anticipating the course of the breast cancer
  - ✓ determining the overall prognosis
- Both the American Joint Committee on Cancer (AJCC) and the National Comprehensive Cancer Network (NCCN) recognize the importance of all three biomarkers in cancer staging and therapy

# Documentation of Receptor Status

- Receptor status is routinely provided in pathology reports with each receptor identified separately:
  - ✓ ER+ / ER-      ✓ PR+ / PR-      ✓ HER2+ / HER2-
- In office and clinic notes, physicians may also document receptor status individually
- Alternately, physicians may generically document Hormone Receptor [HR] status to refer to the *combined* status of ER and PR
  - ➡ If ER *and/or* PR is positive, this may be documented as **HR+**
  - ➡ If *both* ER *and* PR are negative, this may be documented as **HR-**
- ✓ HER2 is then usually documented separately

# Triple Negative Breast Cancer

- When all three receptors are negative (ER– , PR– , HER2–), physicians usually document this as either “triple negative breast cancer” or “TNBC”
- Triple negative breast cancer accounts for about 10-20% of all breast cancers and has several unfortunate distinctions:
  - ✓ more common in younger women under 40
  - ✓ typically found in Black and Hispanic women
  - ✓ also more common in women with BRCA1 mutation
  - ✓ rate of occurrence in Black women is almost three times higher than in white women



# Triple Negative Breast Cancer

- Triple negative breast cancer is very aggressive
- Because it is receptor negative, treatment options are limited
- Chemotherapy is the mainstay of TNBC treatment
- It is also more likely to recur after treatment
- Prognosis is generally poor with a 5 year survival rate of about 25% in the US
- Black women in particular have a worse prognosis with significantly higher mortality

Negative (ER-)

Negative (PR-)

Negative (HER2-)

# Data Issues

- It is essential to identify ER, PR, and HER2 status in national databases
- This will provide a more complete picture of breast cancer for:
  - ✓ breast cancer research
  - ✓ longitudinal data analysis
  - ✓ identification of the relationship with clinical outcomes
- It will also specifically enable further insight into triple negative breast cancer

# **Estrogen and Other Hormones and Factors Receptor Status**

## **Clinical Questions?**