International Journal of Pharmaceutical Sciences and Drug Analysis

E-ISSN: 2788-9254
P-ISSN: 2788-9246
IJPSDA 2023; 3(1): 94-97
www.pharmacyjournal.info
Received: 01-11-2022
Accepted: 05-12-2022

Dr. Jagannath Patro V
Principal and Professor,
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

E Sheela
Assistant Professor,
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

Mamilla Srinavya
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

Adepu Jyothika
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

Manda Sailaja
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

Correspondence
Dr. Jagannath Patro V
Principal and Professor,
Department of Pharmacology,
Browns College of Pharmacy,
Khammam, Telangana, India

A review on pathophysiology of breast cancer

Dr. Jagannath Patro V, E Sheela, Mamilla Srinavya, Adepu Jyothika and Manda Sailaja

Abstract
In the majority of countries around the globe, breast cancer is the most commonly identified malignancy among women. Breast cancer develops due to DNA damage and genetic mutations that can be influenced by exposure to estrogen some times there will be an inheritance of DNA defects or pro-cancerous genes like BRCA1 and BRCA2. Breast cancer is a heterogenous disease with diverse, molecular, genetic, phenotypic and pathological changes. Many models of breast carcinogenesis have been suggested and phenotypic plasticity is exemplified by a distinctive phenotype called Epithelial-to-mesenchymal transition [EMT]. EMT programs may revert through mesenchymal-epithelial [MET] to the pervious phenotypic state before the induction of EMT program. The cells are protected from programmed cell death by different path ways like P13K/AKT pathway and another is RAS/MEK/ERK pathway.

Keywords: Breast cancer, estrogen, phenotypic plasticity, EMT and MET programs

Introduction
Breast cancer is cancer that starts in cells in the breast. The ducts and the lobules are the two parts of the breast where cancer is most likely to start. Breast cancer is one of the most common types of cancer in the U.S. Healthcare providers don't yet know exactly what causes it. Once breast cancer forms, cancer cells can spread to other parts of the body (metastasize), making it life-threatening. The good news is that breast cancer is often found early, when it's small and before it has spread. It is the second most common cause of death from cancer among women in the world. Breast cancer can also occur in males but not as common as in females.

Risk factors
- Age
- Family history
- Over weight
- Dense breast
- Smoking and drinking alcohol

Signs and symptoms
- New lump in the breast or underarm (armpit).
- Thickening or swelling of part of the breast.
- Pulling in of the nipple or pain in the nipple area.
- Nipple discharge other than breast milk, including blood.
- Any change in the size or the shape of the breast.
- Pain in any area of the breast.

Pathophysiology
Breast cancer is a malignant tumor that starts in the cells of the breast. Like other cancers, there are several factors that can raise the risk of getting breast cancer. Damage to the DNA and genetic mutations can lead to breast cancer have been experimentally linked to estrogen exposure. Some individuals inherit defects in the DNA and genes like the BRCA1, BRCA2 and P53 among others. Those with a family history of ovarian or breast cancer thus are at an increased risk of breast cancer. The immune system normally seeks out cancer cells and cells with damaged DNA and destroys them. Breast cancer may be a result of failure of such an effective immune defence and surveillance.

Breast cancer is a heterogeneous disease with diverse, molecular, genetic, phenotypic, and pathologic changes. Tumor heterogeneity results from the genetic, epigenetic, and microenvironmental influences (selective pressure) that tumor cells undergo during cancer progression. Cellular subpopulations from different sections of the same tumor vary in many ways including growth rate, immunogenicity, ability to metastasize, and drug response, demonstrating significant heterogeneity. The biological attributes of a tumor as a whole are strongly influenced by its subpopulation of cells with cellular populations communicating through paracrine or contact-dependent signaling (juxtacrine) from ligands and mediated from components of the microenvironment such as blood vessels, immune cells, and fibroblasts.

Normal cells divide as many times as needed and stop; they attach to other cells and stay in place in tissues. Cells become cancerous when mutations destroy their ability to stop dividing, to attach to other cells, and to stay where they belong. Normal cells will commit cell suicide (apoptosis) when they are no longer needed. Until then, they are protected from cell suicide by several protein clusters and pathways.

One of the protective pathways is the PI3K/AKT pathway; another one is the RAS/MEK/ERK pathway. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of committing suicide when it is no longer needed. This is one of the steps that cause cancer in combination with other mutations. Normally, the PTEN protein turns off the PI3K/AKT pathway when the cell is ready for cell suicide. In some breast cancers, the gene for the PTEN protein is mutated, so the PI3K/AKT pathway is stuck in the "on" position, and the cancer cell does not commit suicide. Mutations that can lead to breast cancer have been experimentally linked to estrogen exposure and failure of immune surveillance, the removal of malignant cells throughout one's life by the immune system. Abnormal growth factor signaling in the interaction between stromal cells and epithelial cells can facilitate malignant cell growth. In breast adipose tissue, overexpression of leptin leads to increased cell proliferation and The familial tendency to develop these cancers is called hereditary breast—ovarian cancer syndrome.

The best known of these, the BRCA mutations, confer a lifetime risk of breast cancer of between 60 and 85%. Some mutations associated with cancer, such as p53, BRCA1 and BRCA2, occur in mechanisms to correct errors in DNA. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which lead to uncontrolled division, lack of attachment, and metastasis to distant organs.

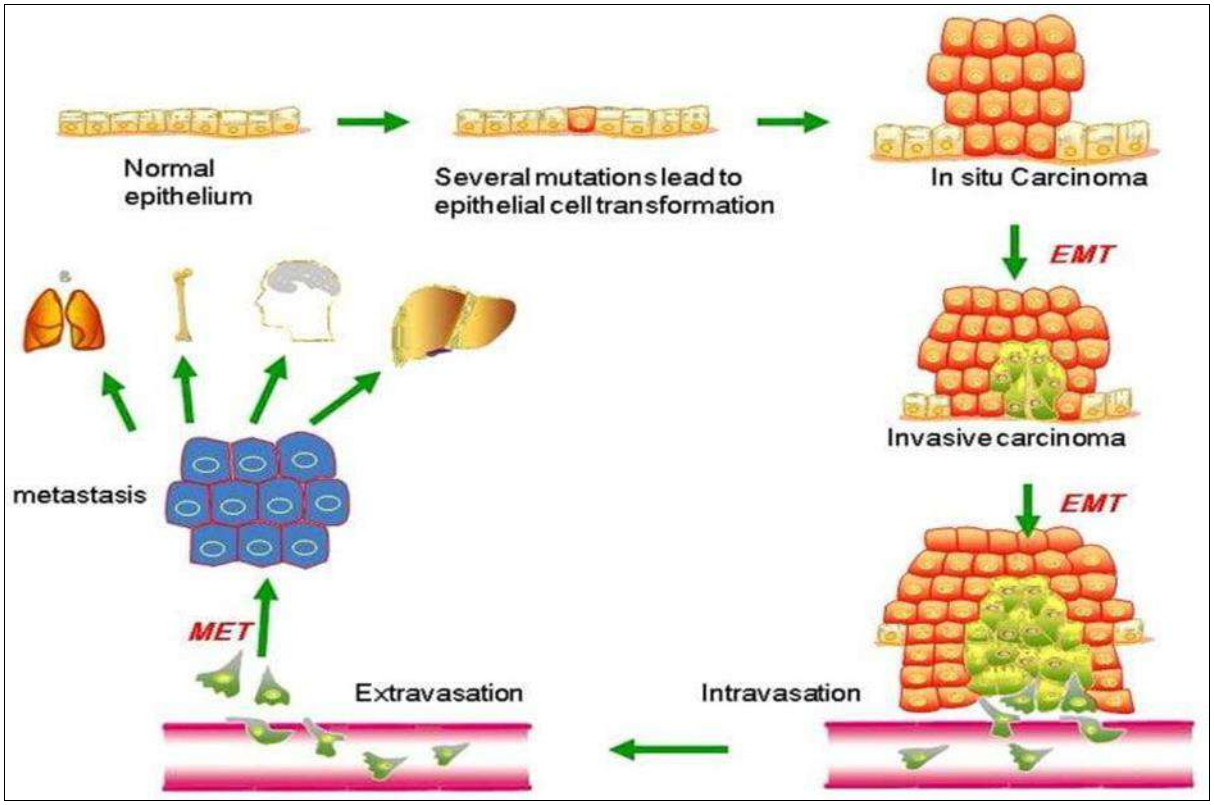
However, there is strong evidence of residual risk variation that goes well beyond hereditary BRCA gene mutations between carrier families; this is caused by unobserved risk factors. It implicates that environmental factors and other causes are triggers for breast cancer. The inherited mutation in BRCA1 or BRCA2 genes can interfere with repair of DNA cross links and DNA double strand breaks (known functions of the encoded protein). Because of this repair deficit, risks from carcinogenic chemicals and ionizing radiation can increase.

These carcinogens cause DNA damage, such as to DNA cross links and double strand breaks that often require repairs by pathways containing BRCA1 and BRCA2. But it is these repair pathways that can be crippled by inherited mutation. There is evidence that cancer risks increase in mutation carriers exposed to such opportunistic carcinogens. Thus, risks for cancers may be reduced by avoiding or compensating for carcinogens that exploit the inherited BRCA gene deficiency However, mutations in BRCA genes account for only 2 to 3% of all breast cancers.

Gene expression profiling studies have identified major subtypes classified as luminal A, luminal B, HER2+, basal-like, Claudin-low, and normal breast. These subtypes have different prognoses and responses to therapy. Tumours can be stratified with gene expression profiles such as Oncotype Dx, Prosigna, and MammaPrint on the basis of genetic profiles. This information helps personalize breast cancer treatment and determine which women need aggressive systemic treatment for high-risk cancers versus close surveillance for indolent tumours. Breast cancer syndromes involve unknown genes.

Many models of breast carcinogenesis have been suggested and the expanding themes include (1) gene addiction, (2) phenotype plasticity, (3) cancer stem cells, (4) hormonal outcomes affecting cell turnover of mammary epithelium, stem cells, extracellular matrix, and immune function.

Phenotypic plasticity is exemplified by a distinctive phenotype called epithelial-to- mesenchymal transition (EMT). EMT is involved in the generation of tissues and organs during embryogenesis, is essential for driving tissue plasticity during development, andis hijacked during cancer progression. The EMT-associated programming is involved in many cancer cell characteristics, including suppression of cell death or apoptosis and senescence. It is reactivated during wound healing and is resistant to chemotherapy and radiation therapy. Re modeling or reprogramming of the breast during post- pregnancy involution is important because it involves inflammatory and “wound healing-like” tissue reactions known as reactive stroma or inflammatory stroma. The reactive stroma releases various signals and interleukins that affect nearby carcinoma cells, inducing these cells to activate their previously silent EMT programs. The activation is typically reversible (i.e., plasticity), and those EMT programs may revert through mesenchymal-epithelial (MET) to the previous phenotypic state before the induction of the EMT program. Reactive stroma increases the risk for tumour invasion and may facilitate the transition of carcinoma in situ to invasive carcinoma. Activation of an EMT program during cancer development often requires signalling between cancer cells and neighbouring stromal cells. In advanced primary carcinomas, cancer cells recruit a variety of cell types into the surrounding stroma. Overall, increasing evidence suggests that interactions of cancer cells with adjacent tumour-associated stromal cells induce malignant phenotypes.



Putative EMT and MET in breast cancer progression

Staging: Once your doctor has diagnosed your breast cancer, he or she works to establish the extent (stage) of your cancer. Your cancer's stage helps determine your prognosis and the best treatment options. Complete information about your cancer's stage may not be available until after you undergo breast cancer surgery. Tests and procedures used to stage breast cancer may include: Blood tests, such as a complete blood count

- Mammogram of the other breast to look for signs of cancer
- Breast MRI
- Bone scan
- Computerized tomography (CT) scan
- Positron emission tomography (PET) scan

Diagnosis

- **Breast ultrasound:** A machine that uses sound waves to make pictures, called sonograms, of areas inside the breast.
- **Diagnostic mammogram:** If you have a problem in your breast, such as lumps, or if an area of the breast looks abnormal on a screening mammogram, doctors may have you get a diagnostic mammogram. This is a more detailed X-ray of the breast.
- **Breast magnetic resonance imaging (MRI):** A kind of body scan that uses a magnet linked to a computer. The MRI scan will make detailed pictures of areas inside the breast.
- **Biopsy:** This is a test that removes tissue or fluid from the breast to be looked at under a microscope and do more testing. There are different kinds of biopsies (for example, fine-needle aspiration, core biopsy, or open biopsy).

Treatment

- **Surgery:** An operation where doctors cut out cancer tissue.
- **Chemotherapy:** Using special medicines to shrink or kill the cancer cells. The drugs can be pills you take or medicines given in your veins, or sometimes both.
- **Hormonal therapy:** Blocks cancer cells from getting the hormones they need to grow.
- **Biological therapy:** Works with your body's immune system to help it fight cancer cells or to control side effects from other cancer treatments.
- **Radiation therapy:** Using high-energy rays (similar to X-rays) to kill the cancer cells.

Prevention

- Try to maintain healthy weight and avoid weight gain
- Eat less meat
- Eat more fruits and vegetables
- Limit alcoholQuit smoking
- Exercise
- Breast feed, if possible
- Evaluate your hormone use
- Know your family history

Conclusion

In summary breast cancer is one of the leading and exponentially advancing cancers worldwide. The pathophysiology of breast cancer includes the physical and hormonal changes associated with cancer and paraneoplastic syndrome its main goal is to cure breast cancer patients or prolong their life considerably ensuring a good quality of life. The patient should go for a check up at least every three years to prevent getting breast cancer on any other cancer. Breast cancer can spread more quickly if left and not cared about resulting to death. Hence diagnosis and treatment at early stages is beneficial for curing at early stages.

References

1. https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=8 5&contentid=p09506
2. https://www.cancer.net/cancer-types/breast-cancer/introduction
3. https://www.breastcancer.org/risk/risk-factors
4. https://www.cdc.gov/cancer/breast/basic_info/symptoms.htm
5. www.cancer.org/acs/groups/cid/documents/webcontent/003090-pdf.pdf
6. http://www.biomedcentral.com/content/pdf/bcr10.pdf
7. https://www.news-medical.net/amp/health/Breast-Cancer- Pathophysiology.aspx
8. https://u.osu.edu/breastcancercasestudy2019/pathophysiology-description/
9. https://www.wikidoc.org/index.php/Breast_cancer_pathophysiology
10. https://www.mayoclinic.org/diseases-conditions/breast-cancer/diagnosis- treatment/drc-20352475
11. https://www.cdc.gov/cancer/breast/basic_info/diagnosis.htm
12. https://www.cdc.gov/cancer/breast/basic_info/treatment.htm
13. https://www.bcrf.org/blog/breast-cancer-prevention-breast-cancer-risk- reduction/
14. Farvid MS, Eliassen AH, Cho E, Liao X, Chen WY, Willett WC. Dietary Fiber Intake in Young Adults and Breast Cancer Risk. Pediatrics; c2016, 137(3). https://doi.org/10.1542/peds.2015-1226
15. What Can I Do to Reduce My Risk of Breast Cancer? (2020, September 14). Centers for Disease Control and Prevention. Retrieved March 1, 2022, from https://www.cdc.gov/cancer/breast/basic_info/prevention.htm