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Biomarkers: An Important Tool for Diagnosing and Treating Breast Cancer

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Authors' contributions

This work was carried out in collaboration among all authors. Author Anil Sharma wrote the first draft of the manuscript. Author TC did the conceptualization, design the study, reviewing and editing. Author SG reviewed the study. Authors Abhishek Sharma and PKP managed the literature searches. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Breast cancer is a type of tumor in which individual cases deviate from each other in morphology, protein expression, molecular phenotype, genetic characteristics, and prognosis. Worldwide, breast cancer is the most-common invasive cancer in women. A patient with breast cancer may have the following symptoms:- lumps, skin dimples, nipple discharge, nipple height, nipple withdrawal, pain and burning sensation. There are many causes and risks of breast cancer, including family history (heriditary), obesity, active smoking, early and late childbearing, breast feeding for less than two weeks, exposure to estrogen and oral contraceptive pills. Most breast cancers are diagnosed through estrogen receptor (ER) -positive determination and rely on estrogen for cell growth and survival. Breast cancer treatment has encountered a few progressions in the previous decades with the revelation of explicit prescient prognostic biomarkers that make conceivable the use of individualized treatments. Blocking estrogen biosynthesis by aromatase inhibitors (AI) has, subsequently, become a first-line endocrine treatment for menopausal ladies with ER-positive breast disease. Various conventional diagnosing and treating methods of breast cancer is available

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but there have limitation of accuracy and treating. For that reason now a day's various biomarkers like Molecule or Biochemical biomarkers like Estrogen receptor, Progesterone receptor, human epidermal growth factor receptor 2 (HER2), human Mammaglobin (H-MAM), Osteopontin, Fibroblast Growth Factor Receptor 2 (FGFR2), Phosphatase and tensin homolog (PTEN), Physiologic Biomarkers like Carcinoma Antigen 15-3(CA 15–3), Cancer Antigen 125 (CA 125), Prostate specific antigen (PSA) and Anatomic Biomarkers Oncotype Dx, and Cystic fibrosis Trans-membrane conductance regulator (CFTR). These biomarkers are of great importance in the evaluation and diagnosis process, which leads to better patient's care and protection of the patients. Due to its various advantages, biomarkers are considered as an innovative tool in the progression of breast cancer diagnosis and treatment.

Keywords: Breast cancer; breast tumor; biomarkers; BRCA1; BRCA2.

1. INTRODUCTION

Breast cancer is a heterogeneous disease in which the individual cases deviate from each other in morphology, protein expression, molecular phenotype, genetic characteristics and prognosis [1]. Breast cancer depend on the different type of gene syndrome like {BRCA1, BRCA2}, PALB2, CHEK2, PTEN, TP53, STK11, BRIT1. On the basis of tumor size, inflammation and the position of the tumor it can be classified in different stages of breast cancer like T1a > 0.5 cm ,T1b > 1 cm, T1c >2 cm, T2 2-5 cm, T3 > 5 cm tumor size, T4d inflammatory carcinoma, Tis ductal carcinoma and lobular carcinoma [1,2]. Patient with breast cancer may have following symptoms i.e. lump, skin dimpling, nipple discharge, nipple elevation, nipple retraction, pain and burning sensation [3,4]. There are many causes and risk factors of breast cancer, these are family history (hereditary, genetic), obesity, active smoker, early period and late child bearing, breast feed for less than two weeks, exposure to estrogen and oral contraceptive pills. Most breast cancers are diagnosed by determining estrogen receptor (ER)-positive and cells depend on estrogen for growth and survival [5,6]. Various conventional diagnosing and treating methods of breast cancer is available but there have limitation of accuracy and treating [7]. For that reason now a day's various biomarkers are using for the diagnosis of breast cancer like Molecule or Biochemical biomarkers like Estrogen receptor, Progesterone receptor, HER2, H-MAM, Osteopontin, FGFR2, PTEN; Physiologic Biomarkers like CA 15–3, CA 125, PSA, and Anatomic Biomarkers Oncotype Dx, CFTR [8]. These biomarkers are of great importance in the evaluation and diagnosis process which leads to better patient's care and protection of the patients [9]. Due to their various advantages, biomarkers are considered as an important tool in the progression of breast cancer diagnosis and treatment.

2. BIOMARKERS

A biomarker is a substance that is used as an indicator of disease status and a feature that is anticipated and evaluated for general, pathological, and pharmacologic responses to therapeutic intervention [1]. World Health Organization (WHO) and in coordination with the United Nations and the International Labor Organization, has described a biomarker as detecting measure of the biological situation. The biomarker is used for frequently detected and estimated the normal as well as abnormal biological activities, bacterial activity viral activity or/and medicinal intervention [10].

Breast cancer biomarkers are of four types:

- Molecule or Biochemical biomarkers,
- Physiologic Biomarkers,
- Anatomic Biomarkers,
- Specific Biomarkers.

3. MOLECULE OR BIOCHEMICAL BIOMARKERS:- [11]

The molecule or biochemical markers are organic atoms found in body liquid or tissues. In disease, sub-atomic biomarkers are frequently qualities items. This is a protein made by prostate cells. Molecular biomarkers are not extensive cramped to a point restricted to a particle. Rather, they may comprise of a board of various biochemical substances that together fill in as a biochemical mark.

Examples [11]

- Estrogen receptor [12],
- Progesterone receptor [13],
- HER2 [14].

3.1 Name: Estrogen Receptor (ER)

Year of discovery: 1996 [15].

3.1.1 Mechanism of action

The estrogen receptor is similar to other steroid receptors. Agonist irrevocable to the ligand-irrevocable area achieves receptor dimerization and its association with "Estrogen Response Element. Gene interpretation is advanced through certain co-activator proteins. On restricting an estrogen rival the receptor expect an alternate adaptation and cooperates with other co-repressor proteins hindering gene reproduction [16].

3.1.2 Function

Estrogen empowers the accompanying organs to work. The body utilizes estrogen in the arrangement of breast tissue. This hormone likewise helps stop the progression of milk flow subsequent to weaning [17]. Particular estrogen receptor modulators (SERMs) offer post-menopausal ladies a significant number of the benefits of estrogen substitution [18].

3.1.3 Limitations

Partial estrogenic agonistic activity.

3.2 Name: The Progesterone Receptor (PR)

Year of discovery: 1929 [19].

3.2.1 Mechanism of action

Where the drug obstructs the site of Progesterone hormone.There is no sign for cell extension [20].

3.2.2 Function

The diverse is very effective in key areas of public health, including emergency contraception. This is a Long phase without estrogen contraception and endometriosis and myoma is a treatment [21]. In hormonal anti-conception medication and the menopausal hormone is a treatment. In gynecological conditions, to help fruitfulness and pregnancy, to bring down sex hormone is a treatment [21].

3.2.3 Limitations

That limitations are nausea, menstrual irregularities, breast tenderness, and headaches [22].

3.3 Name: Human Epidermal Growth Factor Receptor (HER2)

Year of discovery: 1987 [23].

3.3.1 Mechanism of action

A receptor tyrosine kinase plays a significant in tumor cell endurance. Phosphorylated EGFR upon initiation causes phosphorylation of downstream proteins that lead to changes in cell multiplication, attack, metastasis, and hindrance of apoptosis [24].

3.3.2 Function

These applications are- MRI, PET and SPECT, Nuclear medicine imaging, Multimodal imaging, Optical imaging [25]. DNA is truly steady, that is the reason it is impressively less in tissues contrasted and protein and mRNA.

3.3.3 Limitations

This is much time taken and requires a lot of DNA [26].

4. PHYSIOLOGIC BIOMARKERS

Physiologic biomarkers are those that have to do with the practical procedures in the body. For instance, blood stream in cerebrum zones influenced by stroke is being researched as an expected marker of treatment achievement. As imaging procedures become further developed, we are probably to see an expansion in the examination and utilization of physiologic biomarkers [10].

Examples

- CA 15–3,
- CA 125,
- PSA.

4.1 Name: Carcinoma Antigen 15-3 (CA 15–3)

Year of discovery: 1981 [27].

4.1.1 Mechanism of action

CA 15-3 has a place with the MUC1 family. In spite of the fact that the MUC1 quality is found in a few tissues, clearly manufacture an indistinguishable center protein. The variety in the degree of glycosylation (CO_2 content) is the

distinctive element between various tissue sources. In breast tissue, the CO_2 content is around 50% [28]. The exact physiological functions of MUC1 proteins are not completely known, but it appears to reduce cell-to-cell interaction and may also inhibit tumor cell [29].

4.1.2 Function

CA 15-3 amount in the blood can be utilized for screening, for breast cancer as well as for Pancreatic, lung, ovarian, colon and liver cancer, including other tumors [30]. It is Simple and modest to gauge mechanized examines accessible.

4.1.3 Limitations

That limitations are less delicate and specificity [31].

4.2 Name: Cancer Antigen125 (CA 125)

Year of discovery: 1981 [32].

4.2.1 Mechanism of action

It is too much glycosylated it makes hydrophilic environs that work about as a greasing up boundary against remote particles and irresistible specialists on the apical film of epithelial cells [32].

4.2.2 Function

That antigen applications are diagnosis, monitoring therapy, detecting recurrence and prognosis [33]. It is Simple and modest to gauge mechanized examines accessible.

4.2.3 Limitations

It is less delicate and specificity.

4.3 Name: Prostate Specific Antigen (PSA)

Year of discovery: 1970 [34].

4.3.1 Mechanism of action

The physiological capacity of KLK3 is the disintegration of the coagulum, the sperm capturing that gel is made of semenogelin and fibronectin [35]. Its proteolytic activity is compelled in melting the coagulum with which the goal that the sperm can be freed. Its applications are screening, diagnosis**,** and monitoring [36].

4.3.2 Function

Generally used to improve the tumor growth carefulness of Prostate Specific Antigen (PSA) particularly in men with PSA esteems [37].

4.3.3 Limitations

PSA esteems just decide in the 'grey area [37].

5. ANATOMIC BIOMARKERS

Anatomic biomarkers are those that have to do with the structure of a life form and the connection of its parts. Anatomic biomarkers involve the structure of different organs, for example, the brain or liver. The size of certain mind structures according to each other is a biomarker for a disorder known as Huntington disease. The anatomic biomarker are likewise being encouraged by the improvement of imaging strategies [10].

Examples

a) Oncotype Dx,
b) CFTR [38].

5.1 Name: Oncotype Dx.

Year of discovery: 2007 [39].

5.1.1 Mechanism of action

Decide the recurrence risk (RR) in patients with estrogen receptor-positive (ER+) and lymph hub negative (LN−) cancer [40].

5.1.2 Function

Radiology, imaging [41]. The advantage of getting chemotherapy notwithstanding hormone treatment [42].

5.1.3 Limitations

That limitations are less delicate and specificity [41].

5.2 Name: Cystic Fibrosis Trans-membrane Conductance Regulator (CFTR)

Year of discovery: 1989 [43].

5.2.1 Mechanism

Ties to the inadequate protein at the cell surface and opens the chloride channel (holds the door open) with the goal that chloride can move through, managing the measure of liquids at the outside of the cell [44].

5.2.2 Function

The CFTR gene provides guidance for the production of a protein called cystic fibrosis transmembrane conductor regulator. This protein acts as a channel across the cell membrane that produces mucus, sweat, saliva, tears and digestive enzymes [45].

5.2.3 Limitations

Adequacy of the pancreas with mild pulmonary disease, borderline or normal sweating test [46].

6. SPECIFIC BIOMARKERS

Specific biomarkers that have been specifically identified and repeatedly shown to accurately predict relevant clinical outcomes across different treatments and populations, this use is entirely justified and appropriate. However in many cases the “legitimacy” of the biomarkers is assumed where in practice it should continue to be assessed [47].

Examples

a) H-MAM,
b) Osteopontin,
c) FGFR2,
d) PTEN.

6.1 Name: Human-mamma Globin (h-MAM) [47].

Year of discovery: 1966.

6.1.1 Mechanism

Mamma globin shows a little helical globular area and a hydrophobic pocket in its structure; consequently, encouraging official to steroid and biphenyl-like particles. One 90 AA protein isoform created by the loss of 9 BP through elective joining at the second quality exon [48].

6.1.2 Function

Its applications are physical assessment or ultrasound. Atomic tests in quality groupings and articulation with respect to a specific particle [48]. Breast cancer growth cells didn't communicate consistently the mamma globin since its appearance ranges among changed subtypes of tumors. The positive articulation pace of mamma globin biomarker was seen in 69% of breast cancer patients [49].

6.1.3 Limitations

ER-negative and high-grade tumors express lower quantities of mamma globin mRNA particles each cell [49].

6.2 Name: Osteopontin

Year of discovery: 1979 [50].

6.2.1 Mechanism

A phosphorylated glycoprotein that ties integrin and works as a middle person of cell grip, movement, insusceptible reactions, and tissue repair [51,52].

6.2.2 Function

That applications are therapeutic targeting for glioblastoma, radiotherapy [52]. A movement of peripheral blood mononuclear cells (PBMC) articulation is closer to breastfed profiles. It conveys insusceptible security like human milk. Decreases periods of fever [53].

6.2.3 Limitations

Its recurrence rate is high [53].

6.3 Name: Fibroblast Growth Factor Receptor 2 (FGFR2)

Year of discovery: 1998 [54].

6.3.1 Mechanism

ATP serious atoms official to the cytoplasmic kinase space and either restrain the reactant action of FGFRs or the auto-phosphorylation of tyrosine buildups [55,56].

6.3.2 Function

FGFR2 inhibitors for malignancy treatment in patients with FGFR2 transformation or quality enhancement is gainful [57]. FGFR2 articulation is expanded in tissues and associated with tumor action [58].

6.3.3 Limitations

FGFR2 cancer cells are that FGFR2 capacities as an endurance factor and FGFR2 cancer cells are hence disposed of by cell demise during mammary branching [58].

6.4 Name: Phosphatase and Tensin Homolog (PTEN) [59,60]

Year of discovery: 1997 [59].

6.4.1 Mechanism

Phosphatase and tensin homolog (PTEN) assumes a role in the phosphatidyl-inositol-3-kinase (PI3-K) pathway by catalyzing debasement of phosphatidylinositol-(3, 4, 5)-triphosphate created by PI3-K. This represses downstream targets most part protein kinase B (PKB/Akt), cell endurance and multiplication [60,61].

6.4.2 Function

Its applications are gene editing, mRNA targeting. It is helpful in regenerative medicine.

6.4.3 Limitations

It's a dose increaser [62].

7. CONCLUSION

Biomarker is a substance used as an indicator of disease status and a property that is expected and evaluated for general, pathological and pharmacological responses to therapeutic interventions. Various conventional methods of diagnosis and treatment of liver disease are available but there are limitations in accuracy and treatment. Thus, as a result of the above studies, it has been concluded that biomarkers play crucial role in the evaluation and diagnosis process which leads to better care and protection of patients. Due to its various advantages, biomarkers are considered as an important tool in the advancement of breast cancer diagnosis and treatment.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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