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Review Article

An Overview of a Biomarker in Breast Cancer

Gandraju Akhila, Nagashree AG, Asha Spandana KM, Hemanth Kumar S, Harshith HS, Vishnu Vardh R, Shailesh T*

Department of Pharmaceutics, JSS College of Pharmacy, Mysuru, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagar, Mysuru, Karnataka, INDIA.

ABSTRACT

Cancer is one of the leading causes of death across the world, which is caused by tumours. Breast Cancer (BC) is the most common cancer in women and the second most common cancer death in women. A variety of molecular biomarkers are being used to predict BC susceptibility, including hormone receptors for subtyping and several genes involved in genome maintenance. Hence, biomarkers have specific importance in translational and clinical development to improve diagnosis, prognosis, and treatment since they have advantages in detection time and energy efficiency. The impact of breast cancer, as well as BC risk factors, identification of high-risk groups, screening modalities, and guidelines for screening average-risk and high-risk individuals, therapy advancement using various types of biomarkers. This review describes the design, approval, and distribution of biomarkers and outlines the many types of biomarkers currently used in breast cancer.

Keywords: Breast Cancer, Biomarker, Receptors, Tumours.

Correspondence:
Dr. Shailesh T
Lecturer, Department of Pharmaceutics, JSS College of Pharmacy, JSS Academy of Higher Education and Research, SS Nagar, Mysuru-570015, Karnataka, INDIA.
Email: shailesht@jssuni.edu.in

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INTRODUCTION

Cancerous cells lack the components necessary to stop proliferating cancerous cells and cause cell death, so they persist in the body, absorbing oxygen and nutrients that might be utilised by diseased cells if not absorbed by other cells. Benign and malignant are the types of tumours observed, where benign tend to grow slowly and non-invasively, but malignant grow rapidly and are invasive to other parts of the body. Breast Cancer (BC) affects 2.3 million women worldwide, and it is noted that the death rate was 685,000 in 2020. According to a world-by-world study, BC has already been diagnosed in 7.8 million women in the last five years and will be the most common type of cancer by the end of 2020. Although cancer is found all over the world, its prevalence, fatality, and survival rates vary significantly between regions, which might be attributable to a variety of variables such as population structure, lifestyle, genetic factors, and environment. One of the issues associated with BC is early detection. Therefore, biomarkers are becoming increasingly important in identifying and treating individuals with various types of cancer, including breast cancer. These are especially helpful in identifying individuals at high risk for BC in high-risk families, determining the prognosis at initial diagnosis, and identifying the most appropriate systemic, post-operative, and advanced BC surveillance therapies gain. The purpose of this study is to provide a comprehensive overview of BC Biomarkers. In addition, the explanation of the BC biomarkers under development speculates that they can be used on a daily basis.

VARIOUS BC TYPES

Cancer is a collection of diseased cells involving defective genes that provide the persistent proliferating potential of somatic or germinal cells.[1] BC can occur in different areas of the breast, such as the ducts, lobules, and possibly the tissues in between. Various types of BC are shown in Figure 1.

The most common forms of BC are ductal carcinoma and lobular carcinoma. Breast cancer is an invasive BC, meaning cancer cells grow in other parts of the breast tissue outside the ducts. Infiltrative cancer cells can also metastasize or metastasize to other parts of the body. In invasive lobular cancer, cancer cells have spread from the lobule to the surrounding breast tissue. Therefore, invasive BC is the result of cancer cells spreading to other parts of the body, as shown in Figure 2.

BC is a diverse collection of tumours with different morphological and genetic subtypes, resulting in diverse biological activities, symptoms, and prognosis. Breast Tumor, nodules and metastases, treatments at the stage of cancer growth, such as Breast Tumor, nodules and metastases, treatments are based on patients who will benefit from the identified BC stage and specific cancer treatment will be identified.

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The Human Epidermal Growth Factor Receptor (HER), Progesterone Receptor (PR), Human Epidermal Growth Factor Receptor 2 (HER2), and Ki67 Proliferation Index are the most important and well-known hormonal molecular indicators associated with breast cancer. They are used in the clinical treatment of all patients with primary, relapsed, and metastatic breast cancer. The main symptoms are examined immunohistochemically with BC samples. Symptoms are important in the prognosis and management of BC patients because the information is used to inform treatment decisions and reliable tests.

What are Biomarkers?

Biomarkers are detectable biological events that indicate a physiological state. Biomolecules present in blood, other fluids, or tissues indicate that the process is in a healthy or ill state. Biomarkers can be used to determine the effectiveness of treatment when the body is reacting to cancer cells. Biomarkers are also known as signature molecules or molecular markers.

Recompenses of Biomarker in BC

Biomarkers can be employed for patient assessment in a variety of situations (Medical Scenarios), such as risk assessment, screening for occult primary tumours, and distinguishing the type of cancer. Prognosis and prediction for cancer patients, as well as disease status monitoring to detect recurrence or progression to therapy.

The biomarker has several methodologies to identify potential biomarkers. The traditional strategy is that biomarkers are selected based on the type of the tumour and its surroundings or the metabolism of the pharmacological drug.[2] With the increasing number of current cancer scenarios and the introduction of new technologies, biomarker-based identification will be performed using techniques such as high-throughput sequencing, gene expression arrays, and mass spectrometry to accurately identify cancers.[3] It is often developed as biomarkers and has led researchers to design biomarkers that eliminate bias, extensive testing, and validation.[4,5]

Steps in the development of a candidate biomarker have numerous hurdles that a potential biomarker must overcome before it can be applied, such as analytical validity, clinical validity, and clinical utility.[6]

Why biomarker is intended for breast cancer?

Cancer biomarkers include a variety of organisms, including nucleic acids, proteins, carbohydrates, lipids, micro metabolites, cytogenetic and cytokinetic properties, and whole tumor cells in body fluids.

A clear test of biomarkers is important because it is helpful in making an accurate diagnosis of the disease and also in selecting the various treatment strategies that are currently available that can help the patient.

TYPES OF BIOMARKERS

Risk Assessment biomarkers have also been associated with cancer genetic susceptibility and can predict the chances of BC in women. Proteins, gene mutations (changes), gene rearrangements, extra gene copies, defective genes, and other factors are examples of cancer biomarkers that health professionals say are designed for early detection of BC (Figure 3).

Detection/Screening Biomarkers are associated with the screening and detection of cancer and provide information on cancerous cells. In addition to the response to the presence of a tumor by producing antibodies, shedding serum proteins, circulating malignant cells, and nucleotide sequences into the circulation. The diagnostic biomarker is a biopsy method to identify breast cancer, biomarkers aid with determining the main

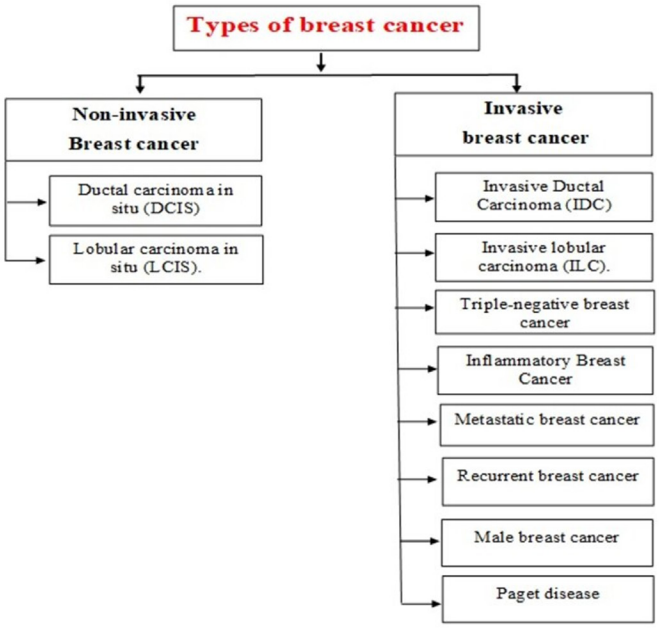

Figure 1: Types of Breast Cancer.

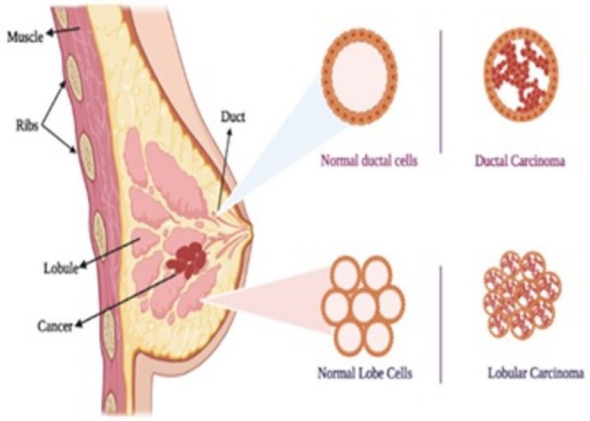

Figure 2: Ductal and Lobular carcinoma.

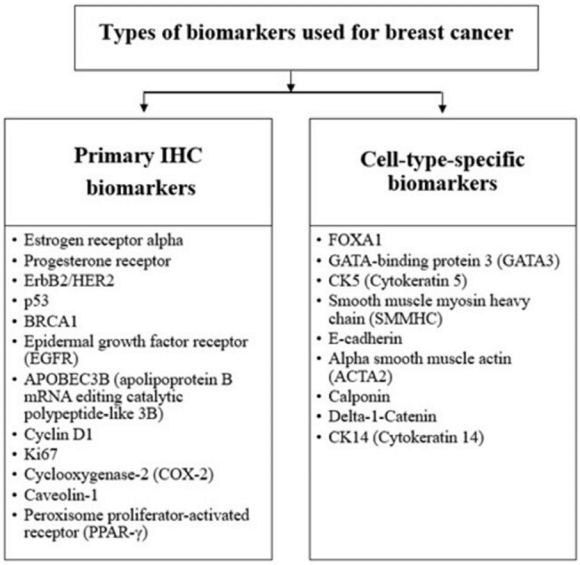

Figure 3: Types of biomarkers used for breast cancer.

origin of the tumor. Diagnose and prognosis biomarkers are measurable properties that assist clinical oncology scientists in their first encounter with a patient with suspected cancer.[7] Such as early diagnosing, selecting the appropriate treatment method, and tracking response to therapy.[8]

The prognostic biomarker is one that indicates progression or disease condition which predicts the upcoming clinical event of cancer.

Predicting Biomarkers can be used to forecast a patient's reaction to medicine or to determine the best dosage. The result predicts the severity or recovery of the patient to the therapy.

Monitoring biomarkers can be used to monitor the treatment progression, side effects, and recovery repeatedly. Key technologies such as the availability of complete human genome sequences, advanced high-throughput DNA sequencing, microarrays, mass spectrometry, and the excess of potentially beneficial cancer biomarkers are the sequences of DNA, RNA, proteins, and metabolites. and provides information about expression levels.[9]

Genetic Biochemical Methods provides precise and susceptible details about the genetic changes that were very beneficial in the recognition of tumours.[10]

For example, with enrichment (Biomarker-positive patients) and randomised controlled trials of pre-approved studies of tumour drugs approved by the United States Food and Drug Administration (USFDA) requiring pharmacological genomics biomarker testing, and with biomarker treatment-interaction The FDA's table contained 137 medicines, and 22 cancer treatments required genetic testing on labels selected from among them. These drugs have responded to 35 approvals backed by 80 clinical trials included in the FDA's medical officer efficacy assessment. All clinical trials were limited to biomarker-positive patients in two-thirds (24/35 or 69%) of the approvals. Biomarker treatment interactions were statistically significant with three approvals, but not with two. Three out of the six approvals, which include non-enriched randomised controlled trials, showed statistically significant biomarker treatment interactions.[11]

PRIMARY ICH BIOMARKER

Immunohistochemistry (ICH) is a term that refers to a range of methodologies for identifying tissue constituents (antigens) using specific antibodies that can be visualised through staining. ICH is used to detect the type of cancer in samples. There are various types of ICH biomarkers mentioned below.

Oestrogen receptor alpha (ER-α)

The Oestrogen Receptor (ER) is the major transcriptional function of BC that promotes breast cell proliferation by binding to the proximal promoters of major oncogenes.

A study of a completely disposable Microfluidic Electrochemical Device (FED) by Carolina V. Uriana *et al.* A breakthrough and economical device for detecting BC electron acceptor alpha biomarkers. Enhancement of magnetic particles and protein-DNA interactions were presented and used for spotting. This is an ultrasensitive BC biomarker in concentrated calf serum. Microfluid electrochemical blood clots allow for simultaneous protein spotting. The FED contains a counter electrode and a reference electrode, as well as eight carbon-based working electrodes that alternate with the DNA sequence called the Oestrogen Response Element (DNAERE). Stable amplified paramagnetic particles with anti-ER antibody and Horseradish Peroxidase (MPAbHRP) were used to productively retain ER from the sample solution. The formed ERMPAb HRP bioconjugate was introduced into FED and incubated with a DNAERE modified electrode. As a result, amperometry detection can be easily constructed and functioned for multiplexed biomarker spots by applying -0.2 V to the FED array, especially in developing countries. This makes the device an excellent economic alternative to cancer diagnosis.[12]

Angeles C. Tecalco Cruz *et al.* describe the mechanism that enhances the stability of the oestrogen receptor in breast cancer. The ER is a transcriptional controller that controls the expression of genes associated with cell proliferation and mutations in typical breast tissue. However, the appearance, quantity, and action of these receptors are improved in 70% of breast cancers. Overexpression of ER is facilitated by molecular mechanisms and protein stability, demonstrating the dominant strategy for maintaining strong and efficient selectivity of ER. Some proteins work together to protect the ER from degradation by the ubiquitin proteasome system. Through a variety of mechanisms, these proteins avoid ER polyubiquitination and degradation,

resulting in increased ER protein levels. Oestrogen signalling and its physiological properties are then enhanced in BC cells. Therefore, increasing protein stability is one of the main reasons ER is upregulated in breast cancer. Various mechanisms involved in ER stability suggest new ways to understand the development of BC.[13]

Progesterone receptor

Progesterone Receptors (PRs) are members of the nuclear receptor superfamily that specifically regulate target gene expression in response to hormonal stimuli.

The oestrogen and progesterone receptor spotting in BC study was carried out by Kimberly H. Allison, MD. PR detection is an invasive method of BC by immunohistochemistry that is an effective marker of cancer in patients, which is an advantage of endocrine therapy, and no other assay has been proposed. BC samples with 1% to 100% positive tumour cores should be evaluated as PR positive. Experts acknowledge that data on the benefits of endocrine therapy in cancer is limited and that 1% to 10% of cells are PR-positive. Samples containing these results should be reported in a new report category and PR positive. A sample is considered PR negative if 1% or 0% of the tumour cell nuclei are immunoreactive. Establishing laboratory-specific standard operating procedures that describe additional procedures used in the laboratory to confirm results is optimal performance and interpretation when PR staining results are financially low or none at all. Another recommended strategy to ensure reporting The PR test is only performed on positive points of ER.[14]

Mauro E. Cenciarini *et al*. Explains the molecular mechanism underlying progesterone receptor action in breast cancer. Progesterone is an ovarian steroid hormone that acts through a nuclear receptor called the Progesterone Receptor (PR), an important regulator of breast cells that functions through proliferation and differentiation. In addition, research and clinical studies have shown its important effectiveness in inhibiting the formation of breast tumours and the progression of breast cancer. PR affects the proliferation and survival of BC cells and the proliferation of BC stem cell populations. In postmenopausal women, exposure to progesterone or synthetic progestin leads to metastatic BC and the potential for death. PR is a phosphorylated protein that plays an important role in regulating the transcriptional activity of PR. PR phosphorylation is caused not only by progestogens, but also by growth factors involved in complex bidirectional interactions with growth factor signalling pathways. Interactions play an important role in the progression of breast cancer. A better understanding of the possible effects of PR isoforms such as B. PR phosphorylated species and their target gene cofactors provides further insights into BC cell proliferation and BCSC biology. The PRA/PRB ratio can be effectively used to design coordinated therapies.[15]

ErbB2/HER2

The HER2 or ERBB2 (human epidermal growth factor receptor 2) gene is found in all cells of our body and belongs to the same family as the EGFR gene. The HER2 protein is a receptor on the surface of almost every cell in our body.

In the BC cell line, Gilbert S. Omennetal. A new class of protein candidates for cancer biomarkers: ERBB2 (HER2/neu) and ERBB1 (EGFR) are differentially expressed splice variants. The interesting evolutionary development of multi-exon genes emphasizes alternative splicing. The splicing and signaling pathways of ERBB2 + and EGFR + BC cell lines are very different. In these studies, splicing patterns are linked to interaction networks and signaling pathways. Methods of predicting functional differences between upstream ligand isoforms and downstream signaling pathways are useful for therapeutic guidance. The combination of RNA sequences and proteomics analysis shows that major protein splicing isoforms are differentially expressed in major cancer pathways and networks, according to RNA sequences and proteomics analysis. This study compared primary tumor cell lines from histologically identical inflammatory breast tumours, hormone receptor-negative cell line amplification ERBB2 (Her2 / neu), and ERBB1 overexpression with low ERBB2 activity (EGFR). But there was a significant difference between these results. Methods for identifying functional variants from protein-protein interaction networks, signal transduction and metabolic processes, and many alternative isoforms. It is a mistake to explain and predict the various expression levels and therapeutic responses of ERBB + tumours in the breast and other organs. It doesn't matter. Alternative splicing is a unique evolutionary phenomenon that allows multi-exotic genes to generate more protein diversity without expanding the genome.[18] It is no longer sufficient to report peaks and valleys of gene expression or protein expression without examining the complexity caused by alternative splicing.[16]

Krit Leemasawat *et al*. have undertaken *in vitro, in vivo*, and medical research in sufferers in British Columbia into the cardiotoxicity-associated mechanisms and feasible remedies for capsules focused on ERBB2. BC is the most common type of cancer in girls across the world. Newly released ErbB2 focused on capsules together with lapatinib, pertuzumab, and trastuzumab mutancin might also result in cardiotoxicity, although early medical trials have proven that they're secure in this regard. Unfortunately, the mechanism that causes cardiotoxicity is presently unknown. In addition, the advantages of trastuzumab-triggered preventive remedies for cardiac dysfunction, B. angiotensin-changing enzyme inhibitors, and beta-blockers are nevertheless controversial. The ErbB/neurregulin pathway is an essential aspect of cardiac strain adaptation. Drugs that focus on ErbB2 can cause cardiac dysfunction, particularly when treating HER2-wonderful breast cancers in aggregate with anthracycline-primarily based chemotherapy. Although

their cardiotoxicity isn't always dose-structured and in large part reversible, capsules focused on ErbB2 nevertheless cause hyperfine shape harm and myocardial mobile death. *In vitro* and *in vivo* research has proven that capsules focused on ErbB2 growth enhance the toxicity of anthracyclines via means of increasing oxidative strain and impairing mitochondrial function. Anthracyclines additionally have an effect on ErbB expression, making them more at risk of the cardiotoxicity triggered by ErbB2 inhibition. Unfortunately, no different powerful preventive approach has been demonstrated. Evidence indicates preferred anthracycline remedy techniques, together with exercise, have no impact on ErbB2 inhibition-triggered cardiac dysfunction.[17]

p53

p53 markers are tumor antigens that contain mutations. Tumor growth is thought to be caused by various stages of genetic damage that can lead to impaired cell cycle regulation mechanisms.

Waldemar Luetzetal. describes p53 mutations, p53 proteins, and anti-p53 antibodies as biomarkers for cancer. With the discovery that genetic mutations and changes in their expression are responsible for cancer, molecular epidemiologists have found that damaged genes or proteins are produced or produced under the control of readily available cellular material in systemic fluids. I was able to identify it. I started development. Cancer performance is thought to be dependent on mutations in the suppressor gene p53. This gene is one of the most important transcriptional, cellular domains, DNA repair, and apoptosis controllers previously discovered. Inactivation of the p53 gene causes a chaotic cell sector, leading to healthy cellular transformation in healing. The discovery that the mutation of the p53 gene develops in the presence of chemical and physical carcinogens such as vinyl chloride, radon or aflatoxin B1 has proved to be very important for work and environmental health. There is. The expression of the gene p53 and changes in the gene's mutation cause variations in the concentration of the cellular protein p53. Increased protein transfer to extracellular fluid and blood is associated with high levels of the cellular protein p53. Elevated serum protein p53 levels have been shown to be prognostically important in the early detection of lung cancer. Several studies have shown that the accumulation of mutated versions of the protein p53 and the large number of wildtypes of this protein in cells can activate the development of antip-53 antibodies. Statistical analysis proved that the Antip-53 antibody is a special biomarker for the cancer process. The Antip-53 antibody has been shown to be associated with the severity of malignant tumours. Antip53 antibodies have been shown to be associated with a high prevalence of mutations in the p53 gene.[18,19]

Ayodeji Aaj Agboola *et al.* describe the main reason for preventing Nigerian women's BC prognosis according to molecular profiling as the change in p53 direction. Advances in BC studies show the differences between tumor behaviour, patient predictions, and therapeutic effects in black and white women. This can be explained by fundamental genetic abnormalities. The tumor suppresser gene P53 act in the biology of three BCs, which are considered to be more common in black women than in white women. P53 protein expression was examined using immunohistochemistry in tissue samples of 308 Nigerian women constructed as Tissue Microarrays (TMA). Nigerian women have clinical characteristics, functional indicators of tumours expressing p53, and patient prognosis for tumours expressing p53, and were compared to the appropriate series of UK women. When the BC of Nigerian women was compared to the BC of British women, there was a significant proprietary P53 expression of Nigerian women's BC. A significant proportion of tumours of the Nigerian series that were positive for p53 were diagnosed at age 50, and the size was greatly diagnosed, and there was a sign of lymphobo transition. Compared with the series of British series, P53 positive expression was compared to the negative representation of ER and PGR (P0.001, P0.03), BRCA1, MDM2 (all P21 and Cadherin) and the UK series. The basis is significantly correlated with Cytokeratin (CK) 5/6 expression and the basal phenotype. In survival studies, Nigerian women with BC did not significantly survive if BC-specific survival rates were low, but such compounds were not seen in any disease. Compared to the BC of Nigerian women from BC women in Britain, there was a large proprietary P53 expression of Nigerian women's BC.[20]

BRCA1

BRCA1 (BC gene 1) and BRCA2 (BC gene 2) are genes that produce proteins that serve to repair damaged DNA. BRCA1, a potential biomarker predictor in breast cancer treatment. Use a graphene kip optical fibre as described by MD. Biplob Hossain *et al.*, developed for BRCA1 and BRCA2BC biomarkers of Surface Plain Resonance (SPR). Early (BRCA1) and BCGENE2 Plasmon Resonance Graphic Processing PR-Biosensor (BRCA2) Gene BC detection is characterised by simple hybrid design and numerical analysis. For numerical detection of breast cancer, two specific mutations were selected in the BRCA1 and BRCA2 genes, 916 DENTT and 6174°C. An Attenuation Total Reflection approach (ATR) is used to identify specific point mutations in Deoxyribonucleic Acid (DNA) hybridization and BRCA1 and BRCA2 genes. SPR angle (minimum: 135% or greater) and surface resonance frequency (minimum: 136% or greater). Target resonance frequency (at least 136% or more). The BRCA1 and BRCA2 genes (at least 136% or more) are target DNA (at least 136% or more). It has been shown to correlate with mutations. The difference between the non-aligned DNA strand and SrF was not important but is important for supplemental DNA strands and is important for the exact detection of the gene biomarkers of early breast cancer (916 DELTT and 6174 DELT). Finally, using commercial FDTD software, it is used to investigate the impact of electric field distribution when inserting a graph leaf using a Finite Difference Time Range (FDTD) approach. This is the first

known example of a very effective biosensor to detect BRCA1 and BRCA2BC. As a result, the proposed biosensor opens a new route for BC diagnostics.[21]

Waks *et al.* has discussed on the process of reversal and non-decline of reversal for PARP inhibitors or platinum chemotherapy in BRCA1 or 2 mutagenic breast cancer were examined. We investigated the pathway of resistance to PARP inhibitor/platinum treatment for metastatic breast cancer with BRCA1 or 2 mutations. Half of the patients showed the return of the genome to functional BRCA1 and 2 proteins. In the other two cases, the high degree of DNA connection resection was used as a mechanism of resistance. Immunohistochemically detected RAD51 lesions are associated with PARP inhibitors and platinum clinical responses. RAD51 fly colouring should be further investigated as a biomarker for clinical use. Mutations in BRCA1 and BRCA2Poly (Adenocynchinic Phosphate) Polymerase Inhibitor (PARPI) and Platinum Treatment for the Platinum Treatment Clinical Cohort the more resistive studies are avoided or overcome treatment failures. can result in the opportunity to Tumor tissues of BRCA1 or 2 patients with the development of resistance to PARAPIC or platinum treatment were obtained. All exotestal sequencing was performed on each tumor, germline DNA, and circulating tumour DNA. Tumours are sequenced to RNA and tumour parts are immunohistochemically coloured for RAD51 lesions, allowing functional evaluation of intact Homologous Recombination (HR). Eight indicates BRCA1 or 2, and genome reversal, which is the most common resistance mechanism. Two people had a new sequence change that brought more terminal DNA.[22]

Epidermal Growth Factor Receptor (EGFR)

EGFR is a protein expressed on the surface of cells. It is most commonly found in skin cells, but it can also be found elsewhere in the body. EGFR is involved in the regulation of breast cancer cell proliferation. Its activated form, phosphorylated EGFR (pEGFR), correlates with a poor prognosis for lung cancer, but has not been well studied in breast cancer.

Malgorzata Banys Paluchowski *et al.* describe patients with metastatic breast cancer whose serum Epidermal Growth Factor Receptor (EGFR) levels have been compared to circulating tumour cells. In breast cancer, overexpression of epidermal growth factor receptors is associated with negative oestrogen receptors, increased histological grade, and tumour enlargement. In metastatic breast cancer, the clinical importance of serum EGFR (sEGFR) was assessed in the context of Circulating Tumour Cells (CTC). A total of 252 participants participated in this prospective multicentre collaborative study. Blood was pulled before starting a new therapeutic line. SEGFR was measured with a sandwich ELISA. CTC was searched by cell search. When SEGFR was measured in 48 healthy controls and 252 patients, there was no significant difference between the two groups. Regardless of the threshold used, clinical pathological features were not correlated with SEGFR. Patients with sEGFR values at the 50th and 75th percentiles were more likely to have 5 CTCs per 7.5 mL of blood (p = 0.007 and 0.003, respectively). Overall survival in patients with sEGFR 73 ng/mL is significantly longer than in patients with sEGFR 73 ng/mL multivariate analysis, with 5 CTCs present, higher ranks, and higher treatment lines all having shorter OS. Although it was an independent predictor of 5 CTCs, higher treatment lines were shorter. It was an independent predictor of PFS.[23]

EGFR-bound FSCN1 as a novel therapeutic strategy for triple-negative BC was proposed by ChaoQun Wang *et al.* Examined. New findings indicate that Fascin1 (FSCN1) is involved in the development of many types of malignancies and may also function as a potential biomarker of aggression in certain cancers. However, the role of FSCN1 in infiltration and migration of Triple-Negative BC (TNBC) cells remains largely unexplored. The expression of FSCN1 was found to be significantly higher in invasive ductal carcinoma compared to both normal ductal hyperplasia and carcinoma *in situ*. Expression of FSCN1 was significantly higher in TNBC cases than in non-TNBC cases. The migration and infiltration of TNBC cells was promoted by overexpression of FSCN1. Activation of MAPK by epidermal growth factor stimulated FSCN1 expression and promoted cell motility and infiltration. Combination therapy with FSCN1 siRNA and gefitinib resulted in a significant reduction in FSCN1 expression compared to treatment with FSCN1 siRNA or gefitinib alone. In addition, we found a link between FSCN1 expression and recurrence-free and shortened overall survival. Therefore, simultaneous targeting of the epidermal growth factor receptor and the dual biomarker FSCN1 is a potential therapeutic approach for TNBC.[24]

APOBEC3B (Apolipoprotein B mRNA Editing Catalytic polypeptide-like 3B)

One of the most prominent mutational signatures in cancer, present in more than half of all human tumours, is called the APOBEC signature or signature 2/13, and is responsible for the activity of the cytosine deaminating enzymes APOBEC3A (A3A) and APOBEC3B (A3B).

It comes from Priority deamination of cytosine under immediate control Activation and regulation of apolipoprotein BmRNA-edited enzyme-catalysed polypeptide-like family genes during carcinogenesis have been reported by Jianlong Gao *et al.* Cancer is already recognised as a disease characterised by increased genomic instability and abnormal epigenome changes. Both extrinsic and endogenous factors promote carcinogenic gene changes in most solid tumours. During RNA editing and restriction of retroviruses or retrotransposons, the catalytic polypeptide-like family (APOBEC) of apolipoprotein B mRNA editing enzymes has a unique deamination activity

that converts cytosine to uracil. A subclass of APOBEC3 has been shown to induce significant mutagenesis in multiple types of cancer genomes. Highly expressed subtypes of APOBEC3 may contribute to treatment resistance and clinical outcome, in addition to the inherent protection against innate immunity. The molecular mechanism underlying the APOBEC-mediated hypermutation phenotype remains unclear. This discusses the role of the Activation-Induced Deaminase (AID)/APOBEC3 enzyme in tumorigenesis as well as the mechanism of APOBEC3 activity deregulation during cancer development. Finally, a possible approach to targeted APOBEC3-mediated mutagenesis for cancer intervention was proposed.[25]

Yan Mao *et al.* reported that the mRNA expression of the mRNA-editing enzyme-catalysed subunit 3B (APOBEC3B) of apolipoprotein B is linked to a worse prognosis for Oestrogen Receptor-positive (ER +) breast cancer. However, the clinical significance of APOBEC 3B protein expression in BC patients is unknown. Therefore, they investigated the association between APOBEC 3B protein expression and Tumours in Lymphocyte (TIL) filtration. Immunohistochemistry and tumour microarrays were used to assess APOBEC 3B protein expression in 120 BC patients. TIL was also stained with haematoxylin and eosin.[27] By studying 116 patients with breast cancer, we explored the role of APOBEC3B mRNA expression. The results indicated that increased APOBEC3B expression correlated with higher levels of ER, progesterone receptors, and TIL. In addition, elevated expression of APOBEC3B mRNA was linked to reduced recurrence-free survival, overall survival, and survival without distant metastases, particularly in the luminal A subtype. Furthermore, the expression of APOBEC3B mRNA was associated with the immune status of breast cancer patients. Ultimately, this research demonstrated that the expression of APOBEC3B mRNA and protein had distinct effects on the prognosis of breast cancer patients.[26]

Cyclin D1

The cyclin D1 protein plays an important role in regulating cell progression during the G1 phase of the cell cycle. The cyclin D1 gene CCND1 is amplified in about 20% of breast cancers, and the protein is overexpressed in about 50% of cases.

BC is by Scott F. Schoninger *et al.* Published by CDK4 inhibitors (CDK4/6i) such as palbociclib, ribociclib, and abemaciclib are approved as first-line treatments for metastatic HR+ and HER2BC in combination with hormone therapy. Their targets, CDK4 and CDK6, are cell cycle regulatory proteins that regulate G1S phase transitions in a variety of tissues. The discovery of biomarkers to identify patients who may benefit from this class of medicine remains an important topic. Adding CDK4/6i to oestrogen-regulated therapy almost doubles the median progression-free survival but does not significantly improve overall survival. In fact, only a small percentage of people who receive treatment respond. Many patients initially develop resistance to CDK4/6 inhibitors and do not benefit from them. Therefore, they often rely on chemotherapy after 6 months. Some individuals respond well to treatment at first, but then develop secondary resistance. This underscores the importance of complementary or incidental diagnosis in identifying patients who will benefit. Because CDK4 is a legitimate target for other tumour types currently being evaluated for CDK4/6i treatment, lack of target identification may obscure the interests of some patients. I have. This review provides an overview of the current status of CDK4/6i biomarker test development in both clinical and laboratory tests, focusing on tests with strong biological evidence and support for clinical data.[27]

Ana C. Garrido Castro *et al.* describe the treatment failure and susceptibility mechanisms of Cyclin-Dependent Kinases (CDKs) 4 and 6 in breast cancer and potential biomarkers of susceptibility and resistance to CDK 4 and 6 inhibitors. A modest number of preclinical and clinical studies in BC address the mechanism of response and resistance to CDK4/6 inhibitors. Oestrogen receptor positivity, luminal gene expression patterns, high cyclin D1 levels, and low p16 levels are all potential response markers. Loss of Rb function, overexpression/amplification of cyclin E, and CDK6 amplification are thought to be mechanisms of resistance. The results show that this percentage is still theoretical and has not been validated in clinical samples. Using the initial results of CDK4/6 inhibitors, the understanding of CDK4/6 biology in BC needs to go beyond the current basic form. Only then can we create meaningful treatment combinations that further enhance the effectiveness of these drugs.[28]

Ki67

Ki67 is an excellent marker for determining the growth rate of a particular cell population. The proportion of Ki67-positive tumour cells (Ki67 labelling index) often correlates with the clinical course of cancer.

Matthew G. Davie *et al.* We announced Ki67 as a prognostic biomarker for invasive breast cancer. BC management has changed dramatically since the advent of molecular medicine. BC is now understood as a heterogeneous disease with a wide range of morphology, molecular properties, tumour behaviour, and therapeutic response. Expression of ki67 has a strong relationship with tumour cell proliferation and is widely used as a proliferation marker. This review describes the therapeutic value, existing problems, and interesting solutions for increasing the Ki67 proliferation index in future breast oncology. Ki67 expression is significantly associated with tumour growth in developing BC and is a known predictor of prognosis and outcome. In certain situations, Ki67 expression levels can be used to guide treatment decisions. Therefore, the Ki67 test is routinely performed as part of the pathological tumour assessment. The purpose of this work was to provide an overview of Ki67 use in clinical practice,

current problems in measurement, and new means of improving the Ki67 proliferation index in future BC patients.[29]

Rita Halder *et al*. Clinical trials in BC patients describe inhibition of intraoperative epinephrine and COX2 signaling. This improves tumour Ki67 expression, serum cytokine levels, and the PBMC transcriptome. The highlight is the inflammatory or rearrangement reaction of BC patients, even before surgery. These reactions were suppressed by propranolol (a blocker) and etodolac (a COX2 inhibitor). Numerous preoperative indicators of metastasis in the blood and resected tumours were improved by propranolol and etodolac. Larger clinical trials are needed to investigate the effects of treatment on cancer recurrence. Translation studies show that catecholamines and prostaglandins are released in large quantities during the perioperative period in response to stress and surgery, promoting tumour spread. The perioperative combination of the blocker propranolol and the COX2 inhibitor etodolac is 38 v.o. tested in a clinical phase II biomarker study. examination for 11 consecutive days from the 5th day before surgery. Chr. Be patient. Blood samples were taken before Treatment (T1), before and after surgery (T2 and T3), and after Treatment (T4). The drug was well tolerated. The results are based on a preferred hypothesis and suggest that serum levels of pro-inflammatory IL6, CRP, IFN, anti-inflammatory cortisol and IL10 are elevated preoperatively (T2). At T2 and/or T3, drug treatment reduced serum levels of the aforementioned pro-inflammatory cytokines and TRAIL, as well as the activity of several inflammation-related transcription factors (including NFB, STAT3, ISRE), but not cortisol. Did not decrease Serum levels did not decrease. IL10, IL18, IL8, VEGF, and TNF. This treatment reduced the expression of the growth marker Ki67 in resected tumours and at the same time had a positive effect on its transcription factors SP1 and AhR.[30]

Cyclooxygenase-2 (COX-2)

Established by Malta Szweda *et al*., the correlation between COX2 expression and angiogenesis and lymph node metastasis in human breast cancer is clear. Increasingly, research is focusing on identifying new biomarkers that can speed up and improve oncological diagnosis and treatment for both humans and animals. COX2 is a promising biomarker that is gaining attention in human cancer and is yet to be used in veterinary oncology. It is known to be highly expressed in certain disease states such as inflammation, pain, and fever and is likewise overexpressed in certain types of tumours in both humans and animals. The value of COX2 as a biomarker with diagnostic, therapeutic, prognostic, and predictive implications in oncology and the clinical importance of reducing its overexpression in tumours is a growing area of research.[31]

Mousumi Majumder *et al*. demonstrated that overexpression of Cyclooxygenase 2 (COX2) in human breast cancer cells produces the carcinogenic microRNA miR655. This expression of miR655 was found to be elevated in all cell lines when they were proliferated as spheroids and is associated with Stem-Like Cells (SLC). MiR655 was found to be responsible for promoting proliferation, migration, infiltration, spheroid formation, and Epithelial-Mesenchymal Transition (EMT). Moreover, it was shown to be linked to SLC-related signalling pathways, activated by EP4 and downstream EP4 signalling pathways such as PI3K/AKT, ERK, and NFkB, resulting in Smad3 phosphorylation resistance to TGF. Injecting MCF7miR655 and SKBR3miR655 cells into the tail vein of NOD/SCID/GUSB null mice resulted in accelerated lung colonisation and micro metastasis in the liver and spleen. Additionally, MiR655 expression was found to be significantly higher in human breast cancer than in nontumor tissue and was associated with reduced patient survival, making it a potential predictive biomarker for breast.[32]

Caveolin-1

Caveolin 1 (Cav1) is a constituent protein of the flask-formed invagination of the plasma membrane known as caveolae. Several studies have found that a lack of interstitial Cav1 predicts normal survival or the development of most cancers in BC.

Expression of interstitial caveolin 1 as a predictor of competitive BC behaviour is Nuket Eliyat *et al*. mentioned that Caveolin 1 (Cav1) is a famous scaffold protein discovered in caveolae, a unique plasma membrane structure. Little interest has been paid to the results of Cav1 on BC carcinogenesis. The motive of this assignment is to provide an explanation for the organic interest of Cav1 in malignant tumours of the breast, given its contrasting twin potential as an oncogene and a tumour suppressor. Between 2007 and 2012, seventy-one girls with BC were diagnosed histopathological in the Private Genes Pathology Laboratory. The common age is 52. Forty-eight years old, and the median age is twelve years old. Patients had been observed for a mean of 47. Ninety-seven to twenty-eight months. No Cav1-effective tumour cells have been discovered. Cav1 interstitial expression was discovered in 36 cases. Expression of Cav1 was discovered within the stroma. Expression of Cav1 becomes related to tumour size, histological grade, and lymph node metastasis, respectively.[33]

XianLing Qian *et al*. describe approximately the multidimensional drivers of the BC boom and its scientific importance. Human BC is one of the most common and common types of most cancers, as well as one of the leading causes of death in females worldwide. incidence, excessive malignancy, excessive mortality, excessive recurrence rate, and negative diagnosis. Caveolin 1 (Cav1) is an important factor in caveolae involved in a variety of organic processes. According to increasingly experimental research, Cav1 plays an increasingly crucial role in the development of breast cancers, together with molecular proliferation, apoptosis, autophagy, infiltration, migration, and BC metastasis. Problems in scientific BC remedies in addition, Stroma Cav1 may be used to expect the diagnosis of BC patients. This evaluation describes the

modern-day studies, development, and position of Cav1 in BC development and scientific control of Cav1 and breast cancers, laying the muse for destiny studies and development of the CAV1 gene as a capacity target. I need the prognosis and remedy for superior breast cancer.[34]

Peroxisome Proliferator-Activated Receptor (PPAR-γ)

Peroxisome Proliferator-Activated Receptor Gamma (PPARγ), a member of the nuclear receptor superfamily, is a ligand-gated transcription factor expressed in many tumours, including breast cancer, and its role in ligand binding is involved in development. It is the role of the tumor. Progression and metastasis.

Early detection of breast cancer (the common type of breast cancer) using biomarkers connected to the PPAR signalling pathway is the main cause of morbidity and mortality in women around the world. According to the GHAZala Sultan *et al.* Report, it represents approximately 12% of all women. The basic changes in gene expression, molecular mechanisms, and metabolic pathways that cause breast cancer onset and progression are not yet known. In this study, potential biomarker genes were involved in the early detection of early progression. *In situ* (DCIS) of non-invasive emulsified cancer (DCIS), Invasive Duktal Cancer (IDC) and normalization, statistical calculation, TG annotations, Protein Interaction (PPI) networks and -GEN profiling and tracking of their expression Regulatory pattern comparison analysis of healthy copies of healthy genes compared the differentiated genes between health and DCIS, healthy and IDC, and DCIS and IDC. Some of the observed expressions were overexpressed, while others were under expressed. Consistently under expressed genes were found in all three pre-invasive and invasive ductal breasts. The active pathways of these genes have been further studied and are found to be deeply involved in the PPAR signalling pathway. A database of gene expression profiles is useful for the early detection of breast cancer.[35]

Iman *et al.* reported an adjunct correlation between transcription factor receptor gamma and nuclear factor omega-3 polyunsaturated fatty acid chemotherapy in BC survivors Sharaf *et al.* PAR is involved in cell proliferation and differentiation pathways in various cancers. PPAR regulates important breast cancer genes that are important for breast cancer progression. The purpose of this study is to determine if there is a connection between PPAR and NFB and the clinical pathology feature of BC patients. The effects of the administration of omega-3 fatty acids in addition to chemotherapy were also studied. A total of 40 obese BC patients were divided into two groups: chemotherapy and omega. The chemotherapy group received only chemotherapy, while the omega group received 2gn3 daily with chemotherapy. The control group consisted of 20 fat women. Blood levels of PPAR and NFB were measured in all groups tested. PPAR was significantly lower than the control. Higher ERP and PR positive levels decreased at higher ERP levels with HER2/neu positive in hyperplasia and postmenopausal BC patients. In British and postmenopausal BC patients, NFB was significantly larger than control and decreased with the increase of ER, PR, and HER2/neutral. Treatment with omega-3 fatty acids in combination with chemotherapy increases the amount of PAR and reduces NFB NFB. The use of omega-3 PUFA as an adjuvant treatment may increase the sensitivity of cancer cells to chemotherapy by correcting disturbances in the PARE/NFB signalling pathway.[36]

CELL-TYPE-SPECIFIC BIOMARKERS

Cell type-specific biomarkers indicate normal or pathological processes in the body. Biomarkers can be specific cells, molecules or genes, gene products, enzymes or hormones.

FOXA1

FOXA1 is a member of the forkhead class of DNA-binding proteins. These hepatocellular nuclear factors are transcriptional activators of liver-specific transcripts such as albumin and transthyretin, and they also interact with chromatin as pioneer factors.

FOXA1 is an important marker for breast cancer forecasting. FOXA1 research is by Xiaofeng Dai *et al.* Effective marking of triple growth breast cancer due to transcriptional suppression of SOD2 and IL6 BC side-working type, especially triple Brive detection, is important to improve patient outcomes in these malignant tumours. The role of Foxa1 in the definition of trihydrogen breast cancer and the role of Foxa1 in triple mitic cancer and lumen cancer identification is systematically promoted, and various transparent levels and expression patterns of translation levels are examined. Hooray! Immunohistochemical staining and clinical patterns and clinical pattern-based prediction evaluation studies Clinical patterns and functional studies such as survival rate analysis of patients can lead to increasing the rhizoma of malignant tumours and cancer. Sexual results are shown. Lumen tyre transcription reduction of SOD2 and IL6 production It is a tight list. *In vitro* and Clinic Continuous Bioinformatics Analysis and Experimental Verification, researchers identify the meaning of FOXA1 to understand the triple import as a biomarker and the meaning of Foxa1 at the molecular level. I first pull you deeply. Our results are validated with larger clinical cohorts and complement existing biomarker modalities and help characterise BC's non-uniformity more accurately.[37]

Xiaoyong Fu *et al.* Research on Overexpression of Foxa1 in Erpospositive BC promotes endocrine resistance by changing error-based and IL8 expression. The interaction between the Oestrogen Receptor (ER) and the growth factor receptor pathway results in the modification activity and reprogramming of the first transcriptome and Oestrogen Receptor (ER) positive (+) thoracic endocrine secretion. It is one of the causes of resistance. However, the basic reproduction of this opponent's transcriptional reprogramming has not yet been identified. By modifying the

Dependent transcriptome, we show that upregulation of fork head box protein A1 (FOXA1) by gene amplification or overexpression contributes to the enhancement of endocrine resistance and the invasive phenotype. As a result, IL8, one of the most highly altered FOXA1/ER effectors, plays an important role in mediating these phenotypes and may be a therapeutic target for high ER +/FOXA1 breast cancer. The findings suggest a novel role for FOXA1 in the ER transcriptional programme in endocrine-resistant breast cancer. Although FOXA1 is a pioneer factor in Oestrogen Receptor (ER)–chromatin binding and function, its role in endocrine resistant (Endor) BC remains uncertain. The authors present preclinical evidence for the function of FOXA1 in Endor breast cancer, as well as clinical evidence for its importance. For surface data of a large number of BC cell line models, the Foxa1 gene is enhanced and/or overexpressed. Induced Foxa1 results in carcinogenic signatures and proteome profiles that are strongly linked to endocrine resistance. According to integrated Omix data, IL8 is one of the disturbing genes regulated by FOXA1 and ER transcriptional reprogramming. Tamoxifen-resistant cell proliferation and infiltration are inhibited by IL8 knockdown, which also partially reduces the effect of overexpression of Foxa1. The work shows Foxa1.[24,38]

GATA-binding protein 3 (GATA3)

GATA3 (GATA Binding Protein 3) is a protein encoding gene, and GATA Binding Protein 3 (GATA3) is a transcriptional activator highly expressed by the luminal epithelial cells of the breast. Jeremy M. Arnold *et al.* discuss GATA3 somatic mutations. It is common in non-BRCA1 and BRCA2 familial breast malignancies, but not in BRCA1, BRCA2, or sporadic breast tumours. Recently, a heterozygous somatic mutation in the GATA3 transcription factor was found in about 5% of breast cancers that have not been evaluated for family history. Examination of the GATA3 gene in 55 breast tumours in women with familial BC revealed seven heterozygous cell mutations. All of these were found in non-BRCA1/2 cases with a 22% chance. In contrast, GATA3 mutations were detected in only 4% of the 81 sporadic cancers examined. In general, GATA3 mutations occur earlier in the onset of BRCAx cancer than in BRCA1, BRCA2, or spontaneous tumours, making it easy to identify direct sequencing in the presence of stromal contamination.[39]

The function of the Rola El Sayed Oestrogen Receptor 1 (ESR1), GATA Binding Protein 3 (GATA3), Fork Headbox Protein A1 (FOXA1), and Runt Related Transcription Factor 1 (RTF1) ER (RUNX1) genomes. Whether to control, as a result, ER+ tumours show a high degree of heterogeneity. Within the ESR1 binding region are the GATA3 and FOXA1 DNA binding sites. ER binding capacity and transcriptional activity are impeded by the absence of such a binding site. Patients with the GATA3 mutation had lower markers of Ki67 proliferation after AI treatment than those without it, suggesting that the GATA3 mutation indicates BC in response to endocrine therapy. Mutations in FOXA1 may indicate BC in response to endocrine therapy, as mutations in GATA3 and FOXA1 are mutually exclusive. Mutations in FOXA1 may also indicate BC in response to endocrine therapy. In contrast, in breast cancer, the RUNX1 transcription factor acts as a tumour suppressor, and in advanced disease, its expression is reduced. Resistance to AI treatment is associated with mutations in RUNX1.[40]

CK5 (Cytokeratin 5)

Cytokeratin 5 (CK5) is an epithelial cell marker in master and progenitor cell activity in gland-rib-type tissue in the Oestrogen Receptor (ES).

Rohit Bhargava *et al.* discusses that sensitive than CK5 than CK5/6. A panel of immunohistochemical staining containing Cytokeratin (CK) 5 is used, including Cytokeratin (CK) 5, corresponding to the CK5 phenotype of breast cancer with "strip" carcinoma. increase. As the CK5 antibody (clone XM26) wanted to see if it had sensitivity or specificity, its expression was compared within the scope of BC patients in the range of CK5/6 (Clone D5/16B4). The test (TMA) used three BC tissue microarrays. TMA1 consists of 59 BCs and they were all diagnosed. TMA2 and TMA3 were previously described morphologically and immunohistochemically breast cancer strips in our plants. CK 5 and CK 5/6,14 was CK 5 positive, and CK 5/14 and 52 were negative. CK5 had a 97% sensitivity of 97% to recognise carrier cancer, while CK5/6 had a 59% sensitivity. Both antibodies were very specific and their specificity exceeded 95%. In the case of positive, the ratio of coloration by CK5 and the strength were significantly higher than CK5/6.[41]

Olivia Mcginnetal discuss that cytokeratin 5 affects the catenin dynamics of BC cells. Subductions from cells expressing the intermediate filament protein cytokeratin 5 are common in Oestrogen Receptor (ER)-positive breasts (CK5). In ER + breast cancer, CK5+ cells are activated by progestin and are rich in CK5 cells of Cancer Stem Cell (CSC) frac with incomplete formation. Due to the deletion and overexpression of CK5, it was discovered that CK5 is required for the development of tumour spheres in the ER+BC cell line. This means that CK5 matches the CSC. Er + WNT Er + BC Cell Er + BC Cell Er + BC Cell Err + BC Cell Err + BC Cell CK5 Interaction Catenin is an essential transcription factor for transduction pathways and cell adhesion molecules and signals. focuses on transducing proteins. We investigated the dual activity of cats associated with CK5. CK5 knockout or knockdown inhibited catenin transcriptional activity in response to progesterone and Want stimuli. Conversely, overexpression of CK5 in the cell membrane or progestin-induced loss of catenin was sufficient to promote the overall loss of cadherin. Single-cell RNA sequencing, remodelling, and cell-binding signalling showed that identical loss of membrane catenin and cadherin in CK5+ but not in intertumoral CK5 cells, single-cell RNA sequencing, remodelling, and cell-binding signaling showed

that. We have shown that transduction is the most concentrated pathway in CK5+ cell clusters. CK5 actively changes the shape of cells and inhibits CK5 catenin compounds. This may help reverse the negative effects of CK5 + breast cancer.[42]

Smooth Muscle Myosin Heavy Chain (SMMHC)

Myosin Curable Smooth Muscle is the heavy chain of smooth muscle myosin, which is important for smooth muscle contraction. Myosin has recently been discovered to play an intracellular function in cellular activity, migration, responsibility, cell trade, and membrane transfers. Myosin uses ATP hydrolysis energy to move filaments and generate muscle strength that plays a role in various cellular processes.[46] Finally, system biology tools, especially PPI networks, can help investigate complex diseases. Bioinformatics Research provides a complete insight into the mechanism behind BC development. Network analysis identifies the hub genes connected to BC, including SMMHC. A total of 433 gene groups and six stroke genes were found and verified as BC target biomarkers. Thorough testing and pathways of this gene molecular mechanism can result in possible goals for monitoring BC therapeutic agents.[43]

Mammographic cleaning has increased BC diagnostics in invasive stages, so it is modelled for early stages of BC infiltration to identify possible biomarkers to share the risk of recurrence. is essential. For such research, invasive lesions and invasive lesions are very important. In a chest channel system, myoga Wal cell cells function as barriers between epithelial cells and the surrounding stroma. Pathologists can use various muscle-up immunohistochemical markers developed and verified in human tissues to identify *in situ* carcinomas of invasive breast cancer. Meanwhile, strong muscular intercourse markers in mouse breast tissue were hardly divided. In the C57BL/6J-MMTVPYMT transgenic model of breast cancer, test results showed the ability

Table 1: Patents on biomarkers for breast cancer.

Sl. No.	Patent number	Title	Outcome	Published year
1	CN113495144	Biomarker for predicting the progress of BC and application of biomarker.	The 4.1 R protein can be used for successfully evaluating incidence and advancement of tumor resulting in targeted treatment.	2021
2	WO2021244423	Methylated biomarker for detecting breast cancer, and use thereof.	Methylated biomarker for detecting BC by low methylation expression of a combination of 3 CpG sites.	2021
3	CN110835650	Biomarker for BC metastasis and prognosis diagnosis.	A new diagnosis and evaluation by *in vitro* and *in vivo* metastasis and progenesis for BC.	2020
4	EP3191845	Biomarkers for assessing breast cancer.	Employment of various strategies and metabolism to specific biomarkers is considered to assess BC.	2019
5	KR102027248	Biomarker for detecting BC Stem Cell (BCSC) and use thereof.	cellular heterogeneity and immunotherapy by cancer stem cells and Drug Delivery Systems (DDSs) by selectively targeting BC for derived cancer stem cells.	2019
6	EP3368684	Biomarker for breast cancer.	the SPAG6-gene, PER1-gene, and NKX2-6-gene promoter promotes the level of methylation is a biomarker for breast cancer.	2018
7	KR1020180001380	Biomarker for predicting prognosis of Triple-Negative BC[TNBC].	The predicting progenesis of TNBC by the expression level of an mRNA of the genetic biomarker treated by concealing the expression of the genetic biomarker involved in an unhealthy prognosis of TNBC.	2018
8	EP3152578	Method and arrays for use in diagnosing early breast cancer.	The method of diagnosing BC consists of proving sample to be tested and detection of the amount of BC cells in biomarker.	2017

of muscle mass marker capabilities (min) and muscle chain (min) to increase myopathy (minimum) differentiation atmosphere. Then SMMHC is found is conserved in early-stage tumours and can be used to distinguish invasive diseases. In addition, prior to the onset of MIN, the proliferation marker Ki67 was an excellent marker for distinguishing between normal and hyperplastic ducts. Based on this, we created a scoring matrix to distinguish between normal, hyperplastic, MIN, and infiltrating lesions in a spontaneous breast tumorigenesis model. This task shows that myoepithelial proteins are differentially expressed during tumor development, providing the most relevant markers in additional early BC models that allow accurate classification of disease. It also emphasizes the need for characterization.[44]

E-cadherin

Cell adhesion molecule catechin is expressed in normal breast tissue, and is often an effective marker for detecting breast cancer. Loss of Ekadechelin has been linked to the development and progression of invasive lung cancer, however, if the tumour is resistant to the treatment of the drug, options are limited. In order to gain better insight into the abnormally effective ILC, a Reverse Phase Protein Array (RPPA), mRNA sequencing, compliant medium proliferation assay, and a combination of CRISPR/CAS9 based knockout experiments (GFR) dependent phosphatidylinositol receptor 4 (PDL) is used. It was found that the responsiveness of 5-bisphosphate-3 kinase (PI3K)/Akt signal transduction activation is high, and GFR signalling and autocrine activation of downstream PI3K/Akt hubs were independent of carcinogenic mutations in PIK3CA, AKT1, or PTEN. Furthermore, analysis of human ILC samples confirmed the production of growth factors and the activity of signalling pathways. Inhibition of Akt using AZD5363 or MK2206 resulted in a strong inhibition of cell proliferation and ILC cell survival, inhibiting tumour proliferation in the mouse.[45]

The integrity of the Cadherin Protein (CDH1 gene) is fundamental to the process of epithelial polarisation and differentiation. Deregulation of cadherin function plays an important role in BC metastases with poor prognosis and short overall survival. This review describes the underlying inactivation mechanism of CDH1 gene activity and its potential translation into clinical practise as a prognostic biomarker and potential targeted therapy.

Alpha smooth muscle actin (ACTA2)

SMA is the first and most commonly used marker to indicate the activation of fibroblasts and is linked to TGF production as well as a highly contractile state. Research demonstrates that SMA-positive CAFs contribute to tumour progression and can make treatments ineffective. Immunosuppressive TME can be controlled by various strategies, for example by paracrine and ECM remodelling.[46]

Calponin

Calponin is responsible for binding many actin-binding proteins and phospholipids to regulate actin-myosin interactions.

With the aid of an intact muscle supermall molecular layer, DCIS is confined to BC within the chest channel and is surrounded with the aid of an intact muscle supermall molecular layer that forestalls neighbourhood intrusion. With the aid of radiation and possibly endocrine chemotherapy, DCIS analysis will increase the danger of lifestyles growing Invasive BC (IBC) and outcomes in surgical resection with the aid of radiation. DCIS is understood to be flawlessly embellished with related coexistence. Patients who are at low risk of developing a disorder require more competitive treatments. The look at the position of muscular molecular differentiation within the barrier characteristic is anticipated to offer perception into DCIS development and distinguish between low harm and excessive lesions. The advanced approach is an ancient stage for comparing the lack of muscle epithelial differentiation markers. This approach is confirmed with the aid of using an excessive correlation with the annotations of pathologists and helps computerised evaluation of clinically suitable histopathological capabilities to guide analytical substrates for more than one Immunohistochemistry (IHC). Calponin1 is known to bind and stabilise actin cytoskelets in clean muscle cells, where it aids in energy production. Expression of the expression of calponin 1 improved with the aid of using approximately 130-fold in adjoining tumour cells expressing inferior prognostic tumour molecular markers. In addition, calponin 1 is covered within the set of 17 genes. This predicts the growth of the danger of metastasis in BC patients. Currently, it isn't regarded as manipulating the lack of muscle.[47]

However, it demonstrates that lymphocyte filtration is similar to mobile cell intermingling within the immune system. Calponin 1 is a tumour suppressor biomarker that may be more accurately diagnosed as a histologic subtype as a histologic subtype and the presence of necrosis or nuclear network. These observations guide additional surveys into the position of calponin 1 as a tumour suppressing protein, which may make contributions to destiny remedy improvement within the prevention of DCIS development.

CK14 (Cytokeratin 14)

CK14+ cells are guide cells for mass infiltration of breast cancer, cause migration of CK14 cells, and show mobility, overhang, and intercellular aggregation. CK14+ cells are significantly enriched in BC cells during metastasis. This is most strongly associated with systemic metastases. Conversely, CK14 cells are significantly enriched during metastasis, which is most strongly associated with proliferation. Interestingly, CK14+ cells were also required for the gene expression of several metastatic effectors involved in niche remodelling.[48]

PATENTS ON BIOMARKERS FOR BREAST CANCER

Biomarkers are being developed to identify individual risks, cancer types, offspring, recurrences, predict treatment outcomes, and monitor breast cancer treatment. The development of new treatments helps diagnose the severity of cancer and its response to treatment. Advances in treatment have led to a variety of powerful and safe biomarkers that can be used to guide the determination of promising responses to early detection and recovery of cancer. Table 1 shows some of the patented biomarkers.

CONCLUSION

Some styles of biomarkers are required for all people with diagnostic breast cancer, regardless of the giant attempt at biomarker discovery. It is important to use analytically and clinically demonstrated assays, execute common inner pleasant manipulation checks, and feature hooked up assay recognition and rejection standards while comparing BC biomarkers for scientific application. The discovery of biomarkers calls for early detection of physical fluid. Breast surgery, which incorporates excisional biopsy and radiation, makes breast-precise fluid samples especially critical for early detection. Biomarker panels are getting extra popular. This multi-evaluation method to optimise the sensitivity and specificity is both sensible and reasonable. Before a biomarker may be extensively used, it has to be demonstrated.

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this work.

ABBREVIATIONS

BC: Breast cancer; **HER:** Human Epidermal Growth Factor Receptor; **ER:** Oestrogen receptor; **PR:** Progesterone receptors; **HER2:** Human Epidermal Growth Factor Receptor 2; **USFDA:** United States Food and Drug Administration; **FDA:** Food and Drug Administration; **ICH:** Immunohistochemistry; **ER α:** Oestrogen receptor alpha; **FED:** Microfluidic electrochemical device; **DNA:** Deoxyribonucleic acid; **RNA:** Ribonucleic acid; **DNAERE:** Oestrogen response element; **HRP:** Horseradish Peroxidase; **BCSC:** Breast Cancer Surveillance Consortium; **PRA:** Progesterone receptor isoforms A; **PRB:** Progesterone receptor isoforms B; **TMA:** Tissue Microarrays; **PARP:** Poly-ADP ribose polymerase; **FDTD:** Finite-Difference Time-Domain; **EGFR:** Epidermal growth factor receptor; **CTC:** Circulating Tumour Cells; **FSCN1:** Fascin1; **TNBC:** Triple-negative Breast cancer; **APOBEC3B:** Apolipoprotein B mRNA editing catalytic polypeptide-like 3B; **AID:** Activation-Induced Deaminase; **TIL:** Tumours in Lymphocyte; **CDK:** Cyclin-Dependent Kinase; **COX-2:** Cyclooxygenase-2; **SLC:** Stem-like cells; **EMT:** Epithelial-Mesenchymal Transition; **Cav1:** Caveolin-1; **PPAR:** Peroxisome proliferator-activated receptor; **DCIS:** Ductal carcinoma *in situ*; **IDC:** Invasive Ductal Cancer; **PPI:** Protein pump inhibitor; **FOXA1:** Forkhead box A1; **CK:** Cytokeratin; **SMMHC:** Smooth muscle myosin heavy chain; **CDH1:** Cadherin Protein; **ACTA2:** Alpha smooth muscle actin.

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