ISSN : 2350-0743

International Journal of Recent Advances in Multidisciplinary Research

Vol. 13, Issue 05, pp.12411-12417, May, 2026
https://doi.org/10.64485/ijramr.6563.05.2026

REVIEW ARTICLE

TRIPLE-NEGATIVE BREAST CANCER: INTEGRATING MOLECULAR BIOLOGY, THERAPEUTIC STRATEGIES, AND PHYTOCHEMICAL INTERVENTIONS

[1]Kirti Sisodiya, [2]Vishakha Jain, [3,*]Aman Upaganlawar and [4]Chandrashekhar Upasani

[1,2,]Research Scholar, Department of Pharmacology, SNJBs Shriman Sureshdada Jain College of Pharmacy, Neminagar, Chandwad, Nashik, India; [3,4]Professor, Department of Pharmacology, SNJBs Shriman Sureshdada Jain College of Pharmacy, Neminagar, Chandwad, Nashik, India.

ARTICLE INFO

Article History:
Received 15th February, 2026
Received in revised form
24th March, 2026
Accepted 19th April, 2026
Published online 28th May, 2026

Keywords:

Triple-Negative Breast Cancer (TNBC); Breast Neoplasms; Signaling Pathways; Epithelial-Mesenchymal Transition (EMT); Targeted Therapy; Apoptosis; Bioactive Compounds.

Corresponding author:
Aman Upaganlawar

ABSTRACT

Triple negative breast cancer (TNBC) represents a clinically aggressive form of breast carcinoma distinguished by the lack of estrogen, progesterone, or HER2 receptors, which limits therapy options and poorer prognosis. This subtype exhibits considerable heterogeneity and is driven by multiple molecular signaling networks mTOR, Wnt, Notch, and NF-kB. Chemotherapy is primary treatment strategy, although new targeted treatment options and immunotherapies, including PARP and immune checkpoints, are polyphenols and flavonoids which can alter cancer pathways. In order to improve patient outcomes, subsequent therapies will focus on a combination of conventional and modern therapies that target the tumor microenvironment.

Citation: Kirti Sisodiya, Vishakha Jain, Aman Upaganlawar and Chandrashekhar Upasani, 2026. *"Triple-Negative Breast Cancer: Integrating Molecular Biology, Therapeutic Strategies, and Phytochemical Interventions" , International Journal of Recent Advances in Multidisciplinary Research, 13(05), 12411-12417.*

INTRODUCTION

Breast cancer continues to be a major contributor to global cancer-related morbidity, with approximately two million new cases reported globally, according to 2018 report(1).TNBC constitutes approximately 10-15% of diagnosed cases and is defined by the lack of ER, PR, and HER2 expression. This subtype is associated with elevated frequencies of BRCA1 mutations, metastasis and death. There are four transcriptional subtypes of TNBC, and in general, it has a poorer 5-year survival rate than tumors that are positive for hormone receptors (2). Diagnostics approaches for TNBC include imaging modalities, biopsy and histological analysis are the main clinical diagnostic techniques for TNBC. However, conventional screening methods often show limited sensitivity for TNBC detection (3).Chemotherapy is presently the main therapeutic approach used to treat TNBC.To increase their treatment effectiveness and survival rates, new therapeutic approaches like immunotherapy and targeted therapy are constantly being researched. Agents like PARP inhibitors have shown significant benefit in BRCA-mutated TNBC cases, while immune checkpoint inhibitors like pembrolizumab and atezolizumab have shown promising outcomes in selected patient groups. Moreover, natural products and herbal medicines are progressively investigated as possible therapeutic agents owing to their varied pharmacological characteristics (4).

Molecular and Pathophysiological Background of TNBC

Molecular subtypes

Basal-like subtype: Basal-like triple negative breast cancer (TNBC) is marked by accelerated proliferative activity, with the BL1 subtype showing increased proliferation markers like Ki-67, indicating responsiveness to antimitotic agents including paclitaxel or docetaxel. In contrast BL2 tumors enhancesignaling through pathways such as EGFand Wnt/β-catenin, experience dysregulation in DNA damage response, and exhibit genomic instability(5).

IM subtype: The IMsubtype is primarily defined by the enrichment of immune-related gene expression profiles.Pathways associated with T-cell receptor signaling, antigen-presenting cell function and cytokine interaction are highly active in this subtype (6).The IM subtype shares molecular similarities with medullary breast carcinoma, which is associated with a comparatively favourable prognosis (7). IM-TNBC patients are likely to get advantages from

immunotherapeutic approaches, particularly those that suppress PD-L1, and CTLA-4 pathways.

Mesenchymal subtype/ M and MSL subtypes: Compared to other subtypes, mesenchymal tumours exhibit greater levels of copy number changes, mutation burden, and genomic instability. These tumors demonstrate activation of growth factor signaling pathways and often exhibit reduced immune cell infiltration, contributing to resistance to immunotherapy(8). Alterations in the mTOR pathway are commonly observed, particularly due to loss of PTEN function. Consequently, inhibitors targeting mTOR signaling have shown potential therapeutic value (9).

Luminal ARsubtype: The Luminal AR subtype is particularly unique subtype. The expression of estrogen metabolism and hormone regulatory pathways in these tumors differs from that of tumors with the other subtypes. Furthermore, A study reported that LAR tumors differ physiologically from other subtypes based on DNA copy number studies. Clinical studies have demonstrated that anti-androgen agents such as bicalutamide, may be effective inpatients with androgen receptor-positive TNBC. Additionally, the frequent presence of PIK3CA mutations suggests that combination therapies involving PI3K inhibitors and androgen receptor antagonists may enhance treatment outcomes (10).

Signaling Pathways Involved in TNBC Progression

mTOR Pathway: The mTOR signaling cascade fundamently involved in cancer progression. Dysregulation of this pathway is strongly associated with poor prognosis(11,12). Activation of PI3K leads to downstream phosphorylation of Akt, which subsequently activates mTOR complexes (mTORC1 and mTORC2), promoting anabolic processes and tumor development (Figure1)(13). mTOR network inhibitors belong into six classes. Furthermore, compared to single PI3K inhibition, the efficiency can be increased by simultaneously targeting mTOR and one PI3K isoform (12).Rapamycin and paclitaxel are important treatments for TNBC because they block the mTOR pathway.Additionally, mTOR antibodies have been reported to be more successful than mTOR inhibitors by itself (14).

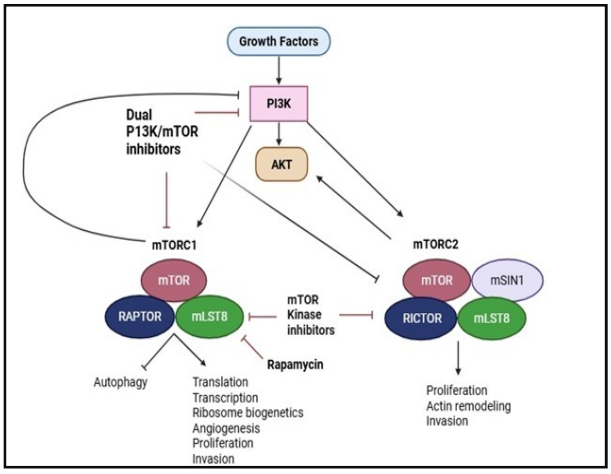

Figure1. mTOR signaling pathway

WntPathway: The Wnt pathway is commonly disrupted in TNBC contributes totumor growth,metastasis, and prevention of cancer stem cells. Activation of this pathway facilitates epithelial-mesenchymal transition (EMT) and increases tumor invasiveness (15).Wnt ligands including WNT3A, WNT5A and WNT11 play critical roles in tumour cell migration and invasion(16).Specifically, enhanced malignant cell motility in TNBC is linked to the FZD6 receptor. Therapeutic targeting of this pathway, including inhibition of Frizzled receptors (Figure 2) using antibodies such as OMP-18R5, has shown promising anti-tumor effects (17).

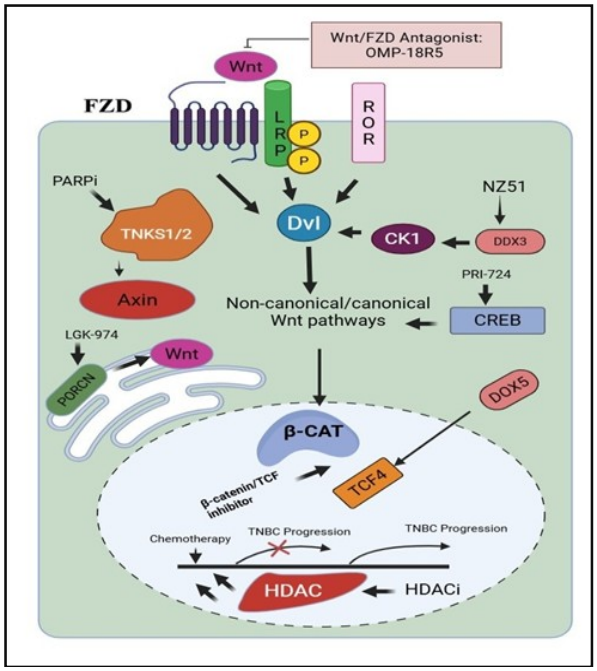

Figure 2. Wntsignaling Pathway

Notch receptor Signaling pathway: The Notch receptor signaling pathway regulates survival, proliferation and differentiation of cells. It involves interaction between Notch receptor and ligands such as Jagged and Delta-like proteins (18,19). Aberrant activation of Notch signaling contributes to tumor development and poor prognosis in TNBC (20–22).

TNBCs have been associated with notch expression, and researchers anticipate that monoclonal antibodies that target receptors can lower the HES and HEY-Lfamilies.The monoclonal antibody targeting the delta-like ligand 4 Notch ligand effectively cured TNBC (23). These medications are called as γ secretase complexes by working at proteolytic cleavage(24).The Notch pathway is displayed, along with the points where it can be inhibited is shown in Figure 3.

NF-κB Pathway: NF- kB is a major transcription factor that is related to inflammation,immune function and cell survival. NF-kB was found to stimulate tumor growth, angiogenesis, and apoptotic resistance in TNBC (25,26).

Inhibitors targeting NF-κBsignalinghave shown potential in preclinical studies, although many lack specificity. Compounds such as plumbagin have demonstrated the capacity to reduce TNBC cell growth and cause apoptosis by inhibiting this pathway (27,28).

Pathophysiological Features of TNBC

Epithelial–Mesenchymal Transition (EMT): Epithelial-mesenchymal transition (EMT) is a dynamic and

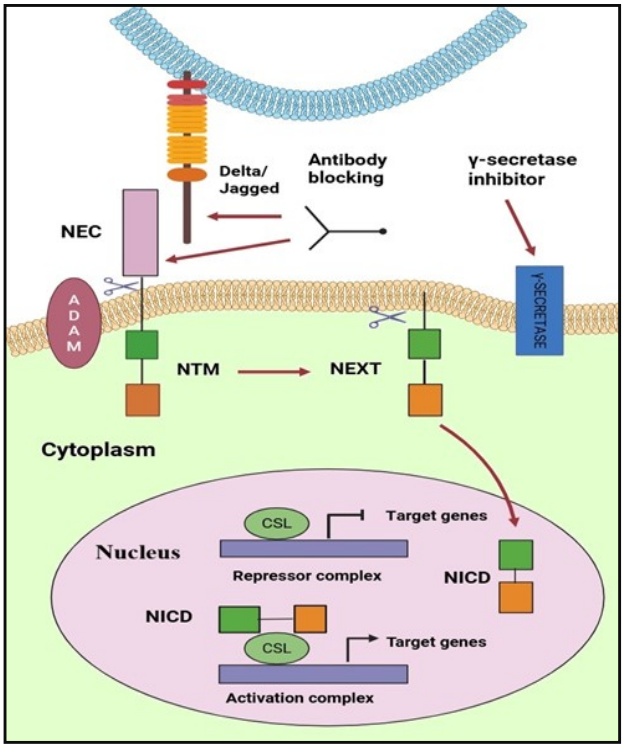

Figure 3. A diagram of Notch signaling in clinical development depicts the activation pathway started by ligand contact with the Notch receptor. γ-secretase and ADAM proteases cleave the receptor, which release the Notch intracellular domain (NICD). γ-secretase inhibitors and monoclonal antibodies that target Notch receptors and block Notch signaling. Once inside the nucleus, NICD associates with CSL, transforming the repressor complex into an activator of Notch target genes. Neuroendocrine Carcinoma (NEC), Notch transmembrane fragment (NTM), truncated extracellular segment (NEXT), CSL, and NICD are all essential components

reversibleprocess influenced by microenvironment signals, with important role in embryonic development, and cancer progression, notably in treatment resistance and tumorigenesis. EMT is characterised by changes in cell polarity, cytoskeletal structure, which are marked by specific proteins.

In TNBC,EMT is indicated by increased levels of mesenchymal markers, along with decreased level of epithelial marker, promotingtumor invasion and metastasis. whereas mesenchymal-epithelial transition (MET) is involved in normal tissue repair and development. Cytokines such as TNF-α and TNF-β from macrophages can stimulate EMT in TNBC, whereas mesenchymal-epithelial transition (MET) occurs during normal tissue repair and development(29,30).

Angiogenesis: Active angiogenesis in TNBC causes irregular blood vessels and prolonged intratumoral hypoxia, promoting an invasive tumor phenotype via activating HIF-α.This activation upregulates which in turn upregulates immunosuppressive factors like PD-L1 and the enzymes CD39 and CD73, causing ATP to be converted to adenosine, suppressing effector and NK cells.

VEGF-induced angiogenesis establishes an immunosuppressive atmosphere that prevents immune cell invasion and is important in regulating endothelial function. Abnormal neovascularisation in TNBC, defined by increased microvascular density and intratumoral VEGF levels, is associated with poorer survival outcomes (30,31).

Therapeutic Strategies for TNBC

Standard Chemotherapy

Anthracyclines (doxorubicin): Anthracyclines like doxorubicin and epirubicincan be used particularly to treat TNBC. A study reported a pCR rate in TNBC is 22%, compared to 11% for non-TNBC, although both groups had similar 3-year disease-free survival rates. In addition, TNBC patients tend to respond more favorably to treatment with cyclophosphamide and doxorubicin. Consequently, anthracyclines in conjunction with cyclophosphamide are extensively used in TNBC treatment (32).

Platinum agents: BRCA-associated breast cancer and basal-like subtypes exhibit similar characteristics, prompting interest in platinum compounds like carboplatin and cisplatin to treat triple-negative breast cancer. Platinum induce double-strand breaks and DNA crosslinks, leading to cell death in BRCA-mutant cells due to impaired DNA repair. Among various platinum agents, cisplatin regimens showed the highest efficacy. To enhance response and survival, platinum should be combined with other chemotherapy drugs, such asepirubicin and 5-fluorouracil, which have been shown to improve treatment outcomes in various cancer types(32).

Taxanes: A class of tubulin polymerizers known as ‘taxanes’, (including paclitaxel, docetaxel, and cabazitaxel) is effective in treating TNBC. Research indicates TNBC patients experience improved outcomes with a treatment regimen comprising four cycles of 5-fluorouracil, epirubicin, and FEC,rather than six cycles of FEC alone. Efficacy improves with reduced treatment frequency. Ixabepilone, amicrotubule Stabiliser, is effectivefor taxane-refractory breast cancer, offering an alternative for patients tolerant to platinum, and enhancing progression- free survival when combined with capecitabine in metastatic TNBC resistant to taxanes and anthracyclines(32).

Targeted Therapies

PARP inhibitors: PARP (poly (ADP-ribose) polymerase) plays a vital role in mending single-stranded DNA breaks via the base excision repair mechanism. BRCA mutations, commonly found in TNBC, hinder proper DNA repair, rendering PARP inhibitors promising for inducing cell death in affected tumors. These inhibitors also enhance the effectiveness of various cancer treatments and are in clinical development, including drugs like BSI-201 and olaparib. However, resistance to PARP inhibition occurs through mechanisms like stabilizing mutant BRCA proteins, necessitating ongoing research to overcome these resistance factors. (32,33).

TK inhibitors: Tyrosine kinases pivotal in cancer progression withinhibitors like dasatinib and pazopanib showing anti-tumoreffect in TNBC by targeting multiple signaling pathways. Specifically, dasatinib, an oral inhibitor initially known as BMS-354825, effectively hinders TNBC cell line proliferation, both alone and in combination with cisplatin. It is under investigation as a singular treatment or alongside chemotherapy for TNBC. A study indicates that combining topotecan and pazopanib considerably enhances anti-tumor effects and survival in a mouse orthotopic implanted breast tumor model, reducing vascularity and increasing apoptosis, although its selectivity for TNBC remains unknown (32).

EGFR inhibitors: Over 50 percent of triple-negative breast tumors (TNBCs) have EGFR overexpression, resulting in an unfavourable prognosis and therapeutic efficacy. This has initiated therapeutic trials employing anti-EGFR agents, such as cetuximab, which attaches to the extracellular domain of EGFR (32).

Immunotherapy: For TNBC recent developments in immunotherapy have showed encouraging outcomes. In clinical trials, Drugs that target PD-1 and PD-L1 in the immune system have been linked to higher survival rates. Pembrolizumab, when used with chemotherapy, has worked very well for people with TNBC. Additional strategies include CAR-T cell therapy and tumor vaccines, which aim to enhance anti-tumor immune responses (34).

Plant-Derived Bioactive Agents in TNBC Treatment

Polyphenols

Curcumin: Turmeric, scientifically known as *Curcuma longa*, comprises the polyphenol curcumin, which has been used in clinical settings for aliments such as depression and arthritis. Curcumin demonstrated anti-inflammatory, antioxidant, and anticancer properties, especially against triple-negative breast cancer. It affects many signaling pathways, including EGFR, mTOR,JAK-STAT, and HIF-1 resulting in apoptosis and reduced cell growth. Research demonstrates that curcumin promotes cell death in TNBC while reducing tumor growth in animal models by blocking essential oncogenic pathways, including Notch-1 and PI3K/Akt. Its capacity to influence gene expression and signaling indicates a significant therapeutic potential in cancer therapy (35,36).

Resveratrol: Resveratrol, a polyphenolic compound found in grape and wine derivatives, enhances apoptosis in triple-negative breast cancer (TNBC) cells by lowering POLD1 expression. Resveratrol interferes with cancer stem cell (CSC) pathways in both TNBC and non-TNBC cells by lowering the levels of phosphorylated PI3K and Akt along with mTOR pathway and suppressing the NF-kB pathway. It also decreases HDAC activity by 50%, activates p44/42 MAPK temporarily, and downregulates MMP-2 and MMP-9, preventing metastasis in TNBC (36,37).

Epigallocatechin-3-gallate: Epigallocatechin-3-gallate (EGCG) has potential anticancer activities, along with anti-inflammatory and antifibrotic effects. It suppresses the proliferation of TNBC cells by targeting DNA methyltransferase and catechol-o-methyltransferase. This leads to the re-expression of critical genes such as RAR-B and MGMT, while also modulating apoptosis-related pathways.

EGCG promotes TNBC cell growth suppression by increasing levels of caspase enzymes and decreasing expression of TP53. Furthermore, it enhances chemotherapeutic efficacy through various signaling pathways, including β-catenin, mTOR, MAPK, and NF-κβ and alters the expression of apoptosis regulators such as RIPK2 and XIAP. Notably, EGCG also downregulates MCL1 and IGF1R and inhibits GOLM1 expression through the β-catenin pathway (35).

Flavonoids

Quercetin: Quercetin, a flavonolwhich primarily exhibits antioxidant properties and can also be found in various fruits and buckwheat. It targets IGF1R and related pathways to inhibit metastasis in MDA-231 line. Quercetin shows a dose-dependent effect, activating IGF1R and downstream kinases, with an IC50 of 20 μM, leading to reduced activity of p21 and GADD45, thus inducing apoptosis. It disrupts nuclear β-catenin accumulation, decreasing cyclin D1 and c-Myc expression by promoting MET (Mesenchymal to-epithelial transition), with an IC50 of 50 μM in vitro. In vivo, quercetin at 50 mg/kg reduces fatty acid synthase (FASN) expression and tumor development, further promoting apoptosis by down-regulating β-catenin and caspase-3 activity (35,37).

Genistein: A naturally occurring isoflavone, genistein (Gen), exhibits anti-breast cancer properties, specifically in triple-negative breast cancer (TNBC). Genistein targets multiple CSC pathways in TNBC by suppressing Notch-1 pathway and inhibiting NF-kB. It lowers TNBC cyclin B, increases p2, reduces CDK-1 transcription, and promotes G2 arrest through upregulation of the MAPKsignaling pathway and phosphorylation of ERK/2, which is also associated with breast cancer metastasis(36,37).

Alkaloids

Berberine: A naturally occurring active principle with promising anticancer action is berberine (BBR) derived form like Berberis and Coptis,demonstrating significant anticancer properties. BBR caused cell cycle arrest across various cancer cell types and downregulates 33 genes associated with cell cycle progression and differentiation. Its antiproliferative effect is enhanced when combined with T. cordifolia extract, which also suppresses colon cancer-related gene expression. Overall, BBR mimics the therapeutic effects of T. cordifolia, indicating its crucial role in mediating these effects(37).

Terpenoids

Ursolic acid: A pentacyclic triterpene commonly present in numerous fruits and vegetables, ursolic acid (UA) exhibits anti-inflammatoryand antioxidant effects. It suppresses Nf-kB and inducing cell cycle arrest, it prevents cancer cells like MDA-231 and N from growing and invanding. Additionally, UA may affect the p53 signaling pathways, which might reduce TNBC cell proliferation by lowering PLK1 and CCNB1 expression, suggesting its potential as a therapeutic agent for TNBC(35).

Future Perspectives and Research Directions: Future perspectives in triple-negative breast cancer (TNBC) treatment emphasise innovativenovel plant-based therapies targeting specific molecular pathways and modulating the tumor microenvironment (TME) to supress metastasis and overcome chemoresistance. Phytochemicals can enhance immunomodulation, potentially through regulatory T cell (Treg) targeting, and their combination with immunotherapies like immune checkpoint inhibitors may improve outcomes. However, there's a need for extensive clinical studies to verify the safety and effectiveness of these treatments. Future research should explore molecular target for these therapies, the reprogramming of the u, and expand clinical studies to integrate personalised treatment approaches using multiomics and immunomolecular strategies (38–40).

CONCLUSION

Plant-derived bioactive compounds have notable potential in managing TNBC by targeting multiple pathways related to tumor growth, metastasis, and immune evasion. These compounds can inhibit cancer stem cell maintenance and immunosuppression, offering a comprehensive strategy for

TNBC treatment. Combining these phytochemicals with existing therapies, such as chemotherapy and emerging targeted therapies, may augment therapeutic effectiveness, mitigate adverse effects, and increase patient outcomes, leading to more effective and personalized treatments for TNBC (36,38).

List of abbreviation

Abbrevation	Full form
ADAM	A DisintegrinAnd Metalloproteinase
ATP	Adenosine triphosphate
BBR	Berberine
BL1	Basal-like 1
BL2	Basal-like 2
BRCA	Breast cancer gene
BRCA1	Breast cancer type 1
CAR-T	Chimeric Antigen Receptor T-cell
CCNB1	Cyclin B1
CD39	Cluster of Differentiation 39
CD73	Cluster of Differentiation 73
CDK-1	Cyclin-Dependent Kinase 1
CSC	Cancer Stem Cell
CSL	CBF1, Suppressor of Hairless, Lag-1
CTLA-4	Cytotoxic T-Lymphocyte-Associated protein 4
DNA	Deoxyribonucleic acid
EGCG	Epigallocatechin-3-gallate
EGF	Epidermal Growth Factor
EGFR	Epidermal Growth Factor Receptor
EMT	Epithelial-Mesenchymal Transition
ER	Estrogen Receptor
ERK/2	Extracellular signal-regulated kinase /2
FASN	Fatty Acid Synthase
FEC	5-fluorouracil, epidoxorubicin and cyclophosphamide
FZD6	Frizzled Class Receptor 6
G2	Grade 2
GADD45	The Growth Arrest and DNA Damage-inducible 45
GOLM1	Golgi Membrane Protein 1
HDAC	Histone Deacetylase
HER2	Human Epidermal Growth Factor Receptor 2
HES	Hairy and Enhancer of Split
HEY-L	Hairy/Enhancer-of-split related with YRPW motif-like family of proteins
HIF-α	Hypoxia-Inducible Factor-1 alpha
HIF-1	Hypoxia-inducible factor-1
IC50	Half-maximal Inhibitory Concentration
IGF1R	Insulin-like Growth Factor 1 Receptor
IM	Immunomodulatory
JAK-STAT	Janus Kinase (JAK)—Signal Transducer and Activator of Transcription (STAT)
MAPK	Mitogen-Activated Protein Kinase
MCL1	Myeloid Cell Leukemia-1
MDA-231	MD Anderson—Metastatic Breast—231
MDA-468	MD Anderson Mammary Breast 468
MET	Mesenchymal-Epithelial Transition
MGMT	O6-methylguanine-DNA-methyltransferase gene
MMP-2	Matrix Metalloproteinase-2
MMP-9	Matrix Metalloproteinase-9
mTOR	mammalian Target of Rapamycin
mTORC1	Mechanistic Target of Rapamycin Complex 1
mTORC2	Mechanistic Target of Rapamycin Complex 2
NEC	Neuroendocrine Carcinoma
NEXT	Notch Extracellular Truncation
NF-kB	Nuclear Factor-kappaB
NICD	Notch intracellular domain
NK	Natural Killer
NTM	Notch Transmembrane Fragment
PARP	Poly (ADP-ribose) Polymerase
pCR	Pathological Complete Response
PD-1	Programmed Cell Death Protein 1
PD-L1	Programmed Death-Ligand 1
PI3K	Phosphoinositide 3-Kinase
PIK3CA	phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.
PLK1	Polo-like kinase 1
POLD1	DNA Polymerase Delta 1, Catalytic Subunit
PR	Progesterone Receptor
PTEN	Phosphatase and Tensin homolog deleted on chromosome 10
RAR-B	Retinoic Acid Receptor beta
RIPK2	Receptor-Interacting Protein Kinase 2 [1]
TME	Tumor Microenvironment
TNBC	Triple-Negative Breast Cancer
TNF-α	Tumor Necrosis Factor-alpha
TNF-β	Tumor Necrosis Factor-beta
UA	Ursolic Acid
VEGF	Vascular Endothelial Growth Factor
WNT3A	Wingless-type MMTV integration site family, member 3A
WNT5A	Wingless-type MMTV integration site family, member 5A
WNT11	Wingless-type MMTV integration site family, member 11
XIAP	X-linked Inhibitor of Apoptosis Protein

REFERENCES

Schick, Jason, Ritchie, Raquel P, and Restini, Carolina, Breast Cancer Therapeutics and Biomarkers: Past, Present, and Future Approaches, Breast Cancer: Basic and Clinical Research 15 (2021).

Dent, Rebecca, Trudeau, Maureen, Pritchard, Kathleen I., Hanna, Wedad M., Kahn, Harriet K., Sawka, Carol A., Lickley, Lavina A., Rawlinson, Ellen, Sun, Ping, and Narod, Steven A., Triple-Negative Breast Cancer: Clinical Features and Patterns of Recurrence, Clinical Cancer Research 13 no. 15 (2007) 4429–4434.

Szulc, Anna, and Woźniak, Marta, Targeting Pivotal Hallmarks of Cancer for Enhanced Therapeutic Strategies in Triple-Negative Breast Cancer Treatment—In Vitro, In Vivo and Clinical Trials Literature Review, Cancers 16 no. 8 (2024) 1483.

Li, Qingzhou, Ye, Zhen, Wang, Guilin, Chen, Yuhui, Deng, Jinghong, Wang, Dong, and Wang, Yumei, Natural Products as Novel Therapeutic Agents for Triple-Negative Breast Cancer: Current Evidence, Mechanisms, Challenges, and Opportunities, Molecules 30 no. 6 (2025) 1201.

Barchiesi, Giacomo, Roberto, Michela, Verrico, Monica, Vici, Patrizia, Tomao, Silverio, and Tomao, Federica, Emerging

Role of PARP Inhibitors in Metastatic Triple Negative Breast Cancer. Current Scenario and Future Perspectives, Frontiers in Oncology 11 (2021).

Yin, Li, Duan, Jiang-Jie, Bian, Xiu-Wu, and Yu, Shi-cang, Triple-negative breast cancer molecular subtyping and treatment progress, Breast Cancer Research 22 no. 1 (2020) 61.

Hubalek, Michael, Czech, Theresa, and Müller, Hannes, Biological Subtypes of Triple-Negative Breast Cancer, Breast Care 12 no. 1 (2017) 8–14.

Akhand, Saeed S., Chen, Hao, Purdy, Stephen Connor, Liu, Zian, Anderson, Joshua C., Willey, Christopher D., and Wendt, Michael K., Fibroblast growth factor receptor facilitates recurrence of minimal residual disease following trastuzumab emtansine therapy, npj Breast Cancer 7 no. 1 (2021) 5.

Zhao, Shen, Zuo, Wen-Jia, Shao, Zhi-Ming, and Jiang, Yi-Zhou, Molecular subtypes and precision treatment of triple-negative breast cancer, Annals of Translational Medicine 8 no. 7 (2020) 499–499.

Lehmann, Brian D, Bauer, Joshua A, Schafer, Johanna M, Pendleton, Christopher S, Tang, Luojia, Johnson, Kimberly C, Chen, Xi, Balko, Justin M, Gómez, Henry, Arteaga, Carlos L, Mills, Gordon B, Sanders, Melinda E, and Pietenpol, Jennifer A, PIK3CA mutations in androgen receptor-positive triple negative breast cancer confer sensitivity to the combination of PI3K and androgen receptor inhibitors, Breast Cancer Research 16 no. 4 (2014) 406.

Fruman, David A., and Rommel, Christian, PI3K and cancer: lessons, challenges and opportunities, Nature Reviews Drug Discovery 13 no. 2 (2014) 140–156.

Zaytseva, Yekaterina Y., Valentino, Joseph D., Gulhati, Pat, and Mark Evers, B., mTOR inhibitors in cancer therapy, Cancer Letters 319 no. 1 (2012) 1–7.

Arcaro, Alexandre, and Guerreiro, Ana, The Phosphoinositide 3-Kinase Pathway in Human Cancer: Genetic Alterations and Therapeutic Implications, Current Genomics 8 no. 5 (2007) 271–306.

Ali, Remah, and Wendt, Michael K, The paradoxical functions of EGFR during breast cancer progression, Signal Transduction and Targeted Therapy 2 no. 1 (2017) 16042.

Pohl, SÖ-G, Brook, N, Agostino, M, Arfuso, F, Kumar, A P, and Dharmarajan, A, Wntsignaling in triple-negative breast cancer, Oncogenesis 6 no. 4 (2017) e310–e310.

Zhu, Yichao, Tian, Yinhui, Du, Jun, Hu, Zhenzhen, Yang, Ling, Liu, Jiaojing, and Gu, Luo, Dvl2-Dependent Activation of Daam1 and RhoA Regulates Wnt5a-Induced Breast Cancer Cell Migration, PLoS ONE 7 no. 5 (2012) e37823.

Dean, Michael, Fojo, Tito, and Bates, Susan, Tumour stem cells and drug resistance, Nature Reviews Cancer 5 no. 4 (2005) 275–284.

Gu, Yisu, Masiero, Massimo, and Banham, Alison H., Notch signaling: its roles and therapeutic potential in hematological malignancies, Oncotarget7 no. 20 (2016) 29804–29823.

Palomero, T, Barnes, K C, Real, P J, Glade Bender, J L, Sulis, M L, Murty, V V, Colovai, A I, Balbin, M, and Ferrando, A A, CUTLL1, a novel human T-cell lymphoma cell line with t(7;9) rearrangement, aberrant NOTCH1 activation and high sensitivity to γ-secretase inhibitors, Leukemia20 no. 7 (2006) 1279–1287.

Speiser, Jodi J., Erşahin, Çağatay, and Osipo, Clodia, The Functional Role of Notch Signaling in Triple-Negative Breast Cancer, pp. 277–306.

Brennan, Keith, and Clarke, Robert B., Combining Notch inhibition with current therapies for breast cancer treatment, Therapeutic Advances in Medical Oncology 5 no. 1 (2013) 17–24.

Soares, R., Balogh, G., Guo, S., Gärtner, F., Russo, J., and Schmitt, F., Evidence for the Notch Signaling Pathway on the Role of Estrogen in Angiogenesis, Molecular Endocrinology 18 no. 9 (2004) 2333–2343.

Benedito, Rui, Roca, Cristina, Sörensen, Inga, Adams, Susanne, Gossler, Achim, Fruttiger, Marcus, and Adams, Ralf H., The Notch Ligands Dll4 and Jagged1 Have Opposing Effects on Angiogenesis, Cell 137 no. 6 (2009) 1124–1135.

Chan, Steven M., Weng, Andrew P., Tibshirani, Robert, Aster, Jon C., and Utz, Paul J., Notch signals positively regulate activity of the mTOR pathway in T-cell acute lymphoblastic leukemia, Blood 110 no. 1 (2007) 278–286.

Fan, Yongjun, Dutta, Jui, Gupta, Nupur, Fan, Gaofeng, and Gélinas, Céline, Regulation of Programmed Cell Death by NF-κB and its Role in Tumorigenesis and Therapy, pp. 223–250.

Ossovskaya, V., Wang, Y., Budoff, A., Xu, Q., Lituev, A., Potapova, O., Vansant, G., Monforte, J., and Daraselia, N., Exploring Molecular Pathways of Triple-Negative Breast Cancer, Genes & Cancer 2 no. 9 (2011) 870–879.

Begalli, Federica, Bennett, Jason, Capece, Daria, Verzella, Daniela, D'Andrea, Daniel, Tornatore, Laura, and Franzoso, Guido, Unlocking the NF-κB Conundrum: Embracing Complexity to Achieve Specificity, Biomedicines 5 no. 3 (2017) 50.

Messeha, Samia S., Zarmouh, Najla O., Mendonca, Patricia, Alwagdani, Hayfaa, Kolta, Malak G., and Soliman, Karam F. A., The inhibitory effects of plumbagin on the NF-κB pathway and CCL2 release in racially different triple-negative breast cancer cells, PLOS ONE 13 no. 7 (2018) e0201116.

Błaszczak, Ewa, Miziak, Paulina, Odrzywolski, Adrian, Baran, Marzena, Gumbarewicz, Ewelina, and Stepulak, Andrzej, Triple-Negative Breast Cancer Progression and Drug Resistance in the Context of Epithelial–Mesenchymal Transition, Cancers 17 no. 2 (2025) 228.

Rosado-Sanz, María, Martínez-Alarcón, Nuria, Abellán-Soriano, Adrián, Golfe, Raúl, Trinidad, Eva M., and Font de Mora, Jaime, Cytokine Networks in Triple-Negative Breast Cancer: Mechanisms, Therapeutic Targets, and Emerging Strategies, Biomedicines 13 no. 8 (2025) 1945.

Zhou, Zijian, and Zhou, Qin, Immunotherapy resistance in triple-negative breast cancer: Molecular mechanisms, tumor microenvironment, and therapeutic implications, Frontiers in Oncology 15 (2025).

Yao, Hui, He, Guangchun, Yan, Shichao, Chen, Chao, Song, Liujiang, Rosol, Thomas J., and Deng, Xiyun, Triple-negative breast cancer: is there a treatment on the horizon?,Oncotarget8 no. 1 (2017) 1913–1924.

Zhu, Shuangli, Wu, Yuze, Song, Bin, Yi, Ming, Yan, Yuheng, Mei, Qi, and Wu, Kongming, Recent advances in targeted strategies for triple-negative breast cancer, Journal of Hematology& Oncology 16 no. 1 (2023) 100.

Xiong, Nating, Wu, Heming, and Yu, Zhikang, Advancements and challenges in triple-negative breast cancer: a comprehensive review of therapeutic and diagnostic strategies, Frontiers in Oncology 14 (2024).

Kaleem, Mohammed, Thool, Mandar, Dumore, Nitin G., Abdulrahman, Abdulrasheed O., Ahmad, Wasim, Almostadi, Amal, Alhashmi, Mohammad Hassan, Kamal, Mohammad Amjad, and Tabrez, Shams, Management of triple-negative breast cancer by natural compounds through different mechanistic pathways, Frontiers in Genetics 15 (2024).

Ke, Danny Yu Jia, El-Sahli, Sara, and Wang, Lisheng, The Potential of Natural Products in the Treatment of Triple-negative Breast Cancer, Current Cancer Drug Targets 22 no. 5 (2022) 388–403.

Ravindra B. Malabadi, Sadiya MR, Kiran P. Kolkar, Simuzar S. Mammadova, Raju K. Chalannavar, Himansu Baijnath, Lavanya L, and Antonia Neidilê Ribeiro Munhoz, Triple Negative Breast Cancer (TNBC): Signalling pathways-Role of plant-based inhibitors, Open Access Research Journal of Biology and Pharmacy 10 no. 2 (2024) 028–071.

Emara, Hadir M., Allam, Nageh K., and Youness, Rana A., A comprehensive review on targeted therapies for triple negative breast cancer: an evidence-based treatment guideline, Discover Oncology 16 no. 1 (2025) 547.

Battogtokh, Gantumur, Obidiro, Onyinyechi, and Akala, Emmanuel O., Recent Developments in Combination Immunotherapy with Other Therapies and Nanoparticle-Based Therapy for Triple-Negative Breast Cancer (TNBC), Cancers 16 no. 11 (2024) 2012.

Malla, Rama Rao, Vasudevaraju, Padmaraju, Vempati, Rahul Kumar, Rakshmitha, Marni, Merchant, Neha, and Nagaraju, Ganji Purnachandra, Regulatory T cells: Their role in triple-negative breast cancer progression and metastasis, Cancer 128 no. 6 (2022) 1171–1183.

****