Breast Cancer: Targets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

The Role of Actin-Binding Proteins in Breast Cancer Progression

Nayla Majeda Alfarafisa[1], Regina Indrasari Herriyanto[2], Karina Fitria Alhaq[2], Mh Busra Fauzi[3], Astrid Feinisa Khairani[1]

[1]Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Jawa, Indonesia; [2]Undergraduate Programme, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Jawa, Indonesia; [3]Departement of Tissue Engineering & Regenerative Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Correspondence: Nayla Majeda Alfarafisa, Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Jalan Raya Bandung – Sumedang Km 21, Jatinangor, Sumedang, Bandung, West Java, 45363, Indonesia, Tel +62-22-7795594, Email nayla.alfarafisa@unpad.ac.id

Abstract: Actin and actin-binding proteins (ABPs) regulate fundamental processes in cancer progression, including migration, invasion, and metastasis. Despite increasing evidence from in vitro and in vivo studies, the role and prognostic significance of actin and ABPs in breast cancer remain unclear due to the lack of a comprehensive review. This review, conducted in 2024 following PRISMA 2020 guidelines, systematically searched PubMed and Scopus using MeSH terms and text words to identify English-language original studies on actin and actin-binding proteins (ABPs) in breast cancer progression. Inclusion criteria were applied during title/abstract screening and full-text review, focusing on studies reporting cell migration, invasion, or metastasis. A total of 176 studies were included, comprising in vitro and in vivo models that investigated ABPs such as Fascin, Cofilin, and Mena, along with key signaling pathways like Rho GTPase, PI3K, and MAPK/ERK. Extracted data included cell lines, interventions, signaling pathways involved in actin or ABP regulation, the mechanism by which each intervention impacted actin remodeling or ABP expression, and outcomes such as migration, invasion, or metastasis. Prominent ABPs such as fascin, cofilin, and Mena were found to influence actin cytoskeletal dynamics, cell motility, and metastatic behavior. Findings highlight the prognostic relevance of ABPs and their therapeutic potential, although clinical translation remains limited by biological complexity and lack of standardized detection tools.

Keywords: actin, actin-binding proteins, biomarker, breast cancer, cancer progression

Introduction

Breast cancer is the most commonly diagnosed cancer among women worldwide and remains a significant cause of cancer-related mortality. According to GLOBOCAN, in 2022, there were nearly 2.3 million new cases and over 650,000 deaths due to breast cancer globally.[1] Despite advances in screening and treatment, challenges such as metastasis and therapeutic resistance continue to limit clinical outcomes. Tumor heterogeneity, shaped by genetic and epigenetic alterations, contributes to variability in treatment response and disease progression.[2] Moreover, invasive breast cancer can evade immune surveillance and adapt to the tumor microenvironment to support its survival and dissemination.[3]

As a result, tumor heterogeneity, therapeutic resistance, and immune evasion, contribute to delays in detecting disease progression, making it more challenging to assess prognosis accurately and initiate timely interventions. Delayed detection can lead to increased mortality rates, delayed treatment initiation, and potentially reduced survival rates for patients. Developing targeted therapies hinges on accurate and timely diagnosis, which could significantly impact patient outcomes and overall survival rates. Conventional prognostic tools such as mammography, ultrasound, Magnetic Resonance Imaging (MRI), and tissue biopsy are widely used in clinical settings. However, they present notable limitations, including low sensitivity in dense breast tissue, operator dependence, high costs, and invasive procedures.[4,5]

The actin cytoskeleton is a critical component of eukaryotic cells, existing in two dynamic forms, G-actin (Globular actin) and F-actin (Filamentous actin), that interconvert to regulate cell shape and movement.[6] G-actin is a monomeric protein that serves as the fundamental unit of F-actin. Through the process of actin polymerization, these monomers

https://doi.org/10.2147/BCTT.S566309
Received: 9 September 2025
Accepted: 3 February 2026
Published: 19 February 2026

assemble into dynamic actin filaments that play a crucial role in cell migration. This process predominantly occurs at the leading edge of the lamellipodium and begins with nucleation, where actin monomers form a stable nucleus assisted by actin-binding proteins such as formin and the Arp2/3 complex. This is followed by elongation, during which ATP-bound actin monomers are added to the barbed ends of filaments, a process supported by profilin. Meanwhile, cross-linking proteins such as filamin-A and α-actinin stabilize and stiffen the filaments, enabling them to exert force on the cell membrane. Actin filaments also undergo treadmilling, in which monomers are added at the barbed end and removed at the pointed end, maintaining filament dynamics. Regulation of this process involves thymosin β4, which sequesters G-actin, capping proteins that control filament growth, and severing proteins like cofilin that generate new barbed ends, collectively enabling the formation of lamellipodia, filopodia, and pseudopodia necessary for cell movement.[7,8] This dynamic remodeling is tightly controlled by actin-binding proteins (ABPs), which govern the polymerization, stabilization, and spatial organization of actin filaments.[9] These include monomer-binding proteins, actin-nucleating proteins, polymerases, capping proteins, severing proteins, cross-linking proteins, bundling proteins, and branching proteins.[10]

In cancer, aberrant expression or regulation of ABPs contributes to increased motility, invasiveness, and drug resistance.[11] ABPs also play key roles in epithelial-to-mesenchymal transition (EMT), a process that facilitates metastasis and is associated with poor prognosis.[11,12] Epithelial–mesenchymal transition (EMT) is a dynamic cellular program in which epithelial cells lose their apicobasal polarity and stable cell–cell adhesion while acquiring mesenchymal traits that enhance motility and invasiveness. A central event in EMT is the downregulation of E-cadherin, a key component of adherens junctions, whose loss destabilizes epithelial integrity and weakens intercellular cohesion. Concurrently, cells undergo cytoskeletal reorganization marked by the upregulation of vimentin, an intermediate filament protein that supports mesenchymal phenotypes by promoting EMT-associated transcriptional programs, facilitating microtubule polarization for directional migration, and maintaining cellular force balance. Together, the loss of E-cadherin–mediated adhesion and the gain of vimentin-dependent cytoskeletal plasticity enable cells to transition toward a migratory and invasive state characteristic of EMT.[13–15] Additionally, actin-rich structures such as lamellipodia, filopodia, and invadopodia enable directional migration and invasion through the extracellular matrix, which is crucial for metastasis.[16–19] Therefore, mutations or dysregulation of ABPs enhance cell motility, invasiveness, and metastatic potential, thereby accelerating cancer progression.

Given their central role in cancer cell migration, invasion, and cytoskeletal reorganization, actin and ABPs hold great potential as prognostic biomarkers in breast cancer. Several studies have linked specific ABPs to aggressive tumor behavior and treatment outcomes, yet their clinical utility remains underexplored. Unlike previous reviews that focus broadly on actin in cancer biology, this review specifically investigates the prognostic value of actin and ABPs in breast cancer. By highlighting mechanistic roles and relevant evidence from in vitro and in vivo studies, this review aims to uncover potential biomarkers that could improve early prognosis, risk stratification, and personalized treatment strategies. Ultimately, understanding actin dynamics may provide new avenues for clinical intervention and better patient outcomes.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines were used. This review was conducted in 2024. This study is guided by the DSEO (Disease, Settings, Exposure, Outcome) research framework. The disease of interest (D) is breast cancer, examined in a global setting (S). The study focuses on actin (E) and its role in the progression of breast cancer (O), specifically in processes such as cell migration, cell invasion, and metastasis. A comprehensive literature search was conducted in PubMed and Scopus without year limitation to identify relevant studies investigating the role of actin and actin-binding proteins (ABPs) in breast cancer progression. The search was conducted in 2024 and followed a structured approach that combined Medical Subject Headings (MeSH) and free-text terms (Title/Abstract), with Boolean operators used to connect relevant domains: (1) actin cytoskeleton, (2) microfilament proteins, (3) breast cancer, and (4) progression/metastasis.

In PubMed, the search strategy utilized MeSH terms such as “Actin Cytoskeleton”, “Microfilament Proteins”, “Breast Neoplasms”, and “Neoplasm Metastasis”. Each MeSH term was expanded using a set of text words (Title/Abstract) to capture variations and synonyms found in the literature. For the actin cytoskeleton domain, text words included: Cytoskeletons, Actin, Cytoskeleton, Actin, Actin Filaments, Actin Filament, Filament, Actin, Filaments, Actin, Actin

Microfilaments, Actin Microfilament, Microfilament, Actin, and Microfilaments, Actin. For the microfilament proteins domain, terms such as Actin-Binding Proteins, Actin Binding Proteins, Binding Protein, Actin, Protein, Actin Binding, and Proteins, Actin-Binding were included. The breast cancer concept was addressed using both MeSH and text words (Title/Abstract), including: Breast Cancer, Breast Carcinoma, Breast Neoplasm, Breast Neoplasms, Breast Tumors, Mammary Cancer, Mammary Cancers, Breast Carcinomas, Breast Malignant Neoplasm(s), Malignant Tumor of Breast, Breast Malignant Tumor(s), Cancer of Breast, Cancer of the Breast, and Human Mammary Carcinomas. To identify studies discussing cancer progression or metastasis, terms such as Metastasis, Progressivity, Progressive, Continuing, Continuous, Growing, Developing, and Gradual were used alongside the MeSH term "Neoplasm Metastasis". Initial search in PubMed applied filters to include only English-language articles, free full text, and to exclude reviews.

In Scopus, where MeSH terms are not available, equivalent free-text keywords were searched within the Title, Abstract, and Keyword fields. Boolean operators was applied consistently to combine synonymous terms within each concept using OR, and different concepts using AND. Initial search in Scopus was filtered to include only English-language articles, exclude review articles, and limited to "All Open Access" documents. The results were limited to articles published in English with full-text availability. Review articles, non-English papers, and documents without full-text access were excluded. The results were imported into Rayyan.ai for blinded screening, duplicate detection, and selection based on inclusion and exclusion criteria.

The selection of studies was conducted in two phases: (1) a screening of titles and abstracts and (2) a full-text evaluation. The initial screening was performed independently by two reviewers (RIH and KFA) using the Rayyan.ai platform, which facilitated blinded review and duplicate detection. Any uncertainties or disagreements regarding study inclusion during this phase were discussed with two additional reviewers (NMA and AFK) for clarification. In the second phase, full-text articles that passed the initial screening were reviewed by RIH, applying the same eligibility criteria. Any uncertainties or questions during this process were discussed with NMA and AFK. Specific reasons for exclusion such as irrelevant outcomes or populations were documented accordingly. This process followed the PRISMA 2020 flow diagram (Supplementary Figure 1), ensuring that all inclusion and exclusion steps were transparently reported. Extracted data were synthesized narratively and thematically, focusing on the mechanisms by which actin and ABPs influence breast cancer progression. Feedback on the manuscript draft was provided by NMA, AFK, and MBF to enhance clarity and scientific precision.

Results

A total of 362 studies were identified through preliminary database searches. The initial step in the process involved excluding articles based on their titles and abstracts. This led to the inclusion of 216 articles. In the subsequent screening phase, which involved a comprehensive evaluation of the complete text, several articles were excluded from the study because they did not provide any data or observations related to actin or ABPs. Alternatively, articles were excluded if they did not employ breast cancer cells as the primary model in their research. A total of 176 articles were included in the analysis. Of these, 167 studies utilized in vitro breast cancer models, with 59 also integrating in vivo validation. An additional nine studies employed in vivo models exclusively, such as murine xenografts and genetically engineered mouse models. The following Venn diagram offers a visual representation of the overlapping study designs observed among the included articles (Supplementary Figure 2).

Experimental manipulation of actin-regulatory pathways consistently demonstrates that breast cancer cell migration is governed by coordinated signaling networks that control cytoskeletal plasticity rather than actin abundance alone (Supplementary Table 1). Among these, the Rho family of GTPases; RhoA, Rac1, and Cdc42 acts as a central signaling hub translating extracellular stimuli into actin reorganization, as evidenced by marked alterations in migratory behavior following their inhibition or dominant-negative expression across multiple breast cancer models. Rac1 and Cdc42 are particularly critical for front-edge dynamics, where they drive lamellipodia and filopodia formation and enable persistent, directional migration.[20] In contrast, RhoA primarily regulates actomyosin contractility and stress fiber assembly. Its contribution to migration appears more context-dependent, reflecting its dual role in maintaining cytoskeletal integrity

and generating rear-end contractile forces, such that its disruption may variably enhance or suppress net cell movement depending on cellular context.

Beyond upstream signaling, proteins that directly regulate actin filament turnover are key determinants of migratory efficiency. Profilin-1, which facilitates actin polymerization by maintaining the ATP–actin monomer pool, exhibits a context-dependent role in invasiveness, while cofilin-mediated filament severing is essential for sustaining actin dynamics required for motility.[21,22] In contrast, fascin functions as a dominant pro-migratory actin-bundling protein by stabilizing filopodia and invadopodia structures. Inhibition of fascin–actin interactions consistently suppresses migration and invasion across diverse breast cancer models, highlighting fascin as one of the most promising cytoskeletal targets for anti-metastatic intervention.[23,24]

Hormonal and transcriptional programs further modulate actin remodeling in breast cancer. Steroid hormones, including estrogen, progestins, and androgens, markedly influence cytoskeletal organization in hormone receptor–positive tumors, underscoring the role of nuclear receptor signaling in licensing migratory competence.[25–28] Similarly, activation of the TGF-β pathway promotes epithelial–mesenchymal transition (EMT), a process characterized by extensive actin cytoskeleton reprogramming, whereas inhibition of this axis reverses metastatic traits.[29–31]

Finally, the actin cytoskeleton functions as an integrative platform for diverse environmental cues. Metabolic inputs such as glucose availability, mechanical signals from the extracellular matrix, pharmacological and natural compounds, and post-transcriptional regulation by microRNAs collectively fine-tune actin dynamics.[32–40] Notably, several miRNAs simultaneously target multiple actin regulators, acting as endogenous suppressors of invasive cytoskeletal programs. Loss of these regulatory miRNAs may facilitate metastasis, while their restoration represents a promising strategy to restrain cancer cell motility by targeting the actin network at multiple levels.[41,42] All associated data are summarized in Supplementary Table 1 and 3.

Most in vitro studies have utilized breast cancer cell lines to assess the effects of gene modifications or novel compounds on actin cytoskeletal dynamics and actin-binding proteins (ABPs), particularly on cell migration and invasion. These findings were often extended in vivo using animal models, with primary outcomes focusing on tumor volume and lung metastasis. The characteristics of the included in vitro studies, including the cell lines used, types of interventions, key signaling pathways involved, evaluated biomarkers (particularly those related to actin and/or actin-binding proteins), and the observed effects on migration and/or invasion, are summarized in Supplementary Table 1. The earliest in vitro studies exploring ABPs in breast cancer appeared in 1998, with the first in vivo studies in 2001, and research has continued to this day, showing ongoing interest in how actin cytoskeletal regulation affects cancer development and its potential clinical applications.

The most commonly used cell lines in vitro included MDA-MB-231, MCF-7, T47D, 4T1, and BT549, representing a spectrum of molecular subtypes from luminal A to triple-negative breast cancer. The frequency of breast cancer cell lines used across the included studies was summarized in Supplementary Table 2. The experimental designs encompassed gene silencing (eg, RNA interference/short hairpin RNA knockdown), overexpression systems, and pharmacological interventions targeting actin polymerization or ABP function. In addition to phenotypic observations, functional assays assessing migration, invasion, morphology, and EMT markers were widely utilized. Despite the diverse study designs, a strong positive correlation was consistently found between the expression of several ABPs and increased migration, invasion, and metastasis. In contrast, several studies also reported that suppression or loss of specific ABPs led to reduced motility and invasive potential, highlighting the nuanced and context-dependent roles of these proteins.

Across the included studies, a recurrent set of ABP, notably Fascin, α-actinin, Arp2/3 complex, Cofilin, and Filamin A, were identified as key modulators of cell motility and cytoskeletal remodeling in breast cancer cells. Changes in F-actin polymerization status were commonly used as readouts of cytoskeletal remodeling. Table 1 below summarizes the biomarkers evaluated for actin cytoskeletal dynamics across the included studies. The standard functional assessments employed included Boyden chamber and Matrigel invasion assays. Notably, suppression of ABP function or that of its upstream regulators consistently reduced the motility and invasive potential of cancer cells. In contrast, overexpression was commonly associated with enhanced migration, EMT, and metastatic spread. Conversely, the upregulation or expression of specific ABPs often resulted in the induction of EMT-like features and the promotion of cell dissemination. However, further analysis shows that ABPs can have varying effects. For example, while Filamin A downregulation has been shown to impair migration in several models, the role of Profilin-1 appears more complex. Reduced expression of Profilin-1 is in fact often associated with increased motility in breast cancer and other cancer cell types, whereas its overexpression tends to inhibit migration. These

Table 1 Frequency of Biomarkers Assessed in in vitro and in vivo Studies

Biomarker/Actin-Related Readout	In vitro	In vivo
Actin/F-actin organization	132	53
Fascin	8	4
Cofilin	5	3
Mena	5	7
MenaINV	3	5
Ezrin	3	0
Cortactin	3	0
Actinin	2	0
Profilin	2	2
Girdin	2	1
Filamin A	2	2
MRTFs	2	0
Moesin	1	0
Tensin	1	1
CNN1	1	1
L-plastin	1	0
MTSS1	1	0
Actin-related protein 2/3 complex (ARPC2)	1	1
WAVE3	1	0
Afadin	1	2
Talin	1	0
Transgelin	1	1
PARVA	1	0
NMIIA	1	0
Paxillin	1	1
Migfilin	1	0
Coronin-1C	1	0
CAPG	1	1
Vinculin	0	1
Anillin	0	1

Notes: Actin and F-actin were classified as structural readouts of cytoskeletal remodeling rather than molecular biomarkers. In vivo evidence was reported only when directly supported by experimentally validated animal studies identified through the predefined search strategy.

findings emphasize that Profilin-1 and Filamin A, though both actin-binding proteins, exert distinct and sometimes opposing effects on cancer cell behavior depending on the cellular context.

In vivo studies have yielded translational insights into the influence of actin or ABPs modulation on tumor progression within a complex physiological environment. Among the 68 studies incorporating animal models (59 in vitro and in vivo and 9 exclusively in vivo), the majority used orthotopic mouse models, in which human or murine breast cancer cells were injected into the mammary fat pad (Supplementary Table 3). The interventions were diverse, most commonly consisting of either gene knockout or overexpression strategies, or the administration of novel compounds that had not previously been tested in breast cancer models. These in vivo studies were typically built upon prior in vitro experiments using the same interventions. The most frequently utilized breast cancer cell lines in the in vivo models were identified as MDA-MB-231, 4T1, MCF-7, and MTLn3 (Supplementary Table 2).

Additionally, the most frequently used animal models were SCID mice. The most frequently evaluated biomarker was filamentous actin, with Mena, the most commonly studied actin-binding protein, being the most frequently studied (Table 1). The majority of studies concentrated on evaluating breast cancer metastasis to the lungs, with fewer studies additionally assessing tumor volume.

The following table (Table 2) presents a comprehensive overview of the signaling pathways that were the primary focus of the majority of investigations in the included studies. The table illustrates the number of studies that have

Table 2 Frequency of Signaling Pathways Investigated in in vitro and in vivo Studies

Pathway	In vitro	In vivo
Rho GTPase	67	20
Actin Binding Protein	23	13
PI3K	15	5
MAPK/ERK	14	7
LIMK/Cofilin	6	2
TGF-β / Smad Signaling Pathway (Canonical Pathway)	5	3
FAK/Src	5	2
NF-κB	4	3
Non-canonical TGF-β Signaling Pathway (p38 MAPK Pathway)	2	0
Wnt/β-catenin	1	0
HIF-1 signaling pathway	1	1
mTORC1/S6K	1	0
Src/ERK	1	0
JAK/STAT	1	0
Integrin/FAK	1	1
RAGE	1	1
miR-206/TWF1/MKL1-SRF/IL11	1	1
Hippo	1	0
Wnt/PCP	1	1
JNK/c-Jun	1	1
PKC/Src/Rho	1	0

investigated each pathway in both in vitro and in vivo contexts, providing insights into the molecular mechanisms frequently examined regarding actin cytoskeletal regulation and breast cancer progression. The findings, when considered as a whole, emphasize the pivotal role of actin dynamics and ABP regulation in the cellular behaviors that are fundamental to the progression of breast cancer. The uniformity of the findings across disparate models and pathways underscores their prospective value as prognostic indicators and therapeutic targets.

Fascin, Cofilin, Mena, MenaINV, Ezrin, and Cortactin consistently emerged as the most frequently studied ABPs. Likewise, although various signaling pathways were explored, only a few pathways such as Rho GTPase, PI3K, MAPK/ERK, and LIMK/Cofilin, appeared repeatedly across studies, yet without consistent temporal focus. In conclusion, while several ABPs and associated signaling pathways have been studied extensively in the context of breast cancer, it remains difficult to determine which specific ABP is most consistently favored or prioritized across studies. Most ABPs such as Fascin, Cofilin, Mena, MenaINV, Ezrin, and Cortactin tend to promote cancer cell migration and invasion when overexpressed. However, certain ABPs like Profilin-1 demonstrate the opposite, where increased expression is associated with reduced migratory behavior. This contrast highlights that not all ABPs uniformly enhance metastatic potential.

Discussion

This review highlights the central role of the actin cytoskeleton and its associated actin-binding proteins (ABPs) in regulating breast cancer progression. The dynamic remodeling of the actin cytoskeleton is essential for key processes such as cell migration, invasion, and metastasis, which are hallmarks of aggressive tumor behavior.[43,44] While the functional involvement of ABPs such as Fascin, Cofilin, and Mena has been extensively characterized, their potential clinical relevance as prognostic or therapeutic biomarkers remains insufficiently elucidated in the current literature. These proteins facilitate the movement and penetration of cancer cells through the extracellular matrix, contributing to tumor dissemination. Notably, their expression levels are often elevated in highly invasive breast cancer subtypes, suggesting their potential value as biomarkers of disease progression and as targets for therapeutic intervention.

The shape and organization of filamentous actin (F-actin) critically influence breast cancer cell migration, invasion, and metastasis by forming specialized protrusions that facilitate movement and tissue penetration. These F-actin assemblies function as viscoelastic materials, combining resistance to flow with elastic energy storage, which enables cells to generate and sustain protrusive forces.[45] Lamellipodia, broad sheet-like F-actin networks at the leading edge of cells, generate protrusive forces through rapid actin polymerization, enabling directional migration in aggressive cancer cells.[43] Filopodia, thin finger-like F-actin bundles, extend beyond lamellipodia to sense the extracellular environment, guiding cell movement and enhancing adhesion to the extracellular matrix (ECM).[46,47] Invadopodia, dense F-actin-rich protrusions, degrade the ECM via protease secretion, allowing cancer cells to breach tissue barriers and metastasize.[48,49] The dynamic remodeling of F-actin within these structures determines their efficiency in promoting motility and invasion. Disrupting F-actin formation impairs these protrusions, reducing cell migration, invasion, and metastatic potential.

Among ABPs examined, fascin impacts actin by cross-linking (bundling) actin filaments into tightly packed, parallel bundles that support cellular protrusions such as filopodia. These filopodia act as dynamic sensory probes at the cell membrane, allowing cells to explore their microenvironment and facilitate processes such as migration and invasion.[50–53] In addition, cofilin dynamically regulates actin by severing and depolymerizing filaments at low concentrations. Cofilin-1 binds along actin filaments, twisting their helical structure and inserting between actin subunits, which weakens lateral contacts and induces fractures, creating new barbed and pointed ends for polymerization and depolymerization.[54] Conversely, at high levels, it stabilizes filaments as cofilactin.[55] It indirectly supports actin bundling by generating free barbed ends and supplying monomers for polymerization, thereby facilitating structures such as lamellipodia (via rapid actin turnover) and filopodia (via localized remodeling). In lamellipodia, cofilin drives protrusion by creating new barbed ends, whereas in filopodia, it fine-tunes length and flexibility by balancing bundled and cofilactin states.[56,57]

On the other hand, Mena promotes actin polymerization and filament elongation at lamellipodial edges and filopodia tips by protecting barbed ends from capping proteins, enchancing actin filament organization without direct bundling.[58,59] This activity leads to the stabilization of membrane protrusions by organizing actin into parallel arrays, which indirectly supports the formation of bundled filopodia structures.[60] Mena, particularly its invasive isoform MenaINV, guides

directional migration (haptotaxis) by binding to α5β1 integrin, enhancing cancer cell sensitivity to fibronectin gradients through increased integrin association, FAK signaling, and actin polymerization, enabling tumor cells to migrate toward ECM-rich areas like blood vessels and metastatic sites.[61] Collectively, these ABPs work synergistically to shape actin architecture that facilitates cancer cell migration and invasion during metastasis.

Numerous signaling pathways influence actin dynamics. Among them, the pathways most frequently identified in this review include the Rho GTPase, PI3K, MAPK/ERK, and LIMK/Cofilin Pathways (Figure 1). The Rho GTPase family, comprising RhoA, Rac1, and Cdc42, regulates the formation of actin filaments into stress fibers, lamellipodia, and filopodia, respectively. RhoA promotes stress fiber formation by activating ROCK, which stabilizes actin filaments through LIMK-dependent cofilin inhibition.[62,63] ROCK functions downstream of RhoA to regulate actomyosin contractility and stress fiber formation by controlling myosin activity together with MLCK. ROCK inhibits myosin phosphatase through MYPT1 phosphorylation, thereby sustaining MLC phosphorylation at Ser19/Thr18 and enhancing non-muscle myosin II ATPase activity, which generates strong and stable contractile forces and promotes central/ventral stress fiber formation. In parallel, MLCK directly phosphorylates MLC at Ser19 to initiate myosin activation, primarily driving peripheral stress fibers that support dynamic protrusion and retraction at the cell edge. Through this coordinated action, MLCK provides localized and rapid myosin activation, while ROCK maintains and reinforces contractility, together managing stress fiber organization and cellular mechanical tension.[64]

In contrast, Rac1 stimulates lamellipodia formation by activating the WAVE complex. WAVE, as part of the WAVE regulatory complex (WRC), which binds to the A- and D-sites of the WRC and induces a conformational change that releases the autoinhibited VCA domain. Once exposed, the V (WH2) motif of WAVE binds a G-actin monomer and

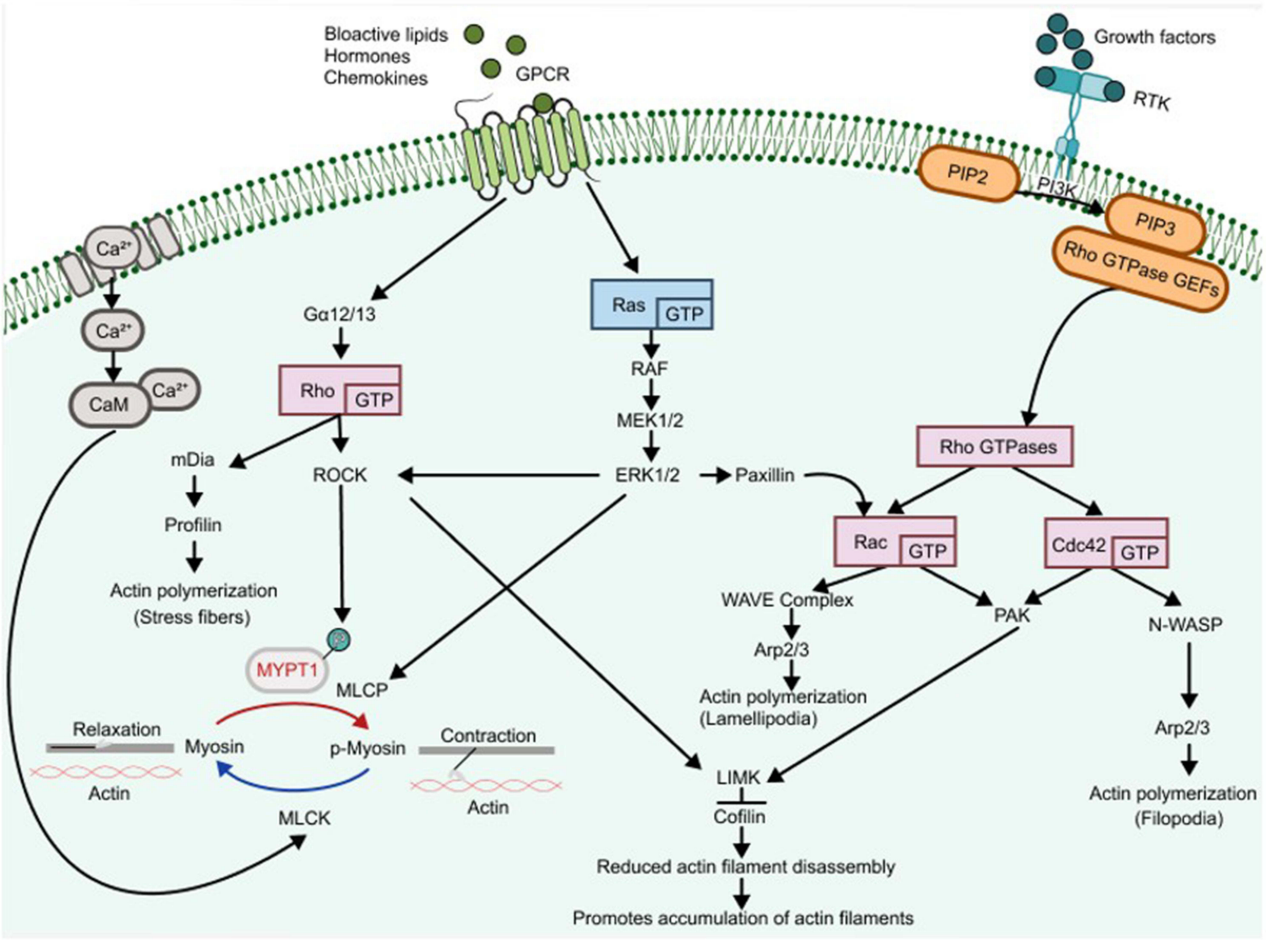

Figure 1 Schematic representation of key signaling pathways regulating actin cytoskeleton remodeling and actin-binding proteins in breast cancer progression.

delivers it directly to the inactive Arp2/3 complex, positioning the actin between Arp2 and Arp3. Simultaneously, the CA region binds Arp2/ARPC1 and Arp3, stabilizing their rearrangement into a short-pitch, actin-dimer–like configuration. The bound G-actin effectively bridges Arp2 and Arp3, promoting the rotation and alignment of Arp3 so that the complex mimics the first two subunits of a new filament. This stabilized nucleation seed then associates with a pre-existing "mother" filament, enabling rapid elongation of a new, branched "daughter" filament from the barbed end at approximately 70°, with additional actin monomers supplied to sustain growth.[65–67] Meanwhile, Cdc42 regulates filopodia assembly by activating N-WASP, another Arp2/3 activator, which nucleates actin filaments that bundle into parallel arrays, enabling directional sensing and polarized migration.[62,63]

The PI3K pathway drives actin cytoskeletal remodeling through its lipid mediators PIP2 (phosphatidylinositol 4,5-bisphosphate) and PIP3 (phosphatidylinositol 3,4,5-trisphosphate), with PI3K phosphorylating PIP2 to PIP3, which engage PH domain-containing GEFs to activate Rho GTPases (Rac1 and Cdc42).[68,69] Rac1 signaling also leads to PAK activation, which in turn activates LIMK, blocking cofilin's ability to break down actin filaments and thereby helping to maintain cytoskeletal structure.[69–71] The PI3K/AKT pathway indirectly regulates RhoA-mediated actin remodeling by inhibiting GSK-3β through serine-9 phosphorylation. Ser9 phosphorylation creates a pseudosubstrate that blocks the kinase active site, thereby reducing GSK-3β dependent phosphorylation of cytoskeletal regulators such as APC and β-catenin. When active, GSK-3β suppresses APC and CLIP-170/CLASP mediated microtubule–actin interactions, favoring RhoA/ROCK driven stress fiber formation while limiting protrusive activity and cell migration.[72–74]

By coordinating both the creation of new actin branches and the protection of existing filaments, this PI3K driven process generates the sustained membrane protrusions that allow cancer cells to move directionally and invade surrounding tissues during metastasis.

The MAPK/ERK pathway coordinates cell migration by linking focal adhesion turnover and actin remodeling through paxillin and Rac signaling. Upon activation, ERK1/2 phosphorylates paxillin, enhancing its role as a scaffold at focal adhesions and promoting dynamic adhesion turnover. Phosphorylated paxillin recruits Rac-specific GEFs such as DOCK180 and PIX, leading to localized Rac activation at the cell's leading edge. Active Rac stimulates actin polymerization via the WAVE/Arp2/3 complex, driving lamellipodia formation and membrane protrusion. This ERK/paxillin/Rac signaling axis enables spatial coordination of protrusive and adhesive forces, supporting directed migration.[75]

Most of the experimental studies included in this review have utilized gene knockdown techniques to investigate the therapeutic potential of targeting ABPs and their regulators. Silencing or knockdown of genes such as Mena, Fascin, Filamin A, Profilin, and Palladin has resulted in reduced motility and invasion of breast cancer cells in both in vitro and/or in vivo models.[21,24,61,76–78] Additionally, several actin/ABP-targeting compounds have been identified that interfere with actin dynamics or ABP function. Chelidonine disrupts actin cytoskeleton reorganization, Vitamin C inhibits F-actin assembly, and Telocinobufagin induces the collapse of actin filaments.[79–81] SH-479, a derivative of betulinic acid, alters microfilament architecture, while NP-G2-044 specifically inhibits fascin activity.[82,83] These compounds suppress breast cancer cell migration and/or invasion in vitro (eg, chelidonine, vitamin C, SH-479, Telocinobufagin), while NP-G2-044 demonstrates anti-metastatic efficacy in preclinical animal models. Their ability to effectively target actin/ABP involved in breast cancer progression makes them promising candidates for breast cancer therapy. However, current direct pharmacological targeting of actin itself is associated with significant cytotoxicity due to its essential role in normal cellular function, limiting its clinical applicability in cancer therapy. These findings are primarily supported by studies employing well-established breast cancer models. In vitro experiments frequently utilized MDA-MB-231, MCF-7, T47D, 4T1, and BT549 cell lines, while in vivo investigations commonly involved MDA-MB-231, 4T1, MCF-7, and MTLn3 models, which were inoculated into animal models to establish primary tumors. Importantly, in vivo studies further validate these mechanistic findings, demonstrating that modulation of ABP expression—either via overexpression, knockdown, or pharmacological inhibition—consistently alters metastatic potential and tumor burden in orthotopic and xenograft mouse models. For instance, inhibition of Mena or Cofilin using small interfering RNA (siRNA) has been shown to significantly reduce lung metastasis and intravasation, underscoring the translational relevance of these targets. This RNA interference–based approach selectively degrades Mena- or Cofilin-specific mRNAs, leading to reduced protein expression and impaired metastatic potential.[22,84]

The current clinical study on actin-binding proteins in breast cancer has reached a significant milestone. Transcriptome analyses and tissue-based studies using datasets such as TCGA and METABRIC have identified several ABPs as potential prognostic markers. Among them, cofilin-1, shows a strong association with metastatic potential.[85] Other ABPs, including transgelin, fascin, and MenaINV, have also demonstrated clinical relevance in relation to disease progression.[61,86–88] A small number of studies have explored ABPs as circulating biomarkers. For example, elevated serum levels of Actinin-4 are associated with aggressive disease features such as higher tumor grade and lymph node involvement, suggesting potential for non-invasive diagnostics.[89] However, therapeutic applications remain limited. To date, only one ABP-targeting compound, the fascin inhibitor NP-G2-044, has progressed into Phase I and II clinical trials. This shows that several actin-binding proteins are associated with breast cancer prognosis and metastasis, with limited evidence supporting their use as circulating biomarkers, while only one ABP-targeting therapy has advanced to early-phase clinical trials.

Among the actin-related components and ABPs investigated in breast cancer, actin itself remains the most extensively analyzed biomarker, particularly in relation to F-actin. Among specific ABPs, Fascin, Cofilin, Mena, MenaINV, and Profilin are the most frequently studied due to their critical roles in reorganizing the cytoskeleton and promoting cancer cell motility. In vivo models, especially those involving Mena and MenaINV, highlight their roles in metastasis. The pathways most commonly associated with ABP activity include the Rho GTPase pathway, which regulates actin-based structures such as lamellipodia, filopodia, and stress fibers through key effectors like Rac1, Cdc42, and RhoA. Other prominent signaling pathways include PI3K and MAPK/ERK, which facilitate actin remodeling through mechanisms such as LIMK-mediated cofilin regulation, activation of the Arp2/3 complex, and regulation of focal adhesion dynamics. Together, these actin regulators and pathways underscore the importance of cytoskeletal remodeling in breast cancer progression, supporting their potential as prognostic biomarkers and therapeutic targets.

Despite promising findings, several barriers continue to hinder the clinical translation of ABPs research in breast cancer. The research landscape remains fragmented, with many studies investigating different ABPs without a consistent or strategic direction. A significant methodological limitation is the overreliance on TNBC models, particularly the MDA-MB-231 cell line, while other molecular subtypes such as HER2-positive and luminal B are significantly underrepresented. This imbalance reduces the generalizability of findings across the diverse landscape of breast cancer. Moreover, only a limited number of studies have explored how ABPs interact with the tumor microenvironment, including critical components such as extracellular matrix stiffness, structural proteins, and immune cell infiltration, which are known to influence tumor progression and therapeutic response.

Beyond experimental design issues, the biological complexity and context-dependent roles of ABPs further complicate their clinical application. ABP expression and function vary across different breast cancer subtypes and disease stages, contributing to inconsistent outcomes in both prognostic and therapeutic studies. The lack of standardized, clinically validated assays for detecting ABP levels adds another layer of difficulty, especially given that ABP expression can be dynamically regulated by microenvironmental factors such as scaffold stiffness.[33] Although certain ABPs show promise as biomarkers, their inconsistent behavior across tumor contexts undermines their reliability in clinical practice. Tumor heterogeneity further complicates their use, as ABP expression varies across breast cancer subtypes and stages.[90]

On the therapeutic side, efforts to target actin and ABPs face significant challenges due to their fundamental roles in essential cellular processes. Actin and ABPs are involved in critical physiological functions, including muscle contraction in the heart and skeletal muscles, making systemic modulation risky due to potential cardiotoxicity.[11] Their pleiotropic involvement in numerous signaling pathways further complicates the design of selective drugs. Although preclinical models have demonstrated that disrupting the actin cytoskeleton can suppress cancer cell migration and invasion, achieving tumor-specific effects without damaging normal tissues remains a significant challenge. Moving forward, the development of effective therapies will depend on strategies that can precisely target cancer-specific actin dynamics while preserving essential functions in healthy cells.

Despite the current limitations, growing research continues to unveil promising opportunities for leveraging actin and ABPs in breast cancer management. Advances in targeted drug delivery systems, such as nanoparticle-based drug delivery, offer the potential to inhibit tumor-associated ABP functions while minimizing systemic toxicity selectively.[91–93] Furthermore, the integration of ABPs into multi-omics approaches and machine learning models may

enhance their utility as prognostic or predictive biomarkers, especially in stratifying patients based on metastatic risk or treatment response. Circulating ABPs such as Actinin-4 also hold promise in the development of minimally invasive diagnostic tools, enabling early detection or disease monitoring through liquid biopsy.[89] In addition, combinatorial strategies that incorporate ABP-targeting agents alongside chemotherapy or immunotherapy are being explored to enhance therapeutic outcomes.[94] Taken together, the current body of evidence highlights the multifaceted role of actin cytoskeletal regulators in promoting breast cancer aggressiveness. Further exploration into their prognostic value, especially when integrated with molecular subtype stratification, may yield clinically actionable biomarkers to enhance precision oncology approaches in breast cancer management.[95–233]

Conclusion

This review emphasizes that remodeling of the actin cytoskeleton, driven by key actin-binding proteins (ABPs) and various signaling pathways, plays a vital role in breast cancer progression by regulating cell motility and invasion. Numerous in vitro and in vivo studies consistently highlight the crucial roles of ABPs such as Fascin, Cofilin, and Mena, along with signaling pathways like Rho GTPase, PI3K, and MAPK/ERK, in mediating actin cytoskeletal changes that promote breast cancer progression. Despite these consistent findings, several challenges hinder the clinical application of ABP-related research. Tumor heterogeneity, the diverse functions of ABPs, and the absence of standardized detection methods limit their use as universal biomarkers or therapeutic targets. Additionally, because actin and ABPs are involved in essential physiological processes, systemic targeting raises concerns about potential toxicity. However, emerging strategies such as nanoparticle-based drug delivery, ABP-targeting agents like fascin inhibitors, and incorporating ABPs into biomarker tools like liquid biopsies and molecular profiling present promising approaches that could unlock the clinical potential of actin dynamics for personalized breast cancer treatment.

Abbreviations

ABP, actin-binding protein; APC, adenomatous polyposis coli; Arp2/3, actin-related protein 2/3; Cdc42, cell division cycle 42; CLASP, cytoplasmic linker–associated protein; CLIP-170, cytoplasmic linker protein of 170 kDa; DOCK180, dedicator of cytokinesis 180; DSEO, Disease, Settings, Exposure, Outcome; ECM, extracellular matrix; EMT, epithelial-to-mesenchymal transition; ERK, extracellular signal-regulated kinase; FAK, focal adhesion kinase; GEF, guanine nucleotide exchange factor; GSK-3β, glycogen synthase kinase-3β; HER2, human epidermal growth factor receptor 2; LIMK, LIM domain kinase; MAPK, mitogen-activated protein kinase; mDia, mammalian diaphanous; METABRIC, Molecular Taxonomy of Breast Cancer International Consortium; MeSH, Medical Subject Headings; MRI, Magnetic Resonance Imaging; N-WASP, neuronal Wiskott-Aldrich syndrome protein; PI3K, phosphoinositide 3-kinase; PIX, PAK-interacting exchange factor; PIP2, phosphatidylinositol 4,5-bisphosphate; PIP3, phosphatidylinositol 3,4,5-trisphosphate; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ROCK, Rho-associated protein kinase; SCID, severe combined immunodeficiency; TCGA, The Cancer Genome Atlas; TNBC, triple-negative breast cancer; WAVE, Wiskott-Aldrich syndrome protein family verprolin-homologous protein.

Acknowledgments

The authors would like to thank all colleagues and institutions who provided valuable support and discussions during the preparation of this manuscript. This work was supported by Universitas Padjadjaran under Grant Hibah Artikel Review (5317/UN6.C/PT.02/2025). The funding body had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.

Disclosure

The author(s) report no conflicts of interest in this work.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: Cancer J Clinicians*. 2024;74(3):229–263. doi:10.3322/caac.21834

2. Proietto M, Crippa M, Damiani C, et al. Tumor heterogeneity: preclinical models, emerging technologies, and future applications. *Front Oncol*. 2023;13(April):1–24. doi:10.3389/fonc.2023.1164535
3. Salemme V, Centonze G, Cavallo F, Defilippi P, Conti L. The crosstalk between tumor cells and the immune microenvironment in breast cancer: implications for immunotherapy. *Front Oncol*. 2021;11(March):1–20. doi:10.3389/fonc.2021.610303
4. He Z, Chen Z, Tan M, et al. A review on methods for diagnosis of breast cancer cells and tissues. *Cell Prolif*. 2020;53(7):1–16. doi:10.1111/cpr.12822
5. Hashimoto K, Nishimura S, Ito T, Oka N, Akagi M. Limitations and usefulness of biopsy techniques for the diagnosis of metastatic bone and soft tissue tumors. *Ann Med Surg*. 2021;68(May):102581. doi:10.1016/j.amsu.2021.102581
6. Dominguez R, Holmes KC. Actin structure and function. *Annu Rev Biophys*. 2011;40(1):169–186. doi:10.1146/annurev-biophys-042910-155359
7. Muñoz-Lasso DC, Romá-Mateo C, Pallardó FV, Gonzalez-Cabo P. Much more than a scaffold: cytoskeletal proteins in neurological disorders. *Cells*. 2020;9(2):1–43. doi:10.3390/cells9020358
8. Bearer EL. Role of actin polymerization in cell locomotion: molecules and models. *Am J Respir Cell Mol Biol*. 1993;8(6):582–591. doi:10.1165/ajrcmb/8.6.582
9. Balta E, Kramer J, Samstag Y. Redox regulation of the actin cytoskeleton in cell migration and adhesion: on the way to a spatiotemporal view. *Front Cell Dev Biol*. 2021;8(January):1–11. doi:10.3389/fcell.2020.618261
10. Pollard TD. Actin and actin-binding proteins. *Cold Spring Harb Perspect Biol*. 2016;8:a018226.
11. Izdebska M, Zielińska W, Hałas-Wiśniewska M, Grzanka A. Involvement of actin and actin-binding proteins in carcinogenesis. *Cells*. 2020;9(10):1–20. doi:10.3390/cells9102245
12. Shankar J, Nabi IR. Actin cytoskeleton regulation of epithelial mesenchymal transition in metastatic cancer cells. *PLoS One*. 2015;10(3):1–12. doi:10.1371/journal.pone.0119954
13. Leggett SE, Hruska AM, Guo M, Wong IY. The epithelial-mesenchymal transition and the cytoskeleton in bioengineered systems. *Cell Commun Signal*. 2021;19(1):1–24. doi:10.1186/s12964-021-00713-2
14. Liu CY, Lin HH, Tang MJ, Wang YKVimentin contributes to epithelial-mesenchymal transition cancer cell mechanics by mediating cytoskeletal organization and focal adhesion maturation. *Oncotarget*. 2015; 6(18):15966.
15. Lamouille S, Xu J, Derynck R. Molecular mechanisms of epithelial–mesenchymal transition. *Nat Rev Mol Cell Biol*. 2014;15(3):178–196. doi:10.1038/nrm3758
16. Vinzenz M, Nemethova M, Schur F, et al. Actin branching in the initiation and maintenance of lamellipodia. *J Cell Sci*. 2012;125(11):2775–2785. doi:10.1242/jcs.107623
17. Schäfer C, Faust U, Kirchgeßner N, Merkel R, Hoffmann B. The filopodium: a stable structure with highly regulated repetitive cycles of elongation and persistence depending on the actin cross-linker fascin. *Cell Adhes Migr*. 2011;5(5):431–438. doi:10.4161/cam.5.5.17400
18. Beaty BT, Condeelis J. Digging a little deeper: the stages of invadopodium formation and maturation. *Eur J Cell Biol*. 2014;93(10–12):438–-444. doi:10.1016/j.ejcb.2014.07.003
19. Svitkina T. The actin cytoskeleton and actin-based motility. *Cold Spring Harb Perspect Biol*. 2018;10(1):1–21. doi:10.1101/cshperspect.a018267
20. Bouzahzah B, Albanese C, Ahmed F, et al. Rho family GTPases regulate mammary epithelium cell growth and metastasis through distinguishable pathways. *Mol Med*. 2001;7(12):816–830. doi:10.1007/bf03401974
21. Zou L, Jaramillo M, Whaley D, et al. Profilin-1 is a negative regulator of mammary carcinoma aggressiveness. *Br J Cancer*. 2007;97(10):1361–1371. doi:10.1038/sj.bjc.6604038
22. Tahtamouni LH, Shaw AE, Hasan MH, Yasin SR, Bamburg JR. Non-overlapping activities of ADF and cofilin-1 during the migration of metastatic breast tumor cells. *BMC Cell Biol*. 2013;14(1):1. doi:10.1186/1471-2121-14-45
23. Majchrzak K, Lo Re D, Gajewska M, et al. Migrastatin analogues inhibit canine mammary cancer cell migration and invasion. *PLoS One*. 2013;8(10):1–13. doi:10.1371/journal.pone.0076789
24. Al-Alwan M, Olabi S, Ghebeh H, et al. Fascin is a key regulator of breast cancer invasion that acts via the modification of metastasis-associated molecules. *PLoS One*. 2011;6(11):e27339. doi:10.1371/journal.pone.0027339
25. Giretti MS, Fu XD, De Rosa G, et al. Extra-nuclear signalling of estrogen receptor to breast cancer cytoskeletal remodelling, migration and invasion. *PLoS One*. 2008;3(5):e2238. doi:10.1371/journal.pone.0002238
26. Fu XD, Giretti MS, Goglia L, et al. Comparative actions of progesterone, medroxyprogesterone acetate, drospirenone and nestorone on breast cancer cell migration and invasion. *BMC Cancer*. 2008;8:1–14. doi:10.1186/1471-2407-8-166
27. Montt-Guevara MM, Shortrede JE, Giretti MS, et al. Androgens regulate T47D cells motility and invasion through actin cytoskeleton remodeling. *Front Endocrinol*. 2016;7(SEP):1–10. doi:10.3389/fendo.2016.00136
28. Tahtamouni L, Alzghoul A, Alderfer S, et al. The role of activated androgen receptor in cofilin phospho-regulation depends on the molecular subtype of TNBC cell line and actin assembly dynamics. *PLoS One*. 2022;17(12). doi:10.1371/journal.pone.0279746
29. Brunet S, Sardon T, Zimmerman T, et al. Characterization of the TPX2 domains involved in microtubule nucleation and spindle assembly in xenopus nucleation around chromatin and functions in a network of other molecules, some of which also are regulated by. *Mol Biol Cell*. 2004;15(December):5318–5328. doi:10.1091/mbc.E04
30. Sun J, He H, Xiong Y, et al. Fascin protein is critical for transforming growth factor β protein-induced invasion and filopodia formation in spindle-shaped tumor cells. *J Biol Chem*. 2011;286(45):38865–38875. doi:10.1074/jbc.M111.270413
31. Taylor MA, Davuluri G, Parvani JG, et al. Upregulated WAVE3 expression is essential for TGF-β-mediated EMT and metastasis of triple-negative breast cancer cells. *Breast Cancer Res Treat*. 2013;142(2):341–353. doi:10.1007/s10549-013-2753-1
32. Oh M, Batty S, Banerjee N, Kim TH. High extracellular glucose promotes cell motility by modulating cell deformability and contractility via the cAMP-RhoA-ROCK axis in human breast cancer cells. *Mol Biol Cell*. 2023;34(8):1–15. doi:10.1091/mbc.E22-12-0560
33. Berger AJ, Renner CM, Hale I, et al. Scaffold stiffness influences breast cancer cell invasion via EGFR-linked Mena upregulation and matrix remodeling. *Matrix Biol*. 2020;85–86(3):80–93. doi:10.1016/j.matbio.2019.07.006
34. Wang Z, Wu Y, Wang H, et al. Interplay of mevalonate and hippo pathways regulates RHAMM transcription via YAP to modulate breast cancer cell motility. *Proc Natl Acad Sci U S A*. 2014;111(1). doi:10.1073/pnas.1319190110

35. Khanfar MA, Youssef DTA, El Sayed KA. Semisynthetic latrunculin derivatives as inhibitors of metastatic breast cancer: biological evaluations, preliminary structure–activity relationship and molecular modeling studies. *ChemMedChem*. 2010;5(2):274–285. doi:10.1002/cmdc.200900430
36. Huang X, Sun D, Pan Q, et al. JG6, a novel marine-derived oligosaccharide, suppresses breast cancer metastasis via binding to cofilin. *Oncotarget*. 2014;5(11):3568–3578. doi:10.18632/oncotarget.1959
37. Menhofer MH, Kubisch R, Schreiner L, et al. The actin targeting compound Chondramide inhibits breast cancer metastasis via reduction of cellular contractility. *PLoS One*. 2014;9(11):1–9. doi:10.1371/journal.pone.0112542
38. Flamini MI, Gauna GV, Sottile ML, Nadin BS, Sanchez AM, Vargas-Roig LM. Retinoic acid reduces migration of human breast cancer cells: role of retinoic acid receptor beta. *J Cell Mol Med*. 2014;18(6):1113–1123. doi:10.1111/jcmm.12256
39. Jurmeister S, Baumann M, Balwierz A, et al. MicroRNA-200c represses migration and invasion of breast cancer cells by targeting actin-regulatory proteins FHOD1 and PPM1F. *Mol Cell Biol*. 2012;32(3):633–651. doi:10.1128/mcb.06212-11
40. Ljepoja B, Schreiber C, Gegenfurtner FA, et al. Inducible microRNA-200c decreases motility of breast cancer cells and reduces filamin A. *PLoS One*. 2019;14(11):1–18. doi:10.1371/journal.pone.0224314
41. Sundararajan V, Gengenbacher N, Stemmler MP, Kleemann JA, Brabletz T, Brabletz S. The ZEB1/miR-200c feedback loop regulates invasion via actin interacting proteins MYLK and TKS5. *Oncotarget*. 2015;6(29):27083–27096. doi:10.18632/oncotarget.4807
42. Pillman KA, Phillips CA, Roslan S, et al. miR-200/375 control epithelial plasticity-associated alternative splicing by repressing the RNA - binding protein Quaking. *EMBO J*. 2018;37(13):1–20. doi:10.15252/embj.201899016
43. Yamaguchi H, Condeelis J. Regulation of the actin cytoskeleton in cancer cell migration and invasion. *Biochim Biophys Acta*. 2007;1773 (5):642–652. doi:10.1016/j.bbamcr.2006.07.001
44. Saha T, Solomon J, Samson AO, Gil-Henn H. Invasion and metastasis as a central hallmark of breast cancer. *J Clin Med*. 2021;10(16):1–12. doi:10.3390/jcm10163498
45. Pollard TD, Cooper JA. Actin and actin-binding proteins. A critical evaluation of mechanisms and functions. *Annu Rev Biochem*. 1986;55 (1):987–1035. doi:10.1146/annurev.bi.55.070186.005011
46. Alieva NO, Efremov AK, Hu S, et al. Myosin IIA and formin dependent mechanosensitivity of filopodia adhesion. *Nat Commun*. 2019;10(1). doi:10.1038/s41467-019-10964-w
47. Pratiwi L, Elisa E, Sutanto H. Probing the protrusions: lamellipodia and filopodia in cancer invasion and beyond. *Mechanobiol Med*. 2024;2 (2):100064. doi:10.1016/j.mbm.2024.100064
48. Bayarmagnai B, Perrin L, Pourfarhangi KE, Graña X, Tüzel E, Gligorijevic B. Invadopodia-mediated ECM degradation is enhanced in the G1 phase of the cell cycle. *J Cell Sci*. 2019;132(20). doi:10.1242/jcs.227116
49. Greco MR, Antelmi E, Busco G, et al. Protease activity at invadopodial focal digestive areas is dependent on NHE1-driven acidic pHe. *Oncol Rep*. 2014;31(2):940–946. doi:10.3892/or.2013.2923
50. Heckman CA, Plummer HK. Filopodia as sensors. *Cell Signal*. 2013;25(11):2298–2311. doi:10.1016/j.cellsig.2013.07.006
51. Vignjevic D, Kojima SI, Aratyn Y, Danciu O, Svitkina T, Borisy GG. Role of fascin in filopodial protrusion. *J Cell Biol*. 2006;174(6):863–875. doi:10.1083/jcb.200603013
52. Jansen S, Collins A, Yang C, Rebowski G, Svitkina T, Dominguez R. Mechanism of actin filament bundling by fascin. *J Biol Chem*. 2011;286 (34):30087–30096. doi:10.1074/jbc.M111.251439
53. Tanaka M, Fujii Y, Hirano K, et al. Fascin in lamellipodia contributes to cell elasticity by controlling the orientation of filamentous actin. *Genes to Cells*. 2019;24(3):202–213. doi:10.1111/gtc.12671
54. Goode BL, Eskin J, Shekhar S. Mechanisms of actin disassembly and turnover. *J Cell Biol*. 2023;222(12):1–20. doi:10.1083/jcb.202309021
55. Bamburg JR, Bernstein BW. Roles of ADF/cofilin in actin polymerization and beyond. *F1000 Biol Rep*. 2010;2(1):1–7. doi:10.3410/B2-62
56. Hylton RK, Heebner JE, Grillo MA, Swulius MT. Cofilactin filaments regulate filopodial structure and dynamics in neuronal growth cones. *Nat Commun*. 2022;13(1):1–11. doi:10.1038/s41467-022-30116-x
57. Kiuchi T, Ohashi K, Kurita S, Mizuno K. Cofilin promotes stimulus-induced lamellipodium formation by generating an abundant supply of actin monomers. *J Cell Biol*. 2007;177(3):465–476. doi:10.1083/jcb.200610005
58. Barzik M, Kotova TI, Higgs HN, et al. Ena/VASP proteins enhance actin polymerization in the presence of barbed end capping proteins. *J Biol Chem*. 2005;280(31):28653–28662. doi:10.1074/jbc.M503957200
59. Bear JE, Svitkina TM, Krause M, et al. Antagonism between Ena/VASP proteins and actin filament capping regulates fibroblast motility. *Cell*. 2002;109(4):509–521. doi:10.1016/S0092-8674(02)00731-6
60. Rajadurai CV, Havrylov S, Coelho PP, et al. 5'-Inositol phosphatase SHIP2 recruits Mena to stabilize invadopodia for cancer cell invasion. *J Cell Biol*. 2016;214(6):719–734. doi:10.1083/jcb.201501003
61. Oudin MJ, Jonas O, Kosciuk T, et al. Tumor cell–driven extracellular matrix remodeling drives haptotaxis during metastatic progression. *Cancer Discov*. 2016;6(5):516–531. doi:10.1158/2159-8290.CD-15-1183
62. Spiering D, Hodgson L. Dynamics of the rho-family small GTPases in actin regulation and motility. *Cell Adhes Migr*. 2011;5(2):170–180. doi:10.4161/cam.5.2.14403
63. Mosaddeghzadeh N, Ahmadian MR. The rho family gtpases: mechanisms of regulation and signaling. *Cells*. 2021;10(7):1831. doi:10.3390/cells10071831
64. Kassianidou E, Hughes JH, Kumar S. Activation of ROCK and MLCK tunes regional stress fiber formation and mechanics via preferential myosin light chain phosphorylation. *Mol Biol Cell*. 2017;28(26):3832–3843. doi:10.1091/mbc.E17-06-0401
65. Lebensohn AM, Kirschner MW. Activation of the WAVE complex by coincident signals controls actin assembly. *Mol Cell*. 2009;36 (3):512–524. doi:10.1016/j.molcel.2009.10.024
66. Ding B, Yang S, Schaks M, et al. Structures reveal a key mechanism of WAVE regulatory complex activation by Rac1 GTPase. *Nat Commun*. 2022;13(1):1–13. doi:10.1038/s41467-022-33174-3
67. Helgeson LA, Nolen BJ. Mechanism of synergistic activation of Arp2/3 complex by cortactin and N-WASP. *Elife*. 2013;2013(2):1–26. doi:10.7554/eLife.00884
68. Johnson C, Rodgers W. Spatial segregation of phosphatidylinositol 4,5-bisphosphate (PIP2) signaling in immune cell functions. *Immunol Endocr Metab Agents Med Chem*. 2009;8(4):349–357. doi:10.2174/187152208787169233

69. Deng S, Leong HC, Datta A, Gopal V, Kumar AP, Yap CT. PI3K/AKT signaling tips the balance of cytoskeletal forces for cancer progression. *Cancers*. 2022;14(7):1–26. doi:10.3390/cancers14071652
70. Burridge K, Wennerberg K. Rho and rac take center stage. *Cell*. 2004;116(2):167–179. doi:10.1016/S0092-8674(04)00003-0
71. Cui D, Jiang X, Chen M, et al. Activation of Rac1 has an opposing effect on induction and maintenance of long-term potentiation in hippocampus by acting on different kinases. *Front Mol Neurosci*. 2021;14(August):1–10. doi:10.3389/fnmol.2021.720371
72. Liu J, Zhang Y, Xu R, et al. PI3K/Akt-dependent phosphorylation of GSK3β and activation of RhoA regulate Wnt5a-induced gastric cancer cell migration. *Cell Signal*. 2013;25(2):447–456. doi:10.1016/j.cellsig.2012.10.012
73. Hervé JC, Bourmeyster N. Rho GTPases at the crossroad of signaling networks in mammals. *Small GTPases*. 2015;6(2):43–48. doi:10.1080/21541248.2015.1044811
74. Kumar P, Lyle KS, Gierke S, Matov A, Danuser G, Wittmann T. GSK-3β phosphorylation modulates CLASP-microtubule association and lamella microtubule attachment. *J Cell Biol*. 2009;184(6):895–908. doi:10.1083/jcb.200901042
75. López-Colomé AM, Lee-Rivera I, Benavides-Hidalgo R, López E. Paxillin: a crossroad in pathological cell migration. *J Hematol Oncol*. 2017;10(1):1–15. doi:10.1186/s13045-017-0418-y
76. Oudin MJ, Barbier L, Schäfer C, et al. MENA confers resistance to paclitaxel in triple-negative breast cancer. *Mol Cancer Ther*. 2017;16(1):143–155. doi:10.1158/1535-7163.MCT-16-0413
77. Xu Y, Bismar TA, Su J, et al. Filamin A regulates focal adhesion disassembly and suppresses breast cancer cell migration and invasion. *J Exp Med*. 2010;207(11):2421–2437. doi:10.1084/jem.20100433
78. Von Nandelstadh P, Gucciardo E, Lohi J, et al. Actin-associated protein palladin promotes tumor cell invasion by linking extracellular matrix degradation to cell cytoskeleton. *Mol Biol Cell*. 2014;25(17):2556–2570. doi:10.1091/mbc.E13-11-0667
79. Kim O, Hwangbo C, Kim J, Li DH, Min BS, Lee JH. Chelidonine suppresses migration and invasion of MDA-MB-231 cells by inhibiting formation of the integrin-linked kinase/PINCH/α-parvin complex. *Mol Med Rep*. 2015;12(2):2161–2168. doi:10.3892/mmr.2015.3621
80. Gan L, Camarena V, Mustafi S, Wang G. Vitamin C inhibits triple-negative breast cancer metastasis by affecting the expression of YAP1 and synaptopodin 2. *Nutrients*. 2019;11(12):1–11. doi:10.3390/nu11122997
81. Gao Y, Shi L, Cao Z, et al. Telocinobufagin inhibits the epithelial-mesenchymal transition of breast cancer cells through the phosphoinositide 3-kinase/protein kinase B/extracellular signal-regulated kinase/snail signaling pathway. *Oncol Lett*. 2018;15(5):7837–7845. doi:10.3892/ol.2018.8349
82. Tang L, Lv SJ, Wu Z, et al. Role of betulinic acid derivative SH-479 in triple negative breast cancer and bone microenvironment. *Oncol Lett*. 2021;22(2):1–8. doi:10.3892/ol.2021.12866
83. Wang Y, Jillian Zhang J, Huang XY. Anti-metastasis fascin inhibitors decrease the growth of specific subtypes of cancers. *Cancers*. 2020;12(8):1–20. doi:10.3390/cancers12082287
84. Pignatelli J, Goswami S, Jones JG, et al. Invasive breast carcinoma cells from patients exhibit Mena INV - and macrophage-dependent transendothelial migration. *Sci Signal*. 2014;7(353). doi:10.1126/scisignal.2005329
85. Müller C, Oliveira-Ferrer L, Müller V, Schmalfeldt B, Windhorst S. Transcriptome-based identification of key actin-binding proteins associated with high metastatic potential in breast cancer. *Front Mol Biosci*. 2024;11(August):1–10. doi:10.3389/fmolb.2024.1440276
86. Liu L, Meng T, Zheng X, et al. Transgelin 2 promotes paclitaxel resistance, migration, and invasion of breast cancer by directly interacting with PTEN and activating PI3K/AKT/GSK-3b pathway. *Mol Cancer Ther*. 2019;18(12):2457–2468. doi:10.1158/1535-7163.MCT-19-0261
87. Jeong BY, Cho KH, Jeong KJ, et al. Rab25 augments cancer cell invasiveness through a β1 integrin/EGFR/VEGF-A/snail signaling axis and expression of fascin. *Exp Mol Med*. 2018;50(1):e435–11. doi:10.1038/emm.2017.248
88. Chen L, Yang S, Jakoncic J, Zhang JJ, Huang XY. Migrastatin analogues target fascin to block tumour metastasis. *Nature*. 2010;464(7291):1062–1066. doi:10.1038/nature08978
89. Fang C, Li JJ, Deng T, Li BH, Geng PL, Zeng XT. Actinin-4 as a diagnostic biomarker in serum of breast cancer patients. *Med Sci Monit*. 2019;25:3298–3302. doi:10.12659/MSM.912404
90. Tsuchiya H. Fascin is Expressed in Basal-Liketype Triple Negative Breast Cancer Associated with High Malignant Potential in Japanese Women. *Int J Cancer Clin Res*. 2015;2(5):35–37. doi:10.23937/2378-3419/2/5/1035
91. Yao Y, Zhou Y, Liu L, et al. Nanoparticle-based drug delivery in cancer therapy and its role in overcoming drug resistance. *Front Mol Biosci*. 2020;7(August):1–14. doi:10.3389/fmolb.2020.00193
92. Yau A, Lee J, Chen Y. Nanomaterials for protein delivery in anticancer applications. *Pharmaceutics*. 2021;13(2):1–23. doi:10.3390/pharmaceutics13020155
93. Zhang P, Ye G, Xie G, Lv J, Zeng X, Jiang W. Research progress of nanomaterial drug delivery in tumor targeted therapy. *Front Bioeng Biotechnol*. 2023;11(July):1–9. doi:10.3389/fbioe.2023.1240529
94. Pfitzer L, Moser C, Gegenfurtner F, et al. Targeting actin inhibits repair of doxorubicin-induced DNA damage: a novel therapeutic approach for combination therapy. *Cell Death Dis*. 2019;10(4). doi:10.1038/s41419-019-1546-9
95. Honda K, Yamada T, Endo R, et al. Actinin-4, a novel actin-bundling protein associated with cell motility and cancer invasion. *J Cell Biol*. 1998;140(6):1383–1393. doi:10.1083/jcb.140.6.1383
96. Adam L, Vadlamudi R, Mandal M, Chernoff J, Kumar R. Regulation of microfilament reorganization and invasiveness of breast cancer cells by kinase dead p21-activated kinase-1. *J Biol Chem*. 2000;275(16):12041–12050. doi:10.1074/jbc.275.16.12041
97. Denoyelle C, Hong L, Vannier JP, Soria J, Soria C. New insights into the actions of bisphosphonate zoledronic acid in breast cancer cells by dual RhoA-dependent and -independent effects. *Br J Cancer*. 2003;88(10):1631–1640. doi:10.1038/sj.bjc.6600925
98. Paradiso A, Cardone RA, Bellizzi A, et al. The Na+-H+exchanger-1 induces cytoskeletal changes involving reciprocal RhoA and Rac1 signaling, resulting in motility and invasion in MDA-MB-435 cells. *Breast Cancer Res*. 2004;6(6):616–628. doi:10.1186/bcr922
99. Sokol JP, Neil JR, Schiemann BJ, Schiemann WP. The use of cystatin C to inhibit epithelial-mesenchymal transition and morphological transformation stimulated by transforming growth factor-β. *Breast Cancer Res*. 2005;7(5). doi:10.1186/bcr1312
100. Nam JS, Kang MJ, Suchar AM, et al. Chemokine (C-C motif) ligand 2 mediates the prometastatic effect of dysadherin in human breast cancer cells. *Cancer Res*. 2006;66(14):7176–7184. doi:10.1158/0008-5472.CAN-06-0825
101. Iwasaki M, Homma S, Hishiya A, Dolezal SJ, Reed JC, Takayama S. BAG3 regulates motility and adhesion of epithelial cancer cells. *Cancer Res*. 2007;67(21):10252–10259. doi:10.1158/0008-5472.CAN-07-0618

102. Jiang P, Enomoto A, Jijiwa M, et al. An actin-binding protein girdin regulates the motility of breast cancer cells. *Cancer Res*. 2008;68(5):1310–1318. doi:10.1158/0008-5472.CAN-07-5111
103. Philippar U, Roussos ET, Oser M, et al. A Mena invasion isoform potentiates EGF-induced carcinoma cell invasion and metastasis. *Dev Cell*. 2008;15(6):813–828. doi:10.1016/j.devcel.2008.09.003
104. Holeiter G, Heering J, Erlmann P, Schmid S, Jähne R, Olayioye MA. Deleted in liver cancer 1 controls cell migration through a dia1-dependent signaling pathway. *Cancer Res*. 2008;68(21):8743–8751. doi:10.1158/0008-5472.CAN-08-0984
105. Cushman I, Casey PJ. Role of isoprenylcysteine carboxylmethyltransferase-catalyzed methylation in rho function and migration. *J Biol Chem*. 2009;284(41):27964–27973. doi:10.1074/jbc.M109.025296
106. Pan H, Wanami LS, Dissanayake TR, Bachelder RE. Autocrine semaphorin3A stimulates alpha2 beta1 integrin expression/function in breast tumor cells. *Breast Cancer Res Treat*. 2009;118(1):197–205. doi:10.1007/s10549-008-0179-y
107. Androulidaki A, Dermitzaki E, Venihaki M, et al. Corticotropin releasing factor promotes breast cancer cell motility and invasiveness. *Mol Cancer*. 2009;8:1–12. doi:10.1186/1476-4598-8-30
108. Quintela-Fandino M, Arpaia E, Brenner D, et al. HUNK suppresses metastasis of basal type breast cancers by disrupting the interaction between PP2A and cofilin-1. *Proc Natl Acad Sci U S A*. 2010;107(6):2622–2627. doi:10.1073/pnas.0914492107
109. Pandey RN, Rani R, Yeo EJ, et al. The eyes absent phosphatase-transactivator proteins promote proliferation, transformation, migration, and invasion of tumor cells. *Oncogene*. 2010;29(25):3715–3722. doi:10.1038/onc.2010.122
110. Pichot CS, Arvanitis C, Hartig SM, et al. Cdc42-interacting protein 4 promotes breast cancer cell invasion and formation of invadopodia through activation of N-WASp. *Cancer Res*. 2010;70(21):8347–8356. doi:10.1158/0008-5472.CAN-09-4149
111. Sanchez AM, Flamini MI, Baldacci C, Goglia L, Genazzani AR, Simoncini T. Estrogen receptor-α promotes breast cancer cell motility and invasion via focal adhesion kinase and N-WASP. *Mol Endocrinol*. 2010;24(11):2114–2125. doi:10.1210/me.2010-0252
112. Zhong Z, Yeow WS, Zou C, et al. Cyclin D1/cyclin-dependent kinase 4 interacts with filamin A and affects the migration and invasion potential of breast cancer cells. *Cancer Res*. 2010;70(5):2105–2114. doi:10.1158/0008-5472.CAN-08-1108
113. Snyder M, Huang XY, Zhang JJ. Signal Transducers and Activators of Transcription 3 (STAT3) directly regulates cytokine-induced fascin expression and is required for breast cancer cell migration. *J Biol Chem*. 2011;286(45):38886–38893. doi:10.1074/jbc.M111.286245
114. Zheng S, Huang J, Zhou K, et al. 17β-Estradiol enhances breast cancer cell motility and invasion via extra-nuclear activation of actin-binding protein ezrin. *PLoS One*. 2011;6(7):1–10. doi:10.1371/journal.pone.0022439
115. Mierke CT. Cancer cells regulate biomechanical properties of human microvascular endothelial cells. *J Biol Chem*. 2011;286(46):40025–40037. doi:10.1074/jbc.M111.256172
116. Hu Q, Guo C, Li Y, Aronow BJ, Zhang J. LMO7 mediates cell-specific activation of the rho-myocardin-related transcription factor-serum response factor pathway and plays an important role in breast cancer cell migration. *Mol Cell Biol*. 2011;31(16):3223–3240. doi:10.1128/mcb.01365-10
117. Bailey CK, Mittal MK, Misra S, Chaudhuri G. High motility of triple-negative breast cancer cells is due to repression of plakoglobin gene by metastasis modulator protein SLUG. *J Biol Chem*. 2012;287(23):19472–19486. doi:10.1074/jbc.M112.345728
118. Aguilar-Rojas A, Huerta-Reyes M, Maya-Núñez G, et al. Gonadotropin-releasing hormone receptor activates GTPase RhoA and inhibits cell invasion in the breast cancer cell line MDA-MB-231. *BMC Cancer*. 2012;12(4). doi:10.1186/1471-2407-12-550
119. Du M, Wang G, Ismail TM, et al. S100P dissociates myosin IIA filaments and focal adhesion sites to reduce cell adhesion and enhance cell migration. *J Biol Chem*. 2012;287(19):15330–15344. doi:10.1074/jbc.M112.349787
120. Montalvo-Ortiz BL, Castillo-Pichardo L, Hernández E, et al. Characterization of EHop-016, novel small molecule inhibitor of Rac GTPase. *J Biol Chem*. 2012;287(16):13228–13238. doi:10.1074/jbc.M111.334524
121. Liao YC, Ruan JW, Lua I, et al. Overexpressed hPTTG1 promotes breast cancer cell invasion and metastasis by regulating GEF-H1/RhoA signalling. *Oncogene*. 2012;31(25):3086–3097. doi:10.1038/onc.2011.476
122. Minea R, Helchowski C, Rubino B, Brodmann K, Swenson S, Markland F. Development of a chimeric recombinant disintegrin as a cost-effective anti-cancer agent with promising translational potential. *Toxicon*. 2012;59(4):472–486. doi:10.1016/j.toxicon.2011.02.020
123. Mezi S, Todi L, Orsi E, Angeloni A, Mancini P. Involvement of the Src-cortactin pathway in migration induced by IGF-1 and EGF in human breast cancer cells. *Int J Oncol*. 2012;41(6):2128–2138. doi:10.3892/ijo.2012.1642
124. Cross AM, Wilson AL, Guerrero MS, et al. Breast cancer antiestrogen resistance 3-p130Cas interactions promote adhesion disassembly and invasion in breast cancer cells. *Oncogene*. 2016;35(45):5850–5859. doi:10.1038/onc.2016.123
125. Döppler H, Bastea LI, Eiseler T, Storz P. Neuregulin mediates F-actin-driven cell migration through inhibition of protein kinase D1 via Rac1 protein. *J Biol Chem*. 2013;288(1):455–465. doi:10.1074/jbc.M112.397448
126. Sneh A, Deol YS, Ganju A, et al. Differential role of psoriasin (S100A7) in estrogen receptor α positive and negative breast cancer cells occur through actin remodeling. *Breast Cancer Res Treat*. 2013;138(3):727–739. doi:10.1007/s10549-013-2491-4
127. Van Impe K, Bethuyne J, Cool S, et al. A nanobody targeting the F-actin capping protein CapG restrains breast cancer metastasis. *Breast Cancer Res*. 2013;15(6):1–15. doi:10.1186/bcr3585
128. Antelmi E, Cardone RA, Greco MR, et al. ß1 integrin binding phosphorylates ezrin at T567 to activate a lipid raft signalsome driving invadopodia activity and invasion. *PLoS One*. 2013;8(9):1–19. doi:10.1371/journal.pone.0075113
129. Li D, Jin L, Alesi GN, et al. The prometastatic ribosomal S6 kinase 2-cAMP response element-binding protein (RSK2-CREB) signaling pathway up-regulates the actin-binding protein fascin-1 to promote tumor metastasis. *J Biol Chem*. 2013;288(45):32528–32538. doi:10.1074/jbc.M113.500561
130. Monteiro P, Rossé C, Castro-Castro A, et al. Endosomal WASH and exocyst complexes control exocytosis of MT1-MMP at invadopodia. *J Cell Biol*. 2013;203(6):1063–1079. doi:10.1083/jcb.201306162
131. Bockhorn J, Yee K, Chang YF, et al. MicroRNA-30c targets cytoskeleton genes involved in breast cancer cell invasion. *Breast Cancer Res Treat*. 2013;137(2):373–382. doi:10.1007/s10549-012-2346-4
132. Li H, Yang L, Fu H, et al. Association between Gαi2 and ELMO1/Dock180 connects chemokine signalling with Rac activation and metastasis. *Nat Commun*. 2013;4:1706–1712. doi:10.1038/ncomms2680
133. Hu X, Guo J, Zheng L, et al. The heterochronic microRNA let-7 inhibits cell motility by regulating the genes in the actin cytoskeleton pathway in breast cancer. *Mol Cancer Res*. 2013;11(3):240–250. doi:10.1158/1541-7786.MCR-12-0432

134. Chen M, Bresnick AR, O'Connor KL. Coupling S100A4 to rhotekin alters rho signaling output in breast cancer cells. *Oncogene*. 2013;32 (32):3754–3764. doi:10.1038/onc.2012.383
135. Wang J, Tsouko E, Jonsson P, et al. miR-206 inhibits cell migration through direct targeting of the actin-binding protein Coronin 1C in triple-negative breast cancer. *Mol Oncol*. 2014;8(8):1690–1702. doi:10.1016/j.molonc.2014.07.006
136. Goicoechea SM, Zinn A, Awadia SS, Snyder K, Garcia-Mata R. A RhoG-mediated signaling pathway that modulates invadopodia dynamics in breast cancer cells. *J Cell Sci*. 2017;130(6):1064–1077. doi:10.1242/jcs.195552
137. Juin A, Di Martino J, Leitinger B, et al. Discoidin domain receptor 1 controls linear invadosome formation via a Cdc42-Tuba pathway. *J Cell Biol*. 2014;207(4):517–533. doi:10.1083/jcb.201404079
138. Zheng S, Zhong Q, Xi Y, et al. Modification and biological evaluation of thiazole derivatives as novel inhibitors of metastatic cancer cell migration and invasion. *J Med Chem*. 2014;57(15):6653–6667. doi:10.1021/jm500724x
139. Elloul S, Kedrin D, Knoblauch NW, Beck AH, Toker A. The adherens junction protein afadin is an AKT substrate that regulates breast cancer cell migration. *Mol Cancer Res*. 2014;12(3):464–476. doi:10.1158/1541-7786.MCR-13-0398
140. Feng S, Cai M, Liu P, et al. Atp6v1c1 may regulate filament actin arrangement in breast cancer cells. *PLoS One*. 2014;9(1):2–6. doi:10.1371/journal.pone.0084833
141. Volakis LI, Li R, Ackerman IVWE, et al. Loss of myoferlin redirects breast cancer cell motility towards collective migration. *PLoS One*. 2014;9 (2):e86110. doi:10.1371/journal.pone.0086110
142. Zhang Z, Yang M, Chen R, et al. IBP regulates epithelial-to-mesenchymal transition and the motility of breast cancer cells via Rac1, RhoA and Cdc42 signaling pathways. *Br Dent J*. 2014;217(1):3374–3382. doi:10.1038/onc.2013.337
143. Beaty BT, Wang Y, Bravo-Cordero JJ, et al. Talin regulates moesin-NHE-1 recruitment to invadopodia and promotes mammary tumor metastasis. *J Cell Biol*. 2014;205(5):737–751. doi:10.1083/jcb.201312046
144. Sollome JJ, Thavathiru E, Camenisch TD, Vaillancourt RR. HER2/HER3 regulates extracellular acidification and cell migration through MTK1 (MEKK4). *Cell Signal*. 2014;26(1):70–82. doi:10.1016/j.cellsig.2013.08.043
145. Singleton DC, Rouhi P, Zois CE, et al. Hypoxic regulation of RIOK3 is a major mechanism for cancer cell invasion and metastasis. *Oncogene*. 2015;34(36):4713–4722. doi:10.1038/onc.2014.396
146. Yu L, Liu X, Cui K, et al. SND1 acts downstream of TGFβ1 and upstream of Smurf1 to promote breast cancer metastasis. *Cancer Res*. 2015;75 (7):1275–1286. doi:10.1158/0008-5472.CAN-14-2387
147. Madsen CD, Hooper S, Tozluoglu M, et al. STRIPAK components determine mode of cancer cell migration and metastasis. *Nat Cell Biol*. 2015;17(1):68–80. doi:10.1038/ncb3083
148. Hughes SK, Oudin MJ, Tadros J, et al. PTP1B-dependent regulation of receptor tyrosine kinase signaling by the actin-binding protein Mena. *Mol Biol Cell*. 2015;26(21):3867–3878. doi:10.1091/mbc.E15-06-0442
149. Henkels KM, Mallets ER, Dennis PB, Gomez-Cambronero J. S6K is a morphogenic protein with a mechanism involving Filamin-A phosphorylation and phosphatidic acid binding. *FASEB J*. 2015;29(4):1299–1313. doi:10.1096/fj.14-260992
150. Hermann MR, Jakobson M, Colo GP, et al. Integrins synergise to induce expression of the MRTF-A-SRF target gene ISG15 for promoting cancer cell invasion. *J Cell Sci*. 2016;129(7):1391–1403. doi:10.1242/jcs.177592
151. Oudin MJ, Miller MA, Klazen JAZ, et al. MenaINV mediates synergistic cross-talk between signaling pathways driving chemotaxis and haptotaxis. *Mol Biol Cell*. 2016;27(20):3085–3094. doi:10.1091/mbc.E16-04-0212
152. Menezes ME, Shen XN, Das SK, Emdad L, Sarkar D, Fisher PB. MDA-9/Syntenin (SDCBP) modulates small GTPases RhoA and Cdc42 via transforming growth factor β1 to enhance epithelial-mesenchymal transition in breast cancer. *Oncotarget*. 2016;7(49):80175–80189. doi:10.18632/oncotarget.13373
153. Gari HH, DeGala GD, Ray R, Lucia MS, Lambert JR. PRL-3 engages the focal adhesion pathway in triple-negative breast cancer cells to alter actin structure and substrate adhesion properties critical for cell migration and invasion. *Cancer Lett*. 2016;380(2):505–512. doi:10.1016/j.canlet.2016.07.017
154. Han S, Huang J, Liu B, et al. Improving fascin inhibitors to block tumor cell migration and metastasis. *Mol Oncol*. 2016;10(7):966–980. doi:10.1016/j.molonc.2016.03.006
155. Park JH, Cho YY, Yoon SW, Park B. Suppression of MMP-9 and FAK expression by pomolic acid via blocking of NF-B/ERK/mTOR signaling pathways in growth factor-stimulated human breast cancer cells. *Int J Oncol*. 2016;49(3):1230–1240. doi:10.3892/ijo.2016.3585
156. Lii CK, Chang JW, Chen JJ, et al. Docosahexaenoic acid inhibits 12-O-tetradecanoylphorbol-13-acetate-induced fascin-1-dependent breast cancer cell migration by suppressing the PKCδ- and Wnt-1/β-catenin-mediated pathways. *Oncotarget*. 2016;7(18):25162–25179. doi:10.18632/oncotarget.7301
157. Teng Y, Bahassan A, Dong D, et al. Targeting the WASF3–CYFIP1 complex using stapled peptides suppresses cancer cell invasion. *Cancer Res*. 2016;76(4):965–973. doi:10.1158/0008-5472.CAN-15-1680
158. Mansour M, Haupt S, Chan AL, et al. TheE3-ligase E6AP represses breast cancer metastasis via regulation of ECT2-Rho signaling. *Cancer Res*. 2016;76(14):4236–4248. doi:10.1158/0008-5472.CAN-15-1553
159. Morris DC, Popp JL, Tang LK, et al. Nck deficiency is associated with delayed breast carcinoma progression and reduced metastasis. *Mol Biol Cell*. 2017;28(24):3500–3516. doi:10.1091/mbc.E17-02-0106
160. Chen ZL, Yang J, Shen YW, et al. AmotP130 regulates Rho GTPase and decreases breast cancer cell mobility. *J Cell Mol Med*. 2018;22 (4):2390–2403. doi:10.1111/jcmm.13533
161. Chonggao YIN, Zhang G, Ruimei SUN, et al. miR-185-5p inhibits F-actin polymerization and reverses epithelial mesenchymal transition of human breast cancer cells by modulating RAGE. *Mol Med Rep*. 2018;18(3):2621–2630. doi:10.3892/mmr.2018.9294
162. De P, Carlson JH, Jepperson T, Willis S, Leyland-Jones B, Dey N. RAC1 GTP-ase signals Wnt-beta-catenin pathway mediated integrin-directed metastasis-associated tumor cell phenotypes in triple negative breast cancers. *Oncotarget*. 2017;8(2):3072–3103. doi:10.18632/oncotarget.13618
163. Samaeekia R, Adorno-Cruz V, Bockhorn J, et al. miR-206 inhibits stemness and metastasis of breast cancer by targeting MKL1/IL11 pathway. *Clin Cancer Res*. 2017;23(4):1091–1103. doi:10.1158/1078-0432.CCR-16-0943
164. Wang H, Zhang J, Zhang M, Wei L, Chen H, Li Z. A systematic study of Girdin on cell proliferation, migration and angiogenesis in different breast cancer subtypes. *Mol Med Rep*. 2017;16(3):3351–3356. doi:10.3892/mmr.2017.6971

165. Gkretsi V, Stylianou A, Stylianopoulos T. Vasodilator-Stimulated Phosphoprotein (VASP) depletion from breast cancer MDA-MB-231 cells inhibits tumor spheroid invasion through downregulation of Migfilin, β-catenin and urokinase-plasminogen activator (uPA). *Exp Cell Res*. 2017;352(2):281–292. doi:10.1016/j.yexcr.2017.02.019
166. Lim JP, Shyamasundar S, Gunaratne J, Scully OJ, Matsumoto K, Bay BH. YBX1 gene silencing inhibits migratory and invasive potential via CORO1C in breast cancer in vitro. *BMC Cancer*. 2017;17(1):1–15. doi:10.1186/s12885-017-3187-7
167. Li D, Wang H, Song H, et al. The microRNAs miR-200b-3p and miR-429-5p target the LIMK1/CFL1 pathway to inhibit growth and motility of breast cancer cells. *Oncotarget*. 2017;8(49):85276–85289. doi:10.18632/oncotarget.19205
168. Gómez-Contreras P, Ramiro-Díaz JM, Sierra A, et al. Extracellular matrix 1 (ECM1) regulates the actin cytoskeletal architecture of aggressive breast cancer cells in part via S100A4 and Rho-family GTPases. *Clin Exp Metastasis*. 2017;34(1):37–49. doi:10.1007/s10585-016-9827-5
169. Alam F, Mezhal F, El Hasasna H, et al. The role of p53-microRNA 200-Moesin axis in invasion and drug resistance of breast cancer cells. *Tumor Biol*. 2017;39(9):101042831771463. doi:10.1177/1010428317714634
170. Berno V, Porrini D, Castiglioni F, et al. The 67 kDa laminin receptor increases tumor aggressiveness by remodeling laminin-1. *Endocr Relat Cancer*. 2005;12(2):393–406. doi:10.1677/erc.1.00870
171. Vadakekolathu J, Al-Juboori SIK, Johnson C, et al. MTSS1 and SCAMP1 cooperate to prevent invasion in breast cancer. *Cell Death Dis*. 2018;9(3). doi:10.1038/s41419-018-0364-9
172. Yang L, Hong Q, Xu SG, et al. Downregulation of transgelin 2 promotes breast cancer metastasis by activating the reactive oxygen species/nuclear factor-κB signaling pathway. *Mol Med Rep*. 2019;20(5):4045–4058. doi:10.3892/mmr.2019.10643
173. Pardo-Pastor C, Rubio-Moscardo F, Vogel-González M, et al. Piezo2 channel regulates RhoA and actin cytoskeleton to promote cell mechanobiological responses. *Proc Natl Acad Sci U S A*. 2018;115(8):1925–1930. doi:10.1073/pnas.1718177115
174. Huang S, Chi Y, Qin Y, et al. CAPG enhances breast cancer metastasis by competing with PRMT5 to modulate STC-1 transcription. *Theranostics*. 2018;8(9):2549–2564. doi:10.7150/thno.22523
175. Acharya S, Yao J, Li P, et al. Sphingosine kinase 1 signaling promotes metastasis of triple-negative breast cancer. *Cancer Res*. 2019;79(16):4211–4226. doi:10.1158/0008-5472.CAN-18-3803
176. Zhang G, Li H, Sun R, et al. Long non-coding RNA ZEB2-AS1 promotes the proliferation, metastasis and epithelial mesenchymal transition in triple-negative breast cancer by epigenetically activating ZEB2. *J Cell Mol Med*. 2019;23(5):3271–3279. doi:10.1111/jcmm.14213
177. Zeng Y, Cao Y, Liu L, et al. SEPT9_i1 regulates human breast cancer cell motility through cytoskeletal and RhoA/FAK signaling pathway regulation. *Cell Death Dis*. 2019;10(10). doi:10.1038/s41419-019-1947-9
178. Jeong M, Jung E, Oh S, Shin SY. Homeobox protein PROX1 expression is negatively regulated by histone deacetylase 1 and c-JUN complex in MDA-MB-231 human breast cancer cells. *Folia Biol*. 2023;69(3):81–90. doi:10.14712/fb2023069030081
179. Thomas C, Karagounis IV, Srivastava RK, et al. Estrogen receptor β-mediated inhibition of actin-based cell migration suppresses metastasis of inflammatory breast cancer. *Cancer Res*. 2021;81(9):2399–2414. doi:10.1158/0008-5472.CAN-20-2743
180. Casanova AG, Roth GS, Hausmann S, et al. Cytoskeleton remodeling induced by SMYD2 methyltransferase drives breast cancer metastasis. *Cell Discov*. 2024;10(1). doi:10.1038/s41421-023-00644-x
181. Choi HS, Jang HJ, Kristensen MK, Kwon TH. TAZ is involved in breast cancer cell migration via regulating actin dynamics. *Front Oncol*. 2024;14(May):1–26. doi:10.3389/fonc.2024.1376831
182. Chang CY, Pearce G, Betaneli V, et al. The F-actin bundler SWAP-70 promotes tumor metastasis. *Life Sci Alliance*. 2024;7(8):1–18. doi:10.26508/lsa.202302307
183. Yousafzai NA, El Khalki L, Wang W, Justin M, Metrohealth S, Sossey-Alaoui K. Kindlin-2 regulates the oncogenic activities of integrins and TGF-β in triple negative breast cancer progression and metastasis. *Oncogene*. 2024;43(45):3291–3305. doi:10.1038/s41388-024-03166-2
184. VanderVorst K, Dreyer CA, Hatakeyama J, et al. Vangl-dependent Wnt/planar cell polarity signaling mediates collective breast carcinoma motility and distant metastasis. *Breast Cancer Res*. 2023;25(1):1–19. doi:10.1186/s13058-023-01651-2
185. Dong Y, Jin Q, Sun M, et al. CLDN6 inhibits breast cancer metastasis through WIP-dependent actin cytoskeleton-mediated autophagy. *J Exp Clin Cancer Res*. 2023;42(1):1–17. doi:10.1186/s13046-023-02644-x
186. Alneyadi A, Nizami ZN, Aburawi HE, et al. Synthesis of New Chromene Derivatives Targeting Triple-Negative Breast Cancer Cells. *Cancers*. 2023;15(10):2682. doi:10.3390/cancers15102682
187. Zhang Y, Lu Q, Li N, Xu M, Miyamoto T, Liu J. Sulforaphane suppresses metastasis of triple-negative breast cancer cells by targeting the RAF/MEK/ERK pathway. *Npj Breast Cancer*. 2022;8(1). doi:10.1038/s41523-022-00402-4
188. Medina JI, Cruz-Collazo A, Del Mar Maldonado M, et al. Characterization of novel derivatives of MBQ-167, an Inhibitor of the GTP-binding proteins Rac/Cdc42. *Cancer Res Commun*. 2022;2(12):1711–1726. doi:10.1158/2767-9764.CRC-22-0303
189. Padilla-Rodriguez M, Parker SS, Adams DG, et al. The actin cytoskeletal architecture of estrogen receptor positive breast cancer cells suppresses invasion. *Nat Commun*. 2018;9(1):1–16. doi:10.1038/s41467-018-05367-2
190. Dvorak KM, Pettee KM, Rubinic-Minotti K, Su R, Nestor-Kalinoski A, Eisenmann KM. Carcinoma associated fibroblasts (CAFs) promote breast cancer motility by suppressing mammalian Diaphanous-related formin-2 (mDia2). *PLoS One*. 2018;13(3):1–22. doi:10.1371/journal.pone.0195278
191. Carter KP, Hanna S, Genna A, Lewis D, Segall JE, Cox D. Macrophages enhance 3D invasion in a breast cancer cell line by induction of tumor cell tunneling nanotubes. *Cancer Rep*. 2019;2(6):1–9. doi:10.1002/cnr2.1213
192. Xiong N, Li S, Tang K, et al. Involvement of caveolin-1 in low shear stress-induced breast cancer cell motility and adhesion: roles of FAK/Src and ROCK/p-MLC pathways. *Biochim Biophys Acta*. 2017;1864(1):12–22. doi:10.1016/j.bbamcr.2016.10.013
193. Chanez B, Ostacolo K, Badache A, Thuault S. Eb1 restricts breast cancer cell invadopodia formation and matrix proteolysis via fak. *Cells*. 2021;10(2):1–14. doi:10.3390/cells10020388
194. Luo S, Wang H, Bai L, et al. Activation of TMEM16A Ca2+-activated Cl− channels by ROCK1/moesin promotes breast cancer metastasis. *J Adv Res*. 2021;33(77):253–264. doi:10.1016/j.jare.2021.03.005
195. Jeong M, Jung E, Lee YH, et al. A novel synthetic compound (E)-5-((4-oxo-4h-chromen-3-yl)methyleneamino)-1-phenyl-1h-pyrazole-4-carbonitrile inhibits tnfα-induced mmp9 expression via egr-1 downregulation in mda-mb-231 human breast cancer cells. *Int J Mol Sci*. 2020;21(14):1–15. doi:10.3390/ijms21145080

196. Wang Z, Li TE, Chen M, Pan JJ, Shen KW. miR-106b-5p contributes to the lung metastasis of breast cancer via targeting CNN1 and regulating Rho/ROCK1 pathway. *Aging*. 2020;12(2):1867–1887. doi:10.18632/aging.102719
197. Chang KC, Diermeier SD, Yu AT, et al. MaTAR25 lncRNA regulates the Tensin1 gene to impact breast cancer progression. *Nat Commun*. 2020;11(1). doi:10.1038/s41467-020-20207-y
198. Liu Y, Li H, Liu F, et al. Heterogeneous nuclear ribonucleoprotein A2/B1 is a negative regulator of human breast cancer metastasis by maintaining the balance of multiple genes and pathways. *EBioMedicine*. 2020;51:102583. doi:10.1016/j.ebiom.2019.11.044
199. Qiao Y, Jin T, Guan S, et al. Long non-coding RNA Lnc-408 promotes invasion and metastasis of breast cancer cell by regulating LIMK1. *Oncogene*. 2021;40(24):4198–4213. doi:10.1038/s41388-021-01845-y
200. Machado RAC, Stojevski D, De Landtsheer S, et al. L-plastin Ser5 phosphorylation is modulated by the PI3K/SGK pathway and promotes breast cancer cell invasiveness. *Cell Commun Signal*. 2021;19(1):1–22. doi:10.1186/s12964-021-00710-5
201. Wang Z, Yang L, Wu P, et al. The circROBO1/KLF5/FUS feedback loop regulates the liver metastasis of breast cancer by inhibiting the selective autophagy of afadin. *Mol Cancer*. 2022;21(1):1–18. doi:10.1186/s12943-022-01498-9
202. Yu J, Shen W, Gao B, Xu J, Gong B. Metastasis suppressor 1 acts as a tumor suppressor by inhibiting epithelial-to-mesenchymal transition in triple-negative breast cancer. *Int J Biol Markers*. 2020;35(1):74–81. doi:10.1177/1724600820905114
203. Peng Y, Chen Z, Chen Y, et al. ROCK Isoforms Differentially Modulate Cancer Cell Motility by Mechanosensing the Substrate Stiffness. *Acta Materialia*. 2019;88: 86–101. doi:10.1016/j.actbio.2019.02.015
204. Cheng Z, Wei W, Wu Z, et al. ARPC2 promotes breast cancer proliferation and metastasis. *Oncol Rep*. 2019;41(6):3189–3200. doi:10.3892/or.2019.7113
205. Alassaf E, Mueller A. The role of PKC in CXCL8 and CXCL10 directed prostate, breast and leukemic cancer cell migration. *Eur J Pharmacol*. 2020;886(January):173453. doi:10.1016/j.ejphar.2020.173453
206. Kansakar U, Wang W, Markovic V, Sossey-Alaoui K. Phosphorylation of the proline-rich domain of WAVE3 drives its oncogenic activity in breast cancer. *Sci Rep*. 2021;11(1):1–14. doi:10.1038/s41598-021-83479-4
207. Song X, Wang W, Wang H, et al. Acetylation of ezrin regulates membrane-cytoskeleton interaction underlying CCL18-elicited cell migration. *J Mol Cell Biol*. 2020;12(6):424–437. doi:10.1093/jmcb/mjz099
208. Wang D, Naydenov NG, Dozmorov MG, Koblinski JE, Ivanov AI. Anillin regulates breast cancer cell migration, growth, and metastasis by non-canonical mechanisms involving control of cell stemness and differentiation. *Breast Cancer Res*. 2020;22(1):1–19. doi:10.1186/s13058-019-1241-x
209. Hu PC, Li K, Tian YH, et al. Creb1/lin28/mir-638/vasp interactive network drives the development of breast cancer. *Int J Biol Sci*. 2019;15(12):2733–2749. doi:10.7150/ijbs.36854
210. Mannion AJ, Odell AF, Taylor A, Jones PF, Cook GP. Tumour cell CD99 regulates transendothelial migration via CDC42 and actin remodelling. *J Cell Sci*. 2021;134(15). doi:10.1242/jcs.240135
211. de Oliveira Moritz MN, Casali BC, Stotzer US, Karina Dos Santos P, Selistre-de-Araujo HS. Alternagin-C, an alpha2beta1 integrin ligand, attenuates collagen-based adhesion, stimulating the metastasis suppressor 1 expression in triple-negative breast tumor cells. *Toxicon*. 2022;210(February):1–10. doi:10.1016/j.toxicon.2022.02.001
212. Wu Y, Yuan MH, Wu HT, et al. MicroRNA-488 inhibits proliferation and motility of tumor cells via downregulating FSCN1, modulated by Notch3 in breast carcinomas. *Cell Death Dis*. 2020;11(10). doi:10.1038/s41419-020-03121-5
213. Kalpana G, Figy C, Feng J, et al. The RhoA dependent anti-metastatic function of RKIP in breast cancer. *Sci Rep*. 2021;11(1). doi:10.1038/s41598-021-96709-6
214. Shechter D, Harel M, Mukherjee A, et al. Breast cancer-derived microparticles reduce cancer cell adhesion, an effect augmented by chemotherapy. *Cells*. 2020;9(10):2269. doi:10.3390/cells9102269
215. Yan T, Zhang A, Shi F, et al. Integrin αvβ3-associated DAAM1 is essential for collagen-induced invadopodia extension and cell haptotaxis in breast cancer cells. *J Biol Chem*. 2018;293(26):10172–10185. doi:10.1074/jbc.RA117.000327
216. Carmona G, Perera U, Gillett C, et al. Lamellipodin promotes invasive 3D cancer cell migration via regulated interactions with Ena/VASP and SCAR/WAVE. *Oncogene*. 2016;35(39):5155–5169. doi:10.1038/onc.2016.47
217. Kim T, Hwang D, Lee D, Kim J, Kim S, Lim D. MRTF potentiates TEAD - YAP transcriptional activity causing metastasis. *EMBO J*. 2017;36(4):520–535. doi:10.15252/embj.201695137
218. Gkretsi V, Louca M, Stylianou A, Minadakis G, Spyrou GM, Stylianopoulos T. Inhibition of breast cancer cell invasion by Ras suppressor-1 (RSU-1) silencing is reversed by growth differentiation factor-15 (GDF-15). *Int J Mol Sci*. 2019;20(1):163. doi:10.3390/ijms20010163
219. Ahn YH, Gibbons DL, Chakravarti D, et al. ZEB1 drives prometastatic actin cytoskeletal remodeling by downregulating miR-34a expression. *J Clin Invest*. 2012;122(9):3170–3183. doi:10.1172/JCI63608
220. Miao B, Skidan I, Yang J, et al. Inhibition of cell migration by PITENINs: the role of ARF6. *Oncogene*. 2012;31(39):4317–4332. doi:10.1038/onc.2011.593
221. Monzavi-Karbassi B, Hine RJ, Stanley JS, et al. Fructose as a carbon source induces an aggressive phenotype in MDA-MB-468 breast tumor cells. *Int J Oncol*. 2010;37(3):615–622. doi:10.3892/ijo_00000710
222. Wu D, Asiedu M, Wei Q. Myosin-interacting guanine exchange factor (MyoGEF) regulates the invasion activity of MDA-MB-231 breast cancer cells through activation of RhoA and RhoC. *Oncogene*. 2009;28(22):2219–2230. doi:10.1038/onc.2009.96
223. Medjkane S, Perez-Sanchez C, Gaggioli C, Sahai E, Treisman R. Myocardin-related transcription factors and SRF are required for cytoskeletal dynamics and experimental metastasis. *Nat Cell Biol*. 2009;11(3):257–268. doi:10.1038/ncb1833
224. Jiang X, Yue J, Lu H, et al. Inhibition of filamin-A reduces cancer metastatic potential. *Int J Biol Sci*. 2012;9(1):67–77. doi:10.7150/ijbs.5577
225. Lorente G, Syriani E, Morales M. Actin filaments at the leading edge of cancer cells are characterized by a high mobile fraction and turnover regulation by profilin I. *PLoS One*. 2014;9(1):e85817. doi:10.1371/journal.pone.0085817
226. Roussos ET, Wang Y, Wyckoff JB, et al. Mena deficiency delays tumor progression and decreases metastasis in polyoma middle-T transgenic mouse mammary tumors. *Breast Cancer Res*. 2010;12(6). doi:10.1186/bcr2784
227. Karagiannis GS, Pastoriza JM, Wang Y, et al. Neoadjuvant chemotherapy induces breast cancer metastasis through a TMEM-mediated mechanism. *Sci Transl Med*. 2017;9(397):1–30. doi:10.1126/scitranslmed.aan0026

228. Anwar T, Arellano-Garcia C, Ropa J, et al. P38-mediated phosphorylation at T367 induces EZH2 cytoplasmic localization to promote breast cancer metastasis. *Nat Commun*. 2018;9(1). doi:10.1038/s41467-018-05078-8
229. Huang LT, Tsai CL, Huang SH, et al. Depleting RhoA/stress fiber-organized fibronectin matrices on tumor cells non-autonomously aggravates fibroblast-driven tumor cell growth. *Int J Mol Sci*. 2020;21(21):1–20. doi:10.3390/ijms21218272
230. Li Q, Cao J, He Y, et al. R5, a neutralizing antibody to Robo1, suppresses breast cancer growth and metastasis by inhibiting angiogenesis via down-regulating filamin A. *Exp Cell Res*. 2020;387(1):111756. doi:10.1016/j.yexcr.2019.111756
231. Wang Y, Song M, Liu M, et al. Fascin inhibitor increases intratumoral dendritic cell activation and anti-cancer immunity. *Cell Rep*. 2021;35 (1):108948. doi:10.1016/j.celrep.2021.108948
232. Tabariès S, McNulty A, Ouellet V, et al. Afadin cooperates with claudin-2 to promote breast cancer metastasis. *Genes Dev*. 2019;33(3–4):180–-193. doi:10.1101/gad.319194.118
233. Goswami S, Philippar U, Sun D, et al. Identification of invasion specific splice variants of the cytoskeletal protein Mena present in mammary tumor cells during invasion in vivo. *Clin Exp Metastasis*. 2009;26(2):153–159. doi:10.1007/s10585-008-9225-8