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REVIEW

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SDC1 is a critical transmembrane proteoglycan in breast cancer

Yingying Mei[1†], Lantao Zhao[2†] and Na Zhou[1*]

Abstract

There has been an increasing incidence of breast cancer around the world in recent years. As a burgeoning model of diagnosis and treatment, precision medicine has become a new trend in breast cancer management. Dysregulated glycometabolism is well established as a tumor feature. SDC1 is a glycometabolism-related gene and participates in the progression, metastasis, resistance and recurrence of malignant tumors. SDC1 promotes the development of breast cancer by disturbing tumor stem cell phenotypes, the cell cycle and apoptosis, and then modulates macrophage migration, epithelial-mesenchymal transformation, angiogenesis and the tumor-bone microenvironment. We summarized the recent advances regarding the role of SDC1 in the mechanism driving the occurrence of breast cancer, and evaluated its potential therapeutic contributions.

Keywords SDC1, Breast cancer, Tumor microenvironment, Targeted therapy

Introduction

According to global cancer statistics [1], the number of new cancer cases reached 19.3 million in 2020, and approximately 10 million people died from cancer. Malignant tumors are one of the primary causes of premature death and reduced life expectancy in many nations as the world population grows and ages, yet the burden of cancer is not equally distributed [2]. Breast cancer recently surpassed lung cancer as the most commonly diagnosed malignancy in women [1].

Breast cancer is a complex disease with high heterogeneity, that involves genomic and transcriptional alterations. Breast cancer is categorized as luminal A (PR+, ER+, HER2-), luminal B (PR+, ER+, HER2+), HER2-overexpressing (PR-, ER-, HER2+) or triple-negative (PR-, ER-, HER2-). The treatment of tumors has entered the age of precision targeting. Molecular targeted therapies are therapies that primarily affect tumor tissues and have better therapeutic effects and bioavailability than traditional therapies. Although some molecular markers including Human EpidermalGrowth Factor Receptor 2 (HER2), Epidermal Growth Factor Receptor (EGFR) and mammalian Target Of Rapamycin (mTOR), have been universally used, there is no significant benefit of targeted treatments in triple-negative breast cancer, indicating a lack of effective targets [3]. The targets for other breast cancer subtypes are also limited, so the need to identify novel effective targets is urgent.

The dysregulation of glucose metabolism is an emerging feature of breast cancer [4, 5]. The overexpression of glucose transporters and key glycolytic enzymes, massive production of ATP and accumulation of lactate can lead to an acidic microenvironment disrupting antitumor immunity and promoting tumor progression synergistically [6]. With the development of bioinformatics,

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Table 1 Research on SDC family structure

Members	Features of intracellular variable region (C1)	Primary binding proteins	Core functional tendencies
SDC1	Short C1 region, containing PDZ binding motif (EFYA)	Src, ERM proteins (Ezrin)	Invasion, immune evasion
SDC2	Long C1 region, containing phosphorylation sites (Tyr/Ser)	CASK、α-actinin、FAK	Adhesion dynamics regulation, EMT
SDC3	Long C1 region, containing PDZ binding motif (DTKN)	Syntenin、Synbindin、PKCδ	Neuronal migration, inhibition of invasion
SDC4	Short C1 region, containing PDZ binding motif (EENY)	PKCα, PIP2, PDZ protein (Synectin)	Stabilizing adhesion, anti-migration

Table 2 Research on SDC family function

Function	SDC1	SDC2	SDC3	SDC4
Adhesion properties	Adhesion dissociation (MMP activation)	Dynamic adhesion (Rac1-dependent)	Neurotrophically specific adhesion	Stable adhesion (RhoA activation)
Invasive tendency	Strong promotion of invasion (EMT-driven)	Bidirectional regulation (dependent on microenvironment)	Inhibition of invasion (MMP inhibition)	Inhibition of invasion (anti-EMT)
Core pathways	Wnt/β-catenin、PI3K/Akt	TGF-β/Smad、Rac1	PKCδ/ERK、PDGFRβ	RhoA/ROCK、PKCα
Prognostic association	Unfavorably poor prognosis (high metastasis)	Colon cancer has poor prognosis, lung cancer has good prognosis	Neuro-oncology has a better prognosis	Preferably good prognosis (low metastasis)
Therapeutic target potential	Antibody targeting (such as Indatuximab)	Inhibition of TGF-β pathway	Recovery of expression (gene therapy)	Enhance adhesion (anti-metastasis)

next-generation sequencing has become a powerful technology that can comprehensively analyze gene expression, screen out differentially expressed genes and identify potential genetic targets [7, 8]. Syndecan1 (SDC1) is a heparin sulfate proteoglycan and is mainly involved in glucose metabolism, which provides energy for tumor proliferation, which was identified by next-generation sequencing to be used as an effective independent biomarker and a potential therapeutic target for breast cancer patients [9, 10]. Additionally, the abnormal expression of SDC1 contributes to tumor development by promoting cell proliferation, migration, invasion and angiogenesis in malignant tumors. In this review, we report the multifunctional role of SDC1 in breast cancer progression to highlight the potential of targeting SDC1 in the individualized management of breast cancer patients. In addition, we highlight that SDC1 is important not only as a potential therapeutic target but also as a novel prognostic biomarker.

Structure and function of SDCs

SDCs are a family of heparin sulfate proteoglycans (HSPGs) including SDC1-4 [11]. SDCs are I-type transmembrane proteins with extracellular amino-termini, transmembrane domains and internal carboxy-termini [12]. Each SDC protein has distinct extracellular and intracellular domains with different coreceptor phenotypes and intracellular signaling pathways. We have provided a detailed description in Tables 1 and 2.

SDC1, also known as CD-138, is mainly expressed in epithelial cells and plasma cells [13]. SDC1 is a cell surface adhesion molecule that can maintain cell morphology and interacts with the surrounding environment by binding to heparin sulfate chains with matrix components, growth factors, enzymes, and enzyme inhibitors [14]. SDC1 can be defined as membrane-bound SDC1 and soluble SDC1. Membrane-bound SDC1 mainly promotes growth and proliferation in the tumor microenvironment, while soluble SDC1 mainly promotes invasion and metastasis [15]. Moreover, there is a wide range of extracellular stimulation and matrix proteolytic enzymes, including MMPs, ADAMs, and gamma-secretase, that can promote the transition of SDC1 from the membrane type to the soluble type [16]. In addition, the expression of SDC1 is mainly regulated by degradation and endocytosis, and degradation of SDC1 stimulates its own expression, forming a positive feedback loop [17, 18].

SDC2, also known as fibroglycan, is mainly expressed in mesenchymal cells [13]. SDC2 is a 48 KDa stable dimer or oligomer transmembrane protein with a short cytoplasmic domain that consists of two constant regions (C1 and C2) separated by a variable region (V) [19, 20]. The large extracellular domain enables it to interact with cell membrane receptors, acting as coreceptor binding ligands, and activating cell adhesion and migration signaling pathways [21, 22]. Additionally, SDC2 inhibits apoptosis and promotes breast cancer growth [23]. Targeting SDC2 can limit immune evasion [24].

SDC3 is the largest syndecan family member, composing 442 amino acids in humans [25]. SDC3 is mainly expressed in neural cells. SDC3 is a specific attachment receptor in dendritic cells for HIV-1, and can present HIV antigens to $CD8^+$ T cells [26]. SDC3 plays an important anabolic role in bone and promotes new bone formation through the stabilization of Frizzled 1 to enhance Wnt signaling in osteoblasts [27]. This prior research documents that SDC3 extracellular core protein can block endothelial cells to produce antiangiogenic effects [28]. In addition, the expression of SDC3 can be increased by HIF-1α depending on the mechanism in

an anoxic environment [29]. Genes related to SDC3 are enriched in the glycolysis pathway (glycolysis refers to the process in which glucose is decomposed into pyruvate in the cytoplasm under anaerobic conditions, which is a type of glucose metabolism), and SDC3 is a new prognostic marker for breast cancer [9, 30], yet the mechanisms need to be further investigated.

SDC4 is ubiquitously expressed in almost all cells [31]. SDC4 is upregulated with the help of IL-1β although the SRC/STAT3 pathway in human islet β-cells [32]. SDC4 can also regulate and control the intracellular calcium balance via transient receptor potential canonicals (TRPCs) [33]. SDC4 accelerates the biosynthesis of Wnt signaling molecules and potentially regulates the migration of breast cancer cells [34]. SDC4 binds to EGFR and RON kinases to maintain the cell cycle [35]. In addition, targeting SDC4 inhibits early bone metastasis formation [36].

Through its heparan sulfate (HS) chains, SDC enhances the interaction with growth factors (such as FGF, VEGF, HGF, etc.) and activates downstream proliferative signaling pathways (such as MAPK, PI3K/AKT, etc.), thereby promoting the survival and proliferation of tumor cells.

SDC1 is widely expressed in breast cancer. SDC1 is a key glycometabolism related gene regulating the immune microenvironment of breast cancer in our previous bioinformatics studies [37], and it is of great significance in guiding the prognosis of breast cancer patients. Therefore, we chose SDC1 as the research target of our review.

SDC1 in breast cancer

Relationship between SDC1 and clinical outcome

SDC1 is an important member of the Syndecan family, and its expression is closely related to the prognosis and treatment response of solid tumors [38]. SDC1 functions as a cell and matrix adhesion receptor and is a classical coreceptor for growth factors, angiogenic factors and chemokines [15]. Compared with that in normal tissues, the expression level of SDC1 was higher in breast cancer, pancreatic cancer, ovarian cancer, endometrial cancer, and prostate cancer tissues, while the expression level was lower in lung cancer, gastric cancer, and colorectal cancer tissues [39–46]. The overexpression of SDC1 was closely correlated with the methylation status of the SDC1 promoter in breast cancer [47]. Moreover, increased SDC1 expression was associated with an ER-negative and HER2-positive aggressive breast cancer phenotype [48] and a reduced response to neoadjuvant chemotherapy in breast cancer patients [49]. Previous studies have shown that SDC1 has a strong predictive contribution to the prognosis of several cancers, including breast and colorectal cancers [48, 50]. In particular, SDC1 results in breast cancer patients who have a worse OS [51, 52]. Additionally, increased SDC1 gene expression is correlated with decreased SDC4 gene expression [53]. The reason why SDC4 overexpression is associated with a better prognosis in breast cancer patients is that SDC4 can promote more cell adhesion and less cell migration [54]. Therefore, pathological expression of SDC1 interferes with complex molecular signals and affects the grade and prognosis of breast cancer patients.

SDC1 and the cancer stem cell phenotype

Cancer stem cells (CSCs) are involved in all stages of breast cancer, including the development and progression of primary tumors, metastasis and recurrence. CSCs are typically regulated by a variety of transcription factors as well as intracellular pathways, such as the Wnt and Notch signaling pathways [55]. CSCs are also regulated by the cellular microenvironment, including cancer-associated fibroblasts (CAFs), extracellular matrix (ECM), tumor-associated macrophages (TAMs), and hypoxia [56]. SDC1 relies on the IL-6/STAT3, Notch and EGFR pathways to regulate the phenotype of breast cancer stem cells (BCSCs) [57, 58]. As a co-receptor, SDC1 can bind to various cytokines (such as IL-6) through its HS chain, enhancing their signal transduction. The IL-6/STAT3 pathway plays a core role in cancer stem cells, and SDC1 can promote STAT3 phosphorylation by binding to the IL-6 receptor complex, thereby maintaining stem cell characteristics. This mechanism has been reported in myeloma, but further verification is needed in breast cancer [59]. The Notch pathway is a key regulator of EMT and stem cell phenotypes. The abscissive form of SDC1 upregulates EMT-associated transcription factors (such as ZEB1, Snail1, and Snail2), thereby promoting the expression of stem cell factors (SOX2, BMI1, OCT4), inducing chemotherapy resistance and metastasis 1. Snail is the core regulatory factor of EMT, and its expression is closely related to the activity of SDC1. Although direct experimental data is limited, SDC1 may indirectly affect Notch signaling by regulating EMT factors such as Snail. For instance, Snail is a downstream target gene of Notch, and SDC1 may form a feedback loop with the Notch pathway through EMT [60]. shed SDC1 can competitively bind to EGFR through its heparan sulfate (HS) chain, activating downstream signaling pathways and promoting chemotherapy resistance in breast cancer cells1. In addition, binding of the HS chain of SDC1 to EGFR has been shown to enhance chemotherapy resistance in colorectal cancer, suggesting that cancer stem cell activity may be maintained through a similar mechanism in breast cancer [61]. In addition, the inhibition of SDC1 expression reduces BCSCs, which is mainly related to a decrease in the IL-6/STAT3 signaling pathway, and can effectively reduce recurrence after successful conventional treatment [62].

SDC1 and the cell cycle

The cell cycle is strictly regulated under physiological conditions and consists of the first gap (G1) phase, synthesis (S) phase, second gap (G2) phase and mitosis (M) phase [63]. Aberrant cell cycle progression is one of the basic mechanisms contributing to tumorigenesis, suggesting that regulation of the cell cycle is a potential anticancer target. Breast cancer is a proliferative disease related to cell cycle dysregulation. Factors known to regulate cell cycle progression, include cyclin-dependent kinases (CDKs) and CDK inhibitors [64]. SDC1, a recently discovered transcription factor regulating the cell cycle, promotes G1 phase arrest by altering the level of heparan sulfate in mesothelioma [65]. Analogously, it was found that a reduction in SDC1 expression reduced the number of cells in S phase and arrested cells in G1 phase, which slowed the progression of the breast cancer cell cycle and inhibited proliferation [57].

SDC1 and cell apoptosis

Cell death is a necessary process for the development of organisms, and cell death types include apoptosis, necrosis, pyroptosis, ferroptosis and other processes [66]. Cell apoptosis is a form of cell suicide triggered by extracellular or intracellular signals and is characterized by cell shrinkage, nuclear fragmentation, chromatin aggregation and the formation of apoptotic bodies [67]. The balance between anti-apoptosis and pro-apoptosis signals maintains cell homeostasis. Once the balance is broken, excessive apoptosis leads to atrophy, while insufficient apoptosis is associated with uncontrolled proliferation, treatment resistance and cancer relapse [68]. The decrease in SDC1 induces caspase-dependent apoptosis by inhibiting Junb-Flip long subtype signaling and reducing the pyrolysis of Caspase 3 and Caspase 8 [69]. Moreover, SDC1 induces apoptosis by inhibiting PDK1/Akt/Bad in prostate cancer [70]. In breast cancer, upregulated SDC1 induces apoptosis by inhibiting the activity of the MEK/ERK signaling pathway to regulate cell proliferation in an orderly manner [71]. Therefore, SDC1 acts as a tumor suppressor molecule by inducing apoptosis.

SDC1 and cell proliferation

SDC1 is a membrane-anchored protein polysaccharide expressed on the basolateral surface of epithelial cells that is abnormally induced in breast cancer stromal fibroblasts and plays a key role in tumor proliferation [72]. SDC1 derived from interstitial fibroblasts participates in the paracrine secretion of breast cancer cells, coordinates the arrangement of extracellular matrix fibers and creates a microenvironment that enables migration and invasion [73]. SDC1 regulates cytoskeletal tissues by contacting extracellular matrix proteins, and results in changes in cell morphology and adhesion [74]. The decrease in SDC1 on the membrane suppresses adhesion and enhances the invasion potential of mammary epithelial cells. Protease facilitates the transformation of SDC1 from the membrane-bound type to the soluble type, marking the transition of breast cancer from the proliferative type to the invasive type, which is of great significance for the diagnosis and treatment of breast cancer based on glycosaminoglycans. In addition, SDC1 acts as a receptor on the cell surface to form a complex with integrin and receptor tyrosine kinase (RTK) to regulate proliferation and migration [75]. In addition, SDC1-deficient mouse models show that SDC1 deletion can inhibit the proliferation of breast tumors induced by the WNT-1 proto-oncogene, suggesting that it may inhibit early tumorigenesis by regulating the Wnt pathway [76]. Although SDC1 is a double-edged sword, more research have confirmed its tumor-promoting effect.

This study delineates the intricate regulatory network mediated by syndecan-1 (SDC1), encompassing its pleiotropic effects on cellular homeostasis, extracellular matrix dynamics, and transmembrane signaling cascades, as systematically mapped in Fig. 1.

SDC1 in the tumor microenvironment

Macrophage migration

The expression of SDC1 is a bridge linking macrophage phagocytosis, polarization and migration. Macrophages in the tumor microenvironment are a group of inflammatory cells different from macrophages in the inflammatory response, called tumor-related macrophages (TAMs). They are macrophages that gradually evolve from monocytes in the circulatory system and migrate to tumor tissue and have different phenotypes and functions [77]; they can be M1-type tumor-suppressing macrophages or M2-type tumor-promoting macrophages. SDC1 expression is unique to M2-type macrophages and is associated with the enhancement of M2-type polarization and migration [78]. SDC1 is able to enhance the movement of macrophages and is involved in the regulation of tissue repair and chronic injury responses, including cell-substrate interactions and matrix remodeling [79]. SDC1 is also critical in regulating the cytoskeletal dynamics of M2-type macrophages [78]. The expression of SDC1 in macrophages is regulated by the CAMP/PKA signaling cascade; treatments such as E-prostaglandin membrane-permeable CAMP analogs or adenosine and other drugs that increase intracellular CAMP can promote the expression of SDC1 protein in macrophages through this pathway [80].

Angiogenesis

Tumor cells are highly active in metabolism, and sufficient nutrients are necessary for their continuous growth.

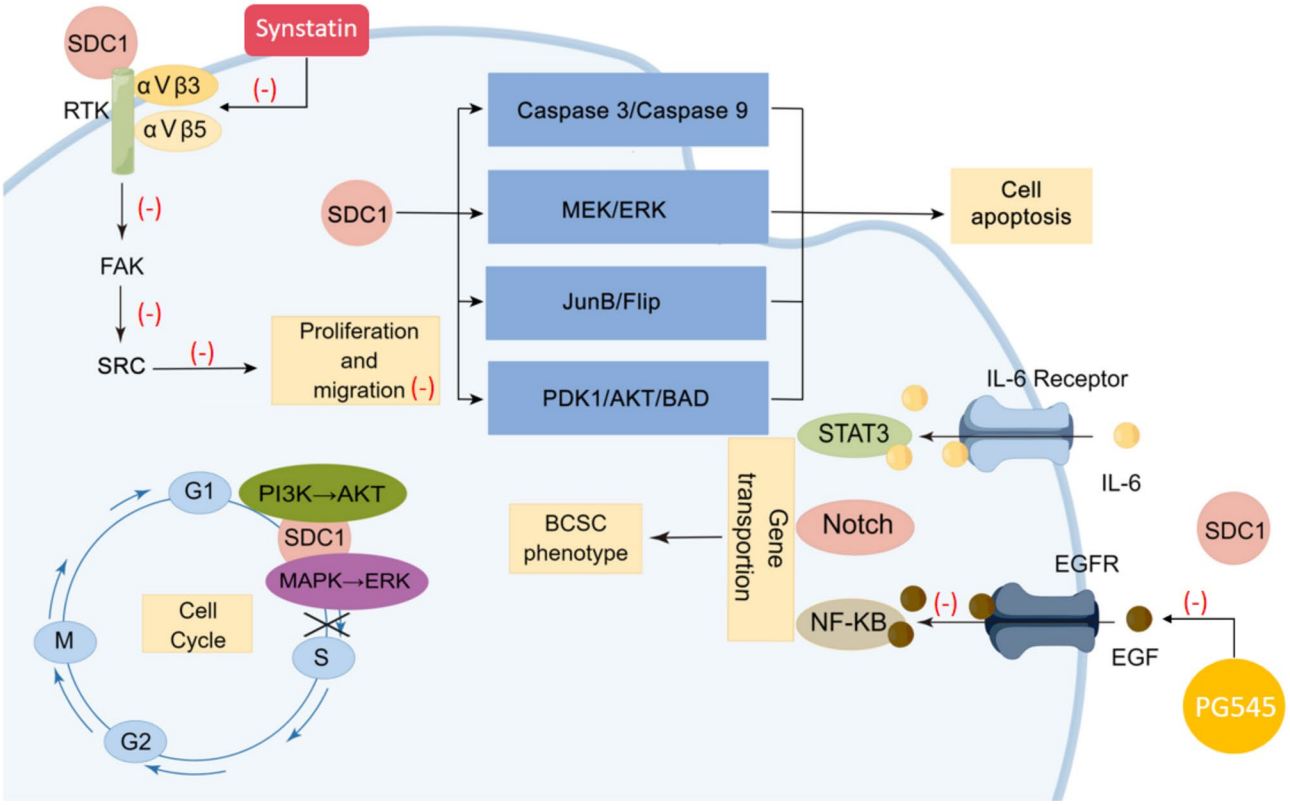

Fig. 1 The cellular activities of SDC1 in breast cancer. ***Proliferation and migration***:SDC1: Syndecan1; RTK: Receptor Tyrosine Kinase; FAK: Focal adhesion kinase; SRC: Sarcoma. ***Cell apoptosis***: Caspase 3/Caspase 9 signal pathway; MEK/ERK signal pathway; JunB/Flip signal pathway; PDK1/AKT/BAD signal pathway. ***Cell cycle***:G1: First Gap; S: Synthesis; M: Metaphase; G2: Second Gap. ***BCSC phenotype***:IL-6: Interleukin-6; EGF (R): Epidermal Growth Factor (Receptor); STAT3: Signal Transducer and Activator of Transcription 3; Notch signal pathway; NF-KB: Nuclear Factor Kappa-B

Angiogenesis is an important process by which tumor cells obtain nutrients [81] and is based on the sprouting of vessels to form new capillaries. Tumor angiogenesis is a cascade process between tumor cells and vascular endothelial cells mediated by various cytokines through paracrine and autocrine pathways. Whether the process can proceed depends on the balance between angiogenesis promoters and angiogenesis inhibitors. SDC1 can bind to angiogenic promotors such as FGF-2 and VEGF, which are presented to their respective receptors on endothelial cells, thereby initiating endothelial cell invasion and sprouting [82]. Therefore, the expression level of SDC1 in human breast cancer stromal fibroblasts is associated with higher microvessel density and larger vessel area [18]. Moreover, the overexpression of SDC1 also results in increased expression of angiogenesis promoters [18] and is part of proangiogenic signaling in early breast cancer. Increased vascularity is associated with advanced tumor stages and a poor prognosis [83].

The tumor-bone microenvironment

SDC1 derived from tumor cells is a novel positive regulator of osteoclastogenesis that plays an important role in the tumor-bone microenvironment [84]. The loss of SDC1 reduces the cell viability of hormone receptor-positive breast cancer cells and increases the expression of osteoprotegerin (OPG), which inhibits the differentiation and activation of osteoclasts [85]. SDC1 alters OPG function not only at the protein level but also at the transcriptional level [85].

Epithelial-mesenchymal transformation

Epithelial-mesenchymal transformation (EMT) refers to the transformation of epithelial cells into mesenchymal cells under certain physiological or pathological conditions. In recent years, EMT has been found to be strongly associated with tumor metastasis. In the process of tumorigenesis, normal epithelial cells undergoing EMT can evolve into carcinoma in situ, and then tumor cells continue to evolve through EMT and gain in situ invasion and lymphatic vessel and blood vessel invasion abilities, eventually leading to distant metastasis [86]. On the one hand, EMT can reduce the expression of intercellular connective molecules, which can decrease adhesion ability, promote migration and enhance the invasion ability of tumor cells [87]. On the other hand, tumor invasion and metastasis are enhanced by changing the microenvironment of tumor growth and vascular formation [87].

The expression levels of SDC1 and E-cadherin were used to assess EMT, and low expression of SDC1 and E-cadherin indicated worse cell connectivity and tumor-promoting development through EMT [88].

This review establishes a paradigm for SDC1-mediated modulation of the tumor microenvironment, particularly its macrophage migration, angiogenesis, tumor-bone microenvironment and Epithelial-mesenchymal transformation, as mechanistically mapped in Fig. 2.

The expression and function of SDC1 (Syndecan-1) in cancer are dynamically regulated by its various ligands, which are often abnormally expressed or have enhanced activity in the tumor microenvironment. These ligands jointly drive cancer progression. For instance, growth factors (such as FGF, VEGF) bind to the sulfate heparan chains of SDC1, activating proliferation-promoting signaling pathways (such as MAPK, PI3K/AKT), and form a positive feedback loop to upregulate SDC1 expression to enhance tumor survival and angiogenesis; extracellular matrix components (such as fibronectin, collagen) promote SDC1 membrane localization through integrin synergy, inducing epithelial-mesenchymal transition (EMT) and metastasis. Additionally, inflammatory factors (such as IL-6, TGF-β) upregulate SDC1 expression through STAT3 or Smad signaling pathways, exacerbating tumor stem cell characteristics and immunosuppressive microenvironment; while proteases (such as MMPs, ADAM17) cleave SDC1 to generate soluble forms, promoting angiogenesis, immune escape, and chemotherapy resistance. The interactions between these ligands and SDC1 are type-specific to tumors, and their co-expression often indicates poor prognosis. Targeting the SDC1-ligand axis (such as antibody blockade, shedding inhibition) or combining with existing therapies provides potential strategies to reverse the malignant phenotype of tumors.

Current therapies targeting SDC1

Clinical treatment of tumors still remains difficult, and several drugs that interfere with SDC1 expression are being investigated, as shown in Table 3. The I^{131}-labeled SDC1 antibody B-B4 induces cell death through radiation

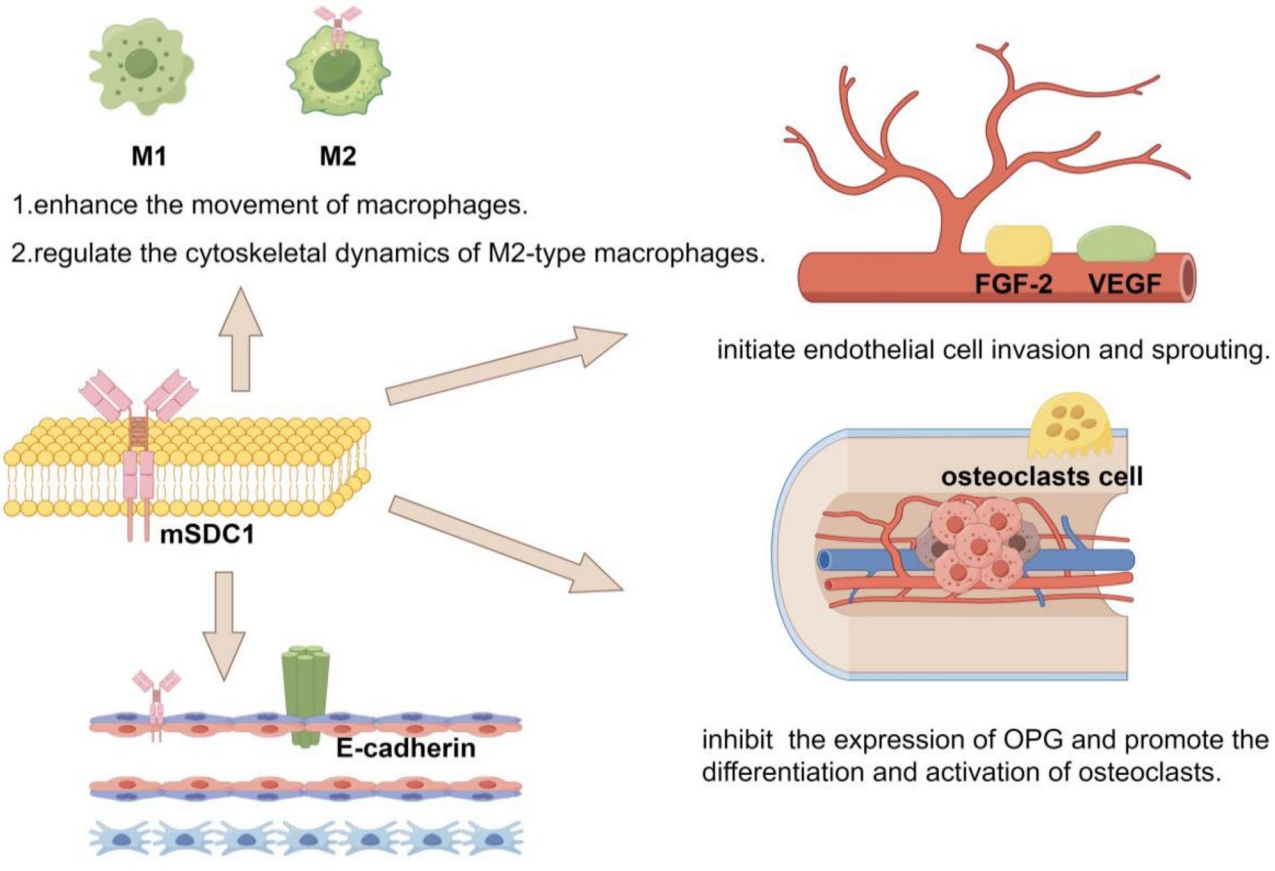

Fig. 2 The microenvironment effects of SDC1 in breast cancer. 1. The expression of SDC1 is a Bridge linking macrophage phagocytosis, polarization and migration. 2. The expression of SDC1 is related to angiogenesis. 3. SDC1 plays an important role in the tumor-bone microenvironment. 4. The expression levels of SDC1 and E-cadherin were used to assess EMT

Table 3 Research on SDC1 targeting in breast cancer

Ligands	Targeted area	Antitumor affect	Research style	Style object	Reference
BB4 (I^{131})	extracellular domain of mSDC1	Inducing the death of tumor cells	Clinical model	Multiple myeloma patients	87
BB-94 (MMP inhibitor)	Inhibiting shedding of mSDC1	Inhibiting of chemotherapy-induced SDC1 shedding to form a microenvironment that promotes tumor recurrence	Pre-clinical model	Mouse	89
All-trans retinoic acid (ATRA)	Reducing expression of sSDC1	Providing chemical protective effect on lung cancer model induced by benzopyrene	Pre-clinical model	Mouse	90
Zoledronic acid	Reducing expression of sSDC1	Inhibiting bone metastasis	Pre-clinical model	Cell	83
SSTN	Destructing of SDC1 and integrin complex	Inhibiting angiogenesis	Pre-clinical model	Mouse	73

by targeting the extracellular domain of membrane-bound SDC1 [89]. As mentioned previously, commonly used chemotherapeutic agents can promote the shedding of SDC1 [90]. BB94 is a broad-spectrum MMP inhibitor that inhibits membrane-type SDC1 shedding, and disrupts the occurrence of breast cancer, ovarian cancer and colorectal cancer [91]. Although benzopyrene has been found to promote lung cancer in mice by increasing SDC1 shedding from epithelial cells, this effect can be inhibited by all-trans retinoic acid (ATRA) [92]. Zoledronic acid inhibits breast cancer metastasis by reducing SDC1 expression and increasing SDC2/SDC4 expression [93]. Synstatin inhibits angiogenesis in breast cancer by disrupting the complex of integrin αVβ3, αVβ5 and SDC1 [75]. Therefore, SDC1 is a potentially attractive molecular target that can guide the personalized diagnosis and treatment of a variety of malignancies with a poor prognosis, such as breast cancer.

Conclusion and perspective

In conclusion, breast cancer is a heterogeneous disease at the population and single-cell levels, with different genotypes and phenotypes that can manifest within the same tumor, and targeted therapy remains a challenge in different subtypes of breast cancer. Although there is limited research on targeting SDC1in breast cancer, the role of SDC1 in breast cancer occurrence and development indicates that SDC1 creates favorable conditions by regulating ECM remodeling to transform the stromal microenvironment from restricting invasion to allowing invasion, which promotes the attack and spread of breast cancer cells. SDC1-targeted therapy shows good antitumor activity, and we believe that monoclonal antibodies or small molecule inhibitors against SDC1, siRNA-based therapy for SDC1 suppression and combination strategies (e.g., SDC1 inhibition + immune checkpoint blockade) will become a very promising therapeutic strategy in the future.

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Author contributions
Yingying Mei: Conceptualization, Writing-Original Draft. Lantao Zhao: Data Curation, Writing-Review & Editing. Na Zhou: Project administration, Conceptualization, Funding acquisition. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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