CXCL1 in triple-negative breast cancer: Mechanisms, challenges, and therapeutic opportunities (Review)

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Abstract. Triple negative breast cancer (TNBC) is an aggressive BC subtype with limited therapeutic options and poor clinical outcomes. This subtype accounts for 15-20% of all BC cases and contributes to nearly 40% of BC mortalities. The chemokine C-X-C motif ligand 1 (CXCL1) is a key player in TNBC progression through several signaling pathways, including NF-κB, MAPK and related cascades. CXCL1 contributes to tumor growth, metastasis, immune modulation and resistance to therapy, however its role and therapeutic potential in TNBC has not been comprehensively described. The present review aimed to summarize CXCL1 biology in TNBC, with a focus on its prognostic relevance, role in the tumor microenvironment and potential as a therapeutic target, as well as emerging strategies aimed at modulating CXCL1 signaling. However, challenges remain in translating these findings into clinical application, including incomplete understanding of certain molecular mechanisms underlying CXCL1 function, unclear prognostic value, the need for validation of potential inhibitors in large and diverse cohorts and the lack of well-designed clinical trials testing CXCL1-targeted approaches. Addressing these challenges through rigorous preclinical work and carefully designed clinical trials is key to define the true therapeutic potential of CXCL1 in TNBC to advance precision medicine strategies and enhance clinical outcomes in patients with TNBC.

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Abbreviations: ACKR1, atypical chemokine receptor 1; BCSC, breast cancer stem cell; BHS, baohuoside I, BL1/BL2, basal-like 1/2; CAF, cancer-associated fibroblast; CCL2/CCL7, chemokine ligand 2/7; CXCL1 EV, C-X-C motif ligand 1-containing extracellular vesicle; CXCR1/CXCR2, C-X-C motif chemokine receptor 1/2; DIF-1, differentiation-inducing factor-1; EED, ectoderm development protein; EGFR, epidermal growth factor receptor; EMT, epithelial-mesenchymal transition; ER, estrogen receptor; GR, glucocorticoid receptor; GRO: growth-regulated oncogene; HER2, human epidermal growth factor receptor 2; HSPC, hematopoietic stem and progenitor cell; IκB, NF-κB inhibitor; IM, immunomodulatory subtype; MDSC, myeloid-derived suppressor cell; PD-L1, programmed death-ligand 1; PGG, pentagalloylglucose; PI3K, phosphoinositide 3-kinase; PMN, pre-metastatic niche; TAM, tumor-associated macrophage; TAN, tumor-associated neutrophil; TGF-α, transforming growth factor α; TME, tumor microenvironment; TNBC, triple-negative breast cancer; tmTNF-α, transmembrane tumor necrosis factor-α; TPCA-1, [(aminocarbonyl) amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide; XPS, XIAOPI formula

Key words: CXCL1, TNBC, CXCR2, tumor microenvironment, chemokine, metastasis, chemotherapy resistance, therapeutic target

Contents

1. Introduction

Triple-negative breast cancer (TNBC) is a highly aggressive subtype of BC (1). It is defined by the absence of expression of the estrogen receptor (ER) and progesterone receptors, as well as the absence of human epidermal growth factor receptor 2 (HER2) upregulation (2). This subtype accounts for 15-20% of all BC cases (3) and contributes to nearly 40% of BC mortality (4). TNBC is typically associated with a poor prognosis and notable risk of recurrence (~25%) (5,6). It is also prone to metastasis which occurs in ~46% of cases (6,7). Despite advancements made in TNBC treatment, it remains challenging

due to the presence of multiple molecular subtypes (8). The molecular subtypes of TNBC include basal-like (BL)1 and 2, immunomodulatory (IM), mesenchymal (M), mesenchymal stem-like (MSL) and luminal androgen receptor (9). Moreover, future integration of additional data sources may help identify definitive TNBC subtypes (10). This tumor heterogeneity and the absence of biomarkers contribute to treatment resistance and relapse in TNBC (1).

Treatment strategies and challenges. Chemotherapy is the standard treatment for TNBC, with commonly used agents including anti-microtubule agents such as taxanes (paclitaxel), anthracyclines (doxorubicin), alkylating agents (cyclophosphamide) and fluorouracil (11). Although chemotherapy can be effective, it is associated with toxicity and variable patient outcomes (8). Another limitation is intrinsic or acquired chemotherapy resistance, which is common in TNBC and is the primary obstacle to effective treatment (12). It is therefore prudent to explore additional therapeutic options. Numerous immunotherapy and targeted therapy strategies, including immune checkpoint inhibitors, PARP inhibitors, and antibody-drug conjugates, are under investigation for their potential effectiveness against TNBC (13). In addition, studying the interaction of TNBC tumors with the tumor microenvironment (TME) may help increase immunotherapy effectiveness (14). Nevertheless, developing new therapies for TNBC remains challenging, with a small number of approved targeted therapies available, such as poly-ADP-ribose polymerase and immune checkpoint inhibitors (13). As such, treatment mostly depends on chemotherapy, surgery and radiation, which typically cause serious side effects and have decreased effectiveness (15,16). These challenges underscore the urgent need for novel therapeutic strategies that may overcome resistance and improve outcomes for patients with TNBC.

C-X-C motif ligand 1 (CXCL1). Chemokines are small proteins that regulate guided cellular movement, with ~50 members identified in mammals (17). The TME is the primary site of interaction between tumor cells and the host immune system (18). Through interactions between chemokines and chemokine receptors, numerous immune cell subsets are recruited into the TME, with differential effects on tumor progression and treatment results (18). The CXC chemokines are a distinct family of cytokines that contain four highly conserved cysteine amino acid residues, with the first two cysteine residues separated by one non-conserved amino acid residue (19). These chemokines are key regulators of the progression and spread of BC due to their ability to control leukocyte infiltration and TME interactions (20). The present review primarily examines CXCL1 chemokine, which is also known as growth-regulated oncogene-α and melanoma growth stimulatory activity-α, due to its role as a key mediator of TNBC progression (21). CXCL1 belongs to the ELR^+ chemokine group due to the presence of the tripeptide motif (Glu-Leu-Arg) at the NH2 terminus (22).

CXCL1 receptors (CXCRs). A total of three receptors for CXCL1 have been identified: CXCR1 and 2 and atypical chemokine receptor 1 (ACKR1) (23). CXCL1 binds CXCR2 with high affinity and CXCR1 with low affinity (24). ACKR1 interacts with CXCL1 with binding characteristics comparable with those observed between CXCL1 and CXCR2 (23). In BC, particularly TNBC, ACKR1 expression is associated with regulation of angiogenesis, metastatic behavior and immune cell infiltration (25). The role of ACKR1 in CXCL1 function, however, is not fully understood and requires further experimental validation (26).

Role of CXCL1 in BC. Numerous reviews have addressed the role of CXCL1 in BC and concluded that CXCL1 promotes cancer cell proliferation and migration (26-28). Beyond its direct tumor effects, CXCL1 influences the TME by recruiting immune cells such as myeloid-derived suppressor cells (MDSCs) and neutrophils, and inducing angiogenesis via endothelial CXCR2 (23,26,27). Notably, Korbecki *et al* (26) summarized the involvement of CXCL1 in BC progression, highlighting its role in tumor progression, metastasis and immune cell recruitment, as well as therapeutic strategies targeting CXCL1 and its receptors in cancer (27).

CXCL1 is typically overexpressed in aggressive BC subtypes, including TNBC (26,27). Recent studies have highlighted CXCL1 as a potential therapeutic target in TNBC (29-31). Despite increasing evidence of its involvement in tumor progression, immune modulation and the TME (21,22,26,27), to the best of our knowledge, no comprehensive review has focused exclusively on the role of CXCL1 in TNBC.

The present review summarizes the value of targeting CXCL1 in TNBC, a subtype marked by poor prognosis and the absence of effective targeted therapy, the expression patterns and cellular sources of CXCL1 in TNBC, along with key signaling pathways associated with its activity, as well as how CXCL1 shapes tumor behavior and the TME, including its interactions with immune cells and involvement in extracellular vesicle (EV)-mediated communication. Finally, it explores therapeutic strategies aimed at modulating the CXCL1 axis and outlines challenges that continue to hinder clinical translation.

2. CXCL1 expression, sources and signaling in TNBC

Expression patterns of CXCL1. Elevated CXCL1 expression in BC tissue is associated with advanced tumor stage and poor prognosis (32). CXCL1 expression may differ between BC subtypes. For example, CXCL1 is highly expressed in ER-negative BC compared with ER-positive subtypes (33,34). Although CXCL1 is expressed in 3.67% of BC cases in the Pan-Cancer dataset, with ~2 million cases diagnosed annually worldwide, this corresponds to ~73,000 CXCL1-positive cases each year (35). As 69% of patients with CXCL1-positive BC are diagnosed with TNBC, CXCL1 expression might serve a role in the malignant phenotype of this disease (35).

Expression of CXCL1 is elevated in TNBC compared with other subtypes in human BC tissues (33,36-38). Elevated CXCL1 expression is associated with BL subtypes of BC (39). The BL subtype is common in TNBC, accounting for 70-80% of cases (40). CXCL1 expression is also elevated in M TNBC (38). Because these subtypes are characterized by distinct molecular characteristics, the functional consequences

Table I. CXCL1 expression patterns and proposed functional roles across TNBC molecular subtypes.

TNBC subtype	CXCL1 expression	Associated pathways	Proposed biological consequences	Subtype-specific uncertainties	(Refs.)
BL	Elevated	Proliferation-related	May contribute to the highly proliferative phenotype characteristic of BL tumors	Lack of direct comparative studies assessing CXCL1 expression and function in BL1 vs. BL2	(9,39)
Mesenchymal	Elevated	EMT and motility-associated	May promote EMT and cell motility	Limited subtype-stratified functional studies linking CXCL1 to EMT programs	(9,38)
IM	Not defined	Immune cell signaling	May influence immune cell recruitment or activation within the TME	Insufficient direct evidence defining CXCL1-driven immune interactions specifically in IM TNBC	(9)

BL1/BL2, basal-like 1/2; CXCL1, C-X-C motif ligand 1; EMT, epithelial-mesenchymal transition; IM, immunomodulatory; TME, tumor microenvironment; TNBC, triple-negative breast cancer.

of CXCL1 upregulation may differ according to subtype context. For example, given that CXCL1 has been reported to promote tumor cell proliferation in TNBC (36), its elevated expression in BL tumors may further contribute to the highly proliferative phenotype characteristic of this subtype (9). Within the BL subtype, BL1 and BL2 differ in their molecular programs, with BL1 exhibiting the strongest enrichment in proliferation-associated pathways (9). However, despite the higher proliferative signature of BL1, the relative contribution and functional impact of CXCL1 in BL1 vs. BL2 remain insufficiently defined, and additional studies are needed to clarify these distinctions.

In M TNBC which is characterized by upregulation of signaling pathways that promote epithelial-mesenchymal transition (EMT) and cell motility (9), CXCL1 may contribute to these processes through its ability to modulate EMT regulators in TNBC cells (36). The IM subtype is highly enriched in immune cell signaling (9). Given its interaction with immune cells in TNBC (41-43), it is important to determine whether CXCL1 interacts differently with immune cells in the IM compared with other subtypes. However, direct experimental evidence linking CXCL1 to specific downstream signaling pathways in individual TNBC subtypes is limited (44). Most studies have examined general TNBC contexts without stratification into BL1, BL2, M or IM subtypes (27,44,45). Accordingly, the proposed subtype-specific roles are largely hypothetical and require validation in subtype stratified cell lines, patient-derived models or single-cell transcriptomic analyses. A summary of CXCL1 expression patterns and proposed functional consequences across TNBC molecular subtypes is provided in Table I.

Beyond molecular subtypes, Bièche *et al* (46) showed that the TNBC cell line MDA-MB-231 produces the highest levels of CXCL1 among BC cell lines. Furthermore, this increased CXCL1 expression is induced by various cancer therapies (27). For example, CXCL1 expression in TNBC is induced by chemotherapeutic agents, such as doxorubicin (47) and paclitaxel (30) in MDA-MB-231 cells. High CXCL1 expression does not occur in all TNBC cell lines, with BT-20 cells being an example (26).

Sources of CXCL1. In TNBC, CXCL1 is produced by multiple cell types, including BC and tumor-associated immune cells in the TME (35). To explore the significance of CXCL1 in TNBC, it is important to identify which cells in the TME are responsible for its production. Tumor-associated macrophages (TAMs), a primary immune cell population within tumors, are broadly classified into pro-inflammatory, anti-tumor M1 macrophages and immunosuppressive, tumor-promoting M2 macrophages, with the latter supporting tumor growth, metastasis and angiogenesis (48). CXCL1 is secreted in high amounts by TAMs (39,48). More specifically, CXCL1 is secreted by M2-polarized TAMs in the TME (49,50).

Cancer associated fibroblasts (CAFs) are another source of CXCL1 in TNBC (37). CAFs arise primarily from tissue-resident (quiescent) fibroblasts and include all fibroblasts present in the tumor that interact with cancer cells (51). CAFs produce extracellular matrix and reprogram immune surveillance in the TME (44). CAFs treated with neoadjuvant chemotherapy release ELR^+ chemokines, which include CXCL1 (52).

In addition, BC stem cells (BCSCs) are a small but key subset of heterogenous BC cells that exhibit potent proliferative and self-renewal abilities (53). TNBC exhibits marked enrichment of BCSCs (54). It has been hypothesized that BCSCs could potentially serve as a notable source of CXCL1 in TNBC (35). Overall, CXCL1 is abundantly expressed in TNBC and originates from multiple cell types.

3. Upstream regulation of CXCL1 signaling

NF-κB pathway. CXCL1 expression is regulated by intracellular signaling pathways and external stimuli within the TME. Chemokine expression is regulated by NF-κB signaling (55-57). CXCL1 is a transcriptional target of NF-κB, which, upon activation, promotes CXCL1 expression (23,58,59). IκB kinase-mediated phosphorylation of the

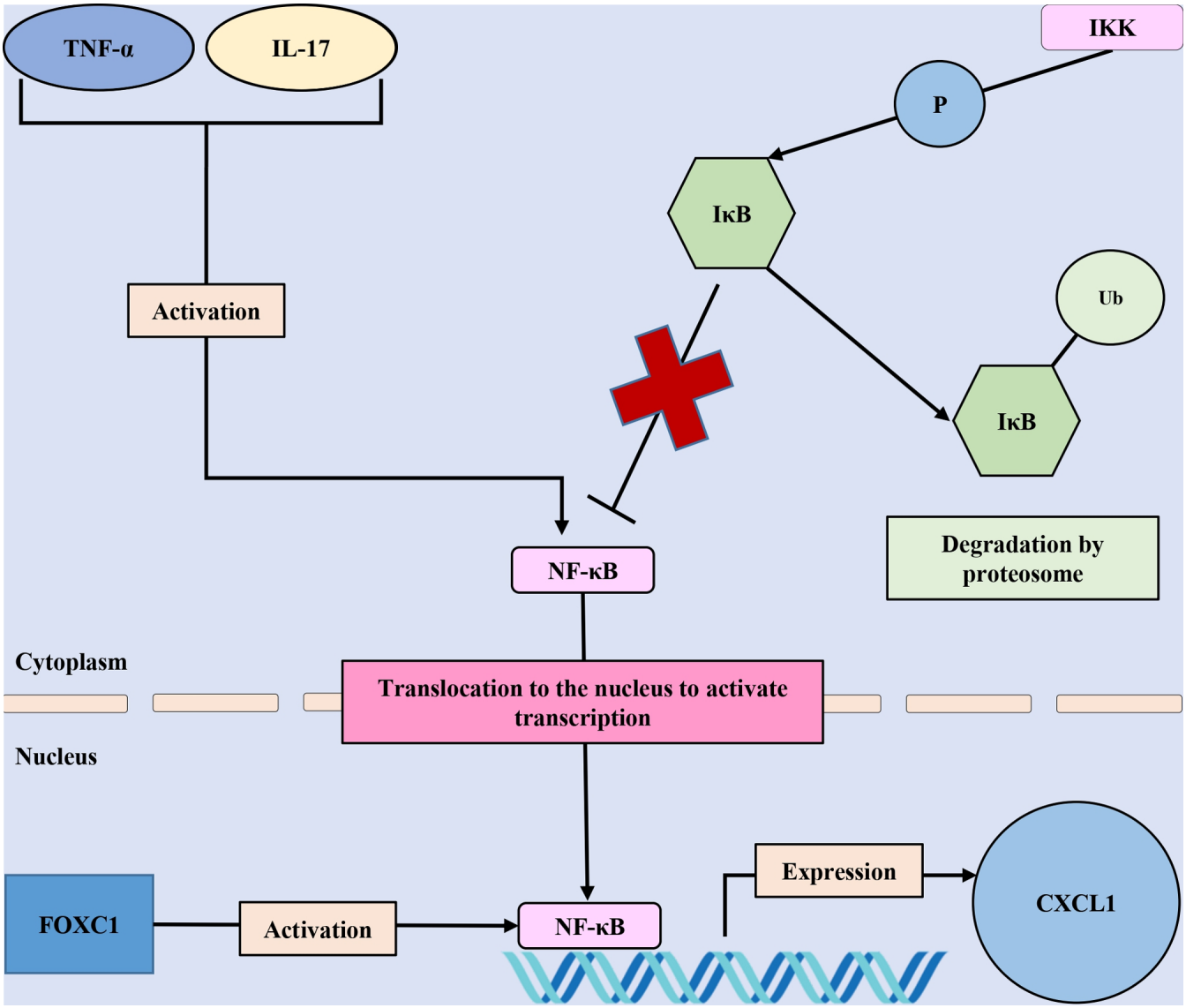

Figure 1. Upstream regulation of CXCL1 expression via NF-κB. IκB is phosphorylated by IKK, which marks it for ubiquitination and leads to its degradation, enabling NF-κB to enter the nucleus and activate transcription of CXCL1. IL-17 and TNF-α activate NF κB signaling. NF-κB may also be induced by the transcription factor FOXC1 in triple-negative breast cancer cells. Created using Canva.com. Ub, Ubiquitin; IKK, IκB kinase.

NF-κB inhibitor (IκB) marks it for ubiquitination and leads to its degradation, enabling NF-κB to enter the nucleus and activate transcription of tumor-promoting chemokines such as CXCL1 (57) (Fig. 1). Elevated NF-κB activity is associated with ER-negative BC, especially BL subtypes (60). TNBC, in particular, is characterized by high levels of constitutively active NF-κB signaling (61). Additionally, the increase of CXCL1 via NF-κB in BC is associated with the use of chemotherapeutics (27,47). This is observed in TNBC, where doxorubicin activates NF-κB in MDA-MB-231 cells resulting in the expression of several genes, including CXCL1 (47).

Regulators of the NF-κB pathway. The NF-κB pathway is regulated by multiple modulators that might affect CXCL1 expression (Fig. 1). For example, IL-17 activates NF-κB signaling (62,63). IL-17 also induces CXCL1 expression in TNBC cells (64,65). Furthermore, chemotherapy increases tumor necrosis factor (TNF)-α expression in the TME, which increases CXCL1 levels in BC cells (7). Consistently, the NF-κB pathway is induced by TNF-α in TNBC cells, leading to increased expression of CXCL1 (41,59). A total of ~84% of TNBC cases exhibit upregulated transmembrane TNF-α (tmTNF-α) (66). This may be associated with increased CXCL1 expression, potentially through NF-κB dependent mechanisms (57-59). This suggests tmTNF-α as a potential tumor biomarker, with further research required. Finally, CXCL1 expression mediated by NF-κB may be induced by the transcription factor forkhead box C1 in TNBC cells (58).

Additional regulators. TNBC cells exhibit increased activation of Akt. These cells express elevated levels of epidermal growth factor receptor (EGFR) and release more transforming growth factor (TGF)-α, the primary ligand for EGFR, compared with other BC subtypes (38). It is hypothesized that TGF-α- and EGFR-mediated activation of Akt may contribute

to the increased expression of proinflammatory chemokines in TNBC (38).

4. Downstream regulation of CXCL1 signaling

CXCL1 expression in TNBC is positively associated with pro-angiogenic factors and tumor progression gene expression (35). Elevated levels of CXCL1 and other CXCR2 ligands lead to a self-stimulating loop that enhances the production of these chemokines through autocrine signaling (27,67). For example, in BCSCs, which are enriched in TNBC, CXCL1 reinforces its own expression through an autocrine feedback loop (35). In addition, CXCL1 binding to CXCR2 activates NF-κB signaling pathways (27,68,69). In BC, CXCL1 derived from tumor-associated macrophages (TAMs) signals via the NF-κB/SRY-box transcription factor 4 pathway (39). CXCL1 also contributes to the upregulation of programmed death-ligand 1 (PD-L1) (70). In TNBC cells, CXCL1 produced by M2 TAMs induces PD-L1 expression by triggering NF-κB activation (49).

Beyond NF-κB, CXCL1 also activates the ERK/MAPK pathway, which enhances the expression of MMP2 and MMP9, thereby promoting BC cell migration (34). Consistent with this, a previous study in TNBC demonstrated that MDA-MB-231 cells display increased invasiveness and migration associated with elevated MMP9 expression (71,72). Notably, TNBC-derived CXCL1 stimulates lung fibroblasts and cancer-associated fibroblasts (CAFs) to secrete additional chemokines, such as C-C motif chemokine ligand (CCL)2 and 7, which subsequently enhance CXCL1 production in TNBC cells, establishing a positive chemokine feedback loop at metastatic sites (58). Although several signaling cascades have been identified downstream of CXCL1, only a subset, including NF-κB and ERK/MAPK pathways, have been thoroughly investigated in TNBC (34,68,69).

5. Role of CXCL1 in TNBC progression and the TME

High CXCL1 expression is associated with decreased survival in patients with BC (73). Several mechanisms mediated by CXCL1 may be involved in this outcome. Previous reviews have highlighted the multifaceted role of CXCL1 in BC via effects on tumor cells and the TME (26,27). These effects include driving carcinogenesis, angiogenesis, immune cell recruitment and polarization, metastatic progression and drug resistance (26,27). As such, it is important to shed light on the role of CXCL1 in TNBC. CXCL1 may promote cell proliferation in TNBC, since CXCL1 knockdown in MDA-MB-231 cells decreases proliferation by ~40% (36). CXCL1 also serves as an autocrine growth factor for BCSCs and sustains their self-renewal (35). Consistently, CXCR2 has been proposed as a potential cancer SC marker in TNBC (74), which suggests that the CXCL1-CXCR2 axis may play a critical role in maintaining BCSC properties and promoting tumor progression in TNBC (26).

CXCL1 may influence invasiveness and metastatic potential of TNBC. A study on TNBC cell lines showed that treatment with CXCL1 promotes MDA-MB-231 cell invasion in a dose-dependent manner, while an increase in migration is observed only at elevated CXCL1 levels (42). Furthermore, CXCL1 is a key component that facilitates the metastasis of BC cells (50,75). This may be explained by the involvement of CXCL1 in the regulation of EMT regulators such as Snail, mesenchymal marker genes such as N-cadherin and the epithelial marker gene E-cadherin in TNBC cells (36). Consistently, elevated levels of CXCL1 contribute to lung metastasis in patients with BC (76). In TNBC, CXCL1, along with CXCL2 and CXCL8, serves an essential role in lung metastasis formation, and high CXCL1/2/8 expression in primary TNBC tumors is key for supporting angiogenesis in this process (58). During TNBC lung metastasis formation, tumor-derived CXCL1/2/8 activate lung resident fibroblasts to secrete CCL2/7, which stimulates cholesterol synthesis in metastatic TNBC tumor cells, driving angiogenesis and metastatic outgrowth (58). In summary, CXCL1 promotes diverse mechanisms that support TNBC progression.

Interaction with immune cells. CXCL1 interacts with immune cells by attracting myeloid cells (41). For example, a recent study in 4T1 TNBC cells revealed that CXCL1 promotes the mobilization of splenic MDSCs to the lung, a key step in pre-metastatic niche (PMN) formation (50). The aforementioned study showed that chronic psychological stress activates TAM/CXCL1 signaling in the TME via the glucocorticoid receptor (GR) pathway, with elevated cortisol levels enhancing GR binding to the CXCL1 promoter in TAMs (50). This upregulation of CXCL1 promotes the proliferation, movement and immunosuppressive functions of MDSCs via CXCR2, facilitating their recruitment and PMN formation (50). Similarly, another study has shown that CXCL1 may indirectly mediate the interaction between macrophages and BC cells in the PMN, which contributes to BC progression (42). Moreover, CXCL1 promotes the recruitment of hematopoietic stem and progenitor cells (HSPCs) from the bone marrow and their differentiation into MDSCs in the TME (77).

In addition to MDSCs, CXCL1 also plays a crucial role in attracting tumor-associated neutrophils (TANs) to the TME (33,43,64). TANs are highly present in the TNBC tumor niche. Tumor-associated factors, including cytokines, are involved in promoting their production in the bone marrow and recruitment to the tumor site (78). TNBC cell lines secrete notably higher levels of neutrophil-activating factors, including CXCL1, compared with ER-positive cells, resulting in strong neutrophil migration (33). This recruitment may depend on the combined effects of Growth-regulated oncogene (GRO) chemokines, such as CXCL1, and TGF-β found in the tumor conditioned media harvested from TNBC cells (33). TGF-β also induces an N2 protumor phenotype of TANs in the TME (79). TAN recruitment is typically mediated via CXCR2 in TNBC (23,80,81). However, neutrophil-recruiting activity of tumor conditioned media remains intact after blocking CXCR2, indicating that CXCL1/CXCR1 signaling may also play a role in neutrophil recruitment in TNBC cell lines (33). Additionally, CXCL1/TAMs are primarily implicated in immune evasion and therapy resistance in TNBC (48,49).

TAM/CXCL1 and EV signaling. TAMs are a key immune population in TNBC. TNBC tissue shows notable infiltration of M2 macrophages (49). M2-TAMs may promote autophagy

and contribute to BC cell resistance to chemotherapy with the involvement of CXCL1 (48). CXCL1 may induce autophagy by regulating the insulin-like growth factor 1/insulin-like growth factor 1 Receptor pathway (48). This promotes chemoresistance to paclitaxel in MDA-MB-231 cells (48).

PD-L1, the primary ligand of the coinhibitory receptor PD-1, regulates immune tolerance by preventing overactive immune responses (82). Cancer cells exploit this process and typically express PD-L1 to evade immune attack, a strategy associated with poor patient outcomes (82). A recent study showed that CXCL1 secreted by M2 macrophages in the TME promotes PD-L1 upregulation in TNBC via activation of the CXCR2-mediated phosphoinositide 3-kinase (PI3K)/AKT/NF-κB signaling pathway, which reveals the immunosuppressive role of M2 macrophages and CXCL1 (49) (Fig. 2).

Additionally, tumor cells release EVs, which have the potential to act as mediators of intercellular communication in the TME, impacting cancer progression (83). This has been described in TNBC (30,84). Chemotherapeutic agents such as paclitaxel induce the release of CXCL1-enriched EVs from dying TNBC cells (30). These CXCL1-containing EVs (CXCL1 EVs) induce macrophage M2 polarization by upregulating PD-L1 expression (30). EVs are phagocytosed by macrophages and the CXCL1 cargo is released into the cytoplasm (30). It is likely that CXCR2 does not serve a role in this process (30). Mechanistically, CXCL1 EVs promote embryonic ectoderm development (EED) protein expression and its nuclear translocation. EED then binds to the PD-L1 promoter, enhancing PD-L1 transcription (30). Through this TAM/PD-L1 signaling pathway, CXCL1 EVs drive TNBC tumor growth and lung metastasis (30). This process also contributes to chemotherapy resistance in TNBC (84). This suggests that chemotherapy may paradoxically drive pathways that promote chemoresistance in TNBC, emphasizing the need for alternative treatment options. Overall, CXCL1 links macrophage polarization, PD-L1 expression and EV-mediated communication into a unified axis of immune evasion and therapy resistance in TNBC (Fig. 2).

6. Therapeutic potential of targeting CXCL1 signaling in TNBC

Current strategies to inhibit CXCL1/CXCR2 pathway. The CXCL1/CXCR2 pathway plays a key role in TNBC, making it a relevant focus for therapeutic development. CXCR2 expression is upregulated by chemotherapeutic agents such as doxorubicin in TNBC cells (85). Elevated CXCR2 expression is associated with poorer prognosis in patients with TNBC, as it is implicated in chemotherapy resistance (85,86). Combining CXCR2 antagonists with traditional chemotherapy or immune checkpoint inhibitors suggests CXCR2 inhibition is a viable approach to counteract chemoresistance and enhance immunotherapy in TNBC (85). Several antagonists targeting CXCR2 such as reparixin, SB225002 and AZD5069 have been developed (27). Reparixin, a non-competitive allosteric inhibitor, does not show an advantage when combined with paclitaxel in patients with advanced TNBC, compared with paclitaxel treatment alone (27,87). Alternatively, SB225002 increases apoptosis in TNBC cells (45). Although SB225002 has shown effectiveness against multiple types of cancer, including TNBC, this compound has not yet been tested in clinical trials (27). For AZD5069, an *in vitro* study using MDA-MB-231 mammospheres has shown that this small-molecule CXCR2 antagonist enhances the effectiveness of the anti-PD-L1 immune checkpoint inhibitor atezolizumab and decreases doxorubicin chemoresistance in 3D TNBC cultures (85). This effect may be mediated through disruption of the aforementioned TAM/CXCL1/CXCR2/PD-L1 signaling pathway (49). In summary, SB225002 and AZD5069 show promise in preclinical models of TNBC but it is crucial to investigate their therapeutic potential in clinical trials.

Conflicting evidence on CXCR2 in prognosis and targeting. There is evidence in the literature that suggests contrasting effects of CXCR2 and its inhibition (37,88,89). A study on metastatic sub-clones of 4T1 breast carcinoma cells has shown that blocking CXCR2 activity leads to an increase in CXCL1 secretion (89). This may be a result of CXCR2 serving as an auto-receptor for its ligands (89). As aforementioned, some pathways mediated by CXCL1 in TNBC may be independent of CXCR2 activation (30,33).

Moreover, higher levels of CXCR2 may be associated with a better prognosis in patients with BC (37,88). Several factors may help explain the inconsistent findings regarding CXCR2 prognosis in BC. One possibility is that differences in cell sources of CXCR2 within the TME influence outcome associations. For example, stromal immune cells, particularly TANs, express high levels of CXCR2 (88), and certain antibodies used in earlier studies may preferentially stain stromal rather than malignant cells (37,88).

TNBC expresses greater levels of CXCR2 compared with luminal or HER2-positive BC. This CXCR2 is mostly expressed by neutrophils in breast tumors (88). TANs facilitate T cell activation in response to chemokines in the TME, which may contribute to their anti-tumor activity (90). Consistently, high CXCR2 expression is associated with increased tumor-infiltrating lymphocytes, a feature typically associated with better prognosis in patients with TNBC (88). This implies that increased CXCR2 expression on infiltrating immune cells may promote improved TNBC outcomes (88).

Although numerous mediators have been implicated in shaping the pro- or anti-tumoral functions of immune cells (91), the mechanisms governing how TNBC cells regulate the expression and secretion of these factors, such as CXCL1 and associated chemokines, and how these mediators interact to influence CXCR2-dependent neutrophil behavior remain incompletely understood. Collectively, the aforementioned findings highlight the need for studies that discriminate between stromal and tumor-intrinsic CXCR2 expression and define how CXCR2-dependent immune infiltration patterns influence clinical outcomes in TNBC. Given the inconsistent evidence on CXCR2 prognosis and inhibition effects, it is important to examine potential CXCL1 inhibitors, as well as the CXCL1/CXCR1 pathway, which may offer a more effective approach in TNBC.

Implications of the CXCL1/CXCR1 pathway in TNBC. While most literature in TNBC focuses on CXCL1 signaling via CXCR2, the CXCL1-CXCR1 axis may also be biologically

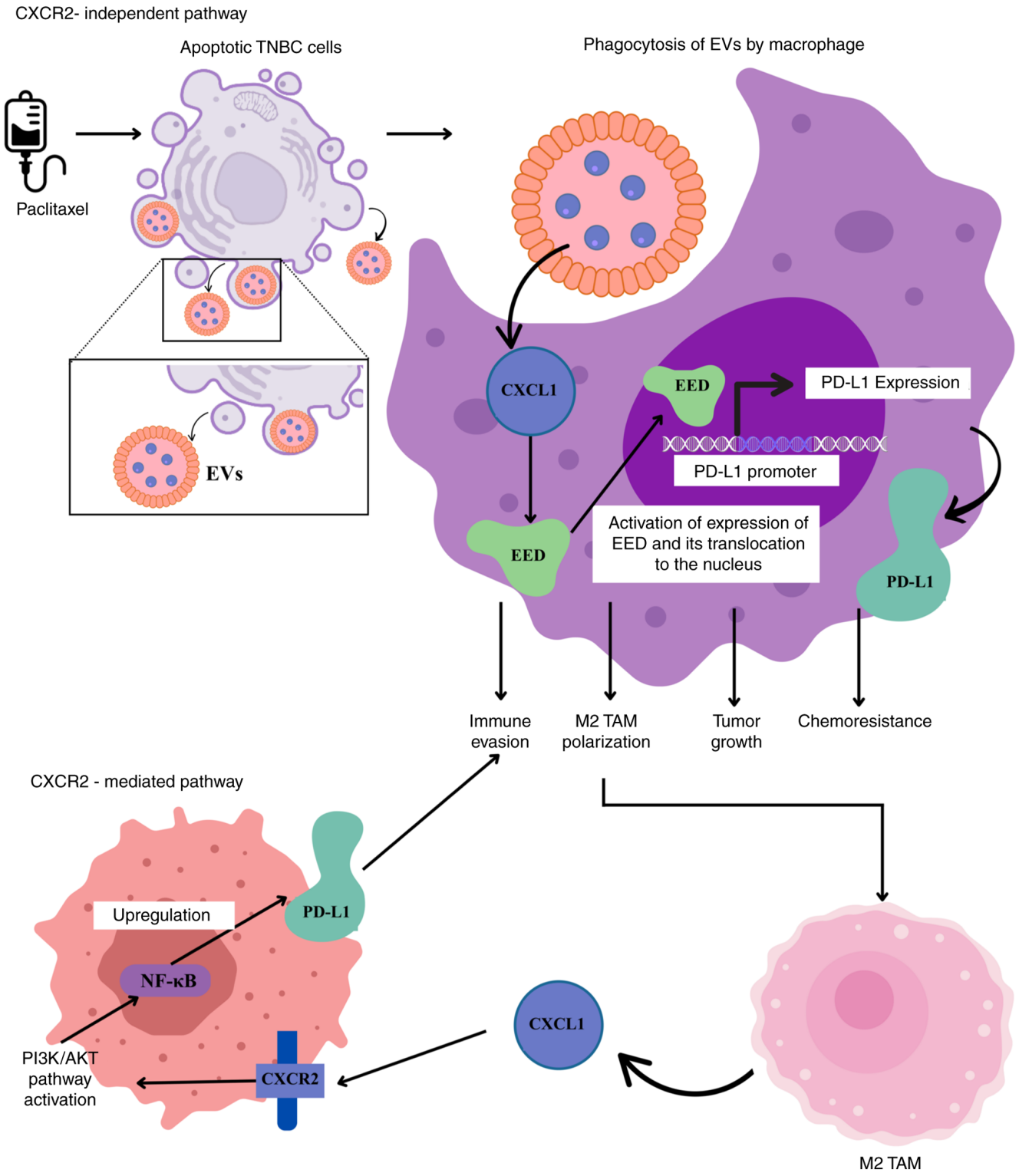

Figure 2. EVs and TAM/CXCL1/PD-L1 pathways.CXCR2-independent pathway. Chemotherapeutic agents such as paclitaxel induce the release of CXCL1-enriched EVs from apoptotic TNBC cells. EVs are phagocyted by macrophages, then the CXCL1 cargo within them is released into the cytoplasm. This promotes EED expression and its nuclear translocation. EED binds to the PD-L1 promoter, enhancing PD-L1 transcription. This pathway drives TNBC tumor growth, M2 TAM polarization, immune evasion and chemoresistance. CXCR2-mediated pathway. CXCL1 secreted by M2 macrophages in the TME promotes PD-L1 upregulation in TNBC via activation of the CXCR2-mediated PI3K/AKT/NF-κB signaling pathway. This pathway contributes to immune evasion. Created using Microsoft PowerPoint 2016. EV, extracellular vesicle; TAM, tumor-associated macrophage; TNBC, triple-negative breast cancer; EED, ectoderm development protein.

and therapeutically relevant in cancer (33,92). CXCR1 is upregulated in breast tumors compared with normal tissue and may serve as a biomarker for malignancy, invasiveness and prognosis (92). Furthermore, CXCR1 blockade selectively depletes CSC populations in MDA-MB-453 TNBC cells, highlighting the role of CXCR1 in CSC maintenance in BC (93).

As aforementioned, the neutrophil-recruiting activity of tumor conditioned media remains intact after blocking CXCR2, indicating that CXCL1/CXCR1 signaling may also play a role in neutrophil recruitment in TNBC cell lines (33). A recent *in vivo* study revealed that CXCR1/2 dual antagonism impairs neutrophil polarization toward immunosuppressive phenotypes (94). This implies that CXCR2 blockade alone may be insufficient, as CXCR1 may sustain certain immune-suppressive functions when CXCR2 is blocked.

Beyond BC, the CXCL1-CXCR1 axis may be implicated in other malignancies. For example, colorectal cancer is associated with elevated circulating levels of both CXCL1 and CXCR1 (22), suggesting that this ligand-receptor pair may act as a biomarker and potentially drive malignant behavior.

Taken together, the aforementioned findings support the hypothesis that CXCR1 signaling represents a potential escape mechanism, which highlights the possibility that compensatory CXCR1 signaling may undermine the efficacy of CXCR2-directed therapy. Consequently, dual CXCR1/2 inhibition or combination regimens may offer superior therapeutic benefit by reducing the likelihood of compensatory escape in TNBC, although this requires further experimental validation. While dual CXCR1/2 inhibition may provide superior therapeutic benefit by limiting compensatory escape, whether blockade of CXCR1 alone is sufficient to achieve anti-tumor effects in TNBC remains to be determined.

7. Potential therapeutic agents targeting CXCL1

Monoclonal antibody HL2401. Targeting CXCL1 might be a useful strategy to limit the BCSC subpopulation within the tumor and enhance the effectiveness of immunotherapeutic treatments for aggressive BC (35). One promising therapeutic approach to target CXCL1 involves HL2401, a monoclonal antibody against human CXCL1 (95). Preclinical studies have shown that HL2401 inhibits tumor cell proliferation, migration and angiogenesis in bladder and prostate cancer models, but it has not yet been evaluated in clinical trials (27,95). Although HL2401 has shown promise in certain types of cancer, its potential in TNBC remains unexplored and requires investigation.

Natural compounds. Given the importance of CXCL1 in TNBC, several natural compounds have been investigated to inhibit CXCL1 and block its downstream effects. One example is the XIAOPI formula (XPS), which has been the focus of preclinical studies in TNBC (29,31,77). XPS is a traditional Chinese medical preparation composed of 10 medicinal herbs and containing 196 compounds (96). XPS has been approved for the treatment of mammary hyperplasia by the National Medical Products Administration of China, and is prescribed to patients at high risk of developing BC (29). In TNBC, a study on 4T1 cells showed that XPS inhibits the proliferation and metastatic ability of cancer cells in the TME (77). More specifically, XPS inhibits the formation of TAM-induced PMN in mice by suppressing CXCL1-mediated MDSC activation, which might inhibit lung metastasis (77). XPS also suppresses the early-stage rise of HSPCs in BC and their mobilization by CXCL1, exhibiting minimal hematopoietic toxicity (77). Furthermore, XPS inhibits M2 phenotype polarization, CXCL1 expression and suppresses breast tumor growth and BCSC activity in mouse 4T1 xenografts without detectable side effects (97). These effects may be due to the inhibition of CXCL1 mRNA and protein expression by XPS (77). A recent clinical study showed that XPS decreases CXCL1 serum levels in patients with TNBC following administration for 3 months, suggesting that it could improve clinical outcomes (29).

Through bioactivity-guided fractionation, baohuoside I (BHS) was identified as the principal active compound in XPS responsible for suppressing CXCL1 transcription and producing the effects of XPS (98). BHS demonstrates strong *in vivo* efficacy, inhibiting BC metastasis in zebrafish (98) and mouse (84) models by targeting the TAM/CXCL1 pathway, while showing no signs of embryotoxicity or teratogenicity in zebrafish embryos (98). Furthermore, a recent study of TNBC cells showed that BHS inhibits CXCL1 cargo in EVs derived from apoptotic tumor cells, which inhibits M2 polarization of TAMs and PD-L1 expression and chemosensitizes BC cells to paclitaxel *in vivo* by suppressing EV/CXCL1/TAM/PD-L1 signaling (84). Moreover, XPS increases TNBC sensitivity to chemotherapy by blocking CXCL1-induced autophagy (99). Similarly, BHS inhibits the autophagic activity induced by paclitaxel in tumor tissue without inducing toxic side effects (84). Thus, BHS, a naturally abundant compound that can be easily synthesized, combines with paclitaxel to effectively suppress breast tumor growth and lung metastasis, offering a potentially safer and more accessible alternative to costly immune checkpoint inhibitors that may lead to adverse effects (84).

Another natural compound is pentagalloylglucose (PGG), a polyphenol found in multiple medicinal herbs, that exhibits biological therapeutic activity for many diseases, including cancer (100). PGG inhibits TNF-α stimulated CXCL1 mRNA and protein expression and induces apoptosis in TNBC cells (59). The decrease in CXCL1 release may be caused by suppressing the translation of genes involved in NF-κ and MAPK signaling (59). Also, ginsenoside panaxatriol (GPT), one of the primary active components in Panax ginseng herb, has been reported to decrease the expression of inflammatory cytokines including CXCL1, thereby resensitizing TNBC cells to paclitaxel treatment (101).

Small molecule inhibitors. Small molecule inhibitors have been investigated for their potential to modulate the CXCL1 pathway in TNBC. One of these agents is [(aminocarbonyl) amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide (TPCA-1), an IκB kinase inhibitor, which has been shown to downregulate inflammatory responses via the inactivation of the NF-κB pathway (102). Similar to the effects observed with XPS and BHS, TPCA-1 enhances TNBC chemosensitivity to paclitaxel, decreases CXCL1 content in EVs derived from apoptotic cells and inhibits tumor growth and lung metastasis *in vivo* (30). TPCA-1 displays minimal toxicity, indicating its potential as a safe adjuvant to eliminate pro-tumor signals from dying cells (30). Although NF-κB pathways may serve a role in the inhibitory effect of TPCA-1 on CXCL1 expression, the findings on mechanisms of TPCA-1 are scarce (30).

Another example of small molecule inhibitors is differentiation-inducing factor-1 (DIF-1), which is secreted by *Dictyostelium discoideum* amoeba and known to exhibit

Table II. Potential CXCL1 inhibitors and their reported effects.

Name	Class	Effect	Result	Clinical trials	(Refs.)
XIAOPI formula (active ingredient, baohuoside I)	Natural compound	Inhibits CXCL1 mRNA and protein expression	Decreases tumor growth and metastasis and increases chemosensitivity in TNBC cells	Randomized controlled trial in patients with TNBC (trial no. 38835647)	(29,77, 97,98)
Pentagalloylglucose	Natural compound	Inhibits TNF-α-stimulated CXCL1 mRNA and protein expression	Induces apoptosis in TNBC cells	No registered clinical trials in TNBC	(59)
Ginsenoside panaxatriol	Natural compound	Decreases the expression of inflammatory cytokines, including CXCL1	Resensitizes TNBC cells to paclitaxel treatment	No registered clinical trials in TNBC	(101)
[(Aminocarbonyl amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide	Small molecule	Decreases CXCL1 content in EVs derived from apoptotic cells	Enhances TNBC chemosensitivity to paclitaxel and inhibits tumor growth and lung metastasis	No registered clinical trials	(30)
Differentiation-inducing factor-1	Small molecule	Decreases CXCL1 and CXCR2 expression in TNBC cells	Suppresses the communication between BC cells and CAFs mediated by the CXCL/CXCR2 pathway	No registered clinical trials	(103)
HL2401	Monoclonal antibody	Neutralizes CXCL1	Decreases tumor growth in preclinical bladder and prostate cancer model	Not yet evaluated in clinical trials	(95)
Belinostat	Epigenetic modulator	Induces CXCL1 upregulation	May cause DNA damage that renders the TME less supportive of tumor cell growth	Ongoing Phase I trials with ribociclib in TNBC (trial nos. NCT04315233 and NCT04315233)	(71)

CAF, cancer-associated fibroblast; CXCL1, C-X-C motif ligand 1; CXCR2, C-X-C motif chemokine receptor 2; EV, extracellular vesicle; TME, tumor microenvironment; TNBC, triple-negative breast cancer.

anticancer activity (103). It is reported to decrease CXCL1 and CXCR2 expression in 4T1 cells (103). The aforementioned study also proposed that the anticancer effect of DIF-1 may be associated with suppression of communication between BC cells and CAFs mediated by the CXCL/CXCR2 pathway (103).

Epigenetic modulators with paradoxical effects. By contrast with the aforementioned agents that suppress CXCL1 activity, belinostat, a histone deacetylase inhibitor, induces CXCL1 expression, leading to enhanced drug sensitivity and a potentially favorable prognosis in TNBC (71). Belinostat-induced CXCL1 upregulation may cause DNA damage that renders the TME less supportive of tumor cell proliferation, yet treatment-driven selective pressure could trigger adaptive resistance, leaving the role of CXCL1 uncertain (71). These contradictory effects require further investigation.

Overview and therapeutic relevance. Given the lack of effective targeted therapy and poor prognosis of TNBC, inhibiting CXCL1 serves as a potentially effective approach that may complement existing treatments. The aforementioned agents modulate CXCL1 in TNBC, affecting tumor progression and highlighting its potential as a therapeutic target. Although multiple CXCL1-targeted strategies have shown promise in preclinical TNBC models (98,102,103), their clinical applicability remains uncertain. Several compounds, such as XPS and BHS, are supported primarily by limited *in vitro* or small animal studies (84,98,99), with no pharmacokinetic, toxicity or efficacy data in humans. These agents should therefore be interpreted as early exploratory tools rather than clinically mature therapeutics. Collectively, the aforementioned findings indicate that CXCL1 inhibition represents a potential therapeutic strategy for TNBC, with certain agents such as XPS/BHS (29,98) demonstrating greater translational readiness (Table II).

Given the heterogeneity of TNBC, it is possible that only specific patient subsets would benefit from CXCL1-targeted approaches. For example, CXCL1-targeted therapy may be most relevant in TNBC tumors characterized by a strong CXCL1/CXCR2 transcriptional signature. In addition, TNBC subtypes characterized by BL or mesenchymal phenotypes, which tend to show elevated CXCL1 activity, might be more responsive to CXCL1 blockade. However, these considerations remain speculative, as no clinical trials have yet stratified TNBC patients according to CXCL1/CXCR2 status. Overall, these considerations underscore the need for biomarker-driven patient selection and well-designed early-phase trials for determining which subgroups could realistically benefit from CXCL1-targeted therapies.

8. Potential resistance mechanisms to CXCL1-targeted therapy

Tumors may develop resistance to CXCL1-targeted interventions. A primary resistance mechanism to CXCL1-targeting in TNBC may arise from functional redundancy among ELR^+ CXC chemokines. Several other ELR^+ chemokines, including CXCL2, CXCL6 and CXCL8, also bind CXCR2, with some (such as CXCL6 and CXCL8) additionally engaging CXCR1 (104). These chemokines may act as compensatory pathways if CXCL1 signaling are inhibited. Expression profiling studies further show that ELR^+ chemokines other than CXCL1 such as CXCL2, CXCL3, CXCL5, CXCL6 and CXCL8 are elevated in TNBC (105,106), reinforcing the possibility of escape via ligand compensation.

CXCL8 expression is upregulated under stimulation by TNF-α in co-culture of TNBC cells and CAFs (106,107). As CXCL8 can engage the same receptors as CXCL1 (CXCR1/2), blockade of CXCL1 may be offset by compensatory CXCL8 signaling. For example, CXCL8 regulates the survival and self-renewal of CXCR1-expressing CSCs (108). Moreover, CXCL1 is implicated in mediating the pro-metastatic effects in TNBC cells (58,106). These findings underscore that inhibition of CXCL1 may be partially circumvented by other ELR^+ chemokines, although it is uncertain whether these chemokines are upregulated specifically in response to CXCL1 inhibition.

Another potential escape mechanism may involve persistent signaling through downstream pathways such as NF-κB via chemokines other than CXCL1. For example, a recent study demonstrated that tumor-infiltrating B cells in TNBC may promote increased MMP activity, migration and invasion, potentially via IL-1β-mediated NF-κB activation (109). Another study showed that TNBC cells and adipocytes engage in reciprocal signaling, activating NF-κB through the production of CXCL1 and IL-6, respectively, which ultimately contributes to tumor progression (110). This suggests IL-6 and IL-1β may potentially continue to drive pro-tumor effects via NF-κB activation in TNBC cells following CXCL1 neutralization. However, this hypothesis remains to be experimentally validated. Collectively, these observations underscore the potential need for strategies that extend beyond single-ligand blockade, such as combining CXCL1 inhibition with disruption of NF-κB signaling or broader chemokine suppression.

9. Challenges for clinical translation

Despite the substantial evidence supporting the role and therapeutic potential of CXCL1 in TNBC (29,31,49), multiple barriers hinder the application of CXCL1-targeted therapy in clinical practice. Several studies are limited by small sample sizes, which pose a challenge for drawing definitive conclusions across diverse TNBC populations (29,37,86). Although preclinical studies suggest several agents have potential anticancer effects by targeting CXCL1 or CXCR2, their efficacy remains modestly examined in TNBC, given the dearth of *in vivo* studies (85,98). Also, the lack of clinical data makes it difficult to evaluate the potential of these agents in enhancing patient outcomes (29,84,85,98). Moreover, in certain studies, some underlying molecular mechanisms were not completely delineated, limiting the ability to interpret the findings and translate them into clinical applications (86,98).

The models used to investigate CXCL1, such as *in silico* approaches (71) or immunodeficient mice (42), may not fully capture the complexity of human TNBC, nor be directly applicable to human patients. Furthermore, the variability among TNBC subtypes limits the applicability of results from certain cell lines or models to all forms of the disease, since genetic diversity may contribute to distinct outcomes clinically (59). Moreover, experimental validation of bioinformatics results is limited, which could affect the reliability of the conclusions (71). Finally, the evaluation of only a single chemotherapeutic agent, such as paclitaxel, in certain studies restricts the applicability of findings to other treatment regimens for TNBC (66,84,101). Recognizing these limitations helps guide future research directions and enhance strategies for translating CXCL1-targeted approaches into clinical practice.

10. Conclusion

CXCL1 serves multiple roles in TNBC, contributing to tumor progression, metastasis and interactions within the TME. Its elevated expression in TNBC is generally linked to poor prognosis. Overall, the present review highlighted the role of CXCL1 and its potential as a target for therapeutic intervention in TNBC. Further preclinical evaluation of CXCL1-targeted agents is required, followed by the development of carefully designed clinical trials across diverse patient populations (29,84,85). Future studies should involve larger and more diverse patient groups to confirm the results (29). Moreover, interventions may need to be customized for the unique characteristics of each TNBC subtype and its TME (59). Given the higher CXCL1 expression in BL and mesenchymal TNBC (38,39), future stratified clinical trials targeting CXCL1 should prioritize these subtypes. Future studies should also assess the benefits of potential therapeutic agents at different stages, including diagnosis, surgery and post-operative therapies (29).

Additional research is needed to elucidate the molecular pathways underlying the interaction between TGF-β and chemokine signaling pathways to regulate neutrophil migration (33), the involvement of CXCL1 in immune escape mechanisms (49), HSPC mobilization via CXCL1 (77) and the diverse biological functions that may be mediated by

EV/CXCL1 signaling (84) in TNBC. The present review did not summarize interactions between CXCL1 and other cytokines in TNBC. Cocktail therapies targeting multiple cytokines simultaneously represent a potential strategy for future investigation (77). Finally, given the contrasting findings regarding CXCR2 prognosis in TNBC, further research is needed to clarify its prognostic value (37). Addressing these gaps is essential to realize the potential of CXCL1 targeted therapies in TNBC to develop novel effective treatments and help overcome current limitations in TNBC management.

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Competing interests

The authors declare that they have no competing interests.

Use of artificial intelligence tools

During the preparation of this work, AI tools were used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the AI tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

References

1. So JY, Ohm J, Lipkowitz S and Yang L: Triple negative breast cancer (TNBC): Non-genetic tumor heterogeneity and immune microenvironment: Emerging treatment options. Pharmacol Ther 237: 108253, 2022.
2. Zagami P and Carey LA: Triple negative breast cancer: Pitfalls and progress. Npj Breast Cancer 8: 95, 2022.
3. Almansour NM: Triple-negative breast cancer: A brief review about epidemiology, risk factors, signaling pathways, treatment and role of artificial intelligence. Front Mol Biosci 9: 836417, 2022.
4. Wu Q, Siddharth S and Sharma D: Triple negative breast cancer: A mountain yet to be scaled despite the triumphs. Cancers (Basel) 13: 3697, 2021.
5. Michaels E, Chen N and Nanda R: The role of immunotherapy in triple-negative breast cancer (TNBC). Clin Breast Cancer 24: 263-270, 2024.
6. Yin L, Duan JJ, Bian XW and Yu SC: Triple-negative breast cancer molecular subtyping and treatment progress. Breast Cancer Res 22: 61, 2020.
7. Deepak KGK, Vempati R, Nagaraju GP, Dasari VR, S N, Rao DN and Malla RR: Tumor microenvironment: Challenges and opportunities in targeting metastasis of triple negative breast cancer. Pharmacol Res 153: 104683, 2020.
8. Obidiro O, Battogtokh G and Akala EO: Triple negative breast cancer treatment options and limitations: Future outlook. Pharmaceutics 15: 1796, 2023.
9. Lehmann BD, Bauer JA, Chen X, Sanders ME, Chakravarthy AB, Shyr Y and Pietenpol JA: Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest 121: 2750-2767, 2011.
10. Ensenyat-Mendez M, Llinàs-Arias P, Orozco JIJ, Íñiguez-Muñoz S, Salomon MP, Sesé B, DiNome ML and Marzese DM: Current triple-negative breast cancer subtypes: Dissecting the most aggressive form of breast cancer. Front Oncol 11: 681476, 2021.
11. Won K and Spruck C: Triple-negative breast cancer therapy: Current and future perspectives (review). Int J Oncol 57: 1245-1261, 2020.
12. Ferrari P, Scatena C, Ghilli M, Bargagna I, Lorenzini G and Nicolini A: Molecular mechanisms, biomarkers and emerging therapies for chemotherapy resistant TNBC. Int J Mol Sci 23: 1665, 2022.
13. Vagia E, Mahalingam D and Cristofanilli M: The landscape of targeted therapies in TNBC. Cancers (Basel) 12: 916, 2020.
14. Hu Y, Wang C, Liang H, Li J and Yang Q: The treatment landscape of triple-negative breast cancer. Med Oncol 41: 236, 2024.
15. Chapdelaine AG and Sun G: Challenges and opportunities in developing targeted therapies for triple negative breast cancer. Biomolecules 13: 1207, 2023.
16. Emara HM, Allam NK and Youness RA: A comprehensive review on targeted therapies for triple negative breast cancer: An evidence-based treatment guideline. Discov Oncol 16: 547, 2025.
17. Laing K and Secombes CJ: Chemokines. Dev Comp Immunol 28: 443-460, 2004.
18. Nagarsheth N, Wicha MS and Zou W: Chemokines in the cancer microenvironment and their relevance in cancer immunotherapy. Nat Rev Immunol 17: 559-572, 2017.
19. Belperio JA, Keane MP, Arenberg DA, Addison CL, Ehlert JE, Burdick MD and Strieter RM: CXC chemokines in angiogenesis. J Leukoc Biol 68: 1-8, 2000.
20. Masrour M, Moeinafshar A, Poopak A, Razi S and Rezaei N: The role of CXC chemokines and receptors in breast cancer. Clin Exp Med 25: 128, 2025.
21. Korbecki J, Bosiacki M, Barczak K, Łagocka R, Chlubek D and Baranowska-Bosiacka I: The clinical significance and role of CXCL1 chemokine in gastrointestinal cancers. Cells 12: 1406, 2023.
22. Łukaszewicz-Zając M, Pączek S, Mroczko P and Kulczyńska-Przybik A: The significance of CXCL1 and CXCL8 as well as their specific receptors in colorectal cancer. Cancer Manag Res 12: 8435-8443, 2020.
23. Korbecki J, Barczak K, Gutowska I, Chlubek D and Baranowska-Bosiacka I: CXCL1: Gene, promoter, regulation of expression, mRNA stability, regulation of activity in the intercellular space. Int J Mol Sci 23: 792, 2022.
24. Loetscher P, Seitz M, Clark-Lewis I, Baggiolini M and Moser B: Both interleukin-8 receptors independently mediate chemotaxis. Jurkat cells transfected with IL-8R1 or IL-8R2 migrate in response to IL-8, GRO alpha and NAP-2. FEBS Lett 341: 187-192, 1994.
25. Talukdar J, Nayek A, Gogoi G, Srivastava TP, Goel I, Sahoo OS, Dhar R and Karmakar S: Investigating the interaction of ACKR1 and c-Myc in the breast carcinoma tumor microenvironment modulation. Discov Oncol 16: 1615, 2025.
26. Korbecki J, Bosiacki M, Barczak K, Łagocka R, Brodowska A, Chlubek D and Baranowska-Bosiacka I: Involvement in tumorigenesis and clinical significance of CXCL1 in reproductive cancers: Breast cancer, cervical cancer, endometrial cancer, ovarian cancer and prostate cancer. Int J Mol Sci 24: 7262, 2023.

27. Korbecki J, Bosiacki M, Pilarczyk M, Kot M, Defort P, Walaszek I, Chlubek D and Baranowska-Bosiacka I: The CXCL1-CXCR2 axis as a component of therapy resistance, a source of side effects in cancer treatment, and a therapeutic target. Cancers (Basel) 17: 1674, 2025.
28. Ullah A, Singla RK, Cao D, Chen B and Shen B: Age-related and postmenopausal breast cancer progression and treatment management: The significance of pro-inflammatory cytokines and CXC chemokines. Genes Dis 12: 101606, 2025.
29. Guo L, Hong SC, Wang X, Wang SQ, Wang N, Wei XQ, Situ HL and Wang ZY: Modulatory effects of XIAOPI formula on CXCL1 and selected outcomes in triple-negative breast cancer: A randomized controlled clinical trial. Breast Cancer (Dove Med Press) 16: 289-303, 2024.
30. Wang S, Li J, Hong S, Wang N, Xu S, Yang B, Zheng Y, Zhang J, Pan B, Hu Y and Wang Z: Chemotherapy-elicited extracellular vesicle CXCL1 from dying cells promotes triple-negative breast cancer metastasis by activating TAM/PD-L1 signaling. J Exp Clin Cancer Res 43: 121, 2024.
31. Wang S, Xu S, Li J, Wang N, Zheng Y and Wang Z: XIAOPI formula inhibits chemoresistance and metastasis of triple-negative breast cancer by suppressing extracellular vesicle/CXCL1-induced TAM/PD-L1 signaling. Phytomedicine 135: 156039, 2024.
32. Zou A, Lambert D, Yeh H, Yasukawa K, Behbod F, Fan F and Cheng N: Elevated CXCL1 expression in breast cancer stroma predicts poor prognosis and is inversely associated with expression of TGF-β signaling proteins. BMC Cancer 14: 781, 2014.
33. SenGupta S, Hein LE, Xu Y, Zhang J, Konwerski JR, Li Y, Johnson C, Cai D, Smith JL and Parent CA: Triple-negative breast cancer cells recruit neutrophils by secreting TGF-β and CXCR2 ligands. Front Immunol 12: 659996, 2021.
34. Yang C, Yu H, Chen R, Tao K, Jian L, Peng M, Li X, Liu M and Liu S: CXCL1 stimulates migration and invasion in ER-negative breast cancer cells via activation of the ERK/MMP2/9 signaling axis. Int J Oncol 55: 684-696, 2019.
35. Ciummo SL, D'Antonio L, Sorrentino C, Fieni C, Lanuti P, Stassi G, Todaro M and Di Carlo E: The C-X-C motif chemokine ligand 1 sustains breast cancer stem cell self-renewal and promotes tumor progression and immune escape programs. Front Cell Dev Biol 9: 689286, 2021.
36. Bhat K, Sarkissyan M, Wu Y and Vadgama JV: GROα overexpression drives cell migration and invasion in triple negative breast cancer cells. Oncol Rep 38: 21-30, 2017.
37. Boissière-Michot F, Jacot W, Fraisse J, Gourgou S, Timaxian C and Lazennec G: Prognostic value of CXCR2 in breast cancer. Cancers (Basel) 12: 2076, 2020.
38. Ignacio RMC, Gibbs CR, Lee ES and Son DS: The TGFα-EGFR-Akt signaling axis plays a role in enhancing proinflammatory chemokines in triple-negative breast cancer cells. Oncotarget 9: 29286-29303, 2018.
39. Wang N, Liu W, Zheng Y, Wang S, Yang B, Li M, Song J, Zhang F, Zhang X, Wang Q and Wang Z: CXCL1 derived from tumor-associated macrophages promotes breast cancer metastasis via activating NF-κB/SOX4 signaling. Cell Death Dis 9: 880, 2018.
40. Prat A, Pineda E, Adamo B, Galván P, Fernández A, Gaba L, Díez M, Viladot M, Arance A and Muñoz M: Clinical implications of the intrinsic molecular subtypes of breast cancer. Breast 24 (Suppl): S26-S35, 2015.
41. Acharyya S, Oskarsson T, Vanharanta S, Malladi S, Kim J, Morris PG, Manova-Todorova K, Leversha M, Hogg N, Seshan VE, *et al*: A CXCL1 paracrine network links cancer chemoresistance and metastasis. Cell 150: 165-178, 2012.
42. Wang YY, Chen HD, Lo S, Chen YK, Huang YC, Hu SCS, Hsieh YC, Hung AC, Hou MF and Yuan SF: Visfatin enhances breast cancer progression through CXCL1 induction in tumor-associated macrophages. Cancers (Basel) 12: 3526, 2020.
43. Yuan M, Zhu H, Xu J, Zheng Y, Cao X and Liu Q: Tumor-derived CXCL1 promotes lung cancer growth via recruitment of tumor-associated neutrophils. J Immunol Res 2016: 6530410, 2016.
44. Jin K, Pandey NB and Popel AS: Crosstalk between stromal components and tumor cells of TNBC via secreted factors enhances tumor growth and metastasis. Oncotarget 8: 60210-60222, 2017.
45. Jeong Y, Yoon SY, Jung SP, Nam SJ, Lee JE and Kim S: Inhibition of interleukin-8/C-X-C chemokine receptor 2 signaling axis prevents tumor growth and metastasis in triple-negative breast cancer cells. Pharmacology 110: 178-190, 2025.
46. Bièche I, Chavey C, Andrieu C, Busson M, Vacher S, Le Corre L, Guinebretière JM, Burlinchon S, Lidereau R and Lazennec G: CXC chemokines located in the 4q21 region are up-regulated in breast cancer. Endocr Relat Cancer 14: 1039-1052, 2007.
47. Dalmases A, González I, Menendez S, Arpí O, Corominas JM, Servitja S, Tusquets I, Chamizo C, Rincón R, Espinosa L, *et al*: Deficiency in p53 is required for doxorubicin induced transcriptional activation of NF-κB target genes in human breast cancer. Oncotarget 5: 196-210, 2014.
48. Yang B, Li G, Wang S, Zheng Y, Zhang J, Pan B, Wang N and Wang Z: Tumor-associated macrophages/C-X-C motif chemokine ligand 1 promotes breast cancer autophagy-mediated chemoresistance via IGF1R/STAT3/HMGB1 signaling. Cell Death Dis 15: 743, 2024.
49. Zhang L, Gu S, Wang L, Zhao L, Li T, Zhao X and Zhang L: M2 macrophages promote PD-L1 expression in triple-negative breast cancer via secreting CXCL1. Pathol Res Pract 260: 155458, 2024.
50. Zheng Y, Wang N, Wang S, Zhang J, Yang B and Wang Z: Chronic psychological stress promotes breast cancer pre-metastatic niche formation by mobilizing splenic MDSCs via TAM/CXCL1 signaling. J Exp Clin Cancer Res 42: 129, 2023.
51. Ganguly D, Chandra R, Karalis J, Teke M, Aguilera T, Maddipati R, Wachsmann MB, Ghersi D, Siravegna G, Zeh HJ III, *et al*: Cancer-associated fibroblasts: Versatile players in the tumor microenvironment. Cancers (Basel) 12: 2652, 2020.
52. Brogna MR, Varone V, DelSesto M and Ferrara G: The role of CAFs in therapeutic resistance in triple negative breast cancer: An emerging challenge. Front Mol Biosci 12: 1568865, 2025.
53. Zhang X, Powell K and Li L: Breast cancer stem cells: Biomarkers, identification and isolation methods, regulating mechanisms, cellular origin, and beyond. Cancers (Basel) 12: 3765, 2020.
54. Olsson M, Larsson P, Johansson J, Sah VR and Parris TZ: Cancer stem cells are prevalent in the basal-like 2 and mesenchymal triple-negative breast cancer subtypes in vitro. Front Cell Dev Biol 11: 1237673, 2023.
55. Burke SJ, Lu D, Sparer TE, Masi T, Goff MR, Karlstad MD and Collier JJ: NF-κB and STAT1 control CXCL1 and CXCL2 gene transcription. Am J Physiol Endocrinol Metab 306: E131-E149, 2014.
56. Punj V, Matta H, Schamus S, Yang T, Chang Y and Chaudhary PM: Induction of CCL20 production by Kaposi sarcoma-associated herpesvirus: role of viral FLICE inhibitory protein K13-induced NF-kappaB activation. Blood 113: 5660-5668, 2009.
57. Richmond A: Nf-kappa B, chemokine gene transcription and tumour growth. Nat Rev Immunol 2: 664-674, 2002.
58. Han B, Alonso-Valenteen F, Wang Z, Deng N, Lee TY, Gao B, Zhang Y, Xu Y, Zhang X, Billet S, *et al*: A chemokine regulatory loop induces cholesterol synthesis in lung-colonizing triple-negative breast cancer cells to fuel metastatic growth. Mol Ther 30: 672-687, 2002.
59. Mendonca P, Alghamdi S, Messeha S and Soliman KFA: Pentagalloyl glucose inhibits TNF-α-activated CXCL1/GRO-α expression and induces apoptosis-related genes in triple-negative breast cancer cells. Sci Rep 11: 5649, 2021.
60. Wang J, Ray PS, Sim MS, Zhou XZ, Lu KP, Lee AV, Lin X, Bagaria SP, Giuliano AE and Cui X: FOXC1 regulates the functions of human basal-like breast cancer cells by activating NF-κB signaling. Oncogene 31: 4798-4802, 2012.
61. Wang W, Nag S and Zhang R: Targeting the NFκB signaling pathways for breast cancer prevention and therapy. Curr Med Chem 22: 264-289, 2015.
62. Hata K, Andoh A, Shimada M, Fujino S, Bamba S, Araki Y, Okuno T, Fujiyama Y and Bamba T: IL-17 stimulates inflammatory responses via NF-kappaB and MAP kinase pathways in human colonic myofibroblasts. Am J Physiol Gastrointest Liver Physiol 282: G1035-G1044, 2002.
63. Sønder SU, Saret S, Tang W, Sturdevant DE, Porcella SF and Siebenlist U: IL-17-induced NF-kappaB activation via CIKS/Act1: Physiologic significance and signaling mechanisms. J Biol Chem 286: 12881-12890, 2011.
64. Khalid F, Takagi K, Sato A, Yamaguchi M, Guestini F, Miki Y, Miyashita M, Hirakawa H, Ohi Y, Rai Y, *et al*: Interleukin (IL)-17A in triple-negative breast cancer: A potent prognostic factor associated with intratumoral neutrophil infiltration. Breast Cancer 30: 748-757, 2023.
65. Ma K, Yang L, Shen R, Kong B, Chen W, Liang J, Tang G and Zhang B: Th17 cells regulate the production of CXCL1 in breast cancer. Int Immunopharmacol 56: 320-329, 2018.

66. Liu J, Wang P, Huang B, Cheng Q, Duan Y, Chen L, Ma T, Zhu C, Li D, Fan W and Yu M: Effective suppression of triple negative breast cancer by paclitaxel nanoparticles conjugated with transmembrane TNF-α monoclonal antibody. Int J Pharm 624: 121969, 2022.
67. Sharma B, Nawandar DM, Nannuru KC, Varney ML and Singh RK: Targeting CXCR2 enhances chemotherapeutic response, inhibits mammary tumor growth, angiogenesis, and lung metastasis. Mol Cancer Ther 12: 799-808, 2013.
68. Bernard S, Myers M, Fang WB, Zinda B, Smart C, Lambert D, Zou A, Fan F and Cheng N: CXCL1 derived from mammary fibroblasts promotes progression of mammary lesions to invasive carcinoma through CXCR2 dependent mechanisms. J Mammary Gland Biol Neoplasia 23: 249-267, 2018.
69. Ruiz De Porras V, Bystrup S, Martínez-Cardús A, Pluvinet R, Sumoy L, Howells L, James MI, Iwuji C, Manzano JL, Layos L, *et al*: Curcumin mediates oxaliplatin-acquired resistance reversion in colorectal cancer cell lines through modulation of CXC-Chemokine/NF-κB signalling pathway. Sci Rep 6: 24675, 2016.
70. Han D, Zhang N, Zhao S, Liu H, Wang X, Yang M, Wang S, Li Y, Liu Z and Teng L: AKIP1 promotes glioblastoma viability, mobility and chemoradiation resistance via regulating CXCL1 and CXCL8 mediated NF-κB and AKT pathways. Am J Cancer Res 11: 1185-1205, 2021.
71. Han XL, Du J, Zheng YD, Dai JJ, Lin SW, Zhang BY, Zhong FB, Lin ZG, Jiang SQ, Wei W and Fang ZY: CXCL1 clone evolution induced by the HDAC inhibitor belinostat might be a favorable prognostic indicator in triple-negative breast cancer. Biomed Res Int 2021: 5089371, 2021.
72. Park SY, Jun JA, Jeong KJ, Heo HJ, Sohn JS, Lee HY, Park CG and Kang J: Histone deacetylases 1, 6 and 8 are critical for invasion in breast cancer. Oncol Rep 25: 1677-1681, 2011.
73. Gibson JT, Orlandella RM, Turbitt WJ, Behring M, Manne U, Sorge RE and Norian LA: Obesity-associated myeloid-derived suppressor cells promote apoptosis of tumor-infiltrating CD8 T cells and immunotherapy resistance in breast cancer. Front Immunol 11: 590794, 2020.
74. Wang Y, Tu L, Du C, Xie X, Liu Y, Wang J, Li Z, Jiang M, Cao D, Yan X and Luo F: CXCR2 is a novel cancer stem-like cell marker for triple-negative breast cancer. OncoTargets Ther 11: 5559-5567, 2018.
75. Li J, Wang S, Wang N, Zheng Y, Yang B, Wang X, Zhang J, Pan B and Wang Z: Aiduqing formula inhibits breast cancer metastasis by suppressing TAM/CXCL1-induced Treg differentiation and infiltration. Cell Commun Signal 19: 89, 2021.
76. Divella R, Daniele A, Savino E, Palma F, Bellizzi A, Giotta F, Simone G, Lioce M, Quaranta M, Paradiso A and Mazzocca A: Circulating levels of transforming growth factor-βeta (TGF-β) and chemokine (C-X-C motif) ligand-1 (CXCL1) as predictors of distant seeding of circulating tumor cells in patients with metastatic breast cancer. Anticancer Res 33: 1491-1497, 2013.
77. Zheng Y, Wang N, Wang S, Yang B, Situ H, Zhong L, Lin Y and Wang Z: XIAOPI formula inhibits the pre-metastatic niche formation in breast cancer via suppressing TAMs/CXCL1 signaling. Cell Commun Signal 18: 48, 2020.
78. Soto-Perez-de-Celis E, Chavarri-Guerra Y, Leon-Rodriguez E and Gamboa-Dominguez A: Tumor-associated neutrophils in breast cancer subtypes. Asian Pac J Cancer Prev 18: 2689-2693, 2017.
79. Fridlender ZG, Sun J, Kim S, Kapoor V, Cheng G, Ling L, Worthen GS and Albelda SM: Polarization of tumor-associated neutrophil phenotype by TGF-beta: 'N1' versus 'N2' TAN. Cancer Cell 16: 183-194, 2009.
80. Kang W, Wang C, Wang M, Liu M, Hu W, Liang X, Yang J and Zhang Y: A key regulator of tumor-associated neutrophils: The CXCR2 chemokine receptor. J Mol Histol 55: 1051-1061, 2024.
81. Ohms M, Möller S and Laskay T: An attempt to polarize human neutrophils toward N1 and N2 phenotypes in vitro. Front Immunol 11: 532, 2020.
82. Kythreotou A, Siddique A, Mauri FA, Bower M and Pinato DJ: PD-L1. J Clin Pathol 71: 189-194, 2018.
83. Clancy JW and D'Souza-Schorey C: Tumor-derived extracellular vesicles: Multifunctional entities in the tumor microenvironment. Annu Rev Pathol 18: 205-229, 2023.
84. Wang S, Li J, Xu S, Wang N, Pan B, Yang B, Zheng Y, Zhang J, Peng F, Peng C and Wang Z: Baohuoside I chemosensitises breast cancer to paclitaxel by suppressing extracellular vesicle/CXCL1 signal released from apoptotic cells. J Extracell Vesicles 13: e12493, 2024.
85. Ghallab AM, Eissa RA and El Tayebi HM: CXCR2 small-molecule antagonist combats chemoresistance and enhances immunotherapy in triple-negative breast cancer. Front Pharmacol 13: 862125, 2022.
86. Chu H, Li W and Li H: C-X-C motif chemokine receptor type 2 correlates with higher disease stages and predicts worse prognosis, and its downregulation enhances chemotherapy sensitivity in triple-negative breast cancer. Transl Cancer Res 9: 840-848, 2020.
87. Goldstein LJ, Mansutti M, Levy C, Chang JC, Henry S, Fernandez-Perez I, Prausovà J, Staroslawska E, Viale G, Butler B, *et al*: A randomized, placebo-controlled phase 2 study of paclitaxel in combination with reparixin compared to paclitaxel alone as front-line therapy for metastatic triple-negative breast cancer (fRida). Breast Cancer Res Treat 190: 265-275, 2021.
88. Boissière-Michot F, Jacot W, Massol O, Mollevi C and Lazennec G: CXCR2 levels correlate with immune infiltration and a better prognosis of triple-negative breast cancers. Cancers (Basel) 13: 2328, 2021.
89. Erin N, Tavşan E, Akdeniz Ö, Isca VMS and Rijo P: Rebound increases in chemokines by CXCR2 antagonist in breast cancer can be prevented by PKCδ and PKCε activators. Cytokine 142: 155498, 2021.
90. Jaillon S, Ponzetta A, Di Mitri D, Santoni A, Bonecchi R and Mantovani A: Neutrophil diversity and plasticity in tumour progression and therapy. Nat Rev Cancer 20: 485-503, 2020.
91. SenGupta S, Hein LE and Parent CA: The recruitment of neutrophils to the tumor microenvironment is regulated by multiple mediators. Front Immunol 12: 734188, 2021.
92. Xue MQ, Liu J, Sang JF, Su L and Yao YZ: Expression characteristic of CXCR1 in different breast tissues and the relevance between its expression and efficacy of neo-adjuvant chemotherapy in breast cancer. Oncotarget 8: 48930-48937, 2017.
93. Ginestier C, Liu S, Diebel ME, Korkaya H, Luo M, Brown M, Wicinski J, Cabaud O, Charafe-Jauffret E, Birnbaum D, *et al*: CXCR1 blockade selectively targets human breast cancer stem cells in vitro and in xenografts. J Clin Invest 120: 485-497, 2010.
94. Kwak JW, Nguyen HQ, Camai A, Huffman GM, Mekvanich S, Kenney NN, Zhu X, Randolph TW and Houghton AM: CXCR1/2 antagonism inhibits neutrophil function and not recruitment in cancer. OncoImmunology 13: 2384674, 2024.
95. Miyake M, Furuya H, Onishi S, Hokutan K, Anai S, Chan O, Shi S, Fujimoto K, Goodison S, Cai W and Rosser CJ: Monoclonal antibody against CXCL1 (HL2401) as a novel agent in suppressing IL6 expression and tumoral growth. Theranostics 9: 853-867, 2019.
96. Wang N, Yang B, Zhang J, Zheng Y, Wang S, Zhang X, Situ H, Lin Y and Wang Z: Metabolite profiling of traditional Chinese medicine XIAOPI formula: An integrated strategy based on UPLC-Q-Orbitrap MS combined with network pharmacology analysis. Biomed Pharmacother 121: 109569, 2020.
97. Wang S, Liu X, Huang R, Zheng Y, Wang N, Yang B, Situ H, Lin Y and Wang Z: XIAOPI formula inhibits breast cancer stem cells via suppressing tumor-associated macrophages/C-X-C motif chemokine ligand 1 pathway. Front Pharmacol 10: 1371, 2019.
98. Wang S, Wang N, Huang X, Yang B, Zheng Y, Zhang J, Wang X, Lin Y and Wang Z: Baohuoside i suppresses breast cancer metastasis by downregulating the tumor-associated macrophages/C-X-C motif chemokine ligand 1 pathway. Phytomedicine 78: 153331, 2020.
99. Wang N, Yang B, Muhetaer G, Wang S, Zheng Y, Lu J, Li M, Zhang F, Situ H, Lin Y and Wang Z: XIAOPI formula promotes breast cancer chemosensitivity via inhibiting CXCL1/HMGB1-mediated autophagy. Biomed Pharmacother 120: 109519, 2019.
100. Zhang J, Li L, Kim SH, Hagerman AE and Lü J: Anti-cancer, anti-diabetic and other pharmacologic and biological activities of penta-galloyl-glucose. Pharm Res 26: 2066-2080, 2009.
101. Wang P, Song D, Wan D, Li L, Mei W, Li X, Han L, Zhu X, Yang L, Cai Y and Zhang R: Ginsenoside panaxatriol reverses TNBC paclitaxel resistance by inhibiting the IRAK1/NF-κB and ERK pathways. PeerJ 8: e9281, 2020.
102. Wang B, Bai S, Wang J, Ren N, Xie R, Cheng G and Yu Y: TPCA-1 negatively regulates inflammation mediated by NF-κB pathway in mouse chronic periodontitis model. Mol Oral Microbiol 36: 192-201, 2021.
103. Seto-Tetsuo F, Arioka M, Miura K, Inoue T, Igawa K, Tomooka K and Sasaguri T: DIF-1 exhibits anticancer activity in breast cancer via inhibition of CXCLs/CXCR2 axis-mediated communication between cancer-associated fibroblasts and cancer cells. Int Immunopharmacol 117: 109913, 2023.

104. Palomino DCT and Marti LC: Chemokines and immunity. Einstein (Sao Paulo) 13: 469-473, 2015 (In English, Portuguese).
105. Mehraj U, Mushtaq U, Mir MA, Saleem A, Macha MA, Lone MN, Hamid A, Zargar MA, Ahmad SM and Wani NA: Chemokines in triple-negative breast cancer heterogeneity: New challenges for clinical implications. Semin Cancer Biol 86: 769-783, 2022.
106. Liubomirski Y, Lerrer S, Meshel T, Rubinstein-Achiasaf L, Morein D, Wiemann S, Körner C and Ben-Baruch A: Tumor-stroma-inflammation networks promote pro-metastatic chemokines and aggressiveness characteristics in triple-negative breast cancer. Front Immunol 10: 757, 2019.
107. Liubomirski Y, Lerrer S, Meshel T, Morein D, Rubinstein-Achiasaf L, Sprinzak D, Wiemann S, Körner C, Ehrlich M and Ben-Baruch A: Notch-mediated tumor-stroma-inflammation networks promote invasive properties and CXCL8 expression in triple-negative breast cancer. Front Immunol 10: 804, 2019.
108. Brandolini L, Cristiano L, Fidoamore A, De Pizzol M, Di Giacomo E, Florio TM, Confalone G, Galante A, Cinque B, Benedetti E, *et al*: Targeting CXCR1 on breast cancer stem cells: Signaling pathways and clinical application modelling. Oncotarget 6: 43375-43394, 2015.
109. Toney NJ, Opdenaker LM, Frerichs L, Modarai SR, Ma A, Archinal H, Ajayi GO and Sims-Mourtada J: B cells enhance IL-1 beta driven invasiveness in triple negative breast cancer. Sci Rep 15: 2211, 2025.
110. Ruan GT, Zhu LC, Xie HL, Zhang HY, Song MM, Deng L and Shi HP: Adipocyte-derived IL6 and triple-negative breast cancer cell-derived CXCL1 co-activate STAT3/NF-κB pathway to mediate the crosstalk between adipocytes and triple-negative breast cancer cells. Cell Death Discov 11: 395, 2025.