ChatGPT 结果：

Introduction

Triple-negative breast cancer (TNBC), defined by the absence of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 expression, is an aggressive breast cancer subtype characterized by a high propensity for invasion and metastasis and relatively limited options for molecularly targeted therapy. Tumor cell dissemination is governed not only by cancer cell-intrinsic signaling but also by interactions between tumor cells and the surrounding extracellular matrix (ECM). In particular, the mechanical properties of the ECM have emerged as important regulators of malignant cell behavior. Changes in matrix rigidity can alter cancer cell morphology, proliferation, metabolism, adhesion, and migration, suggesting that the mechanical microenvironment may influence both tumor progression and therapeutic responses [1–3].

Breast cancer cells exhibit pronounced responses to differences in matrix rigidity. Kostic et al. demonstrated that breast cancer cell proliferation and migration varied according to matrix rigidity and that these responses were associated with the mechanical properties of tissues relevant to metastatic tropism [1]. Similarly, Tilghman et al. showed that cancer cells cultured on compliant substrates displayed altered growth, metabolism, and protein synthesis compared with cells cultured on rigid substrates, emphasizing that conventional rigid culture surfaces may not adequately reproduce the mechanical environments encountered by tumor cells in vivo [2]. Subsequent studies have further shown that increased matrix stiffness can enhance the migratory behavior of metastatic breast cancer cells and alter focal adhesion dynamics [3]. Thus, matrix stiffness represents a biologically relevant variable when evaluating signaling pathways that control breast cancer cell migration.

Citation对应不够精准：[3]主要研究动态基质硬化下乳腺上皮细胞的恶性表型转变，并非此处所述转移性乳腺癌细胞迁移及focal adhesion dynamics。

Focal adhesion kinase (FAK), a non-receptor cytopla
primarily at integrin-associated focal adhesions, is a c
signaling and mechanotransduction. FAK coordinates
turnover with cytoskeletal remodeling and regulates multiple cellular processes relevant to cancer progression, including adhesion, migration, invasion, proliferation, and survival [4]. Autophosphorylation at Tyr397 is a key event in FAK activation, providing a docking site for Src-family kinases and other signaling molecules and facilitating downstream signaling that regulates focal adhesion dynamics and actin organization [4]. Importantly, FAK signaling is sensitive to the mechanical properties of the extracellular environment. Increased collagen matrix stiffness has been associated with enhanced focal adhesion formation and activation of a FAK–Rho signaling network in mammary epithelial models, providing a mechanistic connection between extracellular mechanics and invasive cellular behavior [5]. These

observations place FAK at an important interface between matrix stiffness and the migratory machinery of breast cancer cells.

The involvement of FAK in malignant breast cancer also makes it an attractive therapeutic target. Pharmacological inhibition or genetic suppression of FAK has been reported to impair tumor-cell motility and other malignant phenotypes. Recent work by Masuyama et al. showed that targeting FAK inhibited breast cancer cell migration and non-angiogenic vascularization and provid relevance of FAK inhibition in malignant brea mechanical context in which FAK inhibitors a matrix stiffness regulates focal adhesion maturation, cytoskeletal organization, and FAK-associated mechanotransduction, inhibition of FAK could produce different functional consequences in compliant and rigid microenvironments. In particular, similar degrees of biochemical inhibition of FAK phosphorylation do not necessarily imply equivalent effects on cell migration, because the contribution of FAK-dependent adhesion and cytoskeletal processes to cell motility may itself depend on matrix stiffness. Whether substrate stiffness modifies the functional response of TNBC cells to FAK inhibition therefore remains insufficiently characterized.

由一般机制进一步推导至“相似FAK抑制可产生不同迁移效应”，但此处未提供直接Citation支持该具体判断。

Compound X is a small-molecule FAK inhibitor whose synthesis and FAK-inhibitory activity were previously described by Smith et al. [7]. However, its activity has not been examined in the context of mechanically distinct extracellular environments. Determining whether matrix stiffness alters the cellular effects of Compound X may help clarify the relationship between target inhibition and downstream functional responses and, more broadly, whether the mechanical tumor micro should be considered when evaluating FAK-targeted agents.

‘尚未研究’属于较强的文献空白判断，当前Citation不足以直接支持这一排他性结论。

In the present study, we therefore investigated the effects of Compound X in two TNBC cell lines, MDA-MB-231 and BT-549, cultured on collagen I-coated soft and stiff substrates. We first characterized stiffness-dependent changes in cell spreading, actin organization, and FAK Tyr397 phosphorylation. We then compared the effects of Compound X on FAK phosphorylation, gap closure, focal adhesions, actin organization, and proliferation under the two stiffness conditions. FAK knockdown and the reference FAK inhibitor defactinib were additionally used to assess the involvement of FAK in the observed response. We hypothesized that matrix stiffness would modulate the functional consequences of FAK inhibition, particularly those associated with cell migration and focal adhesion organization. This experimental framework was designed to distinguish the biochemical inhibition of FAK from the stiffness-dependent cellular consequences of such inhibition.

References

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