DeepSeek 结果：

Introduction

Triple-negative breast cancer (TNBC) remains the most aggressive subtype of breast cancer, characterized by the absence of estrogen receptor, progesterone receptor, and HER2 amplification, which renders it unresponsive to endocrine and HER2-targeted therapies . Although cytotoxic chemotherapy remains the mainstay of treatment, a substantial proportion of patients experience recurrence or metastatic progression within five years, underscoring the urgent need for novel therapeutic strategies that target the molecular vulnerabilities of TNBC .

The extracellular matrix (ECM) surrounding breast tumors undergoes profound remodeling during cancer progression, characterized by increased collagen deposition and cross-linking that elevates tissue stiffness . This mechanical alteration is not merely a byproduct of tumor growth but actively contributes to malignant phenotypes, including enhanced proliferation, invasion, and metastasis . Biophysical cues from the stiffened ECM are transduced through integrin-mediated adhesions and the actomyosin cytoskeleton, ultimately influencing intracellular signaling cascades that govern cell behavior .

涉及FAK表达/活化与乳腺癌临床结局的具体论述，但正文未提供对应Citation。

Focal adhesion kinase (FAK), a non-receptor tyr ode in mechanotransduction, relaying signals from integrin-based focal adhesions to downstream effectors that regulate cell migration, survival, and proliferation . Elevated FAK expression and activation are frequently observed in high-grade breast carcinomas and correlate with poor clinical outcomes . Upon ECM engagement, FAK autophosphorylates at tyrosine 397 (Tyr397), creating a binding site for Src-family kinases and initiating signaling complexes that promote cytoskeletal remodeling and migratory capacity . Notably, matrix stiffness potently regulates FAK activation, with stiff substrates enhancing FAK phosphorylation and downstream signaling in breast cancer cells . This mechanosensitive FAK activation positions the kinase as a compelling therapeutic target, particularly in the context of the mechanically heterogeneous tumor microenvironment where stiffness increases from the tumor core to the invasive periphery .

提出肿瘤内部存在由core至invasive periphery的特定stiffness梯度，但未提供对应Citation支持。

Small-molecule FAK inhibitors have demonstrated promising preclinical activity in breast cancer models. Defactinib, a clinically adva migration, suppresses non-angiogenic vascularizat orthotopic models . However, the efficacy of FAK mechanical context in which cancer cells reside. Given that matrix stiffness differentially regulates FAK activity and FAK-dependent phenotypes, it is plausible that the inhibitory potency of FAK-targeted compounds could vary between soft and stiff microenvironments—a consideration that remains largely unexplored in the preclinical evaluation of FAK inhibitors.

Compound X is a potent small-molecule FAK inhibitory activity have been previously characterized [citation:1 — prior work: Smith et al.]. In the present study, we employed two TNBC cell lines, MDA-MB-231 and BT-549, cultured on polyacrylamide gels engineered to mimic soft (2.1 kPa) and stiff (20.4 kPa) breast tumor microenvironments to investigate whether substrate stiffness modulates the cellular response to FAK inhibition. We demonstrate that stiff substrates augment baseline FAK activation and that Compound X's inhibition of gap closure, focal adhesion formation, and actin stress fiber organization is disproportionately greater on stiff gels, despite equi[illegible] phosphorylation across stiffness conditions. In contr[illegible] antiproliferative effect is comparable between soft a[illegible] knockdown and the reference inhibitor defactinib recapitulate the stiffness-dependent pattern of migration inhibition, supporting the involvement of FAK in this mechanosensitive response. These findings reveal that the phenotypic consequences of FAK inhibition in TNBC are stiffness-dependent and suggest that the mechanical tumor microenvironment should be considered when evaluating FAK-targeted therapeutic strategies.

将实验设定的2.1/20.4 kPa进一步解释为模拟乳腺肿瘤微环境，但未提供相应依据或Citation。

Introduction直接报告多项主要实验结果及结果性结论，研究目的与Results内容混杂。

References

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该文献目前未检索到可验证的公开记录，但被直接引用且未提示进一步核查。

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正文除Smith外基本无可识别Citation，而文末列出8篇Reference，具体论述与文献来源无法清晰对应。

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