Targeting cancer cytoskeleton: the mechanical properties of natural anticancer drugs

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X.L. and H.D. cover the projects, X.L., X.S., R.L. and Z.S. wrote and edited the manuscript. X.L. and X.S. draw the figures. R.L., Z.S. and X.H. prepared the table. All authors read and approved the manuscript.

Competing interests
The authors declare no conflicts of interest.

Acknowledgments
This work was funded by “Beijing Natural Science Foundation, grant number 62240460”, “Young Elite Scientists Sponsorship Program by BAST, grant number”, BYE52023192, “Program of Beijing Municipal Education Commission, grant number KM202310020006”, “Beijing University of Agriculture science and Technology Innovation Sparkling support plan, grant number, BUA-HHHD2022007” and “2022 Research and Innovation ability improvement plan for young teachers of Beijing University of Agriculture, grant number QJKC2022028”.

Peer review information
Cancer Advances thanks Qi-Xi Zhai and other anonymous reviewers for their contribution to the peer review of this paper.

Abbreviations
ECM, extracellular matrix; 3D, three-dimensional; G-actin, spherical actin; F-actin, filamentous actin; ATP, adenosine triphosphate; ADP, adenosine diphosphate.

Citation

Executive editor: Zi-Yao Feng.
Received: 14 August 2023; Accepted: 02 November 2023;
Available online: 16 November 2023.
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Abstract
Anticancer drugs are one of the most direct means of cancer therapy. However, the various cancer progressions hamper the development and discovery of anticancer drugs. In fact, the mechanical properties of the tumor cytoskeleton are extremely vital for any phase of cancer, especially in tumor invasion and metastasis. However, in the current category of anticancer drugs, the cytoskeleton-targeting drugs are limited and their role in tumor progression is unclear. Here, we present the mechanical characteristics of tumor stiffness that are tightly regulated by the cancer cytoskeleton, including actin filaments and microtubules during tumor initiation, growth and metastasis, and review the natural drugs that target the cancer cytoskeleton. We define cytoskeleton dynamics as target mechanisms for anticancer drugs and summarize the plant, microbial and marine sources of natural products. Furthermore, this paper also provides a material pathway to study active tumor mechanics, and introduces the unique advantages and future application potential of tumor cytoskeleton-targeting drugs in clinical use. The material approaches to active cancer mechanics are supplied in this review. We aim to promote the development of anticancer drugs that target tumor mechanics by using those material approaches and finding their pharmacological application.

Keywords: anticancer drugs; mechanical microenvironment; tumor stiffness; cytoskeleton dynamics; material approaches
Introduction

Cancer is a malignant tumor that originates from the epithelium. Mechanical regulation has a significant role in both epithelial cells and cancer cells on their physiological and pathological progressions [1, 2]. The mechanical properties of cancer cells are initiated by their mechanical microenvironment including but not limited to the stiffness of the surrounding extracellular matrix (ECM) substrates and further regulated the tumor stiffness [3-5]. Most importantly, mechanical stiffness plays a critical role in cancer progression. For instance, in breast cancer, the increased stiffness of ECM drives tumorigenic phenotype in mammary epithelium [2]. The tumor stiffening is occurred in metastatic colorectal cancer [6]. Actually, cancer cytoskeleton that depends on actin filaments and microtubules to regulate the mechanical properties of tumor tissue plays a key role in homeostasis, morphogenesis and cancer metastasis [7]. Thus, assessing the mechanical characteristics of tumors by cytoskeleton dynamics of cancer cells during cancer progression acts as a good indicator in cancer diagnostics, prophylactics, therapeutics, especially in drug development [8-11].

However, the efforts on the discovery of anticancer drugs most limited in those cytotoxic drugs to induce tumor shrinking [12, 13]. In addition, the unclear mechanism of action of the anticancer drugs and no detailed evaluated manner may prevent the application in clinical trials. Moreover, the focus on cytoskeleton-targeting natural products sourced anticancer drugs is important and relevant to translational therapies in cancer disease from tumor mechanical mechanisms attention to its pharmacological application. Therefore, the mechanical regulations of cytoskeleton-targeting natural anticancer drugs should be illustrated before clinical therapy.

At present, the underlying mechanisms among mechanical stiffness, cancer cells and cytoskeleton are clear [7, 8, 14], while the unknown event is that the relationship between mechanical stiffness and anticancer drug (Figure 1A). Since anticancer drugs have a direct inhibition on cancer cells and cytoskeleton dynamics [11, 15, 16], there must be some connections between the two. Thus, the mechanical mechanisms of tumor progressions and cytoskeleton dynamics should be clarified. As a matter of fact, the cytoskeleton dynamics occur in the polymerization and depolymerization of microfilaments and microtubules and mechanical stiffness response to cancer cytoskeleton [7, 17]. Cancer cytoskeletons promote tumor initiation, growth and tumor metastasis, as displayed in Figure 1B. Yet, more detailed mechanisms of the mechanical properties of tumor tissue are urgent to reveal before the development of anticancer agents for the guidance of anticancer strategies.

Here, we first summarize cytoskeleton-associated mechanical stuff during tumor progressions involving the mechanical stiffness the tumor microenvironment of the surrounding ECM substrates and tumor tissue. We define cytoskeleton dynamics as target mechanisms for anticancer and review present cytoskeleton-targeting natural products. Finally, we also provide an overview of the 2D and 3D substrate materials that are used to active tumor mechanics, which can be applied in drug discovery and the research on its mode actions.

Mechanical microenvironment of tumor tissue

Tumor microenvironments are complex and composed of ECM, which surrounds both normal epithelial cells and activated cancer cells [18]. The mechanical properties of the tumor microenvironment refer to the ECM stiffness and have been implicated that matrix stiffness influenced cancer behaviors. In addition, cellular behaviors are altered with the changes in tissue stiffness to facilitate disease progression [19, 20]. In fact, the emerging researches have revealed that the ECM stiffness were different between normal epithelial cells and cancer cells [21, 22]. The stiffness of ECM substrates surrounding of the normal epithelial cells are ~150 Pa, while breast cancer cells are show an increased ECM stiffness of ~4-5 kPa, as shown in Figure 2A [22]. Indeed, mechanical cues such as increased ECM stiffness promote the progression of cancer cells to form tumor tissue [2]. In addition, cancer cells spread less and have shorter actin filaments on soft substrates, while exhibiting of a polarized morphology and showing stress fibers, moreover, cells have higher proliferation on matrix rigidity than softer one (Figure 2B) [24]. As a response, cancer cytoskeletons including microfilaments and microtubules are participated in the different shapes and grades of cancer cells [7]. The connections of cytoskeleton and ECM displayed in Figure 2B, the actin dynamics regulated by G-actin and F-actin, the main II and integrins linked ECM substrates are all contribute to mechanical stiffness [25-27]. And various reports have revealed that microtubules and microfilaments the mechanical properties of cancer cells, between them the crosslinker plays an action role [28, 29].

The inner mechanical stiffness of tumor tissue

Tumor tissue occurs and survives in a three-dimensional (3D) microenvironment. Precisely, any multicellular tissue has a 3D shape. Mechanical integrity and biological function are maintained within the special tissue volume. Investigation of the mechanical cues in tumor 3D structure is better for the anticancer therapy in vivo. Fortunately, materials and instruments are available to do the depth research of multicellular systems in 3D environments by 3D hydrogels [4, 30]. Therefore, the inner mechanical stiffness of tumor tissue is uncovered, and also reveals the tumor development by physical characteristics of individual cells. As exhibited in Figure 2C, the tumor tissue divides into core and periphery parts. The intratumor stress and cancer stiffness decrease from core to periphery cells, while the volumes of cancer cells are increase [4, 30]. In addition, the cytoskeleton between core cells and periphery cells were significantly different [31]. Most important is that the periphery cells have abundant stress fibers, which tend to facilitate tumor invasion [4]. Take it together, the mechanical stiffness regulated by the cytoskeleton of cancer cells and tumor tissue are key factors and indicators for controlling tumor progression, which should be the best targets for the development of anticancer drugs.

Anticancer drugs originate from cytoskeleton-targeting natural products

In the cancer progression phase, especially in solid cancers, more than 90% of mortality caused by tumor invasion and metastasis [32, 33], anticancer drugs that target cytoskeleton are one of the most effective therapy to control tumor invasion and metastasis [34]. Cytoskeleton-targeting natural products mainly originate from plant, microbial and marine sources [33], we list the classical compounds to illustrate the cytoskeleton function during tumor mechanics. As shown in Figure 3A, cucurbitacins, taxol and vinblastine are the natural products of plants; chondramides and cytochalasins derive from microbial sources; gediamolides, jaspilkinolide and latrunculins are the member from marine source. Among these natural compounds, taxol and vinblastine are target microtubules, while the others are all target microfilaments. The different functional manners of cytoskeleton-targeting anticancer agents to hijack cancer cytoskeleton, are detailed in Table 1 and further discussed below.

Actin-Targeting anticancer drugs

Actin dynamics are critical mechanical components involved in cancer growth, invasion and migration [26, 29]. Drugs that target actin can be categorized as the drugs that destabilize the actin filaments and the agents that stabilize the actin cytoskeleton [11]. As shown in Figure 3B, the processes of actin dynamics are tightly regulated by two actin members, a free monomer called G-actin (spherical actin) or as part of linear polymer microfilaments called F-actin (filamentous actin). F-actin can also be described as microfilaments. The two parallel F-actin chains must be rotated by 166 degrees to be on top of each other properly. This produces the double helix structure of the microfilaments found in the cytoskeleton. The diameter of the microfilament is about 7 nm, and the helix repeats every 37 nm. Each actin molecule binds to either adenosine triphosphate (ATP) or adenosine diphosphate (ADP) molecules, which are associated with Mg\(^{2+}\) cations. Compared with all possible combinations, the most
Figure 1 The relationship between cytoskeleton regulated tumor stiffness and anticancer drugs that target cytoskeleton dynamics. (A): Anticancer drugs that target cytoskeleton dynamics are in unknown function on tumor stiffness. Anticancer drugs can inhibit cancer cells and disrupt cytoskeleton dynamics and both cancer cell and its cytoskeleton dynamics are modulated by mechanical stiffness, while the relationship between anticancer drugs and mechanical stiffness is unknown. Actually, cytoskeleton dynamics promote the growth change of cancer cells. Mechanical stiffness and cancer cells or cytoskeleton dynamics are regulated each other. (B): Tumor stiffness and cancer cytoskeleton are regulated with tumor progression. Cytoskeleton of cancer cells including microfilament and microtubule are increase as well as tissue stiffness from tumor initiation, tumor growth to tumor metastasis.

Figure 2 Mechanical microenvironment of tumor tissue is critical for tumor progression. (A): The mechanical regulations between extracellular matrix (ECM) substrates and cancer cells. ECM stiffness surrounds normal cell are lower than cancer cell. The stiffness of ECM substrates on breast epithelial cells and cancer cells are ~150 Pa and ~4-5 kPa, respectively. (B): Cancer cell spread and tumor growth are fast following with the increased ECM stiffness, which promotes the cancer cells form tumor tissue [24]. Cytoskeleton dynamics of cancer cells including actin and microtubule dynamics are crosslink with each other. (C): Tumor stiffness modulates tumor progression. The intratumour stress gradient reduces from core to periphery and thus leads cell volume turn bigger and tumor stiffness decrease, which together facilitate tumor cell invasion [4].
Figure 3 Functional action of cytoskeleton-targeting natural products. (A): Cytoskeleton-targeting natural products mainly originate from plant, microbial, and marine sources. Plant source: cucurbitacin E, taxol, and vinblastine; Microbial source: chondramides and cytochalasins; Marine source: gediamolides, jasplakinolide, and latrunculins. (B) and (C): The mode of action of anticancer drugs on cancer cytoskeleton of actin filaments and microtubules. The cytoskeleton dynamic process of depolymerization and polymerization are in black arrows, while the drug targets were highlighted in red.
common actin forms are ATP-G-actin and ADP-F-actin. The actin depolymerization occurs on the (-) end of F-actin, while polymerization occurs on the (+) end.

Actin-Destabilizing Drugs

Cytochalasins family mostly derive from the species of fungi (more than 60%). The size of the macrocyclic ring and the substituent of the 4-hydroxyisodolyl-1-one residue at the C-3 position are used to classify the cytochalasin subgroup, the chemical structure of cytochalasin D is shown in Figure 4. Cytochalasins are the actin destabilizers and inhibit actin filaments by binding to its (+) end. Cytochalasins can be used for the treatment of gastric, breast and colorectal cancers (Table 1). In addition, cytochalasin E can be used as the adjuvant of bortezomib to increase the drug sensitivity of human lung cancer A549 cells via inhibition of autophagy [35]. Recently, synthesis technologies further expanded the diverse functional use of cytochalasins [36].

Gedlamioles are actin destabilizers that interfere with actin filaments and are derived from marine sponges. By culturing cancer cell lines in a 3D environment, reports show that gedlamiole H (Figure 4) affects the aggressive of tumor cells and inhibits migration and invasion of Hs578T cells via modifications in the actin cytoskeleton [37].

Lattrunculin are the actin-targeting agents, also derived from marine sponges. Lattrunculin lead to actin depolymerization by the sequesteration of G-actin monomers. The chemical structure of lattrunculin A is shown in Figure 4, and many marine source macrolides have similar functions of disrupting the actin cytoskeleton [38]. The main drug therapy of lattrunculin is inhibiting the invasion of tumor cells [39, 40].

Actin-Stabilizing Drugs

Actin-stabilizing drugs discussed in this work are the typical natural compounds that have the abilities of stabilizing the actin cytoskeleton, trigger deregulated polymerization, and lead to monomer depletion and accumulations of large filament aggregates. Targeting actin stabilizing also has the better.

Cucurbitacins, the family of Cucurbitaceae, belongs to the plant natural products and is reported that has the significant function of stabilizing actin cytoskeleton. Cucurbitacin E can bind to F-actin and form a covalent bond at residue Cys257 [41]. Up to now, research has revealed that cucurbitacin E inhibits breast tumor and lung cancer metastasis by suppressing cell migration and invasion (Table 1) [42, 43].

Chondramides are cyclodepsipeptides that are derived from the myxobacterium Chondromycetes crocatus crocatus [44]. Chondramides bind to F-actin to stabilize the actin cytoskeleton. Chondramides are used as the migrastatic drug to inhibit the invasion of cancer cells [45].

Jasplakinolide is an actin stabilizer that comes from marine sponges. The function of jasplakinolide promotes actin polymerization and its binding to actin filament is competitive with phalloidin [46], which can inhibit lung metastases [15].

Microtubule-Targeting Drugs

Microtubule-targeting agents for cancer therapy are important therapeutic targets in tumor cells [47, 48]. Before drugs that target microtubules work, it is necessary to understand the formation process of microtubules. A microtubule is a heterodimer formed by the polymerization of two protein molecules, namely α-, β- tubulin molecules. As shown in Figure 3C, in order to form microtubules, the dimer of α- and β-tubulin binds to GTP and assembles to the microtubule in the GTP-bound state. The β-tubulin subunit is exposed at the positive end of the microtubule, and the α-tubulin subunit is exposed at the negative end. After the dimer is incorporated into the microtubules, the GTP molecules bound to the β-tubulin subunits are finally hydrolyzed into GDP through contact between the dimers along the microtubule protofilaments. Whether the β-tubulin member of the tubulin dimer binds to GTP or GDP will affect the stability of the dimer in the microtubule. Dimers bound to GTP tend to assemble into microtubules, while dimers bound to GDP tend to split. Therefore, this GTP cycle is essential for the dynamic instability of microtubules. Thus, microtubules are become the major targets to development of anticancer drugs, they display the most effective drugs especially in the therapy of solid tumors [49–51]. The two classical microtubule-targeted natural drugs are introduced following.

Taxol (Paclitaxel) is one of classical microtubule-stabilizing agents that isolates from natural plant, the stem bark of the western yew, Taxus brevifolia Nutt [52]. The structure of paclitaxel shows that it belongs to diterpene with a tetracyclic 17 carbon frame and 11 stereocenters (Figure 4). The stabilized function of paclitaxel on microtubule is that it can preferentially binds to the β-subunit of tubulin, then make tubulin and tubulin dimer lose dynamic equilibrium, finally inducing and promoting microtubule polymerization, assembly and prevent depolymerization [53]. Paclitaxel exhibits a potential broad-spectrum anticancer activity, especially in the therapy of ovarian cancer, breast cancer and non-small cell lung cancer [53]. In addition, Paclitaxel also plays a large role in tumor immunity [54].

Vinblastine is completely opposite to paclitaxel in the anticancer mechanism used as the microtubule-destabilizing drug [55]. This product mainly inhibits the polymerization of tubulin, and hinders the formation of spindle microtubules, so that nuclear fission stops at the middle stage. Vinblastine effective against malignant lymphoma, choriocarcinoma and testicular neoplasms, as well as lung cancer, breast cancer, ovarian cancer and mononuclear leukemia [56, 57].

Cytoskeleton-targeting drugs have been discontinued due to significant toxicity, most of them are caused by the nonspecificity of the target. Although an appropriate protein delivery system can be conjugated to drugs to potent therapeutic benefits, thereby delivering highly specific treatments of cytoskeleton-targeting drugs to neoplastic tissue, the other developed manner need be used in future. Indeed, the cytoskeleton is much difference between normal cells and cancer cells as our summarized (Figure 2 and Figure 3), which further trigger different mechanical behaviors. Therefore, illustration of cytoskeleton modulated mechanics in cancer cells by using modern advanced material approaches is a prerequisite for future development of anticancer drugs.

Application potential of cytoskeletal targeted anticancer drugs

Cell skeleton-targeting anti-cancer drugs have multiple advantages. They can directly act on the cell skeleton of cancer cells, targeting specific molecular markers or signaling pathways for targeted therapy. This can improve treatment accuracy and reduce side effects on normal cells. Moreover, due to the fact that cell skeleton-targeting anti-cancer drugs often act on complex signaling pathways and molecular networks, they exhibit multi-target effects. This can enhance the killing effect of drugs on cancer cells. Additionally, they can inhibit cancer cell proliferation and metastasis. Cell skeleton-targeting anti-cancer drugs can interfere with the processes of cancer cell proliferation, migration, and invasion. For example, microtubule-targeting agents can impede cancer cell mitosis, thereby preventing cancer cell proliferation. Extracellular matrix-targeting inhibitors can disrupt the adhesion and migratory ability of cancer cells to surrounding tissues, thus inhibiting cancer cell metastasis.

There are many potential and expectations for the future application of tumor cytoskeleton targeted drugs. First of all, all forms of anti-tumor treatment. The development and application of tumor cytoskeleton targeting drugs are expected to improve the effect of tumor treatment. By interfering with the function of tumor cytoskeleton, these drugs can inhibit the proliferation, migration and invasion of tumor cells and promote their apoptosis. Future tumor cytoskeleton targeted drugs may have higher selectivity and efficacy, providing better treatment options for patients. Second, compared with traditional treatment methods, drugs targeting tumor cytoskeleton may have better therapeutic effects on drug-resistant tumors. The drug resistance of tumor cells is a major challenge in tumor treatment. Tumor cytoskeletal targeted drugs are expected to...
overcome some of the drug resistance problems, because they act on tumor cells through different mechanisms. Moreover, tumor cytoskeleton targeting drugs may be combined with other anti-tumor drugs to form a combined treatment regimen. Multiple blows are applied to tumor cells through different pathways and mechanisms to improve the therapeutic effect and reduce side effects.

**Material approaches on anticancer drug in future**

In cellular mechanical field, the approaches including 2D and 3D materials are employed for the study of cellular dynamics and mechanics to underly the physiological and pathological processes of cells [58]. Therefore, we overview majority material approaches in Figure 5, and aim to inspire the mechanical research topics and drug targets of anticancer therapy in future. The 2D flat substrates are usually used for recover the flexible substrate environment of cell growth due to the Young’s moduli of the surrounding substrates in vivo mostly are less than 100 kPa [59]. Thus, the mechanical mechanisms of ECM stiffness on the cancer cell growth and initiation, even the differences from normal cells will be clarified by using the 2D flat substrates. Furthermore, the anticancer drugs that target tumor cell proliferation and initiation can be screened by this system. Actually, the tissues have a variety of topological forms, such as coiled structure of small intestine. The microfabricated substrate with topographical patterns can achieve it. By using this material, how tissue structure induces tumorigenesis and the progression of tumor stiffness in different histological structures will be understand. The anticancer drugs that target cancer cell invasion, growth and metastasis can be well developed by this. For the 3D-structure of tumor, 3D hydrogels provide better platform to investigate how mechanical environment modulates tumor stiffness and further affect tumor metastasis. Additionally, the platform is more conducive to screening out drugs for tumor control and prevention and control of tumor growth and migration. Take it together, we believe that material approaches to active the mechanics of tumor tissue can be well applied in discovery of anticancer drug in future.

**Conclusion**

In summary, mechanical properties of tumor stiffness that modulated by cancer cytoskeleton are critical for tumor progression. The anticancer drugs from cytoskeleton-targeting natural products that directly disturb the cytoskeleton dynamics are worth to develop. Furthermore, the material approaches to active cancer mechanics that supplied in this review will provide an in vitro platform for the investigation of anticancer drugs that target tumor mechanics and find its pharmacological application.

The role of cell mechanical properties in tumorigenesis is still under study, and this is often ignored in oncology reviews. The research and development of natural drugs for tumor cytoskeleton is currently in an active development stage. Tumor cytoskeleton is a structural scaffold in cells. It plays an important role in cell growth, migration and transformation. Therefore, by interfering with the function of tumor
<table>
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<tr>
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<td>Cucurbitacin E</td>
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<td>4T1 and MDA-MB-231 breast cancer cells</td>
<td>Breast cancer, lung cancer</td>
<td>[43, 60, 61]</td>
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<td>Inhibition of the depolymerization of actin filaments</td>
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<td>It can promote microtubule polymerization, assembly and prevent depolymerization</td>
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<td>Apocynaceae</td>
<td>Vinblastine</td>
<td>Microtubule destabilizer</td>
<td>Nonsmall-cell subtype</td>
<td>Malignant lymphoma, choriocarcinoma, lung cancer, breast cancer, ovarian cancer and mononuclear leukemia</td>
<td>[56, 57]</td>
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<td>Depolymerization of microtubule</td>
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<td>Microbe</td>
<td>Fungi</td>
<td>Cytochalasins</td>
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<td>AGS, CT26 colorectal carcinoma cells</td>
<td>Gastric cancer; breast cancer and colorectal cancer</td>
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<td>myxobacterium</td>
<td>Chondromycetes crocatus crocatus</td>
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<td>Breast cancer, lung cancer</td>
<td>[44, 45]</td>
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<td>Anti-invasiveness; Anti-phosphorylation of MLC; Anti-contractility</td>
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<td>Marine</td>
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<td>Geodia corticostylifera</td>
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<td>Marine sponges</td>
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<td>It promotes actin polymerization and stabilizes actin filaments. Its binding to F-actin is competitive with phallolidin.</td>
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<td>Latrunculins</td>
<td>Actin destabilizer</td>
<td>G-actin; interaction with thymosin b4; &gt; 95% inhibition of invasiveness at 100 ng/mL; Anti-invasiveness</td>
<td>AMDC-S and AMDC-AS cell Lines; MDA-MB-231 cells; MKN45 and NUGC-4 cells</td>
<td>Breast cancer and gastric cancer</td>
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cytoskeleton, it is expected to achieve the treatment and control of tumors. Natural drugs are drugs extracted from natural resources such as plants, animals or microorganisms, which have good safety and low toxic and side effects. In the search for natural drugs for tumor cytoskeleton, researchers often screen active ingredients from herbs or explore through traditional Chinese medicine prescriptions. At present, some studies have found active natural drugs targeting the tumor cytoskeleton. For example, compounds extracted from certain Chinese herbal medicines have shown inhibitory effects on cytoskeletal proteins, which may inhibit the proliferation and migration of tumor cells. In addition, some marine organisms have also been found to have active components targeting the tumor cytoskeleton, which may have potential ability to treat tumors. However, the research and development of natural drugs for tumor cytoskeleton is still in the early stage, and further research and development are needed. Researchers need to understand the mechanism of action of these natural drugs through more in-depth research, and further optimize their pharmacological properties and efficacy to improve the feasibility of their clinical application. In conclusion, the development of natural drugs targeting tumor cytoskeleton presents potential and prospects, but further research and verification are still needed. The progress of this work will help to develop more effective anti-tumor drugs and provide better treatment options for cancer patients.

Table: Material approaches to active tumor mechanics to develop anticancer drug in future.

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<tr>
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<th>Research topics</th>
<th>Drug targets</th>
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<td>1. Cancer cell growth</td>
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<td>2. ECM stiffness regulates the differences on normal epithelial cells and cancer cells</td>
<td>2. Tumor initiation</td>
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<td>2. Progression of tumor stiffness in different histological structures</td>
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<td>3. Metastasis of cancer cells</td>
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<td>3D hydrogel</td>
<td>1. Mechanical environment modulates tumor stiffness</td>
<td>1. Tumor growth</td>
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<td>2. Tumor stiffness modulates tumor metastasis</td>
<td>2. Tumor cell invasion</td>
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<td>3. Tumor metastasis</td>
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Figure 5 Material approaches to active tumor mechanics to develop anticancer drug in future. The material approaches to active tumor mechanics are including 2D flat substrates, microfabricated substrate with topographical patterns and 3D hydrogels. The research topics exhibited on mechanical stiffness of tumor and cancer diseases are showed. Targets of candidate anticancer drugs are also displayed.

References


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Advances in anticancer drug design.

Geodia sp. breast cancer cell lines.

HIF-1α knockdown promotes cell migration and invasion.

Cucurbitacin B promotes cell migration and invasion.

Microtubule-stabilizing agents for breast cancer therapy.

Antimitotics.

Microtubule-stabilizing agents for breast cancer therapy.

Evaluations, including in vivo and in vitro.

Anticancer activity of the patient microtubulin-targeting compound.

Vinblastine-sensitive and -resistant human prostate cancer cell lines.

Novel microtubule-stabilizing agents.

Anticancer properties of microtubule-stabilizing agents.

http://doi.org/10.1002/jcp.21432

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