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Commentary

Pioneering Antitumor Research through Marine-Derived Fungal Metabolites

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DESCRIPTION

Cancer continues to be one of the most significant health challenges globally, with prostate cancer being one of the most common types affecting men. The search for new and effective treatments is ongoing, and marine-derived fungi have emerged as a source of novel bioactive compounds. One such fungus, *Peniophora* sp. SCSIO41203, has been found to produce metabolites that exhibit significant antitumor activity. These novel metabolites have shown potential as methuosis inducers in PC-3 cells, a human prostate cancer cell line. Methuosis is a form of non-apoptotic cell death characterized by the accumulation of large vacuoles derived from macropinosomes, leading to cell death. This article delves into the discovery, characterization, and antitumor activity of these novel metabolites, highlighting their potential as a new class of anticancer agents. Marine ecosystems are rich in biodiversity, offering a vast array of organisms that produce unique secondary metabolites. Marine-derived fungi, in particular, have attracted significant attention due to their ability to produce bioactive compounds with various pharmacological properties, including antimicrobial, antiviral, and anticancer activities. The unique conditions of the marine environment, such as high salinity, pressure, and low light, drive these organisms to develop distinct metabolic pathways, resulting in the production of novel compounds not found in terrestrial organisms. The fungus *Peniophora* sp. SCSIO41203 was isolated from marine sediments collected from the South China Sea. The isolation process involved several steps, including culturing the fungus on specific media, extracting its metabolites, and characterizing the compounds using advanced analytical techniques. The metabolites were identified through a combination of Mass Spectrometry (MS) and Nuclear Magnetic Resonance (NMR) spectroscopy, which provided detailed information about their molecular structures. The metabolites produced by *Peniophora* sp. SCSIO41203 exhibited antitumor activity against PC-3 cells. Among these metabolites, several novel compounds were identified, which showed significant in vitro antitumor activity. These compounds induced methuosis, a non-apoptotic form of cell death, in PC-3 cells. Unlike apoptosis, methuosis is characterized by the formation of large vacuoles derived from macropinosomes, leading to cell death without the typical hallmarks of apoptosis such as DNA fragmentation and caspase activation. The mechanism by which these novel metabolites induce methuosis involves the disruption of macropinocytosis, a cellular process responsible for the uptake of extracellular fluid and nutrients. The metabolites interfere with the normal trafficking and processing of macropinosomes, leading to their accumulation and the formation of large vacuoles. This disruption ultimately results in cell death. The specific molecular targets and pathways involved in this process are still under investigation, but the unique mode of action offers a promising therapeutic strategy, especially for cancers that are resistant to traditional apoptotic inducers. The antitumor activity of these novel metabolites was evaluated *in vitro* using PC-3 cells. The cells were treated with various concentrations of the metabolites, and several assays were performed to assess their effects on cell viability, proliferation, and death. The results showed a dose-dependent reduction in cell viability, indicating the potent cytotoxic effects of the metabolites. Furthermore, morphological studies using microscopy confirmed the presence of large vacuoles in treated cells, consistent with methuosis induction. The discovery of these novel methuosis-inducing metabolites opens up new avenues for cancer therapy. Their unique mechanism of action makes them potential candidates for treating cancers that are resistant to conventional therapies. Moreover, the ability to induce non-apoptotic cell death could be beneficial in overcoming resistance mechanisms that tumors often develop against apoptosis-inducing agents. Further research and development are needed to optimize these compounds for clinical use, including studies on their pharmacokinetics, toxicity, and efficacy *in vivo*.

The novel metabolites from the marine-derived fungus *Peniophora* sp. SCSIO41203 represent a promising new class of antitumor agents with a unique mechanism of action. By inducing methuosis in PC-3 cells, these compounds offer a potential therapeutic strategy for prostate cancer, especially for cases where traditional treatments have failed. The marine environment

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continues to be a valuable source of bioactive compounds, and further exploration of marine-derived fungi could yield additional therapeutic agents with novel mechanisms of action. The ongoing research into these metabolites will provide deeper insights into their potential applications and facilitated for new cancer treatments.