Screening Strategy for Natural Medicine Active Ingredients Targeting Tumor Signaling Pathway

Minhan Zhou

Zhu Junwen Chinese Medicine Clinic, Huizhou, China

clementineabu@hotmail.com

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Abstract: As an important anti-tumor treatment strategy, natural medicine has gradually attracted the attention of researchers. The screening of active ingredients for tumor signaling pathways helps reveal their potential mechanisms and guide clinical applications. This paper discusses the application of high-throughput screening, molecular docking, and network pharmacology to systematically explore and evaluate the active ingredients in natural drugs, as well as their potential use in targeting tumor signaling pathways. By analyzing existing literature and databases, this paper constructs a target network. It combines bioinformatics technology to identify key signaling pathways related to tumors, thereby screening natural ingredients with significant biological activity and providing a crucial basis for the development of new anti-tumor drugs. In addition, this study emphasizes the combination of computational models and experimental verification, which improves the effectiveness and reliability of the screening strategy. This paper aims to provide new ideas for the in-depth development of natural medicine research in anti-tumor studies. Natural medicines have significant value in the treatment of tumors and provide a new perspective for network pharmacology research.

1. Introduction

1.1 Research Background

In recent years, the prevalence and mortality rates of cancer have been increasing year by year, constituting one of the global challenges. Although conventional cancer treatments such as chemotherapy and radiotherapy have certain effects, their side effects are significant, and they are prone to causing drug resistance. In contrast, natural drugs have attracted considerable attention due to their convenient accessibility, complex structures, and wide range of action sites, and have demonstrated good anticancer potential. A large number of studies have confirmed that many natural drugs can inhibit tumor proliferation and metastasis by regulating the signaling pathways of cancer cells. The abnormal activation of cancer cell signaling pathways is a key factor in the occurrence and development of tumors. By screening active ingredients that target signaling pathways, it is helpful to elucidate the anticancer mechanism and provide possibilities for the development of new drugs. Facing the diversity and complexity of natural drugs, how to systematically screen and evaluate active ingredients to achieve precise treatment has become a core issue that needs to be solved urgently. Therefore, researching the active ingredients of natural drugs that target cancer cell signaling pathways has significant theoretical value and application prospects.

1.2 Research Significance

Research on screening strategies for natural medicine active ingredients targeting tumor signaling pathways has significant scientific and technological value, as well as practical application prospects, providing an innovative perspective for the development of anticancer drugs. Owing to the structural diversity and multi-target synergistic effects, natural drugs can effectively solve the problem of drug resistance. An in-depth exploration of the interactive mechanisms between the active ingredients of natural drugs and tumor cell signaling pathways is crucial for

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revealing the underlying principles of tumor therapy and advancing the development of personalized medicine. Through an efficient screening strategy, it is possible to rapidly identify components with clinical application potential, optimize existing treatment methods, and improve patients' survival chances and quality of life. The comprehensive application of network pharmacology and bioinformatics technologies can enhance the scientific rigor and precision of screening methods, as well as elucidate the complex biological characteristics of tumors and the mechanisms of drug action. In summary, the research can not only improve the existing research framework for anticancer drugs but also promote the translation of basic research into clinical practice.

2. Overview of Related Theories and Technologies

2.1 Introduction of Signaling Pathway

2.1.1 Basic Concepts and Regulatory Mechanisms of Tumor Signaling Pathways

Signal pathways are intracellular signaling networks that regulate biological processes such as cell growth, differentiation, apoptosis, and migration through a series of molecular interactions. In a normal body, signal pathways can keep cells in a stable state. However, when tumors appear and develop, they often become too active or suppressed, which in turn helps tumor cells to proliferate and survive.

The regulatory mechanism involves the binding of exogenous signaling molecules, the activation of cell membrane receptors, and cascades of various intracellular signal transduction molecules. After growth factors bind to their receptors, downstream signaling molecules such as RAS and RAF can be activated, thereby initiating the MAPK pathway to promote cell proliferation. On the contrary, PTEN is a molecule that will block the signal pathway. It can inhibit the growth and survival of cells by dephosphorylation of the PI3K/Akt pathway. The regulation of signal pathways has complex positive and negative feedback characteristics, which not only direct the normal behavior of cells but also reprogram them in response to changes in the tumor microenvironment, thereby promoting tumor initiation and progression. Targeted therapeutic strategies against tumor signaling pathways have become a crucial research direction in cancer treatment [1].

2.1.2 Key Tumor Signaling Pathways

Key tumor signaling pathways play a central role in the occurrence and development of cancer, including the PI3K/Akt pathway, the MAPK/ERK pathway, the Wnt/β-catenin pathway, and the NOTCH pathway. The PI3K /Akt pathway is the key mechanism regulating cell proliferation and survival. Abnormal activation is closely related to the formation of various cancer types, which can enhance the anti-apoptotic ability of cells and promote the survival and diffusion of cancer cells [2-3]. The MAPK/ERK pathway primarily regulates cell proliferation and differentiation, playing a crucial role in cellular growth regulation under normal physiological conditions. In cancer cells, it often exhibits excessive activation, driving tumor progression. The Wnt/β-catenin pathway plays crucial roles in processes such as cell adhesion and stem cell maintenance, with aberrant activation frequently leading to the formation of adenomas and malignant cancers. The NOTCH pathway plays a crucial role in determining cell fate and tissue development, exerting either inhibitory or promotive effects in tumors, depending on specific cellular contexts and microenvironmental conditions. To summarize, research on signaling pathway systems offers effective intervention targets for precision-targeted therapies, thereby advancing cancer treatment.

2.2 Overview of Screening of Active Ingredients of Natural Medicines

2.2.1 Characteristics and Advantages of Screening Active Ingredients of Natural Medicines

Screening active ingredients from natural medicines has unique characteristics and advantages, which is why it has been widely studied in the field of anti-tumor research. Natural medicines have a wide range of sources, encompassing plants, organisms, and microorganisms, which provide a rich diversity of structural features and chemical compositions. Natural medicines often work by

targeting multiple sites simultaneously, which means they can help control multiple biological processes simultaneously, making them more effective in treating diseases and reducing the likelihood of resistance. When compared to man-made drugs, natural medicines usually cause fewer severe side effects. Therefore, they are safer to use for a longer time and help patients feel better. With the development of high-throughput screening technology and bioinformatics, our ability to identify effective ingredients in natural medicines has become faster and more accurate, enabling us to quickly identify those ingredients that may be useful. The screening of active ingredients from natural medicines can not only promote the research and development of new drugs but also facilitate the analysis of tumor biological mechanisms, connecting basic research with clinical practice. Employing screening strategies for active ingredients from natural medicines holds profound value and broad prospects in the field of oncology treatment.

2.2.2 Common Screening Platforms

The core screening technology system for natural product active ingredients primarily encompasses high-throughput screening, molecular docking, cell biology experiments, and network pharmacology. High-throughput screening technology utilizes automated equipment to conduct rapid detection on a large number of natural compounds, evaluating their activity against tumor cells and efficiently identifying anti-tumor substances. Molecular docking, through computational simulation, analyzes the interactions between natural compounds and target proteins, predicting binding strength and modes of action. Cell biology experiments encompass cell proliferation, apoptosis, and migration tests, providing a direct evaluation of the effects of active ingredients on tumor cells and verifying their biological efficacy. Network pharmacology integrates multiple bioinformatics data to construct an interactive network between drug components and tumor signaling pathways, enabling researchers to comprehensively analyze the mechanisms of action and sites of action of active ingredients. The synergistic effects of the system significantly enhance the efficiency and precision of screening for natural product active ingredients, laying a solid foundation for the research and development of anti-tumor drugs [4].

3. Problems with Conventional Screening Methods

3.1 Low Screening Efficiency and Flux Limitation

The screening of active ingredients in traditional natural medicines faces considerable limitations in both effectiveness and efficiency. There are many types of natural sources, and their ingredients are very complex, so it is often impossible to obtain complete information on all active ingredients immediately with only one extraction and separation technology. It leads us to spend a considerable amount of time and resources on screening. Furthermore, when confronted with large compound libraries, standard laboratory screening methods are generally inadequate for high-throughput requirements, which in turn hinders the overall screening process. Many experiments still require direct participation, allowing for personal judgment errors and experimental uncertainties. Qualcomm screening technology is being used more frequently now, which significantly enhances our screening speed. However, we still need to find solutions to some challenging problems, such as determining whether the compound is stable enough, whether it can be dissolved, and whether the body will repel it. To improve our screening efficiency, we must study and enhance the platform and technology of screening, as well as carefully examine how to address the challenges of natural drug screening, thereby enabling us to develop more effective anti-tumor drugs.

3.2 Target Specificity and Off-target Effects

In the process of screening for active ingredients in natural drugs, target specificity and off-target effects are key factors that need to be considered. The former refers to the drug's ability to specifically act on a particular biological target to achieve the desired biological effect. Many natural drug ingredients have complex structures and interact with multiple targets, which affects the drug's efficacy and safety. Off-target effects, on the other hand, refer to the drug's unintended

action on non-targeted targets during targeted therapy, leading to adverse reactions or toxicity, which affects the patient's quality of life and treatment compliance. The heterogeneity of tumor cells increases the complexity of target selection, as there are significant differences in the responses of different patients or tumor types to the same active ingredient. Therefore, in the selection process, it is essential to carefully validate and evaluate target selection technologies. To address this issue, researchers must integrate modern pharmacology and bioinformatics methods to thoroughly investigate the interaction mechanisms between active ingredients and their targets, thereby enhancing the precision and safety of targeted therapy.

3.3 Adaptability of Complex System

3.3.1 Multi-target Synergistic Effect

In the process of anti-tumor drug research and development, the synergistic effect of multiple targets is considered a key concept in screening active ingredients of natural drugs. Many natural drugs achieve comprehensive therapeutic effects by acting on multiple signaling pathways and targets, efficiently inhibiting tumor cell proliferation and transformation. The multi-target characteristics of natural drugs can overcome the limitations of target therapy and reduce the risk of drug resistance. Studies show that certain natural ingredients can achieve multiple effects by regulating the cell cycle, inducing apoptosis, and inhibiting the formation of the tumor microenvironment. Some active ingredients of Chinese herbal medicines target common tumor signaling pathways, such as the PI3K/Akt and MAPK/ERK pathways, resulting in a synergistically enhanced anti-tumor effect. This mechanism can enhance drug efficacy, enable dose reduction to reduce adverse reactions, and an in-depth exploration of the multi-target synergistic effects of natural drugs helps to optimize drug selection strategies, providing new ideas and a basis for personalized anti-tumor therapy [5].

3.3.2 In Vivo Metabolism and Bioavailability

In the process of screening and applying natural drug active ingredients, the degree of biotransformation and absorption utilization is a key factor determining pharmacological efficacy and therapeutic effects. After natural drug ingredients are metabolized in vivo, their molecular structures change, thereby affecting their biological activity. Some active ingredients are metabolized rapidly in the liver or intestine, leading to decomposition before they reach their target sites, which reduces their therapeutic efficacy. Evaluating the in vivo metabolic status of natural drugs is of great value for optimizing the screening and development of active ingredients

Bioavailability, which is defined as the fraction of a drug that enters the systemic circulation, directly influences its therapeutic concentration and overall effectiveness. Many active ingredients from natural medicines have low bioavailability because they are poorly soluble in water or struggle to cross biological membranes. To overcome the issues and sustain effective therapy, clinicians often need to administer high doses or use combination therapies. Formulation science offers a solution by designing better drug delivery systems, which can enhance bioavailability. Furthermore, the use of nanotechnology can significantly amplify the potency of these active compounds. Ongoing research and development will continue to solidify the scientific foundation for the broader clinical use of natural medicines.

3.3.3 Interaction between Ingredients

In the selection and application of active ingredients of natural medicines, the interaction between ingredients is regarded as a key element. The diversity of components has a significant impact on the overall efficacy of drugs. Most natural medicines contain a variety of ingredients that act synergistically in different ways to enhance their anti-tumor effect, and may also have antagonistic or inhibitory effects. An in-depth exploration of their interaction can provide a reliable basis for optimizing the formulation and use of natural medicine. Modern pharmacological techniques, such as network pharmacology and systems biology, can assist researchers in systematically analyzing and identifying interactions, clarifying key components and mechanisms

of action, and providing a reference for the development of new drugs. Paying attention to the interaction between ingredients is a necessary prerequisite for improving the efficacy of natural medicines, and it is also a key path to achieving individualized treatment.

4. Targeted Screening Strategy Based on Multi-omics Integration

4.1 Screening Strategy Based on Network Prediction

4.1.1 Multi-scale Target Prediction and Network Pharmacology Analysis

Multi-scale target prediction and network pharmacology are key pathways to understanding the complex mechanisms of action of natural drugs. This study conducts an in-depth exploration from a systems biology perspective. This technology utilizes bioinformatics tools to screen for known targets and, by analyzing the interaction relationships between components and targets, constructs multi-level target networks. The multi-scale target prediction method encompasses molecular, cellular, tissue, and even organ-level complex systems. During the network pharmacology analysis process, we integrate multi-omics data, including genomics, transcriptomics, proteomics, and metabolomics, to perform functional annotation and enrichment analysis on targets, thereby clarifying their specific roles in tumor signaling pathways. This technology can reveal the multi-target characteristics of natural drugs, identify synergistic effects and regulatory mechanisms, and, through visualization network diagrams, intuitively present the correlations between components, targets, and pathways, providing an important reference for subsequent experimental design and clinical application. The multi-scale target prediction and network pharmacology analysis method has significant constructive value and practical significance in the screening of active components.

4.1.2 Priority Ranking of Active Ingredients Based on Pathway Enrichment

Given that the grading of pathway-enriched active components is a crucial step in screening the active components of natural drugs, we identified candidate substances with high biological activity and a significant targeting effect by integrating and evaluating the effects of different components on specific signaling pathways. Based on bioinformatics methods, we performed pathway enrichment analysis to match natural drug components with related target signaling pathways and identify core pathways that regulate tumor progression. By analyzing the functional performance of active ingredients in related pathways, combined with known biological activity and toxicity data, a multidimensional evaluation system can be constructed to prioritize the division of each component. In view of the priority ranking of pathway-enriched active ingredients, it provides a systematic solution for new drug development. It is beneficial to optimize the application strategy, minimize the deviation in the research and development stage, enhance the efficiency of anti-tumor drug research and development, and expedite the clinical application process [6].

4.2 High-throughput Virtual Screening and Experimental Verification

4.2.1 Virtual Screening of Molecular Docking and Dynamic Simulation

Molecular screening and mechanical simulation strategies serve as key methods for screening the active ingredients of natural medicines, providing an understanding and quantitative prediction of molecular interactions. In the molecular docking, we utilize computer algorithms to deduce the binding patterns between natural medicine components and tumor target proteins, assessing their binding affinity and specificity. This process integrates molecular configuration parameters and target attributes, facilitating the screening of candidate substances with potential pharmacological activity. Real-time mechanical simulation is employed to elucidate the dynamic behavior of molecules in a physiological environment, including binding stability and conformational changes. By running long-term molecular mechanics simulations, we can observe important intermediate steps in how molecules move, determine the roles of key amino acid residues, and refine the structures of active ingredients. The combined application of these two virtual screening strategies can enhance screening efficiency and precision, help to systematically elucidate the mechanisms of action of natural medicines, lay a solid foundation for subsequent experimental validation, and

promote the research and development of anti-tumor drugs.

4.2.2 An Experimental Verification System Based on Cell and Animal Models

In the screening process for active ingredients in natural medicines, cellular and biological model verification systems are essential. These systems provide the biological evidence required to confirm the efficacy and safety of the screening results. At the cellular level, researchers frequently employ a variety of tumor cell lines to mimic tumor biology and its microenvironment. Techniques such as the MTT assay and flow cytometry are used to assess the effects of active compounds on cell proliferation, apoptosis, and migration, enabling the early identification of compounds with potential anti-tumor activity. At the biological level, experimental models typically utilize mice or rats to observe how natural drug components inhibit tumor growth and to study their in vivo metabolism and bioavailability [7]. By developing tumor xenograft or chemically-induced models, investigators can conduct a more thorough evaluation of the pharmacodynamics, toxicity, and mechanisms of action of the active ingredients. Biomarker detection facilitates the analysis of alterations in signaling pathways, enabling the identification of specific targets for intervention. The integrated use of these cellular and biological model verification systems is crucial for establishing a solid foundation for the clinical application of active ingredients in natural medicines.

4.3 Strategies for Improving Screening Accuracy under Complex Systems

4.3.1 In Vivo Active Ingredient Tracking Method Based on Serum Pharmacochemistry

The technique for tracking the chemically active ingredients of drugs in vivo serum is a method used to evaluate the distribution and metabolic efficiency of natural drug components in biological organisms. This technique involves the separation and quantitative analysis of active ingredients in serum to monitor the kinetic characteristics, bioavailability, and pharmacodynamic performance of the drug in the body instantly. During the experiment, researchers typically need to collect serum samples from biological models and utilize precise analytical methods such as High-Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) to separate and quantitatively determine the active ingredients. This allows for the acquisition of concentration changes of the active ingredients at different time points, from which the kinetic parameters of the drug—including absorption rate, distribution range, metabolic pathways, and excretion methods—can be inferred. Tracking the concentration changes of active components in serum enables researchers to analyze their interaction with the tumor microenvironment and evaluate the targeting ability and effects of these components. To summarize, this method provides feedback for optimizing drug design, enabling researchers to adjust the structure of active ingredients and enhance their stability and biological activity in vivo.

4.3.2 Comprehensive Evaluation Model

One of the key means of evaluating the efficacy and mechanism of action of natural drug active ingredients in a multi-target context is the integrated assessment of multi-target synergistic effects. This paradigm is based on the systematic analysis of diverse biological targets, constructing an interaction network among active components, targets, and tumor signaling pathways. We employ both quantitative and qualitative methods to integratively evaluate the inhibitory efficacy of different components on tumors through their synergistic effects on multiple targets. With the aid of systems biology tools, we analyze the integrated impact of signaling pathway interactions on the behavior of tumor cells. Additionally, we consider applying machine learning for deep data mining and pattern recognition in experimental data to optimize the quantitative analysis of multi-target synergistic effects. The multi-target characteristics of natural drugs, as embodied in this integrated assessment paradigm, will provide a scientific basis for new drug research and development, as well as optimization, facilitating the practice of precision medicine in the field of anti-tumor therapy and enhancing the clinical value of natural medicines.

5. Conclusion

In the field of anti-tumor research, this research shows broad application prospects. By integrating multiple technical methods, such as high-throughput screening, molecular docking, and network pharmacology, it is possible to scientifically identify and verify active ingredients, clarify the molecular mechanisms underlying multi-target synergistic effects, and optimize screening efficiency and accuracy. The complexity of the tumor microenvironment poses new challenges for the action of natural drugs. By constructing a multi-omics integrated evaluation system and a multi-target synergistic effect analysis model, the technical and practical aspects of ingredient screening can be significantly enhanced.

Future research should focus on improving virtual screening and experimental verification to meet the needs of personalized treatment and enhance the clinical translation value of natural medicines. This study gives a thorough investigation into the interaction and dynamic change patterns among ingredients. The aim is to develop a systematic theoretical framework for new drug research and development (R&D). This framework seeks to provide patients with safer and more effective diagnosis and treatment options. Additionally, the ongoing exploration of innovative comprehensive approaches to tumor treatment aims to offer fresh perspectives and technical pathways for development.

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