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Network Biology Reveals New Strategies for Understanding the Relationship Between Protein Function and Disease

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Abstract Network biology is capable of comprehensively analyzing the interaction networks among biomolecules, providing crucial theoretical support and practical guidance for revealing disease mechanisms, optimizing drug development, and promoting precision medicine. This review introduces the basic concepts of network biology and its importance in studying the relationship between protein function and disease, while pointing out the limitations of traditional biological methods in research. It further delves into how network biology integrates multi-omics data to reveal the relationship between protein function and disease, and explores its applications in identifying key disease proteins, predicting drug targets, and understanding the mechanisms of disease occurrence and development. Additionally, it discusses the practical applications of new strategies in network biology in disease diagnosis and treatment, including early diagnosis, prognostic assessment, personalized treatment, and drug development and optimization. This review summarizes the significant role of network biology in studying the relationship between protein function and disease and looks forward to future research directions. The research in this review not only helps deepen our understanding of the relationship between protein function and disease, but also provides new strategies and methods for disease diagnosis and treatment.
Keywords Network biology; Protein function; Disease relationship; Multi-omics data; Personalized treatment

With the rapid development of biotechnology, proteins, as vital executors of life activities, play a crucial role in understanding life phenomena, disease mechanisms, and drug development (Liu et al., 2020). However, the complexity and diversity of protein functions pose significant challenges to traditional biological research methods. In recent years, network biology, an emerging interdisciplinary field, has provided new perspectives and strategies for elucidating the relationships between protein functions and diseases.

Network biology employs graph theory and complex network analysis to construct biological network models such as protein interaction networks and metabolic networks, thereby revealing the complex relationships between biomolecules. Through the analysis of network biology, it is possible to more systematically understand the interactions and regulatory mechanisms of proteins within organisms, and thus disclose their critical roles in the development of diseases (Diogo et al., 2018).

The new strategies of network biology offer a novel approach. Network analysis places proteins within the entire biological network to explore their interactions with other biomolecules, thereby uncovering their key roles in the development of diseases. Moreover, network biology can also leverage big data and machine learning technologies to perform high-throughput predictions and analyses of protein functions, greatly enhancing research efficiency and accuracy (David et al., 2020).

This study aims to use the new strategies of network biology to reveal the relationships between protein functions and diseases, providing new ideas and methods for the treatment and prevention of diseases. By network analysis, it hopes to identify key proteins closely related to diseases, unveil their molecular mechanisms in disease development, offer a theoretical basis for early diagnosis and precise treatment of diseases, and promote the application and development of network biology in the study of protein functions and disease relationships, thereby injecting new vitality into biomedical research.

1 Overview of Network Biology

1.1 Basic concepts and research scope of network biology

Network Biology is an interdisciplinary field dedicated to studying biomolecular networks and their interactions. Rooted in the principles of Systems Biology, Network Biology integrates multi-omics data and utilizes graph theory, statistics, and computational algorithms to deeply analyze the complex relationships between biomolecules.

Its research scope is extensive, covering gene regulatory networks, protein interaction networks, metabolic networks, and more. Within gene regulatory networks, Network Biology focuses on the transcriptional regulatory relationships between genes, exploring how they work together to regulate gene expression in organisms. In protein interaction networks, it aims to reveal the interactions between proteins and how these interactions affect cellular functions and life processes (Becerra-Flores and Cardozo, 2020).

Network Biology not only focuses on the topological structure and dynamic characteristics of networks but also delves into the functional significance of these characteristics. By constructing and analyzing biomolecular networks, Network Biology can reveal the mechanisms of synergistic action between biomolecules and how these mechanisms affect growth, development, disease occurrence, and other processes in organisms.

1.2 Applications of network biology in protein interaction networks, gene regulatory networks, etc.

The application of Network Biology in areas such as protein interaction networks and gene regulatory networks not only deepens our understanding of life phenomena but also provides new strategies and tools for disease treatment and new drug development. In protein interaction networks, Network Biology constructs maps of protein interactions, systematically revealing the physical and functional connections between proteins. Li et al. (2019) used high-throughput technologies and bioinformatics methods to identify and quantify the interactions between proteins, thus understanding their key roles in cellular signal transduction, metabolic regulation, and disease occurrence. These studies have deepened our understanding of protein functional diversity and complexity and have provided potential targets and new approaches for disease treatment.

In gene regulatory networks, Network Biology plays an equally important role. Gene regulatory networks are complex systems for gene expression regulation within cells, involving interactions among transcription factors, RNA molecules, and epigenetic modifications. Network Biology can analyze the topological structure of gene regulatory networks, identify key regulatory nodes and pathways, and thereby understand the mechanisms and dynamic changes of gene expression regulation. These studies can reveal the complex relationships between genes and phenotypes, providing strong support for the elucidation of disease mechanisms and the development of precision medicine.

1.3 Unique advantages of network biology in revealing protein functions and disease relationships

Network Biology offers a novel perspective and method for understanding the relationships between protein functions and diseases. It can comprehensively analyze protein interaction networks and systematically study the interactions among proteins, revealing their functional localization and mechanisms of action within cells. This global analysis approach overcomes the limitations of traditional biological methods, which can only study single proteins or simple pathways, allowing for a deeper understanding of the complex roles of proteins in the onset and progression of diseases (Liu et al., 2020).

Network Biology can integrate multi-omics data, merging information from genomics, transcriptomics, proteomics, and other levels, thereby more comprehensively revealing the relationships between protein functions and diseases. This cross-omics analysis method can uncover potential associations that traditional methods may miss, providing new ideas for disease diagnosis and treatment. Qin et al. (2020) found that Network Biology also has predictive capabilities, able to predict new disease-related proteins and drug targets based on known protein interaction networks and gene regulatory networks. This predictive ability not only helps to identify potential disease risks in advance but also provides new candidate molecules for drug development, accelerating the process of pharmaceutical research.

Network Biology also has dynamic and personalized characteristics. It can analyze the dynamic changes in protein interaction networks under different conditions and at different times, revealing the dynamic processes of disease occurrence and development. Moreover, Network Biology can design personalized disease prediction and treatment plans based on an individual's genetic background and environmental factors. This personalized research approach helps to improve the accuracy and effectiveness of disease diagnosis and treatment.

2 Research on the Relationship Between Protein Function and Disease in Network Biology

2.1 Network biology reveals the relationship between protein function and disease

Network biology demonstrates strong capabilities in integrating multi-omics data to reveal the relationship between protein function and disease. It utilizes genomics, transcriptomics, proteomics, and other multi-omics data comprehensively, forming multidimensional and multilevel information networks, thereby providing a more comprehensive and in-depth understanding of the role of proteins in diseases (Huang et al., 2020).

Network biology can integrate genomic data to identify gene variants and expression changes related to diseases. These variants and changes may directly affect the structure and function of proteins, and are closely related to the occurrence and development of diseases. By comparing genomic data from different individuals or disease states, network biology can identify potential disease-related genes, providing important clues for subsequent studies on protein function.

The integration of transcriptomics data helps network biology to reveal the relationship between gene transcription regulatory networks and protein function. By analyzing gene expression profiles and transcription factor activities, network biology can construct gene regulatory networks and identify key transcriptional regulators. These factors regulate the genes encoding proteins, thereby affecting the expression levels and functional states of proteins, which are closely linked to the occurrence and development of diseases. Since protein localization can provide crucial information about function, apart from mapping their interactions, David et al. (2020) assessed the cellular localization of individually expressed coronavirus proteins (Figure 1A). Immunofluorescence localization analysis of all 2xStrep-tagged novel coronavirus, SARS-CoV-1, and MERS-CoV proteins in HeLaM cells highlighted a similar localization pattern for most shared protein homologs (Figure 1B), supporting the hypothesis that conserved proteins have functionally similar roles.

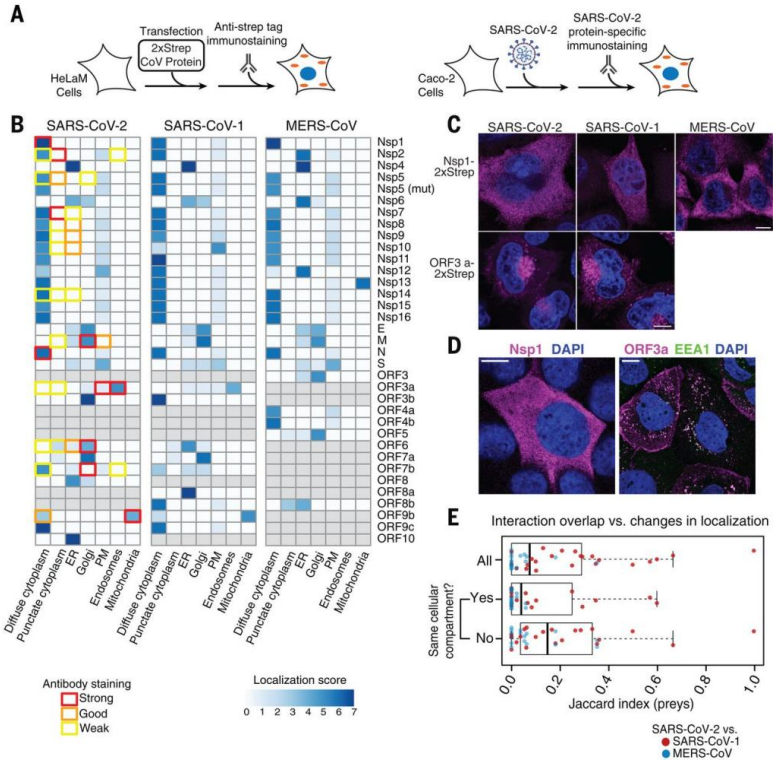

Figure 1 Coronavirus protein localization analysis (David et al., 2020)

Proteomics data integration occupies a crucial role in network biology. Techniques like mass spectrometry and immunoprecipitation help acquire information about protein expression levels, modification states, and interaction relationships. Network biology combines these proteomics data with genomic and transcriptomic data to build protein interaction networks and analyze changes in protein functions in diseases (Figure 1). This cross-omics integration method enables a more comprehensive understanding of the roles proteins play in diseases, providing new insights for the diagnosis and treatment of diseases.

2.2 The application of network biology in identifying key disease proteins and predicting drug targets

Network biology plays a critical role in identifying key disease proteins and predicting drug targets. In identifying key disease proteins, network biology constructs protein interaction networks and can systematically analyze the interactions between proteins, thereby revealing their crucial roles in the onset and progression of diseases. Using bioinformatics algorithms and large-scale datasets, network biology can identify proteins that exhibit abnormal expression or interactions in a diseased state, which are often key molecules in disease onset (Qin et al., 2020).

In predicting drug targets, network biology also shows great potential. Drug targets are specific molecules or structures within a biological system that drugs act upon, which are crucial for the efficacy and safety of the drugs. Network biology, by analyzing protein interaction networks and gene regulatory networks, can predict potential drug targets. For example, by comparing the protein interaction networks of normal and diseased cells, it can identify proteins that show abnormal interactions in a diseased state, which may be effective targets for drug intervention. Additionally, network biology can also analyze gene expression profiles and transcription regulatory networks, predicting genes and transcription factors closely related to disease onset, thus providing new candidate molecules for drug design.

The application of network biology in identifying key disease proteins and predicting drug targets helps to deepen understanding of disease pathogenesis and drug action mechanisms, providing new strategies and tools for precise treatment and new drug development. Combining multi-omics data and network analysis methods allows for more accurate identification of key disease proteins and drug targets, supporting early diagnosis, personalized treatment, and drug development for diseases.

2.3 The important role of network biology in the mechanisms of disease onset and progression

Network biology, by constructing and analyzing biological molecular networks, provides a global and systemic perspective to examine diseases. It integrates genomics, transcriptomics, proteomics, and other multi-omics data, forming multi-level, multidimensional information networks that enable a deeper understanding of the interactions and regulatory relationships between biomolecules. This global analysis method overcomes the limitations of traditional single-molecule studies and can reveal the complexity and diversity of disease onset and progression.

Network biology can reveal key molecules and pathways during the disease development process. Research by Lokau et al. (2020) found that by analyzing the topological structure and dynamics of biological molecular networks, network biology can identify nodes and edges that show abnormal changes in a diseased state, i.e., key molecules and interactions. These key molecules may be critical drivers of disease onset and could also be potential targets for treatment.

Network biology can also predict disease progression trends and individual differences. By analyzing the dynamic changes in biological molecular networks under different times and conditions, network biology can predict the disease trajectory and outcome. Combining an individual's genetic background and environmental factors, network biology can also perform personalized disease prediction and risk assessment. This predictive capability can help identify potential disease risks in advance, develop personalized treatment plans, and improve the accuracy and effectiveness of disease diagnosis and treatment.

3 Applications of New Network Biology Strategies in Disease Diagnosis and Treatment

3.1 Application of new network biology strategies in early diagnosis and prognosis assessment of diseases

New strategies in network biology demonstrate tremendous potential in the early diagnosis and prognosis

assessment of diseases. In early diagnosis, network biology integrates multi-omics data to comprehensively analyze changes in biomolecular networks, thereby identifying early biological markers related to diseases. Samme et al. (2019) found that these biomarkers may include changes in the expression of specific genes and abnormal patterns in protein interaction networks, providing early warning signals before the onset of disease symptoms. By constructing disease-related biomolecular network models, network biology can identify these early biomarkers and develop corresponding detection methods, providing strong support for the early detection of diseases.

In prognosis assessment, new strategies in network biology also play a crucial role. Prognosis assessment is key to determining the trend of disease progression and patient survival expectations. Network biology analyzes the dynamic changes in biomolecular networks to predict the rate of disease progression and patient prognosis. For example, by analyzing the gene expression profiles and protein interaction networks of tumor cells, network biology can reveal the molecular mechanisms of malignant behaviors such as proliferation, migration, and invasion of tumor cells, and thus predict the malignancy of the tumor and the patient's survival period. These predictions can guide doctors in formulating personalized treatment plans and providing prognosis guidance, helping patients better manage their diseases (Jiang et al., 2020).

New strategies in network biology also have high sensitivity and specificity, reducing the incidence of misdiagnosis and missed diagnosis. By integrating multi-omics data and network analysis methods, network biology can comprehensively consider multiple biomarkers and multiple layers of information, improving the accuracy and reliability of diagnoses. This multidimensional analysis approach can more comprehensively assess a patient's disease state, providing a more reliable basis for early diagnosis and prognosis assessment.

3.2 The potential of new network biology strategies in personalized treatment and precision medicine

In personalized treatment, network biology by constructing and analyzing biomolecular networks, can reveal the molecular differences between individuals. These differences include changes in gene expression, protein interactions, and metabolic pathways, which directly affect an individual's disease onset, progression, and drug response. New strategies in network biology can tailor treatment plans for each patient based on individual biomolecular network characteristics, selecting the most appropriate drugs, dosages, and treatment timings. This personalized treatment approach helps enhance treatment effectiveness, reduce unnecessary side effects, and improve patients' quality of life (Chiva et al., 2018).

Precision medicine emphasizes using individualized information and biomarkers for precise decision-making in disease diagnosis, prevention, and treatment. New network biology strategies provide strong support for precision medicine. David et al. (2020) analyzed individual biomolecular networks and identified specific genes, proteins, and metabolites related to diseases. These biomarkers are not only useful for early disease diagnosis but also for predicting disease progression and prognosis, guiding precise treatment. Additionally, network biology strategies can assess individual drug responsiveness and resistance, providing decision-making basis for precision medication. By adopting an integrated and collaborative approach, David et al. (2020) identified conservative mechanisms in three pathogenic coronavirus strains and further researched potential drug targets. This versatile approach is broadly applicable to other pathogens and disease areas.

The application of new network biology strategies in personalized treatment and precision medicine is expected to drive a shift in the medical paradigm. Traditional medical models often base disease diagnosis and treatment on group averages, overlooking individual differences. Network biology strategies can fully consider individual biomolecular network characteristics, achieving truly personalized medicine (Figure 2). This will help improve medical outcomes, reduce medical costs, and promote the sustainable development of the healthcare industry.

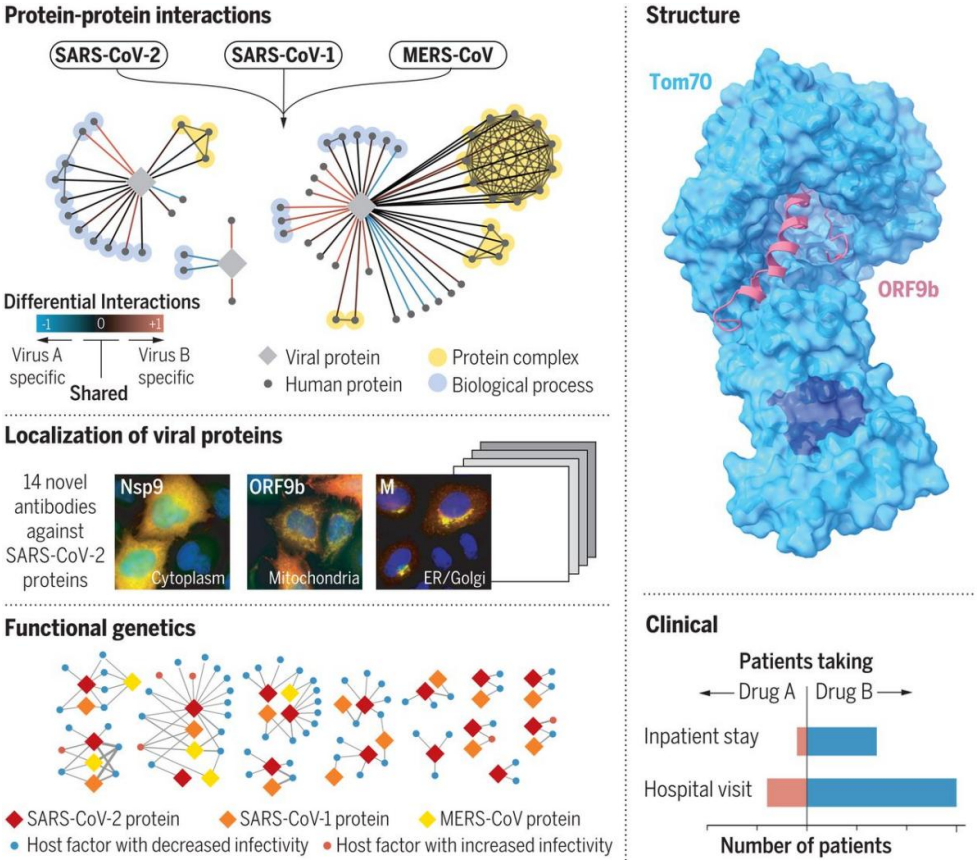

Figure 2 Comparison of host-coronavirus protein interaction networks to reveal pan-viral disease mechanisms (David et al., 2020)

Image caption: Left: Virus-human protein-protein interaction network mapping, viral protein location studies, and functional genetic screening provide key insights into the shared and individual characteristics of each virus; right: Structural studies and hypothesis testing in clinical datasets demonstrate the utility of this approach in prioritizing treatment strategies (Adopted from David et al., 2020)

3.3 Practical applications of new network biology strategies in drug development and optimization

3.3.1 Target identification and validation

In cancer drug development, network biology is used to analyze the gene and protein interaction networks within cancer cells. By analyzing abnormally active signaling pathways in cancer cells, researchers can identify key oncogenes or proteins that can serve as potential drug targets. Subsequently, using network biology experimental validation methods, such as gene knockdown or protein interference techniques, these targets can be further confirmed, providing crucial evidence for subsequent drug design (Giurgiu et al., 2019).

3.3.2 Study of drug action mechanisms

Network biology is used to study the specific mechanisms of drug action within a biological organism. For example, in the development of a new antibiotic, network biology can help researchers analyze how the drug interacts with the biomolecular networks within bacteria, thereby inhibiting bacterial growth. By constructing drug-target interaction network models, researchers can predict the biological processes that may be affected by the drug and verify its effects in actual biological organisms (Yang et al., 2020).

3.3.3 Drug optimization and side effect prediction

In the later stages of drug development, network biology can be used to optimize drug dosage and predict potential side effects. By analyzing the impact of different drug doses on biomolecular networks using network biology methods, researchers can determine the optimal dose range to balance treatment effectiveness and side effects. Additionally, by analyzing the drug's impact on multiple targets within the biological network, potential side effects can be predicted, and risk assessments can be made before clinical trials (Akdel et al., 2020).

3.3.4 Personalized medication guidance

Network biology can combine individual genomic information to provide guidance for personalized medication. By analyzing individual gene mutations and protein expression profiles, network biology can predict individual responses and resistance to specific drugs. This helps doctors tailor personalized medication plans for patients, enhancing treatment effectiveness and reducing unnecessary side effects (Goddard et al., 2018).

These practical applications demonstrate the significant role of new network biology strategies in drug development and optimization. As technology advances and research deepens, these strategies are expected to bring more innovations and breakthroughs to the drug development field, contributing greatly to human health.

4 Summary and Outlook

As bioinformatics and computational biology rapidly develop, network biology has emerged as an interdisciplinary field revealing the complex networks between protein functions and diseases. Network biology integrates multi-omics data, including genomics, transcriptomics, and proteomics, and constructs interaction networks among biomolecules. It offers a global and systemic perspective to deeply analyze the mechanisms of proteins in biological activities. This review aims to summarize the crucial role of network biology in unveiling the relationships between protein functions and diseases and to highlight its new strategies in the practical applications and potential in disease diagnosis and treatment.

Network biology plays a key role in revealing the relationship between protein functions and diseases. By building protein interaction networks, it can systematically analyze the interactions among proteins, thereby identifying those crucial in the onset and progression of diseases. For example, network biology can identify proteins that are abnormally expressed or interact abnormally with other proteins under disease conditions, which are often key molecules in disease onset. Additionally, network biology can analyze the redundancy and complementarity of protein functions, further deepening our understanding of the complexity of protein functions. These research findings not only help understand the pathological mechanisms of diseases but also provide new ideas and methods for disease diagnosis and treatment.

The practical applications and potential of new strategies in network biology in disease diagnosis and treatment are increasingly evident. In diagnostics, network biology can construct disease-related biomolecular network models, predicting the risk and progression speed of diseases. Analyzing individual biomolecular network characteristics can enable early diagnosis and precise classification of diseases, providing personalized treatment plans for patients. In therapeutics, network biology can predict the efficacy and side effects of drugs, guiding the research and optimization of drugs. Identifying key drug targets can lead to the design of more precise and effective drugs, improving treatment outcomes and reducing the occurrence of side effects.

The future of network biology in revealing the relationship between protein functions and diseases holds immense research potential. With the continuous development of high-throughput sequencing technologies, obtaining more accurate biomolecular data will provide a more solid foundation for research in network biology. As artificial intelligence and machine learning technologies advance, more intelligent and efficient network analysis methods will be developed, enhancing the analytical capabilities and predictive accuracy of network biology.

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