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Literature Review: Network Pharmacology as a New Approach and Trend in Medicine

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ABSTRACT

Network pharmacology is a new approach to medicine that aims to understand drug interactions with body tissues more specifically. This concept involves a deep understanding of the mechanisms of drug action, drug metabolism, and the influence of drugs on tissue function. In recent years, network pharmacology has become a significant trend in drug development. This approach allows researchers to design drugs that are more effective and have fewer side effects. By understanding in detail how drugs interact with specific tissues, specific and targeted drug development can be undertaken. Network pharmacology also opens the door to the development of more particular and existent therapies. By taking into account individual differences in response to drugs, this approach allows for more effective and safer treatment. This article presents a literature review of network pharmacology as a new approach and trend in medicine. This literature review also explores the latest research and current trends in the world of medicine using a network pharmacology approach. This article shows that tissue pharmacology has great potential in more effective and safer treatments. With a better understanding of drug tissue interactions, we can develop more targeted therapies and reduce the risk of undesirable side effects.

Keywords: Network Pharmacology, Therapeutics, Computation

I. INTRODUCTION

Network pharmacology is the science that understands the interactions between biological systems and drugs at the network level. The primary focus of network pharmacology is identifying and analyzing complex relationships between drugs, targets, and diseases in biological systems. This approach allows a complete understanding of how the treatment process works and its impact on biological networks, not just individual targets or pathways. Network pharmacology involves computational and systems biology tools to identify, analyze biological and pharmacological data on a large scale (Chandran U.et al. 2017). This approach has been used in the pharmaceutical industry to reduce costs and time in identifying potential lead molecules because initially drug development strategies require several testing steps and, in this process, out of a million selected molecules, only a quarter of drugs pass clinical trials. a stage that takes an average of 7 years or more followed by clinical validation so that only one or two potential candidates receive approval. This entire process is not only complicated but

also requires billions of dollars in investment and includes the costs of all drugs that do not receive FDA approval (Xue et al. in Parihar et al. 2022).

Given the daunting success rates or high failure rates, high costs, and slow pace of drug discovery, by using a drug repurposing approach, one can save time and costs associated with traditional drug development processes and bring successful drugs to market more quickly and providing patients with more effective treatment in less time (Deotarse et al., 2015). Recent advances in computational and bioinformatics-based systems biology processes are driving the drug development process. The systems biology approach mainly uses drug-related data information to reposition drugs and help us better understand the molecular basis of diseases and how drugs work. Because some diseases, including cancer and inflammatory diseases, are usually caused by a combination of many molecular abnormalities, which form a unique network of several related signaling pathways involved in disease complications, it has been shown to be much more complex than previously thought (Barabasi et al., 2011).

II. NETWORK PHARMACOLOGHY

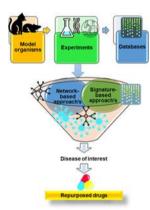


Figure 1. The process of making drugs using the network pharmacology method (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9300680/bin/f13-01-9780323911726.jpg)

Network pharmacology has emerged as a promising approach to accelerate drug development and elucidate the mechanisms of action of various target agents. He understands diseases as disorders of interconnected complex biological networks and determines the mechanism of action of drugs based on network topology with computational power (Waldman SA, et al. 2012). By utilizing information from various biological data sources, such as genetic data, proteomics, and biological pathways, network pharmacology can assist in drug discovery and development in a more efficient and effective way (Hopkins A. 2007).

Systems pharmacology when combined with wet laboratory examinations can have the ability to measure biological components, with the help of which computational approaches and results can be confirmed empirically (Zou et al., 2013.). Systems pharmacology is becoming a more popular technique for identifying new drug targets and therapeutic molecules to design effective therapies for patient care. Furthermore, drug target networks, side effects, predictions of drug target interactions or drug combinations, and drug repositioning can be carried out using a pharmacology-based systems approach (Pandita V, et al. 2022).

III. TRENDS IN MEDICINE

Tissue pharmacology is becoming a trend in medicine because of its ability to deliver drugs into the tissue in precise quantities. This allows treatment without undergoing surgery.

Recently, the therapeutic trend has been widely used in the treatment of therapeutic diseases because it is considered more effective and safe. The influence of network pharmacology in therapy can be explained as a new evolution in the field of pharmacology that allows understanding the effects of drugs not only on single molecular targets, but also on entire tissue systems and integrated biological processes. Systems pharmacology provides a high-level dimension to drug action that more precisely predicts concentration—response relationships, which in turn defines a framework for the field of pharmacometrics that is critical in improving drug development, regulation, and utilization (Waldman SA, et al. 2012). Here are some new trends in medicine:

Nanotechnology

Nanotechnology is the science that studies the manipulation and control of materials on the nanoscale (i.e. a very small scale, namely 1 to 100 nanometers). For applications, nanotechnology can be used to develop new products and technologies with unique sizes and properties, such as nanoparticles, nanosensors and nanorobots. One of the fields where nanotechnology is widely used is the medical field to develop effective and efficient drugs, diagnostic tools and therapies (Abid Haleem et al., 2023). Nanotechnology can be achieved by introducing nanoscale medicines that have enhanced positive attitudes for diagnosis, treatment, screening, sequencing, disease prevention and medical care. Nanotechnology has been applied to regenerative medicine, tissue engineering, and gene therapy, leading to advances in cell therapy, tissue regeneration, and organ repair (Malik S, at al. 2023)

The use of nanotechnology in drug delivery opens the door to the development of more efficient and targeted drug delivery systems. This allows the drug to reach its target tissue. Nanotechnology has many benefits in the medical field, including: Tissue regeneration: Nanotechnology can be used to develop materials that stimulate cell and tissue growth and support the healing process of damaged or lost tissue. Cancer treatment: Nanotechnology can be used to develop more effective cancer treatments, such as nanoparticles that can kill cancer cells. Treating infectious diseases: Nanotechnology can be used to develop better antimicrobial properties in treating infectious diseases, such as silver and gold nanoparticles that can kill bacteria and viruses. Health monitoring: Nanotechnology can be used to develop more accurate and non-invasive health monitoring devices, such as sensors that can be worn on the skin or monitoring devices that can be absorbed into the body (Abid Haleem et al., 2023).

Targeted Therapy

Network pharmacology is a targeted therapy approach that aims to treat diseases that affect specific cells or tissues, rather than entire organs or body systems. As previously explained, targeted therapy also uses nanotechnology to deliver drugs to the target. This targeted therapy is based on an understanding of the molecular and cellular mechanisms of disease, as well as the interactions between the drug and the molecular target. In targeted therapy, specially designed drugs are used to bind to specific molecular targets, such as proteins or enzymes, that are involved in disease development (Satpathy M, 2019). Targeted therapy is a treatment that targets specific molecules in body tissue. Targeted therapy has been used in the treatment of cancer, diabetes, and autoimmune diseases.

J Zhang, et al in their journal article Treatment of acral and mucosal melanoma: Current and emerging targeted therapies" Discusses the use of targeted therapy to treat melanoma tissue and ducts. It targets EGFR (epidermal growth factor receptor), MEK (mitogen-activated protein kinase), PI3K (phosphatidylinositol 3-kinase), mTOR (target of rapamycin). This therapy uses a vaccine attacked by combination therapy such as anti-BRAF, anti-PD-L1, and

anti-CTLA-4. Clinical trials include BRAF inhibitors (vemurafenib, dabrafenib), anti-PD-L1 (atexipar, atezolizumab, durvalumab), and anti-CTLA-4 (ipilimumab) in melanoma.

Some time ago Yan Hu, et al have conducted a promising study on the use of TIM-3 blockade as a potential therapy for diffuse intrinsic pontine glioma (DIPG). In their article TIM-3 blockade: immune and targeted therapy in DIPG they explain the role of TIM-3 in regulating the antitumor response. TIM-3 blockade has been shown to induce persistent antitumor immune memory and change the microtumor environment to an inflammatory state. Effect of TIM-3 blockade on tumor cells and the microtumor environment, TIM-3 blockade directly inhibits tumor formation and survival of DIPG tumor cells by inhibiting the mitogenactivated protein kinase (MAPK) and ERK1 pathways. Possibility of combination therapy and its impact on other immunotherapies In addition to immune check point inhibitor (ICI) therapy, other immunotherapeutic approaches such as adoptive cell transplant therapy, vaccines, and oncolytic virus therapy are important strategies for the treatment of DIPG. Clinical implications and hope for targeted therapy This study highlights the potential of DIPG tumor cells and immunotherapy and highlights its clinical relevance. Additionally, this research provides a promising new therapeutic approach for DIPG, which may play a key role in combating aggressive childhood brain tumors.

Cell Therapy

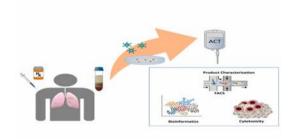


Figure 2. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10701366/bin/fx1.jpg)

Cell therapy is a treatment that uses living cells to treat disease. Cell therapy has been used in the treatment of cancer and autoimmune diseases. Much research has been carried out on cell therapy, one of which is Zhang X, et al. 2022 in his article CAR-T Cell Therapy in Hematological Malignancies: Current Opportunities and Challenges. The research explains the success of cell therapy in treating blood cancer. Basic principles and working mechanism of CAR-T Cell Therapy: CAR-T Cell Therapy is a therapy that uses genetically modified T cells to recognize and destroy cancer cells. T cells are modified by adding a special antigen receptor called CAR (Chimeric Antigen Receptor) which can recognize antigens on the surface of cancer cells. Once modified, these T cells are implanted back into the patient's body to fight cancer cells. Common targets in CAR-T Cell Therapy: Common targets in CAR-T Cell Therapy are antigens on the surface of cancer cells, such as CD19, CD20, and BCMA. These antigens were chosen because they are generally only found on cancer cells and not on normal cells, thus allowing T cells to be modified to recognize and destroy cancer cells without damaging normal cells. Success of CAR-T Cell therapy in treating relapsed or difficult-to-treat B-cell type blood cancers: CAR-T Cell therapy has shown remarkable success in treating relapsed or difficult-to-treat B-cell type blood cancers, such as acute lymphoblastic leukemia and non-steroidal lymphoma. -Hodgkin.

In another study, Charlotte O'G, et al in Pre-treatment with systemic agents for advanced NSCLC elicits changes in the phenotype of autologous T cell therapy products evaluated the phenotypic changes in T cell therapy products in response to pretreatment and subsequent behavior in the presence of certain cell lines. This study included the use of various assays and analytical techniques to assess the effects of pretreatment on T cell therapy products, especially in relation to the frequency of clusters associated with cytotoxic responses and sinterferon-gamma (IFNg) responses. These findings provide insight into the potential impact of pre-therapy on the effectiveness of T-cell therapy in the context of progressive NSCLC.

Gene Therapy

Gene therapy is a treatment that uses genes to treat disease. This therapy has been used in the treatment of cancer and genetic diseases. Gene therapy allows more effective treatment and reduces unwanted side effects. In terms of gene therapy, drug therapy is used in combination with gene delivery techniques to enhance delivery and expression. gene therapy, improving patient outcomes and managing potential side effects. Mendell JR et al, 2021. In his article "Current Clinical Applications of In Vivo Gene Therapy with AAVs. Mol Ther. 2021" revealed the potential of gene therapy using adeno-associated virus (AAV) for the treatment of a variety of hereditary diseases, including neuromuscular disorders, eye disorders, bleeding disorders, and lysosomal storage disorders. Gene therapy using AAV is considered a promising approach due to its safety profile and efficiency in gene transfer. Mendell JR et al, 2021 also highlighted the success of gene therapy in treating spinal muscular atrophy, a devastating neurodegenerative disease, with promising results in improving motor function and quality of life. life.

However, the use of AVV has serious impacts. Alessia A, et al in their research Gene therapy vector-related myocarditis explains the serious effects associated with gene therapy using aav (adeno-related virus) vectors, especially related to the incidence of myocarditis. Several studies and clinical trials related to gene therapy for various diseases, such as Pompe disease and Duchenne disease, have shown myocarditis as a serious effect. This myocarditis occurs after administration of gene therapy with AAV vectors, and some patients may even experience death due to this condition. Efforts to reduce the immunogenicity of vectors and their transgenic products are also discussed to improve the safety and efficacy of future gene therapies. Several efforts have been made to reduce the immunogenicity of the AAV vector, including; Existing immune monitoring: Gene therapy candidates are screened for preneutralizing antibodies (Nab) against AAV, and high neutralizing antibody titers are expected to be an exclusion criterion for clinical trials; NAB saturation strategies: Efforts have focused on methods such as empty capsid and NAB saturation, low prevalence of Nab and AAV serotype selection, novel and engineered AAV structures, and chemical modification of capsids; Use of specific promoters: Use of specific promoters to reduce the expression of transgenic genes that can trigger an immune response; Use of immunosuppressants: Some studies have also attempted to use immunosuppressive regimens to reduce the immune response to vectoraav.

Use of Latest Technology in Network Imaging

The impact of internet technology on the medical field is enormous. Computer network technology has encouraged the development of health information systems, telemedicine and fast access to medical information. With the help of network technology, access and sharing of medical information between various medical institutions becomes easy, improving collaboration between medical professionals and speeding up the process of diagnosis and

treatment of patients. Additionally, network technology supports the development of mobile health applications, electronic medical record management systems, and telemedicine platforms that enable remote medical information. This allows patients to receive better health services, especially in hard-to-reach areas. Therefore, the impact of Internet technology in the medical field is very positive, increasing access to health services, increasing collaboration between health workers, and improving the patient care process (Dan Shan, 2023).

Sandeep Wadekar, Dileep Kumar Singh, in their article A modified convolutional neural network framework for categorizing lung cell histopathological images based on residual networks, 2023, explains the use of the latest technology in tissue imaging, especially in the context of lung cancer detection from histopathological images. Some of the latest technologies used in tissue imaging to detect lung cancer include: Deep Learning: This technology allows the use of deep neural networks such as Convolutional Neural Networks (CNN) to analyze histopathological images with high accuracy; Visual Geometry Group (VGG19): Introduced an improved artificial neural network model using VGG19 pre-trained networks for automatic detection of lung cancer from histopathology imaging datasets; Data Augmentation: Data augmentation techniques are used to increase the number of data samples by organizing, patching, and transforming different forms; Advanced image processing: The use of advanced image processing technologies, such as image segmentation, is also an important part of modern tissue imaging technology for detecting lung cancer.

IV. CONCLUSION

This literature review provides an overview of tissue therapy as a new and innovative therapeutic approach. The success of tissue pharmacology-based treatments lies in a deep understanding of the complex interactions between drugs and body tissues. By using this approach, we hope to create a specific and effective treatment with minimal side effects. With the development of technology and advanced research, tissue pharmacology is expected to change the face of the medical world. This approach opens the door to self-medication and advanced treatment in the face of complex disease challenges. Therefore, the role of pharmacology is not only part of the future of medicine but also a key pillar for optimizing medical outcomes. In summary, we can conclude that tissue medicine is a new hope for addressing global health challenges. By continuing to encourage research and development in this area, we can begin a new chapter in the development of new treatments.

V. REFERENCES

- Chandran U, Mehendale N, Patil S, Chaguturu R, Patwardhan B. Network Pharmacology. Innovative Approaches in Drug Discovery. 2017:127–64. doi: 10.1016/B978-0-12-801814-9.00005-2. Epub 2016 Oct 14. PMCID: PMC7148629.
- Hopkins, A. Network pharmacology: the next paradigm in drug discovery. Nat Chem Biol 4, 682–690 (2008). https://doi.org/10.1038/nchembio.118
- Hopkins, A. Network pharmacology. Nat Biotechnol 25, 1110–1111 (2007). https://doi.org/10.1038/nbt1007-1110
- Pandita V, Parihar A, Parihar DS, Panda S, Shanmugarajan D, Kumari L, Badwaik HR. System and network biology-based computational approaches for drug repositioning. Computational Approaches for Novel Therapeutic and Diagnostic Designing to Mitigate SARS-CoV-2 Infection. 2022;267–90. doi: 10.1016/B978-0-323-91172-6.00003-0. Epub 2022 Jul 15. PMCID: PMC9300680.

- Waldman SA, Terzic A. Advancing pharmacometrics and systems pharmacology. Clin Pharmacol Ther. 2012 Nov;92(5):535-7. doi: 10.1038/clpt.2012.151. PMID: 23085873; PMCID: PMC5540435.
- Bateman DN, McInnes GT, Webb DJ. Clinical pharmacology and therapeutics in a changing world. Br J Clin Pharmacol. 1999 Jul;48(1):1-3. doi: 10.1046/j.1365-2125.1999.00988.x. PMID: 10383551; PMCID: PMC2014879.
- Marius M. Hoeper, Pharmacological therapy for patients with chronic thromboembolic pulmonary hypertension. European Respiratory Society0905-9180,1600-0617, Received February 6, 2015 Accepted March 19, 2015, Published online May 31, 2015. https://doi.org/10.1183/16000617.00001015
- Mendell JR, Al-Zaidy SA, Rodino-Klapac LR, Goodspeed K, Gray SJ, Kay CN, Boye SL, Boye SE, George LA, Salabarria S, Corti M, Byrne BJ, Tremblay JP. Current Clinical Applications of In Vivo Gene Therapy with AAVs. Mol Ther. 2021 Feb 3;29(2):464-488. doi: 10.1016/j.ymthe.2020.12.007. Epub 2020 Dec 10. PMID: 33309881; PMCID: PMC7854298.
- Joules A, Connors J, Johnson R, Van Orsow EA, McKenna DH, Nikiforow S, Ritz J, Gee A, Hubel A. Comparative analysis of cell therapy infusion workflows at clinical sites. Cytotherapy. 2021 Apr;23(4):285-292. doi: 10.1016/j.jcyt.2020.12.008. Epub 2021 Jan 30. PMID: 33531267; PMCID: PMC9013238.
- Furukawa Y, Hamano Y, Shirane S, Kinoshita S, Azusawa Y, Ando J, Nakauchi H, Ando M. Advances in Allogeneic Cancer Cell Therapy and Future Perspectives on "Off-the-Shelf" T Cell Therapy Using iPSC Technology and Gene Editing. Cells. 2022 Jan 13;11(2):269. doi: 10.3390/cells11020269. PMID: 35053386; PMCID: PMC8773622.
- Zhang X, Zhu L, Zhang H, Chen S, Xiao Y. CAR-T Cell Therapy in Hematological Malignancies: Current Opportunities and Challenges. Front Immunol. 2022 Jun 10;13:927153. doi: 10.3389/fimmu.2022.927153. PMID: 35757715; PMCID: PMC9226391.
- Satpathy M, Wang L, Zielinski RJ, Qian W, Wang YA, Mohs AM, Kairdolf BA, Ji X, Capala J, Lipowska M, Nie S, Mao H, Yang L. Targeted Drug Delivery and Image-Guided Therapy of Heterogeneous Ovarian Cancer Using HER2-Targeted Theranostic Nanoparticles. Theranostics. 2019 Jan 24;9(3):778-795. doi: 10.7150/thno.29964. PMID: 30809308; PMCID: PMC6376473.
- Jiaran Zhang, Huichun Tian, Lili Mao, Lu Si, Treatment of acral and mucosal melanoma: Current and emerging targeted therapies, Critical Reviews in Oncology/Hematology, Volume 193, 2024,104221, ISSN 1040-8428, https://doi.org/10.1016/j.critrevonc.2023.104221. (https://www.sciencedirect.com/science/article/pii/S1040842823003098)
- Sandeep Wadekar, Dileep Kumar Singh, A modified convolutional neural network framework for categorizing lung cell histopathological image based on residual network, Healthcare Analytics, Volume 4, 2023, 100224, ISSN 2772-4425, https://doi.org/10.1016/j.health.2023.100224. (https://www.sciencedirect.com/science/article/pii/S2772442523000916)
- Abid Haleem, Mohd Javaid, Ravi Pratap Singh, Shanay Rab, Rajiv Suman, Applications of nanotechnology in medical field: a brief review, Global Health Journal, Volume 7, Issue 2, 2023, Pages 70-77, ISSN 2414-6447, https://doi.org/10.1016/j.glohj.2023.02.008. (https://www.sciencedirect.com/science/article/pii/S2414644723000337)

- Malik S, Muhammad K, Waheed Y. Nanotechnology: A Revolution in Modern Industry. Molecules. 2023 Jan 9;28(2):661. doi: 10.3390/molecules28020661. PMID: 36677717; PMCID: PMC9865684.
- Yan Hu, Peishan Hu, Xiaozhong Peng, TIM-3 blockade: immune and targeted therapy in DIPG, Trends in Molecular Medicine, 2023, ISSN 1471-4914, https://doi.org/10.1016/j.molmed.2023.11.014. (https://www.sciencedirect.com/science/article/pii/S1471491423002769)
- Elizabeth Silver, Alessia Argiro, Kimberly Hong, Eric Adler, Gene therapy vector-related myocarditis, International Journal of Cardiology, 2023, 131617,ISSN 0167-5273, https://doi.org/10.1016/j.ijcard.2023.131617.
 - (https://www.sciencedirect.com/science/article/pii/S0167527323017072)
- Charlotte O'Brien Gore, Amy Billman, Suchete Hunjan, Jayne Colebrook, Desmond Choy, Wilson Li, Jack Haynes, Jennifer Wade, Emily Hobern, Louisa McDonald, Sophie Papa, Martijn Brugman, Shahram Kordasti, Claudia Montiel-Equihua, Pre-treatment with systemic agents for advanced NSCLC elicits changes in the phenotype of autologous T cell therapy products, Molecular Therapy Oncolytics, Volume 31, 2023, 100749, ISSN 2372-7705, https://doi.org/10.1016/j.omto.2023.100749. (https://www.sciencedirect.com/science/article/pii/S2372770523000980)
- Li, L., Yang, L., Yang, L. dkk. Farmakologi jaringan: cahaya penuntun yang terang dalam cara mengeksplorasi pengobatan tepat yang dipersonalisasi dari pengobatan tradisional Tiongkok. Dagu Med 18, 146 (2023). https://doi.org/10.1186/s13020-023-00853-2
- Xue H., Li J., Xie H., Wang Y. Review of drug repositioning approaches and resources. International Journal of Biological Sciences. 2018;14(10):1232–1244. doi: 10.7150/ijbs.24612.
- Barabási A.L., Gulbahce N., Loscalzo J. Network medicine: A network-based approach to human disease. Nature Reviews Genetics. 2011;12(1):56–68. doi: 10.1038/nrg2918.