

Investigation into the Mechanism of Banxia in Treating Stroke Based on Network Pharmacology

Xin Chen^{1*}, Paikun Cheng²

¹ Department of Rehabilitation Medicine, Affiliated Hospital of North Sichuan Medical College, Nanchong, China

² Ziyang Environmental Science and Technology Vocational College, Ziyang, China

Email Address

488874309@qq.com (Xin Chen), 2367429702@qq.com (Paikun Cheng)

*Correspondence: 488874309@qq.com

Received: 8 July 2025; **Accepted:** 15 August 2025; **Published:** 10 September 2025

Abstract:

The purpose of this study is to explore the mechanism of *Banxia* in treating stroke based on network pharmacology. The primary bioactive compounds in *Banxia* and their associated target genes were sourced from the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP), with gene nomenclature standardized using the UniProt database. To identify stroke-related genes, a comprehensive search was conducted across four key databases: OMIM, GeneCards, DrugBank, and TTD. Through the online analysis tool of Venn diagram, the intersection between the target gene of drug active ingredient and the gene of stroke disease was analyzed to determine the potential target of *Banxia* in treating stroke. To identify the core regulatory targets, we first mapped the protein-protein interaction (PPI) network of candidate molecules using the STRING database. The network's topological features were then evaluated through Cytoscape's CytoNCA plugin, enabling us to pinpoint the most biologically significant nodes within this complex web of molecular interactions. To analyze the potential targets, we conducted GO function and KEGG pathway enrichment studies using DAVID, a bioinformatics annotation database. The results were then visualized through R programming for clearer interpretation. The results showed that 50 potential therapeutic targets were obtained after the drug target of *Banxia* crossed with the target of stroke, corresponding to 11 active components. The core targets are ESR1, PTGS2, PPARG, CASP3, BCL2, etc. GO analysis shows that the molecular functions of *Banxia* in treating stroke are mainly to activate adrenergic receptor activity, catecholamine binding, general transcription initiation factor binding and so on. KEGG pathway enrichment analysis showed that *Banxia* therapeutic effect on stroke involved IL-17 signal pathway, TNF signal pathway, HIF-1 signal pathway and so on. The study's findings indicate that *Banxia* exhibits a multifaceted therapeutic effect on stroke, operating through diverse pathways, active compounds, and biological targets. This investigation provides a solid groundwork for future research into *Banxia*'s medicinal properties.

Keywords:

Network Pharmacology, Stroke, Mechanism, *Banxia*

1. Introduction

Stroke is considered to be the main cause of death and disability in the world. According to the World Stroke Organization, the number of stroke cases increased significantly from 1990 to 2019. By 2019, the number of stroke patients had reached 125 million, causing about 5.5 million deaths every year. Most cases are concentrated in developing countries such as Asia, Latin America and Eastern Europe. Stroke has become the second leading cause of death after ischemic heart disease [1]. Ischemic stroke is the most common type. Studies have found that hypertension is the main cause of stroke, and smoking, drinking and bad eating habits will increase the risk of stroke [2]. The treatment and rehabilitation costs of stroke patients are high. According to the statistics of the World Health Organization, the national income loss caused by premature death caused by stroke in China from 2005 to 2015 reached hundreds of billions of dollars [3]. Traditional Chinese medicine is widely used in stroke treatment, with over 140 applicable herbal formulations [4].

Banxia is the dried tuber, a plant of Araceae. It is pungent in taste, warm in nature and toxic, and belongs to the lung, spleen and stomach meridians. It has the effects of eliminating dampness, resolving phlegm, lowering adverse qi, stopping vomiting, eliminating swelling and resolving hard mass. Modern pharmacological research shows that Banxia has antitussive, expectorant and antiemetic effects, anti-tumor, anti-gastric ulcer, blood coagulation, antibacterial and anti-inflammatory effects. At present, there is little research on the mechanism of Banxia in treating stroke. This study intends to explore the mechanism of Banxia in treating stroke through the method of network pharmacology, to provide new ideas for clinical application and research in the future.

2. Materials and Methods

2.1. Prediction of Banxia targets

Search Banxia in TCMSP database [5], set bioavailability (OB) $\geq 30\%$ and drug-like property (DL) ≥ 0.18 to obtain active components of Banxia, select “re-labeled targets” to obtain all targets of active ingredients of Banxia. And the human target genes corresponding to the active components of Banxia were obtained through uniprot database [6].

2.2. Identification of Genes Associated with Stroke Conditions

To identify genes associated with stroke, we conducted a comprehensive search across multiple established databases, including GeneCards [7], OMIM [8], the Therapeutic Target Database [9] and DrugBank [10]. After compiling the initial results, we removed redundant entries to eliminate duplicate genes from our dataset.

2.3. Screening of targets related to Banxia in the treatment of stroke

The obtained Banxia drug targets and stroke-related targets were uploaded to the Venny 2.1.0 platform, and the intersection of the two was taken to initially obtain the target of Banxia in the treatment of stroke.

2.4. Constructing protein interaction maps and pinpointing critical nodes

Import the above-mentioned potential anti-stroke targets of Banxia into the “STRING” database [11]. Import the downloaded files into Cytoscape 3.8.0 software

for visual analysis, build a target protein interaction (PPI) network for Banxia treatment of stroke, and further use the CytoNCA plug-in to conduct network topology analysis to screen key targets in the network.

2.5. GO analysis and KEGG pathway analysis

Input the target of *Banxia* into “DAVID” database [12] for GO and KEGG pathway enrichment analysis, set species as “Homo sapiens”, perform GO function and KEGG signaling pathway enrichment analysis, set $P < 0.05$ as statistically significant difference, output results and draw bubble chart or bar chart.

3. Results

3.1. Prediction of Banxia gene target

The study identified 11 bioactive compounds linked to 173 potential targets. After filtering out non-active components, 50 key targets associated with Banxia were isolated. A network visualization was created (Figure 1) depicting these relationships, with bioactive compounds shown in the outer ring and their corresponding targets in the inner ring. The connections were weighted by interaction strength, revealing four primary active constituents based on their degree centrality: cavidine (MOL002670), β -sitosterol (MOL000358), baicalein (MOL002714), and stigmasterol (MOL000449). These compounds emerged as the core bioactive elements through network analysis.

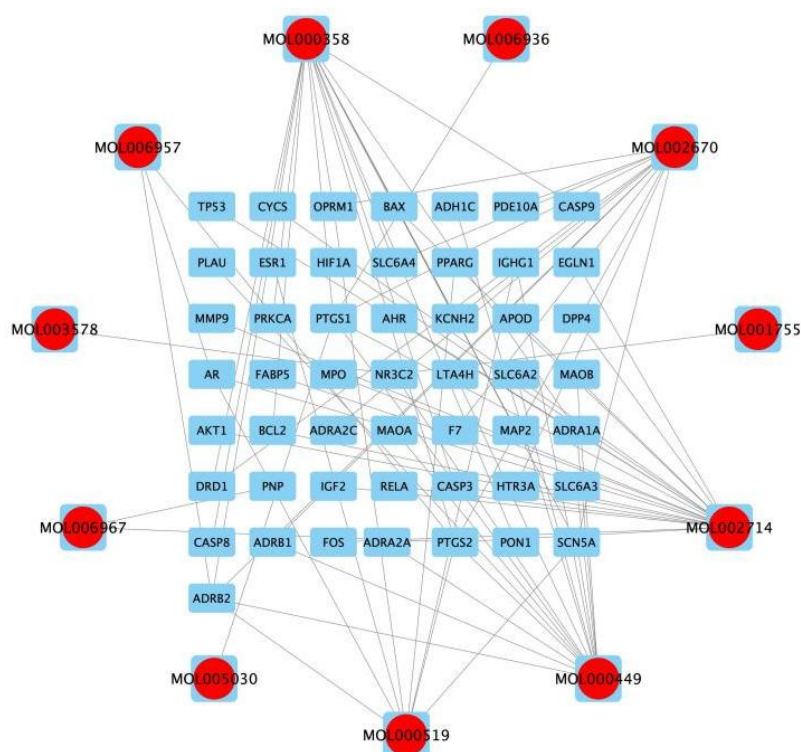


Figure 1. Network Diagram of Genes Influenced by Active Components.

3.2. Identification of gene targets associated with stroke

Utilizing “stroke” as our primary search term, we meticulously combed through each database to narrow down our search: 2845 pertinent entries emerged in GeneCards, a mere 24 were found in OMIM, 35 were identified in TTD, and 207 candidates popped up in DrugBank. After all the targets screened from the above

Figure 1 consists of two Venn diagrams, A and B, illustrating the overlap of drug and disease genes across four databases: DrugBank, OMIM, GeneCards, and TTD.

Panel A: Overlap of all four databases (DrugBank, OMIM, GeneCards, TTD).

Region	Count
DrugBank only	64
OMIM only	0
GeneCards only	0
TTD only	6
DrugBank & OMIM	2757
DrugBank & GeneCards	3
DrugBank & TTD	0
OMIM & GeneCards	1
OMIM & TTD	0
GeneCards & TTD	0
DrugBank & OMIM & GeneCards	56
DrugBank & OMIM & TTD	0
DrugBank & GeneCards & TTD	0
OMIM & GeneCards & TTD	1
DrugBank & OMIM & GeneCards & TTD	27

Panel B: Overlap of DrugBank, OMIM, and GeneCards only.

Region	Count
DrugBank only	31
OMIM only	0
GeneCards only	2865
DrugBank & OMIM	50
DrugBank & GeneCards	0
OMIM & GeneCards	0
DrugBank & OMIM & GeneCards	0

3.3. Compilation of banxia-associated stroke treatment targets

3.4. PPI network construction and core target analysis

www.itspoa.com/journal/hr

Utilizing the CytoNCA plug-in, a thorough topological examination was performed on the protein interaction network. We successfully identified five key hub targets that exceeded the following thresholds: BC values above 2.74, CC values above 0.88, DD values above 12, EC values above 0.27, LAC values above 9.23, and NC values above 11. The primary targets were systematically identified, with preliminary analysis revealing the five most critical contributors to Banxia's efficacy in stroke treatment: ESR1, PTGS2, PPARG, CASP3, and BCL2. These key targets are illustrated in Figure 4.

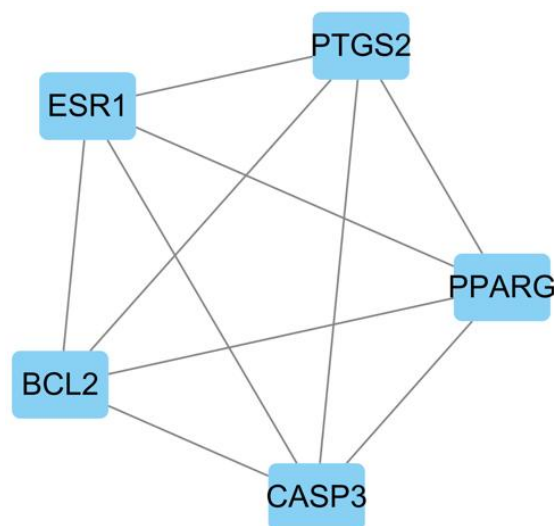


Figure 4. The PPI network construction.

3.5. PPI network construction and critical target evaluation

The 50 potent anti-stroke compounds from Banxia were added to the DAVID online database for GO and KEGG pathway enrichment studies, using a significance threshold of $P < 0.05$. The GO analysis yielded a comprehensive list of 1513 entries. For a closer look, we've pinpointed the top 10 entries under the Biological Process (BP), Cellular Component (CC), and Molecular Function (MF) categories, as illustrated in Figure 5.

Among them, 1537 biological processes were obtained, mainly involving response to decreased oxygen levels, response to oxygen levels, response to xenobiotic stimulus, response to hypoxia, etc. There are 29 cellular components, mainly involving organelle outer membrane, outer membrane, caveola, membrane raft, etc. There are 127 molecular functions, mainly involving adrenergic receptor activity, catecholamine binding, general transcription initiation factor binding, G protein-coupled amine receptor activity, etc. The KEGG pathway enrichment analysis revealed involvement in 185 distinct pathways. For this investigation, the top 30 signaling pathways were chosen and visualized using bubble plots. Notably, the IL-17 signaling pathway contained 15 hub genes, while the TNF and HIF-1 signaling pathways were associated with 14 and 12 hub genes, respectively, as illustrated in Figure 6.

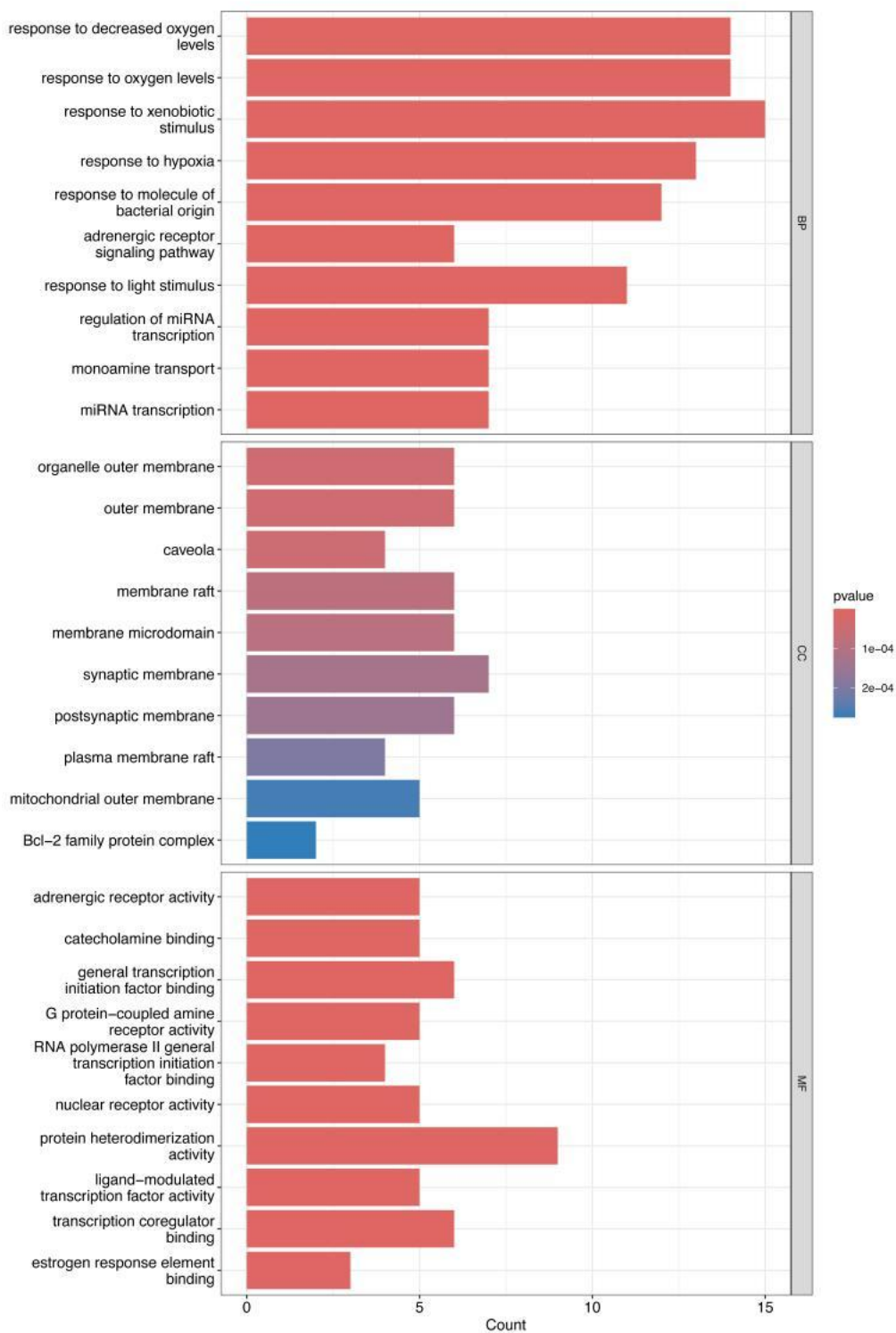


Figure 5. GO Study on Therapeutic aims of banxia for stroke management.

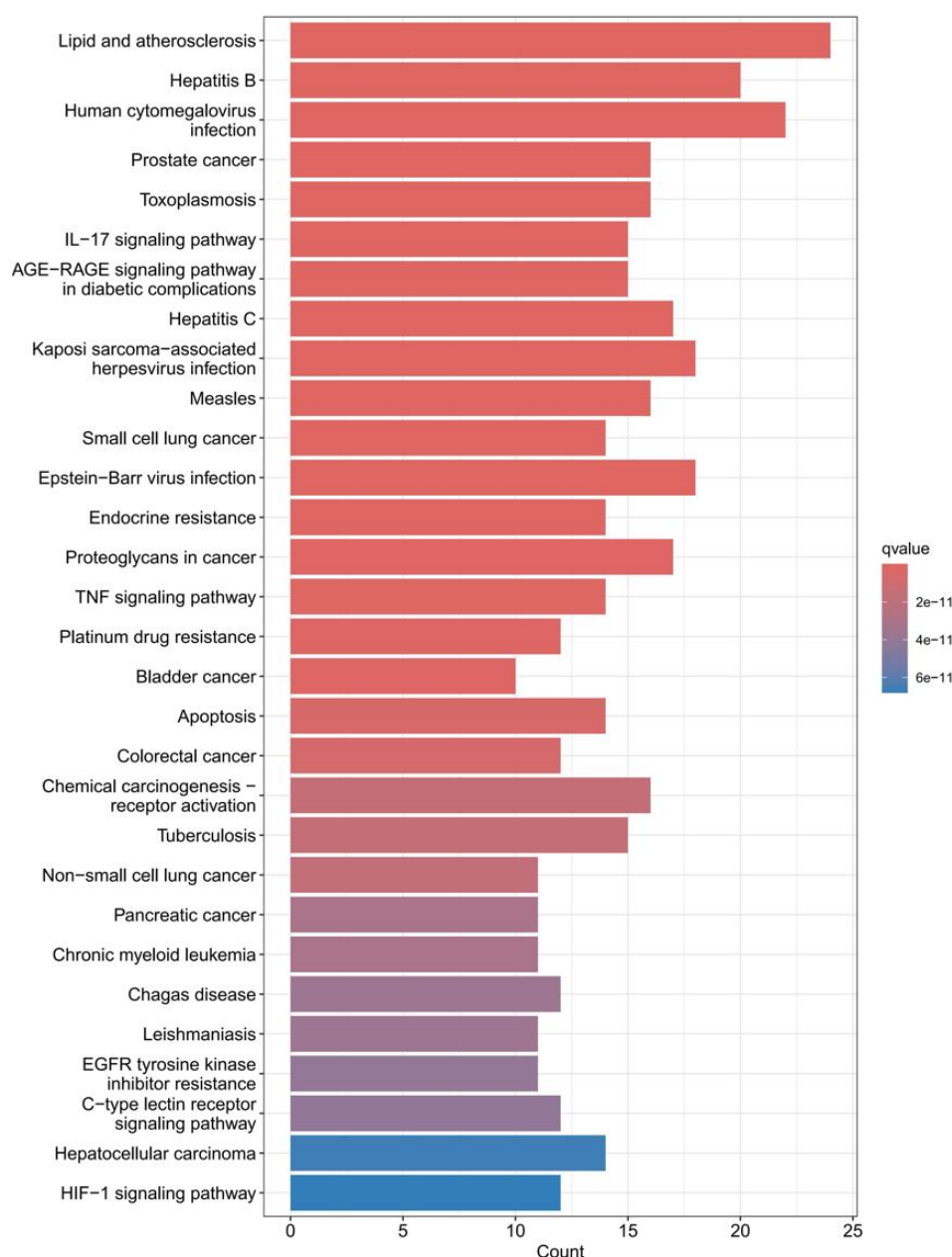


Figure 6. KEGG pathway enrichment study on banxia's therapeutic targets for stroke management (highlighting the top 30 signaling pathways).

4. Discussions

Stroke is a central nervous system disease common in middle-aged and elderly people. It mainly expresses as signs of hemorrhagic or ischemic brain damage, which carries a risk of disability and death [13]. Numerous traditional Chinese medicines show therapeutic potential, yet their molecular mechanisms in stroke treatment remain underexplored [14].

The research findings indicate that, based on shared target analysis, compounds like cavidine and β -sitosterol demonstrate extensive target interactions, positioning them as *Banxia*'s primary bioactive components with therapeutic potential for stroke treatment. Statistical evidence underscores their pharmacological significance in this context. Studies have shown that cavidine protects mice from lipopolysaccharide

induced septic shock by inhibiting the expression of pro-inflammatory cytokines [15]. The anti-inflammatory activity of cavidine may be reflected in reducing the production of pro-inflammatory cytokines such as TNF- α and IL-6 by blocking the activation of the NF- κ B pathway [16]. It is speculated that cavidine can treat stroke through anti-inflammatory effects. β -sitosterol binds best to TP53 targets [17]. β -sitosterol reduces inflammation via the hypothalamic, pituitary, adrenal axis and exhibits antioxidant properties by moderately scavenging reactive oxygen radicals [18].

Key targets identified through PPI network topology examination encompass ESR1, PTGS2, and BCL2, among others. ESR1 is estrogen receptor α . Estrogen has been proved to increase cerebral blood flow, have anti-inflammatory effects, enhance the activity of synapses of neurons, and play a direct neuroprotective and neurotrophic role in brain tissue. PTGS2 is a peroxidase-like enzyme that can catalyze arachidonic acid to be converted into prostaglandin, and it is an important inflammatory mediator, which participates in the whole process from the initial stage of inflammation to the formation of inflammation. Overexpression of PTGS2 can destroy the internal environment balance, participate in the inflammatory reaction after brain injury, and promote the expansion of cerebral infarction area [19]. BCL2 is an anti-apoptosis protein, which mainly inhibits cell apoptosis caused by various reasons. It is found that BCL2 can inhibit the activation of inflammatory corpuscles in NLRP1, thus reducing the apoptosis and inflammation of nerve cells [20].

5. Conclusions

In conclusion, this research employed network pharmacology to investigate *Banxia*'s molecular mechanisms in stroke treatment, identifying critical targets—ESR1, PTGS2, BCL2, and CASP3—as pivotal players in the therapeutic process. These targets interact synergistically across multiple molecular pathways, collectively contributing to stroke intervention via the IL-17, TNF, and HIF-1 signaling cascades. The findings underscore a complex, interconnected network through which *Banxia* exerts its pharmacological effects.

Conflicts of Interest

The author declares that there is no conflict of interest regarding the publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

References

- [1] Feigin, V.L., et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke*, 2022, 17(1), 18-29.
- [2] Kuriakose, D.; Z. Xiao. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. *Int J Mol Sci*, 2020, 21(20).
- [3] Katan, M.; A. Luft, Global Burden of Stroke. *Semin Neurol*, 2018, 38(2), 208-211.

- [4] Kim, J. et al. Neuroprotective effects of human neural stem cells over-expressing choline acetyltransferase in a middle cerebral artery occlusion model. *J Chem Neuroanat*, 2020, 103, 101730.
- [5] Ru, J. et al. TCMSP: a database of systems pharmacology for drug discovery from herbal medicines. *J Cheminform*, 2014. 6, 13.
- [6] UniProt: the universal protein knowledgebase in 2021. *Nucleic Acids Res*, 2021, 49(D1), D480-d489.
- [7] Stelzer, G. et al. The GeneCards Suite: From Gene Data Mining to Disease Genome Sequence Analyses. *Curr Protoc Bioinformatics*, 2016, 54, 1.30.1-1.30.33.
- [8] Amberger, J.S.; A. Hamosh. Searching Online Mendelian Inheritance in Man (OMIM): A Knowledgebase of Human Genes and Genetic Phenotypes. *Curr Protoc Bioinformatics*, 2017, 58, 1.2.1-1.2.12.
- [9] Zhou, Y. et al. TTD: Therapeutic Target Database describing target druggability information. *Nucleic Acids Res*, 2024, 52(D1), D1465-d1477.
- [10] Wishart, D.S. et al. DrugBank: a comprehensive resource for in silico drug discovery and exploration. *Nucleic Acids Res*, 2006, 34(Database issue), D668-72.
- [11] Szklarczyk, D. et al. STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Res*, 2019, 47(D1), D607-d613.
- [12] Sherman, B.T. et al. DAVID: a web server for functional enrichment analysis and functional annotation of gene lists (2021 update). *Nucleic Acids Res*, 2022. 50(W1), W216-w221.
- [13] Diener, H.C.; G.J. Hankey. Primary and Secondary Prevention of Ischemic Stroke and Cerebral Hemorrhage: JACC Focus Seminar. *J Am Coll Cardiol*, 2020, 75(15), 1804-1818.
- [14] Xu, Q. et al. Research progress in the use of botulinum toxin type a for post-stroke spasticity rehabilitation: a narrative review. *Ann Med*, 2025. 57(1), 2521427.
- [15] Li, W. et al. Effects and mechanisms of cavidine protecting mice against LPS-induced endotoxic shock. *Toxicol Appl Pharmacol*, 2016, 305, 46-54.
- [16] Niu, X., et al. Cavidine Ameliorates Lipopolysaccharide-Induced Acute Lung Injury via NF- κ B Signaling Pathway in vivo and in vitro. *Inflammation*, 2017, 40(4), 1111-1122.
- [17] Yuan, Y. et al. Elucidation of the mechanism of Yiqi Tongluo Granule against cerebral ischemia/reperfusion injury based on a combined strategy of network pharmacology, multi-omics and molecular biology. *Phytomedicine*, 2023, 118, 154934.
- [18] Kim, J. et al. Engineering Lipid Nanoparticles for Enhanced Intracellular Delivery of mRNA through Inhalation. *ACS Nano*, 2022, 16(9), 14792-14806.
- [19] Zhang, Z., et al. Genetic Variation of Inflammatory Genes to Ischemic Stroke Risk in a Chinese Han Population. *Pharmgenomics Pers Med*, 2021, 14, 977-986.

- [20]Sung, K.F. et al. Prosurvival Bcl-2 proteins stabilize pancreatic mitochondria and protect against necrosis in experimental pancreatitis. *Exp Cell Res*, 2009, 315(11), 1975-89.



© 2025 by the author(s); licensee International Technology and Science Publications (ITS), this work for open access publication is under the Creative Commons Attribution International License (CC BY 4.0). (<http://creativecommons.org/licenses/by/4.0/>)