*Original Article*

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# Visualization analysis of the use of traditional Chinese medicine in the diagnosis and treatment of rare diseases in mainland China based on CiteSpace

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**SUMMARY**: This study used CiteSpace (version 6.4.R1) to perform a visualization analysis of 3,058 articles on traditional Chinese medicine (TCM) diagnosis and treatment of rare diseases retrieved from the China National Knowledge Infrastructure (CNKI) database, the VIP Chinese Science and Technology Periodical Database (VIP), the Wanfang database (Wanfang), and the Chaoxing database (Chaoxing). The goal was to ascertain the current status of research, hotspots in research, and trends in the development of TCM for rare disease diagnosis and treatment in mainland China, providing insights for future TCM research in this field. Visual maps of annual publication volume, authors, institutions, keywords, and other content have revealed that TCM demonstrates prominent advantages in 5 out of 207 defined rare diseases: idiopathic pulmonary fibrosis, hepatolenticular degeneration (Wilson's disease), osteosarcoma, retinitis pigmentosa, and multiple sclerosis. Potential advantages are identified in treating melanoma, amyotrophic lateral sclerosis, homocysteinemia, primary biliary cholangitis, and lymphangioleiomyomatosis. TCM research on rare diseases focuses on etiology, pathogenesis, and syndrome differentiation-based treatment. Case-control studies and mechanism investigations have been initiated for some conditions, while clinical research is gradually incorporating integrated TCM-Western medicine approaches. However, enhanced team and institutional collaboration, development of multicenter networks, exploration of multidisciplinary research, and clinical studies yielding high-level evidence are still needed to provide quality evidence-based support for clinical decision-making in the TCM treatment of rare diseases.

***Keywords***: CiteSpace, China, rare diseases, traditional Chinese medicine

## 1. Introduction

The World Health Organization (WHO) defines rare diseases as those with a prevalence of 0.65 to 1% of the total population (*i.e.*, 6.5 to 10 individuals per 100,000 people) (*1*). In China, the First (*2*) and Second Lists (*3*) of Rare Diseases were issued in 2018 and 2023 by six government entities in China (*4*), including the National Health Commission, the Ministry of Science and Technology, the Ministry of Industry and Information Technology, the National Medical Products Administration, the National Administration of Traditional Chinese Medicine, and the Logistics Support Department of the Central Military Commission. These lists cover a total of 207 types of diseases (*5*). The updated 2024 list of member hospitals in the National Rare Disease Diagnosis and Treatment Collaboration Network includes 10 traditional Chinese medicine (TCM) or integrated Chinese and Western medicine units (*6*).

This study used the co-occurrence analysis function in the software CiteSpace to visualize authors, institutions, and keywords in TCM literature on rare disease diagnosis and treatment in order to explore the historical context and current status of research while predicting future trends in this field, identifying research hotspots and frontiers.

## 2. Materials and Methods

### 2.1. Retrieval strategy

Since information on TCM diagnosis and treatment of rare diseases is primarily located in TCM databases, the sources examined in this study were all found in Chinese databases, namely the China National Knowledge Infrastructure (CNKI) database, the VIP Chinese

Science and Technology Periodical Database (VIP), the Wanfang database (Wanfang), and the Chaoxing database (Chaoxing). Searches were conducted using the keywords "rare diseases" and "traditional Chinese medicine"; the search query used was "specific rare disease name" AND "traditional Chinese medicine". Based on the first and second national lists of rare diseases issued by the government, we searched for 207 names of rare diseases across all of the databases, ensuring comprehensive coverage. The search covered articles indexed in these databases from their inception until July 31, 2025. Information was collected from the literature, and a total of 5,243 sources were saved in RefWorks text format.

The literature review revealed that the earliest source was from 1958, so the year span for the graphs ranges from 1958 to 2025. This starting year aligns with the history of rare disease research in mainland China, and the TCM diagnosis and treatment of rare diseases has gradually emerged over the past 70 years. After rounds of screening to remove all duplicate entries, sources with incomplete information, and other types of literature, 3,058 papers were ultimately included.

### 2.2. Research methodology

The software CiteSpace (version 6.4.R1) was used in this study. Software parameters: *i*) Time slicing from January 1958 to July 2025, with a 1-year Time analysis slice; *ii*) Term source: Title, Abstract, Author Keywords (DE), Keywords Plus (ID); *iii*) Term type: "Noun phrase" was selected in maps of keywords, otherwise it was not selected; *iv*) Node types: Author, Institution, Keyword; and *v*) Selection criteria were set to g-index, k = 25.

Pruning was done using the Pathfinder and Pruning sliced networks. This resulted in the generation of the following networks: an author collaboration network map, an institution collaboration network map, a keyword co-occurrence network map, a cluster map, a timeline map, and a citation burst map. These networks provide insights into research hotspots, evolutionary trajectories, collaborative dynamics among entities, and the distribution of research capabilities within the field of TCM diagnosis and treatment for rare diseases.

## 3. Results

### 3.1. Annual publication volume

Publications in the field of TCM diagnosis and treatment for rare diseases have tended to increase since 1958. Publications surpassed single digits in 1987, exceeded 30 in 1994, reached over 60 in 2005, stabilized between 80 and 89 from 2008 to 2011, broke the 100-article mark in 2012 by 120, and continued climbing to 158, 141, and 165 articles respectively from 2017 to 2019. A slight decline occurred during the period of the 2020–2022 pandemic, but new highs were consecutively reached after 2023. As of July 2025, 118 articles have been published in 2025 (Figure 1).

### 3.2. Author analysis

In the co-occurrence network of authors, there was a total of 1,236 nodes (N), 1,284 links (E), and a network density (Density) of 0.0017 (Figure 2). Each node represents an author, with node size reflecting the co-occurrence frequency of his or her publications. Links between nodes indicate collaborative relationships among authors. The map reveals that the top authors by publication volume include Wenming Yang, Han Wang, Hui Han, Meixia Wang, Yongzhu Han, Yuanchen Bao, Jiyuan Hu, Juan Zhang, Renmin Yang, Hong Chen, and Wenbin Hu. Node color variations reflect temporal dimensions: orange-yellow nodes represent early authors, while deep red nodes denote recently active authors. The predominance of red nodes indicates that the author collaboration network for TCM treatment of rare diseases has grown annually.

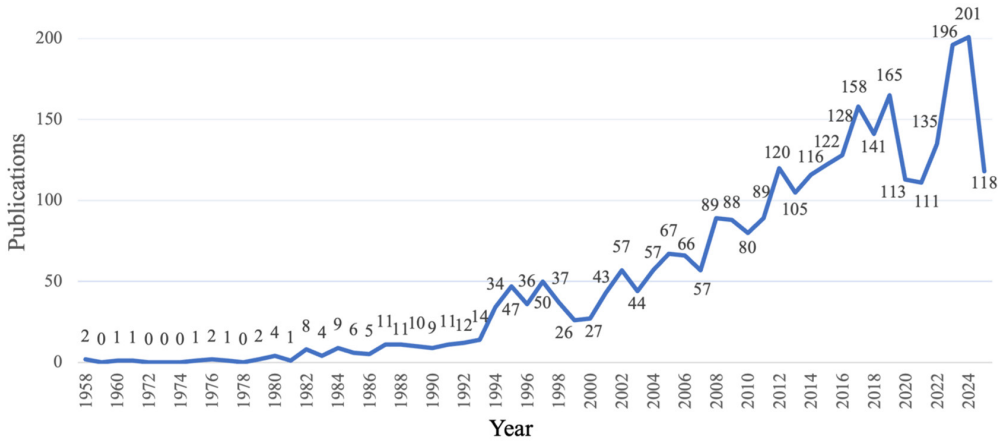


**Figure 1. Annual number of publications for rare disease-related studies.**

3.3. Institution analysis

The institutional network map reveals that research on TCM treatment of rare diseases is primarily concentrated in TCM universities and their affiliated hospitals. The network consists of 721 nodes, 337 links, and a density of 0.0013 (Figure 3). Each node in the diagram represents an institution, with node size proportional to the institution's co-occurrence frequency in the literature. Links indicate collaborative relationships between institutions. The top 3 institutions are Beijing University of Chinese Medicine, Tianjin University of Traditional Chinese Medicine, and Henan University of Chinese Medicine, with research focusing on rare diseases such as multiple sclerosis and idiopathic pulmonary fibrosis. There is close collaboration between universities and

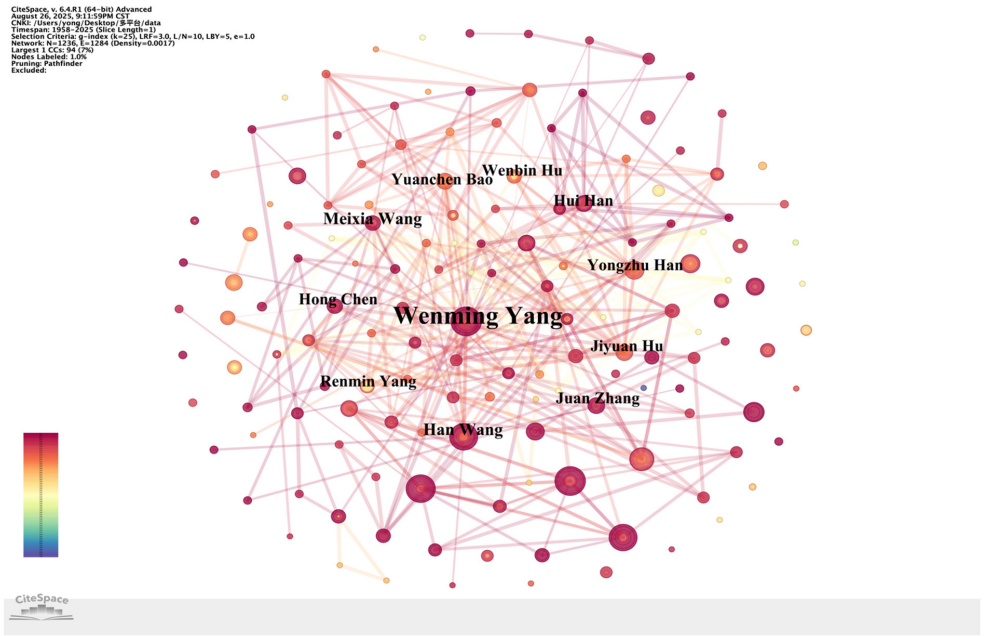


**Figure 2. A network knowledge map of authors in the field of traditional Chinese medicine diagnosis and treatment of rare diseases obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**


**Figure 3. A network knowledge map of institutions in the field of traditional Chinese medicine diagnosis and treatment of rare diseases obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**

their affiliated hospitals, but cooperation between institutions in different regions remains limited.

### 3.4. Keyword analysis

#### 3.4.1. Keyword co-occurrence analysis

Keywords concisely summarize article themes. This map reveals co-occurrence relationships among high-frequency keywords in the literature. There were 1,086 total nodes, 2,619 links, and a network density of 0.0044 (Figure 4). The size of each keyword node correlates positively with its frequency of occurrence. Colors ranging from yellow to purple reflect temporal distribution (yellow indicating earlier years, and purple indicating more recent years). Links between nodes represent the co-occurrence of keywords within the same source; more lines indicate stronger associations. The top five keywords are "TCM therapies", "idiopathic pulmonary fibrosis", "multiple sclerosis", "hepatolenticular degeneration", and "TCM syndrome patterns". The map also highlights names of diseases like "Behcet's disease" and "Retinitis Pigmentosa" and research orientations like "Review", "Treatment based on syndrome differentiation", "Famous doctor's experience", "TCM syndrome", "Etiology and pathogenesis", which to some extent represent the research hotspots in the field of TCM diagnosis and treatment of rare diseases.

#### 3.4.2. Keyword clustering analysis

Noun phrases were selected as the term type, and a keyword cluster map was generated. After displaying the co-occurrence map of keywords through co-word clustering, the log-likelihood ratio algorithm (LLR) was used to generate multiple significant clusters. Each cluster consists of nodes of similar color, with node size reflecting the keyword frequency in the literature. Cluster labels are automatically identified by the algorithm, representing the research themes of each keyword category. The network had an overall modularity (Q) of 0.6158 (Q > 0.3), indicating a significant clustering structure with relatively clear thematic distribution. The weighted mean silhouette (S) was 0.8354 (S > 0.7), demonstrating high internal consistency and reliability within the clusters (Figure 5).

The circular view function was used, and the map clearly displays 15 clusters, including #0 Idiopathic Pulmonary Fibrosis, #1 Hepatolenticular Degeneration, #2 Traditional Chinese Medicine therapy, #3 Multiple Sclerosis, #4 Medication regularity, #5 Syndrome differentiation and treatment, #6 Amyotrophic Lateral Sclerosis, #7 Primary Biliary Cholangitis, #8 Case record, # 9 Retinitis Pigmentosa, #10 Traditional Chinese Medicine intervention, #11 Famous doctor's experience, #12 Traditional Chinese Medicine constitution, #13 Polycythemia Vera, and #14 Gandou Decoction (Table 1). Disease-related clusters include #0 Idiopathic Pulmonary Fibrosis, #1 Hepatolenticular Degeneration, #3 Multiple Sclerosis, #6 Amyotrophic Lateral Sclerosis, #7 Primary Biliary Cholangitis, #9 Retinitis Pigmentosa, #13 Polycythemia Vera, and #14 Gandou Decoction. The corresponding rare diseases, sorted by average publication year in ascending order, are multiple sclerosis (2002), retinitis pigmentosa (2002), polycythemia vera (2007), amyotrophic lateral sclerosis (2010), primary

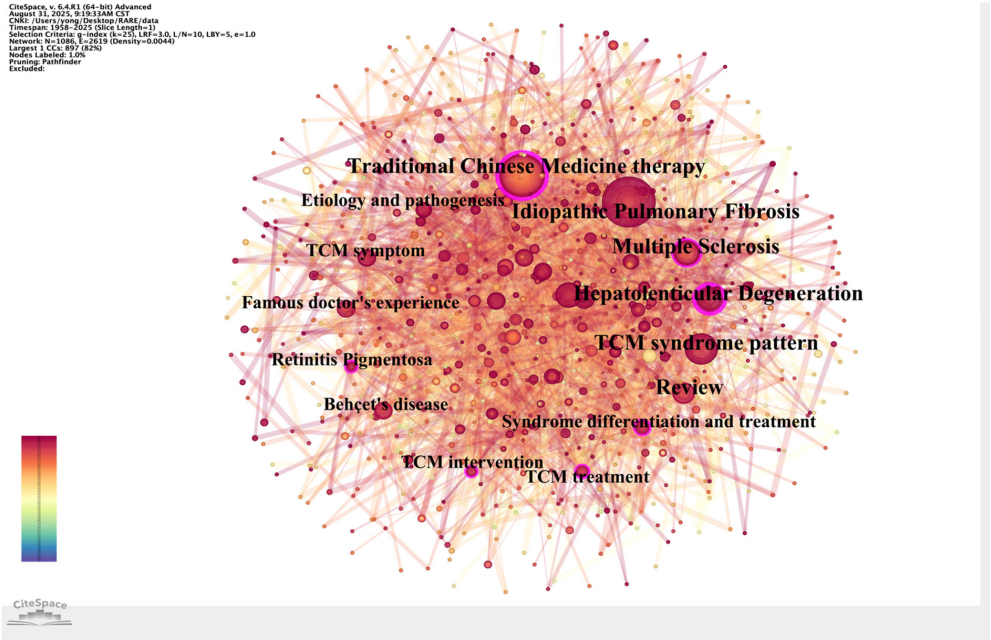


**Figure 4. A network knowledge map of keywords in the field of traditional Chinese medicine diagnosis and treatment of rare diseases obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**

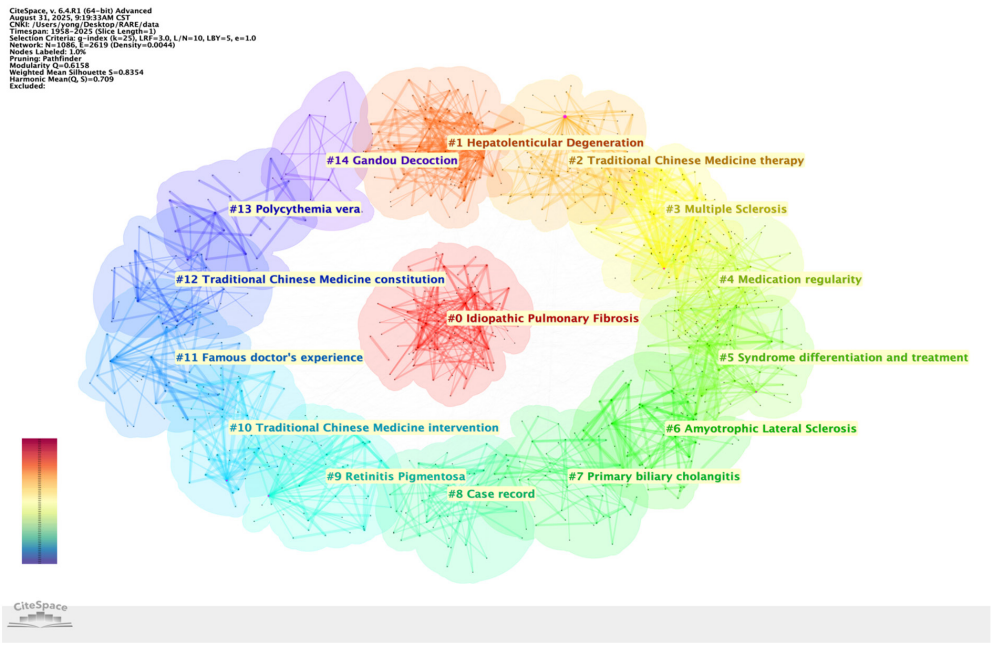


**Figure 5. A clustering map of rare disease keywords obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**

idiopathic pulmonary fibrosis (2012), hepatolenticular degeneration (2012), and primary biliary cholangitis (2017).

3.4.3. Keyword timeline analysis

The keyword timeline map uses clustering as the horizontal hierarchy, with node size representing keyword frequency, color gradient indicating time, and arcs depicting cross-year co-occurrence relationships.

#0 Idiopathic Pulmonary Fibrosis emerged around 1995 and remains prevalent to the present. Related nodes include "experimental research, lung bi (肺痹, fei bi), pulmonary atrophy (肺痿, fei wei), pathogenesis", indicating a high level of interest in rare pulmonary disease topics that was sustained. Key nodes for #1 Hepatolenticular Degeneration emerged after 1985, with "TCM syndrome patterns" appearing after 2000; the last two decades saw the emergence of "hyperhomocysteinemia, homocysteine, H-type hypertension". #2 Traditional Chinese Medicine therapy emerged around 1990, and was associated with keywords like "recurrence, nursing, proven case, bullous pemphigoid, academic research". #3 Multiple Sclerosis appeared before 1985, and was linked to keywords such as "TCM treatment, TCM clinical experience, preventive medicine (治未病, zhi wei bing), latent pathogen theory (伏邪学说, fu xie xue shuo)". #4 Medication regularity: The node "Behçet's disease" emerged before 1990; "osteosarcoma, syndrome differentiation, clinical efficacy" appeared in around 2005; "multiple sclerosis, data mining, medication rules" emerged around 2015; and "network pharmacology, mechanism of action" appeared after 2020. #5 Syndrome differentiation and treatment emerged around 1990, with the node "adult-onset Still disease" appearing around 1995; in around 2000, it was associated with "integrated Chinese and Western medicine, TCM therapy" and was later linked to nodes such as "Behçet's syndrome, systemic sclerosis, quality of life". #6 Amyotrophic Lateral Sclerosis emerged after 1990, with nodes clustering after 2000 alongside "TCM syndrome, Flaccidity Syndrome (痿证, wei zheng), etiology and pathogenesis", indicating the trajectory of research. #7 Primary Biliary Cholangitis appeared in around 1995 and was associated with "clinical observations, clinical experience". #8 Case record emerged in around 1990 and was associated with "Multiple System Atrophy, Neuromyelitis Optica, etiology and pathogenesis, acupuncture". #9 Retinitis Pigmentosa appeared in around 1990 and was linked to nodes such as "Primary Retinitis Pigmentosa, acupuncture therapy, acupuncture, acupuncture treatment". #10 Traditional Chinese Medicine intervention spanned from before 1990 to after 2020 and was associated with "Primary sclerosing cholangitis, Narcolepsy, vessel bi-disease (脉痹, mai bi)". #11 Famous doctor's experience emerged in 1990 and continues to this day, with subsequent nodes including "Multiple Sclerosis, POEMS syndrome, pediatric neuroblastoma, lung flaccidity (肺痿, fei wei), and Retinitis Pigmentosa". #12 Traditional Chinese Medicine constitution emerged in 2000 and was associated with "TCM pathogenesis, acupuncture, clinical characteristics, lung function, syndrome factors, risk factors". #13 Polycythemia Vera appeared in 1985 and was linked to "Chinese medicine, veteran TCM

**Table 1. Summary of major clusters**

| ID | Size | Silhouette | Year | Keywords | Label (LLR) |
|---|---|---|---|---|---|
| 0 | 100 | 0.806 | 2012 | Idiopathic pulmonary fibrosis | Idiopathic pulmonary fibrosis, traditional Chinese medicine, progress of research, clinical research |
| 1 | 89 | 0.936 | 2012 | Hepatolenticular degeneration | Hepatolenticular degeneration, traditional Chinese medicine syndrome patterns, hyperhomocysteinemia, Wilson's disease |
| 2 | 80 | 0.73 | 2002 | Traditional Chinese medicine therapy | Traditional Chinese medicine therapy, pemphigus, case reports, nursing care, pemphigus vulgaris |
| 3 | 77 | 0.895 | 2002 | Multiple sclerosis | Multiple sclerosis, traditional Chinese medicine treatment, integrated Chinese and Western medicine treatment, preventive medicine |
| 4 | 71 | 0.763 | 2012 | Medication regularity | Medication regularity, data mining, Behçet's disease, Chinese herbal medicine, cluster analysis |
| 5 | 69 | 0.826 | 2007 | Syndrome differentiation and treatment | Syndrome differentiation and treatment, traditional Chinese medicine, adult Still's disease, systemic sclerosis, experience |
| 6 | 65 | 0.831 | 2010 | Amyotrophic lateral sclerosis | Amyotrophic lateral sclerosis, ALS, traditional Chinese medicine syndrome, motor neuron disease |
| 7 | 52 | 0.82 | 2017 | Primary biliary cholangitis | Primary biliary cholangitis, clinical experience, ursodeoxycholic acid, traditional Chinese medicine therapy |
| 8 | 51 | 0.812 | 2015 | Case record | Case record, multiple system atrophy, pathogenesis, multiple system atrophy, neuromyelitis optica |
| 9 | 51 | 0.869 | 2002 | Retinitis pigmentosa | Retinitis pigmentosa, primary retinitis pigmentosa, Gaofeng cataract, traditional Chinese medicine ophthalmology |
| 10 | 49 | 0.831 | 2002 | Traditional Chinese medicine intervention | Traditional Chinese medicine intervention, narcolepsy, Takayasu arteritis, primary sclerosing cholangitis |
| 11 | 41 | 0.79 | 2009 | Famous doctor's experience | Famous doctor's experience, multiple sclerosis, inflammatory myofibroblastic tumor |
| 12 | 33 | 0.806 | 2016 | Traditional Chinese medicine constitution | Traditional Chinese medicine constitution, Leber's hereditary optic neuropathy, neuromyelitis optica, clinical features, risk factors |
| 13 | 26 | 0.895 | 2007 | Polycythemia vera | Polycythemia vera, malignant melanoma, experiences of veteran TCM practitioners, Longdan Xiegan decoction |
| 14 | 16 | 0.923 | 2019 | Gandou decoction | Gandou decoction, internal damp-heat pattern, Wilson's disease, hepatolenticular degeneration |

doctor's experience". #14 Gandou Decoction emerged in 2000, with nodes including "research strategies, combination of disease and syndrome, Wilson's disease" (Figure 6).

3.4.4. Keyword emergence analysis

Detecting citation burst terms can provide an intuitive visualization of historical shifts in research hotspots within Chinese literature on TCM treatments for rare diseases. The figure indicates that disease-related keywords — "Retinitis Pigmentosa", "Multiple Sclerosis", "Primary Biliary Cholangitis", and "Idiopathic Pulmonary Fibrosis" — emerged as research focal points during the periods 1993–1999, 2004–2013, 2017–2025, and 2023–2025, respectively. Regarding research methodology-related keywords, "experiences of renowned physicians" emerged as a hot topic from 2010 to 2017, while "data mining" and "medication patterns" gained prominence from 2021 to 2023 (Figure 7).

## 4. Discussion

### 4.1. TCM's primary advantages in diagnosing and treating rare diseases are limited to specific conditions

Based on the above descriptive analysis of 207 rare diseases, TCM demonstrates diagnostic and therapeutic advantages primarily in five conditions: idiopathic pulmonary fibrosis, multiple sclerosis, hepatolenticular degeneration, retinitis pigmentosa, and osteosarcoma. These will now be discussed in detail.

4.1.1. Idiopathic pulmonary fibrosis was studied the most

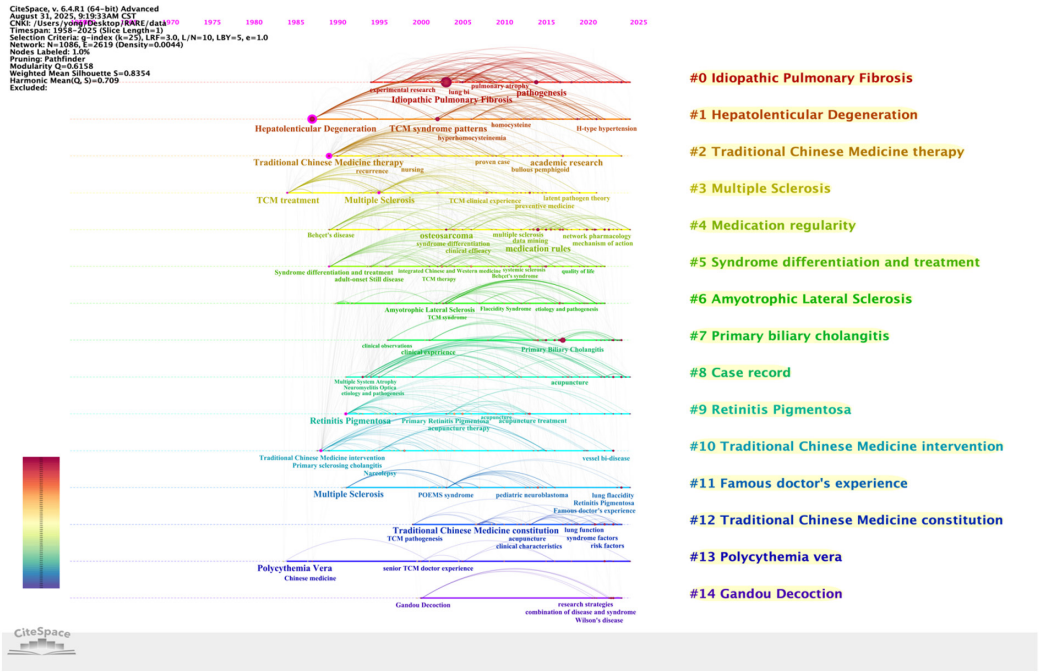


**Figure 6. A timeline map of rare disease keywords obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**

**Top 10 Keywords with the Strongest Citation Bursts**

| Keywords | Year | Strength | Begin | End |
|---|---|---|---|---|
| TCM therapy | 1989 | 65.39 | **1992** | 2010 |
| Retinitis Pigmentosa | 1991 | 14.66 | **1993** | 1999 |
| Multiple Sclerosis | 1995 | 15.02 | **2004** | 2013 |
| Famous doctor's experience | 2003 | 9.38 | **2010** | 2017 |
| Primary biliary cholangitis | 2017 | 14.79 | **2017** | 2025 |
| Traditional Chinese Medicine | 1998 | 9.11 | **2020** | 2025 |
| Data mining | 2014 | 13.82 | **2021** | 2023 |
| Medication regularity | 2015 | 9.82 | **2021** | 2023 |
| idiopathic pulmonary fibrosis | 2014 | 18.5 | **2023** | 2025 |
| traditional chinese medicine | 2014 | 16.75 | **2023** | 2025 |

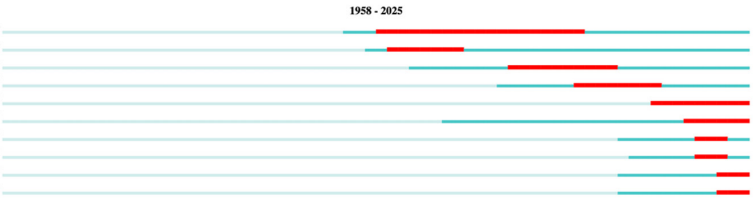


**Figure 7. A citation burst map of rare disease keywords obtained using the software CiteSpace6.4.R1 based on mainstream Chinese databases (CNKI, VIP, Wanfang, and Chaoxing).**

Idiopathic pulmonary fibrosis is a terminal-stage lung alteration in interstitial lung disease (*7*) and falls under pulmonary system diseases in TCM. The primary research institution studying this disease is the Liaoning University of Traditional Chinese Medicine and its affiliated hospitals. The team led by Xiaodong Lyu (core members include Lijian Pang and Li Yang) has significantly influenced research on this disease. In 2007, this team proposed that pulmonary fibrosis falls under the TCM category of pulmonary atrophy (肺痿, fei wei) (*8*) and it suggested treating pulmonary fibrosis based on the principles of pulmonary atrophy. The disease's location is in the lungs, spleen, and kidneys (*9*). Its pathogenesis involves a fundamental deficiency and superficial excess (本虚标实, ben xu biao shi): a lung-kidney deficiency constitutes the fundamental deficiency, while phlegm, dampness, toxins, and blood stasis represent the superficial excess (*10*). Guided by the collateral disease theory (络病理论, luo bing li lun) after 2014, the team proposed that lung heat and collaterals stasis (肺热络瘀, fei re luo yu) constitutes the fundamental pathogenesis of idiopathic pulmonary fibrosis (*11*). Subsequent research identified a qi yin deficiency and phlegm and blood stasis collateral (肺气阴虚, fei qi yin xu, 痰瘀伏络, tan yu fu luo) as the primary pathogenesis (*12*). TCM herbal compounds are commonly based on the therapeutic principles of benefiting qi and nourishing yin (益气养阴, yi qi yang yin), activating blood and dredging collaterals (活血通络, huo xue tong luo), resolving phlegm and dredging collaterals (化痰通络, hua tan tong luo), and regulating the lungs and dredging collaterals (理肺通络, li fei tong luo) (*13*). Potential common therapeutic targets include transforming growth factor-beta 1 (TGF-β1), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), vascular endothelial growth factor (VEGF), and the balance between matrix metalloproteinases and tissue inhibitors of metalloproteinases (MMPs/TIMPs) (*14*). The combination of Shenlong Decoction (primarily containing radix Glehniae and Pheretima)

with pirfenidone serves as a prognostic protective factor for this disease ($p < 0.05$) (*15*). Application of plasters to acupoints is the main method of external treatment, using acupoint combinations focusing on Feishu (BL13) and the Bladder Meridian of Foot-Taiyang, with Semen Sinapis Albae and Asarum as core drugs (*16*). Traditional Chinese nursing specifically proposes methods to enhance healthy Qi, resolve phlegm, remove stasis, and dredge collaterals (*17*). Basic research on the TCM diagnosis and treatment of this disease has amassed nearly 20 years of findings. In recent years, Xiaodong Lyu's team has focused primarily on standardizing TCM pattern differentiation and treatment protocols (*18*). Future research, such as randomized controlled trials (RCTs), may gradually yield high-level evidence following the establishment of standardized TCM diagnostic and therapeutic criteria.

4.1.2. Diagnosis and treatment standards for multiple sclerosis have been devised

Multiple sclerosis is a central nervous system (CNS) disease (*19*), and it falls under the category of brain diseases in TCM. The primary research institution studying this disease is Beijing Tiantan Hospital affiliated with Capital Medical University, where Yongping Fan's team has significantly influenced its study. In 2005, Fan reviewed over two decades of TCM literature, confirming that TCM's advantages in treating this disease lie in effectively alleviating neurological symptoms, regulating immune function, alleviating relapse symptoms, and reducing episode frequency (*20*). He analyzed the medical records of 500 multiple sclerosis patients and summarized 6 combinations of TCM syndrome factors as Liver-Kidney Yin Deficiency, Spleen-Kidney Yang Deficiency, Spleen Qi Deficiency, Blood Stasis, phlegm dampness and phlegm heat, and engendering wind (*21*). This led to the development of the Clinical Diagnosis and Treatment Guidelines for Multiple Sclerosis in Traditional Chinese Medicine, which identified four primary syndromes: a Liver-Kidney Yin Deficiency, a Spleen-Kidney Yang Deficiency, Phlegm-Damp-Heat, and a Qi Deficiency with Blood Stasis. The guidelines also recommended Chinese patent medicines, decoction prescriptions, and acupuncture treatment protocols (*21*). In 2024, an integrated Chinese-Western medicine treatment plan for this disease was further proposed (*22*). Analysis of renowned TCM practitioners' treatment experiences has revealed that the most frequently used categories of drugs are tonics, heat-clearing drugs, and blood-activating stasis-removing drugs. Herbs such as Astragalus, Angelica, Poria, Coix Seed, and Atractylodes demonstrate specific therapeutic effects (*23*). TCM has certain advantages in managing this condition, though future research requires higher-level clinical trials and studies of its mechanisms.

4.1.3. There are effective TCM formulas for hepatolenticular degeneration

Hepatolenticular degeneration is an autosomal recessive inherited copper metabolism disorder (*24*), and it falls under the category of brain diseases in TCM. The primary research institution studying this disorder is Anhui University of Chinese Medicine and its affiliated hospitals, with Wenming Yang's team significantly influencing this field. Yang posits that the TCM pathological nature of hepatolenticular degeneration involves a complex interplay of deficiency and excess. Copper toxicity consistently permeates the disease process, while internal accumulation of damp-heat, phlegm-turbidity, blood stasis, and a deficiency of qi and blood are common pathogenic factors or pathological products. Treatment should focus on resolving phlegm and stasis (*25,26*). Through case-control studies, Yang's team demonstrated that Gandouling decoction improves liver function in patients with this disease (*27*). Combined with swallowing rehabilitation training, it can ameliorate swallowing dysfunction in pseudobulbar palsy caused by hepatolenticular degeneration (*28*); Combined with repetitive transcranial magnetic stimulation, it alleviates depressive disorders (*29*) and enhances cognitive function (*30*) in hepatolithiasis patients. When taken by patients with a liver-kidney deficiency and phlegm-blood stasis, Gandou Fumu granules significantly improved TCM syndrome scores, enhanced clinical efficacy, boosted copper-excretion effects, and demonstrated anti-inflammatory and antioxidant properties (*31*). There is extensive TCM clinical practice regarding this condition, warranting further research into its mechanisms.

4.1.4. TCM's effectiveness at treating retinitis pigmentosa is close to 80%

Retinitis pigmentosa is an inherited retinal neurodegenerative disease (*32*), and it falls under the category of ophthalmological diseases in TCM. The primary research institutions studying this disease include Hunan University of Chinese Medicine and its affiliated hospitals as well as the China Academy of Chinese Medical Sciences. In 1993, Qinghua Peng and Chuanke Li from the First Affiliated Hospital of the Hunan University of Chinese Medicine proposed that the pathogenesis of retinitis pigmentosa involves a deficiency combined with blood stasis. They treated 769 patients using methods to alleviate deficiency and promote blood circulation, achieving an efficacy exceeding 80% (*33*). In 2020, the team categorized syndromes into four patterns: a kidney yang deficiency, a liver-kidney yin deficiency, a spleen qi deficiency, and a qi deficiency with blood stasis. Use of comprehensive TCM therapies in 297 cases yielded an overall efficacy of 78.12% (*34*). A 2021 retrospective analysis of their comprehensive TCM treatments in 973 cases revealed

an overall efficacy of 74.15% (*35*). The Ophthalmic Hospital of the China Academy of Chinese Medical Sciences treated 35 cases with TCM integrated therapy, achieving an overall response rate of 55.37% (*36*). In 2024, a team from Hebei University of Chinese Medicine proposed applying zang-fu syndrome differentiation based on the "Five Wheels Theory" as an approach to this disease's treatment (*37*), though it has yet to be verified clinically. TCM treatment demonstrates distinct advantages in treating this condition, with higher-level clinical studies likely to be conducted in the future.

4.1.5. TCM interventions for osteosarcoma have practical effects

Osteosarcoma is a primary malignant bone tumor (*38*), and it falls under the renal system in TCM. The current study identified 115 TCM-related articles on this condition. The literature indicates that TCM research teams across various regions of China are studying this disease, and yet no mainstream consensus has been reached. Current research primarily involves literature reviews and summaries of renowned physicians' experiences, though it has provided numerous insights into TCM interventions. In 2015, Fuchun Si and Shuaiwei Ding proposed four primary syndromes: a Kidney Yin Deficiency, a Spleen-Kidney Yang Deficiency, Qi and Blood Stagnation, and Phlegm-Heat interaction. Key treatment methods include tonifying a deficiency, activating blood and resolving stasis, and clearing heat (*39*). Professor Guizhi Sun from Guang'anmen Hospital of the China Academy of Chinese Medical Sciences has demonstrated particular expertise in treating this condition. She believes that based on a deficiency in origin and excess in manifestation, syndrome differentiation and treatment should be conducted depending on whether the patient has a spleen and kidney deficiency, the cold or heat nature of the cancer toxin, and the presence of phlegm-dampness and blood stasis (*40*). Professor Yunxia Liu from Hangzhou Third People's Hospital emphasizes distinguishing between Yin patterns (phlegm-dampness and blood stasis obstructing the bones) and Yang patterns (heat-toxin accumulation in the bones) in diagnosis and treatment. She proposes applying the theory of preventive treatment to control lung metastases in this condition (*41*). Ding *et al.* analyzed the role of TCM in bone sarcoma radiotherapy and chemotherapy, finding that TCM enhances immune function, improves liver function, sensitizes bone sarcoma cells to radiotherapy, reverses multidrug resistance in bone sarcoma cells undergoing chemotherapy, promotes hematopoietic function recovery, and prevents distant metastasis of bone sarcoma cells; these effects have been verified (*42*). In recent years, experts from Shanghai, Guangdong, and Henan have collaborated to study this disease. Yin *et al.* analyzed and categorized TCM syndromes in osteosarcoma (*43,44*) and conducted studies on the molecular mechanism of Yiqi-Sanyu-Jiedu Formula (*45*). Further clinical research may follow.

4.2. TCM provides auxiliary support for multiple conditions

Research indicates that TCM can play a supplementary role in specific stages or in particular aspects of managing rare diseases. Numerous conditions fall under this category, including pemphigus, polycythemia vera, Takayasu arteritis, amyotrophic lateral sclerosis, homocysteinemia, primary biliary cholangitis, and lymphangioleiomyomatosis.

4.2.1. TCM can reduce the steroid dosage in pemphigus patients

Pemphigus is a rare and serious autoimmune bullous disease mediated by a group of pathogenic autoantibodies mainly targeting desmoglein 2 (*46*). In TCM, pemphigus is defined as a type of bullous skin disease characterized by initial skin lesions as small as semen Euryales or as large as chess pieces, potentially extending all over the body and causing an intense burning pain (*47*). Unruptured blisters remain firm, while ruptured ones discharge toxic fluid with no foul odor. TCM research on this condition began in the 1990s and was initially dominated by clinical reports of individual case treatments and care. The first case-control study involving 120 cases appeared in 2007 and concluded that while glucocorticoids remain the first-line treatment for pemphigus and pemphigoid, integrating TCM syndrome differentiation can reduce glucocorticoid dosage (*48*). Literature from the 2010s continued to emphasize case reports, including contributions from nationally renowned physicians (*49-51*). These practitioners used pattern differentiation to prescribe internal herbal decoctions or combined them with external herbal washes. Such approaches enabled reduced steroid usage and even prolonged steroid-free periods. Recent studies increasingly emphasize integrated Chinese-Western medicine, elucidating key synergistic points at the protein level (*52*).

4.2.2. There are guidelines for the TCM treatment of polycythemia vera

The main characteristics of polycythemia vera are erythrocytosis, thrombotic and hemorrhagic predisposition, various symptoms and cumulative risks of fibrotic progression and/or leukemic evolution over time (*53*). TCM treatment for polycythemia vera began in the 1970s, and the literature was initially dominated by case reports (*54,55*). Clinical studies emerged after the 1990s. In 2011, Zhejiang Province issued an Evaluation of the

Pathogenesis of Polycythemia Vera and the Efficacy of Combined TCM-Western Medicine for Its Treatment (*56*), proposing standardized diagnosis and treatment criteria from the perspective of the mechanisms of TCM and Western medicine and evaluation of their efficacy. The accumulated experience of famous doctors has also significantly contributed to the TCM management of this condition (*57,58*). In 2022, multiple national academic organizations jointly issued the Expert Consensus on Integrated Chinese and Western Medicine Diagnosis and Treatment of Polycythemia Vera (2022) (*59*), which clearly defines TCM's understanding of this disease and provides specific clinical guidelines.

4.2.3. Staged TCM treatment for Takayasu arteritis can alleviate clinical symptoms

Takayasu arteritis presents as systemic vasculitis (*60*), predominantly affecting the aorta and its major branches (*61*). Clinical reports on TCM treatment for Takayasu arteritis emerged as early as the 1980s (*62*). Treatment outcomes demonstrated that TCM therapy can alleviate clinical symptoms, eliminate a low-grade fever, lower blood pressure, improve renal function, and restore the erythrocyte sedimentation rate (ESR) and anti-streptolysin O (ASO) titer to normal levels, thereby controlling disease activity. Famous doctors have generally had good results in treating this disease. For instance, Jiuyi Xi uses a three-phase approach emphasizing dispelling wind, consolidating the exterior, and fortifying the body's defenses (*63*); Shikui Guo treats the disease and its complications based on the theory of blood stasis (*64*); Baogui Chen focuses on expelling pathogens during the acute phase and fortifying the body during the stable phase, with both methods restoring blood flow in patients (*65*). However, an expert consensus has not yet been reached, and high-level case-control studies still need to be conducted.

4.2.4. TCM tonifying methods can reduce syndrome scores in amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a fatal CNS neurodegenerative disease (*66*) that includes motor decline and cognitive and/or behavioral symptoms (*67*). Chinese ALS cohorts have distinct epidemiological features, including a younger mean age of onset and prolonged median survival (*68*). Famous doctors from Guangzhou University of Chinese Medicine and its affiliated hospitals have influenced research on this disease to an extent. They posit that a spleen-kidney deficiency constitutes the root cause of this disease, while internal wind due to a deficiency and phlegm-stasis obstructing collaterals represent its manifestations (*69,70*). Treatment primarily involves tonifying formulas (*71*) intended to delay disease progression and improve TCM syndrome scores.

4.2.5. TCM can alleviate homocysteinemia and its secondary conditions

An elevated level of homocysteine in the body is known as homocysteinemia (*72*). TCM views a congenital constitutional insufficiency and acquired deficiency of vital substances as primary etiologies, with phlegm-stasis obstruction as the core pathogenesis. Both blood stasis and phlegm turbidity are pathologies that further trigger new pathological changes. Treatment focuses on resolving phlegm, clearing turbidity, promoting blood circulation, and removing stasis (*73*). TCM treatment for this condition has demonstrated efficacy in improving blood pressure and reducing the associated stroke risk (*74,75*) as well as in alleviating angina pectoris in coronary heart disease (*76*).

4.2.6. TCM can alleviate symptoms in non-responders to drugs to treat primary biliary cholangitis

Primary biliary cholangitis (PBC) is a chronic liver disease characterized by an autoimmune attack on the small bile ducts (*77*). Currently, ursodeoxycholic acid (UDCA) is recognized as an effective treatment that significantly alters the natural course of PBC. The advantage of TCM lies in its ability to improve outcomes in 30 to 40% of patients who fail to respond to UDCA (*78*).

4.2.7. TCM can alleviate respiratory symptoms in lymphangioleiomyomatosis

Lymphangioleiomyomatosis is a rare neoplastic disease characterized by the presence of diffuse thin-walled cysts in lungs and angiomyolipomas in kidneys (*79*), and it falls under the category of pulmonary diseases in TCM. By soothing the liver and regulating Qi, tonifying the kidney and astringing the lungs, modified Sini Powder can significantly alleviate clinical symptoms such as dyspnea, coughing, wheezing, and tightness of the chest (*80*).

4.3. Advantages of TCM in diagnosing and treating rare diseases

4.3.1. Comprehensive TCM approaches offer advantages in treating rare diseases

This study has revealed that TCM for rare diseases is rarely a singular treatment. TCM has a holistic advantage in treating rare diseases, guided by theories such as collateral disease theory and preventive treatment theory and adopting comprehensive treatment modalities including Chinese herbs, acupuncture, tuina, and traditional exercises throughout the long course of rare diseases. These comprehensive approaches have been confirmed to improve the quality of life of some rare

disease patients.

4.3.2. TCM interventions offer unique benefits and complement Western medicine in treating rare diseases

An analysis of the clinical research literature on TCM for treatment of various rare diseases has revealed that case-control studies using TCM or integrated TCM-Western medicine approaches primarily observe improvements in TCM syndrome scores and alleviation of specific symptom clusters. Organ structures do not typically differ significantly. Conversely, many Western pharmaceutical interventions fail to improve TCM syndrome scores, indicating that TCM offers a distinct perspective and unique role in treating rare diseases. For instance, TCM can alleviate respiratory symptoms in lymphangioleiomyomatosis, enhancing patients' quality of life; it can also alleviate symptoms in 30 to 40% of patients with primary biliary cholangitis who are unresponsive to standard medications. These cases demonstrate the efficacy of integrated Chinese-Western medicine in treating rare diseases and represent a promising direction for the future management of rare diseases.

4.4. Limitations of TCM in diagnosing and treating rare diseases

4.4.1. Lack of a scaled team for TCM diagnosis and treatment of rare diseases

As rare diseases in mainland China are primarily treated in general hospitals, only about 10 TCM institutions are involved in rare disease care. Consequently, epidemiological data on rare diseases in China are currently limited (*81,82*), and TCM institutions and teams specializing in rare diseases remain scarce. An analysis of 207 rare diseases revealed that, based on Price's law, core authors involved in the TCM treatment of rare diseases should publish more than 4 papers. However, there are only 54 core authors in this field, accounting for approximately 4.4% of all publishing authors. These core authors published 547 papers, accounting for 22.8% of the literature. Since the output of core authors in this field did not reach 50% of the literature, this indicates that a team of core authors has not yet formed in this area. This suggests that TCM research on rare diseases is still in its infancy and that the scope of TCM integration into rare disease diagnosis and treatment should be further expanded.

4.4.2. Lack of high-level evidence-based clinical research on rare diseases in TCM

TCM's involvement in the diagnosis and treatment of rare diseases appears as a scattering of distributed points. Keyword clustering analysis revealed that literature review and data mining are the primary methods used in TCM research on rare diseases. In clinical research, studies typically begin with the long-term clinical experience and accumulated efficacy of famous doctors over decades. From this foundation, research progresses from literature to famous doctors' experience, focusing on TCM classifications of rare diseases to investigate pathogenesis, syndrome patterns, and effective formulas. Building upon this foundation, case-control studies are conducted. For conditions that have been sufficiently studied, their mechanisms are researched—for instance, there is support from the National Natural Science Foundation of China for study of both idiopathic pulmonary fibrosis and retinitis pigmentosa. However, clinical research yielding high-level evidence has yet to be conducted, representing a key direction for the future development of TCM in the area of rare diseases.

## 5. Conclusion

TCM plays a unique role in the diagnosis and treatment of rare diseases in mainland China. Institutions are scattered across the country, with their primary strengths focused on alleviating specific clinical symptoms and improving quality of life. For rare diseases where TCM demonstrates distinct therapeutic advantages, research teams remain relatively singular, concentrating on etiology, pathogenesis, and syndrome differentiation. Case-control studies and studies of mechanisms have been initiated for certain conditions. Clinical research has shifted from purely TCM studies to integrated TCM-Western medicine approaches. However, further efforts are needed to strengthen team and institutional collaboration, develop multicenter networks, explore multidisciplinary research, and conduct high-level clinical studies. This will provide quality evidence-based support for clinical decision-making with regard to the TCM treatment of rare diseases.

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