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# Chinmedomics: A Powerful Approach Integrating Metabolomics with Serum Pharmacochemistry to Evaluate the Efficacy of Traditional Chinese Medicine

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#### ABSTRACT

Evaluation of the efficacy of traditional Chinese medicines (TCMs) is an important prerequisite for discovering effective substances, lead compounds, and quality markers (Q markers). At present, there is an urgent need to develop a biological language that can act as abridge for the scientific elaboration of the efficacy of TCMs, and to further highlight the significant value of TCM. Chinese medicinal syndromes and formulae are two essential parts of TCM that directly relate to its efficacy. Syndromes and formulae have been taken as the research objects. The serum pharmacochemistry of the TCM approach with metabolomics were integrated to establish an innovative chinmedomics strategy, which is able to explore syndrome biomarkers and evaluate TCM efficacy in order to discover effective substances from TCMs. A great deal of concrete work in chinmedomics has already performed to bridge the gap between Chinese and Western medicine, and to provide a powerful approach to enhance the scientific value of TCM theory and clinical practice. This article summarizes the application of chinmedomics in identifying the candidate biomarkers of a syndrome and revealing the efficacy of the related formula. We also highlight the discovery of lead compounds and Q markers from TCMs.

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# 1. Introduction

Due to changes in the human disease spectrum, it is no longer effective to use a simple treatment mode for a single target, or a single drug in Western medicine, to solve complex diseases [1,2]. Precise individualized diagnosis and treatment have been proposed as new challenges for modern medicine. Multi-target therapy, such as traditional Chinese medicines (TCMs), has unique advantages in complex disease treatment over single-target drug use [3–5]. Valuable clinical experience has been accumulated in TCM in finding solutions to complex problems of disease treatment, due to its distinctive features and the benefits of multi-target effects. Syndrome differentiation is an individualized diagnosis and treatment process that contains original thinking in precision medicine and embodies the concept of precise therapy. However, modern scientists find it difficult to fully accept the advantages and value of clinical experience with TCM. Efficacy is

TCM efficacy includes three aspects: clinical effect, mechanism of action, and the material basis. Clinical effect is the basis of TCM development, but it can only be expressed through the state of the formula that corresponds with the syndrome because: ① the effectiveness of TCM is based on syndrome differentiation; and ② the clinical administration of TCM occurs in the form of formulae, rather than single-herb treatments. Precise evaluation of efficacy is the precondition for excavating and revealing the advantages of TCMs. Accurate evaluation is directly related to the two key scientific components of TCM: syndromes and their corresponding formulae. However, syndrome ambiguity and formula complexity have greatly limited the scientific evaluation of formula efficacy and the confirmation of efficacious substances [6]. Current pathological and clinical chemical indicators are limited, which makes it difficult to evaluate the overall role of formulae in the treatment of a syndrome [7]. Accurate treatment can only be achieved

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key to the survival and development of TCM. The question is, how can a biological language be established that can scientifically explain the efficacy of TCM, while being a prerequisite for the use of TCMs in individualized treatment?

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through the precise identification of the TCM syndrome status, a precise understanding of the formula, and the precise evaluation of efficacy in the effective state. Therefore, under the premise of disclosing syndrome biomarkers, the establishment of a precise evaluation system for curative effect is indispensable for the evaluation of the efficacy of TCMs and the discovery of the material bases of formulae.

Based on a great deal of research and practice, a new strategy called chinmedomics has been formed for the evaluation of the efficacy of TCMs [8]. This strategy uses metabolomics to reveal syndrome biomarkers and evaluate formula efficacy; it also uses the serum pharmacochemistry of traditional Chinese medicine (SPT) to discover the active form of the *in vivo* constituents that originate from formulae in an effective condition. The strategy then integrates metabolomics technology with SPT theory by analyzing the correlation relationship between the biomarker and the in vivo constituents, and exploring the constituents associated with clinical efficacy (Fig. 1). Thus, using the research methods of chinmedomics has allowed us to promote an accurate diagnosis of the syndrome, and examine the resulting clinical experience in order to enhance the scientific value of the theory and clinical practice of TCM [9,10]. Chinmedomics can help to establish precision medicine in the Chinese style, while improving the original innovative capability of TCM research and development. This review focuses on the key issues of syndrome biomarkers, TCM efficacy, and the discovery of the efficacy of substances through chinmedomics.

# 2. Overview of the application and challenges of TCM

The development of TCM is deeply influenced by ancient Chinese philosophy that includes the basic concepts of yin-yang theories, holism, syndrome differentiation, and more [11]; this Chinese philosophy is reflected in TCM diagnosis and treatment. TCM treatment is based on holistic symptoms and syndrome

differentiation [12], which are the foundation of disease understanding and clinical efficacy. The millennia-old TCM often promotes combinatory treatment by means of formulae [13]. Combination therapy, which refers to formulae that comprise crude herbs, animals, minerals, and so forth, has long been used as the essential therapeutic method for disease. The formulae in TCM include four elements: the monarch (the component that produces the major pharmacological effect), the minister (which enhances the effect through synergistic action), the assistant (which assists the monarch and minister to achieve their target positions), and the servant (which reduces adverse effects). Chinese practitioners often prescribe a formula in order to achieve an ideal therapy. A single herb contains thousands of compounds, and formulae therefore comprise an enormous system of chemical compositions, which results in many difficulties when searching for the effective substances in a formula.

Many Chinese medical experts are currently working on promoting a global understanding of TCM and demonstrating its advantages. However, due to the complexity of TCM theory, its efficacy cannot be expressed with the limited pharmacological indicators currently available. It is difficult for modern medical scientists—and even for scientists working in the life sciences—to recognize and accept the practical value of clinical experience in TCM. Thus, the scientific interpretation of the efficacy of TCM has become an insurmountable obstacle for medical scientists both at home and abroad, limiting the full utilization of the advantages and clinical experience of TCM.

In the field of international medicine, the overall concept of TCM has gradually become recognized through syndrome differentiation and individualized treatment [4,14]. However, due to the criteria for the diagnosis and evaluation of TCM syndromes, the current reliance on the summary of personal experience and the descriptions of classical medical records have led to a lack of standardization, systematization, and modernization in TCM syndromes and to a lack of objectivity and standardization in clinical use [15]. Thus, progress in TCM is focused on the question



Fig. 1. Chinmedomics: a strategy that integrates metabolomics with serum pharmacochemistry to evaluate the efficacy of TCM. PCMS: plotting of the correlation between marker metabolites and serum constituents; UNIFI: Chinese medicine and natural products discovery and identification database.

of how to express the material bases of formulae and the implications of syndromes. Challenges such as these prevent TCM from advancing into modern sciences, and keep its development stagnant.

# 3. Chinmedomics: Procedures and technology

Syndrome vagueness and formula complexity result in difficult diagnoses and evaluation, and strongly limit discoveries of the effective constituents of TCMs [16–19]. Therefore, the efficacy of formulae and the biological characters of syndromes are important scientific issues that will lead to the discovery of an effective material basis for TCM. The theory and method of SPT were established in the early 1990s, and provide a methodology for discovering the active in vivo constituents in TCMs, as well as exploring their efficacy and related safety issues [20]. By the beginning of the 21st century, SPT theory with the metabolomics method was integrated to develop the innovative strategy of chinmedomics for the purpose of elucidating the essence of syndromes and the efficacy of TCMs in order to discover their effective constituents [21]. As mentioned earlier, a chinmedomics strategy can reveal the candidate biomarkers of a syndrome, the efficacy of the related formulae, and the pharmacological mechanism; it can then promote accurate diagnosis of the syndrome and mine the clinical experience to provide a strategy for enhancing the scientific value of TCM [9,22,23].

# 3.1. Metabolomics technology

Although SPT is an effective method for exploring the ingredients of TCMs, it only considers the qualitative or quantitative chemical ingredients, and does not take efficacy into consideration. It is only under the premise that a treatment is effective that the *in vivo* chemical composition is related to TCM efficacy, and the effective ingredients from TCM are revealed. Therefore, the scientific community introduced metabolomics into the process, and then established a new approach to compensate for the above-mentioned shortcoming of SPT.

Metabolomics (or metabonomics) is an important component of systems biology, with a research idea that is similar to the overall concept of TCM research [24,25]. Taking the integrity and complexity of TCM as a basis, the *in vivo* chemical ingredient changes of TCM formulae were comprehensively considered [26]. This property is consistent with the overall thinking within TCM [27], which implies that metabolomics has the potential to facilitate an understanding of the essence of syndromes and the action mechanisms of formulae.

"Treatment according to syndrome differentiation, formulae corresponding to syndrome" is the basic principle for the understanding and treatment of diseases in TCM. Therefore, the efficacy evaluation of formulae must be based on scientific understanding of the syndromes. A TCM syndrome is considered to be a functional state in which the body responds to various environmental changes and pathogenic factors; its essence is the metabolism or network changes that are caused by the body imbalance. These endogenous metabolic component changes are reflected in biological phenotypes [28].

Systematic metabolomics technology, through the nondiscriminatory analysis of endogenous small-molecule metabolites, reflects changes in the metabolic network disturbance by means of metabolic profiles and fingerprints that reflect the body's functional status [29]. The use of metabolomics to elucidate the biological essence of syndromes helps to characterize syndrome biomarkers that could provide effective evidence for syndrome diagnosis and for the establishment of syndrome-related animal models. The association study of metabolic profiles, metabolic fingerprints, and biomarkers in order to establish a bioevaluation system for efficacy meets both the characteristics and the modernization process of TCM.

# 3.2. SPT theory

The fundamental task of SPT is to analyze the material basis of TCM. Although the components in TCMs are complex, only the components that are absorbed into the blood can play a therapeutic role [30]. These absorbed components include the original components and metabolites. A consensus has been achieved regarding research ideas and methods for screening the effective substances that are absorbed into the body after oral administration. The TCM itself only contains chemical components. However, a specific formula can express the related active substances in vivo in the context of drug interactions. The same TCMs, when used in different formulae and under different pathological conditions, can express different pharmacodynamic substances. Therefore, the use of the SPT method to study the material basis of TCM should start from the effective treatment of clinical formulae. This theory embodies drug interactions (i.e., absorption and metabolism) in vivo and has been used widely.

The detection of components in blood is a key part of SPT. With the rapid development and introduction of liquid chromatography/mass spectrometry (LC/MS) technology, and particularly of ultra-performance liquid chromatography with high-resolution mass spectrometry, the ability to rapidly detect and identify components *in vivo* has greatly improved. This has promoted the popularization of SPT [31]. The combined use of liquid chromatography and mass spectrometry provides an effective detection method for the identification of transitional components in blood, and can be used to obtain information on the direct action of substances in a more comprehensive manner. However, endogenous components *in vivo* are also detected well by this method, which seriously interferes with the identification of components. Therefore, a means of addressing this issue should be introduced into the new method of LC/MS data processing.

Mass defect filtering (MDF) is mainly used for the extraction of homologous components [32]. It processes high-resolution LC/MS spectra by setting an appropriate mass shortage range and performing multiple filters, thus filtering out a great deal of endogenous interference. Background subtraction is a technique that uses the blank sample as a reference to filter out the same ions in the drug-containing biological samples [33]. Some software for drug metabolite analysis, such as MetaboLynx [34] and UNIFI [35] (Waters Corporation, USA), integrate the abovementioned technologies and combine them with the prediction of metabolic pathways in order to achieve automatic data extraction and metabolite-assisted identification.

#### 3.3. Integrating metabolomics with SPT

In the early 1990s, the primary author of this paper proposed and established a research design for the discovery of directacting substances from oral preparation containing serum. However, since the biomarkers of TCM syndromes were not effectively interpreted at that time, a precise evaluation system for formula efficacy had not yet been established. A simple analysis of the composition of a TCM in the body cannot link the *in vivo* components with the efficacy of the TCM. At the beginning of 21st century, the discovery of syndrome biomarkers and *in vivo* components analysis were simultaneously completed for the effective state of formulae, the *in vivo* composition of formulae was correlated with syndrome biomarkers, and potential effective substances were determined according to the degree of association. Chinmedomics is based on the discovery of syndrome biomarkers; taking the

formula as the research object, it uses metabolomics to discover and identify syndrome/disease biomarkers, and then associates them with animal models to establish an evaluation system of formula efficacy. To clarify formula efficacy, the active form of the direct-acting substance during the effective states were analyzed. Then it was associated with the syndrome biomarkers, and identified the components that are highly correlated with the change in biomarker trajectory. In this way, the effective substances were identified, the action mechanism was revealed, and a series of TCM-related problems was solved. To summarize, the metabolomics method is used to reveal the biological mechanism of a syndrome, while SPT is applied to discover the active compounds in vivo. Within the efficacy evaluation study, a correlation relationship analysis is performed between the ingredients in vivo and the endogenous biomarkers after the oral formula, in order to reveal the effective ingredients that are related to formula efficacy.

Chinmedomics, which integrates SPT and metabolomics, has been defined as a method that discovers syndrome biomarkers and related metabolic pathways, reveals the therapeutic properties and metabolism of formulae using analytical techniques, and thereby reveals the scientific value of TCM [36]. In 2015, the book Chinmedomics was published in English by Elsevier [37]. As a hotspot of TCM research and as an efficient strategy for evaluating the efficacy of TCMs in order to identify their effective substances, chinmedomics has gradually drawn extensive attention [38]. To identify the constituents that contribute to a formula's efficacy, the PCMS (i.e., plotting of the correlation between marker metabolites and serum constituents) method was established using Pearson's correlation, with the r coefficient showing the correlation degree between the chemical composition and biomarkers in vivo [39]. PCMS has been used to analyze the dynamic changes of syndrome biomarkers and identify direct-acting substances in vivo in order to discover the key components related to clinical efficacy [6,40]. The biomarkers are affected by the in vivo direct-action substances of the multiple components of a TCM. The dynamic optimization strategy of the key components from the PCMS model should be further established in order to screen optimal multicomponent candidates.

#### 3.4. Key technologies and matters needing attention

As a systemic approach, the chinmedomics method provides the opportunity for a new medical revolution by opening a gateway for TCM therapeutics, the discovery of lead compounds, and the discovery of quality markers (Q markers). Through the study of syndromes and their associated formulae, chinmedomics has broken through the technical bottleneck of effective substance research in TCM: that is, disassociation between formulae and syndromes. Chinmedomics comprises four innovative technologies: ① syndrome biomarker discovery technology; ② formula efficacy evaluation technology; ③ identification technology for effective ingredients *in vivo*; and ④ correlation analysis technology for exogenous ingredients and endogenous biomarkers. The development of a robust chinmedomics method will greatly facilitate various applications, such as revealing the action mechanisms, therapeutic effects, and safety profile of TCMs [41–45].

Application of the tool of chinmedomics must meet the following conditions: ① Syndrome diagnosis should be accurate and should avoid accompanying symptoms; ② syndrome-related animal models should use a preparation method that has been approved by the academic community; ③ the evaluation of the effects of formulae should integrate syndrome elements, clinical chemistry, and syndrome biomarkers; ④ endogenous and exogenous *in vivo* composition analysis should use non-discriminatory full-component analysis, and should use liquid chromatography, nuclear magnetic resonance, gas chromatography, highresolution mass spectrometry, and other equipment; and ⑤ the correlation analysis between the endogenous biomarkers and exogenous formula components must be carried out in multiple ways and be verified by biological testing.

#### 4. Innovations and advantages

Chinmedomics reflects the particularity of the TCM administration form in clinics and the specificity of formulae to corresponding syndromes. Based on these conditions, chinmedomics research is carried out to discover the in vivo effective substances in TCMs. It is known that the same TCM in different formulae will express different ingredients in vivo; thus, this research must focus on formulae in order to discover the therapeutic basis. Therefore, evaluating formula effectiveness is foundational for investigating the efficacy of substances. This method is distinct from other methods that directly analyze the components in vivo and screen the biologically active substances; chinmedomics uses a reverse research strategy to reveal the basis of substances' efficacy. First, this method explores the biological essence of the TCM syndrome/disease in order to establish an evaluation system for the efficacy of the TCM. Based on the formula effectiveness and in order to evaluate the overall effects and effective mechanisms of syndrome/disease treatment, the components of the biological effect are analyzed, and a correlation analysis is performed of the quantitative changes between the ingredients in vivo and the syndrome biomarkers. Finally, the associated components undergo further biological verification to determine the internal pharmacodynamic basis.

In comparison with metabolomics technologies, chinmedomics not only studies endogenous metabolites, but also pays more attention to pharmaceutical ingredients and their metabolites derived from TCMs [46,47]. In early studies on the serum pharmacochemistry of TCM, most studies focused on the in vivo components and metabolism of normal animals, although a few studies were conducted in disease animal models [48-51]. However, the TCM ingredients were not linked to the therapeutic effects: moreover, the *in vivo* components were not associated with syndrome biomarkers. This failure to express the ingredients present in the body during the effective state of the TCM caused the research results to be divorced from TCM practice. In the past, evaluation of a formula's efficacy was only performed using pharmacological and pathological indicators [52,53]. Expressing the overall effect of a syndrome is a challenging task. Chinmedomics provides an integrated analysis of syndrome elements, clinical chemistry, and syndrome metabolic biomarkers for the evaluation of efficacy. An activity-directed separation method for natural products does not adequately reflect the drug interactions of a formula during the absorption process, does not include the role of the human body or the synergy of multiple components, and leads to a loss of activity during the separation process. This makes it difficult to obtain formulae compatibility and embody multi-component synergy [51,54]. As research in this field continues to deepen and methodology continues to improve, chinmedomics will have greater scientific value in the evaluation of the essence of syndromes, TCM efficacy, and quality control, and will promote the modernization and international development of TCM.

#### 5. Recent trends and application of chinmedomics

At present, life science research has entered the age of "omics." Biomarkers have become the main basis for accurate diagnosis, and form a bridge linking basic research with clinical treatment [55– 58]. The use of precise biomarkers of TCM syndromes/diseases can lead to an accurate diagnosis, and can achieve an objective evaluation of the efficacy of TCMs. Precise evaluation of formula efficacy is a prerequisite for revealing the advantages of TCM treatment. Numerous studies have demonstrated the utility of chinmedomics to explore marker metabolites and constituents in vivo, and to provide insights into therapeutic mechanisms [59]. Using chinmedomics, the biomarkers of yanghuang syndrome [60,61], kidney-yang deficiency syndrome [62,63], kidney-yin deficiency syndrome [64], heart-qi deficiency syndrome [65], dampness-heat jaundice syndrome (DHJS) [66], insomnia syndrome [67], and liver-qi and spleen-deficiency syndrome [68], among others, have been developed. Furthermore, the efficacy of formulae such as the Yinchenhao decoction (YCHD) [69], Liuwei Dihuang pill [70], Zhibai Dihuang pill [71], Shenqi pill [72], Wenxin formula [34], Suanzaoren decoction [73], Shengmaisan formula [74–76], Tianqi Jiangtang capsule [77], Shuanghuanglian formula [78], and other formulae for the treatment of related syndromes [79.80], along with an effective material basis, have been clarified. These results demonstrate that high-throughput chinmedomics technologies are valuable for the discovery of effective constituents based on the efficacy of TCMs, and can eventually be used to elucidate the scientific value of TCM.

#### 5.1. Advancing the discovery of effective substances from the YCHD

YCHD has been widely used for DHJS therapy. However, its effective substances and action targets are still unclear. The chinmedomics strategy was used to explore the efficacy of YCHD against DHJS in order to discover the effective substances of YCHD and predict its potential targets [81]. A total of 69 compounds were identified in YCHD, with 41 of them being absorbed *in vivo*. Furthermore, 34 biomarkers in urine were identified from DHJS. Next, PCMS technology was used to perform a correlation analysis of the urine biomarkers and *in vivo* components in order to determine the effective substances responsible for YCHD efficacy (Fig. 2). A total of 12 potential targets were found by means of integrative technology. A further elucidation of the relationships between effective substances and their target pathways may provide the foundation for designing a novel combination agent.

# 5.2. Screening active compounds from Phellodendri amurensis cortex

The high-throughput screening of bioactive ingredients from medical herbs is important for drug discovery [82]. In a recent study [83], the chinmedomics method was used to assess the therapeutic effect of dried *Phellodendri amurensis* cortex (PAC) in

inhibiting prostate cancer, and to explore the active ingredients (Fig. 3). The analysis showed that PAC could decrease the growth of 22RV1 human prostate cancer cell-xenograft tumors (Fig. 3(a)). The *in vivo* constituents and marker metabolites were analyzed using the chinmedomics approach, with a total of 54 compounds in PAC being characterized *in vitro* and 38 compounds being found *in vivo* (Fig. 3(c)). In addition, 29 prototype compounds and nine metabolites were absorbed and identified in serum. A total of 34 biomarkers were related to prostate cancer. PAC can adjust the marker metabolites to a normal level and then regulate the metabolic profile to a healthy state (Fig. 3(b)). It is notable that 10 constituents were absorbed as ingredients that were associated with the overall efficacy (Fig. 3(d)).

#### 5.3. Chinmedomics for quality markers of Kaixinsan

Based on the discovery of the Q markers of TCM, a quality standard was established to reveal its efficacy and safety [84,85]. Kaixinsan (KXS) is a classic formula that has recently been applied to treat Alzheimer's disease (AD). However, its Q markers remain unclear. Chinmedomics has been used to explore the efficacy and potential Q markers of KXS in transgenic AD mice [86]. KXS can reduce the deposition of Aβ1-42 in brain tissue and significantly improve cognitive function. The biomarkers and components in vivo were analyzed using the chinmedomics strategy, which showed that KXS significantly regulates 20 biomarkers by rebalancing lipid and amino acid metabolism abnormalities. Based on the efficacy of KXS against AD, Q markers that included ginsenoside F1, ginsenoside Rf, dehydropachymic acid. 20-O-glucopyranosyl ginsenoside Rf, and E-3,4,5-trimethoxycinnamic acid were determined.

# 6. Future perspectives

Chinmedomics is the science of advancing the discovery of effective substances from TCM formulae and elucidating their action modes. It offers a new method to understand the relationships between syndromes and formulae. Earlier integration of advanced technologies can increase the success rates of lead compound selection and optimization, and can help to explain the therapeutic mechanisms of formulae [87]. Due to the complexity of syndromes, there are some limitations in making use of metabolomics alone to explain the biological essence of a



Fig. 2. An illustration of the use of chinmedomics to advance the discovery of effective substances from the YCHD.



**Fig. 3.** A high-throughput chinmedomics method being used to screen active compounds from PAC. (a) Comparisons of tumor growth between model and treatment groups; (b) the biomarkers analysis using metabolomics; (c) an *in vivo* ingredients analysis by serum pharmacochemistry; (d) identification of effective ingredients that are associated with the overall efficacy by means of the PCMS technique.

syndrome or disease. Much work remains to be undertaken, and it is necessary to overcome these obstacles. In the future, we must focus on upstream functional proteins and genes on the basis of metabolic markers in order to allow more in-depth and specific study of the essence of syndromes, along with more precise treatment. Doing so will make the evaluation of the efficacy of formulae and effective substances more clinically valuable.

Standing now at the beginning of the establishment of chinmedomics theory, these issues must be considered. The research and practice of chinmedomics are closely integrated with those of other "omics." Since metabolomics is the core technology of this theory, the theory is called "chinmedomics." Although it is defined by the "omics" of histology, the introduction and integration of proteomics, transcriptomics, genomics, and other technologies have also been considered, in order for this theory to continue to improve in practice. The next step will be to analyze large samples of common clinical syndromes. Through big data integration analysis, the metabolic contours and biomarkers of syndromes will be established, leading to accurate diagnosis, precise treatment based on biomarker analysis, and the discovery of effective substances. Chinmedomics provides a method for exploring the integration concept of the overall effects of TCM [88]. From the perspective of the life sciences, it is possible to consider the integration of genes, proteins, and the metabolite networks of animals, organ tissues, and cells, including compounds at the subcellular and molecular level, in order to obtain a complete understanding of diseases. Current medical science shows a trend of development in TCM and modern medicine [89–91], and we should seize this major opportunity for a new round of scientific and technological revolution. Chinese and Western medical communities share the unshakable historical mission of gradually breaking through these barriers and realizing the integration of medical science.

#### 7. Conclusion

Precision medicine will surely play an important role in the 21st century. Given the current circumstances of TCM international development, to which all countries attach great importance, China must seize the opportunity to satisfy clinical needs, respect the thinking of TCM, and adopt the concept of precision medicine. In this way, China can integrate the knowledge of multiple disciplines, build a platform for the accurate diagnosis and precise evaluation of therapeutic effects, improve the clinical efficacy of TCM, and provide an effective means of exchange and communication between the practitioners of Chinese medicine and those of modern medical science. Chinmedomics is an important part of precision medicine in the era of big data, and has been extensively used for the precise diagnosis of TCM syndromes and the evaluation of formula efficacy. Chinmedomics uses accurate biomarkers as a bridge, and uses in vivo effective ingredients as a link to establish a precise evaluation system of formulae. Thus, it reveals the correspondence between classic formulae and syndromes, and helps to realize a precise medical model in the Chinese style. We sincerely hope that the vigorous development of a chinmedomics platform will promote the deep integration of basic research in TCM with clinical resources, and will further enhance the original innovative capabilities of research and development in TCM.

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# **Compliance with ethics guidelines**

Ai-Hua Zhang, Hui Sun, Guang-Li Yan, Ying Han, Qi-Qi Zhao, and Xi-Jun Wang declare that they have no conflict of interest or financial conflicts to disclose.

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