Contents lists available at ScienceDirect

Digital Chinese Medicine

journal homepage: http://www.keaipublishing.com/dcmed

Phenomics of traditional Chinese medicine 2.0: the integration with digital medicine

Min XU[a, b†], Xinyi SHAO[a, b†], Donggeng GUO[c], Xiaojing YAN[b, d], Lei WANG[b, d], Tao YANG[b, e], Hao LIANG[f], Qinghua PENG[f*], Lingyu Linda YE[a, b, f*], Haibo CHENG[b, g*], Dayue Darrel DUAN[a, b, c, f*]

a. School of Integrative Medicine, Nanjing University of Chinese Medicine, Nanjing, Jiangsu 210030, China

b. The Academy of Phenomics of Traditional Chinese Medicine, Nanjing University of Chinese Medicine, Nanjing, Jiangsu 210030, China

c. Key Laboratory of Autoimmune Diseases and Precision Medicine, Yinchuan, Ningxia Hui Autonomous Region 750002, China

d. Changzhou Key Laboratory of Human Use Experience Research & Transformation of Menghe Medical School, Changzhou Hospital Affiliated to Nanjing University of Chinese Medicine, Changzhou, Jiangsu 213003, China

e. School of Artificial Intelligence and Information Technology, Nanjing University of Chinese Medicine, Nanjing, Jiangsu 210030, China

f. Research Institute of TCM Zhenghou Phenomics, Hunan University of Chinese Medicine, Changsha, Hunan 410208, China

g. Jiangsu Collaborative Innovation Center of Traditional Chinese Medicine in Prevention and Treatment of Tumor, Nanjing, Jiangsu 210029, China

ARTICLE INFO

Article history
Received 20 May 2025
Accepted 29 August 2025
Available online 25 September 2025

Keywords
Digital medicine
Traditional Chinese medicine
Phenomics
Modernization of traditional Chinese medicine
Artificial intelligence

ABSTRACT

Modern western medicine typically focuses on treating specific symptoms or diseases, and traditional Chinese medicine (TCM) emphasizes the interconnections of the body's various systems under external environment and takes a holistic approach to preventing and treating diseases. Phenomics was initially introduced to the field of TCM in 2008 as a new discipline that studies the laws of integrated and dynamic changes of human clinical phenomes under the scope of the theories and practices of TCM based on phenomics. While TCM Phenomics 1.0 has initially established a clinical phenomic system centered on Zhenghou (a TCM definition of clinical phenome), bottlenecks remain in data standardization, mechanistic interpretation, and precision intervention. Here, we systematically elaborates on the theoretical foundations, technical pathways, and future challenges of integrating digital medicine with TCM phenomics under the framework of "TCM phenomics 2.0", which is supported by digital medicine technologies such as artificial intelligence, wearable devices, medical digital twins, and multi-omics integration. This framework aims to construct a closed-loop system of "Zhenghou–Phenome–Mechanism–Intervention" and to enable the digitization, standardization, and precision of disease diagnosis and treatment. The integration of digital medicine and TCM phenomics not only promotes the modernization and scientific transformation of TCM theory and practice but also offers new paradigms for precision medicine. In practice, digital tools facilitate multi-source clinical data acquisition and standardization, while AI and big data algorithms help reveal the correlations between clinical Zhenghou phenomes and molecular mechanisms, thereby improving scientific rigor in diagnosis, efficacy evaluation, and personalized intervention. Nevertheless, challenges persist, including data quality and standardization issues, shortage of interdisciplinary talents, and insufficiency of ethical and

---

†The authors contributed equally.

*Corresponding author: Dayue Darrel DUAN, E-mail: dduan@medicine.nevada.edu. Haibo CHENG, E-mail: hbcheng@njucm.edu.cn. Lingyu Linda YE, E-mail: lye@njucm.edu.cn. Qinghua PENG, E-mail: pqh410007@126.com.

Peer review under the responsibility of Hunan University of Chinese Medicine.

DOI: 10.1016/j.dcmed.2025.09.002
Citation: XU M, SHAO XY, GUO DG, et al. Phenomics of traditional Chinese medicine 2.0: the integration with digital medicine. Digital Chinese Medicine, 2025, 8(3): 282-299.

legal regulations. Future development requires establishing national data-sharing platforms, strengthening international collaboration, fostering interdisciplinary professionals, and improving ethical and legal frameworks. Ultimately, this approach seeks to build a new disease identification and classification system centered on phenomes and to achieve the inheritance, innovation, and modernization of TCM diagnostic and therapeutic patterns.

1 Introduction

The rapid development of science and technology, including phenomics and digital medicine as new interdisciplinary subjects, is profoundly changing the development pattern of both modern western medicine and traditional Chinese medicine (TCM) [1-17]. As a cutting-edge research direction first introduced in the field of TCM in 2008, TCM phenomics provides a new perspective and paradigm for revealing the scientific connotations and efficacy mechanisms of TCM [5, 8, 9, 16, 18-20]. The TCM phenomic data have become more comprehensive and systematic, building a solid data foundation for subsequent in-depth data analysis and mining work. Integrating the advanced technologies and concepts of digital medicine [21-23] with the research of TCM phenomics may not only help to promote the modernization process of TCM but also offer new ideas and solutions for addressing many problems faced by TCM phenomics 1.0 and modern precision medicine [8-10]. Relevant papers published by leading scholars in recent years provided important references for future studies in this field [8, 12-14, 18, 24-29]. Therefore, in-depth research on the integrated development of digital medicine and TCM phenomics has important theoretical and practical significance.

2 Overview of TCM phenomics 1.0

2.1 Phenome, phenomics, and theoretical innovation

A phenome refers to the overall sum of an organism's phenotypic traits that signify the expression of genome and specific environmental influence [16, 30, 31]. Examples include human skin color, height, behavior, and personality traits. Phenomic differences among individuals can be due to differences in genotypes [such as single-nucleotide polymorphisms and single nucleotide polymorphisms (SNPs)], external environmental influences (such as lifestyle), or a combination of both. The term of "phenome" was first used by DAVIS [32] in 1949. He proposed that "the sum of the extragenic and non-autoreproductive portions of the cell, whether cytoplasmic or nuclear, be named the phenome. The phenome would be the material basis of the phenotype, just as the genome is the material basis of the genotype". With the continuous deepening of research in the field, the concept of the phenome has been expanded and defined more deeply. In 2013, BAKER [33] defined the phenome as "the set of physiological and behavioral characteristics that perfectly match the genome". Dayue Darrel DUAN's team defined the phenome as "the sum of the complete phenotypic characteristics (phenomic traits) expressed by the genome, proteome, and metabolome under the influence of a specific environment" [15-17]. The "Human Phenome Project Development Report 2020" published in 2020 defined the human phenome as the sum of all biological, physical, and chemical characteristics, including macroscopic morphological features, functions, behaviors, and microscopic molecular composition patterns, throughout the life cycle of an organism from embryonic development to birth, growth, aging, and even death (http://hupi.fudan.edu.cn). Currently, it is universally recognized that a phenome is the sum of all interrelated phenotypical traits jointly determined by the genome, proteome, metabolome, lifestyle and environmental influences, epigenome, and metagenome, demonstrating the overall phenotypic traits such as various morphological features and physiological functions of an organism that vary according to time and location [8, 17]. Therefore, a phenotype is the specific manifestation of an individual characteristic of the phenome and the basic unit of the phenome assembly. Phenomic differences between individual organisms are caused by endogenous differences in the transcriptome, proteome, and metabolome determined by one or more SNPs in the genome, external environmental influence differences (such as epigenetic and metagenomic factors), or a combination of both. Evidently, the phenome is the result of the integrated complex internal multi-omics mechanisms. Thus, a phenome has the following attributes. (i) Overall relevance: although each of the phenotypes within the phenome assembly can be separately identified, characterized, and quantified, the phenome is an inseparable whole with an intrinsically related complex network relationship. The individual phenotypes within a phenome are not randomly stacked nor present independently. (ii) Dynamic balance: the relationships and underlying mechanisms of the phenotypes that make up the phenome are determined by multiple omics such as the genome, proteome, metabolome, and epigenome, as well as environmental factors, and exhibit a dynamic balance law that varies from person to person, over time, and with locations. (iii) Multidimensionality of scale: the phenome, formed by the interaction of multi-omics mechanisms, shows cross-scale associations and multi-level manifestations of network structures from microscopic (i.e., molecular) mechanisms to macroscopic traits [8].

The term “phenomics” was first proposed by Steven A. Garan in a lecture at the Institute of Gerontology, University of Waterloo in 1996. It was not until 2003 that he defined the term “phenomics” in the abstract published in the journal *Experimental Gerontology*. Phenomics is a discipline that studies the essential characteristics of the phenome of organisms and its formation mechanisms at a holistic level, especially the internal relationships between the phenome and the entire genome, transcriptome, proteome, interactome, metabolome, and metagenome [8, 15-17, 31, 34]. It measures various phenotypic information of organisms under different environmental conditions comprehensively and dynamically through high-throughput and large-scale technical means, including morphological, physiological, biochemical, behavioral, and other levels, aiming to reveal the complexity and diversity of phenotypes, as well as the influence and regulatory mechanisms of genes and environmental factors on the phenotypes in a phenome [15].

As an emerging discipline, phenomics is constantly evolving and innovating in theory. Here are some of the main theoretical innovations. (i) Systems biology theory for integrating multi-omics data: phenomics emphasizes the integration of multiple omics data such as genomics, transcriptomics, proteomics, metabolomics and metagenomics to understand the formation mechanism of an organism’s phenome at the systematic level [8, 15, 16, 18, 35-37]. This integration not only helps to reveal the complex relationship between genes, proteins, metabolites, microbiotas and phenotypes, but also allows for a more comprehensive analysis of the regulatory mechanisms of biological systems at different levels. By integrating data of genomics, transcriptomics, epigenomics, proteomics, metabolomics, and metagenomics in living organisms and their dynamic changes, it is possible to gain insights into the information flow process from genes to the phenomes of an organism, as well as the interaction and regulation of various links in this process. (ii) Phenotypic plasticity and environmental response theory: phenomics recognizes the plasticity of an organism’s phenome, that is, the same genotype can produce different phenotypes under different environmental conditions [38-41]. This theory emphasizes the important role of environmental factors in shaping an organism’s phenome, prompting researchers to focus on the impact of genome-environment interactions on phenotypes. For example, in order to adapt to different environmental conditions such as light, temperature, food, and water, individuals would adjust their phenomic characteristics of morphology, physiology, and metabolism. Phenomics, by dynamically monitoring phenotypic changes in organisms in different environments on a large scale, helps to reveal the molecular mechanisms and genetic basis of phenotypic plasticity, and how organisms adapt to environmental changes by adjusting their phenotypes, providing a new perspective for understanding biological evolution and ecological adaptation. (iii) Phenotypic networks and module theory: phenomics research has found that there are complex interrelationships between phenotypes in organisms, and these relationships can be constructed into phenomic networks [10, 14, 42-46]. In this network, different phenotypic features are interrelated to form modules with specific functions. For example, in human diseases, different symptoms and pathological features often do not exist in isolation, but are interrelated to form a complex phenomic network [47]. By analyzing the structure and function of phenomic networks, key phenotypic nodes and modules can be discovered, which may play an important regulatory role in the occurrence and development of diseases [48]. Phenome network and module theory provide new ideas for disease diagnosis, treatment and drug development, for example, drugs can be developed for key nodes in phenomic network to achieve the purpose of treating complex diseases. (iv) Dynamic phenomics theory: the phenome of an organism is a process of dynamic change [47]. In the life-span from embryonic development to individual aging, the phenome changes constantly [49-51]. Dynamic phenomics theory emphasizes real-time and continuous monitoring of the phenome of an organism to reveal the laws and mechanisms of phenome changes over time. For example, during the process of tumor occurrence and development, the phenome of tumor cells will continue to evolve over time. By dynamically monitoring the phenomic characteristics such as gene expression, protein expression and modification, and metabolomic changes of tumor cells, the evolutionary process of tumors can be better understood, providing a basis for early diagnosis and personalized treatment of tumors [9]. In addition, dynamic phenomics is also of great significance for the study of developmental biology, aging mechanisms, and TCM Zhenghou (证候, clinical phenome) transformation theory, which helps to understand the dynamic changes and regulatory mechanisms of life processes and disease progression under various environmental conditions [40, 52-55].

2.2 Application of phenomics

2.2.1 Research on precision medicine and TCM

(i) Disease diagnosis and classification. By analyzing a large amount of phenomic data, such as the entire disease-related gene expression profiles, proteomic characteristics, and metabolomic changes, the disease-specific biomarkers can be discovered, which can help in early diagnosis and accurate classification of diseases [56-60]. For example, using multi-dimensional phenomic information such as gene expression data and imaging characteristics of tumor patients can determine more accurately the type, stage, and prognosis of tumors [43, 45]. Since modern biomedicine has long constructed its research paradigms and systems based on phenotypic changes and the definition and classification of diseases are also based on clinical phenotypes in anatomical systems, organs, or even single molecules, western medicine lacks a scientifically or clinically verified theory to guide the definition of the clinical phenome. As a result, it is impossible to correctly define and classify diseases according to the phenome, and there is no way to establish evidence-based medicine grounded on the best external evidence of the clinical phenome. It is unable to understand and re-define diseases at the omics level to improve the accuracy and precision of clinical diagnosis, treatment, rehabilitation, prognosis, prevention, as well as the accuracy and precision of clinical efficacy and safety evaluation and ultimately establish a new precision medicine-science [10, 13, 61]. On the other hand, TCM considers multiple factors such as time, place, and individual patients, and summarizes the comprehensive characteristics and laws of a certain stage of a disease as Zhenghou according to the etiology, location, scope, environment, and characteristics of the dynamic changes in the overall function of the patient. Treatment of disease according to accurate differentiation of Zhenghou or "Bianzheng Lunzhi (辨证论治)" is the fundamental principle and law of TCM. From the perspective of phenomics, Zhenghou is a collection of a specific set of clinical phenotypes that reflect the external manifestations and internal essence of the disease, which is the definition of clinical phenome according to TCM theory (Figure 1). Therefore, while western medicine is a system that defines and classifies diseases based on clinical phenotypes, TCM is a medical system that defines and classifies diseases based on the clinical phenome and takes the transformation of Zhenghou as the efficacy criteria (Table 1). Bianzheng

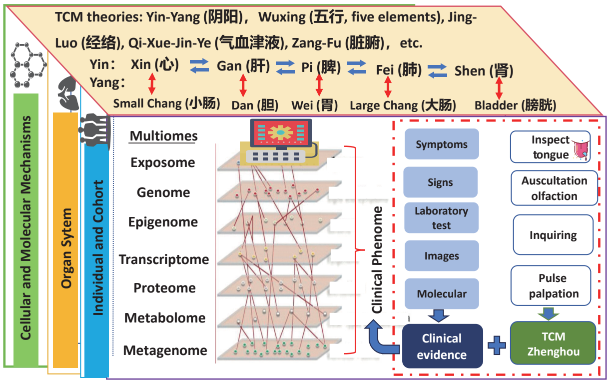

Figure 1 TCM phenomics 1.0

According to the principles of Yin-Yang (阴阳), Wuxing (五行), Jing-Luo (经络), Qi-Xue-Jin-Ye (气血津液), and Zang-Fu (脏腑) theories and assessments of multi-dimensional data collected through four diagnostic approaches of inspection, auscultation and olfaction, inquiry, and pulse palpation, patient constitution, as well as seasonal climate and the surrounding environment appearance, TCM defines and classifies diseased status as Zhenghou. In Zang-Fu theory, the five internal organs, i.e., Xin (心), Gan (肝), Pi (脾), Fei (肺), Shen (肾), and the six external hollow organs, i.e., Dan (胆), Small Chang (小肠), Wei (胃), Large Chang (大肠), Bladder (膀胱), and Sanjiao (三焦), do not exist in isolation. Instead, they form an organic whole of interdependence and mutual restriction through various mechanisms such as Yin-Yang and internal-external relationships, the generation and restriction of the Wuxing, and the metabolism of Qi-Xue-Jin-Ye. This relationship is a core manifestation of the "holistic concept" in TCM and a key to understanding the physiological functions and pathological changes of the human body

Table 1 Differences in the definition and classification of diseases between modern western medicine and TCM

Classification	Definition	
	Modern western medicine	**TCM**
Illness or sickness	The state in which the human body's form and function deviate from the range of normal values	The state in which the human body deviates from the harmony of Yin and Yang
Disease	The International Classification of Diseases (ICD) defines disease categories based on the clinical phenotypic characteristics of the anatomical system, organs, tissues, and cells, as well as their specific pathophysiological molecular mechanisms for their occurrence, development, and progression	Disease is defined and classified based on the holistic view and the theories of Yin-Yang, Wuxing, Zang-Fu, constitution, etc., throughout the entire process of disease occurrence, development, transformation, and progression
Symptom	All abnormal phenomena deviating from the normal physiological range, including symptoms and signs, etc., that is, clinical phenotypes	All manifestations of Yin-Yang disharmony, including the sum of abnormal phenomena, that is, clinical phenomes
Zhenghou pattern	Not available	A comprehensive summary of the nature of the cause, location, pathogenesis, progression, and consequences of disease based on the information obtained from the four diagnostic methods unique to TCM, namely inspection, auscultation and olfaction, inquiry, and palpation, patient constitution, as well as seasonal climate and the surrounding environment, which is a clinical phenome
Clinical treatment	Single-target drugs for clinical phenotypes (precision)	Individualized treatments of clinical phenome (precision) using Fufang, acupuncture, etc.
Evaluation of clinical efficacy	Improvement of symptoms (clinical phenotypes) and physiological indices return to the normal range	Transmission, transformation and prognosis of Zhenghou, return to the harmony of Yin and Yang

Lunzhi is in fact the earliest clinical practice of disease diagnosis and treatment using the science of clinical phenomics and pharmacophenomics. Therefore, phenomics is logically the most suitable cutting-edge science to directly grasp the key issues of TCM Zhenghou and Fufang (复方, pharmacophenomes) and provides straight modern scientific answers (Figure 2).

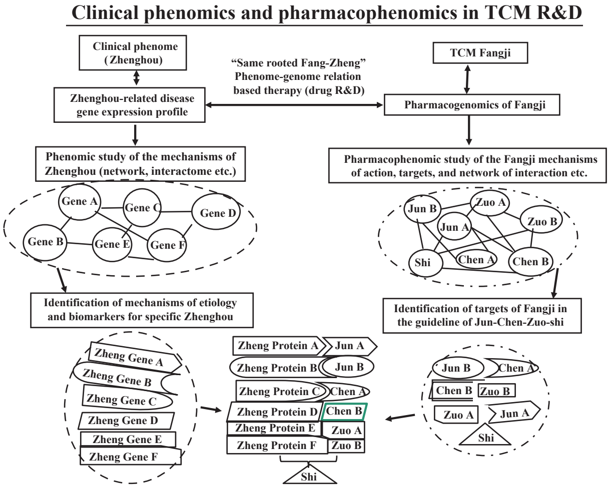

Figure 2 Clinical phenomics and pharmacophenomics in TCM research and development (R&D)

Clinical phenomics studies the genomic/proteomic/metabolomic mechanisms of Zhenghou related disease phenome to identify the biomarkers for the specific Zhenghou, which not only helps precision diagnosis of Zhenghou related disease phenome but also provides multi-omic mechanisms for the effects of TCM Fangji (方剂) or Fufang, which are a combination of multiple herbs according to the principles of Jun-Chen-Zuo-Shi (君臣佐使). With well-defined disease phenome pharmacophenomics offers a suite of new technologies and platforms for the transition from focused phenotype-genotype study of pharmacology to a systematic phenome-genome approach and will identify the corresponding therapeutic targets with systematically-defined drug responses of the specific Jun, Chen, Zuo, Shi roles of the herbs in the Fangji respectively.

The holistic view runs through the whole process of diagnosis and treatment of TCM, which is the core idea that distinguishes it from local symptomatic treatment, and is an important guiding principle for clinical decision-making. In the phenomics point of view, TCM Zhenghou is the earliest definition of clinical phenome. Therefore, phenomics is the most reasonable and practical entry point for the modernization of TCM, and it is the key to unlocking the treasure trove of TCM. As a new discipline TCM phenomics studies the laws of integrated and dynamic changes of human clinical phenomes under the scope of the theories and practices of TCM and combined with the modern clinical evidence TCM phenomics aims to systematically study the occurrence, development, and transformation mechanisms of TCM Zhenghou and disease phenome under the intervention of TCM (Figure 1).

(ii) Drug development of TCM. Phenomics can play an important role in multiple aspects of drug development [14, 19, 20, 34]. With well-defined disease phenome pharmacophenomics offers a suite of new technologies and platforms for the transition from focused phenotype-genotype study of pharmacology to a systematic phenome-genome approach and will identify the corresponding therapeutic targets with systematically-defined drug responses [19] (Figure 2).

In drug target discovery, potential interrelated multi-targets of drug action on complex diseases are characterized by comparing phenomic differences in disease states and normal states. In the drug screening process, phenomic changes in cells or animal models are used to evaluate the efficacy and safety of drugs and improve the success rate of drug development [19]. In addition, the efficacy and adverse reactions of drugs can be predicted according to the individual phenomic characteristics of patients, and personalized medication can be realized [14, 19, 20, 34] (Figure 2).

(iii) Disease mechanism research. In-depth understanding of the molecular and cellular biological mechanisms of disease occurrence and development, as well as the overall pathophysiological process (Figure 1 and 2). For example, through metabolomic analysis of patients with colorectal cancer, disease-related metabolic pathway abnormalities and protein expression changes were found, providing a basis for revealing the pathogenesis of the disease [62]. The significance of applying phenomics to study TCM lies not only in that it can provide a theoretical system to redefine and classify diseases based on the phenome rather than the phenotype, but also that it can scientifically summarize and define the evidence-based clinical practice of TCM with a new integrated omics concept [10].

2.2.2 Plant biology and TCM geoherbs and geo-authentic medicinal materials (i) Understanding plant biology. At the fundamental level, plant phenomics provides valuable insights into the mechanisms of plants, including herbs, growth, development, and evolution. By studying the interrelationship between genomes and phenomes, researchers can uncover the genetic basis of various traits and understand how genes are regulated to control plant morphology and physiology. This knowledge contributes to the overall understanding of the interactions between genomics and environment on plants and promotes the progress of smart breeding and precise cultivation. Plant phenomics can be applied to other areas of research, such as plant ecology and evolution, and shed new lights on the mechanisms of the geoherbs and geo-authentic medicinal materials used in TCM [63, 64].

(ii) Crop production management. Based on phenomics technology, real-time monitoring of crop growth status, nutritional status and occurrence of pests and diseases provides decision support for precision agriculture [65-69]. For example, using remote sensing technology and drone imaging to obtain crop phenotype information in a large area of farmland, timely detection of abnormal growth areas of crops, and targeted fertilization, irrigation and pest control measures to improve agricultural production efficiency and quality [69].

(iii) Crop improvement. Plant phenomics plays a crucial role in crop breeding. Developments in plant phenomic approaches and facilities have gradually caught up with genomic approaches in recent years, providing better opportunities to dissect complex, quantitative traits when both phenome and genome can be assessed at a higher level of details. Field phenomics has been identified as a promising enabling technology to assist plant breeders with the development of improved cultivars for farmers [70]. By accurately measuring and analyzing phenotypic traits, breeders can identify superior plant varieties with desirable traits such as high yield, disease resistance, and stress tolerance. This enables more efficient breeding programs and the development of new crop varieties that are better adapted to changing environmental conditions and meet the growing demand for food security. The accomplishment of whole-genome sequencing of many crops has brought crop functional genomics studies into the big-data and high-throughput era. Recent technological advances have provided potential solutions and methods for large-scale phenotyping data acquisition and high-throughput phenotyping in controlled field conditions and environments as well as its use for post-harvest yield and quality assessment. The latest multi-omics research combining high-throughput phenotyping with genetic studies has gradually bridged the phenotype-genotype gap. Precise measurement and analysis of crop phenotypes, combined with genomic information, to mine genes associated with good agronomic traits, to provide theoretical support for crop breeding [71]. For example, by analyzing phenotypic data such as plant height, yield, and stress resistance in rice, key genes controlling these traits are identified, and new rice varieties with high yield and stress resistance are developed using techniques such as molecular marker-assisted selection [72, 73]. Phenomics technology provides more accurate high-throughput phenotyping and will accelerate crop genetic improvements and promote the next green revolution in crop breeding.

2.2.3 Ecological research Ecological research is a science that explores the dynamic laws of the interrelationships among organisms and between organisms and their environment. It not only focuses on the structure and function of natural ecosystems but also involves the impact of human activities on ecosystems and solutions for sustainable development. It is an interdisciplinary field that bridges natural sciences and social sciences. The objects of ecological research cover multiple scales from micro to macro, with the core being to reveal ecological laws at different levels. Physiological ecology studies how the morphology, physiology, and behavior of organisms adapt to the environment (such as light adaptation in plants and migration behavior in animals) at an individual level. Population ecology analyzes the population dynamics, distribution patterns, evolution, and adaptation of populations (such as population growth models and mechanisms of species endangerment) at population level. Community ecology explores the species composition, diversity, inter-species relationships (competition, predation, and symbiosis), and succession laws of communities (such as the succession of forest communities from bare land to climax communities) at a community level. Ecosystem ecology quantifies the material cycling and energy flow in ecosystems. The application of phenomics in ecology is as follows.

(i) Research on the interaction between organisms and the environment. Studying the phenomic changes of organisms under different environmental conditions may reveal the adaptation mechanism of organisms to the environment and the shaping effect of environmental factors on the phenome of organisms [74, 75]. The study of the morphological and physiological characteristics of plants at different altitudes and geographical areas may help understanding how plants adapt to environmental pressures such as low temperature and low oxygen [76, 77] and the mechanisms for the geoherbs used in TCM [63, 64].

(ii) Ecosystem monitoring and conservation. Ecosystem refers to the unified whole formed by the interaction between a biological community and its non-biological environment (such as climate, soil, and water). Its core characteristics include biotic and abiotic components. The biotic components include encompassing producers (such as plants), consumers (such as animals), and decomposers (such as bacteria and fungi), which transfer energy and matter through food chains. The abiotic components include sunlight, temperature, moisture, minerals, etc., providing the basis for the survival of organisms. The various components maintain relative stability and a dynamic equilibrium through material cycles (such as the carbon cycle and water cycle) and energy flow. Once a certain link is damaged (such as pollution, species extinction), a chain reaction may be triggered. For example, in a forest, trees (producers) produce organic matter through photosynthesis. Deer (consumers) feed on leaves, and wolves (higher-level consumers) prey on deer. Fallen leaves and animal remains are decomposed by decomposers and returned to the soil. At the same time, abiotic factors such as sunlight and rain support this cycle, jointly constituting the forest ecosystem. The health of humans, domestic and wild animals, plants, and the wider environment in the ecosystems are closely linked and interdependent [78]. The skin is the largest organ in the human body. Various skin environments on its surface constitutes a complex ecosystem colonized by millions of microorganisms. Profiling the structure of skin microbial community is the first step to overview the ecosystem and assess its health and trends. Skin microbiota, including bacteria, fungi, and viruses, exerts critical functions in maintaining host skin health. Long-term monitoring of biological phenotypes in skin ecosystem may help understanding the host-microbe interactions from the ecological perspectives and give new inspiration to how skin microbes, by their structures or bioactive molecules, reshape host skin phenotypes, including skin immunity, maintenance of skin physiology such as pH and hydration, ultraviolet (UV) protection, odor production, and wound healing.

2.3 Definition and connotation of TCM phenomics

TCM phenomics is a discipline that studies the laws of integrated and dynamic changes of human clinical phenomes under the scope of TCM theories and practices based on human phenomics [8-10, 20]. It not only focuses on the external manifestations of diseases, such as symptoms and signs, but also delves into the multiomic changes in the human body, such as genomics, proteomics, metabolomics, and metagenomics. It aims to reveal the action mechanisms of TCM on human health and diseases and to provide a scientific basis for the modernization of TCM and development of innovative precision medicine.

2.4 Research status and progress of TCM phenomics

Since 2008 phenomics has entered the field of TCM, giving rise to TCM phenomics as an emerging discipline that studies TCM and pharmacology of TCM Fufang [14, 19, 20, 34, 79]. At present, the phenomic study of TCM has achieved some important advances [8, 9, 14, 18, 34, 62, 80].

At an international conference on “Chloride channels: insight into function from human disease” in Beijing during October 9 – 13, 2008, which was sponsored by *Journal of Physiology-London*, Chinese Association for Physiological Sciences, American Physiology Society, and Canadian Physiology Society, Professor Dayue Darrel DUAN presented his research on the phenomics of chloride channels in the heart. He also explained what the differences between modern western medicine and TCM are and why TCM theory may help to understand the phenomes of chloride channels and their roles in cardiovascular disease through orchestrating six different chloride channels in the same cardiac myocytes [16, 17] or vascular smooth muscle cells [62]. DUAN has been carrying out related new studies since then and pioneered not only the phenomics of chloride channels [16, 17] and cardiovascular disease but also pharmacophenomics [19] and TCM phenomics [34]. In the Research Center for Phenomics of TCM at Southwest Medical University established in 2017, the DUAN’s team elaborated on the research results of TCM phenomics in cardiovascular disease and cancer, providing additional ideas for explaining the scientific connotations of the TCM diagnosis and treatment system and laying a foundation for the further development of TCM phenomics [8]. They studied the metabolomic mechanisms for the clinical phenomes of Pixu Shire (PXSR, 脾虚湿热) and the Shire Yunjie (SRYJ，湿热蕴结) associated with colorectal cancer (CRC) [9]. Compared with control healthy group (n = 62), differences of 12 metabolites in seven metabolic pathways dominated by abnormal energy metabolism were identified in PXSR group (n = 68), and differences of 17 metabolite in 9 metabolic pathways dominated by abnormal lipid metabolism and tricarboxylic acid cycle were discovered in SRYJ group corresponding to the different clinical phenotypes in the respective phenomes. There were four identical characteristic metabolite differences between PXSR and SRYJ groups corresponding to the same clinical phenotypes found in the two different clinical phenomes. It is interesting that they found the histological and pathological properties of the CRC in the two different clinical phenomes were significantly different, with cancer cells in the SRYJ being less differentiated that those in the PXSR [9].

TONG’s team systematically summarized the phenomic characteristics of different types, stages, and Zhenghou of diabetes, as well as the phenomic changes before and after treatment with TCM [18]. They proposed promoting the innovative development of TCM by applying phenomics under the guidance of the "state-target identification and treatment" theory [18, 81-84]. FANG et al [85]. recently reviewed the application of TCM phenomics in glycipid metabolism disorder. By analyzing molecular characteristics of related Zhenghou, they identified differentially expressed genes, metabolites, and gut microbiota biomarkers to elucidate the dynamic evolution patterns of Zhenghou. Simultaneously, they deciphered the multi-target regulatory networks of herbal formulas (Fufang), demonstrating their therapeutic effects through mechanisms including modulation of insulin signaling pathways, improvement of gut microbiota imbalance, and suppression of inflammatory responses [85].

YUAN et al. [12] discussed the similarity in theory and application between TCM and phenomics and named the new discipline “Chinese medicine phenomics (Chinmedphenomics)”. In agreement with DUAN et al., they suggested that the systematisms of phenomics and TCM enables these two disciplines to interlink with each other. Chinmedphenomics is built on classic TCM, combined with phenomics technology, and the development of which needs the mega cohort with TCM syndrome (Zhenghou) and the characteristics of precision medicine as well as multi-disciplinary cooperation, which is personalized, precise and promising, providing unique scientific insights into understanding human health [12].

2.5 Data integration and system construction

Phenomics is an important part of systems biology. It comprehensively and dynamically measures various phenotypic information of organisms under different environmental conditions using high-throughput and large-scale technical means, including morphological, physiological, biochemical, behavioral and other levels, aiming to reveal the complexity and diversity of phenotypes, as well as the influence and regulatory mechanisms of genes and environmental factors on phenotypes. DUAN emphasized the integration of multiple omics data such as genomics, transcriptomics, proteomics, and metabolomics to understand the formation mechanism of organism phenomes at the system level and the key role of data integration in the modernization research of TCM [14]. His research provided a direction for constructing a complete data system of TCM phenomes [14]. Through the collection, collation, and analysis of a large amount of clinical data, DUAN et al. systematically integrated data scattered in different research and clinical practices. This integration covered multi-dimensional data including TCM information through four diagnostic approaches, laboratory test indicators, imaging data, and patients' lifestyles. As a result, the TCM phenomic data became more comprehensive and systematic, building a solid data foundation for subsequent in-depth data analysis and mining work [34].

2.6 Algorithm innovation and application

In the analysis and mining of TCM Zhenghou phenomic data, DUAN and his team have been actively exploring the application of multi-omics and advanced algorithms. They have conducted in-depth research on machine learning, deep learning, and other algorithms, optimized and improved them according to the characteristics of TCM data and improved the efficiency and accuracy of TCM data mining. For example, by improving the clustering algorithm for TCM Zhenghou it is possible to provide a scientific basis for more accurate differentiation and treatment of TCM Zhenghou. Using the association rule of mining algorithm to discover the potential connections between the components of TCM prescriptions (Fangji and Fufang) and treatment effects may assist in drug research and development and help screen out TCM prescriptions and components with potential therapeutic effects [20].

3 Overview of digital medicine

3.1 Definition and connotation of digital medicine

Digital medicine refers to a discipline that uses digital technologies, software and algorithmically driven products to measure, collect, store, process, analyze, and transmit human health and medical information or intervene decision and outcomes [86-90]. Digital medicine covers multiple aspects, including medical imaging, clinical diagnosis, treatment plan formulation, telemedicine, and health management [23, 86-93]. It aims to improve the quality and efficiency of medical services and promote the innovative development of medicine [10, 12, 23, 94]. It realizes the digital management and application of medical information [89]. Digital health and medical data are multimodal and high-dimensional. A patient’s health state can be characterized by a multitude of signals including medical imaging, clinical variables, genome sequencing, metabolomic and metagenomic changes, conversations between clinicians and patients, and continuous signals from wearables. This high volume, personalized data stream aggregated over patients' lives has spurred interest in developing new artificial intelligence (AI) models for higher-precision diagnosis, prognosis, and tracking. Big data and AI approaches will play a pivotal role in data processing and streamlining the phenotype-to-gene identification pipeline. While the promise of these algorithms is undeniable, their dissemination and adoption have been slow, owing partially to unpredictable AI model performance once deployed in the real world. We posit that one of the rate-limiting factors in developing algorithms that generalize to real-world scenarios is the very attribute that makes the data exciting-their high-dimensional nature. We consider how the large number of features in vast digital health and medical data can challenge the development of robust AI models—a phenomenon known as “the curse of dimensionality” in statistical learning theory. We provide an overview of the curse of dimensionality in the context of digital health and medicine, demonstrate how it can negatively impact out-of-sample performance, and highlight important considerations for researchers and algorithm designers.

3.2 Development status and trends of digital medicine

In recent years, digital medicine has achieved rapid development. In the field of medical imaging, digital imaging technologies are constantly innovating, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). CT uses X-rays to perform tomographic scans of the human body. With computer reconstruction technology, CT generates detailed tomographic images of internal organs and tissues of the human body. It can clearly show structures such as bones and lungs, assisting doctors in diagnosing fractures, and lung diseases [25, 95, 96]. MRI uses a strong magnetic field and radio-frequency pulses to make the hydrogen nuclei in human tissues resonate and generate signals [97]. After computer processing MRI has a high resolution for soft tissues and is often used in the diagnosis of lesions or tumors in parts such as the brain, spinal cord, and joints. To diagnose rates of brain growth or atrophy in a genome-wide association meta-analysis of changes in brain morphology across the lifespan longitudinal MRI data from 15 640 individuals were used to compute rates of change for 15 brain structures. Gene set findings implicate both early brain development and neurodegenerative processes in the rates of brain changes. Identifying variants involved in structural brain changes may help to determine biological pathways underlying optimal and dysfunctional brain development and aging. The most robustly identified genes among these MRI data are GPR139, DACH1, and APOE, and they are associated with metabolic processes. Further analysis found a global genetic overlap with depression, schizophrenia, cognitive functioning, insomnia, height, body mass index and smoking [49]. Also to reflect the body's metabolic function PET detects the distribution an injected tracer labeled with a radioactive nuclide in the body [98]. It is often used in the early diagnosis of tumors, differentiation between benign and malignant tumors, and evaluation of treatment efficacy such as determination of whether a tumor has recurred and metastasized [95, 99]. These digital imaging technologies provide strong support for the early diagnosis and precision treatment of diseases. In clinical diagnosis, the application of AI technology has made disease diagnosis more accurate and efficient [99]. The popularization of wearable devices and telemedicine has broken geographical restrictions, enabling high-quality medical resources to benefit more patients [100].

Influenced by genetic and environmental factors disease progression may vary between patients and overtime. The issue of ineffective medication, which is a major healthcare problem causing significant patient suffering and economic costs, stems from the complex nature of diseases and involves altered interactions among thousands of genes across multiple cell types and organs. Medical digital twins (MDTs), which are digital and virtual representations of health and disease processes that can integrate real-time data and simulations to predict and prevent disease progression, personalize treatments, optimize care delivery and improve outcomes, have emerged as a promising approach to address these challenges and have led to international initiatives aiming at clinical implementations [21, 101-105]. Propelled by extensive data collection and advancements in AI, alongside traditional biomedical methodologies, MDTs in precision medicine are increasingly viable. Early clinical applications of MDTs have shown potential in areas like artificial organs, cancer, type 2 diabetes, cardiology, and hospital workflow optimization [21, 101-105]. However, a broader implementation of MDTs in clinics still faces some major challenges [101, 102], including the characterization of the dynamic phenotypic and molecular changes across multidimensional scales, the development of multimodal computation methods for integration of data into MDTs, the prioritization of disease mechanisms and therapeutic targets, the creation of interoperable MDT systems that can learn from each other, the design of user-friendly interfaces for patients and clinicians, the scale of MDT technology for equitable healthcare access globally, and the considerations of ethical, regulatory, and financial issues [102]. Overcoming these hurdles could pave the way for more predictive, preventive, and personalized medicine, potentially transforming healthcare delivery and improving patient outcomes. With the continuous emergence of technologies such as big data, cloud computing, and the internet, the development prospects of digital medicine are even broader, and it will move towards the direction of intelligence, personalization, and precision in the future. The iterative upgrade of digital technologies has created more possibilities for their in-depth application in the medical field [102, 104, 105].

4 Applications of digital medicine in TCM phenomics

4.1 Data collection

TCM is deeply rooted in the unique reasoning paradigm of "Xiangshu (象数, image-number)" or "phenotype-numerology" thinking and TCM theory was deeply influenced by the ancient wisdom of *Hetu Luoshu* (《河图洛书》) and *Yijing* (《易经》), where the relationship between human health, natural phenomena, and the universe are explained using digits and symbols [106]. This traditional phenotype-numerology thinking provides a theoretical basis for TCM digitization and offers an inherent association of TCM with digital medicine [107]. The integration of TCM phenomics and digital medicine for disease diagnosis, classification and treatment typically involve steps of data collection, integration, preprocessing, analysis, mining, feature selection, deep learning, model construction, simulation, prediction, and evaluation (Figure 3).

The key digital tools and methodologies used in TCM phenomics 2.0 are summarized in Table 2.

Digital medical technology can achieve comprehensive and accurate collection of TCM phenomic data related to diseases from multiple sources through various methods. These data sources are extensive, covering various aspects such as clinical symptoms, signs, tongue image and coating, CT, MRI, PET and other imaging examinations, laboratory tests, gene expression profiles, proteomics, and metabolomics. For example, for tumor diseases, not only should clinical the size and location of the tumor in patients be collected, but also multi-omics data such as gene expression data of tumor tissues, protein

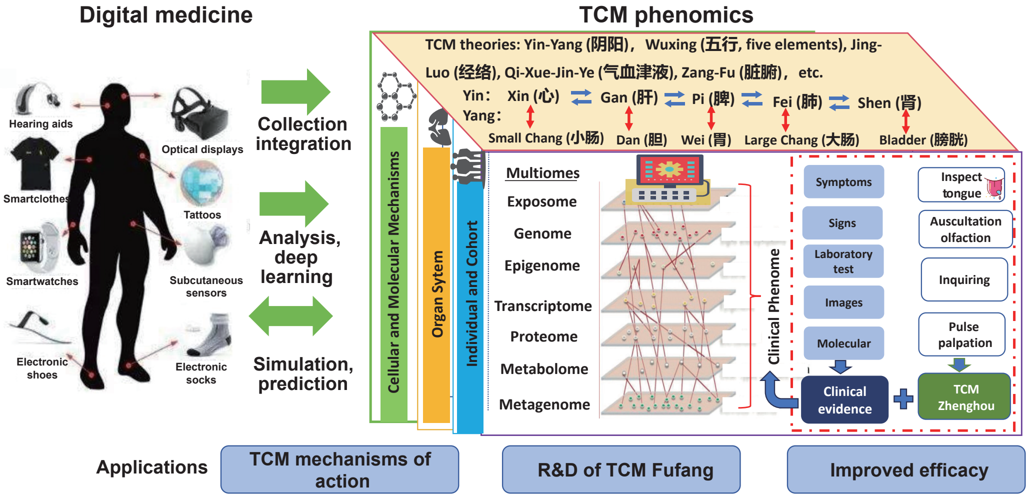

Figure 3 Integration of digital medicine and TCM phenomics

The real-time TCM phenomic data including physiological parameters, constitutions, exercise data, dietary information, clinical symptoms, signs, tongue image and coating, CT, MRI, PET, and other imaging examinations, laboratory tests, profiles of gene expression, proteomics, and metabolomics. will be collected and integrated through various digitalized methods and approaches including wearable devices, sensors, and MDTs. Big data and AI technologies will be used to analyze and integrate these multi-source and heterogeneous data, mining the potential correlations between the data and revealing the mechanisms of TCM Zhenghou and mechanisms of action of TCM Fufang. The integration of TCM phenomics and digital medicine can dynamically integrate multi-omics data (genomics and metabolomics) with clinical TCM diagnostics (tongue coating and pulse patterns) to infer causal relationships between Zhenghou subtypes and molecular pathways. AI technology, such as Bayesian networks, graph neural networks (GNNs) and geometric deep learning (GDL), will be used to dynamically integrate multi-omics data (genomics and metabolomics) with clinical TCM diagnostics (tongue coating and pulse patterns) to infer causal relationships between Zhenghou subtypes and molecular pathways, to reveal the hierarchical structure of Zang-Fu organ networks or time-dependent Yin-Yang transitions, to classify and predict TCM Zhenghou, improving the accuracy and scientific connotation of TCM diagnosis and treatment. Additionally, AI technology can assist in drug research and development by screening out TCM prescriptions of Fufang or Fangji and components with potential therapeutic effects with improved efficacy of treatment.

expression levels, and changes in metabolites in the blood and tongue coating should be collected. Through wearable devices, sensors, and DTs, it is possible to collect real-time physiological parameters, constitutions, exercise data, dietary information, and more from patients. This provides a rich data source for the research of TCM phenomics. At the same time, using big data technology, it is possible to analyze and integrate these multi-source and heterogeneous data, mining the potential correlations between the data and providing support for revealing the mechanisms of TCM Zhenghou and Fufang or Fangji [14, 34, 79, 108].

4.2 Data preprocessing

The raw data collected from phenome defined by integrated criteria of TCM and western medicine [9] often has problems such as noise, missing values, and inconsistencies, and thus requires preprocessing [106]. This includes data cleaning, removing duplicate, incorrect, or invalid data, handling missing values, selecting appropriate filling methods according to the characteristics of the data, such as mean filling, filling based on similar samples, data standardization and normalization, transforming data of different types and magnitudes to the same scale for subsequent analysis [109].

4.3 Data analysis and mining

AI technology has important application value in the research of TCM phenomics. Through machine learning, deep learning, and other algorithms, it is possible to analyze and mine large amounts of TCM phenomic data and discover underlying laws and mechanisms for Zhenghou patterns. For example, using AI technology, such as Bayesian networks, GNNs and GDL, it is possible to classify and predict TCM Zhenghou, improving the accuracy and scientific connotation of TCM diagnosis and treatment. Bayesian networks can dynamically integrate multi-omics data (genomics and metabolomics) with clinical TCM diagnostics (tongue coating and pulse patterns) to infer causal relationships between Zhenghou subtypes and molecular pathways. GNNs excel at non-Euclidean relationships in TCM phenomes, such as the hierarchical structure of Zang-Fu organ networks or time-dependent Yin-Yang transitions can be found. GDL further extends this by capturing spatial-temporal phenomic changes (e.g., tumor evolution) through manifold learning. it is possible to classify and predict TCM Zhenghou, improving the accuracy and scientific connotation of TCM diagnosis and treatment. Additionally, AI technology can assist in drug research and development by screening out TCM prescriptions of Fufang or Fangji and components with potential therapeutic effects [1, 14, 34].

Table 2 Key digital tools and methodologies in TCM phenomics 2.0

Term	Definition
Association rule	A data mining technique to identify relationships between variables (e.g., linking TCM Zhenghou patterns to specific metabolites)
Cloud computing	The delivery of computing services (storage and analysis) over the internet, enabling scalable data processing for phenomics research
Clustering algorithm	Unsupervised machine learning methods that group similar data points (e.g., patient subtypes based on phenomic profiles)
Computer simulation technology	The use of software to mimic real-world processes (e.g., disease progression and drug effects) for hypothesis testing or training
Deep learning	A type of machine learning using multi-layered neural networks to model complex patterns in large datasets (e.g., image recognition and omics analysis)
Digital and virtual representations	Computational models or simulations of real-world entities [e.g., three-dimensional (3D) organ models, virtual patients for drug testing]
Drone imaging	The capture of high-resolution images or videos using unmanned aerial vehicles, commonly used for field phenotyping, crop monitoring, or ecological surveys
High-throughput phenotyping	A method that uses automated, large-scale techniques to rapidly collect and analyze phenotypic data (e.g., plant growth and human clinical traits) for research or precision agriculture
Logistic regression	A statistical model used to predict binary outcomes (e.g., disease presence/absence) based on input variables
Machine learning	A subset of AI that enables systems to learn patterns from data and make predictions or decisions without explicit programming
Phenome-wide association study	A research approach analyzing associations between genetic variants and a wide range of phenotypes to uncover disease mechanisms
Phenotypic networks	Graphical models representing relationships between phenotypic traits, revealing how traits interact within biological systems or diseases
Real-time monitoring	Continuous, instantaneous data collection and analysis to track dynamic changes in systems (e.g., patient vitals)
Recursive feature elimination	A feature selection method that iteratively removes the least important variables to optimize predictive models (e.g., identifying key biomarkers)
Remote sensing technology	The use of sensors to collect data about objects or environments from a distance, often applied in agriculture, ecology, and environmental monitoring

4.4 Feature selection

Accurate screening on features closely related to disease from a large amount of phenomic data at the phenome-genome level contributes to health assessment, disease diagnosis and classification, drug screening, and targeted therapy for precision medicine [10, 13, 98]. This can be achieved through statistical methods, such as calculating the correlation coefficient between features and disease status, conducting analysis of variance, etc., to identify features that show significant differences between the disease phenome and the control healthy phenome. Feature selection algorithms in machine learning [110], such as recursive feature elimination, information gain-based feature selection, Fisher score, logistic regression, etc. can also be used to select the feature subsets that have the most discriminative power for disease classification, reduce the data dimension, and improve the efficiency and accuracy of the model. GE et al. [110] proposed an integrative feature selection algorithm based on the combination of Fisher score, Recursive feature elimination, and Logistic regression (named FRL) to explore potential genomic biomarkers on cancer subsets. Fisher score is initially used to calculate the weights of genes to rapidly reduce the dimension. Recursive feature elimination and Logistic regression are then jointly employed to extract the optimal subset. FRL has greater classification precision than five traditional feature selection algorithms and exhibits excellent performance on accuracy and F1 score and greatly improves computational efficiency. They conducted cluster analysis on 10 diverse cancers with high mortality and form a potential biomarker module comprising 19 genes. All genes in this module can serve as potential biomarkers to provide more information on the overall oncogenesis mechanism for the detection of diverse early cancers and assist in targeted anticancer therapies for further developments in precision medicine [110]. The rapid development of high-throughput sequencing technology has identified abundant genomic biomarkers, but most of them are based on analysis of single-phenotype cohorts. Phenome-Wide Association study (PheWAS) is a powerful tool to screen clinical observations derived from medical records (phenomes) for association with a variable of interest systematically [10, 15, 98]. Despite the wide recognition of their usefulness, few systematic screening of phenotypes associated with clinical phenomes has been done due to the difficulty of clinical phenome definition [10, 15]. TCM phenomics may provide a theoretical system to define clinical phenomes and help establishing cohorts of clinical phenomes for systematic screening of phenotypes associated with clinical [10].

4.5 Model building and evaluation

Common models include support vector machines, decision trees [111], random forests [112], neural networks [4, 113], etc. Appropriate machine learning or statistical models for disease diagnosis and classification need to be selected. The preprocessed data will be divided into a training set and a test set. The training set is used to train the model. By adjusting the parameters of the model, it can accurately learn the relationship between diseases and phenotypic features. For example, when training a neural network-based disease diagnosis model, parameters such as the number of network layers, the number of neurons, and the learning rate need to be adjusted to optimize the performance of the model [5, 114]. The test set is used to further evaluate the constructed model. Commonly used evaluation metrics include accuracy, recall, F1 score, and the area under the receiver operating characteristic curve (AUC). These metrics are used to measure the accuracy and reliability of the model in disease diagnosis and classification. If the evaluation result of the model is not satisfactory, it is necessary to analyze the reasons, such as inappropriate selection of data features, and unreasonable setting of model parameters, and then improve and optimize the model.

4.6 Simulation and prediction

Computer simulation technology and DTs in digital medicine can simulate and predict the action process of TCM. By establishing a mathematical model, it is possible to simulate the impact of TCM on the physiological and pathological processes of the human body and predict the efficacy and safety of drugs. This helps reduce experimental costs and risks in drug research and development, as well as in clinical treatment and improve research efficiency [5].

4.7 Clinical validation and application

The evaluated and verified models need to be further validated and applied in clinical practice. New case data in a real-world clinical environment will be collected to test the generalization ability of the model, ensuring that the model can stably and accurately diagnose and classify diseases in different patient groups and clinical scenarios. Only a model that has undergone sufficient clinical validation can be truly applied to clinical practice, providing strong support for disease diagnosis and treatment (Figure 4).

5 Significance of the integrated development of digital medicine and TCM phenomics

While digital medicine and TCM phenomics differ in their philosophical roots and technical tools, their shared focus on personalization and holism makes them highly complementary (Table 3). For example, digital tools (e.g., smartphone tongue scanners) can solve TCM's subjectivity problem by standardizing phenotype data. TCM phenomics can add a holistic, systemic layer to digital medicine's data-driven models (e.g., explaining why a digital app's "fatigue alert" correlates with TCM's "Qi deficiency"). Therefore, integration of digital medicine and TCM phenomics can create a more comprehensive, patient-centric healthcare system that combines the best of digital innovation and TCM's centuries of holistic wisdom.

5.1 Promoting the modernization process of TCM

The integration of digital medicine and TCM phenomics provides new technical means and methods for the modernization development of TCM [114]. Through digital technology, the theories and practices of TCM can be quantified and standardized, making them more in line with the research paradigm of modern science. This helps to improve the scientificity and credibility of TCM and promote the dissemination and application of TCM internationally (Figure 4).

5.2 Improving the clinical efficacy of TCM

By using digital medical technology to analyze and mine TCM phenomic data, it is possible to better understand the action mechanisms of TCM and provide more accurate guidance for clinical treatment (Figure 4). Through the formulation of personalized treatment plans, the clinical efficacy of TCM can be improved to meet the personalized needs of patients [4].

5.3 Promoting the integration of TCM and western medicine

The integration of digital medicine and TCM phenomics can provide a new entry point and platform for integration of TCM and western medicine [79]. Through the integration and analysis of phenomic data of TCM and western medicine, it is possible to discover the commonalities and differences. This can promote the complementary advantages of TCM and western medicine and advance the in-depth development of their integration (Figure 3 and 4).

6 Challenges faced in the integrated development of digital medicine and TCM phenomics

6.1 Data quality and standardization issues

TCM phenomic data has characteristics such as diversity, complexity, and subjectivity, and the data quality is often uneven [106, 107]. At the same time, there is currently a lack

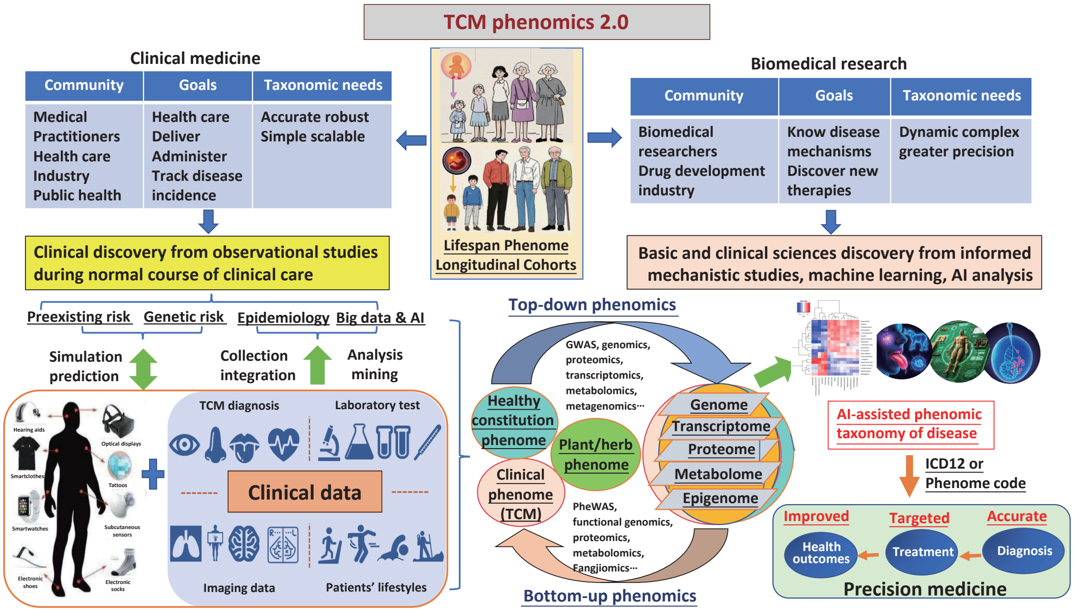

Figure 4 TCM phenomics 2.0

TCM phenomics 2.0 integrates phenomics with digital medicine to investigate the lifespan phenome longditudinal cohorts defined by the integrated criteria of TCM and western medicine. Clinical data from the healthy constitutional phenomes, clinical phenomes and herb/pharmacophenomes as the sources of the best evidence for clinical medicine and biomedical research through top-down or bottom-up phenomics will build a new knowledge network of life science and precision medicine, which will be used as the basis for new taxonomy and classification of disease with phenome codes. The more accurate holistic diagnosis and targeted treatment of disease at the phenomic level will lead to improved health outcomes.

Table 3 The distinct features, the common and overlapping grounds of digital medicine and TCM phenomics

Dimension	Digital medicine	TCM phenomics
Core philosophical foundation	Rooted in western medicine's reductionism and evidence-based medicine: breaks health into measurable variables of phenotypes (e.g., blood pressure and gene expression) and validates interventions via randomized controlled trials (RCTs)	Rooted in TCM's holistic, systemic philosophy: views health as balance between Yin-Yang, Zang-Fu organs, and Qi/Xue; prioritizes Zhenghou differentiation over isolated symptoms
Primary data types	Real-time, dynamic digital data of phenotypes: wearable metrics (HRV and step count), EHRs, imaging (CT/MRI), app-based lifestyle data (diet and stress); focus: quantitative, continuous, and actionable in real time	High-dimensional omics data: genomics, proteomics, metabolomics to quantify TCM Zhenghou TCM-specific qualitative data: tongue coating, pulse quality, subjective symptoms, standardized via digital tools
Technological pillars	Relies on digital infrastructure: IoT (wearables and smart devices), AI/ML (for data analysis/prediction), telehealth platforms, cloud computing (for data storage)	Relies on omics and systems biology: next-generation sequencing (NGS), mass spectrometry (for metabolomics), network biology (to model TCM's systemic effects), and digital tools for TCM symptom standardization
Clinical focus	Emphasizes prevention, acute care augmentation, and remote management: examples include early sepsis detection via AI, remote post-surgery monitoring, and personalized medication dosing	Emphasizes chronic disease management, syndrome validation, and TCM modernization: examples include optimizing herbal formulas for diabetes, validating acupuncture's effects on "Qi stagnation", and integrating TCM with western treatments
Evaluation metrics	Uses phenotypic western medicine clinical endpoints: mortality rate, symptom resolution (e.g., reduced blood glucose), quality of life (QoL) scores (e.g., SF-36), and technical metrics (e.g., AI model accuracy)	Uses TCM-specific + omics endpoints: improvement of Zhenghou (e.g., reduced "Yin deficiency" symptoms), changes in omics markers (e.g., restored metabolomic balance), and TCM QoL scales (e.g., TCM Zhenghou rating scale)

of unified data standards and specifications, which makes it difficult to integrate and analyze the data. Therefore, how to improve data quality and establish unified data standards and specifications is one of the important challenges faced in the integrated development of digital medicine and TCM phenomics.

6.2 Technical and talent issues

The integration of digital medicine and TCM phenomics requires interdisciplinary technical and talent support. Currently, there is a relative shortage of talents who are experts in both digital medical technology and TCM theory and practice. In addition, the application of some advanced digital medical technologies in the field of TCM still faces technical obstacles and needs further research and improvement.

6.3 Ethical and legal issues

With the widespread application of digital medical technology, issues related to patient privacy protection, data security, and ethics are becoming increasingly prominent. In the research of TCM phenomics, how to protect the rights and interests of patients and abide by ethical and legal norms is a problem that needs to be carefully considered and solved.

7 Future prospects for the integrated development of digital medicine and TCM phenomics

7.1 Strengthening data sharing and cooperation

A national data-sharing platform for TCM phenomics should be established to promote data sharing and collaboration among different research institutions. International cooperation should be strengthened by learning from advanced digital medical technologies and experiences abroad, and promote the international development of TCM phenomics (Figure 4).

7.2 Cultivating compound talents

The cultivation of interdisciplinary talent should be strengthened and a comprehensive talent cultivation system should be established. Universities and research institutions should be encouraged to offer relevant majors and courses to cultivate compound talents who are familiar with both digital medical technology and TCM theory and practice, providing talent support for the integrated development of digital medicine and TCM phenomics (Figure 4).

7.3 Improving ethical and legal norms

We should formulate and improve relevant ethical and legal norms, and strengthen the supervision of the application of digital medical technology in the field of TCM. We also need to protect the privacy and rights of patients to ensure that the integrated development of digital medicine and TCM phenomics complies with ethical and legal requirements.

8 Conclusion and prospects

The integrated development of digital medicine and TCM phenomics is an inevitable trend in the modernization of TCM and the integration of TCM and western medicine. Through the application of digital medical technology, new methods and means can be provided for the research of TCM phenomics, promoting the innovative development of TCM. The scholars in the field of TCM phenomics have made significant contributions and provided valuable experience and achievements and prepared well for this integrated development. Although there are still some challenges in the current integrated development of the two fields, with the continuous progress of technology and the cultivation of talents, it is believed that the integration of digital medicine and TCM phenomics will achieve more fruitful results and make greater contributions to the cause of human health.

Fundings

Science and Technology strategic cooperation Programs of Luzhou Municipal People’s Government and Southwest Medical University (2019LZXNYD-P01DUAN), National Key R&D Program of China (2024YFC3505400), and Regional Key R&D Program of Ningxia Hui Autonomous Region (2024BEG01003).

Competing interests

Hao LIANG, Qinghua PENG, and Dayue Darrel DUAN are editorial board members for *Digital Chinese Medicine* and were not involved in the editorial review or the decision to publish this article. All authors declare that there are no competing interests.

References

[1] WANG YL, SHI XM, LI L, et al. The impact of artificial intelligence on traditional Chinese medicine. The American Journal of Chinese Medicine, 2021, 49(6): 1297–1314.

[2] STEINFELDT J, WILD B, BUERGEL T, et al. Medical history predicts phenome-wide disease onset and enables the rapid response to emerging health threats. Nature Communications, 2025, 16(1): 585.

[3] UPADHYAY VR, RAMESH V, KUMAR H, et al. Phenomics in livestock research: bottlenecks and promises of digital phenotyping and other quantification techniques on a global scale. Omics, 2024, 28(8): 380–393.

[4] TIAN Y, YANG ZM, HENG X, et al. Evidence-based medicine review of TCM in combination with chemotherapy and targeted therapy for advanced colorectal cancer. Pharmacology and Clinics of Chinese Materia Medica, 2024, 40(3): 119–123.

[5] LIU ZY, GAO CH, YE LY, et al. Clinical phenome and pharmacophenome of fengre cold. Pharmacology and Clinics of Chinese Materia Medica, 2024, 40(1): 103–106.

[6] ZHU X, WANG FY, MAO J, et al. A protocol for digitalized collection of traditional Chinese medicine (TCM) pulse information using bionic pulse diagnosis equipment. Phenomics, 2023, 3(5): 519–534.

[7] YING WH. Phenomic studies on diseases: potential and challenges. Phenomics, 2023, 3(3): 285–299.

[8] WANG XQ, DU X, CAO Q, et al. Interpretation and application of terms related to phenomics of traditional Chinese medicine. Journal of Nanjing University of Traditional Chinese Medicine, 2023, 39(3): 210–220.

[9] TIAN Y, YANG ZM, DU X, et al. Metabolomic mechanisms for the clinical phenomes of spleen deficiency and dampness-heat syndrome and dampness-heat accumulation syndrome associated with colorectal cancer. Journal of Beijing University of Traditional Chinese Medicine, 2023, 46(12): 1728–1741.

[10] CAO Q, DU X, JIANG XY, et al. Phenome-wide association study and precision medicine of cardiovascular diseases in the post-COVID-19 era. Acta Pharmacologica Sinica, 2023, 44(12): 2347–2357.

[11] ZHANG H, ZHANG JJ, NI WD, et al. Transformer- and generative adversarial network-based inpatient traditional Chinese medicine prescription recommendation: development study. JMIR Medical Informatics, 2022, 10(5): e35239.

[12] YUAN CC, ZHANG WQ, WANG J, et al. Chinese medicine phenomics (Chinmedphenomics): personalized, precise and promising. Phenomics, 2022, 2(6): 383–388.

[13] DENNY JC, COLLINS FS. Precision medicine in 2030-seven ways to transform healthcare. Cell, 2021, 184(6): 1415–1419.

[14] DUAN DD, WANG Z, WANG YY. New omic and network paradigms for deep understanding of therapeutic mechanisms for Fangji of traditional Chinese medicine. Acta Pharmacologica Sinica, 2018, 39(6): 903–905.

[15] ZHANG YP, ZHANG YY, DUAN DD. From genome-wide association study to phenome-wide association study: new paradigms in obesity research. Progress in Molecular Biology and Translational Science, 2016, 140: 185–231.

[16] DUAN DY. Phenomics of cardiac chloride channels: the systematic study of chloride channel function in the heart. The Journal of Physiology, 2009, 587(10): 2163–2177.

[17] DUAN DD. Phenomics of cardiac chloride channels. Comprehensive Physiology, 2013, 3(2): 667–692.

[18] ZHANG BX, ZHOU LJ, CHEN KY, et al. Investigation on phenomics of traditional Chinese medicine from the diabetes. Phenomics, 2024, 4(3): 257–268.

[19] DUAN DD, HAN YS, LI L, et al. Pharmacophenomics: a new paradigm for pharmacology, toxicology, and personalized medicine. Chinese Journal of Pharmacology and Toxicology, 2014, 28(1): 1–9.

[20] YU YN, LIU J, ZHANG L, et al. Clinical Zheng-Hou pharmacology: the missing link between pharmacogenomics and personalized medicine? Current Vascular Pharmacology, 2015, 13(4): 423–432.

[21] DE DOMENICO M, ALLEGRI L, CALDARELLI G, et al. Challenges and opportunities for digital twins in precision medicine from a complex systems perspective. NPJ Digital Medicine, 2025, 8(1): 37.

[22] FORREST IS, PETRAZZINI BO, DUFFY Á, et al. Machine learning-based marker for coronary artery disease: derivation and validation in two longitudinal cohorts. Lancet, 2023, 401(10372): 215–225.

[23] TOPOL EJ. A decade of digital medicine innovation. Science Translational Medicine, 2019, 11(498): eaaw7610.

[24] LIU JJ, BAO CH, ZHANG JX, et al. Artificial intelligence with mass spectrometry-based multimodal molecular profiling methods for advancing therapeutic discovery of infectious diseases. Pharmacology & Therapeutics, 2024, 263: 108712.

[25] ZAMBRANO CHAVES JM, LENCHIK L, GALLEGOS IO, et al. Abdominal CT metrics in 17 646 patients reveal associations between myopenia, myosteatosis, and medical phenotypes: a phenome-wide association study. EBioMedicine, 2024, 103: 105116.

[26] TIAN M, HOOD L, CHITI A, et al. From genome to phenome: opportunities and challenges of molecular imaging. Journal of Nuclear Medicine, 2025, 66(6): 851–855.

[27] TEGTMEYER M, LIYANAGE D, HAN Y, et al. Combining phenomics with transcriptomics reveals cell-type-specific morphological and molecular signatures of the 22q11. 2 deletion. Nature Communications, 2025, 16(1): 6332.

[28] ROSENTHAL EA, WEI WQ, LUO Y, et al. Phenome-wide association study identifies multiple traits associated with a polygenic risk score for colorectal cancer. Human Genomics, 2025, 19(1): 77.

[29] MATENTZOGLU N, BELLO SM, STEFANCSIK R, et al. The Unified Phenotype Ontology: a framework for cross-species integrative phenomics. Genetics, 2025, 229(3): iyaf027.

[30] GERLAI R. Phenomics: fiction or the future? Trends in Neurosciences, 2002, 25(10): 506–509.

[31] HAN YS, LI L, ZHANG YP, et al. Phenomics of vascular disease: the systematic approach to the combination therapy. Current Vascular Pharmacology, 2015, 13(4): 433–440.

[32] DAVIS BD. The isolation of biochemically deficient mutants of bacteria by means of penicillin. Proceedings of the National Academy of Sciences of the United States of America, 1949, 35(1): 1–10.

[33] BAKER M. Big biology: the’omes puzzle. Nature, 2013, 494(7438): 416–419.

[34] DUAN DD, WANG Z, ZHANG BL, et al. Fangjiomics: revealing adaptive omics pharmacological mechanisms of the myriad combination therapies to achieve personalized medicine. Acta Pharmacologica Sinica, 2015, 36(6): 651–653.

[35] MEIER R, WONG W, SRIVATHSAN A, et al. $1 DNA barcodes for reconstructing complex phenomes and finding rare species in specimen-rich samples. Cladistics, 2016, 32(1): 100–110.

[36] MAIORINO E, LOSCALZO J. Phenomics and robust multiomics data for cardiovascular disease subtyping. Arteriosclerosis, Thrombosis, and Vascular Biology, 2023, 43(7): 1111–1123.

[37] CHO J, AHN S, SON DS, et al. Bridging genomics and phenomics of gastric carcinoma. International Journal of Cancer, 2019, 145(9): 2407–2417.

[38] KIEFER AW, ARMITANO-LAGO CN, SATHYAN A, et al. The intelligent phenotypic plasticity platform (IP^3) for precision medicine-based injury prevention in sport. Methods in Molecular Biology, 2022, 2393: 877–903.

[39] KIEFER AW, MARTIN DT. Phenomics in sport: can emerging methodology drive advanced insights? Frontiers in Network Physiology, 2022, 2: 1060858.

[40] KOROMINA M, RAVI A, PANAGIOTAROPOULOU G, et al. Fine-mapping genomic loci refines bipolar disorder risk genes. Nature Neuroscience, 2025, 28(7): 1393–1403.

[41] WANG JL, LU YF, ZHANG R, et al. Modulating and imaging macrophage reprogramming for cancer immunotherapy. Phenomics, 2024, 4(4): 401–414.

[42] CONSORTIUM BOA, HERZOG CMS, GOEMINNE LJE, et al. Challenges and recommendations for the translation of biomarkers of aging. Nature Aging, 2024, 4(10): 1372–1383.

[43] CHEN SP, LIU J, TANG NN, et al. Cancer phenomics research

hotspots and development trends: a bibliometric analysis from 2000 to 2023. Discover Oncology, 2024, 15(1): 811.

[44] DASGUPTA S. Thinking beyond disease silos: dysregulated genes common in tuberculosis and lung cancer as identified by systems biology and machine learning. Omics, 2024, 28(7): 347–356.

[45] DASGUPTA S. Next-generation cancer phenomics: a transformative approach to unraveling lung cancer complexity and advancing precision medicine. Omics, 2024, 28(12): 585–595.

[46] DING ZH, CHEN WJ, WU H, et al. Integrative network fusion-based multi-omics study for biomarker identification and patient classification of rheumatoid arthritis. Chinese Medicine, 2023, 18(1): 48.

[47] TAO XX, WANG XQ, BAI X, et al. Analytical research of graph, text, language, math of Xiang thinking in traditional Chinese medicine. China Journal of Traditional Chinese Medicine and Pharmacy, 2023, 38(4): 1730–1733.

[48] SHAO JW, QIU XY, ZHANG LH, et al. Multi-layered computational gene networks by engineered tristate logics. Cell, 2024, 187(18): 5064–5080. e14.

[49] BROUWER RM, KLEIN M, GRASBY KL, et al. Genetic variants associated with longitudinal changes in brain structure across the lifespan. Nature Neuroscience, 2022, 25(4): 421–432.

[50] POLDRACK RA, LAUMANN TO, KOYEJO O, et al. Long-term neural and physiological phenotyping of a single human. Nature Communications, 2015, 6: 8885.

[51] CONSORTIUM B, ANTTILA V, BULIK-SULLIVAN B, et al. Analysis of shared heritability in common disorders of the brain. Science, 2018, 360(6395): eaap8757.

[52] LU ZL, MO SL, XIE D, et al. Polyclonal-to-monoclonal transition in colorectal precancerous evolution. Nature, 2024, 636(8041): 233–240.

[53] AREND D, PSAROUDAKIS D, MEMON JA, et al. From data to knowledge—big data needs stewardship, a plant phenomics perspective. The Plant Journal, 2022, 111(2): 335–347.

[54] CUELLO HA, SINHA S, VERHAGEN AL, et al. Human-specific elimination of epithelial Siglec-XII suppresses the risk of inflammation-driven colorectal cancers. JCI Insight, 2024, 9(16): e181539.

[55] ZHOU R, JIANG FL, NIU LF, et al. Increase crop resilience to heat stress using omic strategies. Frontiers in Plant Science, 2022, 13: 891861.

[56] HAN SJ, XU QQ, DU YW, et al. Single-cell spatial transcriptomics in cardiovascular development, disease, and medicine. Genes & Diseases, 2024, 11(6): 101163.

[57] HOLMES E, WIJEYESEKERA A, TAYLOR-ROBINSON SD, et al. The promise of metabolic phenotyping in gastroenterology and hepatology. Nature Reviews Gastroenterology & Hepatology, 2015, 12(8): 458–471.

[58] LIU M, LI Y, SUN LY, et al. Integrating multi-organ imaging-derived phenotypes and genomic information for predicting the occurrence of common diseases. Bioengineering, 2024, 11(9): 872.

[59] RUBINO F, CUMMINGS DE, ECKEL RH, et al. Definition and diagnostic criteria of clinical obesity. The Lancet Diabetes & Endocrinology, 2025, 13(3): 221–262.

[60] ZENG CJ, BASTARACHE LA, TAO R, et al. Association of pathogenic variants in hereditary cancer genes with multiple diseases. JAMA Oncology, 2022, 8(6): 835–844.

[61] DENNY JC, BASTARACHE L, RODEN DM. Phenome-wide association studies as a tool to advance precision medicine. Annual Review of Genomics and Human Genetics, 2016, 17: 353–373.

[62] SUN M, LIANG HR, CHEN Y, et al. A retrospective comparison of hyperbaric oxygen and core decompression for mild to moderate avascular necrosis of the femoral head. Medical Gas Research, 2026, 16(1): 1–5.

[63] DUAN DD. A phenomic perspective of the genuine Chinese medicinal materials. The Professional Committee on Multi-dimensional Evaluation of Genuine Medicinal Materials of the World Federation of Chinese Medicine Societies, 2022.

[64] DUAN DD. A new field of research on the formation mechanism of geo-authentic medicinal materials in traditional Chinese medicine: TCM pharmacophenomics. The Professional Committee on Multi-dimensional Evaluation of Genuine Medicinal Materials of the World Federation of Chinese Medicine Societies, 2024.

[65] GILL T, GILL SK, SAINI DK, et al. A comprehensive review of high throughput phenotyping and machine learning for plant stress phenotyping. Phenomics, 2022, 2(3): 156–183.

[66] LI DL, QUAN CQ, SONG ZY, et al. High-throughput plant phenotyping platform (HT3P) as a novel tool for estimating agronomic traits from the lab to the field. Frontiers in Bioengineering and Biotechnology, 2021, 8: 623705.

[67] RESENDE RT, HICKEY L, AMARAL CH, et al. Satellite-enabled enviromics to enhance crop improvement. Molecular Plant, 2024, 17(6): 848–866.

[68] REYNOLDS MP, LEWIS JM, AMMAR K, et al. Harnessing translational research in wheat for climate resilience. Journal of Experimental Botany, 2021, 72(14): 5134–5157.

[69] TAO HY, XU S, TIAN YC, et al. Proximal and remote sensing in plant phenomics: 20 years of progress, challenges, and perspectives. Plant Communications, 2022, 3(6): 100344.

[70] DEERY DM, JONES HG. Field phenomics: will it enable crop improvement? Plant Phenomics, 2021, 2021: 9871989.

[71] YANG WN, FENG H, ZHANG XH, et al. Crop phenomics and high-throughput phenotyping: past decades, current challenges, and future perspectives. Molecular Plant, 2020, 13(2): 187–214.

[72] ZHAO FL, WANG YX, ZHENG JS, et al. A genome-wide survey of copy number variations reveals an asymmetric evolution of duplicated genes in rice. BMC Biology, 2020, 18(1): 73.

[73] SOOD S, JOSHI DC, CHANDRA AK, et al. Phenomics and genomics of finger millet: current status and future prospects. Planta, 2019, 250(3): 731–751.

[74] SHEN SQ, ZHAN CS, YANG CK, et al. Metabolomics-centered mining of plant metabolic diversity and function: past decade and future perspectives. Molecular Plant, 2023, 16(1): 43–63.

[75] CHEN BB, WANG JQ, MENG XH, et al. Putative candidate drug targets for sarcopenia-related traits identified through mendelian randomization analysis of the blood proteome. Frontiers in Genetics, 2022, 13: 923429.

[76] PAUX E, LAFARGE S, BALFOURIER F, et al. Breeding for economically and environmentally sustainable wheat varieties: an integrated approach from genomics to selection. Biology, 2022, 11(1): 149.

[77] REBETZKE GJ, JIMENEZ-BERNI J, FISCHER RA, et al. Review: high-throughput phenotyping to enhance the use of crop genetic resources. Plant Science, 2019, 282: 40–48.

[78] COSTA-NETO G, FRITSCHE-NETO R, CROSSA J. Nonlinear kernels, dominance, and envirotyping data increase the

accuracy of genome-based prediction in multi-environment trials. Heredity, 2021, 126(1): 92–106.

[79] WANG Z, DUAN DD, WANG YY. Editorial: combination therapy of vascular diseases and fangjiomics: when west meets east in the era of phenomics. Current Vascular Pharmacology, 2015, 13(4): 420–422.

[80] SONG C, LIU F, MEI YL, et al. Integrated metagenomic and metabonomic mechanisms for the therapeutic effects of Duhuo Jisheng decoction on intervertebral disc degeneration. PLoS One, 2024, 19(10): e0310014.

[81] PANG B, LI QW, QIN YL, et al. Traditional Chinese medicine for diabetic retinopathy: a systematic review and meta-analysis. Medicine, 2020, 99(7): e19102.

[82] ZHA LH, HE LS, LIAN FM, et al. Clinical strategy for optimal traditional Chinese medicine (TCM) herbal dose selection in disease therapeutics: expert consensus on classic TCM herbal formula dose conversion. The American Journal of Chinese Medicine, 2015, 43(8): 1515–1524.

[83] HUANG ZQ, FAN XM, WANG YM, et al. A new method to evaluate the dose-effect relationship of a TCM formula Gegen Qinlian Decoction: "Focus" mode of integrated biomarkers. Acta Pharmacologica Sinica, 2017, 38(8): 1141–1149.

[84] JIN D, HUANG WJ, MENG X, et al. Chinese herbal medicine TangBi Formula treatment of patients with type 2 diabetic distal symmetric polyneuropathy disease: study protocol for a randomized controlled trial. Trials, 2017, 18(1): 631.

[85] FANG XY, MIAO LX, ZHANG YJ, et al. Traditional Chinese medicine phenomics research on glycolipid metabolism disorder: a review. Digital Chinese Medicine, 2025, 8(1): 49–58.

[86] AHMAD F, MUHMOOD T. Clinical translation of nanomedicine with integrated digital medicine and machine learning interventions. Colloids and Surfaces B, Biointerfaces, 2024, 241: 114041.

[87] ANTO A, SOUSA-PINTO B, BOUSQUET J. Anaphylaxis and digital medicine. Current Opinion in Allergy and Clinical Immunology, 2021, 21(5): 448–454.

[88] ATREJA A, FRANCIS S, KURRA S, et al. Digital medicine and evolution of remote patient monitoring in cardiac electrophysiology: a state-of-the-art perspective. Current Treatment Options in Cardiovascular Medicine, 2019, 21(12): 92.

[89] BERISHA V, KRANTSEVICH C, RICHARD HAHN P, et al. Digital medicine and the curse of dimensionality. NPJ Digital Medicine, 2021, 4(1): 153.

[90] CORAVOS A, GOLDSACK JC, KARLIN DR, et al. Digital medicine: a primer on measurement. Digital Biomarkers, 2019, 3(2): 31–71.

[91] BOTTLES K. Is digital medicine coming soon? Physician Executive, 2013, 39(4): 22–24, 26–27.

[92] CHEN Y, XIAO X, HE Q, et al. Knowledge mapping of digital medicine in cardiovascular diseases from 2004 to 2022: a bibliometric analysis. Heliyon, 2024, 10(3): e25318.

[93] FOGEL AL, KVEDAR JC. Artificial intelligence powers digital medicine. NPJ Digital Medicine, 2018, 1: 5.

[94] WAN JJ, ZHANG Z, WU CN, et al. Astragaloside IV derivative HHQ16 ameliorates infarction-induced hypertrophy and heart failure through degradation of lncRNA4012/9456. Signal Transduction and Targeted Therapy, 2023, 8(1): 414.

[95] YUE YT, LI N, ZHANG GB, et al. Automatic segmentation of esophageal gross tumor volume in ^{18}F-FDG PET/CT images via GloD-LoATUNet. Computer Methods and Programs in Biomedicine, 2023, 229: 107266.

[96] NAIR JKR, SAEED UA, MCDOUGALL CC, et al. Radiogenomic models using machine learning techniques to predict EGFR mutations in non-small cell lung cancer. Canadian Association of Radiologists Journal, 2021, 72(1): 109–119.

[97] CHEN T, ZHU SJ, XU S, et al. Resting-state fMRI reveals changes within the anxiety and social avoidance circuitry of the brain in mice with psoriasis-like skin lesions. Experimental Dermatology, 2023, 32(11): 1900–1914.

[98] ALLAIRE P, ELSAYED NS, BERG RL, et al. Phenome-wide association study identifies new clinical phenotypes associated with *Staphylococcus aureus* infections. PLoS One, 2024, 19(7): e0303395.

[99] ZHANG K, LIU XH, SHEN J, et al. Clinically applicable AI system for accurate diagnosis, quantitative measurements, and prognosis of COVID-19 pneumonia using computed tomography. Cell, 2020, 182(5): 1360.

[100] BRASIER N, WANG J, GAO W, et al. Applied body-fluid analysis by wearable devices. Nature, 2024, 636(8041): 57–68.

[101] OOKA T. The era of preemptive medicine: developing medical digital twins through omics, IoT, and AI integration. JMA Journal, 2025, 8(1): 1–10.

[102] LI XX, LOSCALZO J, MAHMUD AKMF, et al. Digital twins as global learning health and disease models for preventive and personalized medicine. Genome Medicine, 2025, 17(1): 11.

[103] ZHANG Y, QIN GR, AGUILAR B, et al. A framework towards digital twins for type 2 diabetes. Frontiers in Digital Health, 2024, 6: 1336050.

[104] LAUBENBACHER R, MEHRAD B, SHMULEVICH I, et al. Digital twins in medicine. Nature Computational Science, 2024, 4(3): 184–191.

[105] ZHANG K, ZHOU HY, BAPTISTA-HON DT, et al. Concepts and applications of digital twins in healthcare and medicine. Patterns, 2024, 5(8): 101028.

[106] WANG Q. From digits towards digitization: the past, present, and future of traditional Chinese medicine. Digital Chinese Medicine, 2025, 8(1): 4–19.

[107] YE LL, PENG QH, DUAN DD. Unveiling the digital renaissance of traditional Chinese medicine: a leap towards holistic healthcare and precision medicine. Digital Chinese Medicine, 2025, 8(1): 1–3.

[108] LIU ZC, WANG ZL, HUANG CY, et al. Duhuo Jisheng Decoction inhibits SDF-1-induced inflammation and matrix degradation in human degenerative nucleus pulposus cells *in vitro* through the CXCR4/NF-κB pathway. Acta Pharmacologica Sinica, 2018, 39(6): 912–922.

[109] VAN BEZOUW RFHM, KEURENTJES JJB, HARBINSON J, et al. Converging phenomics and genomics to study natural variation in plant photosynthetic efficiency. The Plant Journal: for Cell and Molecular Biology, 2019, 97(1): 112–133.

[110] GE CY, LUO LQ, ZHANG JL, et al. FRL: an integrative feature selection algorithm based on the fisher score, recursive feature elimination, and logistic regression to identify potential genomic biomarkers. BioMed Research International, 2021, 2021: 4312850.

[111] HARDER N, SCHÖNMEYER R, NEKOLLA K, et al. Automatic discovery of image-based signatures for ipilimumab response prediction in malignant melanoma. Scientific Reports, 2019, 9(1): 7449.

[112] MA CC, QIU L. Unveiling the power of R: a comprehensive perspective for laboratory medicine data analysis. Clinical Chemistry and Laboratory Medicine, 2025, 63(8): 1458–1471.

[113] DING ZK, FAHEY PG, PAPADOPOULOS S, et al. Functional connectomics reveals general wiring rule in mouse visual cortex. Nature, 2025, 640(8058): 459–469.

[114] WEN D, TAN RZ, ZHAO CY, et al. *Astragalus mongholicus* Bunge and *Panax notoginseng* (Burkill) F.H. Chen formula for renal injury in diabetic nephropathy—*in vivo* and *in vitro* evidence for autophagy regulation. Frontiers in Pharmacology, 2020, 11: 732.

中医表型组学2.0：与数字医学的融合发展

许敏[a, b†], 邵心怡[a, b†], 郭东更[c], 颜晓静[b, d], 王磊[b, d], 杨涛[b, e], 梁昊[f], 彭清华[f*], 叶玲玉[a, b, f*], 程海波[b, g*], 段大跃[a, b, c, f*]

a. 南京中医药大学中西医结合学院, 江苏 南京 210030, 中国
b. 南京中医药大学中医药表型组学研究院, 江苏 南京 210030, 中国
c. 宁夏自身免疫性疾病精准医学重点实验室, 宁夏回族自治区 银川 750002, 中国
d. 南京中医药大学附属常州医院, 常州市孟河医派人用经验研究与转化重点实验室, 江苏 常州 213003, 中国
e. 南京中医药大学人工智能与信息技术学院, 江苏 南京 210030, 中国
f. 湖南中医药大学中医证候表型组学研究中心, 湖南 长沙 410208, 中国
g. 江苏省中医药防治肿瘤协同创新中心, 江苏 南京 210029, 中国

【摘要】现代西方医学通常侧重于治疗特定症状或疾病，中医学则强调人体各个系统在外部环境下的相互联系，并采用整体方法来预防和治疗疾病。2008年，表型组学作为一门新学科被首次引入中医学领域，它基于表型组学，研究在中医学理论和实践范围内人体临床表型组的综合动态变化规律。虽然中医表型组学1.0初步建立了以“证候”（中医学对临床表型组的定义）为核心的临床表型组体系，但在数据标准化、机制阐释和精准干预方面仍存在瓶颈。在此，我们系统阐述了在“中医表型组学2.0”框架下，数字医学与中医表型组学融合的理论基础、技术路径及未来挑战。该框架以人工智能、可穿戴设备、医疗数字孪生和多组学整合等数字医学技术为支撑，旨在构建“证候-表型组-机制-干预”的闭环系统，实现疾病诊疗的数字化、标准化和精准化。数字医学与中医表型组学的融合，不仅推动了中医学理论与实践的现代化和科学化转型，也为精准医学提供了新范式。在实践中，数字工具有助于多源临床数据的获取和标准化，而人工智能与大数据算法则助力揭示临床证候表型组与分子机制之间的关联，从而提高诊断、疗效评估和个性化干预的科学严谨性。尽管如此，挑战依然存在，包括数据质量与标准化问题、跨学科人才短缺以及伦理和法律规范不完善等。未来的发展需要建立国家数据共享平台、加强国际合作、培养跨学科专业人才，并完善伦理和法律框架。最终，这种方法旨在构建以表型组为核心的新型疾病识别与分类体系，实现中医学诊疗模式的传承、创新与现代化。

【关键词】数字医学；中医学；表型组学；中医药现代化；人工智能