

Integrative network analysis

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Integrative network analysis: Bridging the gap between Western medicine and traditional Chinese medicine

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There is a global movement calling for the integration of Western medicine (WM) and traditional Chinese medicine (TCM)^[1]. The World Health Organization suggests that health care would be improved by integrating traditional and complementary medicines into the practices of health care service delivery and self-health care^[1]. The WM and TCM are commonly integrated in the contemporary practice of medicine in China. About 90% of the general hospitals and 75% of health centers have TCM departments^[2]. Even in WM hospitals, around 40% of the medicines prescribed are TCM. Similarly, in the TCM hospitals 40% of all prescribed drugs are WM^[3]. Meanwhile, over 80% of Chinese patients have received TCM treatment at some point in their lives^[2]. However, differences exist in typical use of prescribed medications between WM and TCM and can result in the incorrect use, thus leading to concerns about the efficacy and safety of integrative treatment^[4].

WM and TCM are different health care systems that developed within the context of different cultures and perspectives on the natural world. The reductionist approach forming the foundation of Western biomedical sciences, arises from ancient Greece and has generated tremendous knowledge of anatomy, physiology, histology, biochemistry and genetics. In contrast, the *Yin/Yang* theory, stating that everything in the world is interconnected in a dynamic balance, lays the foundations of TCM's philosophy, and has been a guiding principle for thousands of years^[5,6].

In TCM, the human body is comprised of functional systems that interact with each other and with the external environment. The healthy body is a well balance system, however illness or injury will disrupt the balance. The pattern of how the balance is disrupted, or more specifically, the comprehensive summary of clinical symptoms and signs gathered by a practitioner using inspection,

auscultation, olfaction, interrogation and palpation of the pulses, is called *Zheng*. The diagnosis of the particular *Zheng* is the first step in TCM treatment. The practitioner will choose compound formulae (*Fufang*), which are designed under the principle “emperor, minister, assistant, courier” (*Jun Chen Zuo Shi*), for the treatment of the particular *Zheng*^[7]. Therefore, correctly explaining *Zheng* and *Fufang* using modern concepts is a key issue in the integration of WM and TCM.

The development of -omics technologies and network pharmacology in recent years offers an opportunity to bridge the gap between WM and TCM. Omics technologies are high-throughput technologies that purify, identify and characterize DNA, RNA, proteins and other kinds of molecules. These methods are usually automated, allowing rapid analysis of a very large number of samples. Many kinds of -omics technologies, including transcriptomics, proteomics, metabolomics, *etc.*, have been introduced to the study of TCM.

We investigated the cold pattern (*Han Zheng*) and heat pattern (*Re Zheng*) of rheumatoid arthritis in TCM using gene expression microarray, which is one kind of transcriptomics technology. This research revealed that the cold pattern was related to a Toll-like receptor signaling pathway, while the heat pattern was related to a calcium signaling pathway, cell adhesion molecules pathway, PPAR signaling pathway and fatty acid metabolism pathway^[8]. Lian *et al*^[9] studied hypertension with blood stasis syndrome (*Xue Yu Zheng*) using digital gene expression sequencing, which is another kind of transcriptomics technology, and identified genes related to blood stasis syndrome.

Fan *et al*^[10] identified potential biomarkers for the TCM syndromes of tuberculosis and established the diagnostic serum proteomic model using proteomic technologies, like matrix-assisted laser desorption–ionization time of flight mass spectrometer and liquid chromatograph–tandem mass spectrometer^[10]. Xu *et al*^[11] identified a new potential biomarker of “toxin syndrome” in coronary heart disease patients using a proteomics method^[11].

Using metabolomics methods, we revealed that betaine and phosphatidylcholine were potential biomarkers for the toxic responses of processed *Aconitum carmichaeli* Debx (*Baifupian*)^[12]. Tian *et al*^[13] performed dynamic analysis of the endogenous metabolites in patients suffering from depression who were treated with TCM formula *Xiaoyaosan*, using urinary nuclear magnetic resonance-based metabolomics, and identified metabolites that changed significantly during the course of the treatment with *Xiaoyaosan*^[13].

In general, the -omics technologies facilitate the accumulation of understanding of *Zheng* and *Fufang*

at the molecular level. Network pharmacology, a strategy for drug design that encompasses systems biology, network analysis, connectivity, redundancy and pleiotropy^[14], helps to integrate this information into human disease networks and drug pharmacology networks. *Zheng* was illustrated by molecular networks of human diseases^[15], while *Fufang* was illustrated in the form of TCM pharmacology networks^[16]. Subsequently, with the help of computational methods, the WM and TCM were evaluated using molecular networks as a common standard^[17]. Thus, the gap between WM and TCM could be bridged by the integrative molecular network of diseases and pharmacology. For example, Li *et al*^[18] studied *Qishen Yiqi*, a Chinese medicine, using network pharmacology and revealed its underlying multi-compound, multi-target, multi-pathway mode of action^[18]. Thus the activity of a TCM drug was illustrated through modern concepts widely used in WM. In conclusion, the integrative analysis of human disease networks, WM pharmacology networks and TCM pharmacology networks (Figure 1) can help to find a common language through which to understand WM and TCM, bridging current gaps, and promoting truly integrative treatment.

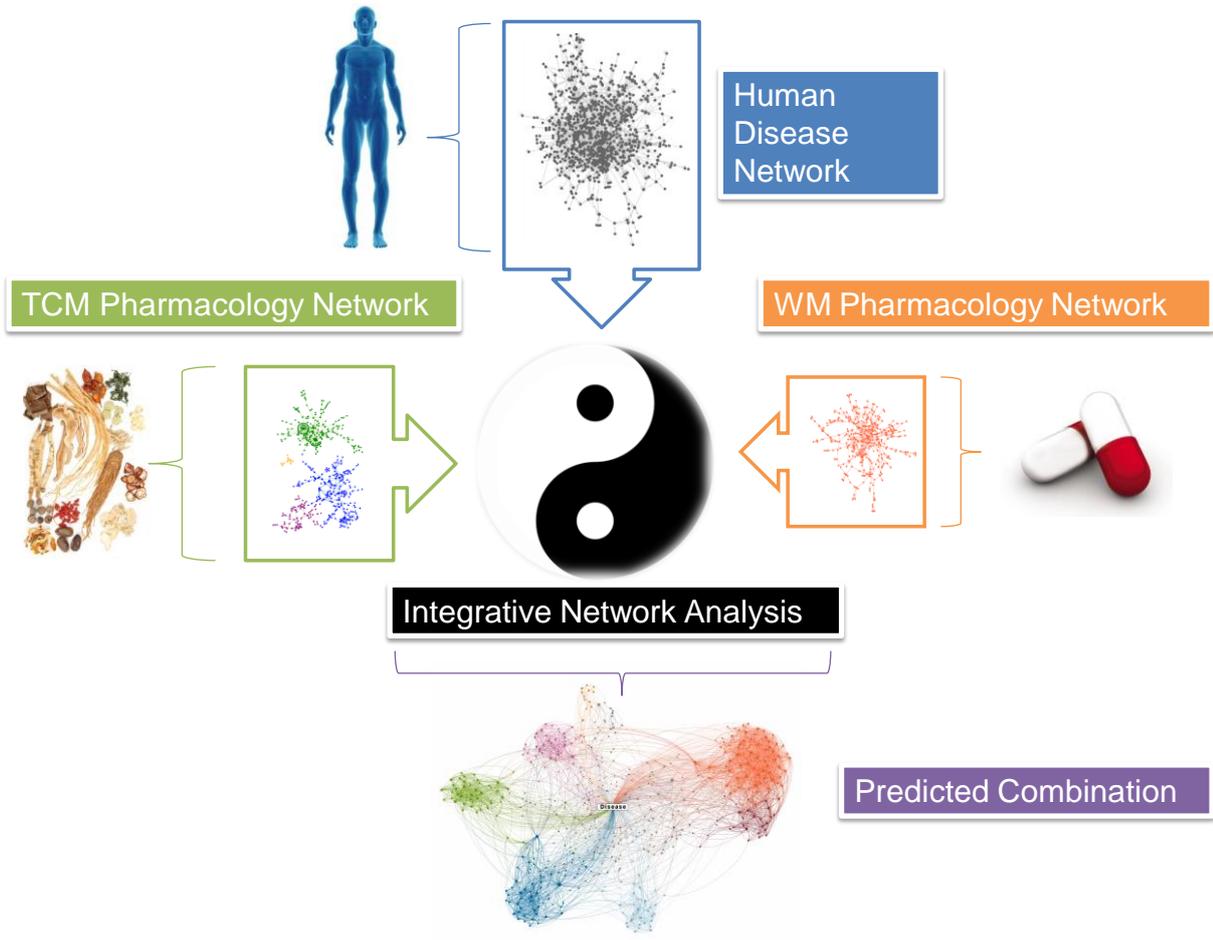


Figure 1 The overview of the integrative analysis of human disease networks, WM pharmacology networks and TCM pharmacology networks.

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