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Editorial

New progress of interdisciplinary research between network toxicology, quality markers and TCM network pharmacology

Traditional Chinese medicine (TCM) has been applied in treating various complex diseases for thousands of years, and has been widely known for its distinguished holistic therapeutic strategy. How to ensure the safety and lower the risk of toxic effects of TCM herbal formulae are of critical importance during the process of the modernization of TCM industry. Due to the complex composition of TCM herbal formulae and its sophisticated interaction between the biomolecules inside the body, there is an urgent need for systematic methodology in the in-depth investigation on TCM herbal formulae regarding its mechanism of action (MoA), which is the basis for its toxicology assessment (Li et al., 2019a; Liu et al., 2017b) and quality control (Liu et al., 2017a).

As a new research paradigm for drug discovery and development, network pharmacology has aroused interests among researchers in the area of TCM since its emergence about 10 years ago (Hopkins, 2007; Li, 2007; Li et al., 2007, 2002). In particular, we proposed the new concept of "network target" (Li, 2011; Li et al., 2011), an elementary entity for the development of TCM Network Pharmacology (TCM-NP), which offer the opportunity to describe and measure the emergence of an ON or OFF effect on the level of network modules, revealing the biological basis of both diseases and drugs by integrating multi-level omics data and temporal-spatial biomedical data with network analysis (Guo et al., 2017; Li, 2015). The network target may offer a powerful computable measurement for evaluating the complex MoA underlying the TCM compounds, herbs and formulae and thus help shift the classical "one target, one drug" research paradigm towards the new "network target, multicomponent therapeutics" strategy. It is suitable for exploring the mysteries of TCM from both the conceptual and the applicable perspective (Li & Zhang, 2013), including toxicology assessment and quality control of the TCM herbal formulae.

To answer the urgent needs in the field of TCM toxicology and quality control, new concepts are continuing to be put forwards, showing compatibility with the strategy of "network target, multicomponent therapeutics", while forming the hot research field together with network pharmacology. In this issue, two reviews (Li et al., 2019b; Wang et al., 2019) on quality marker and network toxicology will be published, discussing the new progress on these two booming research fields, and their integration potential with network pharmacology.

The new concept of the quality marker (Q-marker) was first proposed by Liu et al. in 2016 (Liu et al., 2017a; Liu, Guo, & Liu, 2018), establishing a valuable framework for the rational quality control of TCM. The framework emphasizes both the transitivity and traceability along the intact life-cycle of the TCM herbs, decoction-pieces and formulae. In the recent review (Wang et al., 2019), the role of network pharmacology is further demonstrated and integrated into the strategy for Q-marker prediction and application. The "effect-ingredient-target-fingerprint" is developed as the basis for network pharmacology analysis, and the predicted Q-markers based on the fingerprint are further validated both on the theoretical level of TCM compatibility rules, and on the experimental level of pharmacokinetics, pharmacodynamics and toxicology.

Network toxicology is another important concept, characterizing the interaction and regulation of potential poisonous materials through network models (Liu et al., 2015), which may lead to precise prediction of the toxic components, indication of the biomarkers, and a deeper understanding of MoA related to the side effect. As reviewed in the recent work (Li et al., 2019b), metabolomics with the help of liquid chromatography-mass spectrometry (LC-MS), which provide big data on endogenous metabolites, serve as a powerful method facilitating the network building and analysis. The "toxicity-target-drugs" network is built for network pharmacology analysis, while metabolomics help with the in-depth interrogation of the network and more accurate infer of the toxic components.

There are still many theoretical, methodological and practical challenges that need to be addressed for future developments of the current research area. With the integration of more cutting-edge assays and artificial intelligence, as well as the evolvement of the interdisciplinary research fields of TCM-NP, especially with network toxicology and Q-markers, we are expecting the fast extending of the research area, more and more successful application cases, and eventually innovative breakthroughs for both traditional and conventional medicines.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Guo, Y. C., Nie, Q., MacLean, A. L., Li, Y. D., Lei, J. Z., & Li, S. (2017). Multiscale modeling of inflammation-induced tumorigenesis reveals competing oncogenic and oncoprotective roles for inflammation. *Cancer Research, 77*(22), 6429–6441.

Hopkins, A. L. (2007). Network pharmacology. *Nature Biotechnology, 25*, 1110–1111.

Li, S. (2007). Framework and practice of network-based studies for Chinese herbal formula. *Journal of Integrative Medicine, 5*(5), 489–493.

Li, S. (2011). Network target: A starting point for traditional Chinese medicine network pharmacology. *China Journal of Chinese Materia Medica, 36*(15), 2017–2020.

Li, S. (2015). Mapping ancient remedies: Applying a network approach to traditional Chinese medicine. *Science (New York, N.Y.), 350*(6262 Suppl.), S72–S74.

Li, S., Wang, Y., Ji, L., & Li, Y. (2002). A discussion and case study of complexities in traditional Chinese medicine. *Acta Simulata Systematica Sinica, 14*(11), 1429–1432.

Li, S., & Zhang, B. (2013). Traditional Chinese medicine network pharmacology: Theory, methodology and application. *Chinese Journal of Natural Medicines, 11*(2), 110–120.

Li, S., Zhang, B., & Zhang, N. (2011). Network target for screening synergistic drug combinations with application to traditional Chinese medicine. *BMC Systems Biology, 5*(Suppl. 1), S10.

Li, S., Zhang, Z. Q., Wu, L. J., Zhang, X. G., Li, Y. D., & Wang, Y. Y. (2007). Understanding Zheng in traditional Chinese medicine in the context of neuro-endocrine-immune network. *IET Systems Biology, 1*(1), 51–60.

Li, X. Y., Jin, X., Li, Y. Z., Gao, D. D., Liu, R., & Liu, C. X. (2019a). Network toxicology and LC-MS-based metabolomics: New approaches for mechanism of action of toxic components in traditional Chinese medicines. *Chinese Herbal Medicines, 11*(4), 357–363.

Li, Y. B., Zhang, Y., Wang, Y. M., Li, Y. M., Yang, F. F., & Zhang, P. J. (2019b). A strategy for the discovery and validation of toxicity quality marker of Chinese medicine based on network toxicology. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, 54*, 365–370.

Liu, C. X., Cheng, Y. Y., Guo, D. A., Zhang, T. J., Li, Y. Z., & Hou, W. B. (2017a). A new concept on quality marker for quality assessment and process control of Chinese medicines. *Chinese Herbal Medicines, 9*(1), 3–13.

Liu, C. X., Guo, D. A., & Liu, L. (2018). Quality transitivity and traceability system of herbal medicine products based on quality markers. *Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, 44*, 247–257.

Liu, C. X., Liu, R., Fan, H. R., Xiao, X. F., Chen, X. P., & Xu, H. Y. (2015). Network pharmacology bridges traditional application and modern development of traditional Chinese medicine. *Chinese Herbal Medicines, 7*(1), 3–17.

Liu, S., Li, F., Li, Y., Li, W. F., Xu, J. K., & Du, H. (2017b). A review of traditional and current methods used to potentially reduce toxicity of aconitum roots in traditional Chinese medicine. *Journal of Ethnopharmacology, 207*, 237–250.

Wang, Y. L., Cui, T., Li, Y. Z., Liao, M. L., Zhang, H. B., & Hou, W. B. (2019). Prediction of quality markers of traditional Chinese medicines based on network pharmacology. *Chinese Herbal Medicines, 11*(4), 349–356.