

Editorials

TCM Network Pharmacology

The status quo, challenges and promises



Professor Shao Li Ministry of Education Key Laboratory of Bioinformatics TCM-X Center / Bioinformatics Division, BNRIST Department of Automation Tsinghua University, Beijing, China. E-mail: <u>shaoli@mail.tsinghua.edu.cn</u>

Network pharmacology as a new paradigm for drug discovery and development, has aroused interests among researchers since its emergence about 10 years ago. The aim of network pharmacology is to reveal the biological bases of both diseases and drugs by integrating omics technologies, big biomedical data and network analysis methods. In fact, our lab started research on traditional Chinese medicine (TCM) in terms of system and network since the 1990s, and had already published a series of works [1,2] before the term of "network pharmacology" was raised by Hopkins AL [3]. For instance, a biomolecular network for determining the Cold / Hot ZHENG (syndrome) in TCM was constructed and validated by follow-up Cold / Hot herbal formula experiments [2]. Notably, network pharmacology holds a systematic sight in understanding the disease mechanism and drug efficacy, and poses an update to the classical pharmacology which obeys reductionismIn particular, we proposed for the first time the new concept of "network target" [4,5], an elementary entity for the development of TCM network pharmacology (TCM-NP). It helps shift the drug research paradigm from the classical "one target, one drug" to "network target, multicomponent therapeutics" strategy, and may shed light on future drug development.

TCM has been applied in the treatment of various complex diseases for thousands of years and is widely known for its distinguished holistic therapeutic strategy. TCM herbal formulae are prescribed by TCM practitioners to systematically balance the health status of patients. However, the molecular mechanisms of TCM are still not elucidated, partially because of the complex composition of TCM herbs and the sophisticated interaction between TCM and body. According to the modern studies, most of TCM herbs and compounds may exhibit their efficacy through weakly binding multi-targets. In that case, the characteristics of TCM may not be completely described and measured by the reductionist mode based on a single target. There is an urgent need for systematic methodology in the in-depth mechanistic investigation on TCM. The arrival of TCM-NP emphasizes understanding the mechanism of TCM in the aspect of the interaction between pharmacological network and disease network, which accords with the holistic therapeutic thinking of TCM. Also, the network itself may offer a powerful computable measurement for evaluating the complex mechanism of action (MoA) underlying the TCM compounds, herbs and formulae, and thus is suitable for exploring the mysteries of TCM from both the conceptual and the applicable perspective [6].

TCM network pharmacology, a booming research field which combines TCM with network pharmacology, is promising to efficiently overcome the bottleneck of TCM pharmacology research. What is worth mentioning is that, a continuous effort has been made on the development and dissemination of TCM-NP in China since the late 90s. For example, in our lab, an "effect-on/off" switch model suitable for understanding the MoA of TCM formulae was proposed based on the key concepts of "network target" [7]. As for the applications, the network regulation mechanisms of herbal compounds [8,9], classical formulae including Liu-Wei-Di-Huang (a Yin-nourishing formula) [10] and Qin-Luo-Yin (a Hot-cooling formula) [11], as well as TCM syndromes [12] and complex diseases [13], were analysed by TCM-NP approaches. Some of the results were highlighted by the white paper of NIH/NCI Cancer Complementary and Alternative Medicine Therapeutics Research [14].



For future development of TCM-NP, there are still some theoretical, methodological and applied problems need to be paid attention to. In the aspect of basic theories, the conceptual paradigm of TCM-NP based on "network target" can be further explored and enriched with gradually profound understanding of the correlation between TCM and complex diseases. In the aspect of methodologies, to achieve better performance in correlating the MoA of TCM with the perturbation in disease network, more comprehensive and powerful computational, experimental, and clinical methods with TCM-NP characteristics need to be developed. This may require the researchers to take full advantage of biological big data, cutting-edge assay methods and artificial intelligence for drug development and discovery. In the aspect of applications, more investigations for appropriate validation methods of TCM-NP research results need to be operated.

As a novel approach to decipher the mysteries of TCM developed in the big data and artificial intelligence era, TCM-NP is advancing rapidly and attracting more and more attention from traditional medicine researchers. It is noteworthy that TCM-NP not only promotes the inheritance and development of TCM, but also bring positive impacts on the research of traditional medicine worldwide. With the evolvement of the interdisciplinary research fields of TCM-NP like system biology, bioinformatics and TCM pharmacology, the connotation and application of TCM-NP are extending fast. Moreover, there are more and more evidences indicating the reliability and effectiveness of TCM-NP in uncovering the underlying mechanism of TCM and in further TCM development. In conclusion, TCM-NP may provide an innovative breakthrough point for modernization of TCM, and may contribute to the progress of both traditional and conventional medicines.

Further readings:

- 1. Li S, Zhang Z Q, Wu L J, et al. Understanding ZHENG in traditional Chinese medicine in the context of neuro-endocrineimmune network. IET systems biology, 2007, 1(1): 51-60.
- Li S. Framework and practice of network-based studies for Chinese herbal formula. Journal of Chinese Integrative Medicine 2007;5(5):489-493
- 3. Hopkins AL. Network pharmacology. Nature Biotechnology 2007;25(10):1110.
- 4. Li S. Network target: a starting point for traditional Chinese medicine network pharmacology. China Journal of Chinese Materia Medica 2011;36:2017-2020
- 5. Li S, Zhang B, Zhang NB. Network target for screening synergistic drug combinations with application to traditional Chinese medicine. BMC Systems Biology 2011;5(S1):S10
- 6. Li S, Zhang B. Traditional Chinese medicine network pharmacology: theory, methodology and application. Chinese Journal of Natural Medicines 2013;11(2):110-120
- 7. Li S. Mapping ancient remedies: applying a network approach to traditional Chinese medicine. Science, 2015, 350(6262 Supplement): S72-S74.
- 8. Qi Q, Li R, Li H, et al. Identification of the anti-tumor activity and mechanisms of nuciferine through a network pharmacology approach. Acta Pharmacologica Sinica 2016;37:963-972
- **9.** Zhang B, Wang X, Li Y, Wu M, Wang S, Li S. Matrine is identified as a novel macropinocytosis inducer by a network target approach. Frontiers in Pharmacology 2018; 9;10
- Liang X, Li H, Li S. A novel network pharmacology approach to analyse traditional herbal formulae: the Liu-wei-di-huang Pill as a case study. Molecular BioSystems 2014,10(5):1014-1022
- **11.** Zhang B, Wang X, Li S. An integrative platform of TCM network pharmacology and its application on an herbal formula, Qing-Luo-Yin. Evidence-based Complementary and Alternative Medicine 2013:456747
- Li R, Ma T, Gu J, Liang X, Li S. Imbalanced network biomarkers for traditional Chinese medicine Syndrome in gastritis patients. Scientific Reports 2013;3:1543
- Guo Y, Nie Q, MacLean A, Li Y, Lei J, Li S. Multiscale modeling of inflammation-induced tumorigenesis reveals competing oncogenic and onco-protective roles for inflammation. Cancer Res 2017;77:6429-6441
- 14. Xi D, et al. State of the Science: Cancer Complementary and Alternative Medicine Therapeutics Research—NCI Strategic Workshop Highlights of Discussion Report. JNCI Monographs 2017;52:lgx003





Phytotherapy in the 21st Century



Professor Rob Verpoorte Member of the Board of Directors The GP-TCM RA Emeritus Professor of Pharmacognosy Natural Products Laboratory Leiden University Leiden, The Netherlands verpoort@chem.leidenuniv.nl

To treat patients suffering from cardiovascular diseases, diabetes 2 and other aging related diseases, elderly people get multidrug treatments, often without proper clinical evidence for the efficacy of these combinations. Recent research showed that a placebo can have real measurable phenotypic effects. The development of resistance of microorganisms against the major antibiotics affects the ideas about future drug development. The single target - single compound paradigm of drug development is challenged by the fact that the majority of the medicines (> 90%) only seems to work in 30-50 % of the patients. The single target antibiotics are an example that nature requires more than a single compound to avoid the development of resistance. Just some facts that result in a decrease of the trust in western medicines.

This situation has resulted in rethinking drug development. For the big pharma that means to go away from small molecules, as for all very common diseases already products are on the market. Instead they go for biologicals as precision medicines for life threatening diseases. Antibiotics have low commercial interests from the big pharma, mainly because a compound that cures a patient in a week does not generate sufficient income to cover the development costs. Therefore the development of antibiotics and drugs to treat tropical diseases is moving to academic and governmental research institutions.

Despite the immense investments in drug development still some 80% of the world population is dependent on traditional medicines in primary health care. Though at the end of the 20th century it seemed that phytotherapy in Europe was slowly disappearing. In the past decades many reviews and opinion articles have been published in which the history of global medicine was used to describe the importance of herbal medicines, with morphine, atropine, etc. as the usual examples. However, these are examples of isolated single compounds with an important pharmacological effect that also explain the traditional use. Changing from a complex extract to a pure compound offered better control over the dose and possible side effects. However, in most of the estimated 30,000-70,000 plant species used as medicine, there are no clear single compounds that can explain the traditional use. The fact that one has not yet been able to identify a single active compound in these plants, does not mean that there is no activity. The use of the methods of "the single target - single compound" approach does not necessarily result in evidence for a traditional use, as these methods are mostly in-vitro tests or in-vivo animal tests, which may not show the results found when applied in humans. In fact first of all clinical trials should be made to prove if there is any measurable effect of the traditional medicines.

The 21rst century science has introduced systems biology as a novel approach in which observing the whole system is the key. In fact it goes back to our ancestors who found curare, opium, belladonna, Artemisia, etc., without any of the present day scientific tools. No pharmacology, no pharmacognosy, no medicinal chemistry, it was possibly just trial and error. Now we have all kind of tools to measure things our ancestors could not observe. With all these tools we can now study the whole system, using, among others the omics, physiologic, and pharmacologic tools. By analyzing the results by using all kind of algorithms new hypotheses can be generated and subsequently be tested in the classical hypothesis driven science.

Major drivers in this process of changing paradigm are the Asian medical systems. With thousands of years of written information there is a wealth of knowledge which may be turned into evidence based



traditional uses, and even may result in new leads for drug development. The changing global economy is a further driver for studying traditional medicinal (herbal) treatments. The exponential growth in the quality and quantity of the research in this field in Asia is now setting the scene for studies of medicinal plants. The novel systems biology approach is based on the recognition that a successful treatment of a disease with complex mixtures of compounds present in plant extracts can be a matter of multi-targets, synergy, etc. Consider the treatment of HIV, at the end this became successful by combining several drugs with different modes of action.

Of course we have heard all this many times during the GP-TCM Research Association meetings as well as in many other meetings by other organizations. But what is still missing in my opinion, is courses for young students to teach them the basics of the development of evidence-based herbal medicines, as in the scientific meetings experts show the latest developments, the most sophisticated tools, able to find trace amounts of compounds..... Very interesting but often discouraging for young researchers with only limited facilities, they look up to the "magicians", but forget that science is based on creativity and innovation. These skills are in the heads of the researchers and not in the computer that is registering the data of e.g. an LC-MS chromatogram. We should try to develop a course with teachers from the GP-TCM RA that helps students to find their way in research, learn that even with limited facilities interesting results can be obtained, learn how these can contribute to evidence based traditional medicines. Learn that with 30.000-70.000 medicinal plants not all will be wonder drugs. One has to be critical and make the right choices, not ending every publication that the isolated compound is a very promising drug, when in fact the dose is already quite high in the in-vitro tests if compared to the controls, and nothing is known about stability and bioavailability. Be honest help each other to focus on the most promising ones. For every evidence based traditional medicine that is registered, the interest to support studies of others will increase. To build up such a course that can be organized anywhere might help to attract more support of universities that can offer such a course to their students. The face-to-face aspects of such courses are guite important, it will help the students to appreciate that their teachers have been students as well, and in fact still are students.

Special Features

⁴1. In the Mood for Celebration: 3rd Jury 2018 is the 500th anniversary of the birth of Li Shizhen, the author of Ben Cao Gang Mu (Compendium of Materia Medica).



https://mp.weixin.qq.com/s/aFR8ogMUsdwKjlp2629Fxg (中文)



To mark this important occasion, a series of independently organised events are being held worldwide in honour of LI Shizhen. This includes the 6th GP-TCM RA Annual Meeting to be held at Royal Botanical Gardens Kew and London South Bank University in London, on 4-6 July in London, the UK.

These events will be featured in future newsletters.



To kick-start, we report a grand gathering of international experts in Qichun, Hubei Province, China, the birth place of LI Shizhen, to discuss the worldwide impact of Li Shizhen's work. Attendees included GP-TCM RA Founding President and Current BoD Member Prof Rudolf Bauer (Graz), Newsletter Deputy Editor-in-chief Prof. Yuan-Shiun Chang (Taichung), Life Member Prof Jingyi Wang (Taipei), top materia medica experts and senior GP-TCM RA member Prof. Zhongzhen Zhao (Hong Kong) and Prof Michael Henrich (London), to mention a few.

European Reports

1. Vesper I. €100-billion budget proposed for Europe's next big research programme. Nature 2018;557:150. Initial funding plans for the seven-year Horizon Europe science initiative get a lukewarm reception. The EU is planning to spend €100 billion (US\$120 billion) on its next major research-funding programme, for 2021 to 2027 — a disappointment to some scientists and policy groups who were hoping for up to 60% more. The budget does not include a contribution from the United Kingdom, whose departure from the bloc in 2019 is likely to shake up the distribution of funds among the remaining 27 EU countries. The European Commission issued its opening budget

proposal for Framework Programme Nine (**FP9**) — newly named **Horizon** Europe, and the successor to the current programme, Horizon 2020 on 2 May. The announcement marks the start of tough negotiations between the European Parliament and the Council of the European Union, which comprises government representatives from EU full nations...The proposal for Horizon Europe is expected in June...

https://www.nature.com/articles/d41 586-018-05105-0?WT.ec_id

2. *Nature* &*Science* comments on the EU General Data Protection Regulation

EUROPE'S SCIENCE SPENDING

The European Commission has proposed a €100-billion (US\$120-billion) budget for Horizon Europe, the next instalment of its research-funding programme, which will last from 2021 to 2027.





- Marelli L and Testa G. Scrutinizing the EU General Data Protection Regulation. Science 2018;360:496-498. On 25 May 2018, the European Union (EU) regulation 2016/679 on data protection, also known as the General Data Protection Regulation (GDPR), will take effect. The GDPR, which repeals previous European legislation on data protection (Directive 95/46/EC) (1), is bound to have major effects on biomedical research and digital health technologies, in Europe and beyond, given the global reach of EU-based research and the prominence of international research networks requiring interoperability of standards. Here we describe ways in which the GDPR will become a critical tool to structure flexible governance for data protection. As a timely forecast for its potential impact, we analyze the implications of the GDPR in an ongoing paradigmatic legal controversy involving the database originally assembled by one of the world's first genomic biobanks, Shardna. http://science.sciencemag.org/content/360/6388/496?utm
- Editorial. Science needs clarity on Europe's data-protection law. *Nature* 2018; 557:467. As a commendable European law on prsonal data comes into force, the research community must not let excessive caution about data sharing, however understandable, become the default position. https://www.nature.com/articles/d41586-018-05220-y?WT.ec_id=NATURE-20180524&utm

• GDPR introduction in Chinese: <u>https://mp.weixin.qq.com/s/D8WF7F5BpNbNc-6eHJAgyA</u> (中文)

3. UK Prime Minister's speech on R&D Investment: "As a government, we have set the goal of research and development investment reaching 2.4 per cent of GDP by 2027 - more than ever before. That could translate to an additional £80 billion investment in the ideas of the future over the next decade. <u>https://www.gov.uk/government/speeches/pm-speech-on-science-and-modern-industrial-strategy-21-may-2018</u>

4. UK Government Response to Select Committee's "Brexit, Science and Innovation" Report: <u>https://publications.parliament.uk/pa/cm201719/cmselect/cmsctech/1008/100802.htm</u>

5. All you need to know about FP9

https://www.linkedin.com/groups/164166/164166-6389843788180918276?midToken

46. Wellcome Trust Publishes Brexit Briefings.

https://wellcome.ac.uk/sites/default/files/building-strong-future-european-science-brexit-beyond.pdf https://wellcome.ac.uk/sites/default/files/wellcome-brexit-briefing-for-policymakers.pdf https://wellcome.ac.uk/sites/default/files/uk-access-to-eu-research-framework-programmes.pdf

7. New booklet on EU research & innovation funding.

http://ec.europa.eu/programmes/horizon2020/en/news/newbooklet-shows-how-eu-research-and-innovation-funding-impactsyour-daily-life?utm

8. Innovative Medicines Initiative (IMI) 2018 Call for Proposals: The IMI joint undertaking is a public-private partnership (PPP) between the European Commission and the European Federation of Pharmaceutical Industries and Associations. As part of the H2020 Societal Challenges for Health and Wellbeing, this 2-stage call has an overall estimated budget o €167.2 million. The deadlines for submission of proposals are 14 June and 11 December 2018. Furher information on the different topics and the call can be found at the participant Portal, H2020-JTI-IMI-2018. http://ec.europa.eu/research/participants/portal/desktop/en/opportu nities/h2020/calls/h2020-jti-imi2-2018-14-two-stage.html#c,topics

Reports on China and Chinese-European Cooperation

1. Wang C, Xu J, Yang, L et al. **Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional**





study. *Lancet.* 2018;(published online April 9.) Spirometry-defined COPD is highly prevalent in the Chinese adult population. Cigarette smoking, ambient air pollution, underweight, childhood chronic cough, parental history of respiratory diseases, and low education are major risk factors for COPD. Prevention and early detection of COPD using spirometry should be a public health priority in China to reduce COPD-related morbidity and mortality.

http://dx.doi.org/10.1016/S0140-6736(18)30841-9

2. Ying Ma, Yandong Zhao, Xu Gong et al. **Close the gender gap in Chinese science**. *Nature* 2018; 557: 25-27. Analysis shows that extending the age limit for grants boosts the number awarded to women, but more must be done to achieve parity, say Ying Ma and colleagues. https://www.nature.com/articles/d41586-018-04996-3?WT.ec_id

423. Editorial. **Cancer drugs in China: affordability and creativity.** *Lancet* 2018;391:1866. Cancer is a major public health concern in China. According to the National Central Cancer Registry of China, there were around 4.3 million new cancer cases and 2.8 million cancer deaths in China in 2015. Improving the accessibility and availability of effective treatments is key to tackling the huge burden of cancer in China. However, in terms of local affordability of cancer drugs, China emerges as one of the countries with the least affordable prices in the world. To ease the financial burden of patients with cancer and reduce the price of costly cancer drugs, the Chinese Government has vowed to take immediate steps to exempt tariffs on imported cancer drugs as of May 1, initiate centralised government negotiations and procurement of cancer drugs, and incorporate more cancer drugs into the catalogue of medical insurance reimbursement. Furthermore, as the vice director of the National Health Commission Zeng Yixin pointed out, a long-term strategy of controlling cancer drug pricing further will be built up through four major areas: encouraging new cancer drug discovery and development, accelerating the review and approval procedures for new medicines, reducing circulation costs, and improving cancer diagnosis and rational drug use in China.

4.Yang J, et al. The Tsinghua–Lancet Commission on Healthy Cities in China: unlocking the power of cities for a healthy China. Lancet 2018; 391:2040-84. Over the past four decades, rapid urbanisation in China has brought unprecedented health benefits to its urban population, but has also created new challenges for protection of and promotion of health in cities. With the shift from rural to urban living, more people than ever enjoy the health advantages that cities can provide, such

as better access to health services and improved sanitation. For example, the average life expectancy of male urban residents in 2010 was estimated to be 7.09 years longer than that of their counterparts in rural China; urban females lived 6.64 years longer...

https://doi.org/10.1016/S0140-6736(18)30486-0

5. Zeng H, Chen W, Zheng R, et al. Changing cancer survival in China during 2003-15: a pooled analysis of 17 population-based cancer registries. *The Lancet Global Health* 2018;6:e555-e567. There was a marked overall increase in cancer survival from 2003 to 2015 in the population covered by these cancer registries in China, possibly reflecting advances in the



quality of cancer care in these areas. The survival gap between urban and rural areas narrowed over time, although geographical differences in cancer survival remained. Insight into these trends will help prioritise areas that need increased cancer care.

https://mp.weixin.qq.com/s/8g20GVjxmapAZOZWsXUBRQ (中文)

6. **China continues dominance in THE emerging economies university rankings.** China's domination of the elite Times Higher Education (THE) Emerging Economies Rankings continues, with the nation claiming one in every five positions of the 2018 table released Wednesday 9th May 2018.



http://www.china.org.cn/world/Off the Wire/2018-05/10/content 51201390.htm



7. Lacey B et al. Age-specific association between blood pressure and vascular and nonvascular chronic diseases in 0.5 million adults in China: a prospective cohort study. *Lancet Global Health* 2018; 6: e641–e649. Among adults in China, systolic blood pressure, which grows with age in average, was continuously related to major vascular disease with no evidence of a threshold down to 120 mm Hg. Unlike previous studies in high-income countries, blood pressure was more strongly associated with intracerebral haemorrhage than with ischaemic stroke. Even small reductions in mean blood pressure at a population level could be expected to have a major impact on vascular morbidity and mortality.

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30217-1/fulltext?dgcid

8. Chen Z et al. Adiposity and risk of ischaemic and haemorrhagic stroke in 0.5 million Chinese men and women: a prospective cohort study. *Lancet Global Health* 2018; 6: e630–e640. In Chinese adults, adiposity was strongly positively associated with ischaemic stroke, chiefly through its effect on blood pressure. For intracerebral haemorrhage, leanness, either per se or through some other factor (or factors), might increase risk, offsetting the protective effects of lower blood pressure. https://www.sciencedirect.com/science/article/pii/S2214109X1830216X

9. Summerskill W, Wang HH, Horton R. Healthy cities: key to a healthy future in China. *Lancet* 2018; 391:2086-7. By 2030, up to one in eight people will live in a city in China. As urbanisation accelerates around the world, and particularly in Asia, the pivotal role of cities to influence the health of their inhabitants has never been greater. Hence, the UN Sustainable Development Goal 11 is to make cities inclusive, safe, resilient, and sustainable... https://www.sciencedirect.com/science/article/pii/S0140673618306081?via%3Dihub

⁴⁴⁴10. **China's new regulations regarding the management of scientific data**. In policy news, on 2nd April 2018, the State Counci issued new regulations regarding the management of scientific data. These stipulate that all scientific data generated in China should be submitted to official data centres before being published. The regulations in Chinese, and an English translation, are available here.

http://www.gov.cn/zhengce/content/2018-04/02/content_5279272.htm (中文)

https://www.enago.com/academy/china-open-science-open-data-manadate-released/

11.Belt & Road Initiative features win-win for China and Central & Eastern European countries. Infrastructure investments and other projects within the framework of the China-proposed Belt and Road Initiative are benefitting Serbia as well as the whole of Europe. http://english.scio.gov.cn/beltandroad/2018-05/14/content 51295751.htm

12. China becoming a global leader in innovation: This was illustrated by a series of recent scientific breakthroughs from China

http://en.people.cn/n3/2018/0503/c90000-9456222.html

- Chinese scientists develop DNA nanorobots to treat cancer
 http://www.xinhuanet.com/english/2018-03/02/c_137010384.htm
- China's ambitious brain science project inches forward



http://science.sciencemag.org/content/360/6391/840?utm http://www.xinhuanet.com/english/2018-05/15/c_137180824.htm

- Chinese, American scientists develop tiny gel balls to predict cancer
 http://www.xinhuanet.com/english/2018-05/15/c_137178814.htm
- Chinese researchers identify new leprosy gene variants
 <u>http://en.people.cn/n3/2018/0502/c90000-9455759.html</u>

⁴⁴⁴13. Known species in China has doubled in 10 years! Organized by the Biodiversity Committee of Chinese Academy of Sciences (BC-CAS), Catalogue of Life China 2018 Annual Checklist edition has been compiled by Species 2000 China Node. It is sponsored by the Chinese Academy of Sciences and the Ministry of Ecology and Environment. It is released in Beijing in May,



https://mp.weixin.qq.com/s/NEuZiNsKtq0XCWkas

<u>vLVrA</u>(中文)

2018.

http://www.sp2000.org.cn/

14. Leeming J. Hong Kong builds a science-based future. *Nature* 2018;557:S31. The city is using its proximity to research and development hubs in mainland China to encourage innovation, but barriers to collaboration remain.

https://www.nature.com/magazine-

assets/d41586-018-05213-x/d41586-018-05213-x.pdf

15. Hong Kong-mainland formula for science superpower. Scientists in Hong Kong believe collaboration between the city and the mainland will strengthen the nation's science and technology development. Their remarks follow President Xi Jinping's call for enhanced bilateral collaboration in

science and technology between the mainland and Hong Kong, and support for the region to become an international center of innovative technologies.

https://www.chinadailyhk.com/articles/30/157/18 7/1526353215140.html http://www.china.org.cn/china/2018-05/14/content 51294343.htm

TCM, Acupuncture and Other Traditional Medicine

1. LI Shizhen and Ben Cao Gang Mu (Compendium of Materia Medica)

• Wang P. Perpetuate the spirit of LI Shizhen: Investigation for insights, truth and innovation. China Chinese Medicine. May 2018; 20 (5):

https://mp.weixin.qq.com/s/u1SSh1FKoK3J_Mb6sJ3DWw (中文)

 Wang J, Mei Q. The grand contributions and academic values of Li Shizhen's *Compendium of Materia Medica:* In celebration of the 500th Anniversary of Li Shizhen's birth. *China Chinese Medicine*. May 2018; 20 (5):495-501 <u>https://mp.weixin.qq.com/s/teeDKKTv4XJvZ8C7dlvyXw</u> (中文)





• Further readings:

https://mp.weixin.qq.com/s/krplem9Xa7jQ--kPFZVo9w (中文)

2.Chinese medicines regulated as both food and medicines: An updated official list

https://mp.weixin.qq.com/s/FnHq52igFxGBwKCOOgU8aA (中文)

3. Perspectives: Good Agricultural Practice and Chinese materia medica in China

https://mp.weixin.qq.com/s/nSEYzCJbOyZt7YJDRJrnUw (中文)

4. Baburin I, Varkevisser R, Schramm A, et al. Dehydroevodiamine and hortiamine, alkaloids from the traditional Chinese herbal drug Evodia rutaecarpa, are IKr blockers with proarrhythmic effects in vitro and in vivo. *Pharmacol Res.* 2018;131:150-163.

https://mp.weixin.qq.com/s/T4nNtAq_5w4qsC2ehJZomg (中文)



5. Zhao ZZ, et al. Clarifying the origin of Houzao. *Chin Med* 2018;13:25. Houzao (bezoar) is a valuable imported Chinese medicine that is commonly used as a pediatric medicine to transform phlegm. There are mainly two types of Houzao, "Southeast Asian Houzao" and "Indian Houzao". "Indian Houzao" is the dominant commercial product accounts for over 95% of the actual utilization in the market. However, its origin, formation, composition, efficacy and pharmacology remain unclear. Therefore, we have conducted on-site investigation to clarify the origin of Indian Houzao... https://cmjournal.biomedcentral.com/articles/10.1186/s13020-018-0182-0

46. TCM tongue diagnosis with high-resolution illustrations

https://mp.weixin.qq.com/s/YBA0owHeltizklK61rKb3Q(中文)

<u>https://mp.weixin.qq.com/s/WI1x8S7SnI3Rjk5zh6v_-Q</u>(中文)

https://www.sacredlotus.com/go/diagnosis-chinese-medicine/get/tongue-d



7. A comprehensive collection of TCM diagnosis based on observation of face, eyes, ears, nose, lips, tongue and teeth

<u>https://mp.weixin.qq.com/s/Wh_F4wy_qBFqUKv4ZK_-Bw (中文)</u>

48. TCM massage at 53 acupuncture points

<u>https://mp.weixin.qq.com/s/sao_vSLehs9qs0-u6lcfAQ</u>(中文)

9. Smith CA, et al. Effect of Acupuncture vs Sham Acupuncture on Live Births Among Women Undergoing In Vitro FertilizationA Randomized Clinical Trial. *JAMA*. 2018;319:1990-1998. In this randomized clinical trial of 824 women, the rate of live births was 18.3% among women who received acupuncture vs 17.8% among women who received a sham acupuncture control, a nonsignificant difference. These findings do not support the use of acupuncture when administered at the time of ovarian stimulation and embryo transfer to improve the rate of live births. https://jamanetwork.com/journals/jama/fullarticle/2681194

Commenting on this report published on 15th May 2018, Dr Bingsheng Yuan (Doncaster, UK), a Senior TCM practitioner and acupuncturist questioned the validity of the sham group, the experience and expertise of the acupuncturists and the choice of



acupoints in this study: <u>https://mp.weixin.qq.com/s/T0erTEWMcYeDMIAo0v78dw</u> (中文)

10. Sakagami H, ed. Alternative Medicine. An open-access book published by Intech in 2012. ISBN: 978-953-51-0903-7. Alternative medicine is recognized as medical products and practices that do not belong to the standard cares taken by medical doctors, doctors of osteopathy and allied health professionals. It has developed into a multitude of medical products and practices that significantly improve the body condition and show disease prevention actions. The content of this book does not cover all areas of alternative medicine, but provides the reader with insights into selected aspects of established and new therapies. It consists of 12 chapters that are separated into 4 parts: (1) Historical and Cultural Perception, (2) Compositional Analysis, (3) Therapeutic Potential, and (4) Action Mechanism and Future Direction, written by world experts who are reviewing their original and others' research. Most downloaded and cited chapters include those on "Network Pharmacology and TCM", "Traditional medicine in Hong Kong", "Energy Medicine", "Traditional Medicine in Japan", "Propolis for the Treatment of Oral Microbial Diseases", etc. https://www.intechopen.com/books/alternative-medicine/

411. Ji X, Feng G, Chen G, Shi T. Lack of correlation between aristolochic acid exposure and hepatocellular carcinoma. *Sci China Life Sci*.2018 Apr 20. doi: 10.1007/s11427-018-9288-1.

and hepatocellular carcinoma. Sci China Life Sci.2018 Apr 20. doi: 10.1007/s11427-018-9288-1 [Epub ahead of print] https://link.springer.com/content/pdf/10.1007%2Fs11427-018-9288-1.pdf

12. Zhou G, Zhao X. **Carcinogens that induce the A:T > T:A nucleotide substitutions in the genome.** Front Med. 2018 Apr;12(2):236-238. Recently, Ng et al. reported that the A:T > T:A substitutions, proposed to be a signature of aristolochic acid (AA) exposure, were detected in 76/98 (78%) of patients with hepatocellular carcinoma (HCC) from the Taiwan Province of China, and 47% to 1.7% of HCCs from the Chinese mainland and other countries harbored the nucleotide changes. However, other carcinogens, e.g., tobacco carcinogens 4-aminobiphenyl and 1,3-butadiene, air toxic vinyl chloride and its reactive metabolites chloroethylene oxide, melphalan and chlorambucil, also cause this signature in the genome. Since tobacco smoke is a worldwide public health threat and vinyl chloride distributes globally and is an air pollutant in Taiwan Province, the estimation of the patients' exposure history is the key to determine the "culprit" of the A:T > T:A mutations. Apparently, without estimation of the patients' exposure history, the conclusion of Ng et al. is unpersuasive and misleading. <u>https://link.springer.com/article/10.1007/s11684-017-0611-y</u>

13. International TCM Authentication & Testing Centre Founded in Shanghai.

https://mp.weixin.qq.com/s/BuHEOmrcsujGR3nf7Xs0rA (中文)

14.Jia J et al. Efficacy and safety of the compound Chinese medicine SaiLuoTong in

vascular dementia: A randomized clinical trial. Alzheimer's & Dementia: Translational Research & Clinical Interventions 2018: 4:108-117. No licensed medications are available to treat vascular dementia (VaD). Patients were randomly assigned to experimental groups (SaiLuoTong [SLT] 360 or 240 mg for groups A and B for 52 weeks, respectively) or placebo group (SLT 360 mg and 240 mg for group C only from weeks 27 to 52, respectively). Results: Three hundred twenty-five patients were included in final analysis. At week 26, the difference in



VaD Assessment Scale–cognitive subscale scores was 2.67 (95% confidence interval, 1.54 to 3.81) for groups A versus C, and 2.48 (1.34 to 3.62) for groups B versus C (both P<0.0001). However, at



week 52, no difference was observed among the groups on the VaD Assessment Scale–cognitive subscale (P=0.062) because of the emerging efficacy of SLT in placebo beginning at week 27. This study suggests that SLT is effective for treatment of VaD, and this compound Chinese medicine may represent a better choice to treat VaD.

https://www.trci.alzdem.com/article/S2352-8737(18)30007-6/fulltext

https://mp.weixin.qq.com/s/7rUCxtS_JaZISWrH1KPCCQ (中文)

Omics in Progress

1. Jang C, Chen L, Rabinowitz JD. **Metabolomics and Isotope Tracing.** *Cell* 2018;173:822–837. A roadmap for measuring metabolite concentrations and using isotope tracers to track metabolic activity...

https://doi.org/10.1016/j.cell.2018.03.055

2. Burke JE, et al. Spliceosome Profiling Visualizes Operations of a Dynamic RNP at Nucleotide Resolution. Cell 2018;173:1014–30. Quantitative *in vivo* spliceosome profiling in three divergent yeast species reveals unannotated splicing events and determinants of catalytic efficiency and assesses non-optimal substrates.

https://www.cell.com/cell/fulltext/S0092-8674(18)30300-3

3. Chen W, et al. **Transcriptome-wide Interrogation of the Functional Intronome by Spliceosome Profiling.** *Cell* 2018;173:1031–44. Spliceosome profiling exemplified by transcriptomewide sequencing of RNAs associating with late-stage spliceosomes offers a platform for generation of genome-wide maps for all sites of spliceosome assembly and action in diverse cell types. <u>https://www.cell.com/cell/fulltext/S0092-8674(18)30394-5</u>

4. Plass M, et al. **Cell type atlas and lineage tree of a whole complex animal by single-cell transcriptomics.** *Science* 2018; 360: eaaq1723. Results demonstrate the importance of single-cell

transcriptome analysis for mapping and reconstructing fundamental processes of developmental and regenerative biology at high resolution.

http://science.sciencemag.org/content/360/6391/eaaq1723?utm

5. Fincher CT, et al. **Cell type transcriptome atlas for the planarian** *Schmidtea mediterranea. Science* 2018;360:eaaq1736. <u>http://science.sciencemag.org/content/360/6391/eaaq1736?utm</u>

Other Recommended Readings

1. Editorial. **Mapping the human.** *Nature Methods* 2018; 15:299. The Human Cell Atlas, driven by a collaborative spirit and rapid advances in single-cell methods, is poised to advance both biological understanding and technical development.

https://www.nature.com/articles/nmeth.4685?WT.ec_id

2. Reilly BM. **The Best Medical Care in the World.** *N Engl J Med* 2018:378:1741-1743

https://www.nejm.org/doi/full/10.1056/NEJMms1802026?query=TOC

³3. The *Lancet* publishes "World Healcare League Table" on 23rd May 2018

https://mp.weixin.qq.com/s/wTOhYcXEoZAwS6nr7mNbPg (中文) https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30994-2/fulltext





Meetings Reports

1. The 6th Chinese-European TCM International Cooperation & Development Forum was held at the UNESCO Headquarters in Paris on 16th May 2018, where the WFCMS-France TCM Centre was founded.

https://mp.weixin.qq.com/s/-

<u>cQwJXUrrXTeAa2CEXg47g (</u>中文)

2. The 1st World Acupuncture-Moxibustion Forum *cum* Traditional Medicine Industrial Exchange was held



暨传统医药产业交流大会 Primer Foro Internacional de la Organización Mundial de

首届世界中医针灸论坛

Medicina Tradicional China y Acupuntura

2018年5月19日-20日 阿根廷. 布宜诺斯艾利斯 19-20, Mayo, 2018, Buenos Aires, Argentina



Future Meetings & Events

⁴⁴⁴1. The 6th Annual Meeting of the GP-TCM RA (London, UK, 4-6 July 2018) extended deadline for abstract submission & registration is 31st May 2018. The programme has been designed to address the key areas that impact TCM:

- Availability and quality of the genetic resources used in TCM
- Regulatory environment associated with modern drug development,
- Advances in analytical technique that further our understanding of complex mixtures used in TCM
- Standardization quality and safety of TCM
- New guidelines of, and evidence from, clinical studies
- Integration of acupuncture

Highlights of the meeting: Annual General Meeting; Interest Group activities; meeting Board of Directors, Interest Group Chairs, Newsletter Editorial Board Members and international leaders; presenting your posters and talks; travel grants for PhD students; visiting the lovely royal botanical gardens and London; plus handy attendance of the *Future Trends in Global Healthcare - Fusion of Traditional Medicines and Modern Technologies* meeting in the grand and beautiful city of Cambridge, immediately after the meeting (Register separately below)...

To register and submit abstracts, please visit: http://www.gp-tcm.org/events/upcoming/

2. Future Trends in Global Healthcare - Fusion of Traditional Medicines and Modern Technologies (Cambridge, UK, 7 July 2018). This one-day forum will be held in Cambridge Science Park on 7 July 2018 immediately after the 6th Annual Meeting in Kew/LSBU (4-6 July 2018). An international team of experts and scholars will present and discuss recent advances in traditional



medicine from China, India and Africa and how modern technologies can be used to develop novel therapeutics for the treatment of chronic and infectious diseases. Invited speakers:

- Dr Qi Zhang, Traditional and Complementary Medicine Unit, WHO, Geneva, Switzerland. *The WHO Traditional Medicine Strategy* 2014-2023
- Prof. Christopher Lowe OBE FREng, University of Cambridge, UK. To be announced
- Prof. Zhongzhen Zhao, Hong Kong Baptist University, China. *The Compendium of Materia Medica (Bencao Gangmu) and beyond*
- Prof. Bipin Nair, Amrita University, India. *Natural products from India as novel drug leads old wine in a defined new bottle*
- Prof. Pierre Duez, University of Mons, Belgium. *Traditional African Medicine: validation and modernization*
- Prof. Peng Cheng, Chengdu University of TCM, China. *Conservation and sustainable supply of medicinal plants.*
- Dr Charles Wu, FDA Center for Drug Evaluation and Research, USA. *Evolution of traditional medicines to botanical drugs.*
- Professor Gerhard Franz, University of Regensburg, Germany. Introducing European Directorate for the Quality of Medicines.
- Dr Shifeng Cheng, Beijing Genomics Institute, China. *Medicinal Plants 4.0 Project - the future of medicines from plants.*
- Kan Ding, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, China. *The mechanism underlying anti-*pancreatic cancer polysaccharides from herbal medicine
- Prof.Lie-Fen Shyur, Agricultural Biotechnology Research Center, Academia Sinica, Taiwan. *Phytomedicine polypharmacology: Uncovering novel molecular insights of phytoagents for cancer therapy.*
- Dr Andreas Bender, University of Cambridge, UK. *Cheminformatics and bioinformatics in drug discovery*
- Prof. Ka-Kit Hui, UCLA Center for East-West Medicine, USA. *Integrative East-West Medicine: a commitment to advancing healthcare.*
- Prof. Jaung-Geng Lin, China Medical University. Taiwan. Acupuncture analgesia: issues of clinical practice and research

If you are interested in attending this event, please register ASAP:

https://www.eventbrite.co.uk/e/the-first-cambridge-br-initiative-international-conference-tickets-45297018602?aff=es2&from=singlemessage&isappinstalled=0

For registered participants, coach(es) will be provided to take them from London to Cambridge in the evening of 6 July.

3. The 17th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Kuching-Sarawak, Malaysia on August 8 - 10, 2018. This year's meeting is going to be organized by the Malaysian Institute of Pharmaceuticals and Nutraceuticals, National Institutes of Biotechnology Malaysia. The meeting provides a platform for regulatory-industrial-academic exchanges and potential research collaborations, on various frontiers of Traditional Chinese Medicine among our worldwide CGCM members and guests. You are cordially invited to attend the meetings and submit abstracts. Preliminary programme and more details will soon be announced on our website. Should you have any enquiries, please feel free to contact the CGCM Central Office: Email: centraloffice@tcmedicine.org; Website: www.tcmedicine.org

Information for meeting program, abstract submission, registration and travel grant can be found here: <u>http://www.cgcm2018.com</u> Important dates:

• May 31, 2018 Early Bird Registration





- June 15, 2018 Deadline for abstract submission (extended) and for travel grant application
- July 16, 2018 Registration Deadline

Should you have any enquiries, please feel free to contact <u>cgcm2018@ipharm-nibm.my</u> <u>http://mp.weixin.qq.com/s/R5Ao3tYI7Q2UwzaP94ikTw</u> (中文)

4. The 30th International Symposium on the Chemistry of Natural Products and the 10th International Congress on Biodiversity will be held on Nov. 25–29 2018 in Athens, Greece. <u>http://www.iscnp30-icob10.org/Default.asp?c=6&Ing=1</u> <u>http://www.iscnp30-icob10.org/Default.asp?c=7&Ing=1</u>

5. The 15th World Congress of Chinese Medicine and *Belt and Road* TCM Culture Week to be held in Rome, Italy, Nov. 16-20 2018.

http://c.eqxiu.com/s/O8xACe2w?eqrcode=1&share_level=4&from_user=a294a700-73b5-4d95-9d8bdc428813e7cd&from_id (中文)

Invitation from journals

1. World Journal of Traditional Chinese Medicine: Sincere invitation for submissions. World Journal of Traditional Chinese Medicine (ISSN 2311-8571, CN10-1395/R) is sponsored by WFCMS, and is the official journal of GP-TCM RA. WJTCM dedicates to report the research progress in clinical efficacy and action mechanism of Traditional Chinese Medicine, Chinese materia medica, acupuncture and moxibustion to doctors and biomedical researchers around the world, so as to provide new thoughts and methods for solving complex diseases and knotty diseases. To submit your manuscripts, or to read articles in the past issues, please visit: http://www.wjtcm.net

2. Frontiers in Pharmacology special issue "Can Natural Products Reduce the Side Effects of Cancer Therapies?" invites your submission. Deadline: June 2018.

https://www.frontiersin.org/research-topics/7625/can-natural-products-reduce-the-side-effects-ofcancer-therapies

http://journal.frontiersin.org/researchtopic/7625 (中文)

4 3. Frontiers in Pharmacology and Frontiers in Ethnopharmacology special topic "Metabolomics and Metabolism of Traditional Chinese Medicine"

Submission Deadlines: 3rd September 2018 (Abstract); 1st March 2019 (Manuscript)

https://www.frontiersin.org/research-topics/8155/metabolomics-and-metabolism-of-traditional-chinese-medicine

Sounding Board

This column is reserved for comments, personal views, proposals for collaborations or any other features from our readers across the world. We look forward to hearing from you! Please get in touch with your editors: Dr Qihe Xu (<u>qihe.xu@kcl.ac.uk</u>), Prof. Pierre Duez (<u>pierre.duez@umons.ac.be</u>) and Prof. Yuan Shiun Chang (<u>yschang0404@gmail.com</u>).

Acknowledgements

Contributions from Prof. Rudolf Bauer (Graz), Prof. Pierre Duez (Mons), Dr Tai-Ping Fan (Cambridge), Prof Shao Li (Beijing), Dr Haitao Lu (Shanghai), Prof. Monique Simmonds (London), Prof. Rob Verpoorte (Leiden), Prof Hongxi Xu (Shanghai), Dr Qihe Xu (London), Dr Bingsheng Yuan (Doncaster), and Prof Zhongzhen Zhao (Hong Kong) are gratefully acknowledged. Chinese paintings are selected from the following web link.

https://mp.weixin.qq.com/s/092rLalhpCAFw24jiw2-DA (中文)

