

### editorial

# Systems pharmacology and traditional Chinese medicine



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TCM is based on the traditional Chinese medicine theory to guide the collection, processing, preparation, explain the mechanism of action, and guide the clinical application of drugs. It is the crystallization of the traditional cultural wisdom of the

Chinese nation and has made important contributions to the prevention and treatment of human diseases for thousands of years. In recent years, due to its characteristics of multi-component, multi-target and weak-binding, TCM has become a research hot spot of drug discovery for different disease areas. And studies have shown that many low-affinity drugs that aim for several targets at the same time are found more treatment effects and lower side effects than the high-affinity binders when faced with complex disease conditions [1]. Meanwhile, TCM has been widely applied to clinically treat major diseases such as cancers, Alzheimer's disease and cardiovascular diseases, etc. This provides a favourable reference for the clinical treatment of diseases and development of multi-target drugs. However, the active components of TCM and the mechanism of action of molecules are still unclear.

In the early stages, advances in mass spectrometry, NMR spectroscopy and omics techniques provide technical support for revealing the active components, drug targets, and molecular mechanisms of TCM. Although these technologies have profoundly affected our understanding of pharmacodynamics, pharmacokinetics and drug toxicity, they are time-consuming, costly and relatively difficult to analyse the mechanisms of TCM. Afterward, with the advancement of analytical tools such as bioinformatics, computational biology, systems biology, network biology and network pharmacology, the intricate and holistic mechanisms of TCM may be elucidated in a fast and highly effective way. They have provided new methods and concepts for the modernization of TCM. Nevertheless, despite their great development, there is still room for innovation, and systems pharmacology has emerged.

Systems pharmacology is a novel multidisciplinary cross-product that includes classical pharmacology, chemical biology, biochemistry and structural biology, genomics, pathology, medicine, and applied mathematics, computer technology, bioinformatics, and "-omics" methods. It also covers a wide range of experimental disciplines including research techniques from cells to tissues to organs [2]. It is dedicated to clarifying, validating and applying theoretical calculations combined with experimental methods and techniques to discover molecules, identify targets, study disease pathogenesis and therapeutic mechanisms, thereby providing new strategies and tools for accurate regulation of complex intracellular networks, alteration pathophysiology of diseases, improvement drug efficacy and reduction adverse reactions. Nowadays, systems pharmacology is considered to be the core technology of future translational medicine, and has been successfully applied in various aspects of TCM, including screening bioactive drug ingredients, predicting drug targets, understanding therapeutic mechanisms, revealing rules of drug combination, screening synergistic drug combinations, and so on.

Here, based on systems pharmacology, we constructed a unique systems pharmacology platform of

Chinese herbal medicines, which is different from other databases. The newly developed TCMSP (<u>http://lsp.nwu.edu.cn/tcmsp.php</u>) provides up-to-date, quantitative and systems information about TCM ingredients, ADME-related properties, targets and diseases [3] (Figure. 1). It consists of all the 499 Chinese herbs registered in the Chinese pharmacopoeia with 29,384 ingredients, 3,311 targets and 837 associated diseases. Twelve important





ADME-related properties like human oral bioavailability (OB), half-life (HL), drug-likeness (DL), Caco-2 permeability, blood-brain barrier (BBB) and Lipinski's rule of five are provided for drug screening and evaluation. TCMSP also provides drug targets and diseases of each active compound, which can automatically establish the compound-target and target-disease networks that let users view and analyse the drug action mechanisms. It is designed to fuel the development of herbal medicines and to promote integration of modern medicine and traditional medicine for drug discovery and development. The particular strengths of TCMSP are the composition of the large number of herbal entries, and the ability to identify drug-target networks and drug-disease networks, which will help revealing the mechanisms of action of Chinese herbs, uncovering the nature of TCM theory and developing new herb-oriented drugs.

#### TCMSP : Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform



**Figure 1. TCMSP.** A unique platform that captures the relationships between drugs, targets and diseases.

For example, we can directly retrieve compounds of *licorice* from TCMSP and screen the potential active compounds by appropriate ADME criteria. Finally, these compounds and their predicted /validated targets are integrated into compound-target and target-disease network to systematically analyse the mechanisms of licorice treatment of related diseases. These works were compiled as a book-"Systems Pharmacology- Theory, Methodology and Application".

From the above, TCMSP integrates ADME properties, targets, diseases and networks, so that it can be fully explained the

molecular mechanism from a holistic perspective. This provides a new approach to drug development, clinical diagnosis and personalized treatment. However, ways for further studying the characteristics of multiple targets and weak binding of drugs still need further improvement.

Finally, you are kindly invited to visit the TCMSP website and use this powerful TCM systems pharmacology tool: <u>http://lsp.nwu.edu.cn/tcmsp.php</u>

#### **Further readings**

[1] Wang, J., et al., Weak-binding molecules are not drugs? toward a systematic strategy for finding effective weak-binding drugs. Briefings in Bioinformatics, 2016. **18**(2): p. bbw018.

[2] Huang, C., et al., Systems pharmacology in drug discovery and therapeutic insight for herbal medicines. Briefings in Bioinformatics, 2014. **15**(5): p. 710-733.

[3] Ru, J., et al., TCMSP: a database of systems pharmacology for drug discovery from herbal medicines. Journal of cheminformatics, 2014, **6**(1): 13.

Archives (2008-2019): www.gp-tcm.org/news-list/



#### **Reports from the GP-TCM RA**

1. With the recent co-option of two members from Mainland China, Prof. Rong-Rong He and **Prof. Min Ye, the Board of Directors (BoD) of the GP-TCM RA 2019-2022 have now been finalized.** They are Prof. Aiping Lu (President and chairman of the BoD), Dr Tai-Ping Fan (Past President), Prof. Monique Simmonds (President-elect), Prof. Peter Hylands (Treasurer), Prof. Clara Bik-San Lau (Secretary-General), Dr. Qihe Xu (Newsletter Editor-in-chief), Prof. Pierre Duez (Deputy Newsletter Editor-in-chief), Prof. Rudolf Bauer, Prof. Kelvin Chan, Prof. Thomas Efferth, Prof. Rob Verpoorte, Prof. Vivian Taam Wong, Mr Abraham Chan (Industrial Representative), Rong-Rong He (China Representative) and Min Ye (China Representative).



2. An Update on Membership and Leadership of GP-TCM RA Interest Groups. By January 2019, The Quality Control Interest Group has 49 members; the Pharmacology and Toxicology Interest Group has 64 members; the Clinical Studies Interest Group has 34 members; the Regulatory Aspects Interest Group has 32 members; the Acupuncture – Moxibustion and Meridians Interest Group has 18 members; and the Publication Interest Group has 23 members. Chairs and Co-Chairs of our 6 Interest Group shave now been appointed, as shown in the table below. If you have indicated your Interest Group affiliation on your membership application form, or if you have replied to recent update e-mails from the Secretariat and identified the Interest Groups that you wish to be affiliated to, you should have heard from your Chairs and Co-Chairs for discussions or will hear from them soon. If you have not responded to recent update on your Interest Group affiliations yet, please contact the secretariat: gptcmrasecretariat@gmail.com

Interest Groups	Chairs	Co-Chairs
Quality Control	Kelvin Chan	Christine Leon
Pharmacology and Toxicology	Pierre Duez	Hongxi Xu
Clinical Studies	Zhaoxiang Bian	Myeong Soo Lee
Regulatory Aspects	Mei Wang	Gerhard Franz
Acupuncture – Moxibustion and Meridians	Nicola Robinson	Lixing Lao
Publication	Rob Verpoorte	Thomas Efferth





3. Self-introduction and personal statement of Prof. Rong-Rong He, co-opted BoD member representing Mainland China. Professor Rong-Rong He is the Director of Guangdong Engineering



**nland China.** Professor Rong-Rong He is the Director of Guangdong Engineering Research Center of Chinese Medicine & Disease Susceptibility in Jinan University. She also serves as the Associate Director in the Institute of Traditional Chinese Medicine and Natural Products, College of Pharmacy, Jinan University. She gained her BPharm and PhD in Pharmacy (Chinese Materia Medica) from Shenyang Pharmaceutical University, Shenyang, China. The effectiveness of herbal medicine has always been difficult to evaluate with conventional pharmacological methods. She focuses on using a variety of stress loaded models for anti-stress research and natural product evaluations and improving the effects on homeostasis and disease prevention. These related research projects are supported by dozens of funding sources such as National Natural Science Foundation. As a young researcher, she

has published over 100 scientific articles in peer reviewed journals, presented scientific reports at local, national and international conferences, and is the owner of 6 authorized patents. Dr. He has been awarded with the Guangdong Provincial Science and Technology Progress Award (First Class) and Technological Progress Award from Ministry of Education (Second Class) for her great contribution for the TCM studies.

**Personal statement:** Having known the good reputation of the GP-TCM Research Association from the TCM academic communities, as well as being a participant of the recent annual meetings, I am glad to serve as a member of Board of Directors in order to contribute more towards this influential Association. I have been studying and working in the field of Chinese Materia Medica for almost 20 years. I deeply understand that modernization and internationalization of TCM are the two most important tasks for a TCM researcher. As a member of BoD, I would like to contribute all my expertise to the development of Chinese medicine.

4. Self-introduction and personal statement of Prof. Min Ye, co-opted BoD member representing Mainland China. Prof. Min Ye is a Professor in Pharmacognosy at the School of



Pharmaceutical Sciences, Peking University. He is currently Vice Dean of the School of Pharmaceutical Sciences, and Deputy Director for the State Key Laboratory of Natural and Biomimetic Drugs. He finished his postdoctoral researches in Peking University, Louisiana State University, and Yale University (2003-2007). His research interests are the effective components of traditional Chinese medicines, and biosynthesis of natural products. He has published 105 papers as corresponding author, and his work has been cited for over 4000 times. His h-index is 33. He received two National Awards in 2012 (Natural Science) and 2016 (S&T Progress) for his contribution to the quality control of traditional Chinese medicine. He also received the National Science Fund for Distinguished Young Scholars in 2017. He was elected as a committee member of the Chinese

Pharmacopoeia Commission in 2017. He now serves as associate editor for *Journal of Ethnopharmacology* and *Pharmaceutical Biology*, as well as editorial board member for *WJTCM*, *JPBA*, *APSB*, and other scientific journals.

**Personal statement:** "I have been a member of GP-TCM RA since 2016, and I attended the 3<sup>rd</sup> and 5<sup>th</sup> Annual meeting. It is exciting to see the achievements of GP-TCM RA through the recent years. As a committee member of the Chinese Pharmacopoeia Commission, I am specifically concerned about the quality control of TCM, including raw materials, prepared slices, and formulations. In my research, new strategies have been developed to discover the effective components of TCM, and new methods have been established to evaluate TCM qualities. I would like to contribute to the communication and collaboration regarding TCM research, including quality control, pharmacology, and sustainable TCM resources."



5. The 7<sup>th</sup> Annual Meeting of GP-TCM RA will be held in Daegu Haany University (DHU), Daegu City, Republic of Korea, on July 9<sup>th</sup> – 11<sup>th</sup>, 2019. The meeting will be jointly hosted by National Development Institute of Korean Medicine(NIKOM) and DHU.

Please firmly book your diaries abd watch out for further announcements - Calls for abstracts and registration will be published very soon!



A, B and C: The meeting venues.

#### **Special Features**

### 1. HISTORIC ARCHIVE: The GP-TCM Kick-off Meeting was held in Beijing in January 2009.

A very successful GP-TCM Workshop was held in Beijing (11th-13th January 2009), under the auspices of Ministry of Science & Technology (MOST), Chinese Academy of Medical Sciences (CAMS) and Innovation China UK (ICUK). It was the first time that 26 GP-TCM team members, representing 8 EU countries and all the 10 GP-TCM Work Packages, met with ~40 TCM experts from Beijing, Tianjin, Shanghai, Dalian, Hong Kong, etc. The Opening Ceremony was highlighted by the addresses from Academician Liu Depei. President of Archives (2008-2019): www.gp-tcm.org/news-list/





CAMS, Dr Michael Pulch, Deputy Head of Delegation of the European Commission to China, and Director Jin Xiaoming, Director General of MOST Department of International Cooperation. Significantly, Academicians Li Lian-da, Pei Gang, Yang Shengli, Xiao Peigen and Ms Manyi Cristofoli, ICUK Executive Director also attended the Workshop. We thank MOST for its generous financial support, Directors Xing Jijun, Zou Jiangiang and Zhou Longchao of MOST, Professor Liu Xinmin together with the staff and students of CAMS Institute of Medicinal Plant Development (IMPLAD) for their dedication and professionalism in making this meeting such an enjoyable and memorable one! Led by Dr Qihe Xu, representatives of all the 10 Work Packages (Monigue Simmonds, Peter Proksch, Ian Sutherland, Peter Hylands, Javier de Lucio-Cazana, Pierre Duez, Andrew Flower, Kelvin Chan, Wang Xiaomin, Tai-Ping Fan and Annelies Schulte) gave succinct overviews of their plans for the coming three years, perfectly matching the high quality presentations by top TCM experts from China: Li Lian-da (Safety & Rational Use), Pei Gang (Modernisation), Guo De-an (Quality Control), Lin Ruichao (Quality Control), Liang Xinmiao (Herbalome), Zhao Liping (Top-down Systems Biology), Luo Guo-an (Chemomics), Zhang Weidong (Drug Discovery), Cheng Xiaodong (Anticancer Drugs from TCM), Ye Zuguang (Safety Evaluation of TCM), Wu Chun Fu (Toxicology), Lu Aiping (Pattern Differentiation and Clinical Trials of TCM). By invitation, Ms Lina Svedlund of Tianjin Tasly Pharmaceuticals shared her company's experiences in TCM registration in North America, Europe and Australia. Professors and Drs Bruce Hendry, Jia Weiguo, Alberto Dias, Lin Wenhan, Debbie Shaw, Allan Lau and Ning Wang served as chairpersons, presiding over the enthusiastic discussions each presentation aroused. The Workshop concluded with a very strong desire to combine the expertise and resources in EU and China for advancing the modernisation of TCM. Both MOST and the European Commission were very satisfied with the outcome of this Sino-EU Workshop and pledged to facilitate active collaborations between the two sides.

http://www.gp-tcm.org/2010/02/wp10-kick-off-meeting-the-sino-eu-gp-tcm-workshop/ http://www.most.gov.cn/kjbgz/200901/t20090116\_66843.htm (中文)

2. Dr. Qu Fan, Member of the GP-TCM RA, was awarded a tier-2 prize of the Science & Technology Award of the China Acupuncture and Moxibustion Society. On the New Year's Day, the Chinese Acupuncture and Moxibustion Society issued a notice on the award of the Science & Technology Award of the Society. Dr. Qu Fan, Director of Department of TCM, Obstetrics & Gynaecology Hospital of Zhejiang University School of Medicine, has won a tier-2 prize. His project was entitled "Standardisation of acupuncture and TCM intervention in *in-vitro* fertilisation-embryo transfer". https://mp.weixin.qq.com/s/qlzlevHhDwSn9ucgdBYK9A (中文)



3. Kivelson S. OBITUARY. Shoucheng Zhang (1963–2018). Codiscoverer of topological insulators. *Nature 2019;*565:568. The author Steven Kivelson is professor of physics at Stanford University and a member of the Stanford Institute of Theoretical Physics, California, USA. He was Shoucheng Zhang's adviser on condensed matter for the final year of his PhD, and collaborated with him on many projects thereafter. https://www.nature.com/articles/d41586-019-00268-w?WT.ec\_id

#### **European Reports**

### 1. Horizon 2020: Update on Health-related Funding Opportunities.

- Societal Challenge 1: Health, demographic change and wellbeing https://www.ukro.ac.uk/subscriber/Factsheets/factsheet\_sc1\_health.pdf
- The European & Developing Countries Clinical Trials Partnership (EDCTP) 2018 Calls are still open, including Preparatory Fellowships Joint call with the Africa Research Excellence Fund (deadline 1 February 2019), Senior Fellowships (deadline 28 February 2019 and EDCTP Clinical Research and Product Development Fellowships (deadline 7 March 2019).



http://www.edctp.org/funding-opportunities/calls-for-proposals-for-funding-of-clinical-research-onpoverty-related-infectious-diseases/

The Innovative Medicines Initiative (IMI2) Call 17 is now open, with three topics. Deadline for first stage submissions is on 25 April; https://www.imi.europa.eu/apply-funding/open-calls/imi2-call-17

2. Gibnev E. How UK scientists are preparing for a chaotic no-deal Brexit. Nature 17 Jan. 2019; doi: 10.1038/d41586-019-00191-0. British scientists are ramping up preparations for a 'no deal' Brexit on 29 March — a situation that would instantly affect travel, data collection, clinical trials and crucial laboratory supplies. The widely feared scenario means that the United Kingdom crashes out of the European Union without any trade and migration agreements with the bloc in place. It became more likely on 15 January after the UK Parliament overwhelmingly rejected a hard-negotiated agreement with the EU on the terms of Brexit. The deal would have included a transition period until 2021 during which the UK-EU relationship would have remained largely unchanged, allowing time to negotiate the parties' future relationship. A no-deal split is likely to cause immediate disruption because the many vital supplies that come from mainland Europe would face additional checks and tariffs... https://www.nature.com/articles/d41586-019-00191-0?WT.ec\_id=NATURE-20190124&utm

2. Newton International Fellowships. This scheme is for non-UK scientists who are at an early stage of their research career and wish to conduct research in the UK. This scheme is now open to applications and will close at 3pm on Wednesday 27 March 2019. https://rovalsociety.org/grants-schemes-awards/grants/newton-international/

4. UK biotech funding increased by 85 percent in 2018. UK-based biotech companies raised £2.2billion from investors in 2018, an increase of 85 percent from the year before, a report has found...

https://www.europeanpharmaceuticalreview.com/news/83441/biotechfunding-increased/?utm



4 5. Casassus B. France set to get first national strategy for research. Nature 2019;566:164. Plan promises funding stability and better career

prospects for young researchers, but scientists say significant new investment is crucial. https://www.nature.com/articles/d41586-019-00484-4

4 6. Abbott A. Europe's next €1-billion science projects: six teams make it to final round. Nature 2019;566:164-5. The European Commission has selected six research projects — in areas from health and energy to artificial intelligence and cultural heritage — to compete to become one of its next billion-euro 'flagship' science initiatives, Nature has learned. https://www.nature.com/articles/d41586-019-00541-y?WT

#### **Reports on China and Chinese-European Cooperation**

1. Meyer PK. Why China Thinks It Can Build a Utopian World Order. The National Interest November 2016. China is eager to show the world that it can be a responsible and accountable global leader... https://nationalinterest.org/feature/why-china-thinks-it-can-build-utopian-world-order-18486 https://m.guancha.cn/strategy/2016 11 27 381956.shtml (中文)

2. Cyranoski D. Chinese effort to clone gene-edited monkeys kicks off. Nature 2019;566:15-16. Genetically identical primates could provide improved animal models of human disease, but some researchers raise ethical issues...In Europe and the US, non-human-primate research increasingly faces regulatory hurdles, costs and bioethical opposition. This stands in contrast to China; the country's 2011 five-year plan set primate disease models as a national goal. The science ministry followed up by investing 25 million yuan (US\$3.9 million) into the endeavour in 2014... https://www.nature.com/articles/d41586-019-00292-w?WT.ec id



3. Chen W, et al. **Disparities by province**, age, and sex in site-specific cancer burden attributable to 23 potentially modifiable risk factors in China: a comparative risk assessment. *Lancet Glob Health* 2019;7:e257-e269. The population-attributable fractions (PAFs) of cancers attributable to potentially modifiable risk factors vary substantially across provinces in China. Regional adoption of effective primary cancer prevention strategies has a vast potential to reduce the burden of cancer and disparities in China. Smoking, poor diet, and infection warrant particular policy attention as they contributed a large proportion to the total cancer burden...

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30488-1/fulltext https://mp.weixin.qq.com/s/Ix1zaczggHNIl8fLrH9gjA (中文)

4. Chen C et al. China and India lead in greening of the world through land-use management. Nature Sustainability 2019;2:122-9. Satellite data show increasing leaf area of vegetation due to direct factors (human land-use management) and indirect factors (such as climate change, CO2 fertilization, nitrogen deposition and recovery from natural disturbances). Among these, climate change and CO2fertilization effects seem to be the dominant drivers. However, recent satellite data (2000-2017) reveal a greening pattern that is strikingly prominent in China and India and overlaps with croplands world-wide. China alone accounts for 25% of the global net increase in leaf area with only 6.6% of global vegetated area. The greening in China is from forests (42%) and croplands (32%), but in India is mostly from croplands (82%) with minor contribution from forests (4.4%). China is engineering ambitious programmes to conserve and expand forests with the goal of mitigating land degradation, air pollution and climate change. Food production in China and India has increased by over 35% since 2000 mostly owing to an increase in harvested area through multiple cropping facilitated by fertilizer use and surface- and/or groundwater irrigation. Our results indicate that the direct factor is a key driver of the 'Greening Earth', accounting for over a third, and probably more, of the observed net increase in green leaf area. They highlight the need for a realistic representation of human land-use practices in Earth system models.

<u>https://www.nature.com/articles/s41893-019-0220-7</u> <u>http://world.chinadaily.com.cn/a/201902/13/WS5c6361e3a31010568bdc97b2.html (</u>中文)

### Acupuncture, TCM and Other Traditional Medicine

1. Yuan P et al. **Herbal medicine: abuse and risk in China.** *Pharmacoepidemiol Drug Saf* 2016; 25:606. The past decades have witnessed the rapid development and increasing popularity of Chinese herbal medicine at a global scale. However, the fact that abuse of herbal medicine is exceedingly common and risky in China, as is often neglected, needs a



gain of rational awareness in public... Measures should be taken from all sides' effort to prevent the abuse of herbal medicine from causing harm on man's health, including government's laws and regulations on drug sales and safety, propaganda of media on dangers of drug abuse, social supervision, and people's consciousness on reasonable use of herbal medicine. https://onlinelibrary.wiley.com/doi/full/10.1002/pds.3997

🚾 2. A review on chemistry, PD, PK and quality control of Ziziphi Spinosae Semen (酸枣仁)

published by Prof. Xuemei Qin and colleagues in Chinese Traditional & Herbal Drugs (中草药)

2019;50:299-309. <u>https://mp.weixin.qq.com/s/BFdDKwDsHf6pBp5JTJ3\_oA</u>(中文)

**4**3. **Tropism of TCM drugs:** The four natures and five flavours of TCM drugs are well known; equally fundamental is the concept of tropism, i.e. TCM drugs can be defined as ascending and descending, floating and sinking. How can this be understood? Why is potentially important? This can also be an important area for research. <u>https://mp.weixin.qq.com/s/-nlxhhUC0X7dv7vVD1t3lg</u>



4. Mose KF, Bygum A. Chinese herbal remedy found to contain steroids and antifungals. *Lancet* 2019;393:446. A 14-year-old boy with early-onset guttate psoriasis vulgaris presented at our clinic with several reddish-purple, horizontal streaks on the distal part of his shins. Previously, he had been treated with narrow-band ultraviolet B, topical corticosteroids ranging from mild (hydrocortisone 17-butyrate cream 1 mg/g)



to moderate (mometasone furoate cream 1 mg/g and betamethasone valerate ointment 1 mg/g), and tacrolimus ointment 1 mg/g—but the response to treatment was not long lasting. The family consulted

a licensed practitioner of traditional Chinese medicine who prescribed a so-called herbal cream (神夫

草抑菌乳膏). The patient applied the cream topically on the psoriatic lesions twice a day. After 9 months of doing this, he developed a new rash on his shins that was later confirmed to be striae distensae. We suspected that the cause was exposure to a corticosteroid—but the patient had not been using a corticosteroid either topically or systemically during this time. The so-called herbal cream was suspected as a possible source; however, the content label only listed herbal ingredients including Chinese sumac, *Sophora flavescens, Stemona tuberosa* Lour. Nevertheless, the location of the striae was very unusual, and as a simple test, the herbal cream was applied on the upper arm of the senior physician; after 12 h, a strong vasoconstriction effect was seen (figure), which further raised our suspicion that the cream contained a corticosteroid. We therefore sent it for analysis at the Department of Official Medicines Control Laboratory, Swedish Medical Products Agency, Uppsala, Sweden. The laboratory used liquid chromatography-tandem mass spectrometry and nuclear magnetic resonance, and reported that the cream contained both a potent corticosteroid (0.065% clobetasol propionate) and the antifungals ketoconazole and miconazole. We then reported this herbal product to the Danish Medicines Agency to ensure that it was dealt with appropriately.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30116-3/fulltext https://mp.weixin.qq.com/s/1Z8kMUbQA3F9sMHkgjmBRg

5. Lam WC et al. Hong Kong Chinese Medicine Clinical Practice Guideline for Cancer Palliative Care: Pain, Constipation, and Insomnia. eCAM 2019; Article ID 1038206. It is common for patients with cancers in Hong Kong seeking Chinese Medicine (CM) therapies as supportive care during cancer treatment and to manage treatment-related side effects. This article provides clinical practice guideline (CPG) on the use of CM for specific clinical indications caused by cancer and during cancer treatment, including pain, constipation, and insomnia,

and aims to guide local licensed CM practitioners and provide beneficial reference for social medical decision makers and patients. In this manuscript, we summarize the clinical manifestation, CM pattern classification, and CM intervention including herbal treatment, acupuncture treatment, regulating, and nursing based on pattern differentiation.

https://www.hindawi.com/journals/ecam/2019/1038206/

🥗 6. A WeChat introduction to Salvia miltiorrhiza Bunge (丹参

#### Danshen)

https://mp.weixin.qq.com/s/38PCM89vF nSrkt12tQ7Gw (中文)

### 7. Nature Outlook—Tea. | 07 February 2019

Other than plain water, tea is the world's favourite beverage. Researchers are now uncovering its biological secrets, opening the





door to an array of potential benefits. This Nature Outlook is editorially independent. It is produced with third party financial support, including 9 articles, entitled:

- Tea
- The growth of tea
- Culturing better tea research
- Tea's value as a cancer therapy is steeped in uncertainty
- The science of tea's mood-altering magic
- Leading progress on genomics, health benefits and utilization of tea resources in China
- How climate change might affect tea
- Genomic focus brings tea research to the boil
- Brewing nanotechnology from tea

### https://www.nature.com/collections/rcpzjlzyzf?WT.ec\_id=NATURE-20190207&utm

8. Kuriyama S. The Expressiveness of the Body, and the Divergence of Greek and Chinese Medicine. Zone Books, 1999, pp1-340. At the heart of medical history is a deep enigma. The true structure and workings of the human body are, we casually assume, everywhere the same, a universal reality. But then we look into the past, and our sense of reality wavers: accounts of the body in diverse medical traditions often seem to describe mutually alien, almost unrelated worlds. The Expressiveness of the Body meditates on the contrasts between the human body described in classical Greek medicine and the body as envisaged by physicians in ancient China. It asks how this most basic of human realities came to be conceived by two sophisticated civilizations in radically diverging ways. And it seeks answers in fresh and unexpected topics, such as the history of tactile knowledge, the relationship between ways of seeing and ways of listening, and the evolution of bloodletting.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1118467/ https://mp.weixin.qq.com/s/zCIUvxMCi0UkLEQtJwjAXQ(中文)

### 9. Tongue diagnosis in TCM

https://www.verywellhealth.com/tongue-diagnosis-in-traditional-chinese-medicine-3867931 https://mp.weixin.gg.com/s/ID5Dbl7 bm9AucdgRnM9Nw (中文)

#### **Omics in Progress**

1. **Recent progresses in the field of proteomics** (in Chinese, English references) <u>https://mp.weixin.qq.com/s/R0VaAaedCCIIaH-1G6wyxQ</u> (中文)

2. Almeida A *et al.* **A new genomic blueprint of the human gut microbiota.** *Nature* 2019; 11 Feb. doi:10.1038/s41586-019-0965-1. The composition of the human gut microbiota is linked to health and disease, but knowledge of individual microbial species is needed to decipher their biological roles. Despite extensive culturing and sequencing efforts, the complete bacterial repertoire of the human gut microbiota remains undefined. Here we identify 1,952 uncultured candidate bacterial species by reconstructing 92,143 metagenome-assembled genomes from 11,850 human gut microbiomes. These uncultured genomes substantially expand the known species repertoire of the collective human gut microbiota, with a 281% increase in phylogenetic diversity. Although the newly identified species are less prevalent in well-studied populations compared to reference isolate genomes, they improve classification of understudied African and South American samples by more than 200%. These candidate species encode hundreds of newly identified biosynthetic gene clusters and possess a distinctive functional capacity that might explain their elusive nature. Our work expands the known diversity of uncultured gut bacteria, which provides unprecedented resolution for taxonomic and functional characterization of the intestinal microbiota.

https://www.nature.com/articles/s41586-019-0965-1\_reference.pdf.





#### **Other Recommended Readings**

1. Anniversary celebrations are due for Mendeleev's periodic table. *Nature* 2019;565:535. In 1869 Dmitri Mendeleev published his now-famous system of chemical elements. But by listing elements in columns, and lining up the columns to place elements that have similar properties along the same row, he laid the foundations for the iconic arrangement of elements that we know today. To recognize the 150th anniversary of Mendeleev's achievement, the United Nations declared 2019 to be the International Year of the Periodic Table of Chemical Elements (although the modern version was conceived in the 1940s) https://www.nature.com/articles/d



conceived in the 1940s). https://www.nature.com/articles/d41586-019-00281-z?WT.ec\_id

2. **Perspectives on Plan S recently published in** *Science* 2019;363:461-2. Plan S is an initiative for Open Access publishing that was launched in September 2018. The plan is supported by cOAlition S, an international consortium of research funders. Plan S requires that, from 2020, scientific publications that result from research funded by public grants must be published in compliant Open Access journals or platforms.

https://www.coalition-s.org

- Plan S: Unrealistic capped fee structure <u>http://science.sciencemag.org/content/363/6426/461.1?utm</u>
- Plan S: Overlooked hybrid journal model <u>http://science.sciencemag.org/content/363/6426/461.2?utm</u>
- Plan S: A threat to quality of science? <u>http://science.sciencemag.org/content/363/6426/462.1?utm</u>
- Plan S: Motivations of for-profit publishers <u>http://science.sciencemag.org/content/363/6426/462.2?utm</u>

3. Qiu J. American scientist played more active role in 'CRISPR babies' project than previously known. Statnews.com JANUARY 31, 2019. An American scientist at Rice University was far more involved in the widely condemned "CRISPR babies" experiment than has previously been disclosed. Most notably, STAT has learned that Rice biophysicist Michael Deem was named as the senior author on a paper about the work that was submitted to Nature in late November. Deem's prominent authorship indicates that a respected American researcher played an instrumental role in the controversial project, which sparked a worldwide furor. His involvement could have encouraged volunteers to join the experiment and lent credibility to He Jiankui, the Chinese scientist who led the work. https://www.statnews.com/2019/01/31/crispr-babies-michael-deem-rice-he-jiankui/

4. Editorial. **Ultra-large virtual molecular libraries throw open chemical space.** *Nature* 2019;566:7. A library of 350 million drug-like molecules points to potential drugs. <u>https://www.nature.com/articles/d41586-019-00482-6?WT.ec\_id</u>

5. We need to talk about systematic fraud. Nature 2019;566:9. Software that uncovers suspicious papers will do little for a community that does not confront organized research fraud, says Jennifer Byrne. <u>https://www.nature.com/articles/d41586-019-00439-9?WT.ec\_id</u>

6. Zimmermann M et al. Separating host and microbiome contributions to drug pharmacokinetics and toxicity. *Science* 2019;363:eaat9931. The gut microbiota is implicated in the metabolism of many medical drugs, with consequences for interpersonal variation in drug efficacy and toxicity. However, quantifying microbial contributions to drug metabolism is challenging, particularly in cases where host and microbiome perform the same metabolic transformation. We combined gut

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commensal genetics with gnotobiotics to measure brivudine drug metabolism across tissues in mice that vary in a single microbiome-encoded enzyme. Informed by these measurements, we built a pharmacokinetic model that quantitatively predicts microbiome contributions to systemic drug and metabolite exposure, as a function of bioavailability, host and microbial drug-metabolizing activity, drug and metabolite absorption, and intestinal transit kinetics. Clonazepam studies illustrate how this approach disentangles microbiome contributions to metabolism of drugs subject to multiple metabolic routes and transformations. <u>http://science.sciencemag.org/content/363/6427/eaat9931?utm</u>

7. Li M and Belmonte JCI. Frontiers in Medicine: Organoids — Preclinical Models of Human Disease. *N Engl J Med* 2019; 380:569-579. An organoid is a three-dimensional construct composed of multiple cell types that originates from stem cells by means of self-organization and is capable of simulating the architecture and functionality of native organs. Organoids permit in vivo and in vitro investigation and represent one of the latest innovations in the quest for a model to recapitulate the physiologic processes of whole organisms...

https://www.nejm.org/doi/full/10.1056/NEJMra1806175?query=TOC

8. Coe IR et al. **Organisational best practices towards gender equality in science and medicine.** *Lancet* 2019;393: 587-593. In August 2018, the president of the World Bank noted that "'Human capital'—the potential of individuals—is going to be the most important long-term investment any country can make for its people's future prosperity and quality of life". Nevertheless, leaders and practitioners in academic science and medicine continue to be unaware of and poorly educated about the nature, extent, and impact of barriers to full participation of women and minorities in science and medicine around the world. This lack of awareness and education results in failures to fully mobilise the

human capital of half the population and limits alobal technological and medical The chronic lack advancements. of recruitment, promotion, and retention of women in science and medicine is due to systemic. structural, organisational, institutional, cultural, and societal barriers to equity and inclusion. These barriers must be identified and removed through increased awareness of the challenges combined with



evidence-based, data-driven approaches leading to measurable targets and outcomes. In this Review, we discuss these issues and highlight actions that could achieve gender equality in science and medicine. We survey approaches and insights that have helped to identify and remove systemic bias and barriers in science and medicine, and propose tools that will help organisational change toward gender equality. We describe tools that include formal legislation and mandated quotas at national or large-scale levels (eg, gender parity), techniques that increase fairness (eg, gender equity) through facilitated organisational cultural change at institutional levels, and professional development of core competencies at individual levels. This Review is not intended to be an extensive analysis of all the literature currently available on achieving gender equality in academic medicine and science, but rather, a reflection on finding multifactorial solutions.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33188-X/fulltext?dgcid

9. *Nature Reviews* Collection: Key Advances in Medicine 2019. In 2018, numerous scientific advances revolutionized the biomedical and clinical landscape, delivering on the promise of discoveries from previous years and setting the scene for innovative future research. The Key Advances in Medicine 2019 collection, a product from the eight clinical Nature Reviews journals, features 43 'Year in Review' articles that distil the major developments in 2018 and outline emerging trends to watch for in 2019. https://www.nature.com/collections/nswglzqrbp?utm



10. **FDA commissioner announces plan to modernize regulation of dietary supplements.** FDA announced a goal to implement "one of the most significant modernizations of dietary supplement regulation and oversight in more than 25 years."

https://www.naturalproductsinsider.com/regulatory/fda-commissioner-announces-plan-modernizeregulation-dietary-supplements

44 The set al. Large teams develop and small teams disrupt science and technology. Nature. 2019 Feb 13. doi: 10.1038/s41586-019-0941-9. [Epub ahead of print]. One of the most universal trends in science and technology today is the growth of large teams in all areas, as solitary researchers and small teams diminish in prevalence. Increases in team size have been attributed to the specialization of scientific activities3, improvements in communication technology, or the complexity of modern problems that require interdisciplinary solutions. This shift in team size raises the question of whether and how the character of the science and technology produced by large teams differs from that of small teams. Here we analyse more than 65 million papers, patents and software products that span the period 1954-2014, and demonstrate that across this period smaller teams have tended to disrupt science and technology with new ideas and opportunities, whereas larger teams have tended to develop existing ones. Work from larger teams builds on more-recent and popular developments, and attention to their work comes immediately. By contrast, contributions by smaller teams search more deeply into the past, are viewed as disruptive to science and technology and succeed further into the future-if at all. Observed differences between small and large teams are magnified for higher-impact work, with small teams known for disruptive work and large teams for developing work. Differences in topic and research design account for a small part of the relationship between team size and disruption; most of the effect occurs at the level of the individual, as people move between smaller and larger

teams. These results demonstrate that both small and large teams are essential to a flourishing ecology of science and technology, and suggest that, to achieve this, science policies should aim to support a diversity of team sizes. <u>https://www.nature.com/articles/s41586-019-0941-9</u>

<u>https://m.huxiu.com/article/284488.html</u> (中文)

12. Azoulay P. Small research teams 'disrupt'

science more radically than large ones. *Nature* 2019 Feb 13. https://doi.org/10.1038/d41586-019-00350-3. The application of a new citation metric prompts a reassessment of the relationship between the size of scientific teams and research impact, and calls into question the trend to emphasize 'big team' science. <a href="https://www.nature.com/articles/d41586-019-00350-3">https://www.nature.com/articles/d41586-019-00350-3</a>

### Meeting Reports

1. Translating Fundamental Science of Acupuncture into Clinical Practice for Cancer Symptom Management, Pain, and Substance Abuse, National Institutes of Health, Feb. 11-12, 2019. The meeting was attended by Dr Helen Langevin, Director, National Center for Complementary and Integrative Medicine (NCCIH), NIH experts and experts from the USA and China (Baoyan Liu, Huilong Yang, Xianghong Jing, Bingmei Zhu and Songping Han et al.).

https://mp.weixin.qq.com/s/3bMflmU-kFG\_zelywQmAiQ (中文, with English meeting agenda)

#### Invitation from Future Meetings.

<sup>4</sup>1. The 7<sup>th</sup> Annual Meeting of GP-TCM RA will be held in Daegu Haany University (DHU), Daegu City, Republic of Korea, on July 9<sup>th</sup> – 11<sup>th</sup>, 2019. <u>See page 5</u>.

2. The 18th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Shanghai on August 8 - 10, 2019 (Thursday- Saturday), the Meeting is organized by Shanghai University of Traditional Chinese Medicine, Shanghai. It provides a platform for

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regulatory-industrial-academic exchanges and potential research collaborations on various frontiers of Traditional Chinese Medicine among our worldwide CGCM members and guests.

The following themes will be addressed at the meeting:

- Acupuncture
- Bioinformatics: "Omics" Approach and Data Analysis
- Clinical Investigation
  - § Cancer, Liver Disease and Inflammation
  - § Other Diseases and Safety
  - Chinese Medicine Resources
  - § Authentication
    - § Cultivation and Herbal Quality
    - § Identification, Formulation and Manufacturing
  - § Endangered Species
- Regulation and Interregional Collaborations in Academia, Government and Industry
- Natural Products
  - § Biological Activity
  - § Cancer, Virus and Inflammation
  - § Identification, Bio-transformation and Metabolism
- Polychemical Activities and Mechanism Study
  - § Cancer, Immunomodulation and Inflammation
  - § Metabolic, Neural Diseases, Aging Process and Others
  - § Toxicity and Safety Evaluation of Herbal Medicines
- Preventive Medicine
- TCM Diagnosis

#### Abstract Submission deadline: May 31, 2019 (Friday).

Should you have any enquiries, please contact <u>centraloffice@tcmedicine.org</u>. For further information, please visit: <u>www.tcmedicine.org</u>

**3. 2019** *The Lancet*–CAMS Health Conference: a call for abstracts. The Chinese Academy of Medical Sciences (CAMS) and the *Lancet*family of journals invite abstract submissions for the 2019 *The Lancet*–CAMS Health Conference, to be held on Oct 19–20, 2019, in Chengdu, China. West China Hospital, Sichuan University, will be the local co-organiser with CAMS in Chengdu. 2019 will mark the fifth collaborative conference between CAMS and the *Lancet* family of journals to support medical research in China. Abstracts must be relevant to health science in China and at least one author must be based at an institution in China. Submissions are invited from all aspects of medical research,... https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33176-3/fulltext

4. The 16<sup>th</sup> World Congress of Chinese Medicine will be held in Budapest, Hungary, in November 2019: <u>https://a.eqxiu.com/s/1BpDHw7h (</u>中文)





#### **Invitation from Journals**

1. **Health-care reform in China: a** *Lancet* call for papers. In 2009, China unveiled its ambitious health-care reform plan, with the goal of provision of affordable and equitable basic health care for all by 2020. The reform is anchored in five interdependent areas: expanding coverage to insure more than 90% of the population, establishing a national essential medicines system, improving the primary care system, making public health services available and equal for all, and public hospital reforms. How has China changed since the 2009 health-care reform?

In 2019, *The Lancet* will dedicate a theme issue to evaluate the progress of health-care reform in China on its tenth anniversary. The 2019 China theme issue will be launched at *The Lancet*–Chinese Academy of Medical Sciences Health Conference in Chengdu, China, on Oct 19–20, 2019. While we welcome submissions from China throughout the year and across all *Lancet* family journals, the editors invite submissions of high-quality research from China—or from research teams working on health in China—for this issue.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33054-X/fulltext

2. 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: <a href="http://www.wjtcm.net">http://www.wjtcm.net</a>

**Great news!** Since November 2018, WJTCM has been included in the list of core Chinese scientific journals and magazines! https://mp.weixin.gg.com/s/r5BAEi8uinIpxj0QvhapMA (中文)

**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>gihe.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 Yuan Shiun Chang (Taichung), Prof Pierre Duez (Mons), Prof Rong-Rong He (Guangzhou), Dr Clara Lau (Hong Kong), Dr. Zhihua Li (Xi'an), Dr Fan Qu (Hangzhou), Prof Yonghua Wang (Xi'an), Dr Qihe Xu (London) and Prof Min Ye (Beijing) are gratefully acknowledged.

Pictures of the 2019 Harbin International Ice and Snow Sculpture Festival are borrowed from <u>https://mp.weixin.qq.com/s/BzgcnR332-2iDX5jdDtPdQ</u>(中文) and

https://www.theatlantic.com/photo/2019/01/photos-2019-harbin-ice-and-snow-festival/579607/

