

### **Editorials**

<sup>≪</sup>1. Honoring the 500<sup>th</sup> Anniversary of Li Shizhen (李时珍) : A Season of Celebration



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On May 26<sup>th</sup>, a group of over 800 scholars, scientists and leaders from around the world came together in Li Shizhen's hometown of Qichun to honor the man behind the Ming dynasty masterpiece, the Ben Cao Gang Mu《本草綱目》(Compendium of Materia Medica). While enthusiasm for the 500<sup>th</sup> anniversary celebration of Li Shizhen had been building for years among experts in the field of Chinese materia medica, none were prepared for the pinnacle event that was to come. Beyond the sights and ceremony itself, it felt as though the celebration marked a moment in history, an event that we will one day look back on as the pivotal moment when Li Shizhen moved into the mainstream.



The name of Li Shizhen and his Ben Cao Gang Mu have been well-

known for centuries among scholars and medical scientists in both the East and West, but recent years have seen a spike in interest in Li, and his profound contributions are attracting more and more attention worldwide. For example, the Ben Cao Gang Mu was listed in UNESCO's Memory of the World Register in 2011, and Li Shizhen was honored at the UNESCO Center in Paris to mark the 500<sup>th</sup> anniversary just before the main event in Qichun (蕲春).



Why all the passion for a doctor that lived 500 years ago? In many ways, Li Shizhen embodies the Archives (2008-2018): www.gp-tcm.org/news-list/ 1



essence of Chinese culture with his never-ending dedication to scholarship and his desire to make a positive contribution for future generations. He respected and preserved previous medical classics and perspectives, yet at the same time his scientific mind sought to find new approaches to classification, and he subjected the inherited knowledge of the past to critical analysis and experimentation. Li lived in an eventful time, when world trade was dramatically expanding and new medicines and ideas were constantly arriving. Today, we find ourselves at a similar moment in history, the ancient trade routes that linked distant cultures and brought new medicines to Li Shizhen in the Ming dynasty are being revived, global interest in Chinese medicine is increasing, and it falls to us to emulate Li's spirit by simultaneously preserving traditional knowledge while embracing new innovations and achievements.

#### A Warm Welcome in Qichun

Li Shizhen's hometown of Qichun is located about two hours from Wuhan in Hubei province. Qichun is said to have "four treasures", and the most famous of these is "Qi'ai", the Qichun mugwort that has been prized as the best source of moxa for centuries. Pulling into town, the signs for Qichun moxa are all around, and to the amazement of the international guests, the entire town of Qichun had fundamentally transformed into a medical destination center to welcome to celebration. A vast, modern conference center was the site for an academic forum that brought together top medicinal plant experts from around the world, while the centerpiece of the celebration was held within an impressive museum set in a traditional Chinese courtyard and garden that was built to surround the grave of Li Shizhen and his parents. For the foreign scholars in attendance, it was striking to see such appreciation for traditional medicine and such comprehensive support from society. In the day following the opening ceremony, over 60,000 members of the public came out to enjoy the setting.



The setting of the main celebration was idyllic. Upon arriving at the main gate of a large traditional "*siheyuan*" courtyard, the guests entered to find two large Chinese characters that symbolize the unique role of Li Shizhen: *yi* (醫) and *yao* (藥), since Li's work united both medicine and the study of the herbs themselves. Indeed, in his later years Li Shizhen wrote a text called the *Bin Hu Mai Xue* 

《 瀕湖脈學》(*Lakeside Master's Study of the Pulse*), and today his grave sits next to a lake, much as he enjoyed in life. Elements of plants, minerals, and animals were all together in the garden, just as they are together in the *Ben Cao Gang Mu*. Some medicinal plants such as lily were bright with blossoming flowers, while other medicinal plants in the garden had a unique connection to Li Shizhen, such as datura, which was classified by Li for the first time in his *Ben Cao Gang Mu*. The feeling of *feng shui* was tangible as the Western guests stood in awe of the vast scale of the garden and lake, and the air was rich with emotion as the crowd bowed their heads for a moment to honor Li Shizhen before dropping flowers by his grave.

A large museum dedicated to Chinese medicine and Li Shizhen was opened to celebrate the 500<sup>th</sup> anniversary, and within the museum are several unique treasures. A newly discovered copy of the



Jinling edition of the *Ben Cao Gang Mu* was recently identified, and this rare first printing of the text was exhibited at the museum in honor of the occasion. Continually guarded by heavily equipped police officers, this edition of the text is a national treasure and was the crown jewel of the Qichun exhibit. However, in addition to this centerpiece, the museum was rich with artifacts, including the only remaining portrait of Li Shizhen by the original artist of the now-famous image, as well as an early Japanese complete translation of the *Ben Cao Gang Mu*. From original artifacts to wax statues and texts, the Li Shizhen museum is a fascinating collection that is worth making a special trip to see.



Following the central ceremony, an academic forum was held that brought together experts from across China and the West, as well as local experts Wang Ping from the Hubei University of Traditional Chinese Medicine. Many famous experts in the area of Chinese materia medica were present, including respected leaders such as Professors Zheng Jinsheng, Zhao Zhongzhen, Cao Hui, Mei Quanxi, Deng Jiagang, Lin Ge, Zhang Zhibin, Wang Dequn and many others. European scholars and scientists such as Paul Unschuld and Rudolf Bauer of Germany and Michael Heinrich of the UK praised the work and spirit of Li Shizhen, while Erich Stoger of Austria and Roy Upton and Eric Brand of the USA made a passionate case for preserving traditional knowledge in the process of advancing pharmacopoeia standards. Visiting experts from Japan and Korea made tremendous contributions, including insights on the transmission of the *Ben Cao Gang Mu* to Japan by Prof. Makoto Mayanagi and a presentation on herbal quality control by Prof. Rack Seon Seong of Korea.

This forum was primarily organized by the "*Bencao Club*" (本草讀書會), which was initiated by Professor Zhao Zhongzhen of the School of Chinese Medicine, Hong Kong Baptist University.

After returning from the academic conference, the visiting scholars retired to a brand-new hotel that was finished just before the forum began. Featuring a tasteful mix of traditional and modern styles, the hotel seemed like a natural setting for future conferences, and indeed the town of Qichun seems ready to become a prime destination in China for those with a passion for traditional medicine. Directly across from the hotel was a small village that had been recreated in a Ming dynasty style, and the many small shops that are opening suggest that Qichun will gradually grow to become a famous destination for medicine, tourism, and culture.

At a time of increasing attention on Chinese culture and Chinese medicine worldwide, Li Shizhen serves as an ambassador, reaching across time to inspire us all to preserve traditional knowledge while innovating in new directions. By bringing together experts from around the world to exchange knowledge on medicinal plants, the 500<sup>th</sup> anniversary celebration of Li Shizhen captured the spirit of exchange and scholarship that defined Li Shizhen's life, and will help to spread the news of Li

Shizhen so that his story can help to inspire others around the world.

Further exploration: To watch Prof Zhao's lecture on Li Shizhen and his works, please visit here: <u>https://drive.google.com/file/d/1L2J</u> <u>A8vzKzPKtwoVehVQP2p2XV20oc</u> XxI/view (中文)



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#### New Omic and Network Paradigms for Deep Understanding of Therapeutics: Mechanisms for TCM Fangi



Prof Zhong Wang

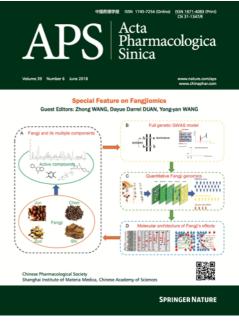
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Combination therapy with multi-drug regimen as an integrated intervention of several pharmacological compounds that interact with multiple targets, rather than monotherapy using a single compound that targets at a single molecule, is a common strategy for combating complex disease in both Western and traditional Chinese medicine (TCM)<sup>[1-3]</sup>. But each is based on different mechanistic principles. In Western medicine, a multi-drug regimen usually combines several monotherapies targeting on different molecules to optimize pharmacodynamics and/or pharmacokinetics to improve therapeutic efficacy and/or reduce toxicity and adverse reactions<sup>[1]</sup>. In TCM, the main therapeutics is the unique TCM medicinal formula, so called Fangji, which is usually composed of multiple herbs and medical materials with integrated multiple therapeutic objects. One of the major principles of Fangji compositions is Zhenghou based "Jun-Chen-Zuo-Shi" to orchestrate and integrate the multiple therapeutic targets for a specific Zhenghou<sup>[4]</sup>. The ingredients in a Fangji were thus composed according to the quaternity of Jun (monarch), which targets at the major etiological mechanisms, Chen (minister), which targets at the secondary etiological mechanisms, Zuo (assistant or associate), which targets at the associated factors to facilitate the therapeutic effects or reduce the adverse effects, and Shi (quide), which quides and orchestrates the targets <sup>[4]</sup>. Therefore, TCM Fangii combination therapy has embodied many principles of modern systems biology and omic theories <sup>[2,3]</sup>. The therapeutic effects of TCM Fangii rely on the integrated whole function through compatibility of the drugs in the multi-drug regimen of Fangji<sup>[2]</sup>. For example, the Duhuo Jisheng decoction (DHJSD) widely used in clinic for effectively combatting lower back pain (LBP) was developed with an integrated combination of 15-ingredients according to the principles of "Jun, Chen, Zuo, and Shi" to specifically target at the primary and secondary causatives of Bi Zheng<sup>[5]</sup>. It eliminates "feng-han-shi" and thus pain of "Bi Zheng" and promotes "Gan" and "Shen" function and therefore strengthens the bones and tendons, respectively. It also improves circulation and removes stasis of "Qi" and "Xue", reduces tissue swelling and relieves pain. Liu et al. found that DHJSD inhibited the generation of

proinflammatory factors and extracellular matrix (ECM) degradation of human intervertebral disc (HID) through an orchestrated targeting at multiple molecules in the SDF-1/CXCR4/NF- $\kappa$ B pathway, thus solved a puzzle of the quarternity of Jun-Chen-Zuo-Shi and added novel mechanistic insights into the clinical effectiveness of DHJSD on LBP<sup>[5]</sup>. Luo et al. studied the Fangji of Yangxin Tongmai formula (YTF) in the treatment of pediatric Graves' disease (GD). They found that YTF enhanced glucose handling in GD children with impaired glucose tolerance through multiple targets to promote the bioactivity of insulin and to avoid the low density of insulin receptors that is induced by the feeble binding affinity of insulin<sup>[6]</sup>.

The modern pharmacological approach to the study of Fangji, however, has been focusing on the isolation and identification of individual active components within a Fangji for cellular and molecular targets. Although this approach has led to the development of many new monomers purified from Fangji as





new drugs widely used in clinical practice such as the antimalarial artemsinin,<sup>[7]</sup> which has earned a Nobel Prize in Physiology or Medicine in 2015,<sup>[8]</sup> the pharmacological bases of these purified effective monomers or active components have lost the TCM characteristics and are far different from the pharmacological theory and clinical applications of Fangji, in terms of the principles of combination therapy based on the composition theories such as the quaternity of Jun-Chen-Zuo-Shi. This not only has led to the misinterpretations of mechanisms of Fangji's therapeutic actions and clinical



effectiveness but also has seriously hampered the scientific research and development of TCM in general.

Clearly, new omic/systematic and networking paradigms are urgently needed for deep understanding of the unique composition theories and mechanisms of effective combination therapy through TCM Fangji. Recent endeavors attributed to this revolutionary paradigm shift has resulted in the current special issue of Fangjiomics. Original studies and reviews on the application of genomics <sup>[9]</sup>, trascriptomis <sup>[10]</sup>, proteomics <sup>[10]</sup>, metabolomics<sup>[11]</sup>, fangjiomics <sup>[12,13]</sup> and network pharmacology <sup>[12,14]</sup> and network medicine [15-17] to the study of several classic Fangjis are incleded. The unbiased genome-wide association study (GWAS) and pharmacogenomics have been applied to dissect the genetic variants underlying complex diseases and individual responses to a given treatment <sup>[9]</sup>. Recent development of a full genetic model for analysis of gene-gene interactions (dominance and epistasis) and gene-environment interactions has substantially increased model power and remarkably improved the detection of association of GWAS and the construction of the molecular architecture <sup>[9]</sup>. This analysis can integrate other omic information and allow for variations of Fangji, which is very promising for Fangjiomic detection of the sophisticated molecular and structural architecture of the function of Fangii<sup>[9]</sup>.

Zhang et al. investigated the mechanisms of Guanxinjing capsules (GXJCs) on coronary heart disease (CHD) complicated with depression <sup>[14]</sup>. A total of 16 GXJC drug-like chemical constituents were identified by UHPLC-LTQ-Orbitrap assay and evaluation of oral bioavailability. Then, 870 genes were identified as the putative targets of these GXJC drug-like chemical constituents by using MedChem Studio. A CHD/depression therapeutic target network of GXJC was then constructed, and four topological features (degree, betweenness, closeness and K-coreness) were calculated. Based on the topological feature values of the GXJC putative targets, 14 main active constituents were identified. Their corresponding putative targets had topological importance in the GXJC putative target-known CHD/depression therapeutic target network, which were defined as the candidate targets of GXJC against CHD complicated with depression <sup>[14]</sup>. Functionally, these candidate targets were significantly involved in several CHD/depression-related pathways, including repairing pathological vascular changes, reducing platelet aggregation and inflammation, and affecting patient depression. Using this integrative pharmacology approach of active chemical constituent identification, drug target prediction and network analysis Zhang et al. identified a list of main active constituents of GXJC acting on CHD complicated with depression. This approach to the identification and characterization of molecular targets of Fangji is more efficient and adequate than the conventional pharmacological approach and provides more accurate information for better understanding of the pharmacological mechanisms of traditional Chinese medicine prescriptions.

Fangjiomics, which was introduced in the previous special issue "Fangjiomics: revealing adaptive omics pharmacological mechanisms of the myriad combination therapies to achieve personalized medicine" in 2015<sup>[3]</sup>, uses rational drug combinations with higher efficacy but fewer adverse effects in a controlled array design by systematically integrating diverse omics data on genomic, proteomic, and metabolomic interactions, in contrast to traditional "omics" techniques focusing on a certain level of cell, tissue, or organ<sup>[2]</sup>. Based on the integration of multi-scale omic data and quantitative modeling of the relationships between complex diseases and combination therapy, Fangijomics-based Archives (2008-2018): www.gp-tcm.org/news-list/



combination therapy presents its feasibility to achieving precision medicine, which would ensure that patients receive the right treatment at the right dose and at the right time, with maximum efficacy and minimum side effects. In this special issue, we continued to introduce its applications to the discovery of rational combination therapy and precision medicine.

The emerging pharmacophenomics studies the orchestrated multi-target pharmacology of combination therapy and provides a systematical paradigm for the pharmacological study of Fangji<sup>[20]</sup>. With well-defined molecular mechanisms of Zhenghou at the level of multi-omics through phenomewide association study (PheWAS) and a suite of new phenomics technologies and platforms, pharmacophenomics may be used to characterize the drug-response phenome of Fangji and to identify the corresponding multiple therapeutic targets according to the TCM theory of jun-chen-zuo-shi. Pharmacophenomic study of Fangji will also lay a theoretical foundation for the new science of precision medicine.



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  - Duan DD. et al. Chin J Pharmacol Toxicol 2014;28:1-9

### **European Reports:**

1. Rabesandratana T. Europe's science spending set for another big boost. Science 2018; 360: 952-953. On 7 June, the European Commission will lay out detailed plans for one of the biggest single research programs on the planet. Horizon Europe could be worth €97.6 billion between 2021 and 2027, up from about €77 billion for the current 7-year program, Horizon 2020. Although Horizon Europe will keep Horizon 2020's main features, the commission has laid the groundwork for several novelties, including a new agency to tackle the continent's perennial innovation problem and a big, separate push on collaborative defense research. But contentious negotiations lie ahead. The United Kingdom is negotiating the terms of its impending exit from the European Union, and some member states want to tighten budgets. Meanwhile, research advocates want more generous spending, noting the low application success rates in Horizon 2020—a frustrating 11.9% so far... http://science.sciencemag.org/content/360/6392/952?utm

#### 2. European Commission Publishes Proposal for Horizon Europe

The European Commission has published its proposal for the next Framework Programme (and the successor to Horizon 2020), Horizon Europe. The programme will aim to strengthen the EU's scientific and technological base, foster the EU's competitiveness and its innovation performance, as well as deliver on the EU's strategic priorities and tackle global challenges.

The total budget announced is €100 billion for 2021-2027, with €97.6 billion for Horizon Europe and €2.4 billion for Euratom. The Horizon Europe funding will be split across three pillars:

• Open Science - €25.8 billion



- Global Challenges €52.7 billion
- Open Innovation €13.5 billion

The main changes from Horizon 2020 highlighted are:

- The creation of the European Innovation Council (EIC) with its early stage and development based funding instruments for start-ups and companies;
- The introduction of Missions, which will unite a body of research in pursuit of a clearly stated goal;
- A new streamlined set of Partnerships with industry, civil society and funding foundations; and
- Further simplification of the programme.



Carlos Moedas, the Commissioner for Research and Innovation, introduced the proposal at a press conference today. The Commissioner explained that the overall structure of the three pillar approach and the vision between having a new Mission-orientated approach. The proposal is the first step of this co-creation process to develop Missions in Horizon Europe, and we can anticipate the launch of a Mission's Board in early 2019. Commissioner Moedas explained the new radical approach to funding innovation under the European Innovation Council in the third pillar of Horizon Europe, with an aim to having a bottom-up approach to funding innovation, rather than a traditional top down approach. The Commissioner confirmed that the Horizon Europe Euratom and ITER proposals are based on continuity, with a specific focus on safety in the Euratom programme.

Attendees had the opportunity to ask questions, several questions related to the position of the UK and the opportunities for countries to associate to Horizon Europe. Moedas highlighted that the rules for association had been expanded in the proposal for Horizon Europe, as can be seen in the relevant part of the proposal. The Commissioner explained that in his view "it's very important for the UK and it's very important for the EU to have a relationship in science and innovation" and he reiterated that "we have Third Countries that are part of the family[...]" but that the details on how this will work still needs to be worked out as part of the negotiations. He explained that the proposal is designed to allow Third Countries to associate to the programme, and that the "doors are open" for the discussion and gives freedom to agree the exact terms of association. In response to later questions he also tackled the topic of 'influence', highlighting that Associated Countries sit at the table and contribute to discussions on all programmes, even if they do not get a formal vote.

A new website on Horizon Europe has been launched by the Commission which includes links to a video, a factsheet on the budget and the research and innovation success stories as well as links to the package of legal texts.

http://europa.eu/rapid/press-release IP-18-4041 en.htm?utm

https://ec.europa.eu/commission/publications/research-and-innovation-including-horizon-europe-iterand-euratom-legal-texts-and-factsheets\_en

https://ec.europa.eu/info/designing-next-research-and-innovation-framework-programme/what-shapes-next-framework-programme\_en

https://www.youtube.com/watch?v=g8BQNnX6\_kY&feature=youtu.be

**4** 3. SME Instrument Report 2018 Published: Here are the main findings from the report:

- Since its start in 2014, the SME Instrument has invested €1.3 billion in a unique selection of 3200 SMEs to get their breakthrough innovations to the market faster.
- In 2017, SME-Instrument-funded companies accounted for 10% of all tech IPOs in Europe and the follow-up equity investments into companies funded by the SME Instrument doubled within just one year.
- Each €1 invested by the SME Instrument generated €1.6 of private investment.
- Companies funded under Phase 2 of the programme had benefitted from a 118% increase in turnover and a 158% increase in employment after two years.



• The Phase 1 feasibility study and the coaching support offered by the SME Instrument build up strategic and managerial capacity within the funded SMEs.

https://ec.europa.eu/easme/sites/easme-site/files/smei\_2018\_impact\_report\_final\_may\_2018.pdf

4. Haug CJ. **Turning the Tables — The New European General Data Protection Regulation.** *N Engl J Med* 2018; 378:2153-2155. "Action required: Make sure you receive important information!" was the alarming message my Internet service provider recently sent me. It turned out they wanted me to review my privacy settings — or, really, to agree that they could continue using data about me just as they had before. People throughout Europe have been inundated with such messages over recent weeks. Almost every Web page or app you open presents you with a pop-up window and an "I agree" button that must be hurdled before you can buy your train ticket, access your music, or browse content. Why this sudden concern about privacy settings? The reason is the General Data Protection Regulation (GDPR), a new European privacy law that will be fully enforced this summer. Given that the regulation was proposed in 2012 and adopted in May 2016, it should come as no surprise that it has become fully enforceable throughout the European Union (EU) now, after a 2-year grace period... https://www.nejm.org/doi/full/10.1056/NEJMp1806637?query=TOC

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

1. *Nature* reports on China's latest move to fight against research misconduct <u>http://www.nature.com/articles/d41586-018-05359-8</u> <u>http://www.nature.com/articles/d41586-018-05359-8</u>

http://www.ebiotrade.com/newsf/2018-6/2018614113200414.htm (中文)

2. Rönkkö TJ et al. Emissions and atmospheric processes influence the chemical composition and toxicological properties of urban air particulate matter in Nanjing, China. *Science of The Total Environment* 2018;639:1290-1310. Ambient inhalable particulate matter (PM) is a serious health concern worldwide, but especially so in China where high PM concentrations affect huge populations. Atmospheric processes and emission sources cause spatial and temporal variations in PM concentration and chemical composition, but their influence on the toxicological characteristics of PM are still inadequately understood. In this study, we report an extensive chemical and toxicological characterization of size-segregated urban air inhalable PM collected in August and October 2013 from Nanjing, and assess the effects of atmospheric processes and likely emission sources. A549 human alveolar epithelial cells were exposed to day- and nighttime PM samples (25, 75, 150, 200, 300 µg/ml) followed by analyses of cytotoxicity, genotoxicity, cell cycle, and inflammatory response. PM<sub>10-2.5</sub> and PM<sub>0.2</sub> caused the greatest toxicological responses for different

endpoints, illustrating that particles with differing size and chemical composition activate distinct toxicological pathways in A549 cells. PM<sub>10-</sub> 2.5 displayed the greatest oxidative stress and genotoxic responses; both were higher for the August samples compared with October. In contrast, PM<sub>0.2</sub> and PM<sub>2.5-1.0</sub> samples displayed high cytotoxicity and substantially disrupted cell cycle; August samples were more cytotoxic whereas October samples displayed higher cell cycle disruption. Several components associated with combustion, traffic, and industrial emissions displayed strong correlations with these toxicological responses. The lower responses for PM<sub>1.0-0.2</sub> compared to PM<sub>0.2</sub> and PM<sub>2.5-1.0</sub> indicate diminished toxicological effects likely due to aerosol aging and lower proportion of fresh emission particles rich in highly reactive chemical components in the PM<sub>1.0-0.2</sub> fraction. Different emission sources and atmospheric processes caused variations in the chemical composition and toxicological responses between PM fractions. sampling campaigns, and day and night. The results indicate different



toxicological pathways for coarse-mode particles compared to the smaller particle fractions with typically higher content of combustion-derived components. The variable responses inside PM

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fractions demonstrate that differences in chemical composition influence the induced toxicological responses.

https://www.sciencedirect.com/science/article/pii/S0048969718319120

3. Watts G. Chen Wang: new President of CAMS and PUMC. Lancet 2018; 391:2407. Professor Chen Wang, Director of the Centre for Respiratory Medicine at Beijing's China–Japan Friendship Hospital, is the new President of the Chinese Academy of Medical *Sciences* (CAMS) and Peking Union Medical College (PUMC). Of the several reasons for welcoming the appointment, the most obvious is Wang's expertise in the respiratory diseases that are a leading cause of morbidity and mortality in his country and impose a great socioeconomic burden. Moreover, he makes no secret of his enthusiasm for curbing tobacco use, which, while now recognised by the Chinese Government as a key public health issue, remains high.



https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31274-1/fulltext?dgcid

4. China Focus: Tech giants tap into AI healthcare market. SHENZHEN, June 19 (Xinhua) --Before 2017, gastroenterologist Cheng Chunsheng had to inspect over 1,000 gastroscopy pictures to search for possible esophageal cancer symptoms, a cancer which appears in the food pipe. However, this painstaking process is no longer needed since the People's Hospital of Nanshan District in Shenzhen where Cheng works introduced "Tencent AIMIS", an AI medical imaging software released in August last year. "The AI system screens through each report and notifies the doctor if further inspection is needed," said Cheng. The system has significantly boosted his efficiency... http://www.xinhuanet.com/english/2018-06/19/c 137265090.htm

5. **Shanghai sets up pioneering brain science center** <u>http://www.xinhuanet.com/english/2018-05/15/c\_137180824.htm</u>

6. China creates medical instrument to culture stem cells automatically <a href="http://www.xinhuanet.com/english/2018-05/15/c">http://www.xinhuanet.com/english/2018-05/15/c</a> 137181160.htm

7. Chen L, Yang M. New opportunities for China in global health. Lancet Global Health 2018; 6:e722-3. In the 5 years since the launch of *The Lancet Global Health*, China has emerged as a major player in global health. In April, 2018, a new International Development Cooperation Agency (IDCA) was launched in China, after deliberation by the country's 19th party congress in October, 2017, and endorsement by the National People's Congress in March, 2018. Similar to the US Agency for International Development and the UK Department for International Development, China's IDCA will be responsible for coordinating and managing the country's foreign aid policy, both financing and implementation...

https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30263-8/fulltext?dgcid=raven\_jbs\_etoc\_email

8. Silver A. **US-Chinese trade war puts scientists in the cross hairs**. *Nature* 2108;**558**:494-495. Scientific research in the United States could become collateral damage in the country's escalating trade dispute with China. Both countries went head-to-head in mid-June over tariffs on a long list of goods that includes lab equipment and reagents. That is likely to increase the cost of scientific research, and the impact could be felt more keenly in US labs. https://www.nature.com/articles/d41586-018-05521-2?WT.ec\_id

#### TCM, Acupuncture and Other Traditional Medicine

1. Steyn M et al. A herbal treatment for type 2 diabetes adulterated with undisclosed drugs. Lancet 2018;391:2411. Patients might be drawn to the use of herbal remedies because they are encouraged to think of them as natural remedies, free from adverse effects. We describe a case in which a patient purchased a purported herbal remedy that was found to be adulterated with commonly prescribed drugs...The patient volunteered that from November, 2015, until May, 2017,

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she had replaced some of her diabetic medicine prescribed at the time with a herbal remedy purchased in India, which the manufacturers claimed was a cure, rather than a treatment, for diabetes. The patient noted some of her Indian acquaintances were taking the same herbal remedy. She stopped taking the product after experiencing recurrent hypoglycaemia. A gradual decline in her renal function, along with hypoalbuminaemia and peripheral oedema, although no albuminuria, was also noted from the time the supplement was started...

https://doi.org/10.1016/S0140-6736(18)31134-6

<sup>2</sup>2. Li Z et al. Challenges in quality assessment of Chinese materia medica and an update on the application of metabolomics in quality assessment of Chinese materia medica. *Chinese Traditional and Herbal Drugs.* 2018; 49: 2221-2229

https://mp.weixin.qq.com/s/jFIU2H6yUZu-DLzGEnrSaw (中文)

<sup>4</sup>3. Chen Keji: Interative Chinese Medicine, an approach that must go on despite all difficulties. <u>https://mp.weixin.qq.com/s/k22qajMjCwp8LhZikq7q8A</u> (中文)

4. **SATCM publish 57 international cooperation projects.** Published on 28<sup>th</sup> May 2018, the projects include 31 overseas TCM centres, 11 TCM international cooperation platforms and 15 TCM international cultural dissemination projects, involving 50M RMB Yuan of investment.

https://mp.weixin.qq.com/s/Ss2KplxGiryIHYdcS-ZpyA (中文)

5. **TRAFFIC: EU-funded project in China has lasting impacts for sustainable use of wild plants by Chinese traditional medicine sector.** Wildlife trade, the commercial use of wild animal and plant resources, is an issue at the heart of the tension between biodiversity conservation and human development. TRAFFIC holds a unique role as a global wildlife trade specialist, combining original research, sound and impartial analysis, and collaborating with a wide range of partners to identify conservation challenges and support solutions linked to trade in wild animals and plants...

http://www.traffic.org/home/2014/10/24/eu-funded-project-in-china-haslasting-impacts-for-sustainab.html



## 1. Willyard C. New human gene tally reignites debate. Nature

2018;558:354-355. Some fifteen years after the human genome was sequenced, researchers still can't agree on how many genes it contains. The latest attempt to plug that gap uses data from hundreds of human tissue samples and was posted on the BioRxiv preprint server on 29 May 2018. It includes almost 5,000 genes that haven't previously been spotted — among them nearly 1,200 that carry instructions for making proteins. And the overall tally of more than 21,000 protein-coding genes is a substantial jump from previous estimates, which put the figure at around 20,000. But many geneticists aren't yet convinced that all the newly proposed genes will stand up to close scrutiny. Their criticisms underscore just how difficult it is to identify new genes, or even define what a gene is...

<u>https://www.nature.com/articles/d41586-018-05462-w?WT.ec\_id</u> This story is also featured in *The Scientist*:

https://www.the-scientist.com/?articles.view/articleNo/54891/title/New-Database-Expands-Number-of-Estimated-Human-Protein-Coding-Genes/&utm

2. Klein JB, Knepper MA. **Protein Mass Spectrometry Made Simple.** JASN 2018, in press. <u>http://jasn.asnjournals.org/content/early/2018/05/02/ASN.2018030244</u>

3. Grams ME, Shafi T, Rhee EP. **Metabolomics Research in Chronic Kidney Disease.** JASN 2018, in press.





http://jasn.asnjournals.org/content/early/2018/05/02/ASN.2018030256

4. Langenberg C, Lotta LA. Genomic insights into the causes of type 2 diabetes. Lancet 2018; 391:2463-474. Genome-wide association studies have implicated around 250 genomic regions in predisposition to type 2 diabetes, with evidence for causal variants and genes emerging for several of these regions. Understanding of the underlying mechanisms, including the interplay between  $\beta$ -cell failure, insulin sensitivity, appetite regulation, and adipose storage has been facilitated by the integration of multidimensional data for diabetes-related intermediate phenotypes, detailed genomic annotations, functional experiments, and now multiomic molecular features. Studies in diverse ethnic groups and examples from population isolates have shown the value and need for a broad genomic approach to this global disease. Transethnic discovery efforts and large-scale biobanks in diverse populations and ancestries could help to address some of the Eurocentric bias. Despite rapid progress in the discovery of the highly polygenic architecture of type 2 diabetes, dominated by common alleles with small, cumulative effects on disease risk, these insights have been of little clinical use in terms of disease prediction or prevention, and have made only small contributions to subtype classification or stratified approaches to treatment. Successful development of academiaindustry partnerships for exome or genome sequencing in large biobanks could help to deliver economies of scale, with implications for the future of genomics-focused research.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31132-2/fulltext?dgcid

4 Science 5. May M. Technology Feature | Translating big data: The proteomics challenge. Science 2018; 360:1255. Getting the most out of protein-related information depends on teamwork among scientists around the world, and that involves sharing large datasets. Simply passing big data back and forth is not a problem, however-the main obstacle is sharing that data in a way that other scientists can use it. Building software that can interpret information from different experiments and equipment remains complicated; likewise, exploring and analyzing large datasets from proteomics experiments even from one lab requires software that is most often developed in-house.

http://science.sciencemag.org/content/360/6394/1255.2?utm campaign=toc sci-mag 2018-06-14&et rid=33953672&et cid=2115504

2018;173: 1581–1592. Machine learning, a collection of data-analytical techniques aimed at building predictive models from multi-dimensional datasets, is becoming integral to modern biological research. By enabling one to generate models that learn from large datasets and make predictions on likely outcomes, machine learning can be used to study complex cellular systems such as biological networks. Here, we provide a primer on machine learning for life scientists, including an introduction to deep learning. We discuss opportunities and challenges at the intersection of machine learning and network biology, which could impact disease biology, drug discovery, microbiome research, and synthetic biology...

https://www.cell.com/cell/fulltext/S0092-8674(18)30592-0

the role of RNAs in genome regulation. Nature Methods 2018;15:405.

https://www.nature.com/articles/s41592-018-0030-2?WT.ec id

2 8. Nawy T. GENOMICS: A pan-cancer atlas. Nature Methods 2018;15:407 (commentary on Hoadley, K. A. et al. Cell 2018;173:291-304) The Cancer Genome Atlas (TCGA), a program funded by the US National Institutes of Health (NIH), has ended over a decade after its inception. The ambitious project coordinated the multi-omic sequencing and clinical annotation of approximately 10,000 tumors across 33 cancer types. The resulting resource, publicly available through the NIH Genomic Data Commons (https://gdc.cancer.gov/), includes data on DNA sequence, DNA methylation, RNA and microRNA expression, and reverse-phase protein array binding, and makes it possible to rigorously characterize the molecular features of Archives (2008-2018): www.gp-tcm.org/news-list/





cancers. A set of 27 analysis papers associated with the final data release (https://www.cell.com/consortium/pancanceratlas) organize our current understanding by cell-of-origin patterns, oncogenic processes and signaling pathways. A flagship paper by Hoadley et al. shows that tumors cluster by histology, tissue type and anatomic origin when classified on the basis of nearly any data type. Integrated data analysis by iCluster defines various pan-cancer groupings of similar tumor types, which will help to orient future work on diagnostics and therapeutic development.

https://www.nature.com/articles/s41592-018-0020-4 https://www.ncbi.nlm.nih.gov/pubmed/29625048

9. Nawy T. **GENOMICS: Tissue-specific oncogene screens.** *Nature Methods* 2018;15:408 (commentary on Sack, L. M. et al. *Cell* 2018;173:499–514). Some genes can lead to cancer when mutated, whereas others drive cancer as a result of copy-number increases. Sack et al. generated a library of almost 30,000 barcoded human open reading frames to screen for genes that either stimulate or suppress proliferation when overexpressed. Their lentiviral screening vectors allowed for inducible expression and tagging, as well as quantitative detection. The researchers carried out screens in mammary, fibroblast and pancreatic cell lines, and found that around 10% of genes regulate proliferation, often in a highly tissue-specific manner. Candidate genes from the screen were enriched for known oncogenes and tumor-suppressor genes, and tissue-specific drivers were typically associated with the tumor tissue of origin. Many of the candidate genes are not commonly mutated in cancers but are associated with tissue-specific focal somatic copy-number alterations. <u>https://www.nature.com/articles/s41592-018-0027-x#auth-1</u>

https://www.ncbi.nlm.nih.gov/pubmed/29576454

### **Other Recommended Readings**

**1. Does Harvard penalize Asian-American applicants?** Harvard Universit has a consistent history of rating Asian-American applicants lower on personality traits such as likability, according to court documents filed on Friday. The filings formed part of a high-profile lawsuit accusing Harvard of discriminating against Asian Americans...

https://mp.weixin.qq.com/s/4S CIL-PZqczsGDVNfFzIA

2. Wang Y, Jiang JD. A new research mode of drug PK-PD mediated by the gut microbiota: insights into the pharmacokinetics of berberine. Acta Pharmaceutica Sinica, 2018, 53(5): 659-666. Berberine is one of the most studied original natural drugs in China in recent years. It is a new lipid-lowering drug with completely different mechanism from statins, which has been used in the multi-center clinical trials. However, berberine is poorly absorbed in the intestinal tract after oral administration leading a significant pharmacokinetic characteristic of low blood concentration (1%) and bioavailability (<5%). That is to say, it is difficult to explain the therapeutical effect in vivo by the current pharmacokinetic results. In fact, this phenomenon also exists in a number of clinically effective natural drugs. This review introduces the pharmacokinetic characteristic of berberine in vivo.

Meanwhile, taking berberine as an example, we emphasized the important role of intestinal bacteria on the pharmacokinetic study on the oral chemical drugs, and put forward a new research mode of drug PK-PD mediated by the gut microbiota.

www.yxxb.com.cn:8081/aps/CN/abstract/abstract17153.shtml https://mp.weixin.qq.com/s/83Kb eXv2t7XO5FPqV1Q-g (中文)

3. Gardening as a form of therapy for depression <u>https://mp.weixin.qq.com/s/KTIjT32S9Fc-NzpEA75ggA</u>

4. Tregoning J. How will you judge me if not by impact factor? *Nature* 2018; **558**:345. Stop saying that publication metrics don't matter, and tell early-career researchers what does, says John





Tregoning. https://www.nature.com/articles/d41586-018-05467-5?WT.ec id

5. Exceptional pharmacology research from Asia

https://bpspubs.onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)2052-1707.ASIARESEARCH

6. Vespignani A. **Twenty years of network science**. *Nature* 2018;558:528-529. The idea that everyone in the world is connected to everyone else by just six degrees of separation was explained by the 'small-world' network model 20 years ago. What seemed to be a niche finding turned out to have huge consequences..... By the 20th anniversary of the paper, more than 18,000 papers have cited the model, which is now considered to be one of the benchmark network topologies. Watts and Strogatz closed their paper by saying: "We hope that our work will stimulate further studies of small-world networks." Perhaps no statement has ever been more prophetic.

https://www.nature.com/articles/d41586-018-05444-y?WT

7. UK Guidelines Quiz: Test Your Knowledge on Smoking Cessation. The UK's National Institute for Clinical Excellence "Stop smoking interventions and services" published guideline [NG92] in March 2018. This guideline covers stop smoking interventions and services delivered in primary care and community settings for everyone over the age of 12. It aims to ensure that everyone who smokes is advised and encouraged to stop and given the support they need. It emphasises the importance of targeting vulnerable groups who find smoking cessation hard or who smoke a lot. This guideline includes recommendations on:

- commissioning and providing stop smoking interventions and services
- monitoring stop smoking services
- evidence-based stop smoking interventions
- engaging with people who smoke
- advice on e-cigarettes
- people who want to quit
- people who are not ready to quit
- telephone quitlines
- education and training
- · campaigns to promote awareness of local stop smoking services
- closed institutions
- employers

The guideline can be found here: https://www.nice.org.uk/guidance/ng92

To test if your understanding of this important issue is in keeping with the state of the art, please visit: https://www.medscape.com/viewarticle/896618\_4

### **Future Meetings & Events**

1. The 6<sup>th</sup> Annual Meeting of the GP-TCM RA will be held in London, UK, 4-6 July 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)...

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. The WHO Traditional Medicine Strategy 2014-2023
- Prof Christopher Lowe OBE FREng, University of Cambridge
- Prof Zhongzhen Zhao, Hong Kong Baptist University. The Compendium of Materia Medica and beyond
- Prof Bipin Nair, Amrita University. Natural products from India as novel drug leads: old wine in a defined new bottle
- Prof Pierre Duez, University of Mons. *Traditional African Medicine: validation and modernization*
- Prof Peng Cheng, Chengdu University of TCM. Conservation and sustainable supply of medicinal plants.
- Dr Charles Wu, FDA Center for Drug Evaluation and Research. Evolution of traditional medicines to botanical drugs.
- Prof Gerhard Franz, University of Regensburg. Introducing European Directorate for the Quality of Medicines.
- Dr Shifeng Cheng, Beijing Genomics Institute. Medicinal Plants 4.0 Project the future of medicines from plants.
- Dr Kan Ding, Shanghai Institute of Materia Medica, Chinese Academy of Sciences. The mechanism underlying antipancreatic cancer polysaccharides from herbal medicine
- Prof Lie-Fen Shyur, Agricultural Biotechnology Research Center, Academia Sinica. *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. Integrative East-West Medicine: a commitment to advancing healthcare.
- Prof Jaung-Geng Lin, China Medical University. 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 17<sup>th</sup> 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 contact the enquiries. please feel free to CGCM Central Office: Email: any 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:

- 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 cgcm2018@ipharm-nibm.my

http://mp.weixin.gq.com/s/R5Ao3tYI7Q2UwzaP94ikTw (中文)

4. The 15<sup>th</sup> World Congress of Chinese Medicine and *Belt and Road* TCM Culture Week to be held in Rome, Italy, Nov. 16-20 2018. <u>http://c.eqxiu.com/s/O8xACe2w?eqrcode=1&share\_level=4&from\_user=a294</u> a700-73b5-4d95-9d8b-dc428813e7cd&from\_id (中文)

5. The 19<sup>th</sup> International Congress of Oriental Medicine will be held in Taipei, Taiwan on 24-26 November 2018. The theme of the conference is "The Applications of Traditional Medicine in Acute and Critical Care." http://www.19icom2018.org.tw/index





6. The 30<sup>th</sup> 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> http://www.iscnp30-icob10.org/Default.asp?c=7&Ing=1

#### 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: <u>http://www.wjtcm.net</u>

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)

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

**Submission Deadlines:** 3<sup>rd</sup> September 2018 (Abstract); 1<sup>st</sup> 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), Dr **Eric Brand** (Hong Kong), Prof **Pierre Duez** (Mons), Dr **Christine Leon** (London), Prof **Zhong Wang** (Beijing), Dr **Qihe Xu** (London) and Prof **Zhongzhen Zhao** (Hong Kong) are gratefully acknowledged. Photos of miniature trees are selected from the following web link: <u>https://mp.weixin.qq.com/s/u92v0AHQCQ4JfSZKBdwrdA</u>

