

The March 2019 Newsletter of The GP-TCM Research Association



Editorial

The GP-TCM RA Regulatory Aspects Interest Group: An Introduction and Plans

Chair: Dr Mei Wang

Co-Chair: Prof Dr Gerhard Franz



Dr Mei Wang

Chair, Leiden University-European Center for Chinese Medicine and Natural compounds (LUCEEM); CEO, SU Biomedicine

Email: m.wang@biology.leidenuniv.nl; mei.wang@subiomedicine.com

Professor Dr Gerhard Franz

Chair, Herbal Drug Working Party of the German Pharmacopoeia Former Chair, TCM Working Party of the European Pharmacopoeia

Email: gerhard.franz@ur.de

The focus of the Regulatory Aspects Interest group will be concentrated on several actual problems of TCM which mainly are obvious in the European Member States.

There is still a concern about the ongoing elaboration of TCM herbal drug quality monographs for the European Pharmacopoeia Ph Eur. The actual number of monographs implemented in the 9th edition and supplements is still not satisfying the need of the TCM practitioner who should dispose of about 300 of such monographs for his daily practice. It is important that some EU Member States such as Germany and the UK work as well on the establishment of TCM herbal drug monographs for their National Pharmacopoeias.

A second effort should be concentrated on the urgent quality needs of TCM Granules which are imported for the EU market. At the moment no stringent proof of identity is documented, no production processes are declared and no content of important active or analytical compound is declared. Consequently, the so called 'phytoequivalence' of granules compared to the corresponding decoction is not obvious.

A third important topic of Regulatory Aspects is the urgently needed licensing of TCM phytomedicines from the Chinese market to European market. Only four single herb preparations have been registered in the Netherlands and in UK. An important step forward is the ongoing registration of a classical KAMPO medicine YamatoGast film coated tablets, composed of nine defined herbal extracts by the German Bundesinstitut für Arzneimittel BfArM. Hopefully more of these medicinal products will follow in the near future.

Finally an important Regulatory Aspect should be underlined, which will be essential for the future of TCM in Europe. Herbal Drug Monographs on Efficacy and Safety for Community Monographs of the European Medicines Agency HMPC should be elaborated and implemented in parallel to the ongoing activities of the EDQM for the Ph Eur: TCM herbal Drug monographs. The concentrated efforts of HMPC and the Ph Eur will be a very promising basis for a fruitful implementation of TCM in the EU Member States. Some of the TCM drugs are listed in the public statements of EMA, additional scientific evidence for safe use of these herbs are urgently needed.

References:

1. Wang M. and Franz G. The role of the European Pharmacopoeia (Ph Eur) in Quality Control of Traditional Chinese Herbal Medicine in European Member States. World J. of TCM. 2015;1:5-15.
2. Qu L., Zou W.J., Zhou Z., Zhang Z., Van der Greef J., Wang M. Non-European traditional herbal medicines in Europe: A community herbal monograph perspective. J Ethnopharmacology 2014;156: 107–114.
3. Qu L., Wang Y.T., Zou W.J., Wang M. European regulation model for herbal medicine: The assessment of the EU monograph and the safety and efficacy evaluation in marketing authorization or registration in Member States. Phytomedicine 2018;42:219-225.

The March 2019 Newsletter of The GP-TCM Research Association



Special Features

NEW 1.

Develop a Good Publication Network for Clinical Study of TCM



Prof. Aiping Lyu¹, The GP-TCM RA President and
Prof. Zhaoxiang Bian², Chair, GP-TCM RA Clinical Studies Interest
Group

School of Chinese Medicine, Hong Kong Baptist University

¹Dean and Chair Professor; aipinglu@hkbu.edu.hk

²Chair Professor; bianzxiang@gmail.com



The Hong Kong Chinese Medicine Clinical Study Centre (CMCS) has published a series of reporting guidelines for clinical trial research with traditional Chinese medicine (TCM). Reporting guidelines are tools that help researchers to remember every needed detail when writing up their research. With the publication number of TCM clinical research has increased considerably each year, the reporting quality of TCM studies, however, is not optimal because some TCM-specific items are not

included in the available general reporting guidelines such that researchers are not required to report the TCM-specific items. To address these issues, the CMCS Centre, led by Prof. Bian Zhao Xiang and Prof. Lyu Ai Ping, aim to develop a “Good publication network for clinical study with TCM (GPNTCM)”, which mainly composed of i) publishing a series of reporting guidelines for TCM clinical studies; and ii) establishing an international network, as the Asia Centre of EQUATOR Network, for enhancing the quality and transparency of TCM research.



The HK CMCS research team has classified and drafted thirteen reporting guidelines of TCM clinical studies, including 1) [Consensus-Based Recommendations for Case Report in Chinese medicine \(CARC\)](#); 2) [Standard Protocol Items for Clinical Trials with Traditional Chinese Medicine 2018: Recommendations, Explanation and Elaboration \(SPIRIT-TCM Extension 2018\)](#); 3) [Extending the CONSORT Statement to Moxibustion \(STRICTOM\)](#); 4) [CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation and Elaboration](#); 5) WHO Trial Registration Data Set (TRDS)-TCM Extension; 6) Extending the PRISMA Statement to Moxibustion; 7) Extending the PRISMA Statement to Chinese Herbal Medicine; 8) Extending the CONSORT Statement to Cupping; 9) Extending the CONSORT Statement to Tuina; 10) Multi-center Clinical Trial Reporting Guidelines; 11) Guideline for Placebo Design in TCM; 12) Consent Form for TCM Clinical Trials; and 13) Clinical Practice Guideline for TCM in HK. These guidelines should be used in conjunction with the main reporting guidelines, such as CONSORT for clinical trials, PRISMA for systematic reviews and meta-analysis, etc.

Among the above guidelines, four of them have been published, such as CARC—used for case report in TCM; SPIRIT-TCM Extension 2018—used for protocol of TCM clinical trial; CONSORT Extension for Moxibustion—used for randomized control trial of moxibustion; and CONSORT Extension for CHM 2017—used for randomized control trial of CHM. The case reports and RCTs contributed larger proportion in TCM researches, thus related reporting guidelines were published in the first step, particular in the extensions of SPIRIT (used for protocol) and CONSORT (used for RCT). While other guidelines are under development. You can keep up-to-date with the latest issues in the reporting guidelines of TCM research and with the work of GPNTCM with the <https://cmcs.hkbu.edu.hk/>

The HK CMCS research team has classified and drafted thirteen reporting guidelines of TCM clinical studies, including 1) [Consensus-Based Recommendations for Case Report in Chinese medicine \(CARC\)](#); 2) [Standard Protocol Items for Clinical Trials with Traditional Chinese Medicine 2018: Recommendations, Explanation and Elaboration \(SPIRIT-TCM Extension 2018\)](#); 3) [Extending the](#)

The March 2019 Newsletter of The GP-TCM Research Association



[CONSORT Statement to Moxibustion \(STRICTOM\)](#); 4) [CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation and Elaboration](#); 5) WHO Trial Registration Data Set (TRDS)-TCM Extension; 6) Extending the PRISMA Statement to Moxibustion; 7) Extending the PRISMA Statement to Chinese Herbal Medicine; 8) Extending the CONSORT Statement to Cupping; 9) Extending the CONSORT Statement to Tuina; 10) Multi-center Clinical Trial Reporting Guidelines; 11) Guideline for Placebo Design in TCM; 12) Consent Form for TCM Clinical Trials; and 13) Clinical Practice Guideline for TCM in HK. These guidelines should be used in conjunction with the main reporting guidelines, such as CONSORT for clinical trials, PRISMA for systematic reviews and meta-analysis, etc.

Among the above guidelines, four of them have been published, such as CARC—used for case report in TCM; SPIRIT-TCM Extension 2018—used for protocol of TCM clinical trial; CONSORT Extension for Moxibustion—used for randomized control trial of moxibustion; and CONSORT Extension for CHM 2017—used for randomized control trial of CHM. The case reports and RCTs contributed larger proportion in TCM researches, thus related reporting guidelines were published in the first step, particular in the extensions of SPIRIT (used for protocol) and CONSORT (used for RCT). While other guidelines are under development. You can keep up-to-date with the latest issues in the reporting guidelines of TCM research and with the work of GPNTCM with the <https://cmcs.hkbu.edu.hk/>

To access the publications please visit:

- [Consensus-Based Recommendations for Case Report in Chinese medicine \(CARC\). *J Integr Med.* 2016; 22\(1\): 73-79.](#)
- [Standard Protocol Items for Clinical Trials with Traditional Chinese Medicine 2018: Recommendations, Explanation and Elaboration \(SPIRIT-TCM Extension 2018\). *Chin J Integr Med.* 2018 Nov 27. doi: 10.1007/s11655-018-2999-x.](#)
- [STRICTOM: Extending the CONSORT Statement to Moxibustion. *J Integr Med.* 2013; 11\(1\): 54-63.](#)
- [CONSORT Extension for Chinese Herbal Medicine Formulas 2017: Recommendations, Explanation and Elaboration. *Ann Intern Med.* 2017; 167\(2\):W7-W](#)

 2.

Taming the fire of nephrotoxic botanicals

Francesca Holden^a, Vanisha Amin^a, Dominic Kuek^a,
Jeffrey B Kopp^b, Bruce M Hendry^a and Qihe Xu^{a,*}

^a Co-Director, King's Centre for Integrative Chinese Medicine, Department of Renal Medicine, King's College London, London, United Kingdom;

^b Head, Kidney Disease Branch, NIDDK, NIH, Bethesda, MD, USA.

* Correspondence: Dr Qihe Xu, e-mail: qihe.xu@kcl.ac.uk



Criteria for diagnosing nephropathy and urothelial neoplasms induced by botanicals containing aristolochic acids (AAs) are well established. Highlights of recent research on AAs include mechanisms of AA intrarenal transport and metabolism and vibrant debates on whether AAs may also cause liver cancers. Many other botanicals may also cause renal injury, but a generalised framework for diagnosing botanical-induced kidney injury (BIKI) is lacking. Based on what we have learnt about the wide spectrum of phenotypes of BIKI attributed to AAs and a recently published standardised phenotypic framework of drug-induced kidney disease, we propose that BIKI may be categorised into six phenotypes (acute kidney injury, tubular dysfunction, glomerular disorders, nephrolithiasis, chronic kidney disease and neoplasms) and four mechanistic types (A, predictable; B, idiosyncratic; C, chronic; and D, delayed). We call for international cooperation assembling a taskforce to develop, refine and regularly appraise an online BIKI database, documenting botanical use, phenotypes, mechanisms and levels of evidence. Once established, such a database may be linked with electronic patient records and pharmacovigilance channels to generate alerts, guide clinical decision making, direct future research, support evidence-based regulation of herbal medicines and education of healthcare professionals and the public. Finally, to prevent BIKI, we propose that a proactive approach integrating the triad of botanicals, users and stakeholders will be needed.

The March 2019 Newsletter of The GP-TCM Research Association



Lead author Dr Qihe Xu comments: “Botanicals, just like any other drugs, are like fire. If we know their effects and mechanisms of action and use them properly, they can benefit us and become an important part of our civilisation. Otherwise, we would miss the opportunities they offer and could even be harmed. Given the complexity of botanicals and weakness in research so far, I’d cordially invite investment and collaborations in this important research field.”

Read the full publication in WJTCM and a related press release, please visit:

http://www.wjtcn.org/ch/reader/view_abstract.aspx?file_no=20180028&flag=1

<https://www.kcl.ac.uk/news/news-article?id=3b151982-ff7d-4bb5-a457-e2031d45fe8b>

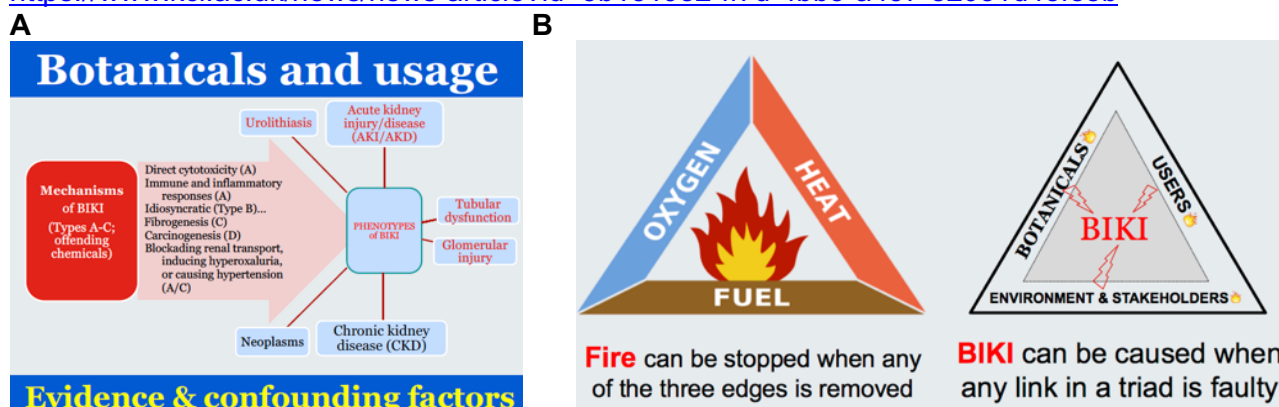


Figure. Keys to taming the fire of nephrotoxic botanicals. **A:** Establishing an integrated database of BIKI is a priority; **B:** BIKI is trickier than fire and demands an integrated approach to prevention.

Now 3. The 2nd Lecture Contest on the Natural History of Materia Medica Held in BUCM



Translated from a report on People.com.cn on 13th March
by Elizabeth R. Qi, PharmD, Hong Kong Baptist University
elizabeth_qi@hkbu.edu.hk

The 2nd Lecture Contest on the Natural History of Materia Medica was successfully held in Beijing University of Chinese Medicine on the 11th March 2019.

Ms Lu Ying, the Curator of the Chinese Medicine Museum at Beijing University of Chinese Medicine, said, “With the success of the first lecture contest, our contest today links the Belt and Road Initiative with the culture of traditional Chinese medicine. This perfectly reflects the spirit and essence of the idea: *The world of materia medica and the materia medica of the world*. This contest aims to promote and advance Chinese medicine culture to the world.”

Professor Zhao Zhongzhen, a renowned scholar in research of materia medica, TCM, and traditional medicines worldwide, commented: “This contest has three keywords. The first keyword is 香 (*xiāng*), meaning both spice and fragrant herbs. Spices and fragrant herbs have always been an important point of Chinese-foreign culture and trade exchange. The second keyword is 一带一路 (*yī dài yī lù*), also known as Belt and Road Initiative (BRI). This initiative is a modern-day recognition to the ancient trade routes as China exported silk, porcelain, and tea while importing fragrant herbs. The third keyword is 本草博物 (*běn cǎo bó wù*), or historic materia medica. For instance, Li Shizhen’s 本草纲目 (*běn cǎo gāng mù*), or *Compendium of Material Medica*, is a record of scientific thought and an encyclopedia of practical knowledge. This book can be regarded as a book introducing one day, one year, and the entire lifetime of a Chinese person. It gives us an understanding of the plant life surrounding us. This book is an ancient Chinese encyclopedia of plants and flowers, attempting to answer all types of questions about the natural world.”

The March 2019 Newsletter of The GP-TCM Research Association



At the contest, the “*Materia Medica in All Aspects of Life*” project was also launched. According to the announcements, the project will actively implement a national strategy to promote the development and dissemination of Chinese medicine culture. Contestants will be invited to be the first batch of volunteers to awaken, ignite, pursue, and disseminate Chinese medicine culture into primary and secondary schools.

A video report can be found here:

<https://tv.sohu.com/v/dXMvMjY1NjQ5MDYzLzEyMzk3ODcxNy5zaHRtbA==.html>

A brief report in Chinese:

<http://health.people.com.cn/n1/2019/0313/c14739-30974504.html>



Reports from the GP-TCM RA

1. The 48th GP-TCM RA BoD meeting was held on 1st March 2019 as a teleconference. Attendees included BoD members: Aiping Lu (President), Tai-Ping Fan (Past-President), Monique Simmonds (President-Elect), Clara Lau (Secretary-General), Peter Hylands (Treasurer), Rudi Bauer, Rong-Rong He, Vivian Wong, Qihe Xu, Min Ye, as well as IG chairs (excluding those BoD members): Zhaoxiang Bian, Nicola Robinson. Grace Yue also attended on behalf of the Secretariat to take minutes. Apologies were received from Abraham Chan, Kelvin Chan, Pierre Duez, Thomas Efferth and Rob Verpoorte. Aiping welcomed Ye Min and He Rong Rong as co-opt BoD members and welcomed all IG chairs who join the BoD meeting for the first time. The meeting approved minutes of the 47th BoD meeting and discussed the following business: Update on Charity Commission Annual Return, Update on Corporate or Institutional Members. At the meeting, the revised Bylaws were approved and chairs and co-chairs of all 6 IG were reappointed. Updates by the Treasurer, on recently approved members and the 7th GP-TCM RA Annual meeting in 2019 (hosted by NIKOM in South Korea) were discussed. The next BoD meeting will be scheduled on Monday 1 April 2019.

2. The 7th Annual Meeting of GP-TCM RA will be held in Daegu Haany University (DHU), Daegu City, Republic of Korea, on July 9th – 11th, 2019. The meeting will be jointly hosted by National Development Institute of Korean Medicine (NIKOM) and DHU. Please kindly note the deadline of abstract submission is **30 April 2019**. The tentative program of our 7th GP-TCM RA Annual Meeting and the call for abstracts can now be found on our website <http://www.gp-tcm.org/>



A, B and C: The meeting venues.

The March 2019 Newsletter of The GP-TCM Research Association



More details regarding registration and accommodation will follow.

3. Several members of GP-TCM attended the 11th International Advisory Board Meeting of the Hong Kong Chinese Materia Medica Standards. These included BoD members, IG Chairs/Co-Chairs Rudolf Bauer, Kelvin Chan, Yuan-Shiun Chang, Gerhard Franz, Monique Simmonds and Prof. Zhongzhen Zhao.

http://www.cmd.gov.hk/html/eng/health_info/publication.html



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 Feb.), Senior Fellowships (deadline 28 Feb.) and EDCTP Clinical Research and Product Development Fellowships (deadline 7 March).
<http://www.edctp.org/funding-opportunities/calls-for-proposals-for-funding-of-clinical-research-on-poverty-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. Millar NL et al. Europe rules on harm from fluoroquinolone antibiotics. *Nature* 2019;566:326. The European Medicines Agency held a public hearing last year on the potentially permanent side

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

The March 2019 Newsletter of The GP-TCM Research Association



effects of quinolone antibiotics. The resulting report from the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) incorporates the views of patients, health-care professionals and academics. Its recommendations, such as restricting the use of these drugs, have been adopted by the EMA's Committee for Medicinal Products for Human Use, and will be ratified by the European Commission next month...

<https://www.nature.com/articles/d41586-019-00619-7?WT>



3. Stephen King. The new isolationism takes us back to the Seventies. This is not a good thing. *Evening Standard* 4th March 2019. The author is HSBC senior economist and author of the *Grave New World*. He concluded: "No wonder I'm turning grey."

<https://www.standard.co.uk/comment/comment/the-new-isolationism-takes-us-back-to-the-seventies-this-is-not-a-good-thing-a4081976.html>

4. Gibney E. Paul Nurse on Brexit: 'UK is sleepwalking into a disaster'. *Nature* 2019;567: 18-19. As departure day approaches, chief of top UK lab says he fears science will drop off the government's agenda. <https://www.nature.com/articles/d41586-019-00694-w>

<https://mp.weixin.qq.com/s/fgEflaqr4xYGIB-tetSqlQ> (中文)

5. 101 Ideas on the Future of Research and Innovation in Europe. On 5 March, the Research, Innovation and Science Expert (RISE) group presented its new publication entitled '101 Ideas on the future of Research and Innovation in Europe'. These ideas are the result of Group's Tour d'Europe, which took place during 2017 and 2018 and which stemmed from the experts' desire to take the discussion on the role of research and innovation in the future of Europe out of the 'Brussels Bubble', to include research and innovation experts, advisors and policy makers from the national and regional level. The publication contains a collection of specific topics intended to provide inspiration for the ongoing reflection on the role of research and innovation within the broader framework of Europe's 2030 policy. The RISE group is a high-level group of policy experts, set up in 2014, who advise the Commissioner for Research, Science and Innovation.

https://ec.europa.eu/info/sites/info/files/research_and_innovation/rise/rise_101_ideas_brochure_032019.pdf

Reports on China and Chinese-European Cooperation

1. Hong Kong has established the standards for 299 Chinese materia medica
<http://www.wtcmq.com/190221/0E411A56.shtml?from=timeline&isappinstalled=0> (中文)

2. Shen T et al. Incidence and Etiology of Drug-Induced Liver Injury in Mainland China. *Gastroenterology*. 2019 Feb 8. pii: S0016-5085(19)30364-6. In a retrospective study to determine the incidence and causes of drug-induced liver injury (DILI) in mainland China, the annual incidence in the general population was estimated to be 23.80 per 100,000 persons-higher than that reported from western countries. Traditional Chinese medicines, herbal and dietary supplements, and anti-tuberculosis drugs were the leading causes of DILI in mainland China.

<https://www.sciencedirect.com/science/article/pii/S0016508519303646?via%3Dihub>

https://m.thepaper.cn/newsDetail_forward_3019079 (中文)

https://m.thepaper.cn/newsDetail_forward_3037987 (中文)

3. Cancer in China 2019. A Report from China's State Cancer Centre published in January 2019. <https://mp.weixin.qq.com/s/P9exl3tyAV4uH1D-O6ValQ> (中文)

4. Chinese Academy of Sciences to strengthen international cooperation. BEIJING, Feb. 6 (Xinhua) -- The Chinese Academy of Sciences (CAS) has said it will enhance its

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

The March 2019 Newsletter of The GP-TCM Research Association



internationalization strategy through international collaborative science projects and gathering international high-level talent.

Zhang Yaping, vice president of CAS, said the academy had seen fruitful results in international cooperation in 2018. The academy launched the Alliance of International Science Organizations in the Belt and Road Region in November last year, creating a platform for countries along the Belt and Road to deepen cooperation in science and tackle common challenges. Through active participation in multilateral collaboration platforms such as The World Academy of Sciences for the advancement of science in developing countries, the academy has enhanced China's role in global governance and deeply integrated into global innovative networks. The academy has played an active role in several international "big science" projects including the Third-pole Environment program, the International Meridian Circle Program and the brain science program. The academy has also recruited more international talent, especially top-level innovation talent for its science projects such as China's Five-hundred-meter Aperture Spherical Radio Telescope and stem cell research.



http://www.xinhuanet.com/english/2019-02/06/c_137802738.htm

5. American and Chinese Scientists Call for International Collaboration in Science Research. BEIJING, Feb. 18 (Xinhua) --American and Chinese scientists have called for international collaboration in science research at the ongoing annual meeting of American Association for the Advancement of Science (AAAS) to build more trust between two countries...

http://www.bjreview.com/Latest_Headlines/201902/t20190218_800156797.html

6. China gets world's first 5G-powered rail station in Shanghai. By Chen Qingqing in Shanghai Source:Global Times Published: 2019/2/18 21:13:39. 5G moved from hype to reality on Monday in China. Thanks to that reality, passengers at the Shanghai Hongqiao Railway Station can soon enjoy ultra-fast mobile networks, where downloading a high-definition movie will only take 20 seconds... <http://www.globaltimes.cn/content/1139289.shtml>

7. Zhao F, Qiao Y. Cervical cancer prevention in China: a key to cancer control. *Nature* 2019;393:969-70. With two powerful weapons—human papillomavirus (HPV) vaccine and screening—cervical cancer has become an important preventable cancer success story. In May, 2018, the Director-General of WHO called for action towards the elimination of cervical cancer. China, however, as one of the top contributors to the global burden of cervical cancer, still has a long way to go before elimination. Since the world's first HPV vaccine became available in 2006, the authorities in China finally approved Cervarix in 2016, Gardasil 4 in 2017, and Gardasil 9 in 2018 in mainland China. Despite the government's enormous investment in cervical cancer screening since 2009, China's national screening system still needs substantial improvement in health service capacities; optimising screening strategies; prioritising health investment; and engaging a wide range of stakeholders. Hence, for China, the goal of cervical cancer elimination seems tantalisingly within sight yet beyond reach.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)32849-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32849-6/fulltext)

8. Normile D. China tightens rules on gene editing. *Science* 2019;363:1023. In the wake of one of its scientists creating genetically altered babies, the Chinese government last week issued draft regulations that would require national approval for clinical research involving gene editing and other "high-risk biomedical technologies." Although Chinese researchers welcome the move to tighten oversight, some worry that the rules could hamper less controversial areas of research...

The March 2019 Newsletter of The GP-TCM Research Association



<http://science.sciencemag.org/content/363/6431/1023.2?utm>



9. China's trading day is starting to influence global markets. *The Economist* 9th March 2019. The importance of opening time in Shanghai...
<https://www.economist.com/finance-and-economics/2019/03/09/chinas-trading-day-is-starting-to-influence-global-markets>

10. Sun L et al. Causal associations of blood lipids with risk of ischemic stroke and intracerebral haemorrhage in Chinese adults. *Nat Med.* 2019 Mar 11. doi: 10.1038/s41591-019-0366-x. [Epub ahead of print]. Stroke is the second leading cause of death worldwide and accounts for >2 million deaths annually in China. Ischemic stroke (IS) and intracerebral hemorrhage (ICH) account for an equal number of deaths in China, despite a fourfold greater incidence of IS. Stroke incidence and ICH proportion are higher in China than in Western populations, despite having a lower mean low-density lipoprotein cholesterol (LDL-C) concentration. Observational studies reported weaker positive associations of LDL-C with IS than with coronary heart disease (CHD), but LDL-C-lowering trials demonstrated similar risk reductions for IS and CHD. Mendelian randomization studies of LDL-C and IS have reported conflicting results, and concerns about the excess risks of ICH associated with lowering LDL-C may have prevented the more widespread use of statins in China. We examined the associations of biochemically measured lipids with stroke in a nested case-control study in the China Kadoorie Biobank (CKB) and compared the risks for both stroke types associated with equivalent differences in LDL-C in Mendelian randomization analyses. The results demonstrated positive associations of LDL-C with IS and equally strong inverse associations with ICH, which were confirmed by genetic analyses and LDL-C-lowering trials. Lowering LDL-C is still likely to have net benefit for the prevention of overall stroke and cardiovascular disease in China.

https://mp.weixin.qq.com/s/tpB2H2kl_lwda6P8UNDhaw (中文)

<https://www.nature.com/articles/s41591-019-0366-x>

Acupuncture, TCM and Other Traditional Medicine

1. Professor Jingcheng Dong's Academic Thoughts on TCM. Hongying Zhang *et al* summarise the main academic thoughts of Prof. Dong, Huashan Hospital Affiliated to Fudan University, including comparison and integration of traditional medicines of different Chinese ethnic groups, tripartite division of TCM and Lung-Kidney relationship in TCM diagnosis and intervention.

Part 1: https://mp.weixin.qq.com/s/Q_FtsC3ojAfsv8aPvkW4bQ (中文)

Part 2: https://mp.weixin.qq.com/s/BgmyVjmPnnA_brFbqQp_Xw (中文)

2. 14 held accountable, time-honored company punished for expired products.

http://www.xinhuanet.com/english/2019-02/12/c_137816343.htm

3. Wang T et al. Ion Channel Targeted Mechanisms of Anti-arrhythmic Chinese Herbal Medicine Xin Su Ning. *Front. Pharmacol.* 06 February 2019 | <https://doi.org/10.3389/fphar.2019.00070>. Xin Su Ning (XSN) is a China patented and certified herbal medicine used to treat premature ventricular contractions (PVCs) since 2005. A recent completed clinical trial of 861 patients showed that XSN had similar PVC inhibition rate to the class I antiarrhythmic drug mexiletine, at 65.85% for XSN and 63.10% for mexiletine. We have previously reported that XSN prolongs action potential duration (APD) and suppresses action potential amplitude (APA) of the cardiac ventricular myocytes. In this report we aim to reveal the effect of XSN on the ionic channels that govern APD and APA, ... In conclusion, the clinical antiarrhythmic efficacy of XSN is based on its class I and Class III antiarrhythmic properties by suppression hNaV1.5

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

The March 2019 Newsletter of The GP-TCM Research Association



channel and hERG channels, which are directly responsible for XSN's effect on APA suppression and APD prolongation.

<https://www.frontiersin.org/articles/10.3389/fphar.2019.00070/full>

<https://www.dpag.ox.ac.uk/news/ma-group-research-aims-to-reveal-the-clinical-ability-of-chinese-herbal-medicine-xsn-to-treat-cardiac-arrhythmia-in-patients>

NEW 4. Yin Chen (Herba Artemisiae Scopariae), *Artemisia capillaris* Thunb.
<https://mp.weixin.qq.com/s/sIV0QV3bbkuAqdJ79zKukg> (中文)

NEW 5. Sharma T. et al. **Wound healing activity of certain root drugs - a review from classical and ethnomedicinal claims.** *International Journal of Green Pharmacy* 2019;13: 21-41. Research articles, and books have been published highlighting the use of medicinal plant for the management of wound. Recent research reveals that some of these plants are renowned either clinically or experimentally for their wound healing activities. Many plants are yet to be studied for their traditional claims. Single hand information regarding these plants with their specific parts used is still lacking. Present study reports the wound healing activity of 221 root drugs, being reported in 14 books and 70 research articles, related to ethnobotany and ethnomedicine. It is noticed that roots of ethnomedicinal plants belonging to 72 families (Fabaceae - 13, Rubiaceae - 12, Vitaceae - 11, Euphorbiaceae - 11, Asteraceae - 9, etc.) are reported for their wound healing activity. Among them, 122 plants reported for topical application, 6 for oral administration, and 6 for both oral and topical. Maximum drugs are used in paste form followed by juice, decoction, and ash form.

<https://www.greenpharmacy.info/index.php/ijgp/article/view/2333/1020>

NEW 6. Balogun FO, Ashafa AOT. **A Review of Plants Used in South African Traditional Medicine for the Management and Treatment of Hypertension.** *Planta Med* 2019; 85: 312-334. South Africa contains 9% of the world's higher plants, and despite its rich biodiversity, it has one of the highest prevalence of hypertension in Africa. This review provides information on medicinal plants embraced in South Africa for hypertension management, with the aim of reporting pharmacological information on the indigenous use of these plants as antihypertensives. This review not only focuses on the activity of antihypertensive medicinal plants but also reports some of its phytochemical constituents and other ethnopharmacological and therapeutic properties. Information obtained from scientific and or unpublished databases such as Science Direct, PubMed, SciFinder, JSTOR, Google Scholar, Web of Science, and various books revealed 117 documented antihypertensive plant species from 50 families. Interestingly, Asteraceae topped the list with 16 species, followed by Fabaceae with 8 species; however, only 25% of all plant species have demonstrated antihypertensive effects originating from both *in vitro* and *in vivo* studies, lending credence to their folkloric use. Only 11 plant species reportedly possess antihypertensive properties in animal models, with very few species subjected to analytical processes to reveal the identity of their bioactive antihypertensive compounds...

<https://www.thieme-connect.de/products/ejournals/html/10.1055/a-0801-8771>



Omics in Progress

NEW 1. Chakrabarti AM et al. **Target-Specific Precision of CRISPR-Mediated Genome Editing.** *Mol Cell* 2019;73:699-713. The CRISPR-Cas9 system has successfully been adapted to edit the genome of various organisms. However, our ability to predict the editing outcome at specific sites is limited. Here, we examined indel profiles at over 1,000 genomic sites in human cells and uncovered

The March 2019 Newsletter of The GP-TCM Research Association



general principles guiding CRISPR-mediated DNA editing. We find that precision of DNA editing (i.e., recurrence of a specific indel) varies considerably among sites, with some targets showing one highly preferred indel and others displaying numerous infrequent indels. Editing precision correlates with editing efficiency and a preference for single-nucleotide homologous insertions. Precise targets and editing outcome can be predicted based on simple rules that mainly depend on the fourth nucleotide upstream of the protospacer adjacent motif (PAM). Indel profiles are robust, but they can be influenced by chromatin features. Our findings have important implications for clinical applications of CRISPR technology and reveal general patterns of broken end joining that can provide insights into DNA repair mechanisms.



[https://www.cell.com/molecular-cell/fulltext/S1097-2765\(18\)31001-3?dgcid](https://www.cell.com/molecular-cell/fulltext/S1097-2765(18)31001-3?dgcid)

2. Lambert S. Unstable genomes promote inflammation. *Nature* 2019; online publication. Faulty DNA replication can make genomes unstable. It now seems that, in mice, severe disruption of DNA replication triggers inflammation in the placenta, and female embryos are more sensitive to this than are male ones...

https://www.nature.com/articles/d41586-019-00510-5?WT.ec_id

3. Wang X-W et al. A microRNA-inducible CRISPR–Cas9 platform serves as a microRNA sensor and cell-type-specific genome regulation tool. *Nature Cell Biol* 2019; online publication. microRNAs (miRNAs) are small noncoding RNAs that play important regulatory roles in plants, animals and viruses. Measuring miRNA activity in vivo remains a big challenge. Here, using an miRNA-mediated single guide RNA (sgRNA)-releasing strategy and dCas9–VPR to drive a transgene red fluorescent protein, we create an miRNA sensor that can faithfully measure miRNA activity at cellular levels and use it to monitor differentiation status of stem cells. Furthermore, by designing sgRNAs to target endogenous loci, we adapted this system to control the expression of endogenous genes or mutate specific DNA bases upon induction by cell-type-specific miRNAs. Finally, by miRNA sensor library screening, we discover a previously undefined layer of heterogeneity associated with miR-21a activity in mouse embryonic stem cells. Together, these results highlight the utility of an miRNA-induced CRISPR–Cas9 system as miRNA sensors and cell-type-specific genome regulation tools.

<https://www.nature.com/articles/s41556-019-0292-7>

<https://mp.weixin.qq.com/s/VlhX9DSViFIOMQdF3YJ74g> (中文)

4. Nelson CE et al. Long-term evaluation of AAV-CRISPR genome editing for Duchenne muscular dystrophy. *Nat Med* 2019; 10.1038/s41591-019-0344-3 (2019). Duchenne muscular dystrophy (DMD) is a monogenic disorder and a candidate for therapeutic genome editing. There have been several recent reports of genome editing in preclinical models of Duchenne muscular dystrophy, however, the long-term persistence and safety of these genome editing approaches have not been addressed. Here we show that genome editing and dystrophin protein restoration is sustained in the mdx mouse model of Duchenne muscular dystrophy for 1 year after a single intravenous administration of an adeno-associated virus that encodes CRISPR (AAV-CRISPR). We also show that AAV-CRISPR is immunogenic when administered to adult mice; however, humoral and cellular immune responses can be avoided by treating neonatal mice. Additionally, we describe unintended genome and transcript alterations induced by AAV-CRISPR that should be considered for the development of AAV-CRISPR as a therapeutic approach. This study shows the potential

The March 2019 Newsletter of The GP-TCM Research Association



of AAV-CRISPR for permanent genome corrections and highlights aspects of host response and alternative genome editing outcomes that require further study.

<https://www.nature.com/articles/s41591-019-0344-3>

5. Jiang Y et al. Proteomics identifies new therapeutic targets of early-stage hepatocellular carcinoma. *Nature* 2019; one-line-first publication. The proteomic stratification of early-stage hepatocellular carcinoma presented in this study provides insight into the tumour biology of this cancer, and suggests opportunities for personalized therapies that target it.

https://www.nature.com/articles/s41586-019-0987-8?WT.ec_id

https://mp.weixin.qq.com/s/7H_JTQhM0CNHtmCQrD35zA (中文)

6. Four *Engl J Med* papers on genome and DNA editing.

• Charo RA. **Rogues and Regulation of Germline Editing.** *NEJM* 2019; 380:976-80

<https://www.nejm.org/doi/full/10.1056/NEJMms1817528>

• Rosenbaum L. **The Future of Gene Editing — Toward Scientific and Social Consensus.**

NEJM 2019; 380:971-5. <https://www.nejm.org/doi/full/10.1056/NEJMms1817082?query=TOC>

• Porteus MH. **A New Class of Medicines through DNA Editing.** *NEJM* 2019; 380:947-59

<https://www.nejm.org/doi/full/10.1056/NEJMra1800729>

• Daley CG et al. **After the Storm — A Responsible Path for Genome Editing.** *NEJM* 2019;

380:997-9. <https://www.nejm.org/doi/full/10.1056/NEJMp1900504>

Other Recommended Readings

1. Editorial. How editors edit. *Nature Methods* 2019;16:135. We shed some light on how the *Nature Methods* editorial team evaluates papers submitted to the journal.

<https://www.nature.com/articles/s41592-019-0324-z>

2. Saxena S et al. Countdown Global Mental Health 2030. *Lancet* Published online February 21, 2019 [http://dx.doi.org/10.1016/S0140-6736\(19\)30424-6](http://dx.doi.org/10.1016/S0140-6736(19)30424-6). Today, we announce the establishment of Countdown Global Mental Health, an independent, multistakeholder monitoring and accountability collaboration for mental health, within an initial timeframe of the UN Sustainable Development Goals (SDGs). The scope of the Countdown will be global since mental health is an issue relevant to all countries. The unit of analysis will be countries or states or provinces within large federated countries. Given the huge disparities between and within countries, we expect the Countdown to be a strong instrument for accountability to decrease population-level disparities for mental health

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)30424-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30424-6/fulltext)

3. Dietary supplement regulation: FDA's bitter pill. *Lancet* Published online February 23,

2019 [https://doi.org/10.1016/S0140-6736\(19\)30406-4](https://doi.org/10.1016/S0140-6736(19)30406-4). The use of dietary supplements has risen precipitously in the past decade, with the fastest growth in Asia Pacific, but also substantially in Europe and North America. At least three-quarters of Americans report regularly using dietary supplements, most commonly reporting taking multivitamins. That translates into an exceedingly lucrative industry, with an estimated US\$40 billion market in the USA alone...

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)30406-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30406-4/fulltext)

4. Hoy AQ. Nobel laureate Steven Chu assumes term as AAAS president. *Science* 2019;363:827-9. Naturally, Steven Chu cites his work on laser cooling and optical trapping as the most recognized of his scientific career. In 1997, Chu, Claude Cohen-Tannoudji, and William Phillips were



The March 2019 Newsletter of The GP-TCM Research Association



honored with the Nobel Prize in Physics for the development of techniques to cool and trap atoms with laser light. The discovery has since led to precision clocks for space navigation, improved construction of small electronic components, and advanced geospatial positioning systems. It continues to spark emerging applications. Chu's scientific career is full of achievements driven by a fierce strand of independence and a grounding in experimentation that dates to childhood. His journey offers budding scientists guidance: seek out inspiring professors, be flexible, and find courage to dive into unfamiliar areas at every turn...

<http://science.sciencemag.org/content/363/6429/827?utm>



5. Finkel A. To move research from quantity to quality, go beyond good intentions. *Nature* 2019;566:297. Australian chief scientist Alan Finkel calls for formal action to bake in better research practices. <https://www.nature.com/articles/d41586-019-00613-z?WT>

6. Mullard A. 2018 FDA drug approvals. *Nat Rev Drug Discov* 2019; 18, 85-89. The FDA approved a record 59 drugs last year, but the commercial potential of these drugs is lacklustre. <https://www.nature.com/articles/d41573-019-00014-x>

7. Baedeker M, et al. 2018 FDA approvals hit all time high - but average value slips again. *Nat Rev Drug Discov.* 2019 Feb;18(2):90. <https://www.nature.com/articles/d41573-019-00004-z>

8. Micklus A, Muntner S. Biopharma dealmaking in 2018. *Nat Rev Drug Discov.* 2019 Feb;18(2):93-94. <https://www.nature.com/articles/d41573-019-00013-y>

9. Mervis J. NIH queries on foreign ties rattle universities. *Science* 363:1020. ScienceInsider has learned that at some institutions, every researcher flagged by NIH is Chinese-American... the message it could be sending to U.S. researchers: If you want to avoid trouble, don't stray beyond the border in pursuit of the next breakthrough in science. <https://www.sciencemag.org/news/2019/03/nih-letters-asking-about-undisclosed-foreign-ties-rattle-us-universities>

10. Fuchs Y. The therapeutic promise of apoptosis. *Science* 2019;363:1050-1051. Stem cells are classically defined by their unlimited proliferative potential and capacity to differentiate into diverse cell types. For many years, investigations in the stem cell field have focused specifically on the self-renewal and differentiation aspects, leaving the mechanisms of stem cell elimination relatively unexplored (1). What may at first appear to be a trivial question—how can an “immortal” self-renewing stem cell commit cellular suicide?—struck me as biologically important. Are there distinct mechanisms enabling such elimination, I wondered, and, if so, to what extent does this process affect tissue regeneration?... <http://science.sciencemag.org/content/363/6431/1050?utm>

11. Beall RF et al. Major Events in the Life Course of New Drugs, 2000–2016. *N Engl J Med* 2019;380:e12. An interactive graphic allows viewers to explore data — gathered by Reed F. Beall, Thomas J. Hwang, and Aaron S. Kesselheim — on the time required for investigational drugs to reach important U.S. milestones, such as new drug applications, FDA approval, expiration of market exclusivity, and market entry of a generic version. Data may be viewed by individual drug, therapeutic class, approval pathway, and approval year, as well as in aggregate... <https://www.nejm.org/doi/full/10.1056/NEJMp1806930>

12. Ciallella H and Zhu H. Advancing Computational Toxicology in the Big Data Era by Artificial Intelligence: Data-Driven and Mechanism-Driven Modeling for Chemical Toxicity. *Chem. Res. Toxicol.*, Just Accepted Manuscript. DOI: 10.1021/acs.chemrestox.8b00393.

The March 2019 Newsletter of The GP-TCM Research Association



Publication Date (Web): March 14, 2019. In 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act became the first US legislation to advance chemical safety evaluations by utilizing novel testing approaches that reduce the testing of vertebrate animals. Central to this mission is the advancement of computational toxicology and artificial intelligence approaches to implementing innovative testing methods... <https://pubs.acs.org/doi/10.1021/acs.chemrestox.8b00393>

Invitation from Future Meetings.

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

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 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

centraloffice@tcmedicine.org. For further information, please visit: www.tcmedicine.org

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

The March 2019 Newsletter of The GP-TCM Research Association



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](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33176-3/fulltext)

4. The 16th World Congress of Chinese Medicine will be held in Budapest, Hungary, in November 2019: <https://a.eqxiu.com/s/1BpDhw7h> (中文)

Invitation from Journals

1. **Health-care reform in China: a *Lancet* call for papers.** 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](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: <http://www.wjtcn.net>

Great news! Since November 2018, WJTCM has been included in the list of core Chinese scientific journals and magazines! <https://mp.weixin.qq.com/s/r5BAEi8uinlpxj0QvhapMA> (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 (qihe.xu@kcl.ac.uk), Prof Pierre Duez (pierre.duez@umons.ac.be) and Prof Yuan Shiun Chang (yschang0404@gmail.com).

Acknowledgements: Contributions from Prof Rudolf Bauer (Graz), Prof Zhaoxiang Bian (Hong Kong), Prof Yuan Shiun Chang (Taichung), Prof Pierre Duez (Mons), Prof Gerhard Franz (Regensburg), Dr Clara Lau (Hong Kong), Prof Aiping Lyu (Hong Kong), Dr Elizabeth Ren Qi (Hong Kong), Dr Mei Wang (Leiden), Dr Qihe Xu (London) and Prof Zhongzhen Zhao (Hong Kong) are gratefully acknowledged.

Pictures of springtime scenery: <https://mp.weixin.qq.com/s/KBvxtsoVznlUOFKiKiGQNQ> (中文)

