

The October 2019 Newsletter of The GP-TCM Research Association



Dear GP-TCM RA Members and Friends,

Greetings from London, Mons, Shiyan and Taichung!

Highlights of the GP-TCM RA Newsletter October 2019:

- On 5 Tastes in TCM
- The manifestation of the genome
- 10 years of health-care reform in China
- China: How science made a superpower
- Remodelling the genome with DNA twists
- China's new 4 + 4 medical education programme
- Bridging the GP gap: nurse practitioners in China
- Xi Jinping: No force can stop China forging ahead
- Cells' Oxygen Sensing Discovery Earns Nobel Prize
- TCM regulation of bone marrow hematopoietic niche
- China's health-care reform: an independent evaluation
- Healthy China 2030: an opportunity for tobacco control
- How Brexit has already taken a toll on five researchers
- Measuring progress in health in China and its provinces
- Memorial Service for Prof Peter Hylands held in London
- The 2nd International Qi-Blood Conference was held in Beijing
- A comparison of Western and Traditional Chinese Medicine
- Chinese Materia Medica of the Month: Safflower and saffron
- Orphan drug development in China: progress and challenges
- Europe seeks broader support and impact for science projects
- Expert Opinions on Aristolochic Acid-Related Safety Concerns
- Seminar on R&D of Chinese Medicines was held in Hong Kong
- Prof Peter Hylands' contributions to integrative Chinese medicine
- The 6th International Conference & Exhibition of TCM held in Chengdu
- Talking about Toxicity — "What We've Got Here Is a Failure to Communicate"
- Metabolomics and its application in TCM treatment of coronary heart disease
- The 2019 Traditional Medicine International Cooperation Forum was held in Macao
- The 1st International Scientific Forum of Traditional Natural Medicines in Mexico City
- Cardiotoxicity and clinical safety evaluation method of Chinese materia medica
- Xenohormesis: Understanding TCM from an Evolutionary and Ecological Perspective
- The 3rd China-ASEAN Training Workshop for Medicinal Study on Traditional Medicine
- KCNQ5 activation is a unifying molecular mechanism of botanical hypotensives
- Seven decades of TCM development in China illustrated by 46 invaluable pictures



Acknowledgements: Contributions from Prof. **Rudolf Bauer** (Graz), Prof **Hubiao Chen** (Hong Kong), Prof. **Pierre Duez** (Mons), Dr **Tai-Ping Fan** (Cambridge), Dr **Ping Guo** (Hong Kong), Prof **Jingyan Han** (Beijing), Prof Michael Heinrich (London), Dr **Erwei Hao** (Nanning), Prof **Jiqing Liu** (Shenzhen), Dr **Elizabeth Qi** (Hong Kong), Dr. **Hongyi Qi** (Chongqing), Prof **Xuanbin Wang** (Shiyan), Dr **Qihe Xu** (London) and Prof **Zhongzhen Zhao** (Hong Kong) are gratefully acknowledged. We acknowledge the contribution of Dr **Bun Tsoi** (Hong Kong) in drafting the editorial of Prof **Jiangang Shen** (Hong Kong) published in the September issue.

Mr WU Guanzhong's paintings in this issue are borrowed from here:
<https://mp.weixin.qq.com/s/P6FmH3G6R6mxFiQK9zJyOQ>

Best wishes,

Qihe Xu, London; Pierre Duez, Mons; Yuan-Shiun Chang, Taichung; Xuanbin Wang, Shiyan

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Editorials

1. Professor Peter Hylands' contributions to integrative Chinese medicine

—A tribute to our Founding Treasurer at his Memorial Service in London, 9th Oct. 2019¹

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Chairman, Steering Committee, The FP7 GP-TCM Consortium (2009-2012)
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Dear Debbie & family,

Dear Principal,

Dear colleagues & friends,

It's no secret that Peter loved China. He first lectured in China when I was still in medical school. And he had been there numerous times ever since.

As a pharmaceutical scientist, of course, he understood the huge value of Chinese Medicine as a source for drug development.

Passionate about international collaboration, Peter knew that Chinese Medicine is an integral part of mainstream medicine in China. If we wish to develop a truly engaged partnership with China in the field of health sciences, Chinese Medicine ought to be an important player!

Hence, it's completely natural that Peter had championed the King's Centre for Integrative Chinese Medicine initiative, which aims to integrate wisdoms from the West and the East to catalyse innovation and to promote collaboration.

It was Peter who first coined the name "King's Centre for Integrative Chinese Medicine". The name indicates that Chinese Medicine will be the focus of our study and that we will do this via an integrative approach.

It was also Peter who brought the new centre to life. In 2012, upon my annual appraisal, I proposed that my long-term goal was to found a new centre at King's, dedicated to Chinese Medicine-inspired research, education and care. My appraiser Professor Bruce Hendry advised that, if we believed in its value, we should work on it ASAP! And this was agreed by Peter. Together, we worked hard to convey our messages to stakeholders, and one year later, we were invited to present our case to the decision-makers. An excellent speaker, Peter was naturally the best person to present our case. He did. And we were officially accepted a King's new initiative in May 2013!

In the following years, Peter chaired 14 follow-up meetings and led the development of a business plan. We conducted omics-guided research of Chinese Medicine, offered Chinese Medicine-related teaching, and trained the first PhD student of our new Centre. By 2016, we have won King's fundraising priority!

Peter had also played important roles nationally and internationally. He was a senior leader of the FP7 GP-TCM Project. Funded 1m Euro by the EU in 2009, it was the 1st ever major EU-China cooperation on Chinese Medicine and it was widely acclaimed a success. As a member of the Steering Committee and Coordination Office, Peter chaired the Scientific & Technological Advisory Committee and one of our ten work packages. Three years later, the GP-TCM Research Association was founded. It quickly grew into a UK-based charity, a reputable international society and an

¹ A report of Peter's Memorial Service is available in the "Special Features" column

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Interested Party of the European Medicines Agency. Since the outset, Peter had been the Treasurer, sitting on the Board and the Executive Council.

For the wider community of Chinese Medicine, Peter had been a much-admired lecturer and an important advisor to the herbal industry. He sat on the Advisory Committees of the HMRA, the British medicines regulatory agency, as well as the British Pharmacopoeia Commission.

I was truly lucky to have worked with Peter on many of the aforementioned milestones. From him, I have learnt a lot.

All this started 13 years ago, when we had successfully co-applied for a Kidney Research UK research grant on antifibrotic Chinese herbs—the first of its kind in the history of the charity. Since then, we had worked closely on a number of projects, and he had constantly impressed me with his frankness, sharp awareness of the difficulties ahead, and the extraordinary ability to make complex things simple.

Throughout these years, I found him **a great listener, motivator and enabler.**

One day, in his office, we discussed about a hypothesis inspired by Chinese Medicine. If proven, it may lead to groundbreaking advances in prevention and treatment of major kidney diseases. He listened attentively and encouraged me to publish it. After the meeting, he walked me to the lift. As the lift doors closed, I saw excitement about new ideas and invaluable support in his eyes!

In the recent months, the hypothesis has been presented and well received at a few national and international meetings. And it has now been published in the current issue of *Nephron*, the primary international journal of nephrology. Fittingly, this Special Article titled “The Renal Collecting Duct Rises to the Defence” has been dedicated to Peter for **“his irreplaceable mentorship, invaluable collaboration and inspirational encouragement and support”**.

Thank you, Peter!

Further readings:

1. Xu Q. *In memoriam* Peter John Hylands (1946-2019). *GP-TCM RA Newsletter*, Jun. 2019: <http://www.gp-tcm.org/wp-content/uploads/2019/06/Jun-2019-GP-TCM-RA-NL.pdf>
2. Xu Q, Hylands PJ. Integrative Chinese Medicine. *GP-TCM RA Newsletter*, Apr. 2017: <http://www.gp-tcm.org/wp-content/uploads/2017/05/GP-TCM-RA-NL-28-3-2017-compressed.pdf>

2.

Xenohormesis: Understanding TCM Mechanisms and Mode of Action from an Evolutionary and Ecological Perspective



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The Question. In general, most of drugs used in western medicine are synthesized in Chemical labs and directed against the single target of the specific disease. They play a therapeutic role with a “S” shape dose-response curve.

In traditional Chinese medicine (TCM), however, the vast majority of drugs are derived from medicinal plants in nature with multi-components acting on multi-targets. Their clinical application follows the principles of “intervention before disease arises” and “prevention and treatment put at equal importance” and finally achieves the goal of “the right qi exists inside; evils cannot make disturbance”, which means the resistance to disease.

Thus, there is a basic scientific question that we can't help wanting to ask: Why the TCM components derived from natural plants can act on targets in human body and produce the prevention and/or treatment effects on human diseases?

Xenohormesis hypothesis existing in interaction between plants and insects/human. Cells are constantly subjected to a variety of exogenous stressors, such as heat, radiation, chemical toxicants, xenobiotics, and pathogens that may destroy cellular homeostasis and ultimately lead to

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damage or cell death. To re-establish homeostasis and mitigate damage, cells have adaptively evolved diverse survival mechanisms termed, the cellular stress response [1, 2].

Subtoxic stressors typically only activate a moderate cellular stress response, which may confer resistance or tolerance to more severe stress that might otherwise be lethal, or cause dysfunction and disease. This theory fits into a general concept known as hormesis, which is characterized by biphasic dose responses (stimulation/promotion at low dose and inhibition at high dose) with an inverted U shape or J shape dose response curve [3].

As living organisms are all interconnected and an inter-species hormesis concept known as xenohormesis has also been proposed. Xenohormesis most often refers to a process in which animals appear to have evolved the ability to sense molecules from stressed plants and benefit from the evolutionarily conserved stress responses activated by such stressors [4, 5].

In an ecological environment, plants face various biotic stresses (e.g., insect feeding and pathogenic microorganism infection) and abiotic stresses (e.g., ultraviolet radiation, high temperature, high salt, drought, and heavy metal). As plants cannot simply change location to avoid disadvantages or gain additional benefits, they have evolved metabolic pathways to synthesize phytochemicals as a chemical defense mechanism, which is an adaptive stress response to environmental factors that leads to tolerance against such environmental stresses [6].

The major biotic factor that interacts with plants in the microenvironment is invertebrates, particularly insects, which have evolved to feed on plants for ~4 billion years, thereby establishing a close co-evolutionary relationship [7]. As an adaptive stress response, insects suffering stress from the noxious phytochemicals of their feeding plants have accordingly evolved numerous enzymes to mitigate the toxicity of the phytochemicals, which contributes to the development of resistance [4, 5]. Phytochemicals derived from stressed natural plants may interact with insects in a hormesis way. Natural selection during the co-evolution between plants and insects may be the primary force that led to the diversity of species and functions of phytochemicals and detoxifying enzymes in insects.

Although the contribution to plant evolution is minor, humans share several biological similarities to insects due to the common ancestor of all multicellular organisms, evolutionary conservation, and adaptive convergence [1, 8]. Thus, phytochemicals playing a role in the chemical defense of plants may also act in a hormetic manner and activate evolutionarily conserved cellular stress response pathways at subtoxic doses after ingestion by humans. Moreover, such pathways may reduce the risk or enhance the tolerance to the insult of disorders, including neurodegenerative diseases, inflammatory and cardiovascular diseases, cancer, and inflammatory diseases [9-11].

TCM-xenohormesis and our work. The holistic view is one of the key features of TCM, emphasizing learning from nature and harmony between the nature and the mankind. In the production of genuine medicinal materials, it is also understood that adversity may promote quality. According to the results of the third national survey of the Chinese materia medica resources, there are 11,146 herbal species out of 12,807 medicinal materials identified in TCM. Plants used in TCM are also living in an environment with diverse stresses and accordingly produce numerous phytochemicals like ginsenosides, which function as chemical defense mechanisms. Thus, the action of TCM may also abide by the xenohormesis hypothesis. That is TCM-xenohormesis, which was proposed by us in *China Journal of Chinese Materia Medica* in 2013 [12]. This hypothesis has also been subsequently recognized by other researchers [13-15].

In TCM-xenohormesis, the first point, we think, is that the evolutionarily conserved cellular stress response mechanisms may serve as the main therapeutic targets of components derived from natural plants in TCM, which has been systematically elaborated by us with ginseng as an example in *Medicinal Research Reviews* in 2018 [16]. The second point is that the components derived from natural plants in TCM may act in a hormesis way to produce the prevention and/or treatment effects

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on human diseases. The third point is that natural selection during the coevolution and arms race between plants and insects may lay the foundation for “multi-components and multi-targets” characteristic of natural plants used in TCM.

Our research work based on this hypothesis can be temporarily summarized as followings: (i) In the ecological environment, the feeding of insects (*Spodoptera litura* Larvae) enhanced the accumulation of Z-ligustilide in *Rhizoma Chuanxiong*, while Z-ligustilide exhibited a chemical defense effect against insects in a hormesis way with an inverted U shape dose response curve, which was highly correlated to the biphasic modulation of detoxifying enzymes in insects by Z-ligustilide. (ii) From three different levels, including: single compounds (Z-ligustilide and ginsenoside Rh2), active component (panaxatriol saponins) and classical formulation (Taohong Siwu Decoction), we found TCM exhibited the prevention (at low dose range) and/or treatment (at high dose range) effects in a hormesis way against cerebral ischemic injury, acute myeloid leukemia or breast cancer through the modulation of evolutionarily conserved cellular stress response mechanisms, such as: Nrf2, HSP70, NR4A1/NR4A3, autophagy. (iii) The α , β , γ , δ -cross conjugated system existing in Z-ligustilide may be the structural basis for the xenohormesis effect of Z-ligustilide.

In conclusion, TCM-xenohormesis may help elucidate the mechanisms and the action mode of TCM from an evolutionary and ecological perspective and provide an original explanation and novel research methods for the prevention and treatment benefits of TCM.

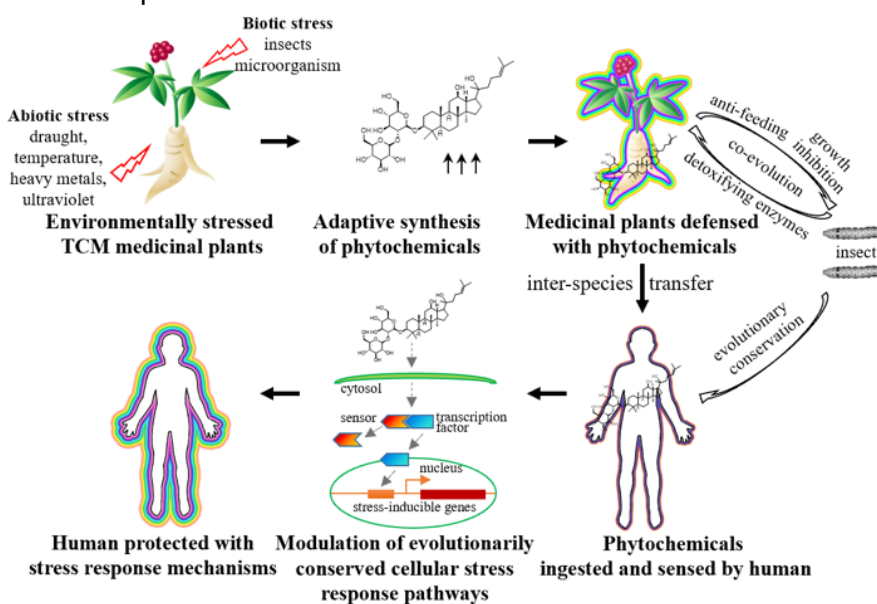


Figure 1. The proposed TCM-xenohormesis (with ginseng as an example)[12]

References:

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16. Qi, H.Y., et al. *Med Res Rev*, 2018. **38**(2): p. 625-654.

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Special Features

1. Top National Honours Mark the 70th Anniversary of the Birth of New China. Among those awardees there is Youyou Tu, whose Nobel-winning research was inspired by TCM classics.
https://mp.weixin.qq.com/s/rjAaY-hjmlASmAYd_qDnRA (中文)
<https://mp.weixin.qq.com/s/bef90bDBeiHHCKoagXefbg> (中文)



2. Makowski E. Cells' Oxygen Sensing Discovery Earns Nobel Prize. *The Scientist* 7th October 2019. For the Physiology or Medicine award, Peter Ratcliffe, William Kaelin, and Gregg Semenza are credited with figuring out molecular and genetic responses to oxygen levels.

<https://www.the-scientist.com/news-opinion/cells-oxygen-sensing-discovery-earns-nobel-prize-66538?utm>

<https://tech.qq.com/a/20191007/004183.htm> (中文)



3. Memorial Service for Prof Peter Hylands, Former Treasurer of the GP-TCM RA, was held in the King's College London Chapel on 9th October 2019. Following a welcome message



from the Chaplain of KCL, the Reverend Tim Ditchfield and hymn "I vow to thee my country", the event was chaired by Professor Ben Forbes, Head of Institute of Pharmaceutical Sciences, KCL. The events comprised four parts, "Peter the academic", "Peter the researcher", Peter's contribution to KCL and "Tributes from the Family". In the first part, Professor Peter Houghton, Emeritus Professor of Pharmacognosy, KCL, fondly introduced Peter's contribution to the early years of academic pharmacognosy in the UK; Professor Graham Davies, Professor of Clinical Pharmacy and Therapeutics, KCL, lovingly described how Peter

had been a great Head of the Pharmacy Department; Professor Kristin Ingolfsson, Vice Chancellor, University of Iceland, prescribed her life as a PhD student training with Peter and having learnt how important "precision" is and how this has impacted on her career and life. This was followed by tributes from Professor Robert Hider, Emeritus Professor of Medicinal Chemistry, KCL, highlighting Peter's contributions to drug discovery and development, and from your editor Dr Qihe Xu, highlighting Peter's contributions to integrative Chinese medicine. Professor Anne Greenough, Professor of Neonatology and Clinical Respiratory Physiology and Former Head of KCL School of Medicine, and Professor Ed Byrne, Principal and President of KCL commended the huge contributions of Professor Peter Hylands to the academic life of KCL and King's Health Partners. Peter's family received a Special Contribution Award to King's College London to Peter from the Principal. Peter's wife Debbie and children Kate and Jonty paid their tributes, before the memorial service concluded in Peter's favourite music "Entry of the gods to Valhalla" by Wagner. During an

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after-the-service reception and a dinner for speakers, family members and invited friends, Peter's kindness, b4raveness and generosity as a person, a teacher and a scientist were widely appreciated. The event was attended by more than 100 colleagues and friends of Prof. Peter Hylands.



4. The 3rd China-ASEAN Training Workshop for Medicinal Study on Traditional Medicine and Agricultural Residues & The 2nd Annual Meeting on China-ASEAN Joint Laboratory for International Cooperation in Traditional Medicine Research was successfully held on 24th Sept. 2019 in Nanning, China. Reported by Dr Erwei Hao, Associate Professor, Guangxi Key Laboratory of Efficacy Study on Chinese Materia Medica, Guangxi University of Chinese Medicine, ewhao@163.com.



More than 20 renowned scientists were invited to the meeting, including Academician Changxiao Liu, Chinese Academy of Engineering; Director Chun Yao, Guangxi Administration of TCM; Director Jiawen Li, Science & Education Department of Guangxi; Vice President Jing Leng, Guangxi University of Chinese Medicine; Director Jiagang Deng, Guangxi Key Laboratory of Chinese Medicine Research; Prof. Zhongzhen Zhao, Hong Kong Baptist University; Prof. Gangsheng Zhong, Beijing University of Chinese Medicine; Prof. Gang Bai, Nankai University; Prof. Chung-Der Hsiao, Chung Yuan Christian University; Prof. Shumei Wang, Guangdong Pharmaceutical University; Associate professor Justin Jang Hann Chu, National University of Singapore; Associate professor Jintanaporn Wattanathorn, Khon Kaen University; Associate professor Panee Sirisa-ard, Chiang Mai University; Prof. Chheang Sena, Dean of the School of Pharmacy, Cambodian University of Health Sciences; Dr. Ch'ng Soo Ee, National Innovation Club of Malaysia; Associate Dean Ounneua Keokongtanh, Lao Traditional Medicine Research Institute.

Among them there are 9 members of the China-ASEAN Joint Laboratory for International Cooperation in Traditional Medicine Research. Meanwhile 19 trainees from 9 ASEAN countries joined the training program. More than 300 staff and students of the Guangxi University of Chinese Medicine participated in the opening ceremony and benefited from the lectures.

In the training class, Academician Changxiao Liu and other 12 experts from China and ASEAN provided special lectures, combining theory with experimentation, and imparting cutting-edge academic ideas and experimental techniques.

Academician Liu's talk was entitled *Chinese Medicine Quality Markers*, while the title of Prof. Zhao's talk

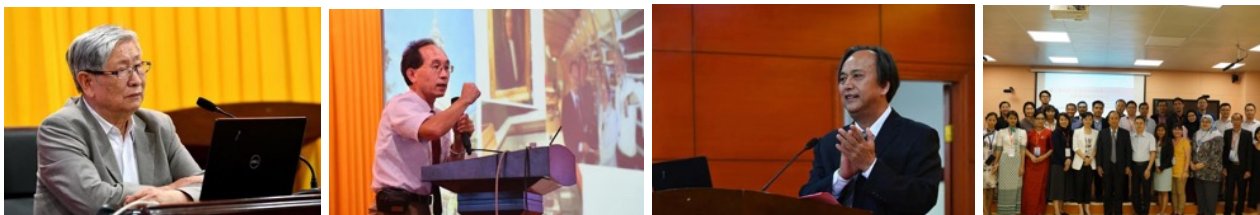


The Third China-ASEAN Training Workshop for Medicinal Study on Traditional Medicine and Agricultural Residues & The Second Annual Meeting on China-ASEAN Joint Laboratory for International Cooperation in Traditional Medicine Research Nanning China 2019.9.29

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was Certification is the basis of herbal standardization and globalization.



Associate professor Chu's talk showed *Natural product flavanone glycoside as antiviral against Hand, Foot and Mouth Disease*. Prof. Zhong's talk focused on *the Analysis on Formula Characteristics of Health Food with Auxiliary Protective Function in Chemical Liver Injury*. The food supplement containing mulberry extract improves non-communicating disorders was given as a theme highlight by Associate professor Jintanaporn.

Guangxi University of Chinese Medicine hosted the training workshop and the annual meeting of the joint laboratory. The other co-organizers were China-ASEAN Joint Laboratory for International Cooperation in Traditional Medicine Research, Guangxi Collaborative Innovation Center for Research on Functional Ingredients of Agricultural Residues, Guangxi Key Laboratory of Efficacy Study on Chinese Materia Medica, School of Chinese Medicine, Hong Kong Baptist University, State Key Laboratory of Pharmaceutical Preparation and Release Technology, Tianjin Institute of Pharmaceutical Research and State Key Laboratory of Medicinal Chemistry Biology, Faculty of Pharmacy, Nankai University.

5. The 2019 Traditional Medicine International Cooperation Forum was held in Macao, China on 25th-26th September 2019 and attended by senior GP-TCM RA members, including GP-TCM RA Honorary Member Academician Prof Xinsheng Yao, GP-TCM RA Founding President and current BoD member Prof Rudolf Bauer, GP-TCM RA BoD member and Newsletter Deputy Editor-in-chief Prof Pierre Duez, GP-TCM RA Interest Group Chairperson Dr Mei Wang and Newsletter Deputy Editor-in-chief Prof Yuan-Shiun Chang.



6. The 2nd International Qi-Blood Conference was held in Beijing, 13-15 September 2019.
https://mp.weixin.qq.com/s/OzKe4_ul8aMcmSfF5Bx9sw (中文)



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7. International Standard Chinese-Japanese-English Basic Nomenclature of Chinese medicine has been published as a publication of the WFCMS.

8. Seminar on Research and Development of Chinese Medicines 2019 was successfully held in Hong Kong on 24th September 2019. The meeting was organised by the Innovation and Technology Commission, Hong Kong Central Government Office and was attended by hundreds of TCM practitioners, researchers and representatives of the TCM industry. BoD members of the GP-TCM RA Professors Aiping Lu, Clara Lau, Vivian Wong and Qihe Xu were among the invited session chairs and speakers. The meeting was also attended by GP-TCM RA Interest Group Leaders and editorial board members of the GP-TCM RA Newsletters, e.g. Professors Zhongzhen Zhao and Zhaoxiang Bian. After the meeting, your editor Dr Qihe Xu visited Professors Clara Lau, Ge Lin and Zhixiu Lin, Chinese University of Hong Kong, and delivered an invited talk at School of Chinese Medicine, Hong Kong Baptist University.



9. The 1st International Scientific Forum of Traditional Natural Medicines in Mexico City. Report translated by Dr Elizabeth Qi (Hong Kong Baptist University). The first “International Scientific Forum of Traditional Natural Medicines” was held at the National Autonomous University of Mexico in Mexico City. This forum was jointly organized by experts in Mexico, China, and the United States from October 5th to 7th. The main aim was to exchange information on TCM, Mexican



herbal medicine, the current laws and regulation, and identification techniques and clinical applications.

Scientists, practitioners, and government officials participated in the forum. Speakers included Prof Qian Zhongzhi from the Chinese Pharmacopoeia Commission, Prof Zhao Zhongzhen from Hong Kong Baptist University, Dr Ren Liping, Chairman of American Nutritional Supplements and Medicines Association, Dr Lizette Clavel, Mexican House Representative Lic. and Dr Ubaldo Juarez Sevilla from the Mexican Pharmacopoeia Committee.

Prof Qian shared the current workings of the Chinese Pharmacopoeia while Representative Clavel and Dr. Sevilla shared the current situation for herbal medicinals in Mexico. Prof Zhao began the exchange on the most modern techniques in identifying and cultivating herbal medicinals. Ren Liping, also a TCM practitioner, shared an interesting comparison of the herbs used in both Chinese and Mexican traditional medicine but for slightly different indications.

This conference was a lively discussion among experts and scholars, hoping to further the advancement in traditional natural medicines research in Mexico. The exchange of information brought forth interest in new collaborations and discussions about Mexican and Chinese traditional medicine.



<http://www.chinesenewsusa.com/news/show-26395.html> (中文)

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10. The 6th International Conference & Exhibition of TCM was successfully held in Chengdu, Sichuan on 21st-22nd October 2019. The meeting was co-organised by 13 Ministries and Commissions of the Central Chinese Government together with the host, the government of Sichuan Province. The meeting was opened on the 21st October morning, which was followed by 12 theme-focused meetings on TCM theories, sustainable development of Chinese materia medica, TCM innovation and internationalisation, development of TCM technologies and devices, acupuncture, prevention and treatment of major diseases and evidence-based medicine, protection and development of traditional medicines of minority ethnic groups, TCM life style and disease prevention, development of TCM S&T industry, TCM Ecology, as well as TCM and biomedicine industry. GP-TCM RA Founding President (2012-2014) and current BoD member Prof Rudolf Bauer chaired the plenary session along with GP-TCM RA Honorary Member Prof Kaixian Chen. GP-TCM RA Former President Prof De-an Guo (2014-2016), your Newsletter editor and current BoD member Dr Qihe Xu, and Honorary Members Prof Gerhard Franz attended the meeting as invited speakers.

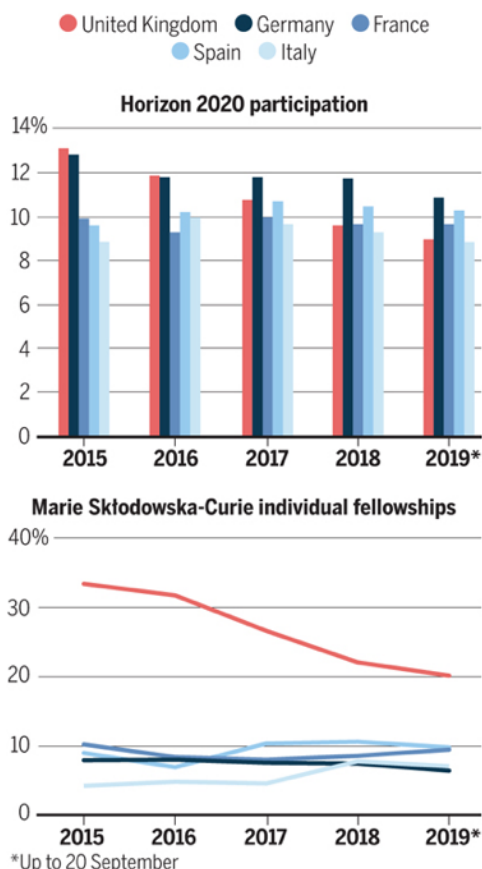


European Reports

1. Rabesandratana T. Europe seeks broader support and impact for science projects. *Science* 2019;366:22. “We need to learn the art of listening.” “There's no taboo, no bad ideas.” “I can assure you your contribution will be considered.” These sound like the messages you hear at a small-team brainstorming session—not a 3-day science policy congress with 5000 attendees. But the encouraging words were spoken here last week at the European Research and Innovation Days, where policy bigwigs working with the European Commission invited the audience to help shape Europe's next 7-year research funding program, Horizon Europe, set to begin in 2021. Their message: Anyone can help “cocreate” the program's outlines. “Our instruction to staff was: Don't promote, listen,” says Kurt Vandenberghe, director for policy development and coordination at the commission's Directorate-General for Research and Innovation here...

<https://science.sciencemag.org/content/366/6461/22?utm>

2. Stokstad E. Split decisions: How Brexit has already taken a toll on five researchers. *Science* 2019;366:24-7...Last year, U.K. researchers were involved in considerably fewer EU research projects than in the year before the Brexit vote (see middle graphic). Prestigious EU fellowships that give early-career researchers 2 years of funding to work in another country offer another ominous indicator. From 2015 to 2019, the proportion of fellows choosing U.K. universities fell from 33% to 22% (see bottom



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graphic). ... In 2017, the (UK) government set a 10-year goal of increasing R&D from 1.7% to 2.4% of gross domestic product, the average for wealthy nations...

<https://science.sciencemag.org/content/366/6461/24?utm>

3. UK guidance on Horizon 2020 funding after Brexit, last updated 4th Oct. 2019.

<https://www.gov.uk/guidance/horizon-2020-funding-after-brexit?utm>

Reports on China and China's International Cooperation

1. Xi Jinping: No force can stop China forging ahead.

CGTN.com 1st October 2019

<https://news.cgtn.com/news/2019-10-01/Xi-Jinping-delivers-speech-to-mark-National-Day--KqHhW91enK/index.html>

2. The Lancet. China's health-care reform: an independent evaluation. *Lancet* 2019;394:1113. When *The Lancet* visited the National Health Commission of China in 2018, Ma Xiaowei, the minister of health, said he would welcome independent assessment of the progress of China's health reforms. Today, *The Lancet* dedicates the ninth China-themed issue to evaluate progress of China's health-care reform since 2009, which coincides with the fifth *Lancet*-Chinese Academy of Medical Sciences Health Conference, held in Chengdu on Oct 19–20... **From 2008 to 2017, Chinese Government health expenditures on health care quadrupled from ¥359 billion to ¥1.52 trillion. It's high time for an independent evaluation of current progress and future directions.** [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)32210-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32210-X/fulltext)

3. Yang G, Wan X. Measuring progress in health in China and its provinces. *Lancet* 2019;394:1115-6. In *The Lancet*, Maigeng Zhou and colleagues present a systematic analysis for the Global Burden of Disease Study (GBD) 2017 on mortality, morbidity, and risk factors in China and its provinces, from 1990 to 2017. Their report is, to our knowledge, the first comprehensive subnational assessment of health in the Chinese population after previous GBD China 2010 on mortality, morbidity, combined health loss, and risks at the national level and GBD China 2013 on mortality at the national and province level...

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)31343-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31343-1/fulltext)

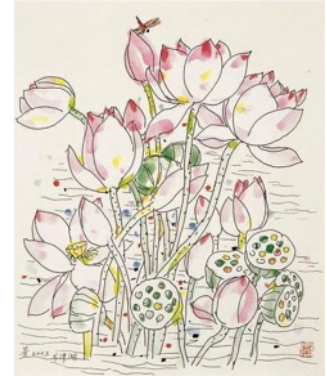
The above is a commentary on Zhou M et al. **Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017.**

Lancet 2019;394:1145-58, which concluded "China has made substantial progress in reducing the burden of many diseases and disabilities. Strategies targeting chronic diseases, particularly in the elderly, should be prioritised in the expanding Chinese health-care system."

[http://dx.doi.org/10.1016/S0140-6736\(19\)30427-1](http://dx.doi.org/10.1016/S0140-6736(19)30427-1)

4. Wang C et al. China's new 4 + 4 medical education programme. *Lancet* 2019;394:1121-3. 2019 is the tenth anniversary of China's latest health system reform. Over the past decade, China has invested much time and effort in improving health-care access and equity. Most noticeably, China has expanded health insurance coverage to more than 95% of its population. However, gaps in health-care quality remain, and resolving these gaps will be key to realising Healthy China 2030, an important long-term national strategic plan. [https://doi.org/10.1016/S0140-6736\(19\)32178-6](https://doi.org/10.1016/S0140-6736(19)32178-6)

5. Li X, Galea G. Healthy China 2030: an opportunity for tobacco control. *Lancet* 2019;394:1123-5. The 2018 China Tobacco Survey shows progress as a result of China's concerted tobacco control efforts in the past decade. People in China are less likely to be harmed by second-hand smoke than they were in 2010, as evidenced by the decrease in second-hand smoke exposure in indoor public places such as workplaces (from 63.3% to 50.9%), government buildings (from 58.4% to 31.1%), health-care facilities (from 37.9% to 24.4%), public transport (from 34.1% to 12.9%), and restaurants (from 88.5% to 73.3%). The survey has once again shown that most people in China embrace policies of smoke-free indoor public places. Although overall adult smoking



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prevalence showed little improvement, the 1.5 percentage point decline in overall smoking prevalence in a population the size of China could be a first signal that the epidemic is peaking. There was a relative decline of about 10% in smoking prevalence among people aged 25–44 years and those aged 45–64 years between 2010 and 2018, from 31.0% to 27.5% and from 33.6% to 30.2%, respectively. Meanwhile, the percentage of ever smokers who quit smoking increased from 16.0% to 20.1% during the same period... [https://doi.org/10.1016/S0140-6736\(19\)32048-3](https://doi.org/10.1016/S0140-6736(19)32048-3)

6. Zhan Q et al. Bridging the GP gap: nurse practitioners in China. *Lancet* 2019;394:1125-7. China's 2009 national health reform focused on health insurance, drugs, public health, hospitals, and primary care. On its tenth anniversary, evaluations of the reforms are underway. There has been good progress in some areas, such as medical insurance coverage through National Healthcare Security Administration. Obstacles, however, hinder progress in other areas. Primary care and large hospitals have been the most resistant to reform efforts. The Chinese Government has set the goal of achieving 300 000 general practitioners (GPs) by 2020—or two to three GPs per 10 000 population by 2020—and a net GP workforce of 700 000, or five GPs per 10 000 population by 2030. GP specialty training is among 36 specialties in China's national standardised residency training. Government policies had prioritised the GP workforce for primary health care through favourable policies and more public investments. Free scholarships have been offered for medical students who commit to serving 6 years after graduation at the township level. One study showed that only 1.6% of recipients of GP scholarships from rural areas are willing to serve at the rural township level; 80% of them reported to duty at the rural township level right after graduation... [https://doi.org/10.1016/S0140-6736\(19\)32209-3](https://doi.org/10.1016/S0140-6736(19)32209-3)

7. Zhang S et al. Orphan drug development in China: progress and challenges. *Lancet* 2019;394:1127-8. On Aug 26, 2019, the National People's Congress (NPC) Standing Committee approved the new revision of the Drug Administration Law of China that allows orphan drug approval to be based on evidence from foreign clinical trials through the green channel mechanism with priority review and accelerated approval. Medical institutions can now legally purchase small amounts of urgently needed orphan drugs from overseas markets. This is welcome news for China's 16 million patients with rare diseases... [https://doi.org/10.1016/S0140-6736\(19\)32179-8](https://doi.org/10.1016/S0140-6736(19)32179-8)



8. Yip W. 10 years of health-care reform in China: progress and gaps in Universal Health Coverage. *Lancet* 2019;394:1192-1204. In 2009, China launched a major health-care reform and pledged to provide all citizens with equal access to basic health care with reasonable quality and financial risk protection. The government has since quadrupled its funding for health. The reform's first phase (2009–11) emphasised expanding social health insurance coverage for all and strengthening infrastructure. The second phase (2012 onwards) prioritised reforming its health-care delivery system through: (1) systemic reform of public hospitals by removing mark-up for drug sales, adjusting fee schedules, and reforming provider payment and governance structures; and (2) overhaul of its hospital-centric and treatment-based delivery system. In the past 10 years, China has made substantial progress in improving equal access to care and enhancing financial protection, especially for people of a lower socioeconomic status. However, gaps remain in quality of care, control of non-communicable diseases (NCDs), efficiency in delivery, control of health expenditures, and public satisfaction. To meet the needs of China's ageing population that is facing an increased NCD burden, we recommend leveraging strategic purchasing, information technology, and local pilots to build a primary health-care (PHC)-based integrated delivery system by aligning the incentives and governance of hospitals and PHC systems, improving the quality of PHC providers, and educating the public on the value of prevention and health maintenance. [https://doi.org/10.1016/S0140-6736\(19\)32136-1](https://doi.org/10.1016/S0140-6736(19)32136-1)

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9. Wu S. China: How science made a superpower. *Nature* 2019; 574:25-28. Shellen Wu traces the rise of the dominant force in science, in the second of a series of essays on the ways in which the past 150 years have shaped today's research system, marking Nature's anniversary...

<https://www.nature.com/articles/d41586-019-02937-2>

Acupuncture, TCM and Other Traditional Medicine

1. Qiyue. A comparison of Western and Traditional Chinese Medicine. *Meipian.cn* 5th July 2019.

https://www.meipian9.cn/28j775gg?first_share_uid=60161770& (中文)

2. On 5 Tastes in TCM. *jiankyd999 WeChat* 2nd October 2019.

https://mp.weixin.qq.com/s/-NeeJ7ptkFzD_twaeVF5aA (中文)

3. Wu GS et al. Metabolomics and its application in the treatment of coronary heart disease with traditional Chinese medicine. *Chin J Nat Med.* 2019;17:321-330. This article summarizes the application of metabolomics in diagnosis, biomarker discovery and TCM treatment of coronary artery disease. <https://www.sciencedirect.com/science/article/pii/S1875536419300378>

4. Seven decades of TCM development in China illustrated by 46 invaluable pictures. *Tieganyixun WeChat* 28th September 2019.

https://mp.weixin.qq.com/s/zRq54IH3JGu74XHDtVJ_rw (中文)

5. Manville RW, et al. KCNQ5 activation is a unifying molecular mechanism shared by genetically and culturally diverse botanical hypotensive folk medicines. *Proc Natl Acad Sci U S A.* 2019 Sep 30. pii: 201907511. Botanical folk medicines have been used throughout human history to treat common disorders such as hypertension, often with unknown underlying mechanisms. Here, we discovered that hypotensive folk medicines from a genetically diverse range of plant species each selectively activated the vascular-expressed KCNQ5 potassium channel, a feature lacking in the modern synthetic pharmacopeia, whereas nonhypotensive plant extracts did not... Discovery of botanical KCNQ5-selective potassium channel openers may enable future targeted therapies for diseases including hypertension and KCNQ5 loss-of-function encephalopathy.

<https://www.pnas.org/content/early/2019/09/26/1907511116.long>

https://mp.weixin.qq.com/s/ceKoP54fwkn_4LlbfheL5g (中文)

6. Yu R et al. Consideration on cardiotoxicity and clinical safety evaluation method of Chinese materia medica. *Chinese Traditional and Herbal Drugs* 2019; 50:4485-4489. Cardiotoxicity assessment is an important index that must be considered before clinical trials of drugs. It also plays an important role in the research and development of new Chinese medicines and the standardized application of clinical safety of Chinese medicines. Then, how to identify the cardiotoxicity of Chinese materia medica (CMM), grasp the clinical characteristics, detection indicators, evaluation methods, and diagnostic elements are the main problems we are facing. In this paper, we summarize many researches and pre-clinical evaluation techniques of cardiotoxicity of CMM in recent years and discuss the clinical evaluation methods of cardiotoxicity of CMM.

http://www.tippress.com/zcy/ch/reader/view_abstract.aspx?file_no=20191831&flag=1

https://mp.weixin.qq.com/s/dla55ZNz9xEXmA9uUyY_Ew (中文)

7. Shen F et al. Research progress on regulation and construction of bone marrow hematopoietic niche by TCM. *Chinese Traditional and Herbal Drugs* 2019; 50:4470-4476. The bone marrow hematopoietic niche is the place where hematopoietic stem cells and progenitors survive. It is not only related to the hematopoiesis function, but also its steady-state disorders and abnormalities can induce a variety of hematologic diseases, which will even be adapted by malignant cells such as leukemia stem cells, so as to cause seriously



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poor prognosis. Therefore, it is of great significance to the regulation and construction of the bone marrow niche. In this review, we outline the composition, physiological and pathological basis of bone marrow hematopoietic niche, from the regulation of Chinese materia medica components and TCM formula to graphically analyze the target and effect of drug efficacy. Then, combined with the clinical practice for integrating and summarizing decentralized research, aiming to provide new directions and perspectives for the TCM research and treatment of hematologic diseases.

http://www.tiprpress.com/zcy/ch/reader/view_abstract.aspx?file_no=20191829&flag=1

<https://mp.weixin.qq.com/s/4WnDXMa4KFUq7nJL4HBBig> (中文)

8. Ye Z, Xiao XH et al. Invited Expert Opinions on Aristolochic Acid-Related Safety Concerns. *wst-mtcm* WeChat 7th October 2019.

<https://mp.weixin.qq.com/s/x5H1ODEnNzPYjaWTcnjNgQ> (中文)

Omics in Progress

1. Puno MR et al. SnapShot: The RNA Exosome. *Cell* 2019;179:282. The RNA exosome is a 3' to 5' ribonuclease that plays a fundamental role in maturation, quality control, and turnover of nearly all types of RNA produced in eukaryotic cells. Here, we present an overview of the structure, composition, and functions of the RNA exosome, including various cytoplasmic and nuclear exosome co-factors and associated protein complexes. To view this SnapShot, open or download the PDF. [https://www.cell.com/cell/fulltext/S0092-8674\(19\)31011-6](https://www.cell.com/cell/fulltext/S0092-8674(19)31011-6)

2. Zahn LM et al. The manifestation of the genome. *Science* 2019;365:1394-5. This special issue expands our view of genotype and phenotype and explores recent advances in understanding the factors that influence the development of the human phenotype. We examine cases in which various cells and traits are specified by DNA mutation or epigenetic changes, but we also highlight cases in which phenotype is affected by suites of genes and gene products from commensal bacteria. This special issue illustrates the diverse approaches that together are increasing our understanding of the complex relationship between genotype and phenotype, with the potential to drive discoveries that promote human health.

<https://science.sciencemag.org/content/365/6460/1394?utm>

- Young AI et al. **Deconstructing the sources of genotype-phenotype associations in humans.** *Science* 2019; 365:1396-400.

<https://science.sciencemag.org/content/365/6460/1396?utm>

- Camp JG et al. **Mapping human cell phenotypes to genotypes with single-cell genomics.** *Science* 2019; 365:1401-5. <https://science.sciencemag.org/content/365/6460/1401?utm>

- Lynch JB, Hsiao EY. **Microbiomes as sources of emergent host phenotypes.** *Science* 2019; 365:1405-9. <https://science.sciencemag.org/content/365/6460/1405?utm>

- Zeggini E et al. **Translational genomics and precision medicine: Moving from the lab to the clinic.** *Science* 2019; 365:1409-13. <https://science.sciencemag.org/content/365/6460/1409>

3. Bowman GD, Deindl S. Remodeling the genome with DNA twists. *Science* 2019;366: 35-6. In complex organisms such as humans, a single genetic blueprint can give rise to a multitude of different cell types, from nerve to liver to muscle. Such cellular diversity relies on restricting which portions of genomic DNA are accessible and therefore can be read by cellular machinery. Ultimately, access to DNA depends on placement of a repetitive, spool-like structure called the nucleosome, the basic packaging unit of chromosomes. The nucleosome occludes two tight loops of DNA and thus represents a fundamentally repressive element. When and where nucleosomes are positioned can affect complex transcriptional programs, and therefore disruptions in the factors responsible for nucleosome positioning often result



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in cancers and multisystem developmental diseases. Although the mechanism of shifting nucleosomes along DNA has long proved elusive, a recent flurry of structural, biophysical, and biochemical work has revealed a core mechanistic framework explaining how nucleosomes are actively repositioned throughout the genome...
<https://science.sciencemag.org/content/366/6461/35?utm>

Other Recommended Readings

1. Mervis J. NIH reveals its formula for tracking foreign influences. *Science* 27 Sept. 2019; doi:10.1126/science.aaz6589. The U.S. National Institutes of Health (NIH) thinks it may have figured out how China's foreign talents recruitment program is undermining its system for making awards and ensuring ethical behavior by its grantees...
<https://www.sciencemag.org/news/2019/09/nih-reveals-its-formula-tracking-foreign-influences>

2. Capturing the value added to a paper during peer-review. *prelights.biologists.com* 26th September 2019. Preprints accelerate science by making research accessible prior to journal publication, but peer-review often substantially improves papers. While for a long time the review history of a paper was not visible to anyone apart from the authors and reviewers/editors, recently, increasing numbers of journals have started publishing this information alongside the paper (including The Company of Biologists journals *Development* and *Journal of Cell Science*). This can provide insightful details to the reader about how the authors dealt with reviewer concerns, but there is still a long way to go until most journals adopt transparent peer review, and even then, readers might wish to get a more succinct overview about the improvements that happened from preprint to the version of record...
<https://prelights.biologists.com/news/>
<https://mp.weixin.qq.com/s/GZa0EnFZVSliuLEwGMZRjw> (中文)



3. Krashes MJ, Chesler AT. Acid Tongues Cause Sour Thoughts. *Cell* 2019;179:287-9. Animals use their sense of taste to evaluate the quality and safety of food before ingestion. In this issue of *Cell*, Zhang and colleagues provide a comprehensive exploration into the elusive mechanisms underlying sour detection...
<https://www.cell.com/action/showPdf?pii=S0092-8674%2819%2931020-7>

4. Sacks CA et al. Talking about Toxicity — “What We’ve Got Here Is a Failure to Communicate”. *N Engl J Med* 2019;381:1406-1408. “A Google Scholar search reveals more than 50,000 occurrences of “generally well tolerated” since 2000.” The authors suggest “...we can take the small step of avoiding sweeping language that oversimplifies and underestimates what patients endure. Vague, meaningless phrases used to describe the toxic effects of drugs are not helpful to patients or their physicians. The language we use to describe short- and long-term toxic effects should more accurately reflect the range of effects the patient can anticipate. Specific language by itself won't improve our patients' lives, but it may be one small step toward better conveying our understanding of their experience. It's a manageable place to start.”

Invitation from Future Meetings

1. The 16th World Congress of Chinese Medicine will be held in Budapest, Hungary, in November 2019: World Congress of Chinese Medicine (WCCM), organized by World Federation of Chinese Medicine Societies (WFCMS), is a global academic event in the field of traditional Chinese medicine. It is convened annually and has been successfully organized 13 times in different countries. The 16th WCCM under the theme of the “Belt & Road TCM Academic Communications” will be held in Budapest, Hungary in November, 2019.

<https://www.medmeeting.org/MiniSiteEn/index/7888>
https://mp.weixin.qq.com/s/SpqrG4XwKKmOJC1QRZ_dWg (中文)

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2. **The 8th GP-TCM RA Annual Meeting will be held in Vytautas Magnus University, Kaunas, Lithuania.** More information will be published in the near future.

<https://www.vdu.lt/en/vmu-will-host-the-annual-meeting-of-traditional-chinese-medicine/>

3. **The 6th World TCM Summer Summit will be hosted by Hong Kong Registered Chinese Medicine Practitioners Association (HKRCMP).** For an introduction of HKRCMP and TCM in Hong Kong, please watch the film below.

https://drive.google.com/file/d/1KbPcYUMwS88YepXulryvfD_RPmPkyx7i/view

4. 13th European Congress of Integrative Medicine announces 2020 will be held in London, UK, 11-13 September 2020. The congress will be held at the prestigious Queen Elizabeth II Centre in London, the largest dedicated conference, events and exhibition space in central London. Located less than five minutes' walk from the Houses of Parliament, the venue is perfectly positioned to house delegates from across Europe and the rest of the world. The following video gives you a good taste of the prime location www.ecimcongress.com/video

Organised on behalf of The European Society for Integrative Medicine and in association with the National Centre for Integrative Medicine (NCIM), The College of Medicine, the University of Southampton and the Academy of Integrative Health & Medicine (AIHM). Featuring world-class experts presenting the latest research and success stories in clinical care, alongside poster sessions and an international exhibition, the congress aims to bring together medical practitioners, healthcare professionals, scientists, researchers, therapists and healthcare politicians from across the globe. All interested parties are invited to register their interest via the website www.ecimcongress.com or by emailing the organisers at info@ecimcongress.com. For more information, please visit: www.ecimcongress.com



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 TCM, 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>

The latest issue of WJTCM focusing on toxicity & safety of traditional medicines has been published on 30th September. <http://www.wjtcn.net/currentissue.asp?sabs=n>

Sounding Board:

1. 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), Prof Yuan Shiun Chang (yschang0404@gmail.com) and Prof Xuanbin Wang (459560483@qq.com).

2. Advised by Professor Zhongzhen Zhao, an Editorial Board member of, and a regular contributor to, our Newsletter, we will highlight a couple of medicinal plants used in TCM a new column in the end page of our newsletters, featuring beautiful photos of the plants by Prof Hubiao Chen, an English introduction to the plants and its medicinal use in TCM by Prof Ping Guo, as well as Chinese poems on the plants by Prof Jiqing Liu. Please read on. The last page is the best yet...

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Monthly Chinese Materia Medica Highlights

Safflower (*Carthamus tinctorius* L., Asteraceae, 红花, left) and saffron (*Crocus sativus* L., Iridaceae, 番红花 or 西红花, right)



Both safflower and saffron are multipurpose resource plants with high economic value. In Chinese *materia medica*, the dried tubular flower (not including ovary) of the former and the dried stigma of the latter are used as Chinese medicinal *honghua* and *xihonghua* respectively. Under the same category of medicinals that invigorate the blood and eliminate blood stasis, *honghua* unblocks menstruation and relieves pain, while *xihonghua* cools the blood, resolves toxicity, relieves stagnancy, and calms the mind.

The good agricultural practice of both plants is mature and successful. However, it takes 140,000~160,000 flowers to produce a single kilogram of saffron stigma. It seems that the total output of saffron is not able to meet the demand from herbal market and food industry, resulting in its higher price in commerce.

红花

番红花

= 红花欲垂未曾凋
独立风中分外娇
不与邻争香作罢
只为故里人逍遥

西域圣草番红花
涉水依香苦作涯
百载深闺犹是客
亭亭玉立贵邻家

Photographs by Prof **Hubiao Chen** (Hong Kong), texts by Dr **Ping Guo** (Hong Kong) and poem by Prof **Jiqing Liu** (Shenzhen).

We thank Prof **Zhongzhen Zhao** (Hong Kong) for advising this new column and thank Dr **Qihe Xu** (London) for help with editing.