

# The November 2017 Newsletter of The GP-TCM Research Association



## Editorials

### TCM and derivatives for microcirculation dysfunction and ischemia/reperfusion injury



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Upon the invitation by the Editor-in-chief of the GP-TCM RA Newsletter, we'd like to summarise our findings of our recent review published in *Pharmacology and Therapeutics*. The review was co-authored with Dr. Quan Li, Professor Jing-Yu Fan and Professor Zhi-Zhong Ma.

Ischemia and reperfusion (I/R) caused microcirculatory disturbance dysfunction and organ injury occur following thrombolysis or intervention in coronary diseases, ischemic stroke, crush injury, trauma, shock, and major surgery. Clinically, only anticoagulant therapy is recommended, and there is no effective cure.

There are clinical advantages in the prevention and treatment of I/R injury in traditional Chinese medicine (TCM), and the related treatment methods have obtained the expert consensus and recommendation of TCM and the integration of Chinese and western medicine. Several hundred papers have been published in SCI journals in the study of the role and mechanism of Chinese medicine in improving I/R injury, but there is a lack of systematic collation and extraction.

Professor Jing-Yan Han and his team systematically studied the effects and mechanisms of compound Chinese medicine and its main ingredients on improving the I/R injury, and published 27 research paper in the SCI journals, such as International Journal of Cardiology, Free Radical Biology and Medicine, Experimental Neurology, Scientific Reports, American Journal of Physiology-Heart and Circulatory Physiology, Microcirculation. In 2008, he was invited to publish a review in the journal of "Pharmacology and Therapeutics", summarizing the pathogenesis of I/R injury and the mechanism of TCM treatment. In 2017, professor Jing-Yan Han was invited again to write a relevant research review for the journal of "Pharmacology and Therapeutics". This review systematically summarizes the 250 papers in the research field, analysis and sorting out of the mechanisms of compound Chinese medicine and its main ingredients in improving the heart, brain, liver and intestinal microcirculatory dysfunction and organ injury, partly explores the scientific connotation of Qi deficiency and blood stasis and tonifying Qi and activating blood.

#### **1. I/R-induced microcirculatory disturbance dysfunction and tissue injury progress stepwise involving ischemia phase, acute, subacute and chronic phases after reperfusion.**

In ischemia phase, mainly manifested as energy metabolism disorder and cell necrosis. During the acute phase of within 24 hours of reperfusion, mainly manifested as oxidative stress, endoplasmic reticulum stress, mitochondrial damage, release of pro-inflammatory factor, adhesion molecule expression, the interaction between leukocytes and vascular endothelial cells, mast cells degranulation and abnormal microvascular permeability, hemorrhage and micro-thrombus. During the



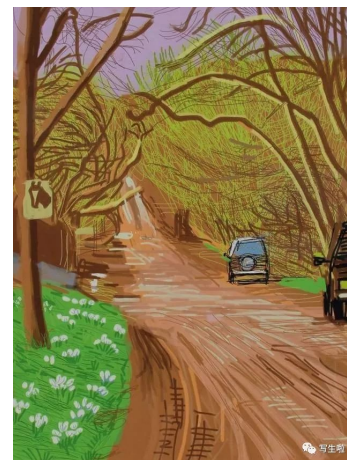
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subacute phase of the period from 24 hours to 7 days after reperfusion, injured vascular endothelial cells and perivascular tissues release chemokines, which attract recruitment of monocytes to interstitial releasing transforming growth factor- $\beta$ 1 that activates fibroblasts, resulting in deposition of collagen via Smad and remodeling and fibrosis of perivascular tissues. During the chronic phase of 7 days after perfusion, CD4-positive lymphocytes extravasate which initiate a chronic inflammatory process. In clinical practice, there is a lack of the theory and method of multi-link regulation aim to the different stages of I/R injury.

### 2. Compound Chinese medicines ameliorating damage induced by I/R usually contain Chinese materia medicas that tonify Qi and/or activate blood and promote blood circulation for removing blood stasis.

For the Chinese materia medica that can tonifying Qi, include *Astragalus membranaceus* (Huang Qi), *Radix Ginseng* (Ren Shen) and *Panax notoginseng* (San Qi), in which, the mainly absorbed ingredients include Astragaloside IV (ASIV), Ginsenoside Rb1 (Rb1), Ginsenoside Rg1 (Rg1), and Notoginsenoside R1 (R1). ASIV, Rb1 and R1 have been found to up-regulate the expression of ATP5D in mitochondrial respiratory chain, thereby improving energy metabolism, attenuating cardiac structure and function injury and alleviating heart microcirculatory dysfunction. For the Chinese materia medica that can activating blood, include *Salvia miltiorrhiza* (Dan Shen), *Radix Paeoniae Alba* (Chi Shao) *Rhizoma Ligustici Chuanxiong* (Chuan Xiong), in which, the mainly absorbed ingredients include dihydroxyphenyl lactic acid (DLA), Caffeic acid (CA), Salvianolic acid B, salvianolic acids, Paeoniflorin, Tetramethylpyrazine. DLA and CA can binds to Sirt1 and Sirt3, respectively, restoring NDUFA10 (a subunit of complex I) expression, or preventing acetylation of NDUFA9 and succinate dehydrogenase complex subunit A, restoring electron transfer in mitochondria, which eventually resulted in a relief of oxidative stress, improving microcirculatory dysfunction and organ injury.



### 3. CP is consisted of *Salvia miltiorrhiza* (Dan Shen), *Panax notoginseng* (San Qi), and *Borneolum Syntheticum* (Bing Pian). QS YQ is consisted of *Astragalus membranaceus* (Huang Qi), *Salvia miltiorrhiza* (Dan Shen), *Panax notoginseng* (San Qi) and *Dalbergia odorifera* (Jiang Xiang).

The major activating blood ingredients in which can inhibit oxidative stress and restore electron transfer through acting on the mitochondria complex I, providing a basis for ATP production. The major tonifying Qi ingredients have been shown to up-regulate ATP5D, a subunit of ATPase, restoring ATP production, improving energy metabolism, and attenuating cardiac structure and function injury.

### 4. Nearly all CCM act at multiple targets, which attributes to the diverse major bioactive components contained in them and accounts for their superiority in fighting against I/R-induced microcirculatory dysfunction and organ injury.

**Reference:** Han JY, Li Q, Ma ZZ, Fan JY. Effects and mechanisms of compound Chinese medicine and major ingredients on microcirculatory dysfunction and organ injury induced by ischemia/reperfusion. *Pharmacol Ther.* 2017;177:146-173.

### Special Features



**1. Warmest congratulations go to Professor Gerhard Franz**, Honorary Member of the GP-TCM RA, the awardee of **the 4<sup>th</sup> Cheung On Tak International Award for Outstanding Contribution to Chinese Medicine 2018**. The award presentation is scheduled for March 2018 at Hong Kong Baptist University. Prof. Franz was chairman of the TCM Working Party, European Pharmacopoeia Commission (2008-2016). Among many other outstanding achievements, Professor Franz's expert leadership in developing TCM herbal monographs and integrating them into European Pharmacopoeia has been widely acclaimed. Interested parties

are referred to his recent paper in WJTCM, the official journal of the GP-TCM RA.

[www.wjtcn.org:8080/ch/reader/create\\_pdf.aspx?file\\_no=20140021&year\\_id=2015&quarter\\_id=1&falq=1](http://www.wjtcn.org:8080/ch/reader/create_pdf.aspx?file_no=20140021&year_id=2015&quarter_id=1&falq=1)

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**2. Warmest congratulations to Professors Rob Verpoorte and Thomas Efferth**, board members of the GP-TCM RA, and Professor Ikhlas Khan, for being awarded the **2017 Qihuang International Prize of China Association of Chinese Medicine**.

**3. Warmest congratulations go to Professor Rudolf Bauer**, Founding President GP-TCM RA (2012-2014) and current BoD member, along with a few other experts, for being awarded an **Outstanding Contribution Award at the 10<sup>th</sup> Shanghai International Conference on TCM and Natural Medicine 2017!**



**4. Warmest congratulations go to Dr Fan Qu and his colleagues** in Zhejiang University for being awarded the sole TCM-related **First Prize at the 2017 China Maternal and Children's Health Scientific and Technological Award**, which was held at the Beijing Diaoyutai State Guest House on 26<sup>th</sup> November 2017. He received this prestigious award for his research on acupuncture and herbal treatment of polycystic ovary syndrome. The deliverables of the project include 21 peer-reviewed papers indexed in Web of Science and two Chinese national patents and one international patent. Fan is Co-Chair of the Pharmacology & Toxicology Interest Group, GP-TCM RA.



<https://mp.weixin.qq.com/s/VC9pArHnFmBdfcY7Vw1ugg> (中文)

**5. The Standardisation Law of the P.R. China (Amended Edition)** was approved by China's top legislature on the 4<sup>th</sup> November 2017.

**6. Classification and Requirements for Registration of Chinese Medicines and Natural Medicines(Draft)**

[http://mp.weixin.qq.com/s/KIP0anfiXqdB\\_g1-0Zk4uA](http://mp.weixin.qq.com/s/KIP0anfiXqdB_g1-0Zk4uA) (Part 1)

[http://mp.weixin.qq.com/s/5HSXmlevKHTB4xbEYI\\_37Q](http://mp.weixin.qq.com/s/5HSXmlevKHTB4xbEYI_37Q) (Part 2)

[http://mp.weixin.qq.com/s/LFiXr0Q\\_AArl0ZWT478qCw](http://mp.weixin.qq.com/s/LFiXr0Q_AArl0ZWT478qCw) (Part 3)

**7. Digital resources of medicinal plants in the Wudang Mountainous Region**, curated by Dr Xiaoyan Zhang, Hubei Medical College.

<http://wdbc2014.sys.sy0719.com.cn/wap/?action=list&id=1&from=groupmessage&isappinstalled=0> (中文)

## European Reports

**1. 2018 EU Budget Agreed.** On Friday 17<sup>th</sup> November, the Council and the European Parliament reached an agreement on the 2018 EU budget, which includes €160.1 billion in new commitments and

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€144.7 billion in payments. Like in 2017, the 2018 budget focuses on the main EU priorities such as boosting economic growth and job creation, strengthening security and addressing the challenges posed by migration. The budgets of multi-annual programmes, such as Horizon 2020 and Erasmus+ received a small boost compared to the Commission's proposal from May this year, despite the Council's plans to cut the former's budget by approximately €500 million. Consequently, the 2018 budgets for Horizon 2020 and Erasmus+ are just over €11.1 billion and €2.3 billion respectively. Once the Council officially adopts the newly agreed budget, the Parliament will need to vote on it on 30 November in Brussels.

<http://ec.europa.eu/budget/library/biblio/documents/2018/statement-of-estimates-of-the-european-commission.pdf>

<http://data.consilium.europa.eu/doc/document/ST-10939-2017-ADD-1/en/pdf>

**2. Gibney E. UK government appoints next chief scientific adviser.** *Nature* 2017;282:551. Patrick Vallance, president of research and development at the pharmaceutical giant GlaxoSmithKline, has been appointed as chief scientific adviser, the UK government announced on 8 November. Vallance, a clinical pharmacologist who previously led the medical division at University College London, will replace Mark Walport in April 2018. Walport has left the government to become head of a powerful new funding body called UK Research and Innovation. As chief scientific adviser, Vallance will advise the prime minister and her cabinet, the government's most senior decision-making body. He will also lead the Government Office for Science, which promotes the use of scientific evidence in policymaking across government... The creation of UK Research and Innovation, intended to increase the power of UK research-funding bodies, means Walport will continue to wield great influence over science in government. The chief scientific adviser has traditionally been the voice of science in government, ...The relationship between Vallance and Walport will be an interesting dynamic to watch,...

[http://www.nature.com/news/uk-government-appoints-next-chief-scientific-adviser-1.22956?WT.ec\\_id](http://www.nature.com/news/uk-government-appoints-next-chief-scientific-adviser-1.22956?WT.ec_id)

**3. Latest Statistics on UK's Participation in Horizon 2020 published.** According to the statistics, the UK ranked second in terms of the overall number of participations in Horizon 2020 projects and also in terms of EU funding received with the UK share of all participations and EU funding awarded equalling 12.6% and 14.9% respectively (including EURATOM).

<https://www.gov.uk/government/statistics/uks-participation-in-horizon-2020-september-2017>

**4. Calendar of H2020 calls for 2018 and 2019.**

<https://www.linkedin.com/groups/164166/164166-6335797344583368708?midToken>



### China Reports

**1. Normile D. Medical centers spearhead China's pharma push.** *Science* 2017;358:709. China's pharma industry has limited R&D capabilities. Struggling under heavy patient loads, clinicians have little time for research and academics are under pressure to churn out peer-reviewed papers. As a result, universities have spun off few biotech ventures. Also hindering innovation are a slow regulatory review process and lax intellectual property protection. Now, China is endeavoring to raise its game in biomedicine. It's launching five new translational medicine centers, each showered with \$150 million in startup funds for buildings and instruments. And last month, China issued guidelines for overhauling the nation's drug approval process by reforming clinical trial management, speeding reviews, allowing submission of foreign clinical trial data, and promoting innovation in drug and medical device development.

[http://science.sciencemag.org/content/358/6364/709?utm\\_campaign](http://science.sciencemag.org/content/358/6364/709?utm_campaign)

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**2. Essential Science Indicators put 6 Chinese universities in top-200 worldwide (112-181).** They are Peking University, University of Chinese Academy of Sciences, Tsinghua University, Shanghai Jiaotong University and Fudan University.

<https://mp.weixin.qq.com/s/Ap-SOlrCvj7Y01c2K0pgw> (中文)

**3. ENRICH – European Network of Research and Innovation of Centres and Hubs, China has been officially launched on October 25th and 27th in Chengdu and Beijing, respectively.** Promoted by the European Commission through Horizon 2020, ENRICH is a global network of centres and hubs that promotes the internationalisation of European science, technology and innovation (STI). The ENRICH service portfolio covers the needs of European STI organisations for the Chinese market such as RDI Consultancy and Coaching, STI RDI Intelligence, Soft Landing and Co-working, Fostering Open Innovation through Training, Cooperation Enabling Events, RDI Briefings and Innovation Support Certification. The ENRICH Centre has its headquarters in the economically vibrant city Beijing, hosted by the EU SME Centre and a regional hub, located in Chengdu, in the brand new building CCEC (Center for China-Europe Cooperation).

More than 50 European organisations from over 20 EU Member States participated in the Matchmaking Tour organised by ENRICH. The participants had the chance to attend the launch ceremonies, as well as B2B matchmaking meetings and business visits in Chengdu, Beijing and Qingdao. The launch ceremonies counted with the participation of representatives from the European Commission, the Chinese government, EU Member States, universities, science parks, private companies, research and innovation agencies, SMEs, start-ups, among others.

<http://www.eucentres.eu/china/>



### TCM, Acupuncture and Other Traditional Medicine

**1. Nature Editorial: Traditional Chinese medicine needs proper scrutiny.** *Nature* 2017;551:541. New laws that promote centuries-old herbal remedies are a backwards step for China. Only controlled clinical trials can satisfy concerns.

[https://www.nature.com/articles/d41586-017-07650-6?WT.ec\\_id](https://www.nature.com/articles/d41586-017-07650-6?WT.ec_id)

**2. Cyranoski D. China to roll back regulations for traditional medicine despite safety concerns.** *Nature* 2017;551:552–553. Scientists fear plans to abandon clinical trials of centuries-old remedies will put people at risk. <http://www.nature.com/news/china-to-roll-back-regulations-for-traditional-medicine-despite-safety-concerns-1.23038>

**3. Qiu J. Traditional medicine: A culture in the balance.** *Nature* 2017; 448, 126–128. Traditional Chinese medicine and Western science face almost irreconcilable differences. Can systems biology bring them together?

<https://www.nature.com/articles/448126a>

**4. International standard for Panax notoginseng root and rhizome (三七) published by ISO.**

Known as ISO 20409:2017, the standard derives from the plant *Panax notoginseng* (Burk.) F.H. Chen, and is applicable to notoginseng root and rhizome that are sold and used as food supplements, functional food or natural medicines in international trade, including Chinese materia medica (whole medicinal materials) and decoction pieces derived from this plant.

<https://www.iso.org/standard/67921.html>

<http://mp.weixin.qq.com/s/7kcfjN2HY-2NRt6zAQcwFg> (中文)

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**5. Zia FZ, et al. The National Cancer Institute's Conference on Acupuncture for Symptom Management in Oncology: State of the Science, Evidence, and Research Gaps. *J Natl Cancer Inst Monogr.* 2017 Nov 1;2017(52). doi: 10.1093/jncimonographs/lgx005.** The Division of Cancer Treatment and Diagnosis, Office of Cancer Complementary and Alternative Medicine, at the National Cancer Institute (NCI) held a symposiumon "Acupuncture for Cancer Symptom Management" on June 16 and 17, 2016. Invited speakers

included 19 scientists and scholars with expertise in acupuncture and cancer research from the United States, Europe, and China. The conference reviewed the NCI's grant funding on acupuncture, analyzed the needs of cancer patients, reviewed safety issues, and assessed both the current scientific evidence and research gaps of acupuncture in oncology care. Researchers and stakeholders presented and discussed basic mechanisms of acupuncture; clinical evidence for specific symptoms; and methodological challenges such as placebo effects, novel biostatistical methods, patient-reported outcomes, and comparative effectiveness research. This paper, resulting from the conference, summarizes both the current state of the science and clinical evidence of oncology acupuncture, identifies key scientific gaps, and makes recommendations for future research to increase understanding of both the mechanisms and effects of acupuncture for cancer symptom management.

[http://mp.weixin.qq.com/s/3GdAm8l0FDUVHt\\_JzBdkZw](http://mp.weixin.qq.com/s/3GdAm8l0FDUVHt_JzBdkZw) (中文)

**6. MacPherson H, Vickers A, Bland M, et al. Acupuncture for chronic pain and depression in primary care: a programme of research. *Programme Grants Appl Res* 2017;5(3).** A systemic review sponsored by UK's National Institute for Health Research, the largest national clinical research funder in Europe, concluded that acupuncture has benefits for treatment of some chronic pain beyond placebo effects. The authors concluded: "We have provided the most robust evidence from high-quality trials on acupuncture for chronic pain. The synthesis of high-quality IPD found that acupuncture was more effective than both usual care and sham acupuncture. Acupuncture is one of the more clinically effective physical therapies for osteoarthritis and is also cost-effective if only high-quality trials are analysed. When all trials are analysed, TENS is cost-effective. Promising clinical and economic evidence on acupuncture for depression needs to be extended to other contexts and settings. For the conditions we have investigated, the drawing together of evidence on acupuncture from this programme of research has substantially reduced levels of uncertainty. We have identified directions for further research. Our research also provides a valuable basis for considering the potential role of acupuncture as a referral option in health care and enabling providers and policy-makers to make decisions based on robust sources of evidence."

<https://www.ncbi.nlm.nih.gov/pubmed/28121095>

<https://discover.dc.nih.ac.uk/portal/article/4000746/acupuncture-shown-to-have-benefits-for-treatment-of-some-chronic-pain>

**7. JAMA publishes discussions on acupuncture for infertility in polycystic ovary syndrome.** Wu X, et al. *JAMA*, 2017, 317(24): 2502; Li Y. *JAMA*. 2017; 318(15):1501-1502.

<http://mp.weixin.qq.com/s/lvnZjO675h5jX6XmIgp-Nw> (中文)

**8. Medicinal Plants Image Database, Hong Kong Baptist University:**

<http://www.hkbu.edu.hk/lib/electronic/libdbs/mpd/index.html>

**The Chinese Medicinal Material Image Database, Hong Kong Baptist University: :**

<http://www.hkbu.edu.hk/lib/electronic/libdbs/mmd/index.html>

**The Phytochemical Image Database, Hong Kong Baptist University:**

<http://www.hkbu.edu.hk/lib/electronic/libdbs/pid/index.html>

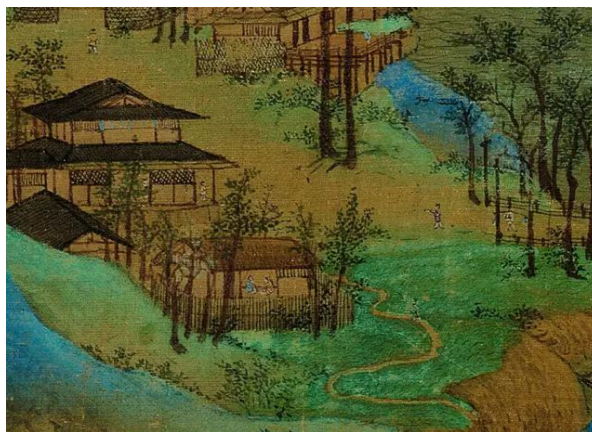
**Chinese Medicine Games, Hong Kong Baptist University:**

<http://lib-nt2.hkbu.edu.hk/cmgame/user.asp>

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**9. First International Guidelines for Chinese Medicine-Based Diagnosis and Treatment of Diseases Issued in Bangkok.** On Oct. 23<sup>rd</sup> 2017, a committee of the World Federation of Chinese Medicine Societies (WFCMS) comprising Chinese and foreign experts released the first international guidelines for the diagnosis and treatment of specific diseases with TCM at the 14<sup>th</sup> World Conference on TCM in Bangkok. The WFCMS, founded in 2003, has published eight international standards for TCM to date. This marks the first release of guidelines for the diagnosis and treatment of specific diseases, said Sang Binsheng, secretary-general of the federation. The guidelines create an international standard for the treatment of diabetes, a disease with high incidence, high mortality and disability, said Tong Xiaolin, chief researcher at the China Academy of Chinese Medical Sciences...



<https://www.yicaglobal.com/news/first-international-guidelines-chinese-medicine-based-diagnosis-and-treatment-diseases-issued>

<http://xhpfmapi.zhongguowangshi.com/share/index.html?docid=2430136&from> (中文)

**10. Academician Prof. Kaixin Chen: The Value and Roles for TCM Nowadays**

<https://mp.weixin.qq.com/s/0GGfQJ3NVDbaL5n-95j2qA> (中文)

**11. The Top-10 Classic TCM Formula:**

<http://mp.weixin.qq.com/s/9TYDRhCG6HqWAQ6RTf2gHw> (中文)

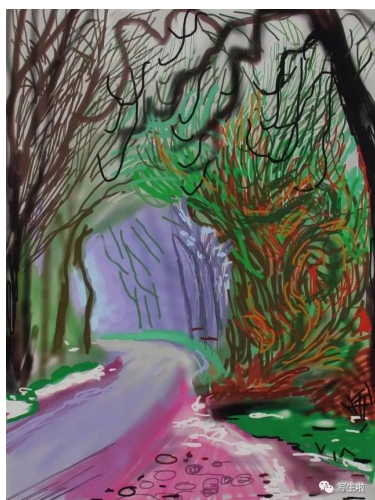
**12. Use of Acupuncture in US Military Service:**

<http://mp.weixin.qq.com/s/Yn-ipeYPrDYo6xuBcUGyEg> (中文)

**13. Aiping Lyu and Zhaoxiang Bian: Improving the accuracy of trial data in China. *The BMJ Opinion* November 20, 2017**

<http://blogs.bmj.com/bmj/2017/11/20/aiping-lyu-and-zhaoxiang-bian-improving-the-accuracy-of-trial-data-in-china/?from=groupmessage&isappinstalled=0>

**14. Gao K, et al. Mechanism of Chinese Medicine Herbs Effects on Chronic Heart Failure Based on Metabolic Profiling. *Front. Pharmacol.* 2017;8:864.** Chronic heart failure (CHF) is a major public health problem in huge population worldwide. The detailed understanding of CHF mechanism is still limited. Zheng (syndrome) is the criterion of diagnosis and therapeutic in Traditional Chinese Medicine (TCM). Syndrome prediction may be a better approach for understanding of CHF mechanism basis and its treatment. The authors studied disturbed metabolic biomarkers to construct



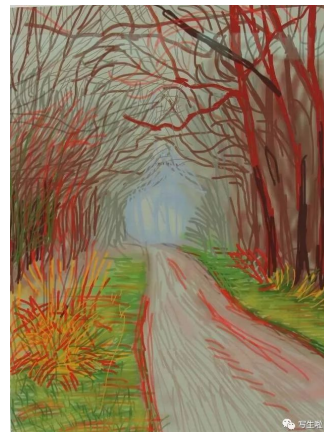
a predicting mode to assess the diagnostic value of different syndrome of CHF and explore the Chinese herbal medicine (CHM) efficacy on CHF patients. A cohort of 110 patients from 11 independent centers was studied and all patients were divided into 3 groups according to TCM syndrome differentiation: group of Qi deficiency syndrome, group of Qi deficiency and Blood stasis syndrome, and group of Qi deficiency and Blood stasis and Water retention syndrome. Plasma metabolomic profiles were determined by UPLC-TOF/MS and analyzed by multivariate statistics. About 6 representative metabolites were highly possible to be associated with CHF, 4, 7, and 5 metabolites with Qi deficiency syndrome, Qi deficiency and Blood stasis syndrome, and Qi deficiency and Blood stasis and Water retention syndrome (VIP > 1, p < 0.05). The diagnostic model was further constructed based on the metabolites to diagnose other CHF patients with satisfying sensitivity and specificity (sensitivity and specificity are 97.1 and 80.6% for CHF

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group vs. NH group; 97.1 and 80.0% for QD group vs. NH group; 97.1 and 79.5% for QB group vs. NH group; 97.1 and 88.9% for QBW group vs. NH group), validating the robustness of plasma metabolic profiling to diagnostic strategy. By comparison of the metabolic profiles, 9 biomarkers, 2-arachidonoylglycerophosphocholine, LysoPE 16:0, PS 21:0, LysoPE 20:4, LysoPE 18:0, linoleic acid, LysoPE 18:2, 4-hydroxybenzenesulfonic acid, and LysoPE 22:6, may be especially for the effect of CHM granules. A predicting model was attempted to construct and predict patient based on the related symptoms of CHF and the potential biomarkers regulated by CHM were explored. This trial was registered with NCT01939236 (<https://clinicaltrials.gov/>).


<https://www.frontiersin.org/articles/10.3389/fphar.2017.00864/full?utm>




### Omics in Progress

#### 1. Advances in Research of Non-coding circular RNAs

[http://mp.weixin.qq.com/s/V\\_OsxoS29MTxH4WUFf5-Uw](http://mp.weixin.qq.com/s/V_OsxoS29MTxH4WUFf5-Uw) (中文)

 2. Editorial. **Accounting for sex in the genome.** *Nat Med* 2017; 23:1243. Genetic association studies of the human genome often omit the X chromosome because of the unique analytical challenges it presents. A concerted effort to undo this exclusion could offer medically relevant insights into basic biology that might otherwise be missed... In the past, genotyping chips contained very few X-chromosome markers, which created a bottleneck on data. This has since improved, but the significance of variants on the X chromosome still remains harder to assess than for variants on autosomal chromosomes. One reason is simply that there are two copies of X in women and one in men, so the signals for variants on this chromosome obtained with standard array genotyping platforms are comparatively lower for men. Another reason is the phenomenon of X inactivation—the process by which one of the two X chromosomes is randomly silenced in women's cells. It is not yet possible for standard sequencing technologies to discern which genetic variants are on the silenced version of the X chromosome. To make matters more complicated, X inactivation can vary within the body... It is not just the X chromosome that has been neglected in genetic analyses. A review paper last year noted that the Y chromosome is “too often ignored by researchers but could potentially be the key to understanding the [coronary artery disease] prevalence differences between men and women”... The failure to assess the influence of sex chromosomes in studies of the genome doesn't necessarily boil down to a lack of tools: there is also a challenge of a lack of will. It takes a bit more effort to include sex chromosomes in certain genomic analyses, and so this step is sometimes skipped. Now is a time to reverse this trend of omission. There are no shortcuts to good science.

[https://www.nature.com/articles/nm.4445?WT.ec\\_id](https://www.nature.com/articles/nm.4445?WT.ec_id)

 3. Cox DBT, et al. **RNA editing with CRISPR-Cas13.** *Science* 2017;358:1019-1027. Efficient and precise RNA editing to correct disease-relevant transcripts holds great promise for treating genetic disease. Cox *et al.* took advantage of the ability of Cas13b, an effector from a type VI CRISPR-Cas system, to target specific RNAs directly (see the Perspective by Yang and Chen). They fused Cas13b with the ADAR2 adenosine deaminase domain and used rational protein engineering to improve the resultant enzyme. These approaches yielded an RNA knockdown and editing platform that allowed efficient and specific RNA depletion and correction in mammalian cells.

[http://science.sciencemag.org/content/358/6366/1019?utm\\_campaign](http://science.sciencemag.org/content/358/6366/1019?utm_campaign)

 4. Dolgin E. **The most popular genes in the human genome.** *Nature* 2017;551:427-431. A tour





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through the most studied genes in biology reveals some surprises.

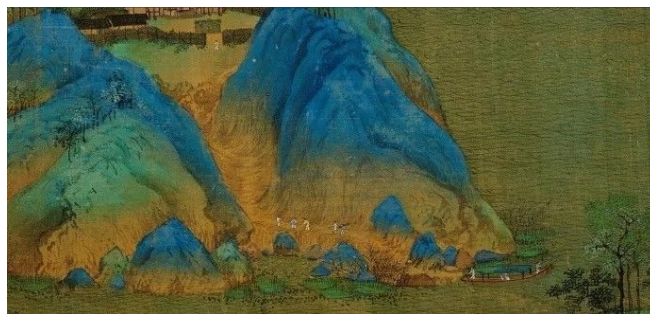
[https://www.nature.com/articles/d41586-017-07291-9?WT.ec\\_id](https://www.nature.com/articles/d41586-017-07291-9?WT.ec_id)

**5. Gaudelli NM et al. Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage.** *Nature* 2017;551:464–471. A new DNA ‘base editor’ can change targeted A•T base pairs to G•C, allowing disease-associated mutations to be corrected and disease-suppressing mutations to be introduced into cells.  
[https://www.nature.com/articles/nature24644?WT.ec\\_id](https://www.nature.com/articles/nature24644?WT.ec_id)

**6. Dodd D, et al. A gut bacterial pathway metabolizes aromatic amino acids into nine circulating metabolites.** *Nature* doi:10.1038/nature24661. A pathway for the production of aromatic amino acid metabolites in *Clostridium sporogenes* is described; modulation of serum levels of these metabolites in gnotobiotic mice affects intestinal permeability and systemic immunity.  
[https://www.nature.com/articles/nature24661?WT.ec\\_id](https://www.nature.com/articles/nature24661?WT.ec_id)

### Other Recommended Readings.

**1. Boncler M, et al. A new approach for the assessment of the toxicity of polyphenol-rich compounds with the use of high content screening analysis.** *PLoS ONE* 2017;12: e0180022. The toxicity of *in vitro* tested compounds is usually evaluated based on AC<sub>50</sub> values calculated from dose-response curves. However, there is a large group of compounds for which a standard four-parametric sigmoid curve fitting may be inappropriate for estimating AC<sub>50</sub>. In the present study, 22 polyphenol-rich compounds were prioritized from the least to the most toxic based on the total area under and over the dose-response curves (AUOC) in relation to baselines. The studied compounds were ranked across three key cell indicators (mitochondrial membrane potential, cell membrane integrity and nuclear size) in a panel of five cell lines (HepG2, Caco-2, A549, HMEC-1, and 3T3), using a high-content screening (HCS) assay. Regarding AUOC score values, naringin (negative control) was the least toxic phenolic compound. Aronox, spent hop extract and kale leaf extract had very low cytotoxicity with regard to mitochondrial membrane potential and cell membrane integrity, as well as nuclear morphology (nuclear area). Kaempferol (positive control) exerted strong cytotoxic effects on the mitochondrial and nuclear compartments. Extracts from buckthorn bark, walnut husk and hollyhock flower were highly cytotoxic with regard to the mitochondrion and cell membrane, but not the nucleus. We propose an alternative algorithm for the screening of a large number of agents and for identifying those with adverse cellular effects at an early stage of drug discovery, using high content screening analysis. This approach should be recommended for series of compounds producing a non-sigmoidal cell response, and for agents with unknown toxicity or mechanisms of action.  
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0180022>



**2. Li F et al. A water-soluble nucleolin aptamer-paclitaxel conjugate for tumor-specific targeting in ovarian cancer.** *Nature Communications* 2017;8:1390. Paclitaxel (PTX) is among the most commonly used first-line drugs for cancer chemotherapy. However, its poor water solubility and indiscriminate distribution in normal tissues remain clinical challenges. Here we design and synthesize a highly water-soluble nucleolin aptamer-paclitaxel conjugate (NucA-PTX) that selectively delivers PTX to the tumor site. By connecting a tumor-targeting nucleolin aptamer (NucA) to the active hydroxyl group at 2' position of PTX via a cathepsin B sensitive dipeptide bond, NucA-PTX remains stable and inactive in the circulation. NucA facilitates the uptake of the conjugated PTX specifically in tumor cells. Once inside cells, the dipeptide bond linker of NucA-PTX is cleaved by cathepsin B and then the conjugated PTX is released for action. The NucA modification assists the selective

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accumulation of the conjugated PTX in ovarian tumor tissue rather than normal tissues, and subsequently resulting in notably improved antitumor activity and reduced toxicity.

<https://www.nature.com/articles/s41467-017-01565-6>

**WeChat introduction on this paper:**

<http://mp.weixin.qq.com/s/uIej7GrK4qyqiu0SpTEF2g> (中文)



**3. Kiley R, et al. Data Sharing from Clinical Trials — A Research Funder’s Perspective.** *N Engl J Med* 2017;377:1990-1992. The Wellcome Trust, the Medical Research Council, Cancer Research UK, and the Bill and Melinda Gates Foundation share a common vision for maximizing the value of data that are generated through the trials we fund. We are committed to ensuring that the data from published clinical trials can be accessed by researchers so they can validate key findings, stimulate further inquiry, and ultimately deliver lifesaving results...

<http://www.nejm.org/doi/full/10.1056/NEJMs1708278?query=TOC>

**4. Chawla DS. Need a paper? Get a plug-in.** *Nature* 2017;551:399-400: Scientists “shouldn’t be spending hours finding papers”, but “spending hours reading them”. Kopernio, Unpaywall and Open Access Button: a collection of web-browser plug-ins is making the scholarly literature more discoverable...

[https://www.nature.com/articles/d41586-017-05922-9?WT.ec\\_id=NATURE-20171116&spMailingID](https://www.nature.com/articles/d41586-017-05922-9?WT.ec_id=NATURE-20171116&spMailingID)

**Kopernio:** <https://kopernio.com>

**Unpaywall:** <http://unpaywall.org>

**Open Access Button:** <https://openaccessbutton.org>



**5. Mullard A. FDA unveils searchable adverse events system.** *Nature Reviews Drug Discovery* 2017;16:743. The FDA has launched a new adverse event portal that enables drug developers, doctors and patients to search for safety red flags for approved drugs. This **FDA Adverse Event Reporting System (FAERS)** could offer a powerful post-marketing pharmacovigilance resource and a means of guiding preclinical drug development...

<https://www.nature.com/articles/nrd.2017.224>

<https://fis.fda.gov/sense/app/777e9f4d-0cf8-448e-8068-f564c31baa25/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis>

**6. Nature Index 2017 Science Cities.** Science is an urban enterprise. In 2016, some 60% of the share of authorship in the Nature Index came from 100 cities. The top 10 metropolises accounted for 17% of the total research output, which is 17 times their global population weight. With two-thirds of the world's population projected to live in urban areas by 2050, cities will become even more distinctly the domain of knowledge and innovation...Agglomeration is the term used by urban economists to describe the added benefits that come from companies clustering in cities. Spatial proximity also seems to amplify knowledge. The relatively small city of Boston-Cambridge has two of the top 10 academic institutions in the Nature Index 2016, ranked by their weighted fractional count — Harvard University and MIT. China's top two institutions are less than a kilometre apart in Beijing. And King's College London, Imperial College London and UCL form a successful triangle, north of the river Thames...For London, The city centre is less than an hour from both Cambridge and Oxford, forming the central node of the **UK's** scientific golden triangle.

<https://www.nature.com/articles/550S160a>

<https://www.nature.com/articles/550S157a>

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## Reports on Meetings & Events

**1. The 10<sup>th</sup> Shanghai International Conference on TCM and Natural Medicine was held in Shanghai on 29-31 October 2017.** The meeting was attended by 33 speakers and more than 350 delegates from 6 countries. <http://mp.weixin.qq.com/s/1jaY4fkl9EuVVNn49Z5gQ> (中文)



**2. The Third China-Africa TCM International Cooperation and Development Forum was held in Cairo, Egypt, on 9-15 November 2017:** [http://news.xinhuanet.com/health/2017-11/22/c\\_1121995507.htm](http://news.xinhuanet.com/health/2017-11/22/c_1121995507.htm) (中文)

**3. The 3<sup>rd</sup> Hunan International Forum for Innovation and Development of Biomedicine and Chinese Medicine was held in Changsha, 2-3 November 2017.** GP-TCM RA BoD member Prof. Rudolf Bauer delivered a talk at the meeting.



**4. The Symposium on Herbal Medicine Biotechnology of One Power Innovative Phytomedicine Co. (Taipei, Taiwan) was held on September 21, 2017 at The Grand Hotel, Taipei, Taiwan.** This meeting was to our knowledge the first of such activity in Taiwan which combined both academic activity and industrial applications in a mission oriented R&D fashion in the field of herbal medicine and biotechnology. Invited speakers, guests and distinguished research scientists came from countries including USA, Germany, Netherlands, Bulgaria and Taiwan. Approximately 400 guests participated in the ceremony and the subsequent symposium.

The ceremony opened with a short magnificent show of a Chinese dragon dance and a Chinese orchestra. The opening remarks were delivered by Dr. Ning-Sun Yang and Chairwoman Ms. Shu-Hui Lin, serving as Co-founders of the One Power Innovative Phytomedicine Co. (OIPM). Dr. NS Yang then shared his company's vision, including future R&D program projects, innovative ideas and milestones for future botanical drug development.

Followed by the opening ceremony, a Symposium on Herbal Medicine Biotechnology was held in the same premises, Dr. Robert Verpoorte from Leiden University, Netherlands shared his opinions and in-depth thinking on the topic of "Synergy, Easier to Say than to



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Prove". Dr. James Timmins from Univ. of Nevada, USA gave a very updated review of the future potential for phytomedicines and human genomics, Dr. Jen Chen, Chairman of Genovate Biotechnology Co. in Taiwan, presented a talk on "Innovative New Product Development in Taiwan". Dr. Milen Georgiev from Bulgarian Academy of Sciences delivered a talk on "From Plant to Pharmacy Shelf: Can we accelerate this long Journey?" emphasizing the proper and efficient use of NMR technology. Dr. Thomas Efferth from Johannes Gutenberg Univ. of Mainz, Germany gave a highly informative and elegant talk on his work entitled "Beyond Malaria: The various Antiviral Activities of Artesunate".

Dr. NS Yang took the liberty on providing a key summary and an interpretation in Chinese at the end of each talk. He and a number of participants then gave comments, questions and useful suggestions, truly can serve as take home lessons to digest. Dr. Ru-Chih Chow Huang, distinguished professor from Johns Hopkins University, commented that this was such a wonderful symposium, and this is very much needed for any biotech company for future R&D efforts.

The ceremony and symposium ended with a gala dinner in The Grand Hotel, with a short presentation of Chinese Opera act.

Following the symposium on second day, there was a Scientific Advisory Committee meeting, via recruiting all of the symposium speaker members in the premises of OIPM facility in Taipei. The research scientists and staff members presented their



future R&D projects and candidate product lines to the committee members. Advisory members indeed gave a series of valuable suggestions regarding the feasibility, setting priorities, and use of new technology platforms. Comments were made on the use of NMR for much of the planned future experimental studies, pre- and post- harvest treatments for augmenting metabolite levels of medicinal phytochemicals, the tricks and skills for herbal extract preparations, the definition and focus on health foods, nutritional foods, medicinal foods and botanical drugs. Comments and suggestions were made on prioritizing short term vs. long term goals and many aspects on type and shape of future candidate products.

A great majority of our meeting participants considered and believed that we had great, stimulating and rewarding meetings in such a mission-oriented research gathering. And both Academia and industry may greatly benefit from such meetings in the future.

### Future Meetings & Events

 1. The 15<sup>th</sup> World Congress of Chinese Medicine and *Belt and Road* TCM Culture Week to be held in Rome, Italy, 16-20 November 2018.

[http://c.eqxiu.com/s/O8xACE2w?eqrcode=1&share\\_level=4&from\\_user=a294a700-73b5-4d95-9d8b-dc428813e7cd&from\\_id](http://c.eqxiu.com/s/O8xACE2w?eqrcode=1&share_level=4&from_user=a294a700-73b5-4d95-9d8b-dc428813e7cd&from_id) (中文)

2. WeChat report on international celebration of the 500 anniversary of Li Shizhen's birth to be held in Li's hometown Jichun County, Hubei Province, China, on 26<sup>th</sup> May, 2018.

<http://mp.weixin.qq.com/s?biz=MzAxMjMyMTEwNA==&mid=2660692447&idx=1&sn=3895e03e994d2f1c98befd9f4beb8eca&chksm> (中文)

### Invitation from Journals

 1. The third issue of *World Journal of Traditional Chinese Medicine (WJTCM)* 2017 published, and invitation for submissions from the journal. WJTCM, ISSN 2311-8571, a peer-

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reviewed journal (quarterly) launched in 2014, is the official journal of the World Federation of Chinese Medicine Societies (WFCMS) and the GP-TCM RA. **Aim & Scope:** Introduce clinical efficacy and mechanism of TCM to doctors and biomedical researchers around the world, so as to provide new ideas and methods for solving the complicated and difficult cases.

- WJTCM includes reviews and original articles focused on four aspects:
- Modern Research on Chinese Materia Medica: theories of processing, property, and compatibility of Chinese materia medica; safety of Chinese materia medica; active principles and mechanism and efficacy of crude drugs and Chinese compound formulas
- Research on TCM Theory: scientific connotation and biological foundation of TCM basic theories
- TCM clinical Research: disease and syndrome, TCM safety, efficacy evaluation, evidence-based and systematic evaluation
- Acupuncture and Moxibustion: effect mechanism of acupuncture and moxibustion, specificity of acupoint effect, acupoints compatibility, efficacy evaluation of acupuncture and moxibustion.

**Good news!** WJTCM has initiated an official cooperation with the Wolters Kluwer Publishing Group. From the 3<sup>rd</sup> issue in 2017, all articles published in WJTCM will be indexed in the VID database and can be retrieved in the Pubmed database. We believe that this latest progress will greatly improve the international influence of WJTCM. Welcome to submit or recommend articles to WJTCM!

**Submission to the Journal:** All the articles can be submitted via ScholarOne: <https://mc03.manuscriptcentral.com/wjtcn>, Detailed information about requirements of manuscript and format can be found in "Instruction&Forms" by the above URL, or by accessing WJTCM home page [www.wjtcn.org](http://www.wjtcn.org).

New articles in the 3<sup>rd</sup> issue of 2017 are as follows.

- Xiao-Ping Zheng, et al. **The Effects of Different Compatibilities of Qing'e Formula on Scopolamine-induced Learning and Memory Impairment in the Mouse**
- Ying Zhang, et al. **Traditional Chinese Herbal Medicine for Perimenopausal Depression of Chinese Women: A Meta-analysis**
- Zhi-Jie Ding, et al. **Interactions Between Traditional Chinese Medicine and Anticancer Drugs in Chemotherapy**
- Yi Wang, et al. **Xiao Chai Hu Tang for Liver Diseases: A Literature Review**
- Qian-Ru Zhang, et al. **Progress of Studies on Traditional Chinese Medicine Based on Complex Network Analysis**
- Yukihiro Shoyama. **Monoclonal Antibody Usage Strategies for Natural Products in Traditional Chinese Medicine**
- Mahmoud A. et al. **New Orally Active Artemisinin Dimer Antimalarials**



All WJTCM articles are published online ([www.wjtcn.org](http://www.wjtcn.org)) and are freely available to global readers.

**NEW** 2. **CALL FOR PAPERS** from *Frontiers in Physiology Vascular Physiology* "Traditional Chinese/Asian Medicine and Cardiovascular/ Complex Disease". Topic Editors: Professor Jing-Yan Han, Peking University, Beijing, China, and Professor Gerald A Meininger, University of Missouri, Columbia, United States. Submission Deadline: 5th January 2018. Manuscripts can be submitted to the journal directly: <http://journal.frontiersin.org/researchtopic/6490/traditional-chinese-and-asian-medicine-and-cardiovascular-disease>.

Or you can contact Prof. Jing-Yan Han: [hanjingyan@bjmu.edu.cn](mailto:hanjingyan@bjmu.edu.cn)

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### Sounding Board.

**NEW** 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](mailto:qihe.xu@kcl.ac.uk)), Prof. Pierre Duez ([pierre.duez@umons.ac.be](mailto:pierre.duez@umons.ac.be)) and Prof. Yuan Shiun Chang ([yschang0404@gmail.com](mailto:yschang0404@gmail.com)).

### Acknowledgements

Contributions from Prof. **Rudolf Bauer** (Graz), Prof. **Hubiao Chen** (Hong Kong), Prof. **Pierre Duez** (Mons), Dr **Tai-Ping Fan** (Cambridge), Prof. **Gerhard Franz** (Regensburg), Prof. **Jing-Yan Han** (Beijing), Prof. **Aiping Lyu** (Hong Kong), Dr **Fan Qu** (Hangzhou), Prof. **Xuanbin Wang** (Shiyan), Dr. **Ning-Sun Yang** (Taipei), Dr. **Robert Verpoorte** (Leiden), Ms **Hui Xu** (Beijing), Prof. **Zhongzhen Zhao** (Hong Kong) and Dr. **Qihe Xu** (London) are gratefully acknowledged.

Traditional Chinese paintings are portions of *A Panorama of Rivers and Mountains* 《千里江山图》 by Wang Ximeng (王希孟), Song Dynasty, and oil paintings were by David Hockney OM, CH, RA.

<https://mp.weixin.qq.com/s/mV0HHp2Au1sG15nEGm9EGg> (中文)

[http://mp.weixin.qq.com/s/smT-aV3E9nXipxspJ85\\_iA](http://mp.weixin.qq.com/s/smT-aV3E9nXipxspJ85_iA) (中文)

