

#### **Presidential Editorial**

#### The GP-TCM Research Association: Six Years On



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As summarised in the article "Traditional Chinese medicine research in the post-genomic era: Good practice, priorities, challenges and opportunities", the GP-TCM Consortium made great efforts to address some fundamental issues in TCM research, including developing guidelines, as well as identifying priorities, challenges and opportunities. These consortium guidelines and consensus will need dissemination, validation and further development through continued interregional, interdisciplinary and intersectoral collaborations. To promote this, the GP-TCM Research Association was established in April 2012.<sup>1</sup>

How time flies! The GP-TCM RA is 6 years old, and it has been 16 months since I took up presidency of the GP-TCM RA in January 2017. As your 3<sup>rd</sup> President, I have been trying to revitalise the GP-TCM Research Association through reorganisation, outreach and implementation.

**Reorganisation**: To serve you better, we have reallocated our Secretariat to Hong Kong, hosted by the Institute of Chinese Medicine, The Chinese University of Hong Kong. Now we have an up-to-date database of our members. We have also added weblink to our official journal – *World Journal of TCM* (WJTCM). Significantly, the Interest Groups have been revitalised by appointment of new chairs and/or co-chairs as well as creation of a Publication Interest Group, to be chaired by Rob Verpoorte and Thomas Efferth who have much experience in editing *Journal of Ethanopharmacology* and *Phytomedicine*.

To draw in new blood, I have been canvassing for new corporate members. It is most pleasing that 6 organisations have accepted my personal invitation to be Corporate Members: Wenzhou Medical University, Zhejiang University College of Pharmaceutical Sciences, Heilongjiang University of Chinese Medicine, Dalian Fusheng Natural Medicine Development Co., Ltd., Hutchison Whampoa Guangzhou Baiyunshan Chinese Medicine Co. Ltd. and International Universities Innovation Alliance.

**Outreach:** At the invitation of the Czech Minister of Health, Dr Miloslav Ludvik, I co-organised a TCM Roundtable Meeting "Possible Synergies between Western and Traditional Chinese Medicines" in Prague on 23 February 2017. This high-profile meeting was held in the Chamber of Deputies of the Parliament of the Czech Republic (see March 2017 edition of our newsletter). The purpose of the meeting was to highlight the global state-of-the-art of TCM and convince the Czech Parliament about

the clinical value and scientific rigor of TCM research and development. Much to our pride and delight, such public consultations and debates led to the legislation of TCM acupuncturists and TCM therapists in the Czech Republic in June 2017.

I also reached out to the US with two visits to the NIH National Center for Complementary and Integrative Health (May 2017), as well as attending the Inaugural UCLA Chinese Herbal Medicine Summit & Symposium on the Potential of Chinese Medicine in the U.S. (13-16 July 2017).

**Implementation:** Despite a year's delay, the 6<sup>th</sup> GP-TCM RA Annual Meeting (4-6 July 2018) will be held in Royal Botanic





Gardens Kew and London South Bank University (Kew/LSBU). This long-awaited event will celebrate Li Shizhen's birth in 1518, and promise to bring in new approaches in TCM research and development while adhering to our core good practices (GxPs) value. GxPs meant good practice guidelines at every stage of TCM research and development, focusing on research into acupuncture and Chinese herbal medicine, and including Good Agriculture and Collection Practice, Good Laboratory Practice, Good Research Practice, Good Manufacturing Practice, Good Clinical Practice, and Good Information Technology Practice, Good Literature Review and Publication Practice, etc.

Immediately after the Kew/LSBU event, I will host a one-day forum in Cambridge on 7 July - *Future Trends in Global Healthcare* - as part of the First International Conference of One-Belt-One-Road International@Cambridge, in association with International Universities Innovation Alliance (IUIA).

As European Coordinator of Medicinal Plants 4.0 project, I shall be working closely with colleagues in Guangxi Botanic Garden of Medicinal Plants, Beijing Genomics Institute (BGI) and other partners and engage GP-TCM RA Board of Directors and appropriate members in this monumental project. To help materialise GxPs, I have recently cooperated with Professor Xiang-Cheng Zhang at Cambridge University and organised a two-day event in Hui-Xian City in Henan Province, China. With unprecedented support from the local government, the 20-plus delegates signed up to Baiquan Declaration as a first step towards working with various stakeholders to set up plots of land for cultivation and production of good quality medicinal plants in Europe, Asia and Africa.

#### References:

1. Uzuner H, Bauer R, Fan TP, Guo DA, Dias A, El-Nezami H, Efferth T, Williamson EM, Heinrich M, Robinson N, Hylands PJ, Hendry BM, Cheng YC, Xu Q. Traditional Chinese medicine research in the post-genomic era: good practice, priorities, challenges and opportunities. J Ethnopharmacol. 2012;140:458-68.

### **Special Features**

1. The 6<sup>th</sup> Annual Meeting of the GP-TCM RA will be held in London, UK, 4-6 July 2018. Extended deadline for abstract submission and registration: 31 May 2018. The programme has been designed to address the key areas that impact TCM:

- Availability and quality of the genetic resources used in TCM
- Regulatory environment associated with modern drug development,
- Advances in analytical technique that further our understanding of the complex mixtures used in TCM
- Standardization quality and safety of TCM
- New guidelines of, and evidence from, clinical studies
- Integration of acupuncture

# The 6th Annual Meeting of Good Practice in Traditional Chinese Medicine Research Association Second Announcement 4-6 July 2018 Royal Botanic Gardens, Kew and London South Bank University, United Kingdom

#### Aims of conference:

- 1. To provide an overview of new methods that can be used to enhance our knowledge about plants and fungi used in TCM.
- 2. To identify what evidence is needed to further the development of TCM in the West.
- 3. To identify key issues associated with the supply and quality of plants and fungi used in TCM and how this could be improved.
- 4. What are the regulatory challenges that TCM faces in the East and West and how could these be addressed.
- 5. What are the commercial opportunities for quality TCM products in China and the West: how can scientists help?



#### Highlights of the meeting:

- Professor Zhongzhen Zhao (Hong Kong Baptist University, China) Materia Medica: From Li Shizhen to now and our future
- Professor Mei Wang (Leiden University, the Netherlands) Challenge and opportunity for TCM in Europe
- Dr Linda Anderson (Medicines and Healthcare Products Regulatory Agency, United Kingdom) Title to be confirmed
- Professor Clara Lau (The Chinese University of Hong Kong, China) New concept of 'good practice' on pharmacological research exploration of beneficial herb-drug combined efficacies
- Professor Gert Laekeman (University of Leuven, Belgium) Safety Pharmacology of Herbal Products
- Dr Andreas Bender (Cambridge University) Chemogenomics for studying pharmacology and toxicology of medicinal plants
- Professor Pang Chui Shaw (The Chinese University of Hong Kong) *Use of DNA techniques in the identification of granule extracts*

Extended deadline for abstracts and registration is 31 May 2018.

Please visit: http://www.gp-tcm.org/events/upcoming/

2. Warm congratulations to Prof Zhongzhi Qian, Chinese Pharmacopoeia Commission, for being the recipient of an Outstanding Contribution Award at the 18th Annual Oxford International Conference on the Science of Botanicals held at Oxford, Mississippi USA, 9-12 April 2018.

https://mp.weixin.gg.com/s/96WweRwo4ggZidobUh1hvw (中文)



3. Medicines from Plants and TCM Forum was held in Baiquan International Hotel, Hui-Xian City, Henan, China on 2-3 April 2018. Co-organised by Prof.Dr. Xiangcheng Zhang, Royal Society Industry Fellow at University of Cambridge & Principal Consultant at Lucideon, and Dr Tai-Ping Fan, President of the GP-TCM RA, and supported by the local government, more than 20 experts and scholars from the UK, USA, Zhengzhou, Hong Kong, Macao, Beijing, Shanghai, Hangzhou, Suzhou, Chengdu and Xi'an attended the meeting and signed up to Baiquan Declaration as a first step towards working with various stakeholders to set up plots of land for cultivation and production of good quality medicinal plants in Europe, Asia and Africa.

Attendees, including GP-TCM RA Board Members Tai-Ping Fan (University of Cambridge), Vivian Wong (University of Hong Kong), Qie Xu (King's College London), and senior GP-TCM RA members



Zhongzhen Zhao (Hong Kong Baptist University), representatives of GP-TCM RA Corporate Members (Prof. Cheng Peng, Chengdu University of TCM; Xiaohui Zheng, Northwest University; Xuesong Liu and Yuwan Lin, Zhejiang University), et al joined local governmental officials and experts to advise on the development of plantation compliant with Good Agricultural Practice. focusing on edible medicinal plant species, integration of herbal plantation, herbal culture the **TCM** with industry, conservation of environmental, cultural and historic legacies, and development of tourism and economy.







Hui-Xian City (辉县 or 輝縣) sits at foot of the south Taihang Mountain. Baiquan Town, part of Hui-Xian City, is one of China's ancient trading centres of Chinese herbal drugs. Due to its proximity to the Jiaozuo City, home of "Huai" Daodi Chinese herbs, Taihang Mountain and rich water resources, it has historically been not only an important trading centre of Chinese herbs, but also a great tourist and cultural centre. With joint efforts by local government, experts and international collaboration, the City, as the birth place of the Baiquan Declaration, is well placed to serve as a starting point for international development of TCM within and beyond the Belt and Road initiative.





4. The 3<sup>rd</sup> Natural Product Symposium & Hong Kong, Macao and Taiwan Natural Product Forum 2018 was held in Shanghai Ocean Hotel from April 12 to 13. Hosted by the Investment Promotion Agency of the Ministry of Commerce, P.R. China and Bioon, the Meetings comprised 3 sessions, i.e. the Origins and Discoveries of Natural Products, Total Synthesis and Structure Optimization of Natural Products and Conversion of Natural Products into Innovative Drugs. On April 12 morning, Dr Daijie Chen (China State Institute of Pharmaceutical Industry), Dr. Chunming Rao (National Institutes for Food and Drug Control of China), Dr. Shaoxiong Chen (Shanghai Biopharmaceutics Industry Association), . Li Chen (Hua Medicine), Dr. Jianguo Ma (Shanghai Medicilon) and Dr. Jingrong Li (CStone Pharmaceuticals Co.) led to explore the status quo and progress of R&D in new drugs in China through keynote speeches and discussions.

In the afternoon, Dr. Hongxi Xu (Shanghai University of TCM) delivered an opening speech. He shared whis personal journey of studying and working aboard and back in China and thoroughly described his work on TCM-derived bioactive compounds and their anti-viral, anti-bacterial and anti-tumor mechanisms of action, particularly focusing on more than 10 *Garcinia* species. and their compounds. Using a series of state-of-the-art technologies, he has established anti-tumor bio-screening platforms at molecular, cellular and animal levels, clarified the bioactive compounds, pharmacodynamics and mechanisms of a series of TCM products, leading to publication of 84 SCI-



cited papers on *Garcinia* species, over 20 American and Chinese patents, while laying a solid foundation for development of new drugs — For a flavour of Dr Xu's speech, please visit: https://mp.weixin.gg.com/s/entwKHRCiDO8d p4xbHB3g (中文).



Dr. Zhixiu Lin (Chinese University of Hong Kong) introduced effects of Chinese herbs in Alzheimer's disease, particularly focused on a health product containing Herb Uncaria for treatment of cognitive disorders. Dr. Zhihong Jiang (Macau University of Science and Technology) systematically separated lignanamides from Semen Cannabis and investigated the bioactivities of the corresponding isomers, leading to discovery of novel lignanamides that effectively inhibit neuronal cytotoxicity caused by endoplasmic reticulum stress. Dr. Shilin Chen (Chinese Academy of Chinese Medical Sciences) shared his perspective on herbal genome and gene mapping, analyzed the transcriptomes of Chinese medicine and the biosynthetic pathways of bioactive components. The talks were followed by lively panel discussions on new drug R&D.



In the morning session next day, Dr. Jun Xu (Sun Yat-sen University) talked on molecular elementary recombination of natural products and new drug discovery. He explored the application of multiple molecular drug design techniques for the discovering bioactive components from natural products and identifying dominant chemical elements. Targeted chemical recombination of these dominant chemical elements was then performed to acquire lead compounds with high druggability. After that, Dr. Wen Liu (Chinese Academy of Sciences) talked on biosynthesis and molecular innovation of thiopeptide antibiotics and Dr. Xiaoguang Lei (Peking University) talked about natural product synthesis and its contributions to biomedicine and innovative drug research. They co-elaborated on the total synthesis and structural optimization of natural products.





In the afternoon, Dr. Yongxun Zhang (China Medical University, Taiwan) focused on the status quo and future of Chinese traditional medicine development in Taiwan and described the current regulations and quality management of TCM products in Taiwan. This was followed by an excellent talk by Dr. Ge Zhang (Hong Kong Baptist University), whose study shows not only novel mechanisms of leflunomide but also contributes to precision medicine-based drug development. Furthermore, Dr. Jianhui Rong (University of Hong Kong) reported that tripterine could reduce fat storage in obese mice and the development of novel GRP78 inhibitors could become a novel strategy for the treatment of obesity. Finally, Drs Boyan Chen and Zhongjuan Xue (National Ilan University) presented their innovative ideas and unique insights, from an outstanding angle of bioenergy, on

the drug properties of Chinese herbal medicine.

#### A WeChat report on this meeting can be found here:

https://mp.weixin.qq.com/s/CwDGqVYH0xArg1zafyWPNg (中文)

### **European Reports**

1. New booklet on EU research & innovation funding. The European Commission has published a new booklet showing a few examples where EU support for research and innovation is making a real difference in the lives of citizens and society as a whole. It is aimed at all age groups so everyone can understand the good work EU funding can do.

http://ec.europa.eu/programmes/horizon2020/en/news/new-booklet-shows-how-eu-research-and-innovation-funding-impacts-your-daily-life?utm

2. Innovative Medicines Initiative 2018 Call for Proposals: The European Commission Directorate-General for Research and Innovation has just launched the Innovative Medicines Initiative (IMI) 2018 Call. The IMI joint undertaking is a public-private partnership (PPP) between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA). As part of the H2020 Societal Challenges for Health and Wellbeing, this 2-stage call has an overall estimated budget of €167.2 million. The deadlines for submission of proposals are 14 June and 11 December 2018. Furher information on the different topics and the call can be found at the participant Portal, H2020-JTI-IMI-2018.

 $\frac{http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/calls/h2020-jti-imi2-2018-14-two-stage.html\#c,topics$ 

### Reports on China and Chinese-European Cooperation

1. Editorial. Health-care system transition in China. Lancet 2018;391:1332. On March 27, the

National Health Commission replaced China's National Health and Family Planning Commission (NHFPC) as the ministry responsible for health. The new commission is now headed by Ma Xiaowei, who was the former deputy head of the dismantled NHFPC. Chinese media have described Xiaowei as the person who understands China's health and hospital situation best, owing to his strong background in medicine. Since his graduation from the medical treatment department of China Medical University in 1982, Xiaowei has served many key roles in various health sectors such as the president of the First Affiliated Hospital of China Medical University and director of Liaoning Provincial Health Department. He is also the president of the Chinese Medical Association as





well as vice president of the Red Cross Society—China's biggest charity organisation.

Under Xiaowei's leadership, several new functions of the commission to improve health promotion in China are particularly worth mentioning. First, the new health commission will take over from the Ministry of Industry and Information Technology ("One of the biggest barriers to tobacco control efforts in China", according to a report published in *The Lancet Respiratory Medicine*) as the government body responsible for implementation of the WHO Framework Convention on Tobacco Control. Second, China's National Committee on Ageing, which leads national efforts to tackle the ageing society is now fully integrated into the National Health Commission to incorporate health care with elderly care.

The non-communicable disease (NCD) burden in China is huge, with tobacco use and ageing as the leading risk factors. Additionally, China's health delivery system is fragmented and hospital-centred. Restructuring the government bodies sends a strong signal of the health-care system transition from disease treatment to health promotion and disease prevention in China. Three forthcoming *Lancet* Commissions, led by Chinese specialists, on healthy cities, primary care, and NCDs in China will be timely contributions to this transition, examining ways of transforming the imminent health challenges that confront China into opportunities to achieve a healthy nation.

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30737-2/fulltext?%7B\$trackingTag%7D

2. China to restructure its FDA and demands pharmaceutical industry to take the responsibilities in pharmacovigilance. China is looking to restructure its Food and Drug Administration, according to a new report from the Regulatory Affairs Professionals Society. With the reorganization, the CFDA will cease being a standalone department and will become part of the country's National Market Supervision Association, according to the report. The CFDA group is slated to add an additional 100 new individuals focused on regulating devices, and will drop its oversight of food, according to the report. The CFDA will also pursue increased inspections of foreign entities and penalties for noncompliance. According to the report, the CFDA is also looking to create systems to enforce manufacturer compliance of reporting adverse events, and what will affect day-to-day work, and possible approval times, are previously announced efforts to increase transparency around regulatory decision making. The CFDA is also looking to be more receptive to feedback from US and multinational companies who want to establish a formal channel for such feedback, and work with companies to improve approval timelines.

https://www.massdevice.com/report-china-to-restructure-its-fda/https://mp.weixin.gg.com/s/X65hOw0p7o2cz9rjaD5ufA (中文)

3. Cyranoski D. **Beijing launches pioneering brain-science centre**. *Nature* 2018;**556**:157-158. The Chinese Institute for Brain Research was officially established in Beijing on 22 March, with an

agreement signed representatives of the Beijing municipality and seven research organizations based in the capital. The agreement named two neuroscientists Peking University's Rao Yi and Luo Minmin of the National Institute Biological Sciences Beijing — as co-directors.



The new Beijing facility will be one of the first concrete developments in the national China brain-research project, which has been under discussion for five years but has yet to be formally announced... <a href="https://www.nature.com/articles/d41586-018-04122-3?WT.ec\_id">https://www.nature.com/articles/d41586-018-04122-3?WT.ec\_id</a>



4. Tackling drug resistance: UK-China funding competition opens. A competition has opened that will make up to £10 million available to UK academic and industrial organisations to work in a consortium with Chinese partners. The Chinese Ministry of Science and Technology (MoST) will invest up to 60 million RMB to fund the Chinese partners. The aim is to support novel projects that neither country would be able to conduct within the same timeframe without the other's expertise. These should develop new products or services against antimicrobial resistance (AMR). The closing date for registration is 15 May 2018 for Chinese applicants and 30 May 2018 for UK applicants. For more guidance on how to apply and assessment criteria please read the competition guidance:

For UK applicants: <a href="https://apply-for-innovation-funding.service.gov.uk/competition/98/overview">https://apply-for-innovation-funding.service.gov.uk/competition/98/overview</a>
For Chinese applicants:

http://www.most.gov.cn/mostinfo/xinxifenlei/fgzc/gfxwj/gfxwj2018/201803/t20180326\_138789.htm For further information please get in touch with the contacts listed in the above links.

5. A recent medicinal liquor scandal in China reported by *Nature*: Entitled "Chinese physician released after 3 months in jail for criticizing a traditional medicine" the Nature news report by David Cyranoski concluded: "Lawyers and physicians fear the case could silence scientific debate on traditional remedies."

https://www.nature.com/articles/d41586-018-04886-8

http://3g.dxy.cn/bbs/topic/38745738?from=groupmessage&isappinstalled=0 (中文)

## TCM, Acupuncture and Other Traditional Medicine

1. Zhao Z, Guo P, Brand E. A concise classification of bencao (materia medica). Chin Med. 2018;13:18. Books that record the sources and applications of medicinal materials are commonly known as bencao (materia medica) in China. Bencao (materia medica) literature review is the very first step in the standard authentication procedure of Chinese medicinals. As an important part of China's cultural heritage, these various bencao (materia medica) texts represent centuries of accumulated wisdom in combating disease and preserving health. In this short review, bencao (materia medica) classics of China are broadly divided into three major categories in our routine practice: mainstream bencao (materia medica), thematic bencao (materia medica) and regional bencao (materia medica). The overall significance and current situation of exploration of bencao

(materia medica) literature are summarized as well. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC589">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC589</a> 4148/

2. A collection of different "nicknames" of Chinese medicines

https://mp.weixin.qq.com/s/fBG76SnAwihMsl3fVA pAA (中文)

## 3. How to name plants and Chinese medicines correctly?

https://mp.weixin.qq.com/s/0nsy3Lq\_RKQFYBAan5 p4HQ (中文)

https://www.sciencedirect.com/science/article/pii/S0 378874112000517?via%3Dihub

https://www.sciencedirect.com/science/article/pii/S0 378874113009021?via%3Dihub

4. Huang T et al. Uncovering the Mechanisms of Chinese Herbal Medicine



(MaZiRenWan) for Functional Constipation by Focused Network Pharmacology Approach. Front Pharmacol.2018;9:270. MaZiRenWan (MZRW, also known as Hemp Seed Pill) is a Chinese Herbal Medicine which has been demonstrated to safely and effectively



alleviate functional constipation (FC) in a randomized, placebo-controlled clinical study with 120 subjects. However, the underlying pharmacological actions of MZRW for FC, are still largely unknown. We systematically analyzed the bioactive compounds of MZRW and mechanism-of-action biological targets through a novel approach called "focused network pharmacology." Among the 97 compounds identified by UPLC-QTOF-MS/MS in MZRW extract, 34 were found in rat plasma, while 10 were found in rat feces. Hierarchical clustering analysis suggest that these compounds can be classified into component groups, in which compounds are highly similar to each other and most of them are from the same herb. Emodin, amygdalin, albiflorin, honokiol, and naringin were selected as representative compounds of corresponding component groups. All of them were shown to induce spontaneous contractions of rat colonic smooth muscle in vitro. Network analysis revealed that biological targets in acetylcholine-, estrogen-, prostaglandin-, cannabinoid-, and purine signaling pathways are able to explain the prokinetic effects of representative compounds and corresponding component groups. In conclusion, MZRW active components enhance colonic motility, possibly by acting on multiple targets and pathways.

https://www.frontiersin.org/articles/10.3389/fphar.2018.00270/full

5. Yang L, et al. Holistic TCM quality control based on standardised decoctions. Chinese Journal of Experimental Traditional Medical Formulae 2018;24(8):1-6. In recent years, great progress has been made in the quality control of traditional Chinese medicine (TCM), a series of research strategies and methods have been put forward successively by scholars at home and abroad. With the extensive application of fingerprint, multi-measurement with a single standard, multi-component thin-layer chromatography in the 2015 edition of Chinese Pharmacopoeia, the framework of the whole quality control of TCM is more and more clear. In the meantime, some scholars put forward the concept of standard decoction of prepared slices of Chinese crude drugs, and they described the connotation and denotation of standard decoction initially, and summed up its preparation technology

and quality control method. This paper defined the concept of standard decoction and discussed its properties and preparation methods; and illustrated its function and significance in product development, quality control, and postmarketing drug evaluation single or classical formulas. The whole quality control mode of TCM



based on standard decoction were investigated based on case analysis. The paper provides a method and reference for the whole quality control of TCM.

http://mp.weixin.qq.com/s/qBPIsBbscFZMY4 ehF58uw (中文)

http://www.syfjxzz.com/ch/reader/view abstract.aspx?file no=20180801&flag=1 (中文)

## **Omics in Progress**

1. Hutter C, Zenklusen JC. The Cancer Genome Atlas: Creating Lasting Value beyond Its Data. *Cell* 2018;173: 283-5. The Cancer Genome Atlas (TCGA) team now presents the Pan-Cancer Atlas, investigating different aspects of cancer biology by analyzing the data generated during the 10+ years of the TCGA project.

https://www.cell.com/cell/abstract/S0092-8674(18)30374-X?code=cell-site https://www.cell.com/pb-assets/consortium/pancanceratlas/pancani3/index.html?code=cell-site

2. Hoadley KA et al. Cell-of-Origin Patterns Dominate the Molecular Classification of 10,000 Tumors from 33 Types of Cancer. *Cell* 2018;173: 291-304. Comprehensive, integrated Archives (2008-2018): www.gp-tcm.org/news-list/



molecular analysis identifies molecular relationships across a large diverse set of human cancers, suggesting future directions for exploring clinical actionability in cancer treatment. https://www.ncbi.nlm.nih.gov/pubmed/29625048

3. Ding L et al. Perspective on Oncogenic Processes at the End of the Beginning of Cancer Genomics. *Cell* 2018;173:305-320. A synthesized view on oncogenic processes based on PanCancer Atlas analyses highlights the complex impact of genome alterations on the signaling and multi-omic profiles of human cancers as well as their influence on tumor microenvironment. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29625049">https://www.ncbi.nlm.nih.gov/pubmed/29625049</a>

4. Sanchez-Vega F et al. **Oncogenic Signaling Pathways in The Cancer Genome Atlas\_***Cell* 2018;173:321-37. An integrated analysis of genetic alterations in 10 signaling pathways in >9,000 tumors profiled by TCGA highlights significant representation of individual and co-occurring actionable alterations in these pathways, suggesting opportunities for targeted and combination therapies. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29625050">https://www.ncbi.nlm.nih.gov/pubmed/29625050</a>

5. Chen H et al. A Pan-Cancer Analysis of Enhancer Expression in Nearly 9000 Patient Samples. *Cell.* 2018;173:386-399. Causal enhancer-target-gene relationships are inferred from a systematic analysis of 33 cancer types...

https://www.cell.com/cell/fulltext/S0092-8674(18)30307-6

6. Liu J et al. An Integrated TCGA Pan-Cancer Clinical Data Resource to Drive High-Quality Survival Outcome Analytics. *Cell.* 2018;173(2):400-416.e11. Analysis of clinicopathologic annotations for over 11,000 cancer patients in the TCGA program leads to the generation of TCGA Clinical Data Resource, which provides recommendations of clinical outcome endpoint usage for 33 cancer types. https://www.sciencedirect.com/science/article/pii/S0092867418302290?via%3Dihub

7. Gilbet JA, et al. Current understanding of the human microbiome. Nature Medicine volume 24, pages 392–400 (2018) Our understanding of the link between the human microbiome and disease, including obesity, inflammatory bowel disease, arthritis and autism, is rapidly expanding. Improvements in the throughput and accuracy of DNA sequencing of the genomes of microbial communities that are associated with human samples, complemented by analysis of transcriptomes, proteomes, metabolomes and immunomes and by mechanistic experiments in model systems, have vastly improved our ability to understand the structure and function of the microbiome in both diseased and healthy states. However, many challenges remain. In this review, we focus on studies in humans to describe these challenges and propose strategies that leverage existing knowledge to move rapidly from correlation to causation and ultimately to translation into therapies. https://www.nature.com/articles/nm.4517

8. Editorial. **CRISPR off-targets: a reassessment.** *Nature Methods* 2018; 15: 229-230. There was insufficient data to support the claim of unexpected off-target effects due to CRISPR in a paper published in *Nature Methods*, which has now been retracted. More work is needed to determine whether such events occur *in vivo*.

https://www.nature.com/articles/nmeth.4664

9. Off-targets in epigenome editing. A *Nature Methods* research highlight on Galonska, C. et al. Nat. Commun. 9, 597 (2018). Everybody agrees that DNA methylation has important regulatory roles, but many blanks regarding the details of this regulation remain to be filled in. The advent of CRISPR brought the promise of targeted modification of cytosines by fusing a methyltransferase to dCas9 and directing it to

a locus of interest via guide RNAs (gRNAs). Galonska et al. examined this promise in a mouse embryonic stem cell line devoid of any DNA methylation and observed unexpectedly high background methylation, independent of gRNAs. The researchers replicated this finding in two somatic human cell lines; although they saw on-target activity at loci with low endogenous methylation, they





also observed high genome-wide off-target activity. dCas9 fused to epigenetic effector proteins is a valuable tool, but more work is needed to ensure specificity.

http://www.nature.com/articles/nmeth.4650

http://www.nature.com/articles/s41467-017-02708-5

10. **Genome editing with ease.** A *Nature Methods* research highlight on Yoon, Y. et al. Nat. Commun. 9, 412 (2018). Genetic manipulations in mice have become easier with the CRISPR-Cas9 system; however, the delivery of the necessary components into embryos, as well as the embryo handling, remains challenging. Yoon et al. now show that nucleic acid delivery methods such as microinjection and electroporation can be replaced by transduction of pre-implantation embryos with recombinant adeno-associated viruses (rAAVs). Many AAV serotypes can successfully transduce embryos, but serotype 6 proved to be the most efficient. When targeting the tyrosinase gene (involved in eye pigmentation and coat color), the researchers obtained chimeras with up to 100% efficiency, with most of the animals in the experiment developing into albinos. The researchers further simplified the genome-editing process in mice by introducing the rAAVs into oviducts of pregnant females, where embryos could be transduced in situ. Thus, this approach makes genome editing possible within pregnant animals, which avoids the need for embryo handling outside of the female reproductive tract.

https://www.nature.com/articles/nmeth.4652 https://www.nature.com/articles/s41467-017-02706-7



#### **Other Recommended Readings**

1. Lazarev VS & Nazarovets SA. Don't dismiss citations to journals not published in English. Nature 2018;556:174. "Papers should be evaluated on academic criteria, not on superficial grounds of communication..."

https://www.nature.com/articles/d41586-018-04169-2?WT.ec id

2. Goldstein P et al. Brain-to-brain coupling during handholding is associated with pain reduction. PNAS 2018;115:E2528-E2537. The mechanisms that underlie social touch analgesia are largely unknown. Here, we apply a hyperscanning approach with real-life interaction of dyads to examine the association between brain-to-brain coupling and pain relief. Our findings indicate that hand-holding during pain increases the brain-to-brain coupling network that correlates with the magnitude of the analgesia and the observer's empathic accuracy. These findings make a unique contribution to our understanding of physiological mechanisms of touch-related analgesia.

http://www.pnas.org/content/115/11/E2528

3. Spector JM, Harrison RS and Fisherman MC. Fundamental science behind today's important medicines. Science Translational Medicine. 2018:10: eaaq1787. Today's most



transformative medicines exist because of fundamental discoveries that were made without regard to practical outcome and with their relevance to therapeutics only appearing decades later.

http://stm.sciencemag.org/content/10/438/eaaq1787?utm

4. Zambetti LP. Convert your weaknesses into assets. *Nature* 2018;556:265. "I'm afraid I won't renew your contract. I am giving you as much advance notice as I can so that you can find something else." Hearing these words from my supervisor's mouth left me reeling. As a native of Italy, and as a postdoctoral researcher in a nation outside the European Union, I had a visa that depended on my having a work contract. Without a job, I would have to leave the country shortly after the end of my contract. Furthermore, the words felt like a death knell for my research career. Surely no one would ever hire me for a



second postdoc when this one had failed to yield any research papers. What would I do in a few months' time when my postdoc ended? I was literally dizzy — I needed a strategy to find another position, and fast. That was a tough week, but I am now grateful for that shocking announcement: it gave me clarity and enough time to make a plan...

https://www.nature.com/magazine-assets/d41586-018-04162-9/d41586-018-04162-9.pdf

5. Darrow JJ, Avorn J, Kesselheim AS. The FDA Breakthrough-Drug Designation - Four Years of Experience. N Engl J Med. 2018;378(15):1444-1453. In 2012, Congress created the "breakthrough therapy" designation to expedite Food and Drug Administration (FDA) testing and approval of medications that were intended to treat serious or life-threatening conditions and that preliminary evidence suggested may provide a substantial improvement over existing treatments with regard to one or more clinically significant end points. The creation of this designation was motivated by the concept that advances in precision medicine would enable the development of therapies with large treatment effects that were seen early, such that random assignment to receive placebo might be unethical and phase 2 trials could provide sufficient evidence for approval. One of the sponsors of the law. Senator Michael Bennet (R-CO), explained that the pathway was intended to speed the approval of drugs that showed "exceptional results for patients." Manufacturers reacted vigorously. According to Janet Woodcock, the head of the FDA Center for Drug Evaluation and Research, the agency was "inundated" with hundreds of requests, despite expectations that only about 2 drugs per year would receive the designation. From 2014 to 2016, a total of 26 (24%) of the 108 new molecular agents and original biologic agents that were approved by the FDA received the breakthrough designation...

http://www.nejm.org/doi/10.1056/NEJMhpr1713338

#### **Meetings & Events**

- 1. The 6<sup>th</sup> Annual Meeting of the GP-TCM Research Association will be held at Royal Botanic Gardens, Kew, UK on 4-6 July 2018. Please refer to Special Features in page 2.
- 2. **TROPHARM seminar Pharmaceutical opportunities in DR Congo / BE: an interdisciplinary approach**, Faculty of Pharmaceutical Sciences, Campus Heymans, Ottergemsesteenweg 460, 9000 Ghent, THURSDAY 17 MAY 2018 | 13:30-16:30, followed by Reception and network event ,16:30.
- Experience and management in the domain of sickle cell disease or sickle cell anemia
- Traditional foods as putative nutraceuticals in Konzo
- Use of traditional drugs in obstetrics
- Quality and safety of food consumed in DR Congo



Introductory talks by deans Prof. José Lami and Prof. Jan Van Bocxlaer. Notes by professors of University of Kinshasa, DRC: Prof. Christophe Masiala, Prof. Dr. Roger Mbungu, Prof. Pius Mpiana and Prof. Nadege Ngombe.

MORE INFORMATION: ciska.deruyver@ugent.be

REGISTER BEFORE 15th MAY 2018 at

https://webappsx.ugent.be/eventManager/events/TROPHARMseminar

- 3. International celebration of the 500 anniversary of Li Shizhen's birth to be held in Li's homehown Jichun County, Hubei Province, China, on 26th May, 2018. <a href="http://mp.weixin.qq.com/s?">http://mp.weixin.qq.com/s?</a> biz=MzAxMjMyMTEwNA==&mid=2660692447&idx=1&sn=3895e03e994 d2f1c98befd9f4beb8eca&chksm (中文)
- 4. The 17th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Kuching-Sarawak, Malaysia on August 8 10, 2018. This year's meeting is going to be organized by the Malaysian Institute of Pharmaceuticals and Nutraceuticals, National Institutes of Biotechnology Malaysia. The meeting provides a platform for regulatory-industrial-academic exchanges and potential research collaborations, on various frontiers of Traditional Chinese Medicine among our worldwide CGCM members and guests. You are cordially invited to attend the meetings and submit abstracts. Preliminary programme and more details will soon be announced on our website. Should you have any enquiries, please feel free to contact the CGCM Central Office: Email: centraloffice@tcmedicine.org; Website: www.tcmedicine.org

Information for meeting program, abstract submission, registration and travel grant can be found here: <a href="http://www.cgcm2018.com">http://www.cgcm2018.com</a>

- Important dates:
  - May 31, 2018 Early Bird Registration
  - July 16, 2018 Registration Deadline
  - May 31, 2018 Abstract Submission Deadline
  - June 15, 2018 Travel grant application deadline
- 5. The 15th 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 (中文)

http://mp.weixin.qq.com/s/R5Ao3tYI7Q2UwzaP94ik Tw (中文)

6. Xuetao Cao, Helena Hui Wang, Limin Li, William Summerskill, Richard Horton. *The Lancet*—CAMS Health Summit 2018: a call for abstracts. *Lancet* 2018;391:188-9. Please submit your abstract as a Word document through The Lancet's online submission system no later than May 31, 2018, stating in your covering letter that the submission is in response to this call for abstracts from China. Please note, abstracts submitted later than May 31 will not be considered.

https://ees.elsevier.com/thelancet/default.asp?pg=login.asp

#### **Invitation from journals**

1. World Journal of Traditional Chinese Medicine: Sincere invitation for submissions. World Journal of Traditional Chinese Medicine





(ISSN 2311-8571, CN10-1395/R) is sponsored by WFCMS, and is the official journal of GP-TCM RA. WJTCM dedicates to report the research progress in clinical efficacy and action mechanism of Traditional Chinese Medicine, Chinese materia medica, acupuncture and moxibustion to doctors and biomedical researchers around the world, so as to provide new thoughts and methods for solving complex diseases and knotty diseases. To submit your manuscripts, or to read articles in the past issues, please visit: <a href="http://www.wjtcm.net">http://www.wjtcm.net</a>

2. Frontiers in Pharmacology special issue "Can Natural Products Reduce the Side Effects of Cancer Therapies?" invites your submission. Deadline: June 2018.

 $\underline{https://www.frontiersin.org/research-topics/7625/can-natural-products-reduce-the-side-effects-of-cancer-therapies}$ 

http://journal.frontiersin.org/researchtopic/7625 (中文)



### **Sounding Board**

1. A unique opportunity: an MSc in Plant and Fungal Taxonomy, Diversity and Conservation that the Royal Botanic Gardens, Kew offers, in partnership with Queen Mary University of London. Designed to help support the training of plant and fungal scientists, the course covers taxonomy, phylogenetics, systematics, conservation and biological data. It also includes a field trip and a six-month research project, supervised by one of Kew's scientists. This year, Royal Botanic Gardens, Kew are delighted to be able to offer the first of five annual scholarships funded through The PuraPharm Traditional Medicine (TM) Scholarship. This scholarship will cover all course fees, course expenses and all student travel and living expenses. Suitable applicants for this bursary must be able to speak Chinese and English, and have an interest in Traditional Chinese Medicine. The student will also be required to complete their six-month MSc research project on Chinese Medicine, and be willing to travel to China as part of this. If you would like any further information about the MSc, please don't hesitate to contact us at kewmsc@kew.org or visit www.kew.org/msc

2. Traditional medicine: A new look at nature's treasures Adventures in Genomics. Traditional medicine provides us with a huge untapped resource of potentially effective and safe drugs, that have been tested in humans for thousands of years. In this episode, Jacques and Irene traveled to Beijing, China, to interview Dr. Chang Liu, the Deputy Director of the Center for Bioinformatics at the Institute of Medicinal Plant Development (IMPLAD) Chinese Academy of Medical Sciences. Dr Chang is applying genomic technologies to study the herbs used in Chinese traditional medicine to ensure the efficacy and safety of such compounds.

https://www.youtube.com/watch?v=rUsd2-dxmyc&feature=youtu.be http://3g.dxy.cn/bbs/topic/38745738?from=groupmessage&isappinstalled=0

This column is reserved for comments, personal views, proposals for collaborations or any other features from our readers across the world. We look forward to hearing from you! Please get in touch with your editors: Dr Qihe Xu (qihe.xu@kcl.ac.uk), Prof. Pierre Duez (pierre.duez@umons.ac.be) and Prof. Yuan Shiun Chang (yschang0404@gmail.com).



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