

The October 2018 Newsletter of The GP-TCM Research Association



Corporate Member Special Feature

China Medical University, Taiwan



中國醫藥大學
China Medical University

Established in 1958, China Medical University (CMU) in Taichung, Taiwan, has since developed into one of the world's premiere medical research universities with 8 colleges total: The College of Medicine, the College of Chinese Medicine, the College of

Pharmacy, the College of Biopharmaceutical and Food Sciences, the College of Public Health, the College of Health Care, the College of Dentistry, and the College of Humanities and Technology. Its Joint Commission International (JCI)-accredited hospitals have a total of over 5,000 beds, and it offers the second largest healthcare system nationwide.

To achieve research excellence, China Medical University establishes Centers of Excellence for Tumor Medical Science, Traditional Chinese Medicine and Acupuncture, Brain Diseases, Aging, Integrative Stem Cell Research, New Drug Development and Cancer Immunology. In 2018, CMU received a five year "Higher Education Sprout Project" awarded by Ministry of Education of the Government. New Drug Development Center and Chinese Medicine Research Center received additional funding under the Featured Area Research Center Program. To further promote research momentum, China Medical University is investing 1 billion US dollars to build a new branch of Taichung Campus including the setup of the Proton and Carbon Ion Radiotherapy Center and aims to recruit 10 outstanding research teams by offering 100 million US dollars in the next 3 years. China Medical University welcomes outstanding scholars and students to join the CMU family.

As a leader in several research fields with a culture of collaboration and innovation, CMU has made important breakthroughs in cancer treatment such as lengthening the survival of glioblastoma patients, discovering ANK-199, a promising anticancer drug that treats head and neck cancer, and identifying the receptor protein IL17RB that is strongly associated with pancreatic cancer. For cultivating talent and advancing the boundaries of knowledge, outstanding international experts have been recruited from around the world to join the 500 full-time, dedicated CMU faculty members who are all passionate about making the world a better place.

Devoted to improving health through sciences, CMU's high ranking in many surveys and lists reflects its effort and determination for excellence: it was placed in the top 151~200 of universities in the 2017 Academic Ranking of World Universities (ARWU); it was in the top 150 in the field of Clinical Medicine and Pharmacy in the 2016 Academic Ranking of World Universities (ARWU); it was 46th in the Times Higher Education Asia University Rankings; it was in the top 401~500 universities in the World University Rankings; and it was in the top 101~150 in Pharmacy and Pharmacology and in the top 200 in Medicine in the 2018 QS World University Rankings by Subject.

International collaborative partnerships with prestigious institutions such as Stanford University, the M.D. Anderson Cancer Center, National University of Singapore and Seoul National University have been firmly established. Additionally, over 80 international healthcare companies and venture capitalists are assisting the university with its knowledge transfer mission. Thus far, over 60 new drugs have emerged from CMU's research laboratories, as well as 9 new spin-off companies.

As a provider of medical services to the community, an educator of future health care professionals, and a contributor to the world's knowledge in health sciences, CMU will continue to strive for excellence in clinical care, education, and research.

For more info, please visit: <http://english.cmu.edu.tw>



The 2nd Joint Symposium of CMU with National University of Singapore was held in Taichung on May 21-22, 2018.

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Special Feature

Now 1. Jocelyn Kaiser, Jennifer Couzin-Frankel.

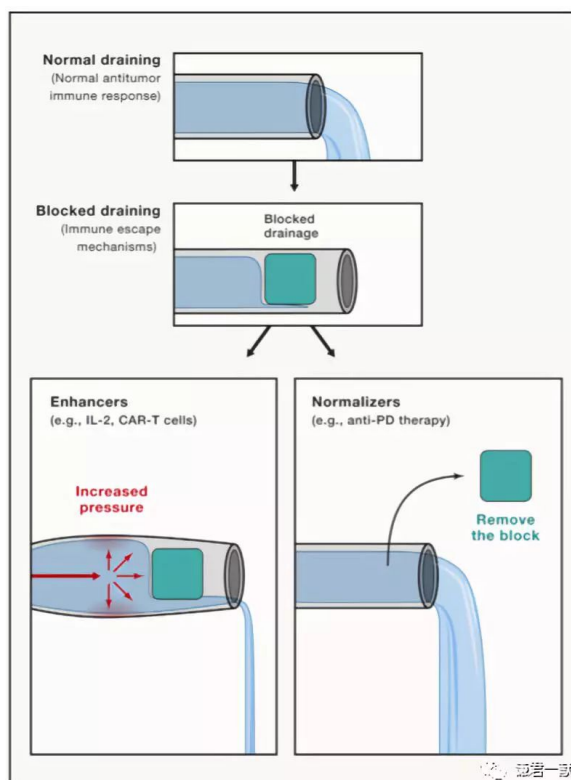
Cancer immunotherapy sweeps Nobel for medicine

Science 2018;362:13. Fittingly, James Allison heard the news at a conference of the very field his work helped launch. At a New York City hotel where he was staying for a meeting on cancer immunotherapy, Allison, an immunologist at University of Texas MD Anderson Cancer Center in Houston, received a 5:30 a.m. phone call on 1 October from his son, then answered a knock at his door to find colleagues carrying champagne. That day, he and Tasuku Honjo of Kyoto University in Japan were awarded the Nobel Prize in Physiology or Medicine for work underpinning a new class of drugs called immune checkpoint inhibitors, which have revolutionized the treatment of certain types of cancer... <http://science.sciencemag.org/content/362/6410/13?utm>



Now 2. Miguel F. Sanmamed and Lieping Chen. **A Paradigm Shift in Cancer Immunotherapy: From Enhancement to Normalization.** *Cell* 2018;175:313-326.

Harnessing an antitumor immune response has been a fundamental strategy in cancer immunotherapy. For over a century, efforts have primarily focused on amplifying immune activation mechanisms that are employed by humans to eliminate invaders such as viruses and bacteria. This “immune enhancement” strategy often results in rare objective responses and frequent immune-related adverse events (irAEs). However, in the last decade, cancer immunotherapies targeting the B7-H1/PD-1 pathway (anti-PD therapy), have achieved higher objective response rates in patients with much fewer irAEs. This more beneficial tumor response-to-toxicity profile stems from distinct mechanisms of action that restore tumor-induced immune deficiency selectively in the tumor microenvironment, here termed “immune normalization,” which has led to its FDA approval in more than 10 cancer indications and facilitated its combination with different therapies. In this article, we wish to highlight the principles of immune normalization and learn from it, with the ultimate goal to guide better designs for future cancer immunotherapies.



[https://www.cell.com/cell/pdf/S0092-8674\(18\)31247-9.pdf](https://www.cell.com/cell/pdf/S0092-8674(18)31247-9.pdf)

<https://mp.weixin.qq.com/s/mvxRD7XNv0m5WgjRc1MTXQ> (中文)

Now 3. Service RF. **Protein evolution (and phage displays) earn chemistry Nobel.** *Science* 2018;362:142. Breeders of everything from horses to tomatoes long ago learned to speed evolution by selecting and propagating offspring with desired traits. The Nobel Prize in Chemistry went on 3 October to researchers who developed tools to do the same with biological molecules. The findings have led to many commercial products, notably treatments for autoimmune diseases and cancer. Chemistry Nobel 2018 has been awarded to Frances Arnold, George Smith and Gregory Winter “for the directed evolution of enzymes” and “for the phage display of peptides and antibodies”. Thanks to the breakthroughs honored last week, evolution has become as powerful a force in technology as it is in nature. <http://science.sciencemag.org/content/362/6411/142.full>

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European Reports:

1. EDITORIAL. Brexit is already damaging European science. *Nature* 2018;561:433-4. With six months to go, uncertainty posed by the decision to leave the European Union is taking its toll.

https://www.nature.com/articles/d41586-018-06826-y?WT.ec_id=NATURE-20180927&utm

2. Medicines and Healthcare Products Regulatory Agency Consultation on EU Exit No-Deal Legislation: The Medicines and Healthcare products Regulatory Agency (MHRA), Department of Health and Social Care, seek your views on how the MHRA legislation and regulatory processes would need to be modified in the unlikely event that the UK does not secure a deal with the EU after the UK's exit. The consultation covers no-deal proposals on medicines, clinical trials and medical devices and closes at 23:45 on 1 November 2018.

<https://consultations.dh.gov.uk/mhra/mhra-no-deal-contingency-legislation-for-the-regul/>

3. The Wellcome Trust Publishes "Brexit and Beyond: Impact Case Studies of EU Funding". The Wellcome Trust have published a series of case studies, which present the positive impact that the European Union Framework Programmes have had on different participants.

The case studies look at the following themes, with the contributor in parentheses:

- Excellence (University of Cambridge)
- Collaboration (GlaxoSmithKline)
- Reputation (Switzerland)
- Long-term Innovation (Aerospace Technology Institute)
- Competition (Norway)

<https://wellcome.ac.uk/sites/default/files/brexit-and-beyond-impact-case-studies-201810.pdf>

Reports on China and Chinese-European Cooperation

1. Nature Index 2018: Challenger states. *Nature* 2018;561:S20-1. Strength in different sectors, subjects and regions contributes to a country's success. Six countries have experienced the highest absolute and percentage increases in their contribution to the *Nature Index* since 2015. While China is making waves among the traditional scientific powers, the other five nations are disrupting lower-tiered research strongholds.

<https://www.nature.com/articles/d41586-018-06623-7>



2. Beddoes ZM. China has designs on Europe. Here is how Europe should respond. *The Economist* 2018; 4th October 2018. As Chinese investment pours into the European Union, the Europeans are beginning to worry...

<https://www.economist.com/leaders/2018/10/04/china-has-designs-on-europe-here-is-how-europe-should-respond?cid1=cust/ednew/n/bl/n/2018/10/4n/owned/n/n/nwl/n/n/UK/155544/n>

3. Taiwan, Hong Kong and Macao residents no longer required to obtain work permit for employment in Mainland China. The State Council published on 28 July 2018 the Circular GuoFa [2018] No. 28 (the "Circular"), abolishing 11 administrative licenses in China, among which the work permit for Taiwan, Hong Kong and Macao residents ("THKM"). Under the Circular, THKM residents will be treated the same as local mainland Chinese residents and will thus no longer need work permits to work in Mainland China.

4. In 2017, China investment into R&D grew to 1,760 billion RMB Yuan, accounting for 2.13% of annual GDP. It was a 12.3% increase compared with the figure of 2016. People's Daily reports.

https://app.peopleapp.com/Api/600/DetailApi/shareArticle?type=0&article_id=2591498

5. Normile D. China narrows U.S. lead in R&D spending. *Science* 2018;362:276. Already the world's second biggest R&D spender behind the United States, China is steadily narrowing the gap, according to a government report. It shows that the total R&D outlay by government and industry rose 12.3% last year to a record 1.76 trillion yuan (\$254 billion). Whereas China spent about 34% as much as the United States in 2012, the proportion is now closer to 45%, figures from the Organisation for

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Economic Co-operation and Development (OECD) and U.S. agencies show. In purchasing power, China's 2016 spending was equivalent to 88% of U.S. spending, according to OECD.

<http://science.sciencemag.org/content/362/6412/276?utm>

6. China has included 17 more cancer drugs in its national basic medical insurance program, the latest progress in government efforts to make drugs more affordable for cancer patients. <https://mp.weixin.qq.com/s/9nXEvgj0AuzeAABjC5zlw>

7. Mullard A. Chi-Med scores key approval for 'discovered in China' cancer drug. *Nature Reviews Drug Discovery* 2018;17:697. Chinese drug regulators approved the VEGFR inhibitor fruquintinib of Hutchison China MediTech Limited ("Chi-Med") (AIM/Nasdaq: HCM) for the treatment of metastatic colorectal cancer, providing the first unconditional approval for a homegrown new drug in China that has been tested in randomized clinical trials. Although industry has long been ramping up its investments in China, many of the early ventures were focused on outsourcing chemistry and manufacturing services. Some firms have been building end-to-end drug discovery capabilities in China as well (*Nat. Rev. Drug Discov.* 16, 443–446; 2017). Chi-Med, one such company, has now scored a landmark approval that they hope will prove their ability to discover and develop follow-on drug contenders with best-in-class potential.

<https://www.nature.com/articles/nrd.2018.176>

8. Cyranoski D. China awaits controversial blacklist of 'poor quality' journals. *Nature* 2018 16 October 2018; doi: 10.1038/d41586-018-07025-5. But some researchers say the policy won't succeed in improving research quality.

<https://mp.weixin.qq.com/s/8ciX5bbEb2Pc7HwPzu4OMg> (中文)

<https://www.nature.com/articles/d41586-018-07025-5>

9. Zhou Y, Liu Y. China's fight against soil pollution. *Science* 2018;362:298. Soil pollution caused by human activities in China threatens agricultural productivity, food safety, and human health. The Chinese government has taken a series of measures, including the Soil Contamination Prevention and Control Action Plan, to combat soil pollution. Recently, the country took another positive step by passing the Law on Soil Pollution Prevention and Control, legislation that was 12 years in the making.

<http://science.sciencemag.org/content/362/6412/298?utm>

10. Westlake University launched on 20 October 2018 in Hangzhou, Zhejiang, China.

<https://mp.weixin.qq.com/s/FwtodBTWVuzswBSjBtL4fw> (中文)

<https://mp.weixin.qq.com/s/FwtodBTWVuzswBSjBtL4fw> (中文)



TCM and other traditional medicine

1. Encyclopedia of Medicinal Plants, 2nd Edition (当代药用植物典中文版；第二版) edited by Professors Zhongzhen Zhao and Peigen Xiao published on 21st October 2018—A celebration commemorating the 500th anniversary of the Birth of LI Shizhen.

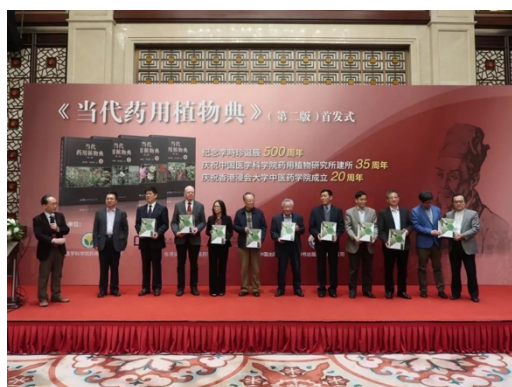
Co-organized by the Institute of Medicinal Plant Development (IMPLAD) of the Chinese Academy of Medical Sciences (CAMS), the School of Chinese Medicine (SCM) of the Hong Kong Baptist University (HKBU), and the World Publishing Corporation (WPC) of the China Publishing Group (CPG), a grand ceremony to celebrate the first publication of *Encyclopedia of Medicinal Plants* (2nd edition) and to commemorate the 500th anniversary of the birth of LI Shizhen was held in Beijing. This event also served as an activity to commemorate the 35th anniversary of IMPLAD of CAMS and the 20th anniversary of SCM of HKBU.



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The ceremony was hosted by XU Hongxi, the dean of the School of Pharmacy of the Shanghai University of Traditional Chinese Medicine (TCM). SUN Xiaobo expressed his gratitude in his welcoming speech to all the friends from Chinese medicine professionals and the press at home and abroad. LYU Aiping delivered a speech to congratulate the successful publication of the 2nd edition of *Encyclopedia of Medicinal Plants*. The editors-in-chief, XIAO Peigen and Prof. ZHAO Zhongzhen (the associate dean of SCM of HKBU) introduced the background information and recalled stories related to the compiling procedure of *Encyclopedia of Medicinal Plants*. “The book is a most valuable reminder of the richness of herbal medicine traditions in East and West”, said Paul U. Unschuld. LI Yan thanked the kind support in his summing up speech to the publishing enterprise from the public and expected continuous contributions from WPC of CPG to the development of TCM.



As a classic monograph with the features of vivid illustration, up-to-date and professional information, *Encyclopedia of Medicinal Plants* was based on first-hand data collected years from field investigation on the distribution and production areas of those original medicinal plants and raw medicinal materials in Asian and European countries. Its traditional Chinese version was first published in 2006. Later on, its simplified Chinese, English, and Korean versions were published to meet the market demand internationally. Awarded a highest national prize for outstanding publication and rich in original and prospective contents, *Encyclopedia of Medicinal Plants* has been commended by numerous experts at home and abroad. This is an “extensive collection

of past and present, distinguished assembly of Chinese and western”, said Chen Keji, an academican of the Chinese Academy of Sciences.

Encyclopedia of Medicinal Plants is co-edited by ZHAO Zhongzhen and XIAO Peigen. As a world renowned pharmacognosist, ZHAO Zhongzhen has been conducting field investigation in more than 40 countries. He has accumulated a large amount of digital data that show the macroscopic and microscopic characteristics of medicinal plants and thus laid a solid foundation for this publication. As one of the founder and academic leaders of Chinese medicinal research, XIAO Peigen was the first mainland China scientist to be in charge of the compilation of monographs on medicinal plants of the world at the World Health Organization headquarters. Under the leadership of ZHAO Zhongzhen and XIAO Peigen, the editorial team fulfilled the task to make this unique and innovative monograph on medicinal plants a reality. Cooperating again between WPC and ZHAO Zhongzhen and XIAO Peigen’s editorial team, the 10-year’s efforts to keep abreast of the latest development in medicinal plant research will make this completely new edition with attempts of digital technology reveal the academic and commercial values of medicinal plants of the world.

This year, a series of international activities have been held to commemorate the 500th anniversary of the birth of LI Shizhen, a great scholar of TCM and the author of the *Compendium of Materia Medica*. As a gift dedicated to commemorate the 500th anniversary of the birth of LI Shizhen, may this new edition make greater contributions to the internationalization of the time-honored TCM!

<https://mp.weixin.qq.com/s/daE6mFHDm-H34mISf1DJrw> (中文)

<https://view.inews.qq.com/a/CUL2018102100593000?openid> (中文)

<https://web.shobserver.com/wx/detail.do?id=111765&time=1540125139286&from=singlemessage&isappinstalled=0> (中文)

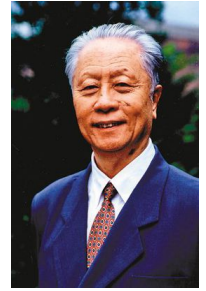
2. In commemoration of the 60th Anniversary of Chairman Mao’s instruction on TCM as a treasure house and on strengthening R&D of TCM. <https://mp.weixin.qq.com/s/Cp-L4uQp148rbkkNawTflg> (中文)

中國醫學
一個偉大的寶庫
應努力發掘，加
以提高
毛澤東

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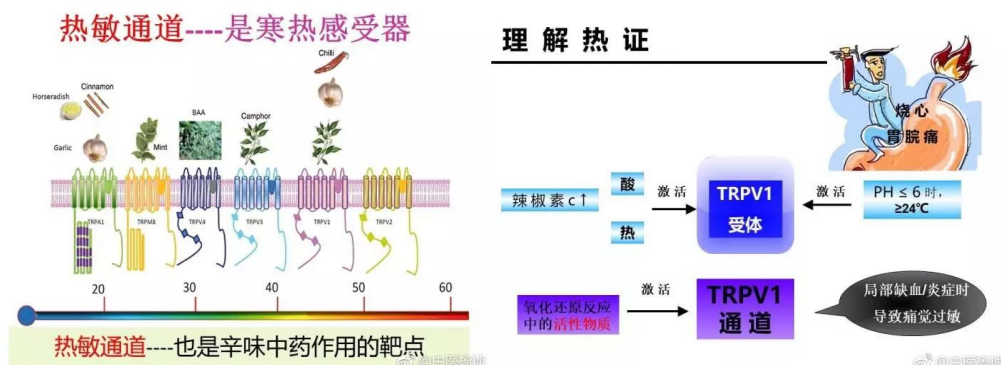
3. He P, Li LD, Li Y. On Ten Grand Issues of TCM. *Journal of Traditional Chinese Medicine* 2017;(21): 1808-1810. This paper is recommended in honour of Professor LI Lianda, a pioneering TCM pharmacologist and an Academician of China's Academy of Engineering, who passed away on 18th October 2018.
<https://mp.weixin.qq.com/s/XlylsgJaAd2fh3QY5ZOXMq>



4. Huang W, Long C, Lam E. Roles of Plant-Associated Microbiota in Traditional Herbal Medicine. *Trends Plant Sci.* 2018;23:559-62. The microbiome of medicinal plants may directly impact the metabolome of the host, and thus could influence the efficacy of herbal medicine. We advocate a herb for traditional Chinese medicine (TCM), *Salvia miltiorrhiza*, as a prime model system to study how microbes may interact with medicinal plants to modify phytochemical production.
<https://www.sciencedirect.com/science/article/pii/S1360138518300979?via%3Dihub>

5. Schwarze J-E et al. Does acupuncture the day of embryo transfer affect the clinical pregnancy rate? Systematic review and meta-analysis. *JBRA Assisted Reproduction* 2018; doi: 10.5935/1518-0557.20180057. The effects of acupuncture on IVF outcomes is still unknown. We carried out a systematic review and meta-analysis of RCT to determine whether acupuncture performed at the time of ET improves outcomes. We searched Medline and Embase from January 1990 to June 2017, for the following terms: (acupuncture; acupuncture therapy) and (reproductive techniques, assisted; in vitro fertilization; embryo transfer). We selected RCT that compared acupuncture with sham acupuncture or no treatment. We included only trials in which acupuncture involved the insertion of needles into traditional meridian points. We evaluated the methodological quality of the trials using the Cochrane risk of bias tool. The measure of treatment effect was the pooled odds ratio of achieving a clinical pregnancy, ongoing pregnancy, or live birth for women in the acupuncture group compared with women in the control group. For pooled data, summary test statistics were calculated using the Mantel-Haenszel method, using the Rev-Man software, version 5.1. We analyzed six studies, including 2,376. In all trials, there were no significant differences between the groups concerning the mean numbers of embryos transferred, the mean age of the women undergoing the procedure, diagnose and use of ICSI. Acupuncture performed the day of ET was associated with a reduced risk of clinical pregnancy (0.87, 95% confidence interval 0.77 to 0.98). The pooled rate difference was -0.06 (-0.12 to -0.01) for clinical pregnancy. None of the trials reported significant adverse effects of acupuncture. Conclusion: acupuncture performed on the day of ET has a significant effect on embryo implantation, however, a negative one. Therefore, clinicians should encourage their patients to avoid this technique the day of ET.
<https://www.ncbi.nlm.nih.gov/pubmed/30132627>

6. Z Yang. Thermosensitive TRP ion channels: Their roles in interpreting heat and cold TCM syndromes and hot, warm, cool and cold natures of TCM drugs, *Songmingshuyuan WeChat*. 13 October 2018.
<https://mp.weixin.qq.com/s/zJroHo3TiGSG3f5wDiHc9w> (中文)



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7. On The “Rising, Descending, Falling and Floating” properties of Chinese materia medica. Jin Ri Tou Tiao WeChat Platform. 22 October 2018.

https://www.toutiao.com/i6614799286586573326/?iid=39509493232&app=news_article (中文)

8. G Wu. Yang Qi is the best remedy but is too often insufficient to cause illness. Yidaoliufang WeChat Platform. 12 October 2018.

<https://mp.weixin.qq.com/s/VlvBdJdXv-i16t2jv7-N3Q> (中文)

9. Why does TCM emphasise boosting positive Qi? Yidaoliufang WeChat Platform. 16 October 2018.

https://mp.weixin.qq.com/s/wfG_e_QggSzJqKxxRnca0w (中文)



10. Cyranoski D. Why Chinese medicine is heading for clinics around the world. *Nature* 2018;561:448-50. For the first time, the World Health Organization will recognize traditional medicine in its influential global medical compendium.

https://www.nature.com/articles/d41586-018-06782-7?WT.ec_id

11. Jingcheng Dong. The evolution of the term “中医”, which is historically more than TCM. Fudan University Institute for Integrative Chinese Medicine WeChat Platform. 16th August 2018. “中医”, now widely accepted as a school of traditional medicine derived from China, in contrast to conventional or Western medicine, which is derived from the West, the term was historically used to refer to a second-class doctor and was considered by some a medicine that emphasised Yin-Yang harmony. In term of TCM, it has grown to include not only the traditional medicine originated from the Han ethnic group to all traditional medicines derived from all ethnic groups in China, and grown from pure TCM to modernised Chinese medicine and integrative Chinese medicine...

https://mp.weixin.qq.com/s/dS8UYM5GEYZp_gP14Mt7Lq (中文)

Omics in Progress

1. Adams DR, Eng CM. Frontiers in Medicine: Next-Generation Sequencing to Diagnose Suspected Genetic Disorders. *N Engl J Med* 2018;379:1353-1362. Clinical next-generation sequencing is being used frequently in medical practices in which genetic testing has traditionally taken place — for example, medical genetics and medical subspecialties such as neurogenetics. Emerging diagnostic applications include rapid-reporting approaches in intensive care settings (especially neonatal and pediatric) and use early in the course of complex disease. Large-scale projects in the United States, China, and elsewhere are exploring and developing the role of clinical next-generation sequencing in precision medicine. This suggests a future in which genomic data will influence medical decision making for a diverse and growing group of patients...

<https://www.nejm.org/doi/full/10.1056/NEJMra1711801>

2. Harris S. Ambitious Plans for Genomic Medicine in the UK. *Medscape UK* 3rd October 2018. The Health and Social Care Secretary has announced plans for a major expansion in genomic medicine. He wants to sequence five million genomes in the UK in the next 5 years. Matt Hancock made the announcement at the Conservative Party Conference. He said: "I'm proud to announce we are expanding our 100,000 Genomes Project so that one million whole genomes will now be sequenced by the NHS and the UK Biobank. I'm incredibly excited about the potential for this type of technology to improve the diagnosis and treatment for patients to help people live longer, healthier lives – a vital part of our long-term plan for the NHS. Today's commitments form part of our bold aspiration to sequence five million genomes in the UK, using ground-breaking technology to do this within an unprecedented 5-year period."...

<https://www.medscape.com/viewarticle/902874>

3. Liu S et al. Genomic Analyses from Non-invasive Prenatal Testing Reveal Genetic Associations, Patterns of Viral Infections, and Chinese Population History. *Cell* 2018;175:347-59.e14. We analyze whole-genome sequencing data from 141,431 Chinese women generated for

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non-invasive prenatal testing (NIPT). We use these data to characterize the population genetic structure and to investigate genetic associations with maternal and infectious traits. We show that the present day distribution of alleles is a function of both ancient migration and very recent population movements. We reveal novel phenotype-genotype associations, including several replicated associations with height and BMI, an association between maternal age and EMB, and between twin pregnancy and NRG1. Finally, we identify a unique pattern of circulating viral DNA in plasma with high prevalence of hepatitis B and other clinically relevant maternal infections. A GWAS for viral infections identifies an exceptionally strong association between integrated herpesvirus 6 and MOV10L1, which affects piwi-interacting RNA (piRNA) processing and PIWI protein function. These findings demonstrate the great value and potential of accumulating NIPT data for worldwide medical and genetic analyses.



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[https://www.cell.com/cell/fulltext/S0092-8674\(18\)31032-8?dgcid](https://www.cell.com/cell/fulltext/S0092-8674(18)31032-8?dgcid)

4. The Tabula Muris Consortium. Single-cell transcriptomics of 20 mouse organs creates a *Tabula Muris*. *Nature* October 2018; <https://doi.org/10.1038/s41586-018-0590-4>. Here we present a compendium of single-cell transcriptomic data from the model organism *Mus musculus* that comprises more than 100,000 cells from 20 organs and tissues. These data represent a new resource for cell biology, reveal gene expression in poorly characterized cell populations and enable the direct and controlled comparison of gene expression in cell types that are shared between tissues, such as T lymphocytes and endothelial cells from different anatomical locations. Two distinct technical approaches were used for most organs: one approach, microfluidic droplet-based 3'-end counting, enabled the survey of thousands of cells at relatively low coverage, whereas the other, full-length transcript analysis based on fluorescence-activated cell sorting, enabled the characterization of cell types with high sensitivity and coverage. The cumulative data provide the foundation for an atlas of transcriptomic cell biology.

<https://www.nature.com/articles/s41586-018-0590-4>

4. Ravindran S. Integrating Multiple -Omics in Individual Cells. *The Scientist* October 1, 2018; A defining shift in molecular biology over the past decade has been the application of whole genome and whole transcriptome sequencing methods to single cells. With advances in cell isolation and next generation sequencing, researchers no longer need to average out the signal from multiple cells in a population, but can instead study the DNA, RNA, proteins, and chromatin cell by cell.
<https://www.the-scientist.com/lab-tools/integrating-multiple--omics-in-individual-cells-64829>

5. RUSK N. Toward a 3D genome in high resolution. *Nature Methods* 2018;15:647. Hidden in the 3D structure of the genome are answers to many questions about processes from transcriptional regulation to genome stability. Striving to understand how exactly the long DNA polymer is folded into the small nucleus, many researchers are developing ever more intricate methods, but several formidable challenges remain. Two of these were recently tackled from two very different angles, from groups in the Netherlands and France, with the similar goal of improving the resolution of genomic interaction maps.

<https://www.nature.com/articles/s41592-018-0130-z>

<https://www.nature.com/articles/s41588-018-0161-5>

<http://msb.embopress.org/content/14/7/e8293>

6. Marx V. Profiling the dress codes of RNA-binding proteins. *Nature Methods* 2018;15:655. Clothes can be enabling. RNAs in a eukaryotic cell can be clothed, as some scientists phrase it, or unclothed. Some RNAs in a cell, including noncoding RNAs, wear proteins

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that cloak certain RNA regions and expose others. RNA-binding proteins (RBPs) are powerful, versatile regulatory units. They play roles in cellular housekeeping, development, differentiation, metabolism, health and disease, a functional diversity that labs are beginning to characterize. Part of this research is profiling RBPs, for example, to learn which RNAs and proteins are connected...
<https://www.nature.com/articles/s41592-018-0117-9>

7. Camp JG et al. Single-cell genomics to guide human stem cell and tissue engineering. *Nature Methods* 2018;15:661. To understand human development and disease, as well as to regenerate damaged tissues, scientists are working to engineer certain cell types in vitro and to create 3D microenvironments in which cells behave physiologically. Single-cell genomics (SCG) technologies are being applied to primary human organs and to engineered cells and tissues to generate atlases of cell diversity in these systems at unparalleled resolution. Moving beyond atlases, SCG methods are powerful tools for gaining insight into the engineering and disease process. Here we discuss how scientists can use single-cell sequencing to optimize human cell and tissue engineering by measuring precision, detecting inefficiencies, and assessing accuracy. We also provide a perspective on how emerging SCG methods can be used to reverse-engineer human cells and tissues and unravel disease mechanisms.
<https://www.nature.com/articles/s41592-018-0113-0>

9. Guo L, et al. The opium poppy genome and morphinan production. *Science* 2018;362:343-347. Morphinan-based painkillers are derived from opium poppy (*Papaver somniferum* L.). We report a draft of the opium poppy genome, with 2.72 gigabases assembled into 11 chromosomes with contig N50 and scaffold N50 of 1.77 and 204 megabases, respectively. Synteny analysis suggests a whole-genome duplication at ~7.8 million years ago and ancient segmental or whole-genome duplication(s) that occurred before the Papaveraceae-Ranunculaceae divergence 110 million years ago. Syntenic blocks representative of phthalideisoquinoline and morphinan components of a benzyloisoquinoline alkaloid cluster of 15 genes provide insight into how this cluster evolved. Paralog analysis identified P450 and oxidoreductase genes that combined to form the *STORR* gene fusion essential for morphinan biosynthesis in opium poppy. Thus, gene duplication, rearrangement, and fusion events have led to evolution of specialized metabolic products in opium poppy.



<http://science.sciencemag.org/content/362/6412/343?utm>

Other Recommended Readings

1. Baker M. Cryo-electron microscopy shapes up. *Nature* 2018;561:565-7. As the imaging technique produces ever-sharper protein structures, researchers are racing to develop tools to assess how accurate they are...

<https://www.nature.com/articles/d41586-018-06791-6?WT.ec>

2. Woolston C. The quest for postdoctoral independence. *Nature* 2018;561:569-71. How to step out from the shadow of your principal investigator...

https://www.nature.com/articles/d41586-018-06794-3?WT.ec_id

3. Smith R. The business of academic publishing: “a catastrophe”. *Lancet* 2018;392:1186-7. As I watched *Paywall: The Business of Scholarship*, I was taken back 30 years to when I thought for the first time about the business aspects of academic publishing. I was an assistant editor at the *BMJ*, and the editor asked me to join a meeting with a group of rheumatologists who wanted a share in the *Annals of Rheumatic Diseases*, a journal we owned. “We do the research published in the journal”,

Archives (2008-2018): www.gp-tcm.org/news-list/

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said one of the rheumatologists. “We do the peer review, we edit the journal, we read it, and we store it in our libraries. What do you do?” “Tell them what we do”, said the editor to me. I was at a complete loss... *Paywall* makes the same point through an almost bewildering succession of talking heads, most of them academics. Publishers are consistently making profit margins of 30–40%, higher than almost any other business, because they are given their valuable content, the academic research, for free... [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)32353-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32353-5/fulltext)

To watch the film *Paywall: The Business of Scholarship*, please click here:

<https://paywallthemovie.com/>

4. Rasmussen K et al. Collaboration between academics and industry in clinical trials: cross sectional study of publications and survey of lead academic authors. *BMJ* 2018;363:k3654. **Conclusions: Industry employees and academic authors are involved in the design, conduct, and reporting of most industry funded trials in high impact journals. However, data analysis is often conducted without academic involvement. Academics view the collaboration as beneficial, but some report loss of academic freedom. <https://www.bmj.com/content/363/bmj.k3654>**

*This study has been featured in The Scientist on 5th October 2018 by Offord C, entitled **Industry Partners Extensively Involved in Trials They Fund:** <https://www.the-scientist.com/news-opinion/industry-partners-extensively-involved-in-trials-they-fund-64906?utm>*

5. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective: The Third Expert Report of the World Cancer Research Fund and American Institute for Cancer Research is published. <https://www.wcrf.org/dietandcancer/contents>

<https://mp.weixin.qq.com/s/GFg8FZMnlKhCZYHFhnsUQ> (中文)

6. Chekroud SR, et al. Association between physical exercise and mental health in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study. *Lancet Psychiatry* 2018;5:739-46. In a large US sample, physical exercise was significantly and meaningfully associated with self-reported mental health burden in the past month. More exercise was not always better. Differences as a function of exercise were large relative to other demographic variables such as education and income. Specific types, durations, and frequencies of exercise might be more effective clinical targets than others for reducing mental health burden, and merit interventional study. <https://www.ncbi.nlm.nih.gov/pubmed/30099000/>

Commentary found in: Cooney G. **Exercise and mental health: a complex and challenging relationship. *Lancet Psychiatry*. 2018;5:692-3.**

7. Shekelle PG. Clinical Practice Guidelines: What's Next? *JAMA*. 2018;320:757-8. Clinical practice guidelines are a key component of medicine, as they provide evidence-based recommendations for physicians and other health care professionals about the management of care for patients with diseases or other clinical conditions. A number of important developments involving clinical practice guidelines have emerged in the past few years. This Viewpoint discusses some of the more important of these. These are: (1) The Institute of Medicine Report; (2) The GRADE Framework; (3) Too Many Guidelines; (4) The Demise of the National Guideline Clearinghouse; (5) Conflict of Interest; and (6) Updating Guidelines.

<https://mp.weixin.qq.com/s/WFX0FNd54b2TBGIXXgkFQg> (中文)

9. It's not simply one Aspirin a day keeps doctors away. McNeil JJ et al. *N Engl J Med* 2018;379:1499-1539 —*NEJM* report series on Aspirin for healthy elderly and diabetic patients. They concluded:

- Aspirin use in healthy elderly persons did not prolong disability-free survival over a period of 5



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years but led to a higher rate of major hemorrhage than placebo.

- The use of low-dose aspirin as a primary prevention strategy in older adults resulted in a significantly higher risk of major hemorrhage and did not result in a significantly lower risk of cardiovascular disease than placebo.
- Higher all-cause mortality was observed among apparently healthy older adults who received daily aspirin than among those who received placebo and was attributed primarily to cancer-related death. In the context of previous studies, this result was unexpected and should be interpreted with caution.
- Aspirin use prevented serious vascular events in persons who had diabetes and no evident cardiovascular disease at trial entry, but it also caused major bleeding events. The absolute benefits were largely counterbalanced by the bleeding hazard.



<https://www.nejm.org/doi/full/10.1056/NEJMoa1800722?query=TOC>

<https://www.nejm.org/doi/full/10.1056/NEJMoa1805819?query=TOC>

<https://www.nejm.org/doi/full/10.1056/NEJMoa1803955?query=TOC>

<https://www.nejm.org/doi/full/10.1056/NEJMoa1804988?query=TOC>

10. Ridker PM. Should Aspirin Be Used for Primary Prevention in the Post-Statins Era? *N Engl J Med* 2018;379:1572-1574. Editorial concluded: "What can we conclude about the use of aspirin for prophylaxis 150 years after its chemical synthesis? For secondary prevention, in which risk is determined largely by the extent of atherosclerotic disease, the benefits of aspirin outweigh the risks of bleeding. In contrast, for primary prevention, in which risk is determined largely by age and the presence or absence of diabetes, the benefit–risk ratio for prophylactic aspirin in current practice is exceptionally small. Thus, beyond diet maintenance, exercise, and smoking cessation, the best strategy for the use of aspirin in the primary prevention of cardiovascular disease may simply be to prescribe a statin instead." <https://www.nejm.org/doi/full/10.1056/NEJMe1812000?query=TOC>

11. Foreman KJ et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *Lancet* open-access online first publication, October 16, 2018.

- In 2040, Japan, Singapore, Spain, and Switzerland had a forecasted life expectancy exceeding 85 years for both sexes, and 59 countries including China were projected to surpass a life expectancy of 80 years by 2040. At the same time, Central African Republic, Lesotho, Somalia, and Zimbabwe had projected life expectancies below 65 years in 2040, indicating global disparities in survival are likely to persist if current trends hold.
- From 2016–40, the reference forecast showed the potential for major shifts in the leading causes of YLLs. While the leading three causes of YLLs in 2016 remained the same in 2040 (ie, ischaemic heart disease, stroke, and LRI), most of the top ten causes fell in rank by 2040. The primary exception was COPD, which was forecasted to rise from 9th to 4th between 2016 and 2040. Several other NCDs were projected to rise in ranking by 2040, particularly diabetes (from 15th to 7th), chronic kidney disease (from 16th to 5th), and Alzheimer's disease (from 18th to 6th).

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(18\)31694-5/fulltext?dgcid](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31694-5/fulltext?dgcid)

- Comment: Blakely T. **Major strides in forecasting future health.** *Lancet* open-access online first publication, October 16, 2018. [http://dx.doi.org/10.1016/S0140-6736\(18\)31861-0](http://dx.doi.org/10.1016/S0140-6736(18)31861-0)

Meeting Reports

1. Grand Gathering in The People's Hall in Beijing on 11th October 2018, Commemorating Mao's Instruction for Doctors Specialised in Western Medicine to Learn TCM:

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2. On 13 October, WFCMS and Hubei Province of China Coorganised a World TCM Health Forum in Shennongjia Forestry District in Hubei, China. The international meeting was attended by over 400 delegates.
<https://mp.weixin.qq.com/s/Thlanx1ZHOGhnH1CZrf2dQ> (中文)



3. Quintennial Celebration of Li Shi-Zhen: International Conference on Smart Medicine, Regimen, and Culture was held in Taipei on September 28th. Supervised by the Department of Chinese Medicine and Pharmacy under the Ministry of Health and Welfare, and jointly organized by Taipei Medical University (TMU)'s College of Pharmacy, College of Management and Center for General Education, the conference was hosted by TMU. A number of leading experts explored new possibilities of TCM in modern medical pursuits. TMU's big data research team also demonstrated its initial results of Database Creation (data archiving) of Chinese medicine texts collection so far.



One aim of the conference was to integrate traditional and modern medicine in an innovative way. As President Lin Chien-Huang stressed in his opening ceremony speech, some integrative therapies that combine western and Chinese medicines have been gaining wide attention in recent years, while botanical drugs, herbal health products, cosmetic products, and even therapeutic food materials are being well received by more and more consumers. This is especially true as artificial intelligence (AI) has already come of age. Thanks to the Memorandum of Understanding between TMU and the National Palace Museum, it would be a worthwhile effort to connect AI and big data architecture, making extensive research into the Compendium of Materia Medica (CMM), of which 60% of the uncommonly applied herbs were worth examining.

The keynote speech was given by renowned Prof. Zhao Zhong-Zhen (from Hong Kong); he gave an account of CMM's foreword written by Wang Shi-Zhen. The first session was contributed by Liu Shih-Hsun, a research fellow at the National Palace Museum Library; he made a succinct introduction to the ancient medical texts collected by the Library. Three other scholars from the United Kingdom, Japan, and the United States also delivered their invited talks on how the theory and ancient texts of

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traditional Chinese medicine have spread and developed in other countries. In Session 2, Chen Chi-Fang, a Chinese medicine practitioner at MacKay Memorial Hospital, successfully took the audience to explore the “treasure of the original texts” from the clinical perspective. Also, our renowned Assistant Professor Tseng Lin-Yi, and project research fellow Kuo Zhong-Hao (both are from the Center for General Education and cultural historians) gave a lively introduction to the Taiwanese food culture, such as Chinese medicinal liquor and food therapy, and how traditional Chinese medicine has seeped into our culture and everyday life. This was followed by the Dean of the College of Management, Shia Ben-Chang, who reported the initial results on the database creation of the Chinese medicine texts collection on behalf of TMU’s big data research team. Dr. Huang Yi-Tsau, Director-General of the Department of Chinese Medicine and Pharmacy, gave a speech titled “Prospects and Challenges of Chinese Medicine in the 21st Century.” Last but not least, the panel discussion was presided over by TMU’s Vice President Wu Chieh-Hsi, where “the current development and prospects of Chinese medicine across the globe” were explored by Dr. Huang Yi-Tsau (Director-General of the Department of Chinese Medicine and Pharmacy), Chang Kuang-Hsiung (Chairman of Min Tong Pharmaceutical Co., Ltd), Prof. Chang Yuan-Shiun (China Medical University) and Dr. Shia Ben-Chang (Dean of the College of Management). These leaders in various fields gathered to provide their informed advice about policy formulation, industry development, academic research, and innovative applications.

In his closing address, Dr. Wu Chieh-Hsi stressed that this conference was designed to make a crossover effort by integrating medical achievement into our everyday life, just as the sub-theme of this conference indicated. The Compendium of Materia Medica written by Li Shi-Zhen was not merely the first step toward Chinese medicine, but has served as an important symbol that combines the advanced development of artificial intelligence and big data architecture, programming, and cross-disciplinary innovation. This way, more enthusiasm and energy will be brought to future research, and more talented pharmacists and physicians will be inspired in younger generations. They will create a promising prospect for medical development and healthcare systems in the foreseeable future.



4. A Consensus Camp of Taiwan Herbal Pharmacopeia Was Held on September 12, 2018.



Dr. Robin J. Marles, Senior scientific advisor, Bureau of nutritional sciences, Food Directorate, Health Canada was invited to give a plenary lecture on the quality control of herbal medicine and related dietary supplements in US and Canada in the Consensus Camp of Taiwan Herbal Pharmacopeia on September 12, 2018. The 2nd Taiwan herbal Pharmacopeia was published in 2013 with 300 herbal items. In 2016, four sub-committees of Taiwan Herbal Pharmacopeia (THP) was organized, namely herb origin, quality specification, herbal preparation and clinical. Twelve to fifteen experts from government, academic and industry were recruited in each subcommittee. Professor Yuan Shiun Chang was called as PI for Overall editing project for the 3rd Taiwan Herbal Pharmacopeia. Through the efforts of the teams, the 3rd edition of Taiwan Herbal Pharmacopeia will be promulgated in late 2018 with 355 herb items and two extracted granule preparations. The quality specification of the herb items was greatly enhanced. To celebrate the completion of the 3rd edition of Taiwan herbal Pharmacopeia, Professor Tuan Shiun Chang was called to organize the Consensus Camp of Taiwan

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Herbal Pharmacopeia. Members from four THP subcommittees and the THP editorial committee together with TCM practitioners from academic, government and industry participated in the consensus camp. Professor Yi-Tsao Huang, Director-General of the Department of Chinese Medicine and Pharmacy, Ministry of Health and Welfare chaired the consensus camp. Besides plenary lecture given by Dr. Robin Marles, Professor Yi-Tsao Huang talked on Retrospect and Prospect of Taiwan Herbal Pharmacopeia, Professor Yuan Shiun Chang talked on International Trend of Quality Control Specification of TCM. Four PIs from four subcommittees also reported their progress on their subcommittees. A total of 120 people participated in the consensus camp.



Future Meetings & Events

1. The 1st International Conference on the Forefront of Complementary and Integrative Medicine will be held at the Joseph B. Martin Conference Center of Harvard Medical School in Boston October 29-30, 2018. The central theme of this conference is to bring traditional medicine to a new horizon by integrating the latest advances in genomic, metabolomic, and system biological approaches. These new approaches will provide an excellent opportunity to re-examine the wisdom and knowledge of traditional medicine as represented by the Chinese and Ayurvedic traditions, which have been used for centuries. We now know that human diseases are highly complicated, and the current strategy of treating the disease site locally can in many cases only provide temporary or symptomatic relief because the disease site is interconnected pathologically and functionally to many other parts of the body. For instance, the body's own immunological function is now recognized as being of the utmost importance in fighting diseases, including cancer. Traditional herbal remedies that consist of many plant components work by a multi-targeted approach that is far better than a single chemical entity targeting a single enzyme or receptor. This conference brings together world renowned investigators to present their research, exchange ideas, and seek future collaborations. It is an opportunity to share and discuss the forefront of complementary and integrative medicine. And besides great science, the beautiful autumn foliage of New England offers an unforgettable experience. <http://www.icfcim.com>; <http://u6788908.viewer.maka.im/pcviewer/DHORYY4Z> (中文)

2. The 19th International Conference on Oriental Medicine (ICOM 19) will be held in Taipei 24-26 November 2018.

<https://m.youtube.com/watch?v=cxioTU0qGOk>

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: <http://www.wjtcn.net>

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2. Call for Papers: Phytomedicine Special Issue Entitled “systems pharmacology and Metabolomics of Traditional Medicine”

Deadline for submission of manuscripts is **December 31st 2018**.

Edited by

Prof. Thomas Efferth, Johannes Gutenberg University

Prof. Liang Liu, Macau University of Science and Technology

Prof. Xijun Wang, Heilongjiang University of Chinese Medicine

Prof. Hua Zhou, Macau University of Science and Technology

Prof. Haitao Lu, Shanghai Jiao Tong University

<https://www.journals.elsevier.com/phytomedicine/call-for-papers/systems-pharmacology-and-metabolomics-traditional-medicine>

Sounding Board

This column is reserved for comments, personal views, proposals for collaborations or any other features from our readers across the world. We look forward to hearing from you! Please get in touch with your editors: Dr Qihe Xu (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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