The September 2018 Newsletter of The GP-TCM Research Association

New Corporate Member Special Feature

Dalian Fusheng Natural Medicine Development Co Ltd

Dalian Fusheng Pharmaceutical Co., Ltd. (No.5 Tieshan MidRoad, DDR, Liaoning, China. TEL:4008-613-365) is a high-tech enterprise integrated by innovation, research and development, manufacture and sales of modern natural medicine, natural health products and traditional Chinese medicine. It is also a national-level enterprise post-doctoral scientific research workstation, an international science and technology cooperation center in the field of Chinese medicinal chemistry as well as provincial, municipal and regional Engineering Technology Research Center. The company has been granted 30 domestic and foreign patents, and received the first and second prizes of provincial and national technological inventions, the enterprise achievement awards of major research and development, the outstanding national patent awards, outstanding contributions awards to medicinal and pharmaceutical innovation and other honors.

Dr. Fuli meeting President Xi Jinping

Fusheng devotes herself to the botanic drug development of high-purity ginsenoside Rg3 which has significant therapeutic effects in anti-tumor metastasis, the improvement of fatigue, the reduction of adverse effects of radiotherapy and chemotherapy, and the improvement of quality of life, as well as in cardiovascular and cerebrovascular diseases, diabetes, and delaying aging. Shenbaiyi and Nuoyamei capsules are 2 natural health products made from the core components of ginsenoside Rg3 as their raw materials.

National Technical Invention Award

Postdoctoral Research Team

The first-class quality of Fusheng products has become a well-known brand in the Chinese pharmaceutical market, and also gained the trust of doctors, patients and the public. Fusheng actively cooperates with international pharmaceutical companies, continuously researches and develops new varieties, moves toward specialization, standardization, and internationalization, takes more responsibilities for societies and promotes the common prosperity of the company and society.

American and EU Patents

The company has a modern Quality Inspection Center, a GMP Workshop Corridor, a GMP Production Line and its main products include Ginsenbesty capsules(参百益胶囊), an anti-fatigue functional food made from ginseng, phmllanthi fructus, lily, ginkgo, etc, and Nuoyamei capsules (诺雅美胶囊), an anti-ageing functional food made from rhizoma polygonate, ginseng, dried rehmannia root and lucid asparagus etc.

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Special Feature

New 1. **NIH names Dr. Helene Langevin director of the National Center for Complementary and Integrative Health.** National Institutes of Health Director Francis S. Collins, M.D., Ph.D., announced today the selection of Helene M. Langevin, M.D., C.M., as director of the National Center for Complementary and Integrative Health (NCCIH). Dr. Langevin is expected to join NIH in November 2018.

As NCCIH director, Dr. Langevin will oversee the federal government's lead agency for scientific research on the diverse medical and health care systems, practices and products that are not generally considered part of conventional medicine. With an annual budget of approximately $142 million, NCCIH funds and conducts research to help answer important scientific and public health questions about natural products, mind and body practices and pain management. The center also coordinates and collaborates with other research institutes and federal programs on research into complementary and integrative health.

Dr. Langevin comes to NIH from the Osher Center for Integrative Medicine, jointly based at Brigham and Women's Hospital and Harvard Medical School, Boston. She has served as director of the Osher Center and professor-in-residence of medicine at Harvard Medical School since 2012. She has also served as a visiting professor of neurological sciences at the University of Vermont Larner College of Medicine, Burlington.

As the principal investigator of several NIH-funded studies, Dr. Langevin's research interests have centered around the role of connective tissue in low back pain and the mechanisms of acupuncture, manual and movement-based therapies. Her more recent work has focused on the effects of stretching on inflammation resolution mechanisms within connective tissue.

https://www.nih.gov/news-events/news-releases/nih-names-dr-helene-langevin-director-national-center-complementary-integrative-health

European Reports:

New 1. Burki T. **Health in the UK in a no-deal Brexit.** *Lancet* 2018;392:721. Documents published by the UK Government give an insight into what a so-called no-deal Brexit would mean for medicine, research, and pharmaceutical industries. Talha Burki reports…
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31993-7/fulltext

New 2. **European funders commit to science without paywalls by 2020.** In a bold commitment to Open Access, 11 national research funding organizations, supported by the European Commission and the European Research Council (ERC), have announced their plan to make full and immediate Open Access to research publications a reality. This coalition of European funders is implementing fundamental principles to mandate that from 1 January 2020, any scientist they fund publishes their research Open Access. For details please read a perspectives paper by Marc Schiltz, President of Science Europe, published in *Front. Neurosci.* 04 September 2018.
https://www.frontiersin.org/articles/10.3389/fnins.2018.00656/full?utm

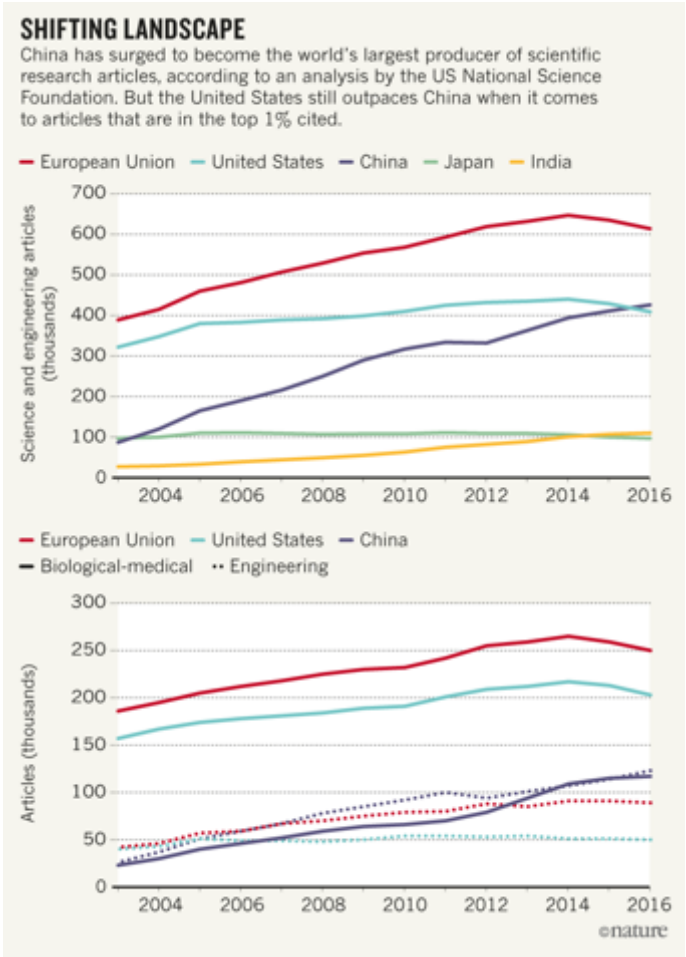
New 3. **cOAlition S, a new initiative aiming to make full and immediate Open Access to research publications a reality**, has been announced in early September by Science Europe. cOAlition S is formed by 11 national research funding organisations, with the support of the European Commission, including the European Research Council (ERC). Other research funders are also invited to join cOAlition S. This new initiative is built around Plan S, which was announced at the EuroScience Open Forum in Toulouse in July 2018, consisting of one target and 10 principles. cOAlition S aims to implement, by 1 January 2020, the necessary measures to fulfil its main principle: "By 2020 scientific publications that result from

research funded by public grants provided by participating national and European research councils and funding bodies, must be published in compliant Open Access Journals or on compliant Open Access Platforms."
https://www.scienceeurope.org/wp-content/uploads/2018/09/cOAlitionS_Press_Release.pdf
https://www.scienceeurope.org/wp-content/uploads/2018/09/Plan_S.pdf

New 4. **President Juncker's 'State of the Union' 2018 Address.** On Wednesday 12 September morning, Jean-Claude Juncker, President of the European Commission, delivered his annual 'State of the Union Address' at the European Parliament. In his address, Mr Juncker highlighted a number of challenges facing the EU in the coming months, including those related to Brexit and the migration crisis, and proposed concrete steps towards building a 'more united, stronger and more democratic Union', which was the theme of his 2017 address. While research and innovation were not addressed directly in the speech, Mr Juncker urged European institutions to reach an agreement on the next Multiannual Financial Framework of the EU (2021-2027) before the new European Parliament is in place in mid-2019 *"to give our researchers and start-ups more opportunities, and prevent funding gaps costing jobs"*. The Commission's proposal for Horizon Europe – successor to Horizon 2020 – was published in June this year and an ambitious timeline envisages its approval by the Council of Ministers and the current European Parliament before the EU leaders' meeting in Sibiu, Romania on 9 May 2019. https://ec.europa.eu/commission/sites/beta-political/files/soteu2018-speech_en.pdf

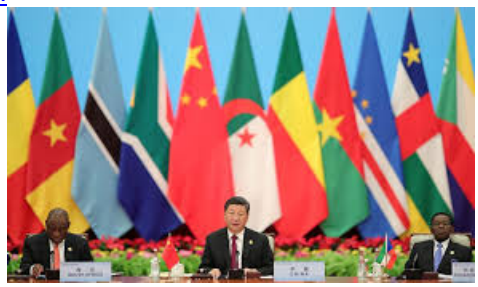
Reports on China and Chinese-European Cooperation

New 1. **China declared world's largest producer of scientific articles.** *Nature* 2018:553:390. China has overtaken the United States in terms of the total number of science publications, according to statistics compiled by the US National Science Foundation (NSF) released on 18 January 2018. The report documents the United States' increasing competition from China and other developing countries that are stepping up their investments in science and technology. Nonetheless, the report suggests that the United States remains a scientific powerhouse, pumping out high-profile research, attracting international students and translating science into valuable intellectual property.
https://www.nature.com/articles/d41586-018-00927-4



New 2. **Forum on China-Africa Cooperation Beijing Action Plan (2019-2021).** The 2018 Beijing Summit of the Forum on China-Africa Cooperation was held on 3 and 4 September 2018 under the theme "China and Africa: Toward an Even Stronger Community with Shared Future through Win-Win Cooperation". The summit was attended by the Heads of State, Government and Delegations of the People's Republic of China and 53 African countries, the Chairperson of the African Union Commission, United Nations Secretary-General and the Executive Secretary of the Economic Commission for Africa. The Summit adopted the Beijing Declaration which, among other things, emphasized that the cooperation between China and Africa under the Belt and Road Initiative will generate more resources and means, expand the market and space for

African development, and broaden its development prospects. The Declaration also underscores the importance of forming a strong synergy between the Belt and Road Initiative and the 2030 Agenda for Sustainable Development of the United Nations, Agenda 2063 of the African Union as well as the development strategies of African countries. To implement the outcomes of the Summit and to chart the course of China-Africa friendly and mutual beneficial cooperation, the two sides adopted a three-year Action Plan (2019-2021) that cuts across the following areas, political cooperation, economic cooperation, social development cooperation, cultural and people-to-people exchanges, and peace and security cooperation. China also announced that it will provide US$60 billion - of which US$15 billion will be in the form of grants - to accompany the agreed Beijing Action Plan.
https://allafrica.com/stories/201809100728.html
https://www.fmprc.gov.cn/mfa_eng/zxxx_662805/t1593683.shtml

New 3. Green A. **Forum on China-Africa Cooperation: what it means for health.** *Lancet* 2018;392:998-9. Investment in health is an essential component of the Forum on China-Africa Cooperation (FOCAC). Whereas some laud China's investment strategy, others deplore that gains to health are hard to track. Andrew Green reports.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32285-2/fulltext

TCM, Acupuncture and Other Traditional Medicine

New 1. **A video in honour of Li Shizhen's and in celebration of the 500th Anniversary of Li Shizhen's birth is now freely available online, both in English and Chinese.**
https://v.qq.com/x/page/q0771v3iby8.html (English)

https://v.qq.com/x/page/e07731lbqgo.html (中文)

New 2. Xiaohe Xiao and Luqi Huang. **Please pay attention to quality control of materia medica: Traditional Chinese medicine cannot be allowed to die from poor materia medica.** *China Traditional Chinese Medicine.* September 20, 2018. Published through WeChat

https://mp.weixin.qq.com/s/KwTwJ1PgnwC1wnL8fjAVPQ (中文)

New 3. Wu X , et al**. Transporter modulation by Chinese herbal medicines and its mediated pharmacokinetic herb-drug nteractions.** *J Chromatogr B Analyt Technol Biomed Life Sci.* 2016;1026:236-253. This review article focuses on two major transporter superfamilies, the solute carrier (SLC) and the ATP-binding cassette (ABC) transporters, to provide the recent advanced knowledge on CHMs and their inherent phytochemicals that interact with these transporters, and their induced pharmacokinetic HDIs from both preclinical and clinical aspects. In addition, the challenges and strategy for studying HDIs are also discussed.
https://www.sciencedirect.com/science/article/pii/S1570023215302889?via%3Dihub

New 4. Chen S, et al. **Chinese Herbal Medicine for Myasthenia Gravis: A Systematic Review and Meta-Analysis.** *Front Pharmacol.* 2018;9:969. Meta-analysis showed a significant effect of Chinese herbal medicine (CHM) as adjuvant therapy for improving the effectiveness compared with Western conventional medicine (WCM) alone or placebo in treating Myasthenia gravis (MG) ($p < 0.01$). Moreover, there were fewer adverse effects and relapse rate in total when compared with the control group. The possible mechanisms of CHM for MG are associated with immunoregulation by reconstituting the functional ability of Tregs. In conclusion, despite the apparent positive results, the

present evidence supports, to an extent, that CHM can be used for MG patients because of the methodological flaws and CHM heterogeneity. Further rigorous RCT for MG is needed.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00969/full?utm

New 5. Chen G, et al. **Efficacy and Safety of Xuebijing Injection Combined With Ulinastatin as Adjunctive Therapy on Sepsis: A Systematic Review and Meta-Analysis.** *Front Pharmacol.* 2018;9:743. Conclusions: Comparing with UTI alone, XBJ and UTI combination therapy appeared to be more effective for sepsis. However, owing to the limitations of this meta-analysis, additional RCTs with higher-quality and more rigorous design are needed to confirm our findings.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00743/full

New 6. Peng Y, et al. **Salvia Miltiorrhiza Ameliorates Liver Fibrosis by Activating Hepatic Natural Killer Cells in Vivo and in Vitro.** *Front Pharmacol.* 2018;9:762. This work provided a new insight into the anti-fibrotic mechanism that SM could enhance the activities of NK cell to reduce liver fibrosis in vivo and in vitro.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00762/full?utm

New 7. Qiu T et al. **Exploring the Mechanism of Flavonoids Through Systematic Bioinformatics Analysis.** *Front Pharmacol.* 2018;9:914. Results highlight the common and preference functions of flavonoids and their subclasses, concerning their pharmacological and biological properties.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6104453/

New 8. Cai X et al. **The Bone-Protecting Efficiency of Chinese Medicines Compared With Western Medicines in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis of Comparative Studies.** *Front Pharmacol.* 2018 Aug 30;9:914. Conclusions: Chinese medicine may provide an efficiently alternative choice for the treatment of RA in terms of the bone-protecting efficiency. Given the inherent limitations of the included studies, future well-designed RCTs are required to confirm and update the findings of this analysis.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00914/full

Omics in Progress

New 1. **The 3D genome: A *Nature* Collection.** This collection includes recent articles from across the *Nature* group of journals and showcases both the latest advances in the methodologies used to study genome organization, and our recent understanding of how genome organization and nuclear architecture regulate gene expression, cell fate and cell function in physiology and disease.
https://www.nature.com/collections/rsxlmsyslk?utm_source=naturecomnewsl&utm

New 2. Dor Y, Cedar H. **Principles of DNA methylation and their implications for biology and medicine.** *Lancet* 2018;392:777-86. DNA methylation represents an annotation system for marking the genetic text, thus providing instruction as to how and when to read the information and control transcription. Unlike sequence information, which is inherited, methylation patterns are established in a programmed process that continues throughout development, thus setting up stable gene expression profiles. This DNA methylation paradigm is a key player in medicine. Some changes in methylation closely correlate with age providing a marker for biological ageing, and these same sites could also play a part in cancer. The genome continues to undergo programmed variation in methylation after birth in response to environmental inputs, serving as a memory device that could affect ageing and predisposition to various metabolic, autoimmune, and neurological diseases. Taking advantage of tissue-specific differences, methylation can be used to detect cell death and thereby monitor many common diseases with a simple cell-free circulating-DNA blood test.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31268-6/fulltext

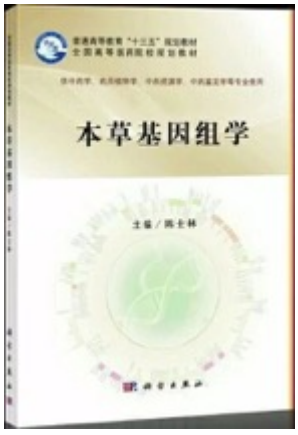
New 3. Camacho DM et al. **Next-Generation Machine Learning for Biological Networks.** *Cell* 2018; 173: 1581-92. Machine learning, a collection of data-analytical techniques aimed at building predictive models from multi-dimensional datasets, is becoming integral to modern biological research. By enabling one to generate models that learn from large datasets and make predictions on likely outcomes, machine learning can be used to study complex cellular systems such as biological networks. Here, we provide a primer on machine learning for life scientists, including an introduction to deep learning. We discuss opportunities and challenges at the intersection of machine learning and network biology, which could impact disease biology, drug discovery, microbiome research, and synthetic biology. https://www.cell.com/action/showPdf?pii=S0092-8674%2818%2930592-0

New 4. Silva R. **After 18 years, research into genome is bearing fruits.** *Evening Standard* 2018; 6th September. When it comes to new technologies, we tend to overestimate the impact in the short term but underestimate the impact in the long term. In Silicon Valley this is known as Amara's Law, named after Stanford university professor Roy Amara, who first observed this behaviour several decades ago. If you want to see this law in action there's nowhere better to look than healthcare and medicine. In June 2000 the human genome — the entire genetic code contained in our cells — was published for the first time… https://www.standard.co.uk/comment/comment/after-18-years-research-into-genome-is-bearing-fruit-a3929276.html

New 5. Rusk N. **Toward a 3D genome in high resolution.** *Nature Methods* 2018;15:647. Independent efforts shine light on the 3D genome structure by looking at multiple contacts along an allele or equalizing the distance between restriction sites for higher-resolution Hi-C maps… https://www.nature.com/articles/s41592-018-0130-z?WT.ec_id

New 6. Camp JG, et al. **Single-cell genomics to guide human stem cell and tissue engineering.** *Nat Methods* 2018;15:661-7. A review on how single-cell sequencing methods can be used to improve human stem cell and tissue engineering. https://www.nature.com/articles/s41592-018-0113-0?WT.ec_id

New 7. **Akcakaya P et al. In vivo CRISPR editing with no detectable genome-wide off-target mutations.** *Nature* **2018;** http://www.nature.com/articles/s41586-018-0500-9.pdf CRISPR–Cas genome-editing nucleases hold substantial promise for developing human therapeutic applications but identifying unwanted off-target mutations is important for clinical translation. A well-validated method that can reliably identify off-targets in vivo has not been described to date, which means it is currently unclear whether and how frequently these mutations occur. Here we describe 'verification of in vivo off-targets' (VIVO), a highly sensitive strategy that can robustly identify the genome-wide off-target effects of CRISPR–Cas nucleases in vivo. We use VIVO and a guide RNA deliberately designed to be promiscuous to show that CRISPR–Cas nucleases can induce substantial off-target mutations in mouse livers in vivo. More importantly, we also use VIVO to show that appropriately designed guide RNAs can direct efficient in vivo editing in mouse livers with no detectable off-target mutations. VIVO provides a general strategy for defining and quantifying the off-target effects of gene-editing nucleases in whole organisms, thereby providing a blueprint to foster the development of therapeutic strategies that use in vivo gene editing.
https://www.nature.com/articles/s41586-018-0500-9.pdf

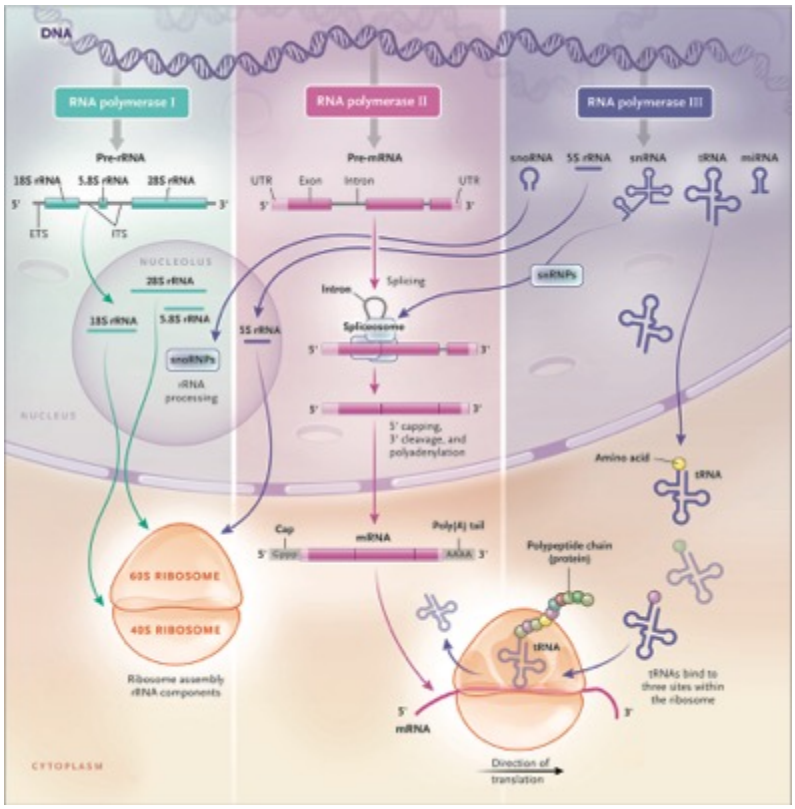


New 8. Chen S. Ed. **Genomics of Materia Medica** – a new textbook for higher education is published by China's Science Press.
https://mp.weixin.qq.com/s/_0iZkKgThStqZDiJv8xK7Q (中文)

New 9. Lieberman J. **Unveiling the RNA World.** *N Engl J Med* DOI: 10.1056/NEJMcibr1808725. The 2018 Lasker–Koshland Special Achievement Award in Medical Science, announced September 11, 2018 recognizes Joan A. Steitz, who has made pioneering contributions to the understanding of RNA biology and, as a woman scientist, has led the way as a role model and strong advocate for removing the barriers to welcoming and ad- vancing women and minorities into the scientific community. This paper highlights the achievements of Dr Steitz in RNA research and summarises our current knowledge on the interrelations and roles for different RNA polymerases and RNA types.
https://www.nejm.org/doi/full/10.1056/NEJMcibr1808725?query=TOC

New 10. Feng X et al. **Tibetan Medical Formula Shi-Wei-Gan-Ning-Pill Protects Against Carbon Tetrachloride-Induced Liver Fibrosis – An NMR-Based Metabolic Profiling.** *Front Pharmacol.* 2018;9:965. The results showed that SWGNP could significantly attenuate the pathological changes and decrease the levels of fibrosis markers (ColIV, HA, LN, and PCIII), and regulate the disordered elements distribution. Multivariate analysis and correlation network analysis revealed that SWGNP could protect rats against CCl4-induced liver fibrosis through anti-oxidation, repairing the impaired energy metabolisms and reversing the disturbed amino acids and nucleic acids metabolisms. In conclusion, this integrated metabolomics approach provided new insights into the mechanism of the hepatoprotective effect of SWGNP in liver fibrosis disease.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00965/full

New 11. Liang L et al. **Integrating Targeted and Untargeted Metabolomics to Investigate the Processing Chemistry of Polygoni Multiflori Radix.** *Front Pharmacol.* 2018;9:934. Polygoni Multiflori Radix (PMR, Heshouwu in Chinese), derived from the tuberous roots of Polygonum multiflorum Thunb., is a widely-used Chinese medicinal material. For traditional clinical use, raw PMR (RPMR) is processed by nine cycles of steaming and drying to generate processed PMR (PPMR); RPMR and PPMR have distinct medicinal purposes based on the theory of traditional Chinese medicine. While PMR has been processed for hundreds of years, including the present, the chemistry of that processing has not been well studied. In this study, targeted and untargeted metabolomics analyses using ultra-performance liquid chromatography-quadrupole/time-of-flight mass spectrometry (UPLC-QTOF-MS/MS) and ultra-performance liquid chromatography-quadrupole/triple quadrupole mass spectrometry (UPLC-QqQ-MS/MS) were integrated to investigate the processing chemistry of PMR. The results demonstrate that processing by nine cycles of steaming and drying qualitatively and quantitatively alters the chemical profile of PMR. Several mechanisms, namely hydrolysis, dehydration, isomerization, and Maillard reaction appear to be involved in the chemical transformation that occurs. The qualitative and quantitative data further suggest that nine cycles might be necessary for the preparation of PPMR, as PPMR that has been processed nine times shows significant differences in its chemical profile.
https://www.frontiersin.org/articles/10.3389/fphar.2018.00934/full



New 12. Liao J, et al. **Network pharmacology study reveals energy metabolism and apoptosis pathways-mediated cardioprotective effects of SHENQI FUZHENG.** *J Ethnopharmacol.* 2018 Aug 23. pii: S0378-8741(18)31179-6. CONCLUSION: In conclusion, our results suggest that SQ injection exerts protective effect against myocardial ischemia-reperfusion injury through multiple pathways, including myocardial energy metabolism improvement, cell adhesion inhibition, inflammatory reaction perturbation, myocardial apoptosis reduction and ventricular remodeling avoidance.

https://mp.weixin.qq.com/s/2DgeInNAOWLWwt7Us4CIXA (中文)

New 13. Guo L et al. **The opium poppy genome and morphinan production**. *Science* 2018:eaat4096 Morphinan-based painkillers are derived from opium poppy. We report a draft of the opium poppy genome, with 2.72 Gb assembled into 11 chromosomes with contig N50 and scaffold N50 of 1.77 Mb and 204 Mb, respectively. Synteny analysis suggests a whole genome duplication at approximately 7.8 million years ago (MYA) and ancient segmental or whole genome duplication(s) that occurred before the Papaveraceae-Ranunculaceae divergence 110 MYA. Syntenic blocks representative of phthalideisoquinoline and morphinan components of a benzylisoquinoline alkaloid cluster of 15 genes provides insight into how it evolved. Paralog analysis identified P450 and oxidoreductase genes that combined to form the *STOR* 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/early/2018/08/29/science.aat4096

http://www.ebiotrade.com/newsf/2018-8/2018831113506345.htm (中文)

Other Recommended Readings

New 1. Kinzler KD, Shutts K. **Ways to promote and foster collaborative research in your lab.** *Nature* 2018;560:673…

- **Eliminate a 'zero-sum' mindset.** Collaboration can help to direct students to 'growing the pie' — creating more resources together that they can ultimately share. As graduate students, we developed a shared research programme that generated multiple studies and articles, so determining authorship was never stressful for us. We encouraged the students in the anecdote above to think about generating a pipeline of collaborative projects. By treating the project as the first step in an important, long-term programme, neither student felt as worried about the final authorship decision.
- **Establish parameters.** Recently, a new student in one of our labs wanted to collaborate with a postdoc, yet devoted significant attention to dissecting her role in the project and how much time she (compared with the postdoc) was spending on it. All this worry risked stagnating the science and ending the collaboration. We explained the benefits of this type of partnership, and pointed to how our own successes, as well as those of previous students, have been bolstered by sharing credit with other scientists.
- **Encourage students to make authorship decisions after they collect data**. In our experience, determining authorship later in the process puts the science (rather than the publication process) front and centre, and helps students to think of growing the total amount of research, rather than angsting over whether they plan to contribute 49% or 51% of any given project…

https://www.nature.com/articles/d41586-018-06037-5?WT.mc_id

New 2. Rubenson D. **Prioritize the needs of the audience when giving a presentation.** *Nature* 2018; doi: 10.1038/d41586-018-06021-z. Speakers inadvertently prepare presentations for themselves rather than their audiences. A few mental exercises can help presenters to avoid this pitfall.

- Take some time to consider who might attend.

- Think about what attendees will remember 24 hours after your talk.
- Identify the core message of each slide.
- Prepare for a time crunch.

https://www.nature.com/articles/d41586-018-06021-z?WT.mc_id

New 3. Shah R et al. **Circulating Extracellular Vesicles in Human Disease.** *N Engl J Med* 2018; 379:958-966. It is well known that cells release fluid-filled sacs (vesicles) to the extracellular environment during cell death, or apoptosis, but it has been increasingly recognized that healthy cells may also release vesicles in the process of normal functions. Vesicles that are released by healthy cells have a wide variety of names (e.g., ectosomes, microparticles, microvesicles, exosomes, and oncosomes), with the term "extracellular vesicles" typically used as a generic reference to secreted vesicles. Extracellular vesicles are found in circulation and contain cell-derived biomolecules (e.g., RNA, protein, and metabolites). Extracellular vesicles are implicated in trafficking of molecules between cells and as such have an effect on physiologic function and serve as biomarkers for disease (see video). Nevertheless, important limitations — including practical difficulties in assaying low concentrations of extracellular vesicles in circulation, identifying their tissue of origin, and specifying which molecular cargo is most relevant — have restrained enthusiasm for research into the role of extracellular vesicles in vivo. The goal of this article is to provide a brief introduction to extracellular vesicles, with a specific focus on translational and clinical studies to highlight emerging evidence that suggests a potential role in human disease. Given the explosion of work in this field, it is difficult to cover the breadth of diseases in which extracellular vesicles may be functionally relevant. As such, the reader is referred to the expanding literature in this field for more details…
https://www.nejm.org/doi/full/10.1056/NEJMra1704286?query=TOC

New 4. **BMJ Best Practice** was ranked equal first in an independent review of CDS tools for breadth of disease coverage, editorial quality and evidence-based methodology. The other guidelines recommended for clinicians include Dynamed and UptoDate.
https://www.ncbi.nlm.nih.gov/pubmed/26786976
BMJ Best Practice: https://bestpractice.bmj.com/?utm
Dynamed: https://dynamed.com/home/
UptoDate: https://www.uptodate.com/home

New 5. Aly M. **The key to a happy lab life is in the manual.**
Nature 2018;**561**:7. A well-crafted set of guidelines and advice can save time, reassure trainees and promote a positive lab culture.
https://www.nature.com/articles/d41586-018-06167-w?WT.ec_id

New 6. **Real World Study Guideline 2018 published in August 2018.** Sponsored by WU Jieping Medical Foundation, the guideline is now available in Chinese on WeChat:

https://mp.weixin.qq.com/s/Oo00rRtyRM4nJrvQSX21zw (中文)

New 7. Bothwell L et al. **Adaptive design clinical trials: a review of the literature and ClinicalTrials.gov**. *BMJ Open* 2018;**8**:e018320
Objectives This review investigates characteristics of implemented adaptive design clinical trials and provides examples of regulatory experience with such trials.
Design Review of adaptive design clinical trials in EMBASE, PubMed, Cochrane Registry of Controlled Clinical Trials, Web of Science and ClinicalTrials.gov. Phase I and seamless Phase I/II trials were excluded. Variables extracted from trials included basic study characteristics, adaptive design features, size and use of independent data monitoring committees (DMCs) and blinded interim analyses. We also examined use of the adaptive trials in new drug submissions to the Food and Drug Administration (FDA) and European Medicines Agency (EMA) and recorded regulators' experiences with adaptive designs.

Results 142 studies met inclusion criteria. There has been a recent growth in publicly reported use of adaptive designs among researchers around the world. The most frequently appearing types of adaptations were seamless Phase II/III (57%), group sequential (21%), biomarker adaptive (20%), and adaptive dose-finding designs (16%). About one-third (32%) of trials reported an independent DMC, while 6% reported blinded interim analysis. We found that 9% of adaptive trials were used for FDA product approval consideration, and 12% were used for EMA product approval consideration. International regulators had mixed experiences with adaptive trials. Many product applications with adaptive trials had extensive correspondence between drug sponsors and regulators regarding the adaptive designs, in some cases with regulators requiring revisions or alterations to research designs.

Conclusions Wider use of adaptive designs will necessitate new drug application sponsors to engage with regulatory scientists during planning and conduct of the trials. Investigators need to more consistently report protections intended to preserve confidentiality and minimise potential operational bias during interim analysis.

https://bmjopen.bmj.com/content/bmjopen/8/2/e018320.full.pdf
https://www.fda.gov/downloads/drugs/guidances/ucm201790.pdf
https://mp.weixin.qq.com/s/8vVvbrQfAcu86D_kM_jK8Q (中文)

New 8. Bray S et al. **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.** CA: A Cancer Journal for Clinicians 2018;0:1-31. This article provides a status report on the global burden of cancer worldwide using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, with a focus on geographic variability across 20 world regions. There will be an estimated 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer) and 9.6 million cancer deaths (9.5 million excluding nonmelanoma skin cancer) in 2018. In both sexes combined, lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths), closely followed by female breast cancer (11.6%), prostate cancer (7.1%), and colorectal cancer (6.1%) for incidence and colorectal cancer (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. Lung cancer is the most frequent cancer and the leading cause of cancer death among males, followed by prostate and colorectal cancer (for incidence) and liver and stomach cancer (for mortality). Among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death, followed by colorectal and lung cancer (for incidence), and vice versa (for mortality); cervical cancer ranks fourth for both incidence and mortality. The most frequently diagnosed cancer and the leading cause of cancer death, however, substantially vary across countries and within each country depending on the degree of economic development and associated social and life style factors. It is noteworthy that high-quality cancer registry data, the basis for planning and implementing evidence-based cancer control programs, are not available in most low- and middle-income countries. The Global Initiative for Cancer Registry Development is an international partnership that supports better estimation, as well as the collection and use of local data, to prioritize and evaluate national cancer control efforts.

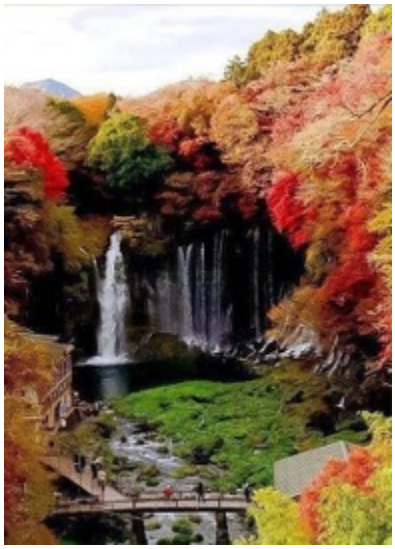
https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21492
https://mp.weixin.qq.com/s/G6yVZIuo4KAGvgQzMGWMMg (中文)

New 9. Burki T. **Cochrane review methods called into question.** *Lancet* 2018; 392:906. Cochrane is contesting allegations that a human papillomavirus vaccine review missed 20 eligible trials in its analysis. Talha Burki reports. Cochrane published a response denying the findings of a *BMJ Evidence-Based Medicine BMJ EBM*) article that criticised Cochrane's human papillomavirus (HPV) review. The authors of the *BMJ EBM* paper had claimed that Cochrane had inadequately assessed adverse events and failed to take into account "nearly half of the eligible trials". Cochrane countered that the *BMJ EBM* article "substantially overstated its criticisms". The dispute is unlikely to be resolved anytime soon… https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32251-7/fulltext

New 10. Offord C. **Cochrane Collaboration Expels Cofounder, Prompts Resignations.** *The* Scientist 2018; The Cochrane Collaboration, a respected medical organization that conducts systematic reviews of research and helps guide clinical practice, has expelled one of its governing board members, Danish physician and Cochrane cofounder Peter Gøtzsche, *STAT News* reported on September 16. The grounds for the decision, which led to the resignations of several other board members who had voted against the move, have not yet been made public, but the resulting controversy has cast a cloud over the organization's 2018 annual meeting, now (18 September 2018) underway in Edinburgh in the UK… The expulsion of an elected member of the board has created heated debate among scientists, both within and outside the organization. Of the 13-person board, six voted in favor of Gøtzsche's expulsion and two did not vote, *STAT* reports. According to a statement published on Saturday (September 15) on Cochrane's website, four board members have since resigned as a result of the decision. "We consider the Board's use of its authority to expel Peter from Cochrane to be disproportionate," wrote the four members in a statement, *Science* reports. "We believe that the expulsion of inconvenient members from the Collaboration goes against Cochrane ethos and neither reflects its founding spirit nor promotes the Collaboration's best interests."
https://www.the-scientist.com/news-opinion/cochrane-collaboration-expels-cofounder--prompts-resignations-64817
http://www.sciencemag.org/news/2018/09/evidence-based-medicine-group-turmoil-after-expulsion-co-founder

New 11. Veuthey TL, Thompson S. **Why you need an agenda for meetings with your principal investigator.** *Nature* 2018; 561:277. A list of talking points can help with navigating potentially difficult topics and sticky negotiations.
https://www.nature.com/articles/d41586-018-06619-3?WT.ec

New 12. Avorn J, Kesselheim A, Sarpatwari A. **The FDA Amendments Act of 2007 — Assessing Its Effects a Decade Later.** *NEJM* 2018; 379:1097-1099. …In the early 2000s, the crisis and reform centered around rofecoxib (Vioxx), which became an important trigger for changes in how the Food and Drug Administration (FDA) collects, analyzes, and acts on evidence of drug risks…By 2006, the public, the scientific community, and Congress were demanding to know how one of the country's best-selling drugs could carry such important risks without the FDA's being aware of their magnitude and importance…Disturbing accounts had also surfaced in the early 2000s about limited access to the clinical trial data that formed the basis of FDA approval decisions…Responding to these concerns in the post-Vioxx era, Congress used the 2007 renewal of FDA user-fee legislation to make seminal reforms in the management of data on drug effects. The resulting FDA Amendments Act (FDAAA) instructed the FDA to build a population-based surveillance system to harness the enormous reservoir of data on medication use and clinical events generated automatically during routine electronic recording of filled prescriptions and virtually all other medical encounters. The FDAAA also increased the FDA's power to require manufacturers to conduct postapproval studies, such as by giving it authority to impose monetary penalties for noncompliance. The Act further required that



information on the design of all clinical trials be recorded in a public database, ClinicalTrials.gov, soon after a trial's inception, and it set in motion rulemaking to require that summary results also be included in the database within 12 months after the trial's primary completion date. The law also mandated the implementation of risk evaluation and mitigation strategies (REMS) which can require physician certification, mandatory risk communications, or laboratory testing when specific high-risk medications are used. These provisions have now been in place for more than a decade, offering an opportunity to assess their effects…
https://www.nejm.org/doi/full/10.1056/NEJMp1803910?query=TOC

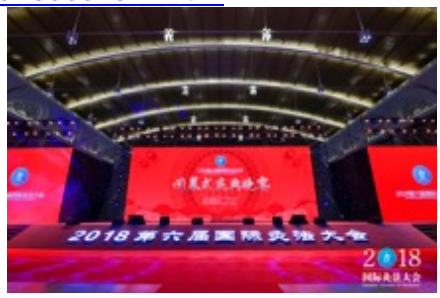
Meeting Reports

New 1. **International Symposium on Clinical and Translational Medicine: Chinese medicine Scientific Evaluation & International Development was held in Shanghai on 11 September 2018.**

New 2. **The Second Congress on Clinical Chinese Medicine cum CHINA-CIOMS Drug-Induced Liver Injury Assessment and Pharmacovigilance Roundtable Meeting was held in Beijing 4-5 September 2018.** At the meeting, an *International Consortium on Studies of the Safe Use of Traditional Medicines* was founded and the *Beijing Declaration on Safe Use of Traditional Medicines* was published. The meeting was attended by some 400 delegates

https://mp.weixin.qq.com/s/Qoo1uNrRR-sNMs6s-hJ2bg (中文)


New 3. **A gallery of the 6th International Convention on Moxibustion, which was held in Kunming, Yunnan, China on 9-10 September 2018.**
http://www.pailixiang.com/album_ia130667824.html


New 4. **The University of Hong Kong Chinese Medicine Alumni (HKCMA) met in Hong Kong on 12 September in celebration of the 20th Anniversary of the HKCMA Association.**

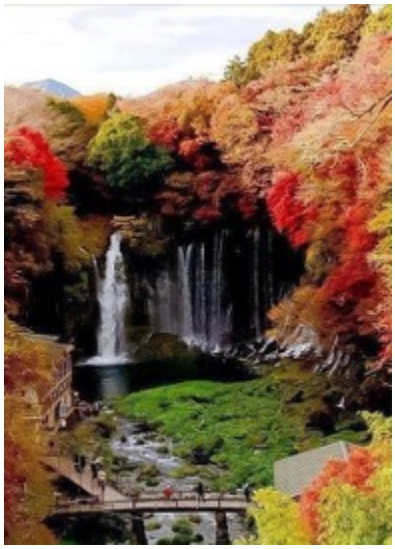

New 5. ***China-ASEAN Traditional Medicine*** **launched at the 6th Forum of China-ASEAN Technology Transfer & Collaborative Innovation in Nanning, China, on 12 September 1018.**

New 6. **A pictorial report on the 10th TCM Expo (Yulin, China) held on 14th September 2018**

Report on the opening ceremony: https://mp.weixin.qq.com/s/EBrgUHzP3xxmJ_pV5nKEIA (中文)

Amazing TCM practice on display: https://mp.weixin.qq.com/s/_JHVcy5RQ2Mr1P4zWUrReQ (中文)

Future Meetings & Events



New 1. **NBI International Congress** "**Natural products: Evidence based effectiveness/solutions for the future". 3rd and 4th October 2018, The Beursgebouw Eindhoven – The Netherlands.** Considerably reduced registration fee of €25 only for students! Worldwide, there is an increasing demand for natural products. They could provide the answer to many of the questions that modern healthcare is struggling with. This is why the Netherlands Association for Phytotherapy (NVF) is organizing a conference in partnership with NBI on October 3rd and 4th 2018. International speakers from diverse disciplines will ensure a top-quality conference that you shouldn't miss out on! The conference will be held concurrently with the MAP-Expo trade fair, at the same venue, and will provide plenty of opportunities for visiting the fair. The programme is under supervision of moderator Prof. Dr Rob Verpoorte, Natural products laboratory, IBL, Leiden University.

Besides the meeting there is a fair for around 80 companies active in the field of phytotherapy and natural products. The program offers among others interesting lectures on the role of the microbiome for our health, synergy, nanoparticles, natural products drug development, cannabinoids and the role for phytotherapy in health care. All topics which are of interest for natural products research. From the fair students may get some ideas about the opportunities for future jobs.

The organizers have decided to offer all students a considerably reduced registration fee of €25 only for the two-day meeting, including coffee, tea, lunch and entrance to the fair. Of course people are also welcome for only one day if they are unable to come to both days.

The meeting will be in the Beursgebouw in Eindhoven, close to the station. Please contact Prof Rob Verpoorte ASAP if you or your students want to participate: verpoort@chem.leidenuniv.nl

Venue: The Beursgebouw Eindhoven (Lardinoisstraat 8, 5611 ZZ Eindhoven) is only a 2-min walk from the railway station. From the platform you take the stairs down and then you turn right (signposted "Beursgebouw"). At the exit you turn left. Now you will see Beursgebouw on your left. You walk right around the building, and through the bicycle and pedestrian tunnel via the shopping promenade you will see the main entrance to Beursgebouw at your left.
https://www.eventbrite.nl/e/international-congres-natural-products-evidence-based-effectivenesssolutions-for-the-future-tickets-47553679335

2. **The 15th World Congress of Chinese Medicine and *Belt and Road* TCM Culture Week to be held in Rome, Italy, Nov. 16-20 2018.**

http://c.eqxiu.com/s/O8xACe2w?eqrcode=1&share_level=4&from_user=a294a700-73b5-4d95-9d8b-dc428813e7cd&from_id (中文)

3. **The 19th International Congress of Oriental Medicine will be held in Taipei, Taiwan on 24-26 November 2018.** The theme of the conference is "The Applications of Traditional Medicine in Acute and Critical Care."
http://www.19icom2018.org.tw/index

4. **The 30th International Symposium on the Chemistry of Natural Products and the 10th International Congress on Biodiversity will be held on Nov. 25–29 2018 in Athens, Greece.**

http://www.iscnp30-icob10.org/Default.asp?c=6&lng=1
http://www.iscnp30-icob10.org/Default.asp?c=7&lng=1

5. **The 6th World Integrative Medicine Congress is to be held in Shanghai, China, December 6-9, 2018.** The past 60 years have witnessed fruitful results in integrative medicine, coupled with its significant role in promoting medical innovation and progress. To further facilitate the international exchange in integrative medicine, the World Integrative Medicine Congress now meets every year instead of every five years. The 6th World Integrative Medicine Congress, co-hosted by Chinese Association of Integrative Medicine and Shanghai Association for Science and Technology, will be held December 6-9, 2018 at Shanghai Fuyue Hotel. http://www.wimco2018.com/weben2018/
http://wimco2018.shcim.org.cn/m2018/index.asp?from=groupmessage&isappinstalled=0 (中文)

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.wjtcm.net

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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Special note: 24th September 2018 was the mid-Autumn Festival, a festival to celebrate harvest, family harmony and union. In celebration of the beautiful autumn, we have selected a few nice autumn views from the following website to decorate this newsletter. Wherever you are, we wish you enjoy good harvest and family harmony!
http://www.geimian.com/wx/50047.html