

Corporate Member Special Feature

PuraPharm International (H.K.) Ltd

https://www.purapharm.com



Since its inception in 1998, PuraPharm (HKEX stock code: 1498.HK) has dedicated itself to the modernization and internationalization of traditional Chinese medicine (TCM). Actively collaborating with internationally renowned academics, PuraPharm has established itself as the technological front-runner within the industry. Through continuous innovation, PuraPharm has come to be recognized as one of the leading companies in research and development (R&D),

manufacturing, marketing and selling, quality control and basic scientific research of TCM.

PuraPharm has invested in its TCM research and production facilities in Nanning, Guangxi Province, China. The factory complies with the PRC Good Manufacturing Practice (GMP) standards as well as the Australia's Therapeutic Goods Administration (TGA) standards – one of the strictest certification standards in the world. Our laboratory is certified by the China National Accreditation Service for Conformity Assessment (CNAS), the international multilateral recognition system that is equivalent to an accreditation, in accordance with the ISO 17025 standards. Our manufacturing facilities are

regarded as one of the most advanced TCM research and manufacturing facilities in Asia.

Our R&D goals and strategies

Our research strategy is based on the PuraPharm's mission and vision to research on drug discovery from natural sources and/or "drug fostering" through clinical studies from TCM formulas used in treatment and prevention of disease and complementary health.

Currently, we are focusing on two main projects, one is to develop new drug in treating IBS (Irritable bowel syndrome) on the basis of regulation over new drug application, of which Phase-II clinical trials in mainland China and Hong Kong SAR, have been carried out respectively. Another is a single herb from TCM which is found to be effective on rheumatoid arthritis in our preclinical study. To assess its safety and efficacy, a randomized, double-blind and placebo-controlled trial will be started at two different clinical trial facilities in Canada and Australia, respectively in 2019.

Besides new drug development, strengthening "drug fostering" is one of the strategic priorities under our management plan.

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Through collecting drug information from clinical use or evaluation, those medicines such as from TCM formulas are furthermore developed and improved with strict quality control so that they could be used more easily in the modern healthcare system. In other words, to accomplish modernization and internationalization of TCM based on the foundation of scientific evidence.

Taking into account the characters of TCM, in particular, the quality can be affected by various factors not only from plantation and process of raw materials but also from pharmaceutical technology. Therefore, our R&D team, which is divided into different units per their functionality, is based in Guizhou (seeding, plantation and process), Nanning (standard building, manufacturing process and quality control), Beijing (clinical trials and regulations), Hong Kong (clinical trials, regulations and planning) and Japan (technological development). They cooperate with each other to achieve the mission of developing products, which matches with our company strategy. R&D team in Japan is also responsible for developing and manufacturing healthcare products including both OEM and ODM products.

Editorial

GP-TCM Research Association – Back to the Future



Dr Tai-Ping Fan
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On behalf of the Board of Directors (2017-2018)
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(Drafted by Dr Clara Lau, Secretary-General, Hong Kong, China)

It gives me great pleasure, as out-going President, to reflect on the collective achievements of the current BoD over the past two years, and to share some of my thoughts for the next two years under the leadership of our new President, Prof. Aiping Lu.

Establishment of Secretariat Office An important milestone during my presidency was the establishment of the Secretariat office at Institute of Chinese Medicine, The Chinese University of Hong Kong, with Dr Grace Yue appointed as paid part-time secretariat staff to assist Secretary-General Clara Lau in coordinating the evergrowing activities of GP-TCM RA:

- Hosting 15 BoD Skype teleconferences, one of them was a face-to-face meeting held at Kew in July 2018.
- · Renewing membership and updating membership database
- Maintaining and updating website http://www.gp-tcm.org (linked to World Journal of Traditional Chinese Medicine since early 2018 and regularly uploaded newsletters)
- Disseminating newsletters (by sending mass email to all members)
- With the New Data Protection Act effective from May 2018, email messages with various reminders had been sent out to all members requesting their acceptance receiving any future emails from the Association. For those members who did not reply, they would no longer receive the newsletters distributed by emails from September 2018 onwards.

Revision of Bylaws At the GP-TCM RA, we pride ourselves for our collective efforts in good practice. Thus, a working group was formed (comprising of Rudi Bauer, Rob Verpoorte, Qihe Xu, Clara Lau, Monique Simmonds and I) to review how much we have adhered to, or deviated from, our Bylaws. This exercise led to the complete revision of Bylaws in September 2018, and approved by the entire membership via email.





6th GP-TCM RA Annual meeting held at Royal Botanic Gardens, Kew and LSBU, UK (**Left**); Annual General Meeting 4 July 2018, Jodrell Laboratory, Royal Botanic Gardens, Kew, London, UK (**Right**).

Invigorating Interest Groups To capitalize on the wide-ranging talent pool of our members, more GP-TCM RA members (other than BoD members) have been invited to serve as chairs and co-chairs for the 6 Interest Groups.

- i. Quality Control Chair & Co-chair: Kelvin Chan, Christine Leon
- ii. Pharmacology & Toxicology Chair & Co-chair: Pierre Duez, Kevin Hongxi Xu
- iii. Regulatory Aspects Chair & Co-chair: Gerhard Franz, Mei Wang
- iv. Clinical Studies Chair & Co-chair: Zhaoxiang Bian, Myeong Soo Lee
- v. Acupuncture Chair & Co-chair: Nicola Robinson, Lixing Lao



vi. Publication - Chair & Co-chair: Robert Verpoorte, Thomas Efferth

Global participation and influences To widen the global footprint of the GP-TCM RA, I co-organised a TCM Roundtable meeting "Possible Synergies between Western and Traditional Chinese Medicines" in Prague on 23 February 2017 under the auspices of the Czech Ministry of Health. Our team was strengthened by the participation of Prof. Tommy Yung-Chi Cheng (Chairman of CGCM), Prof. Gerhard Franz (Chairman of EDQM TCM Working Party), Prof. Mei Wang (Leiden University) and Prof. Jean-Pierre Armand (Gustave Roussy Paris), contributing significantly to the legislation of TCM in the Czech healthcare system in June 2017. As part of the First Cambridge Belt and Road Initiative International Conference, I also organised a one-day forum "Future Trends in Global Healthcare: Fusion of Traditional Medicines and Modern Technologies" on 7 July 2018, featuring UCLA Center for East-West Medicine, as well as traditional medicines from Africa and India.



Improving services to our members

- Creating a new membership category: Institutional members (membership
 fee same as Corporate Members). If an Institutional Member has difficulties in paying the membership fee,
 the fee can be exempted upon approval by the Board of Directors. This resolution is specifically aimed at
 maintaining the largest numbers of academic institutions worldwide whose active participation is critical to
 the future success of our Association. Thus, over the coming months, some ex-Corporate Members may be
 re-instated as Institutional Members when they re-apply to renew their status.
- For new industrial partners, we now have *Infinitus*, *Dalian Fusheng*, *Hutchison Whampoa Guangzhou Baiyunshan*. *Zhejiang University* and *Heilongjiang University* of TCM have joined while two universities of TCM (Nanjing and Zhejiang) are being actively recruited.
- As benefits to Corporate members, online training programmes on regulatory issues and good practices which lead to the issue of certificates should be considered as future initiatives.
- Rob Verpoorte has recently proposed courses on "Production of Phytomedicines for the Global Market" and GxP course. Details for implementation are being discussed and the course will be launched in Spring 2020.

Future prospective developments of GP-TCM RA As of November 2018, we have 150 members, including ordinary full members, life members, student members, honorary members and corporate members. To be a global champion of TCM, we certainly need more active members. Thus, I would like to urge new President Aiping Lu and the new BoD to re-engage former members and enthuse new ones, aiming to double the membership number by December 2020.

The postponement of the 6th GP-TCM RA Annual Meeting at the Royal Botanic Gardens, Kew (UK) from July 2017 to July 2018 was a disappointment to the BoD and many members. To prevent this from happening again, the BoD has now set up a Standard Operating Procedure on inviting, scrutinizing and accepting bids to host



future meetings. A contingency plan should also be in place. I am particularly pleased that the planning of the 7th GP-TCM RA Annual meeting in 2019 (hosted by NIKOM in South Korea) is in progress, and discussions on the 8th GP-TCM RA Annual meeting in 2020 (hosted by Vytautas Magnus University in Kaunas, Lithuania) has been initiated.

Summing up This has been a term of presidency (January 2017 to December 2018) that I shall look back with gratitude, pride and undiluted pleasure. I would like to thank all the BoD members, particularly Clara Lau (Secretary-General) and Qihe Xu (Editor-in-chief of Newsletter) for their exemplary professionalism and comradeship. My very best wishes go to Aiping Lu, our New President, who I strongly believe, will lead our Association to new heights.

Finally, on behalf of the out-going BoD, I would like to wish you all—

Merry Christmas and Happy New Year!



Special Features

1. Introducing the Board of Directors (BoD) of the GP-TCM RA (2019-2022). From 1st Jan. 2019, Prof. Aiping Lu will become President and chairman of the BoD, while President Dr Tai-Ping Fan will become Past President, who will join Prof. Monique Simmonds, President-elect, to serve as Vice-Presidents. In addition to elected BoD members, Prof. Rudolf Bauer, Prof. Kelvin Chan, Prof. Pierre Duez, Prof. Thomas Efferth, Prof. Clara Bik-San Lau, Prof. Rob Verpoorte, Prof. Vivian Taam Wong and Dr. Qihe Xu, Prof. Peter Hylands (Treasurer) and Mr Abraham Chan (Industrial Representative) have been co-opted into the BoD at the 36th BoD teleconference on 23 Nov. 2018. More BoD members could be co-opted upon needs at future BoD meetings.



2. The 7th Annual Meeting of GP-TCM RA will be held in Daegu Haany University (DHU), Daegu City, Republic of Korea, on July 9th – 10th, 2019. The meeting will be jointly hosted by National Development Institute of Korean Medicine(NIKOM) and DHU. Don't miss this great chance to experience Daegu with an exciting conference programme and rhe networking opportunities!







Left: NIKOM; Middle: DHU; Right: Venue at DHU (Https://Goo.Gl/Maps/9ujccwriyrz)

3. Warmest congratulations to Prof. Olavi Pelkonen, Member of the GP-TCM RA Newsletter Editorial Board, for being awarded an Honorary Doctoral Degree of Semmelweis

University, Budapest, Hungary. The Award Ceremony was held on on 16.11.2018. Prof. Olavi Pelkonen (Department of Pharmacology, University of Oulu, Finland) Olavi received the honour together with seven other internationally well-recognized scientists, including Prof Jianguang Xu, President of the Shanghai University of TCM. Olavi has decades-long collaboration with Hungarian scientists at Semmelweis and other Universities and the Hungarian drug industry.

http://semmelweis.hu/english/news/2018/11/eight-professors-receive-semmelweis-universitys-doctor-honoris-causa-award/





4. Warmest congratulations to Prof. Jing Yan Han, Co-Editor-in-chief of the World Journal of Traditional Chinese Medicine, the official journal of the GP-TCM RA, and Member of the GP-TCM RA Newsletter Editorial Board, for being awarded a tier-1 Prize of the Chinese Society of Integrated Medicine for his research on mechanisms of the TCM formula Qishenyiqi Dripping Pills in treating heart diseases.

http://www.stdaily.com/02/difangyaowen/2018-

12/19/content 740965.shtml (中文)



European Reports:

1. Council Endorses Agreement on EU Budget for 2019. On Friday 20 Nov. 2018, the European Commission proposed its second draft EU budget for 2019, which includes, €12.5 billion for Horizon 2020 and €2.73 billion for Erasmus+. With the imperative of reaching a timely adoption of the 2019 budget, the Commission's proposal for a second draft budget for 2019 builds on the progress made in that committee, with some significant reinforcements in commitment appropriations for key programmes contributing to growth and jobs such as Erasmus+ and the Youth Employment Initiative. Overall, the proposed 2019 EU budget amounts to €166 billion in commitments (the total amount the EU is allowed to spend) and €149 billion in payments (actual amount the EU needs to pay in a given year to the beneficiaries of its funds). On 11 December 2018, the Council of Ministers has endorsed the provisional agreement with the European Parliament on EU budget for 2019, thus bringing the EU a step closer to having a budget for next year. On 12 December, the European Parliament also formally adopted the budget for 2019 at its plenary session.

Why is this relevant for Horizon 2020? The so-called 'commitment appropriations' are the maximum amounts the European Commission is allowed to sign new contracts for in a given year with beneficiaries of its funds (i.e. Horizon 2020 grant agreements). The higher the commitment appropriations, the more projects the Commission will be able to fund, thus reducing the problem of oversubscription in the programme.

https://eur-lex.europa.eu/budget/data/DB2/2019/en/SEC00.pdf

2. Horizon Europe – What Will It Look Like? Horizon Europe will keep the three-pillar structure, but can say good-bye to 'Societal Challenges' and hello to 'Clusters'.

Pillar I 'Excellent Science'

- European Research Council (ERC)
- Marie Skłodowska-Curie Actions (MSCA)
- Research Infrastructure

Pillar II 'Global Challenges and European Industrial Competitiveness'

- a) Cluster 'Health'
- b) Cluster 'Culture and Inclusive Society'
- c) Cluster 'Civil Security for Society'
- d) Cluster 'Digital, Industry and Space'
- e) Cluster 'Climate and Energy'
- ee) Cluster "Mobility"
- f) Cluster 'Bio economy, Food, Natural Resources and Environment'
- g) Cluster 'Non-nuclear Direct Actions of the Joint Research Centre (JRC)'

Social sciences and humanities (SSH) shall play an important role across all seven clusters. The proposed Missions will principally be realised within Pillar II, though they may also benefit from actions carried out within other parts of the programme. The Missions themselves will be defined and implemented in accordance with the Specific Programme, thereby ensuring early involvement of the Member States.





Pillar III 'Innovative Europe'

- a) European Innovation Council (EIC)
- b) European Innovation Ecosystems
- c) European Institute of Innovation and Technology (EIT)

Part 'Widening participation and strengthening the European Research Area'

- a) Widening Participation and Sharing Excellence
- b) Reforming and Enhancing the European Research and Innovation System

3. EC phase out the Participant Portal and replace it by the Funding & Tenders Portal.

https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/home





1. The first "vertical forest" community is being built in Chengdu. (People's Daily Online), November 23, 2018. On Nov. 23, the construction of a new residential community in Xindu District of Chengdu was in full swing. The residential area is the first fourth-generation housing project in China. The balcony of each apartment is home to a private garden, complete with greenery which looks impressive from above, and is also the first "vertical forest" residential community in the area. This generation of housing focuses on increasing the flat area available for planting, raising the rate of greenery and finding new space for the growth of plants, therefore developing vertical greening has become a useful measure to improve the ecological environment of modern cities. http://en.people.cn/n3/2018/1123/c90000-9521642.html

2. **UK** and Chinese ministers celebrate 40th anniversary of scientific relations - GOV.UK. On 28 November, the 9th biennial UK-China Joint Commission on Cooperation in Science, Technology and Innovation brought a delegation of senior Chinese officials to London led by the Vice-Minister of Science and Technology, Zhang Jianguo. Meeting with the Minister of State for Universities, Science, Research and Innovation Sam Gyimah, UK government and academic leaders, they jointly celebrated successes to date and mapped out collaboration for the coming years. The UK and China are established science and innovation partners, November 2018 marks four

The UK and China are established science and innovation partners, November 2018 marks four decades since the first bilateral scientific treaty was signed between the UK and China...

https://www.gov.uk/government/news/uk-and-chinese-ministers-celebrate-40th-anniversary-of-scientific-relations

http://www.most.gov.cn/kjbgz/201812/t20181205 143978.htm (中文)

3. **CRISPR babies:** "Following Dr He Jiankui's announcement that he genetically modified human embryos, he has been condemned by Chinese health officials and is facing investigation by the Chinese Ministry of Science and Technology amongst others. The implantation of gene-edited embryos is considered illegal in China. Former Vice Minister of Health Dr. Huang Jiefu called for the establishment of a central authority and complete legal system to supervise bioscience experiments in China. China is moving towards the implementation of international guidelines, having become a member of the International Council for Harmonization in 2017." Science and Innovation Network China reports.

4. Healthy ageing a priority for UK-China collaboration in 2019. "On 28 November, the 9th biennial UK-China Joint Commission on Cooperation in Science, Technology and Innovation was held in London, landing on the UK and China's 40th anniversary of science collaboration. At the meeting, former Science Minister Sam Gyimah met with Chinese Vice-Minister for Science & Technology, Zhang Jianguo, to set out strategic approaches for new areas of collaboration. The ministers



announced healthy ageing as the Flagship Challenge for 2019 under the UK-China Joint Strategy for Science, Technology and Innovation Cooperation. "Science and Innovation Network China reports. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/66 5199/uk-china-strategy-science-technology-innovation-cooperation.pdf

5. Oxford and Cambridge universities both opened research centres in China in November 2018. The Cambridge-Nanjing Centre of Technology and Innovation is the university's first enterprise outside the UK at this scale. OSCAR, the Oxford-Suzhou Centre for Advanced Research, is Oxford's first overseas centre for physical science and engineering research. Science and Innovation Network China reports.

http://english.nanjing.gov.cn/govaffairs/newsevents/201811/t20181106_5835700.html https://oscar.web.ox.ac.uk

6. Schiermeier Q. China backs bold plan to tear down journal paywalls. *Nature* 2018;564:171-2. Officials pledge support for European-led 'Plan S' to make research papers immediately free to read — but it's unclear whether China will adopt all the plan's policies...

https://www.nature.com/articles/d41586-018-07659-5?WT.ec_id=NATURE-20181213&utm

7. **Nature Index 2018 China.** China's rise is the story of the century in science. Its scientific output has already overtaken that of the United States, but on measures of quality, such as articles published in the high-quality journals tracked by the Nature Index, it still has a big gap to close. Some exceptional disciplines, though, are leading the way to overcoming the quality deficit. https://www.nature.com/collections/brmrwyvdvp?WT.ec id=NATURE-20181213&utm



Top 50 Chinese institutions:

https://www.natureindex.com/supplements/nature-index-2018-china/tables/overall

Top 50 Chinese institutions in Chemistry:

https://www.natureindex.com/supplements/nature-index-2018-china/tables/chemistry

Top 50 Chinese institutions in Earth & Environmental sciences: https://www.natureindex.com/supplements/nature-index-2018-china/tables/earth-and-environmental-sciences

Top 50 Chinese institutions in Life Sciences:

https://www.natureindex.com/supplements/nature-index-2018-china/tables/life-sciences
Top 50 Chinese institutions in Physical Sciences:

https://www.natureindex.com/supplements/nature-index-2018-china/tables/physical-sciences

8. China approves snake venom antimicrobial peptide cathelicidin-BF as novel antibiotic: Related research by Ren Lai's laboratory in Yunnan, China.

http://www.kiz.ac.cn/xwzx/kydt/201812/t20181214 5212325.html (中文)

https://pubs.acs.org/doi/abs/10.1021/acs.jmedchem.5b01264

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0003217

9. Zhang Z. Chinese Pharmaceutical industry in the past 40 years illustrated in 15 graphs. Saibolan WeChat. 11th September 2018.

https://mp.weixin.gq.com/s/KH74vov1yGwGT46ABPTc5A(中文)

Acupuncture, TCM and other traditional medicine

1. Li Ke. **TCM Yang-tonic intervention before disease arises.** *Yi Dao Liu Fang WeChat Platform.* 1st December 2018. Mr Li Ke, a famous senior TCM practitioner of the Shanxi Province, China, emphasises that "intervention before disease arises" is a strategic feature of TCM and Yang-tonic TCM therapies hold the key in this both strategically and in practice.





https://mp.weixin.qq.com/s/I7CqdyDw9zLiD672dneFHw (中文)

2. Are medicinal plants the fresher (more preserved) the better? The following links contain an appendix enlisting 64 freshly prepared herbal drugs according to the Chinese Pharmacopoeia 2015 and the discussions on the six classical "preserved" herbal medicines and more.

The fresher the better? https://mp.weixin.qq.com/s/-WAX2pm3Aftz095phHbsmQ (中文)

The more preserved the better? https://mp.weixin.qq.com/s/a SV6 -YU2A26JJVfF0vnw (中文)

3. Hershman DL, et al. Effect of Acupuncture vs Sham Acupuncture or Waitlist Control on Joint Pain Related to Aromatase Inhibitors Among Women With Early-Stage Breast Cancer: A Randomized Clinical Trial. JAMA. 2018;320:167-176. CONCLUSIONS: Among postmenopausal women with early-stage breast cancer and aromatase inhibitor-related arthralgias, true acupuncture compared with sham acupuncture or with waitlist control resulted in a statistically significant reduction in joint pain at 6 weeks, although the observed improvement was of uncertain clinical importance. https://www.ncbi.nlm.nih.gov/pubmed/29998338

Comments by Liu C et al: https://www.ncbi.nlm.nih.gov/pubmed/30512093
Comments by Mao JJ et al: https://www.ncbi.nlm.nih.gov/pubmed/30512093
Reply by Hershman DL et al: https://www.ncbi.nlm.nih.gov/pubmed/30512093

4. A TCM special issue of the Chinese Journal of Evidence-based Medicine. 2018;18(11).

https://mp.weixin.qq.com/s/k3xJI59PUB my w5TxjeCA (中文)

* Now 5. Li J. et **Production of plant**specific flavones baicalein and scutellarein in an engineered E. coli from available phenylalanine and tyrosin e. Metab Eng. 2018 Nov 26. pii: S1096-7176(18)30332-X. Baicalein and scutellarein are bioactive flavones found medicinal plant Scutellaria baicalensis Georgi, used in TCM. Extensive previous work has demonstrated the broad biological activity of these flavonoids, such as antifibrotic, antiviral and anticancer properties. However, their supply from plant material is insufficient to meet demand. Here, to provide an



alternative production source and increase production levels of these flavones, we engineered an artificial pathway in an Escherichia coli cell factory for the first time... https://www.sciencedirect.com/science/article/pii/S109671761830332X?via%3Dihub

6. Lin L, et al. **Fighting Liver Fibrosis with Naturally Occurring Antioxidants.** *Planta Med.* 2018;84:1318-1333. In this review, the pathogenesis of liver fibrosis and the role of oxidative stress in liver fibrosis were discussed. Naturally occurring antioxidants that can treat and prevent liver fibrosis were summarized. Advances in clinical trials were also presented. The main purpose of this review is to provide a comprehensive and up-to-date knowledge from the biological importance of oxidative stress in liver fibrosis to representative antioxidants for treating liver fibrosis. Naturally occurring antioxidants show a potential for further investigations as lead compounds in fighting liver fibrosis.

https://www.thieme-connect.com/products/ejournals/abstract/10.1055/a-0757-0008

7. Academician Prof. Huang Luqi appointed President of the China Academy of Chinese Medical Sciences. https://mp.weixin.qq.com/s/EPIY7ZPeDI wcKwO6xIOBQ (中文)

8. China's State Administration of TCM nominated leading TCM researchers, including many GP-TCM RA members, as Qihuang Scholars:

https://mp.weixin.qq.com/s/W-HT45KORNfzMZrgayO_NQ (中文)



9. Gale J & Yuan H. Chinese Soup Ingredients May Hold Key to Fighting Dementia (Bloomberg)... The resulting blend of ginkgo biloba, ginseng and saffron extracts, called Sailuotong or SLT, is due to enter a late-stage study in Melbourne this month, and a larger clinical trial to validate its impact is slated to begin in China later this year...

https://www.bloomberg.com/news/articles/2018-09-26/key-to-fighting-dementia-may-lie-at-bottom-ofchinese-soup-pot

10. Dr Tang Tiejun: On the Academic Thoughts of TCM Master Professor Deng Tietao. New York TCM Forum. 9th December 2018: https://mp.weixin.qq.com/s/ozRHp0ITsJLcAHXaqfYrMq (中文)

11. 182 TCM formulae authoritatively illustrated – the free-access HKBU TCM Formulae Image Database created by Professor Hubio Chan Group.

http://lib-nt2.hkbu.edu.hk/database/cmed/cmfid/index.asp?lang=eng https://www.toutiao.com/i6634671147784864263/?iid=53264082866&app =news article (中文)

12. Information of 350 TCM decoction pieces charted: Source materials, nature, functions, clinical indications and usage.

https://mp.weixin.gg.com/s/vgx7IQ48BzEkniPpvHtvMA (中文)

13. Role for calligraphy in TCM:

https://mp.weixin.gg.com/s/5HoRBX8ACPd2BhIUIO2n5g (中文)



1. Shen MW et al. Predictable and precise template-free CRISPR editing of pathogenic variants. Nature 2018; 563:646-651. Following Cas9 cleavage, DNA repair without a donor template is generally considered stochastic, heterogeneous and impractical beyond gene disruption. Here, we show that template-free Cas9 editing is predictable and capable of precise repair to a predicted genotype, enabling correction of disease-associated mutations in humans. We constructed a library of 2,000 Cas9 guide RNAs paired with DNA target sites and trained inDelphi, a machine learning model that predicts genotypes and frequencies of 1- to 60-base-pair deletions and 1-base-pair insertions with high accuracy (r = 0.87) in five human and mouse cell lines. inDelphi predicts that 5-11% of Cas9 guide RNAs targeting the human genome are 'precise-50', vielding a single genotype comprising greater than or equal to 50% of all major editing products. We experimentally confirmed precise-50 insertions and deletions in 195 human diseaserelevant alleles, including correction in primary patient-derived fibroblasts of pathogenic alleles to wild-type genotype for Hermansky-Pudlak syndrome and Menkes disease. This study establishes an approach for precise, template-free genome editing. https://www.nature.com/articles/s41586-018-0686-x

2. Azvolinsky A. Fathers Can Pass Mitochondrial DNA to Children. The Scientist Dec 4, 2018. Typically, humans inherit mitochondria and mitochondrial DNA from their mothers only. But using sequencing data from the mitochondrial genomes of members from three unrelated families, researchers have identified 17 individuals who inherited mtDNA from both parents. The results were published last week (November 26) in PNAS (S. Luo et al., "Biparental inheritance of mitochondrial DNA in humans." *PNAS*.https://doi.org/10.1073/pnas.1810946115. 2018)...

https://www.the-scientist.com/news-opinion/fathers-can-pass-mitochondrial-dna-to-children-65165?utm

Other Recommended Reading

1. Coiera E. The fate of medicine in the time of Al. Lancet 2018;392: 2331-2332. What does it mean to be a doctor? Is it still medicine we practise when a machine knows better than us our



patient's diagnosis, treatment, or fate? Would the hand we hold at the bedside still be reassured by our words and care? It remains hard to predict when artificial intelligence (AI) will become so powerful that it outreasons human beings. Some see that day arriving soon, and extreme predictions see whole disciplines like radiology or dermatology disappearing, replaced by AI. The truth is much less clear. The prospect of AI is a Rorschach blot upon which many transfer their technological dreams or anxieties. That AI is improving is not in question...

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31925-1/fulltext

2. Kroemer G et al. Carbotoxicity—Noxious Effects of Carbohydrates. *Cell* 2018;175: 605-

14. Modern nutrition is often characterized by the excessive intake of different types of carbohydrates ranging from digestible polysaccharides to refined sugars that collectively mediate noxious effects on human health, a phenomenon that we refer to as "carbotoxicity." Epidemiological and experimental evidence combined with clinical intervention trials underscore the negative impact of excessive carbohydrate uptake, as well as the beneficial effects of reducing carbs in the diet. We discuss the molecular, cellular, and neuroendocrine mechanisms that link exaggerated carbohydrate intake to disease and accelerated aging as we outline dietary and pharmacologic strategies to combat carbotoxicity.

https://www.cell.com/cell/fulltext/S0092-8674(18)30972-3

3. Canada clinical trial on personalised medicine for prostate cancer. European Pharmaceutical Review. 28 November 2018. A clinical trial could be the world's first to look at personalised medicine in prostate cancer, with patients taking a therapy

based on their DNA markers...https://www.europeanpharmaceuticalreview.com/news/81729/can

ada-clinical-trial-on-personalised-medicine-for-prostate-cancer/

Fox MD Frontiers in Medicine: Manning Symptoms to Brain

4. Fox MD. Frontiers in Medicine: Mapping Symptoms to Brain Networks with the Human Connectome. *N Engl J Med* 2018;379:2237-2245. Complex neurologic and psychiatric syndromes cannot be understood on the basis of focal brain lesions. Functional neuroimaging, maps of interrelated regions called the connectome, and the combination of lesion analysis with networks of the connectome offer a new way to understand neurologic function and disease...

https://www.nejm.org/doi/full/10.1056/NEJMra1706158?query=TOC

5. The Scientist Staff. **2018 Top 10 innovations.** *The Scientist* 1st December 2018. Biology happens on many levels, from ecosystems to electron transport chains. These tools may help spur discoveries at all of life's scales: Cyto-Mine, Tapestri Precision Genomics Platform, Fluidity One, Chromium Immune Repertoire Profiling Solution, Omnitrap, AcouWash, Dharmacon Edit-R Fluorescent Cas9 Nuclease mRNA, MAD7, Tycho NT.6 and BD AbSeq Assay. https://www.the-scientist.com/features/2018-top-10-innovations-65140

6. Goodman SN. **How sure are you of your result? Put a number on it.** *Nature* 2018;564:7. Picture our bafflement if weather forecasts said, "There is a non-statistically significant chance of rain tomorrow," rather than, "There is a 60% chance of rain." Or the confusion among Florida residents if, instead of being told, "Tallahassee has an 85% chance of a direct hit by Hurricane Michael," they heard: "Tallahassee will be hit, P = 0.03." When the stakes are high, we need accurate and understandable risk estimates to make informed decisions. We demand that weather services clearly convey the chance of rain or hurricane, because lives and livelihoods are at stake. That's why forecasts distil immensely complex models into one number. Scientists should do the same... https://www.nature.com/magazine-assets/d41586-018-07589-2/d41586-018-07589-2.pdf

7. Framework for FDA's Real-World Evidence Program, December 2018. The 21st Century Cures Act (Cures Act), signed into law on December 13, 2016, is designed to accelerate medical product development and bring new innovations and advances faster and more efficiently to the



patients who need them. Among other provisions, the Cures Act added section 505F to the Federal Food, Drug, and Cosmetic Act (FD&C Act). Pursuant to this section, the Food and Drug Administration (FDA) has created a framework for evaluating the potential use of real-world evidence (RWE) to help support the approval of a new indication for a drug already approved under section 505(c) of the FD&C Act or to help support or satisfy drug postapproval study requirements. In addition to drug and biological products approved under section 505(c), this framework is also intended for application to biological products licensed under the Public Health Service Act...

https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RealWorldEvidence/UCM627769.pdf https://mp.weixin.qq.com/s/Uatj9-yTRf48MXzsKgHPig (中文)

8. A Nature Guideline on Reporting Life Sciences Research: This non-exhaustive list summarizes several elements of methodology that are frequently poorly reported. Inconsistent reporting may lead to incorrect interpretation of results and a lack of reproducibility. To improve the transparency and the reproducibility of published results, *Nature* ask that authors include in their manuscripts relevant details about these elements of their experimental design. https://www.nature.com/documents/nr-reporting-life-sciences-research.pdf

9. The 2018 Altmetric top 100. In the past year, Altmetric has tracked over 25 million mentions

of 2.8 million research outputs. This page highlights the top 100 most-mentioned scholarly articles published in the past year – those which have truly captured the public imagination. Among the top 100, scientists from USA, UK, and Australia contributed 72, 29 and 17, respectively. Scientists from China contributed to 11 of the top 100.

https://www.altmetric.com/top100/2018/

https://www.linkresearcher.com/information/c1fc1d2a-adc6-47fa-89cf-8b822ae11533 (中文)

10. A brief history of the British tea culture unveiled by the British Library.

https://mp.weixin.qq.com/s/hQuRieyd9PnYZdyF7q0rUA (中文)

11. Guyton KZ et al. **Key Characteristics Approach to Carcinogenic Hazard Identification.** *Chem Res Toxicol* 2018;31:1290–2. Evaluating carcinogenic mechanisms is a challenging part of hazard identification, as mechanistic data are both voluminous and diverse. An evaluation approach based on 10 key characteristics of human carcinogens provides a holistic and unbiased way to https://pubs.acs.org/doi/10.1021/acs.chemrestox.8b00321



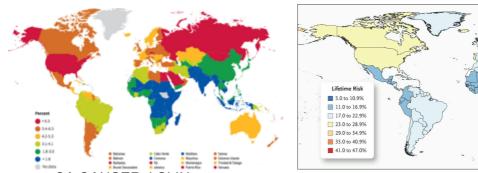
tackle this challenge.

12. Sung H et al. **Global patterns in excess body weight and the associated cancer burden.** *CA CANCER J CLIN* 2018;0:1–25. The prevalence of excess body weight and the associated cancer burden have been rising over the past several decades globally. Between 1975 and 2016, the prevalence of excess body weight in adults—defined as a body mass index (BMI) ≥ 25 kg/m²—increased from nearly 21% in men and 24% in women to approximately 40% in both sexes. Notably, the prevalence of obesity (BMI ≥ 30 kg/m²) quadrupled in men, from 3% to 12%, and more than doubled in women, from 7% to 16%. This change, combined with population growth, resulted in a more than 6-fold increase in the number of obese adults, from 100 to 671 million. The largest absolute increase in obesity occurred among men and boys in high-income Western countries and among women and girls in Central Asia, the Middle East, and North Africa. The simultaneous rise in excess body weight in almost all countries is thought to be driven largely by changes in the global food system, which promotes energy-dense, nutrient-poor foods, alongside reduced opportunities for physical activity. In 2012, excess body weight accounted for approximately 3.9% of all cancers (544,300 cases) with proportion varying from less than 1% in low-income countries to 7% or 8% in



some high-income Western countries and in Middle Eastern and Northern African countries. The attributable burden by sex was higher for women (368,500 cases) than for men (175,800 cases)... https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21499 https://mp.weixin.qq.com/s/1Awwq1VaFDTxmTZgkr6dFQ (中文)

13. The GBD 2016 Lifetime Risk of Stroke Collaborators. **Global, Regional, and Country-Specific Lifetime Risks of Stroke, 1990 and 2016.** *N Engl J Med* 2018; 379:2429-2437. In 2016, the global lifetime risk of stroke from the age of 25 years onward was approximately 25% among both men and women. There was geographic variation in the lifetime risk of stroke, with the highest risks in East Asia, Central Europe, and Eastern Europe. https://www.nejm.org/doi/full/10.1056/NEJMoa1804492



Left. *CA CANCER J CLIN*: International variation in proportion of cancer cases attributable to overweight. **Right.** NEJM reports global risks of stroke 2009-2016, highlighting China is a hot spot.

14. Till BM, et al. Who is pirating medical literature? A bibliometric review of 28 million Sci-Hub downloads. Lancet Glob Health 2018;7:e30-e31. Our analysis illuminates the large volume of medical literature being downloaded illegally in nearly all countries of the world. A significant relation exists between the nation of origin and the density of these requests. This continued inequity in legal access to the medical literature demands the attention of both the publishing industry and policymakers. https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(18)30388-7/fulltext

15. Nature's 10: Ten People who mattered in 2018.

https://www.nature.com/immersive/d41586-018-07683-5/index.html https://mp.weixin.qq.com/s/oO3JLXj36BKPH1C19fXHzA

Meeting Reports

1. The 2nd International Conference on DNA technology for authentication, quality control and conservation of herbal material was held in Hong Kong on 2-5 December 2018. Organized by Li Dak Sum Yip Yio Chin R&D Centre for Chinese Medicine, The Chinese University of Hong Kong, the conference focusd on 3 themes: a) DNA Barcodes – development and application; b) New DNA technology; c) Genome and database. Around 100 participants attended the conference. GP-TCM RA board members Prof Monique Simmonds, Prof Clara Lau and Prof Kelvin Chan attended the meeting.







Left: Photo taken at the conference opening ceremony (from right to left: Prof PC Shaw, Prof Fanny Cheung, Dr Edwin Tsui, Prof Clara Lau, Prof ZX Lin and Dr Stanley Cheung); **middle:** Prof Monique Simmonds was invited to give a talk; **right:** Prof Kelvin Chan gave his talk.



3. The WFCMS TCM Diagnosis Specialty Committee held its 5th Annual Meeting in Changsha, Hunan, China, on 30th November to 2nd December 2018. https://mp.weixin.qq.com/s/0KEWJV2m5QleC6cujkXUqqc (中文)







4. 1st WFCMS TCM Science Conference and International Contribution Award (Scientific & Technological Advance) Ceremony were successfully held in Hangzhou, Zhejiang, China on 8th December 2018. https://mp.weixin.qq.com/s/2TMvFmnikQ9iNVurzuMkBw (中文)









5. The 6th World Integrative Medicine Congress was held in Shanghai, China, 6-9 Dec. **2018**. Programme of the meeting can be found here: http://www.wimco2018.com.cn/weben2018/

Invitation from future meetings

1. The 7th Annual Meeting of GP-TCM RA will be held in Daegu Haany University (DHU), Daegu City, Republic of Korea, on July 9th – 10th, 2019. The meeting will be jointly hosted by National Development Institute of Korean Medicine(NIKOM) and DHU. Don't miss this great chance to experience Daegu with an exciting conference programme and rhe networking opportunities!







Left: NIKOM; Middle: DHU; Right: Venue at DHU (Https://Goo.Gl/Maps/9ujccwriyrz)

2. **2019** *The Lancet*–CAMS Health Conference: a call for abstracts. The Chinese Academy of Medical Sciences (CAMS) and the *Lancet* family of journals invite abstract submissions for the 2019 *The Lancet*–CAMS Health Conference, to be held on Oct 19–20, 2019, in Chengdu, China. West China Hospital, Sichuan University, will be the local co-organiser with CAMS in Chengdu. 2019 will mark the fifth collaborative conference between CAMS and the *Lancet* family of journals to support medical research in China. Abstracts must be relevant to health science in China and at least one author must be based at an institution in China. Submissions are invited from all aspects of medical research,...

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33176-3/fulltext

3. The 16th World Congress of Chinese Medicine will be held in Budapest, Hungary, in November 2019: https://a.eqxiu.com/s/1BpDHw7h (中文)



Invitation from journals

1. **Health-care reform in China:** a *Lancet* call for papers. In 2009, China unveiled its ambitious health-care reform plan, with the goal of provision of affordable and equitable basic health care for all by 2020. The reform is anchored in five interdependent areas: expanding coverage to insure more than 90% of the population, establishing a national essential medicines system, improving the primary care system, making public health services available and equal for all, and public hospital reforms. How has China changed since the 2009 health-care reform?

In 2019, *The Lancet* will dedicate a theme issue to evaluate the progress of health-care reform in China on its tenth anniversary. The 2019 China theme issue will be launched at *The Lancet*–Chinese Academy of Medical Sciences Health Conference in Chengdu, China, on Oct 19–20, 2019. While we welcome submissions from China throughout the year and across all *Lancet* family journals, the editors invite submissions of high-quality research from China—or from research teams working on health in China—for this issue.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)33054-X/fulltext

2. 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

Great news! Since November 2018, WJTCM has been included in the list of core Chinese scientific journals and magazines! https://mp.weixin.gq.com/s/r5BAEi8uinIpxi0QvhapMA (中文)





3. 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

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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).

