

Special Feature

⁴⁴⁴1. The 6th Annual Meeting of the Good Practice in Traditional Chinese Medicine Research Association (GP-TCM RA) will be held on 4th - 6th July 2018 in Royal Botanic Gardens, Kew and London South Bank University, United Kingdom.

The meeting aims to address the current challenges and opportunities that face the global development of traditional Chinese medicine (TCM) and will be highlighted by the following themes:

- Good practices (GxPs) in TCM research;
- International celebration of the 500th anniversary of Li Shizhen's birth in 1518;
- State of the art in clinical and acupuncture research;

The programme has been designed to address the key areas that impact TCM:

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

Registration will be open on 10th February 2018



The 6th Annual Meeting of Good Practice in Traditional Chinese Medicine Research Association Second Announcement





Editorials

1. From biopiracy to fair access and benefit sharing of natural resources



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Our modern view of the world is mainly coined by knowledge gained from life sciences. In contrast to former ages, approaches to interpret the world by the humanities lost at least in part their former relevance. The same took place in medicine. Modern technology-driven treatment concepts are dominating. In traditional medicine, mystical elements lost more and more ground. The use of medicinal plants, which relies on century- to millennia-old experience-based knowledge of indigenous tribes and communities is nowadays supported by pharmacological research to understand the chemical and cellular principles of action. The advancements in life sciences in general and specifically in medicinal plant research raise the question, whom the knowledge belongs to. One might get into a dilemma, if knowledge about the therapeutic potential of biological resources is patented and commercially exploited. Debates on bio-patenting reached central relevance in numerous disciplines in pharmaceutical sciences, but also beyond, *e.g.* in agriculture, nutritional sciences, botany, zoology, microbiology, biotechnology, gene technology, etc. As this topic affects many aspects of everyday life, it cannot be adequately understood without simultaneous interdisciplinary discourses of juridical, ethical and cultural perspectives.

Prior to 1980, the US-American courts in USA interpreted the patent statute in a way that living organisms *per se* represent products of nature and are, therefore, not patentable. However, non-naturally occurring purities, concentrations or combinations of these substances are conditionally patentable. Considerable efforts of the United Nations were necessary to issue the Convention on Biological Diversity (CBD) in 1992. The idea was to find political consensus to stop the exploitative use of biodiversity without including the countries or regions of origin. Around the globe, 196 member countries agreed that biological resources belong to the country of their origin. While there is consensus about that, the situation is less clear in cases, where biological materials have been modified with knowledge derived from other sources than the countries of origin.

In 2010, the Nagoya Protocol (NP) regulated the access to biological resources in combination with benefit sharing deriving from their commercial use. The main aim of the Nagoya Protocol was to regulate research and development for commercial uses. Nevertheless, many regulations also apply to non-profit-oriented basic research in academia. While it sounds straightforward to regulate access of biological resources by the countries of origin and sharing commercial benefits from those, who receive the resources and generate marketed products, it may pose considerable problems in individual cases. As academic research is mainly paid by public funding, *i.e.* the tax payer, scientists

are bound to international regulations. In the EU, additional regulations demand an obligatory declaration of *due diligence* by the researcher. Although commercial and industrial applications may be separately discussed from more basic investigations performed in academia, the European Commission proposed to consider any kind of research on biological resources as potential basis of a production chain ultimately resulting in commercial products. Therefore, the Commission proposed the corresponding formal procedures for registration and control to any kind of research. All biological materials as well as products derived from them belong to the countries of origin and must not be used without permission (CBD Art. 15). A key role of violations related to access and benefit sharing is linked to historical exploitations without



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recognition of local rights, regulations and without benefits to the source countries.

Of utmost importance for phytotherapy as our field of research is the traditional knowledge on genetic resources, which is also the property of countries of origin (Art. 8j, CBD and Art 7, 12 NP). Therefore, research and development related to medicinal plants requires the permission by the country of origin.

The term *biopiracy* was developed in the 1990s by non-governmental organizations and activists beyond the scientific community. Although scholars of jurisprudence criticized this term, it has been frequently used in media and the general public. Biopiracy describes the exploitation of biological resources and/or traditional knowledge of indigenous tribes or communities without sharing the benefits of such resources (Brody, 2010). Another related issue is the ownership of knowledge (Shiva, 1999). It was critically considered that the patenting of medicinal herbs or their isolated chemical constituents disregards the ownership of indigenous knowledge by pharmaceutical corporations without these plants. The patenting of indigenous knowledge by pharmaceutical corporations without recognition of the corresponding communities was seen as a new form of colonialism (Shiva 1999). Thus, any discussions on biopiracy are meaningful, if they contribute to the protection of intellectual rights of those people, where the knowledge of these indigenous sources comes from.

While some drastic cases of biopiracy have been documented, the use of natural resources is not only promising for many applications, but is also realized in a good and fair manner in many cases. The term *biopiracy* is emotional and negative and therefore wrong to describe the proper use of natural resources respecting the rights of indigenous communities. A more general term is *bioprospecting*, which means the identification and commercialization of bioproducts.

At the moment, there is still a lack of research and development opportunities based on these internationally binding agreements. Industrial and academic partners on the one hand and indigenous communities represented by their countries on the other hand should seek for opportunities for fair access and benefit sharing and at the same time conserve biodiversity by sustainable use of biological resources. Measures for good practices have to be developed and routinely implemented to further on allow the development of novel medicines based on natural sources (Efferth, 2016).

Possibilities, how this aims could be reached have been discussed at the International Conference on Science and Society: "Phytomedicine and Biopiracy" (ICSS-2017), which was held in Mainz, Germany,

on July 24-28, 2017 (**Photos**). The concept of the conference was to foster a dialogue between scholars from the life sciences and the humanities.

In conclusion, the international legislations, which were initiated by the Nagoya protocol are reality. Both academia and industry have to find solutions to include legal frameworks for potential commercial use that allow research on medicinal plants without scientific restrictions or hindrance on the one hand. One the other hand, future research on medicinal plants have to cope with the rights of indigenous tribes and communities for fair solutions for both sides.

Further reading (all web pages were accessed on Jan. 31, 2018)

- Brody, B. A. Intellectual property, state sovereignty, and biotechnology. Kennedy Inst. Ethics J. 2010;20:51–73.
- Convention on Biological Diversity. <u>https://www.cbd.int/convention/</u>
- Efferth, T. et al. Biopiracy of natural products and good bioprospecting practice. Phytomedicine 2016 23, 166-73.
- International Conference on Science and Society: "Phytomedicine and Biopiracy" (ICSS-2017), Hilton Hotel, Mainz, Germany, July 24–28, 2017. https://biopiracyconference2017.uni-mainz.de/
- Nagoya Protocol on Access and Benefit sharing. <u>https://www.cbd.int/abs/</u>
- Shiva, V. Biopiracy: The Plunder of Nature and Knowledge. South End Press, 1999.





2. TCM in Nordic Countries: Some reflections at the 16th CGCM Meeting



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Organized by the Guangdong Provincial Hospital of Chinese Medicine, the 16th Consortium for Globalization of Chinese Medicine (CGCM) Meeting was held in Baiyun International Convention Center, Guangzhou, China, August 18-20, 2017. As Co-Chairman (together with Prof. Rudolf Bauer) and a speaker of the Polychemical Activities and Mechanism Study III (Metabolism, Drug Interaction and Toxicity) session, I had some reflections as a scientist from a Nordic country.

Just because I was a toxicology co-opted member of the HMPC of the EMA 2005-2016, I have a lot of experience about herbal medicines of European origin, both efficacy and safety. On the other hand, one could argue with good reasons that herbals in Europe are really rather peripheral, at least from the conventional medicines point of view, and thus do not reflect the situation in other parts of the world. Thus it was of interest to participate in the 16th Meeting of the CGCM in Guangzhou August 18-20, 2017. Especially because the Guangzhou Meeting was the first one for me in China (mainland), and because most of the participants were from the mainland China, the meeting gave me a good opportunity to reflect variable approaches and future prospects of the place of herbal-based medical approaches vi-a-vis conventional medicines.

First of all, it was of interest to notice that China uses a lot of resources and efforts for the scientific inquiry of TCM and that the scientific tools include most of the modern and up-to-date methodologies such as advanced analytical techniques such as omics approaches, systems and network biology and pharmacology and bioinformatics. It was also of interest to visit in a hospital employing traditional Chinese medical treatment modalities. Now it may be a bit difficult to foresee what kind of integrated medicine we'll have a decade or two into the future, but I am sure that Chinese research in the field will be at the forefront when we try to lay grounds for more individualistic precision medicine which uses treatment modalities best applied for the optimal benefit of an individual patient.

How about countries like Finland or other Scandinavian or Nordic countries (Sweden, Norway, Denmark, Iceland) for that matter? In these countries, which belong to the highest tier of public health systems globally, TCM has only a very peripheral unofficial role (if any)in public health. Also the medical establishment is very much opposed to TCM or any CAM. In most Nordic countries there are laws executed to "protect people from treatments not officially accepted within the public health practices". This is not to say that CAM are not used by people, quite the contrary; for example, many people use herbal medicinal products obtained from pharmacies (about 30 products have been approved for use by the Finnish Medicines Agency) or from "health shops" (under the name of "dietary supplements" or other analogous names). In some universities and applied science institutes researchers are working on Finnish traditional herbs and studying also their potential effects by modern scientific tools. In any case, traditional medicinal approaches are not included into the mainstream medical research or practise; actually most of them are excluded by laws or opposition by the medical establishment, and there are very few prospects that any integration or even recognized coexistence will be achieved within a foreseeable future.

At least explicitly, it is mainly about science. Public health authorities and the medical establishment are of the opinion that only the approaches that are evaluated and justified by reliable scientific research, clinical research in the final count, could be endorsed within the public health system. For example, medicines mentioned in the current practise guidelines, which are semi-official recommendations for physicians, are classified according to the quality and quantity of (clinical)



research of a specific disease and indication. Not a single herbal medicine is currently in the highest classes (admittedly there are only a few officially endorsed for use in any diseases or symptoms).

In my opinion, in the foreseeable future the acceptance of TCM or other traditional medicines in Finland (or other Nordic countries) is dependent on the advance of high-quality science on the benefits of TCM and CAM within the public and private health care systems. More specifically, this means research on the treatment of chronic complex diseases, for which the current treatments mean polypharmacy with all its inherent problems especially in the aged patients. It means observance of quality of life aspects in long-term clinical research. Often multi-drug treatments of chronic diseases fail because of problematic adverse effect decreasing quality of life. It means head-to-head comparisons between conventional and TCM-concept-based



treatments. And it means also research on a very basic background of diseases, their multi-faceted aetiologies and symptoms, and intertwined genomic and environmental mechanisms, for which individualized selection of treatment modalities would provide (hopefully) an optimal chance of prevention and treatment. In my opinion, the groundwork for real globalization and harmonization will be created by joint scientific efforts with the highest standards. We (or those following us) will see.

European Reports

1. Horizon 2020: Calendar of main open calls for 2018 and 2019:

http://www.zabala.co.uk/sites/default/files/documentos/publicaciones/zabala17_h2020_deadlines_201 8-2019.pdf

2. Horizon 2020 proposals, success rates, funded projects & participants per country: http://ec.europa.eu/research/participants/portal/desktop/en/projectresults/index.html

3. The Innovative Medicines Initiative (IMI) has launched its 13th call for proposals. The deadline for the stage 1 submission is 28 February 2018 - 17:00 (CET). Applications should be made through the Participation Portal:

http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/calls/h2020-jti-imi2-2017-13-two-stage.html

4. Commission Publishes Booklets on Horizon 2020 Focus Areas on 18 Jan. 2018.

• Boosting the effectiveness of the Security Union

https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/su_booklet.pdf • Building a low-carbon. climate resilient future:

https://publications.europa.eu/en/publication-detail/-/publication/6e0b3746-ca81-11e7-8e69-01aa75ed71a1/language-en

• Connecting economic and environmental gains – the Circular Economy:

https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/ce_booklet.pdf

• Digitising and transforming European industry and services

https://ec.europa.eu/programmes/horizon2020/sites/horizon2020/files/dt booklet.pdf

Reports on China and Chinese-European Cooperation

1 What is China? A WeChat article offers a breathtaking answer, geographically, historically, culturally and economically.

<u>http://mp.weixin.qq.com/s/Z aN lo2uz2cXa9EOTPnNw</u> (中文)

2. China's Big Data on Health & Healthcare.

http://mp.weixin.qq.com/s/z1am_1eHSjOpU6MVBSt4yQ (中文)

4 3. China's Big Data on Its TCM Pharmaceutical Industry.





http://mp.weixin.qq.com/s/zgj13SLLCgursQlgVSNUuw (中文)

4. China launches world's largest human genome research project.

foreign policy.

<u>http://mp.weixin.qq.com/s/ntnLaJ9nMR2llsgJISKaCg</u> (中文) http://www.chinese-embassy.org.uk/eng/EmbassyNews/t1523961.htm

6. Hu C, Jia W. Diabetes in China: Epidemiology and Genetic Risk Factors and Their Clinical Utility in Personalized Medication.

Diabetes. 2018;67:3-11. The incidence of type 2 diabetes (T2D) has rapidly increased over recent decades, and T2D has become a leading public health challenge in China. Compared with European descents, Chinese patients with T2D are diagnosed at a relatively young age and low BMI. A better understanding of the factors contributing to the diabetes epidemic is crucial for determining future prevention and intervention programs. In addition to environmental factors, genetic factors contribute substantially to the development of T2D. To date, more than 100 susceptibility loci for T2D have been identified. Individually, most T2D genetic variants have a small effect size (10–20% increased risk for T2D per risk allele); however, a genetic risk score that combines multiple T2D loci could be used to predict the risk of T2D and to identify individuals who are at a high risk. Furthermore, individualized antidiabetes treatment should be a top priority to prevent complications and mortality. In this article, we review the epidemiological trends and recent progress in the understanding of T2D genetic etiology and further discuss personalized medicine involved in the treatment of T2D.

http://diabetes.diabetesjournals.org/content/67/1/3.long

<u>https://www.toutiao.com/i6510152517962170884/?tt_from=weixin&utm</u> (中文)

wagstaff A, et al. Progress on catastrophic health spending in 133 countries: a retrospective observational study. Lancet Glob Health. 2018;6:69-79. We defined health spending as catastrophic when it exceeded 10% or 25% of household consumption. The global incidence of catastrophic spending at the 10% threshold was estimated as 9.7% in 2000, 11.4% in 2005, and 11.7% in 2010. Globally, 808 million people in 2010 incurred catastrophic health spending. Across 94 countries with two or more survey datapoints, the population-weighted median annual rate of change of catastrophic payment incidence was positive whatever catastrophic payment incidence measure was used. Incidence of catastrophic payments was correlated positively with GDP per person and the share of GDP spent on health, and incidence correlated negatively with the share of total health spendina channelled through social security funds and other government agencies. INTERPRETATION: The proportion of the population that is supposed to be covered by health insurance schemes or by national or subnational health services is a poor indicator of financial protection. Increasing the share of GDP spent on health is not sufficient to reduce catastrophic payment incidence: rather, what is required is increasing the share of total health expenditure that is prepaid, particularly through taxes and mandatory contributions. https://www.ncbi.nlm.nih.gov/pubmed/29248367

8. Zheng H. **To build a China-UK Science & Technology Innovation Community.** *Science & Technology Daily 17th Jan. 2018.* This is a report on an interview of Mr Jiang Sunan, Minister Counsellor of S&T at the Chinese Embassy in the UK.

http://www.stdaily.com/index/kejixinwen/2018-01/17/content_624114.shtml=

9. Editorial. Chinese science is ready to step up (online title: China needs to listen to its researchers to become a scientific superpower). *Nature* 2018;553:249. ... China is right to praise itself for its accomplishments in building a successful scientific community. And its stated goals of becoming an attractive place for foreign or returning scientists and a more desirable partner for international collaborations are the right ones for a country ready to take up a much needed

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leadership role and act as a model for other nations. But China will need to make more effort to listen to its scientists and survey the needs of researchers elsewhere to find out what problems — including those mentioned above — might hamper attainment of those goals.

https://www.nature.com/articles/d41586-018-00659-5?WT.ec_id

https://www.nature.com/magazine-assets/d41586-018-00659-5/d41586-018-00659-5.pdf

10. The Chinese Way. *Nature* 2018;553:S1-S32. China needs your expertise as its plans to become a world-leading science and technology power gather momentum. This *Naturejobs* career guide to China explains how to find a job, outlines the pros and cons of working and living there, and describes the country's AI and biotech ambitions. Also, meet researchers who have relocated there to develop their careers. <u>https://www.nature.com/collections/bxzInkkfnf/content/articles?WT.mc_id</u>

⁴⁴⁴11. Ellis S. **Biotech booms in China** *Nature* 2018;553:S20-S22. <u>https://www.nature.com/magazine-assets/d41586-018-00542-3/d41586-018-00542-3.pdf</u> http://mp.weixin.gg.com/s/iN87JOIEw-qs54cAUdLpHA (中文)

12. Zhao J. Secular Trends in Energy and Macronutrient Intakes and Distribution among Adult Females (1991–2015): Results from the China Health and Nutrition Survey. *Nutrients* 2018;10:115.

http://www.mdpi.com/2072-6643/10/2/115

13. Tollefson J. China declared world's largest producer of scientific articles. *Nature* 2018;553:390. Report shows increasing international competition, but suggests that United States remains a scientific powerhouse.

https://www.nature.com/magazine-assets/d41586-018-00927-4/d41586-018-00927-4.pdf

14. Macias-Fauria M. Satellite images show China going green. *Nature* 2018; doi:10.1038/d41586-018-00996-5. Large-scale tree-planting projects have taken place in regions of China prone to soil erosion. Satellite imagery reveals the effects of this work, and shows that a predicted vegetation decline didn't occur during a period of drought.

https://www.nature.com/magazine-assets/d41586-018-00996-5/d41586-018-00996-5.pdf

TCM, Acupuncture and Other Traditional Medicine

1. Youyou Tu Group at CACMS: New Breakthoughs and Outlook for 2018 <u>http://m2.people.cn/r/MV8wXzEwMzU1MTE1XzIwM18xNTE1MTE0MTM3?tt from=weixin&tt group i</u> d=6507367917179372035&from=groupmessage&isappinstalled=0 (中文)

2. Top-10 World News on TCM 2017 published on 11th Jan. 2018. Organised by the World Federation of Chinese Medicine Societies and sponsored by Beijing Tong Ren Tang Co. Ltd., the annual ranking of TCM-related news was compiled by representatives of public media and experts. Since 2013, this has been the fourth consecutive year for the ranking to be published by WFCMS.

<u>http://mp.weixin.qq.com/s/2Mt597RyxPusYpB8FpYR9Q</u>(中文)

http://www.worldtcm.org/180118/05404160N.shtml?from=groupmessage&isappinstalled=0 (中文)

3. China's Ministry of Science & Technology call for proposals on modernisation of TCM. Investing 600 million Chinese Yuan and to start in 2018, it focuses on TCM prevention and treatment of major diseases, TCM treatment before disease arise and TCM R&D and quality control and covers 6 themes (TCM theoretical heritage and innovation, TCM prevention and treatment of major diseases, TCM resources, TCM big health industrial & scientific showcase, TCM internationalization and heritage and innovation of ethnomedicine), and is further divided into 25 research directions.

http://mp.weixin.qq.com/s/VW1ZhXrIZp8 lgOKQ-1NHg (中文)

4. Yang W, et al. **Approaches to establish Q-markers for the quality standards of traditional Chinese medicines.** *Acta Pharmaceutica Sinica B* 2017;7:439-446.



http://www.sciencedirect.com/science/article/pii/S2211383517300734?via%3Dihub

<u>http://mp.weixin.qq.com/s/zTVIRkttxK8vs7crr8hxpQ</u>(中文)

5. **TCM Centre launched at Oxford University.** On 6th December 2017, Oxford University and Shaanxi Momentum Pharmaceutical Co. Ltd. China signed an agreement to launch Oxford Chinese Medicine Research Centre, which is built on a Chinese herbal medicine research lab founded by Dr Yuling Ma at Oxford in 2015.

http://m.health.china.com/html/zixun/jiankangkuaixun/201712/14-

<u>368870.html?from=singlemessage&isappinstalled=0</u>(中文)

Yuling is the Director of the Centre. Her research on Chinese herbal medicines can be found here: <u>https://www.dpag.ox.ac.uk/team/yu-ling-ma</u>

6. TCM music therapy

http://mp.weixin.qq.com/s/5DZZHJe4aurfH-zml4zjdA (中文)

<u>https://mp.weixin.qq.com/s/8jJu YuEZFw2pgaL9yE4tQ</u> (中文)

7. Ding Z, et al. Interactions Between Traditional Chinese Medicine and Anticancer Drugs in Chemotherapy. WJTCM 2018;3:38-45. Herbal medicines, includingtraditional Chinese medicines (TCMs), have been used in Eastern countries for treatingdiseases such as cancer for thousands of

years. With the growing knowledge of tumorgenesis and cancer therapy, some natural compounds have been developed asclinical anticancer drugs. In addition, many compounds and TCMs have beencharacterized as complementary and alternative treatments, with synergeticeffects on enhancing the efficacy or reducing the side effects of the therapeutics. In this review, we summarized the recent studies focusing on the combination of natural compounds or TCM decoction with chemotherapeutics. The detailed mechanisms of action of the combinations and the application of analytical methods on TCM development are also discussed.

http://www.wjtcm.net/article.asp?issn=2311-

<u>8571;year=2017;volume=3;issue=3;spage=38;epage=45;aulast=Ding;type=3</u> https://mp.weixin.gg.com/s/PwJCCZH8fxOMSx7o7a4k2g (中文)



48. Yongyan Wang. **On the Scientific Nature of TCM and Modern Innovation.** *Guangming Daily*. 17th Jan. 2018.

http://mp.weixin.qq.com/s/BKTQfWmsEqzWB5dMiCpwhA (中文)

⁴9. Kunwen Wang. What are core values of TCM? Qihuanghuoju WeChat Forum. 18 Jan. 2018 <u>http://mp.weixin.gg.com/s/3stW7_YdnCl0y2jDqtKRPQ</u> (中文)

10. Xijun Wang, ed. Chinmedomics: Annual Advances in Metabolomic TCM Studies.

Science Press. <u>http://mp.weixin.qq.com/s/2BYZgv4c3I6-Ittl9kFIMA</u> (中文)

11. Chinese Materia Medica for Us All, a TV show series by Professor Zhongzhen Zhao, Hong Kong Baptist University, and a free-access Christmas gift on the HKBU website.

https://scm.hkbu.edu.hk/tc/knowledge_transfer/compendium_of_materia_medica_cultural_project_fun d/chinese_materia_medica_for_us_all/episodes/

12. TCM is among the flagged topics in *Briefing on Opportunities for UK Collaboration with Chinese Organisations in Horizon 2020.*

https://www.ukro.ac.uk/authoring/researcher/Documents/171220_eu_china_partnerships_briefing.pdf

13. Liu J, et al. **BOKP: A DNA Barcode Reference Library for Monitoring Herbal Drugs in the Korean Pharmacopeia.** *Frontiers in Pharmacology.* 2017;8:931. https://www.frontiersin.org/articles/10.3389/fphar.2017.00931/full



14. Xu Z, et al. **Regulate prescription of Chinese medicines.** *Nature* 2018;553:405. <u>https://www.nature.com/articles/d41586-018-01079-1?WT.ec id</u>

Omics in Progress

1. Nawy T. Special Feature: Method of the Year 2017. **Spatial transcriptomics.** *Nature Methods* 2018;15:30. Spatial gene expression is critical for understanding cell identity and function in the tissue context. The popularity of model organism expression atlases and the Allen Institute for Brain Science's mouse and human brain atlases attest to the power of spatial gene expression. However, existing atlases were largely created using reporter genes or *in situ* hybridization—low throughput methods that make it painstaking to construct references and that limit the ability to assess multiple samples. A bevy of recent tools offer greater flexibility and



scale; highly multiplexed fluorescence *in situ* hybridization, *in situ* sequencing of imaged sections or three-dimensional tissues, and algorithmic methods that project gene expression onto limited existing spatial information, among others, offer very different solutions. There is good reason to expect the innovation to continue...

https://www.nature.com/articles/nmeth.4542.pdf

2. Rusk N. Special Feature: Method of the Year 2017. **Towards a dynamic 3D genome**. *Nature Methods* 2018;15:31. The plethora of methods for probing a genome's 3D architecture all share the same principle: jointly isolate and sequence genomic regions that are distant from one another in linear space but in close proximity in 3D. Methods differ in whether they probe interactions genome wide, such as Hi-C, or around specific loci, such as 3C and 4C. Some approaches enrich for genomic loci that interact with a certain protein, such as ChIA-PETs or the recent Hi-ChIP (Nat. Methods 13, 919–922, 2016); others work with sparse input material, such as the recent single-cell Hi-C (Nature, 502, 59–64, 2013; Nat. Methods 14, 263–266, 2017). In addition to these techniques, which rely on cross-linking interacting loci, the year 2017 also saw a ligation-free method, genome architecture mapping (Nature 543, 519–524, 2017)...

3. Lai Z et al. Identifying metabolites by integrating metabolome databases with mass spectrometry cheminformatics. *Nature Methods* 2018;15:53-6. Novel metabolites distinct from canonical pathways can be identified through the integration of three cheminformatics tools: BinVestigate, which queries the BinBase gas chromatography–mass spectrometry (GC-MS) metabolome database to match unknowns with biological metadata across over 110,000 samples; MS-DIAL 2.0, a software tool for chromatographic deconvolution of high-resolution GC-MS or liquid chromatography–mass spectrometry (LC-MS); and MS-FINDER 2.0, a structure-elucidation program that uses a combination of 14 metabolome databases in addition to an enzyme promiscuity library. We showcase our workflow by annotating N-methyl-uridine monophosphate (UMP), lysomonogalactosyl-monopalmitin, N-methylalanine, and two propofol derivatives. https://www.nature.com/articles/nmeth.4512.pdf

4. Norn H, et al. **NetSig: network-based discovery from cancer genomes.** *Nature Methods* 2018;15:61-6. Methods that integrate molecular network information and tumor genome data could complement gene-based statistical tests to identify likely new cancer genes; but such approaches are challenging to validate at scale, and their predictive value remains unclear. We developed a robust statistic (NetSig) that integrates protein interaction networks with data from 4,742 tumor exomes. NetSig can accurately classify known driver genes in 60% of tested tumor types and predicts 62 new driver candidates. Using a quantitative experimental framework to determine in vivo tumorigenic potential in mice, we found that NetSig candidates induce tumors at rates that are comparable to those of known oncogenes and are ten-fold higher than those of random genes. By reanalyzing nine tumor-inducing NetSig candidates in 242 patients with oncogene-negative lung





adenocarcinomas, we find that two (AKT2and TFDP2) are significantly amplified. Our study presents a scalable integrated computational and experimental workflow to expand discovery from cancer genomes. https://www.nature.com/articles/nmeth.4514.pdf

5. Piazza I, et al. **A Map of Protein-Metabolite Interactions Reveals Principles of Chemical Communication.** *Cell* 2018;172:1-15. Metaboliteprotein interactions control a variety of cellular processes, thereby playing a major role in maintaining cellular homeostasis. Metabolites comprise the largest fraction of molecules in cells, but our knowledge of the metaboliteprotein interactome lags behind our understanding of protein-protein or protein-DNA interactomes. Here, we present a chemoproteomic workflow for the systematic identification of metabolite-protein interactions directly in their native environment. The approach identified a network of known and

novel interactions and binding sites in *Escherichia coli*, and we demonstrated the functional relevance of a number of newly identified interactions. Our data enabled identification of new enzyme-substrate relationships and cases of metabolite-induced remodeling of protein complexes. Our metabolite-protein interactome consists of 1,678 interactions and 7,345 putative binding sites. Our data reveal functional and structural principles of chemical communication, shed light on the prevalence and mechanisms of enzyme promiscuity, and enable extraction of quantitative parameters of metabolite binding on a proteome-wide scale.

http://www.cell.com/cell/fulltext/S0092-8674(17)31448-4

41-54. Hauser AS, et al. Pharmacogenomics of GPCR Drug Targets. Cell. 2018;172:41-54.

Natural genetic variation in the human genome is a cause of individual differences in responses to medications and is an underappreciated burden on public health. Although 108 G-protein-coupled receptors (GPCRs) are the targets of 475 (~34%) Food and Drug Administration (FDA)-approved drugs and account for a global sales volume of over 180 billion US dollars annually, the prevalence of genetic variation among GPCRs targeted by drugs is unknown. By analyzing data from 68,496 individuals, we find that GPCRs targeted by drugs show genetic variation within functional regions such as drug- and effector-binding sites in the human population. We experimentally show that certain variants of μ -opioid and Cholecystokinin-A receptors could lead to altered or adverse drug response. By analyzing UK National Health Service drug prescription and sales data, we suggest that characterizing GPCR variants could increase prescription precision, improving patients' quality of life, and relieve the economic and societal burden due to variable drug responsiveness. https://www.ncbi.nlm.nih.gov/pubmed/29249361

7. Giladi A, Amit I. Single-Cell Genomics: A Stepping Stone for Future Immunology Discoveries. *Cell* 2018;172:14-21. The immunology field has invested great efforts and ingenuity to characterize the various immune cell types and elucidate their functions. However, accumulating evidence indicates that current technologies and classification schemes are limited in their ability to account for the functional heterogeneity of immune processes. Single-cell genomics hold the potential to revolutionize the way we characterize complex immune cell assemblies and study their spatial organiza- tion, dynamics, clonal distribution, pathways, function, and crosstalks. In this Perspective, we consider recent and forthcoming technological and analytical advances in single-cell genomics and the potential impact of those advances on the future of immunology research and immuno-therapy. http://www.cell.com/cell/pdf/S0092-8674(17)31320-X.pdf

8. Dunbar CE, et al. **Gene therapy comes of age.** *Science* 2018;359:eaan4672. Nearly 50 years after the concept was first proposed, gene therapy is now considered a promising treatment option for several human diseases. The path to success has been long and tortuous. Serious adverse effects were encountered in early clinical studies, but this fueled basic research that led to safer and more efficient gene transfer vectors. Gene therapy in various forms has produced clinical benefits in patients with blindness, neuromuscular disease, hemophilia, immunodeficiencies, and cancer.

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Dunbar et al. review the pioneering work that led the gene therapy field to its current state, describe gene-editing technologies that are expected to play a major role in the field's future, and discuss practical challenges in getting these therapies to patients who need them. http://science.sciencemag.org/content/359/6372/eaan4672?utm

9. Cowell AN et al. Mapping the malaria parasite druggable genome by using in vitro evolution and chemogenomics. *Science* 2018;359:191-9. Malaria is a deadly disease with no effective vaccine. Physicians thus depend on antimalarial drugs to save lives, but such compounds are often rendered ineffective when parasites evolve resistance. Cowell *et al.* systematically studied patterns of *Plasmodium falciparum* genome evolution by analyzing the sequences of clones that were resistant to diverse antimalarial compounds across the *P. falciparum* life cycle (see the Perspective by Carlton). The findings identify hitherto unrecognized drug targets and drug-resistance genes, as well as additional alleles in known drug-resistance genes. http://science.sciencemag.org/content/359/6372/191?utm

10. Harvey ZH. **Protein-Based Inheritance: Epigenetics beyond the Chromosome.** *Mol Cell* 2018; 69:195-202. Epigenetics refers to changes in phenotype that are not rooted in DNA sequence. This phenomenon has largely been studied in the context of chromatin modification. Yet many epigenetic traits are instead linked to self-perpetuating changes in the individual or collective activity of proteins. Most such proteins are prions (e.g., [*PSI*+], [URE3], [*SWI*+], [*MOT3*+], [*MPH1*+], [*LSB*+],

and [*GAR*+]), which have the capacity to adopt at least one conformation that self-templates over long biological timescales. This allows them to serve as protein-based epigenetic elements that are readily broadcast through mitosis and meiosis. In some circumstances, self-templating can fuel disease, but it also permits access to multiple activity states from the same polypeptide and transmission of that information across generations. Ensuing phenotypic changes allow genetically identical cells to express diverse and frequently adaptive phenotypes. Although long thought to be rare, protein-based epigenetic inheritance has now been uncovered in all domains of life.

http://www.cell.com/molecular-cell/fulltext/S1097-2765(17)30807-9

11. Chen Z et al. **Highly accurate fluorogenic DNA sequencing with information theory-based error correction.** *Nat-Biotechnol* 2017;35:1170-8. Eliminating errors in next-generation DNA sequencing has proved challenging. Here we present error-correction code (ECC)



sequencing, a method to greatly improve sequencing accuracy by combining fluorogenic sequencingby-synthesis (SBS) with an information theory-based error-correction algorithm. ECC embeds redundancy in sequencing reads by creating three orthogonal degenerate sequences, generated by alternate dual-base reactions. This is similar to encoding and decoding strategies that have proved effective in detecting and correcting errors in information communication and storage. We show that, when combined with a fluorogenic SBS chemistry with raw accuracy of 98.1%, ECC sequencing provides single-end, error-free sequences up to 200 bp. ECC approaches should enable accurate identification of extremely rare genomic variations in various applications in biology and medicine. https://www.nature.com/articles/nbt.3982

Other Recommended Readings.

1. Buenz EJ, Verpoorte R, Bauer BA. **The Ethnopharmacologic Contribution to Bioprospecting Natural Products.** *Annu Rev Pharmacol Toxicol.* 2017 Oct 27. doi: 10.1146/annurev-pharmtox-010617-052703. [Epub ahead of print]. Descriptions of the use of natural products in traditional medicine have served as starting points for new therapeutics. The details of the traditional use of these organisms can provide important information for future drug discovery and development efforts. Recent technologic advances provide the framework to leverage ethnopharmacologic data in the drug discovery process. Information on the traditional harvest,

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preparation, storage, and administration of the organisms, and the natural products they contain, provides valuable details regarding characteristics of the active compounds. Importantly, researchers can now rapidly analyze and identify the multiple, and often synergistic, compounds contained in these natural products. Although we are entering the acme of ethnopharmacology, where information regarding the traditional use of organisms can provide valuable natural product leads and accelerate the identification of new therapeutics, this ethnopharmacologic resource is threatened by the loss of traditional medicine knowledge and extinction of organisms.

http://www.annualreviews.org/doi/abs/10.1146/annurev-pharmtox-010617-052703

2. The Lancet. The NHS at 70 and Alma-Ata at 40. Lancet 2018;391:1. 2018 welcomes two important anniversaries for health. In the UK, the National Health Service (NHS) will be 70 years old in July, and the global health community will mark the 40th anniversary of the Alma-Ata Declaration at a conference on Oct 25-26 in Almaty, Kazakhstan. Common to both anniversaries will be recognition of universal health coverage (UHC) as a goal, and the place of primary health care in achieving that goal...http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)30003-5/fulltext?elsca1=etoc

and clearly described methods and evidence are one of the cornerstones of science. After several publications indicated that a substantial number of scientific reports may not be readily reproducible, the scientific community and public began engaging in discussions about mechanisms to measure and enhance the reproducibility of scientific projects. In this context, several innovative steps have been taken in recent years. The results of these efforts confirm that improving reproducibility will require persistent and adaptive responses, and as we gain experience, implementation of the best possible practices. A framework has been developed to promote transparency and openness in scientific publications—the Transparency and Openness Promotion (TOP) guidelines (http://science. sciencemag.org/content/348/6242/1422.full)...

http://science.sciencemag.org/content/sci/359/6371/9.full.pdf

4. Method of the Year 2017: Organoids. Nature Methods 2018;15:1. The ability to prod stem cells into three-dimensional tissue models makes for a powerful way to study human biology. But these exciting tools are still works in progress.

https://www.nature.com/articles/nmeth.4575.pdf

4 2 5. Petersen KS, et al. Healthy dietary patterns for preventing cardiometabolic disease: the role of plant-based foods and animal products. Curr Dev Nutr 2017.117.001289; DOI: https://doi.org/10.3945/cdn.117.001289.

http://cdn.nutrition.org/content/early/2017/11/06/cdn.117.001289

44 6. Latest Nature Index Report

https://www.natureindex.com/supplements/nature-index-2017-science-inc/index

https://mp.weixin.gg.com/s/9mPJ1V1OBCWOztpL9p48Zg (中文)



7. Chapman CD, et al. Experimenter gender and replicability in science. Science Advances 2018;4:e1701427. There is a replication crisis spreading through the annals of scientific inquiry. Although some work has been carried out to uncover the roots of this issue, much remains unanswered. With this in mind, this paper investigates how the gender of the experimenter may affect experimental findings. Clinical trials are regularly carried out without any report of the experimenter's gender and with dubious knowledge of its influence. Consequently, significant biases caused by the experimenter's gender may lead researchers to conclude that therapeutics or other interventions are either overtreating or undertreating a variety of conditions. Bearing this in mind, this policy paper emphasizes the importance of reporting and controlling for experimenter gender in future research. As backdrop, it

explores what we know about the role of experimenter gender in influencing laboratory results, suggests possible mechanisms, and suggests future areas of inquiry. Archives (2008-2017): www.gp-tcm.org/news-list/



http://advances.sciencemag.org/content/4/1/e1701427

https://www.npr.org/sections/health-shots/2018/01/10/577046624/a-scientists-gender-can-skew-research-results

8. Powell K. **Technology to watch in 2018**. *Nature* 2018;553:531-534. Thought leaders reveal the technologies and topics likely to transform life-science research in the year ahead. <u>https://www.nature.com/magazine-assets/d41586-018-01021-5/d41586-018-01021-5.pdf</u>

9. Santos R, et al. A comprehensive map of molecular drug targets. *Nat Rev Drug Discov.* 2017;16:19-34. ...Here, we present an updated comprehensive map of molecular targets of approved drugs. We curate a total of 893 human and pathogen-derived biomolecules through which 1,578 US FDA-approved drugs act. These biomolecules include 667 human-genome-derived proteins targeted by drugs for human disease. Analysis of these drug targets indicates the continued dominance of privileged target families across disease areas, but also the growth of novel first-inclass mechanisms, particularly in oncology. We explore the relationships between bioactivity class and clinical success, as well as the presence of orthologues between human and animal models and between pathogen and human genomes. Through the collaboration of three independent teams, we highlight some of the ongoing challenges in accurately defining the targets of molecular therapeutics and present conventions for deconvoluting the complexities of molecular pharmacology and drug efficacy.

https://www.nature.com/articles/nrd.2016.230 http://mp.weixin.gq.com/s/kYatmLT0DjsKW4gZnGy85w (中文)

Meeting & Event Reports

⁴⁴⁴1. Representatives of the World Federation of Chinese Medicine Societies attended the 142nd Executive Meeting of the WHO. At the meeting on 22 Jan. 2018, the WFCMS representatives Dr Jialang He and Dr Chunbiao Guo met Dr. Tedros Adhanom Ghebreyesus, the WHO Secretary-General and Dr. Qi Zhang, Head of the Traditional Medicine Department. Both have agreed to attend the 15th World Congress of Chinese Medicine and *Belt and Road* TCM Culture Week to be held in Rome, Italy, 16-20 November 2018.

http://mp.weixin.qq.com/s/Z-AfAraUYmN0_FGzW8cWKw (中文)

2. Photo gallery of the 10th Pong Ding Yuen International Symposium on TCM, Hong Kong, December 2-3, 2017. Dr. Yibin Feng, University of Hong Kong, reports. http://www.scm.hku.hk/pdy2017/photoalbum/p hotoalbum-page-index.html

3. The 18th International Congress of International the Society for Ethnopharmacology (ISE) jointly with the 5th Meeting Annual of Society for Ethnopharmacology, India, was successfully held in Dhaka, Bangladesh on January 13-15, 2018.

The theme of the meeting was *Ethnopharmacology & Drug Development: Innovation meets Tradition.* As Past President and Board Member of ISE, Professor Rudolf Bauer, who is also GP-TCM RA Former President and current BoD Member, attended the board meeting of ISE and gave a plenary lecture on "Application of holistic concepts in Archives (2008-2017): www.gp-tcm.org/news-list/





ethnopharmacological research" (which will be featured in our newsletters as an editorial). Rudi was honoured by the "SFE Outstanding international scientist award" (Pranab Banerji Memorial Award) from the Society for Ethnopharmacology India, for "the outstanding contributions in the field of ethnobotany, ethnopharmacology and medicinal plant research". The award was handed over by Architect Yeafesh Osman, Minister of Science and Technology, Government of Bangladesh.

Professor Zhongzhen Zhao, Hong Kong Baptist University, was invited to talk at the meeting. Our deputy editor-in-chief Professor Yuan-Shiun Chang (Taichung) and senior GP-TCM RA member Professor Hongxi Xu (Shanghai) also attended the meeting. The meeting attracted delegates from 36 countries. More information on the interesting congress with several contributions on TCM can be found here: <u>https://ise2018bd.com/event/conference/</u>

4. The 5th World Congress of Integrative Medicine which was held in Dongguan, Guangdong, China, on December 8-9, 2017. The meeting attracted ca. 3000 delegates from all over the world and was attended by Senior GP-TCM RA members Prof. Rudolf Bauer, Prof. De-an Guo, Prof. Nicky Robinson, Prof. Vivian Wong, Prof. Kelvin Chan, Prof. Werner Knöss, et al. Wang Guoqiang, deputy director of the State Health and Family Planning Commission and Director of the State Administration of Traditional Chinese Medicine, gave a welcome address and pointed out at the conference that the key to developing the integration of traditional Chinese and western medicine is to grasp the dialectical relationship between "keeping" and "changing". Rudi chaired a session and gave a keynote lecture on "The role of the gut microbiome in the activity of herbal medicine".

http://www.ky3h.com/index.php/Show/cid/8/aid/651 (中文)

http://wimc2017.fumed.com.cn/2017web/newslist.asp?3,2



Future Meetings & Events

⁴⁴⁴1. The 6th Annual Meeting of the GP-TCM Research Association will be held at Royal Botanic Gardens, Kew, UK on 4-6 July 2018. Please refer to the front-page special feature.

²2. International celebration of the 500 anniversary of Li Shizhen's birth to be held in Li's homehown Jichun County, Hubei Province, China, on 26th May, 2018.



http://mp.weixin.qq.com/s?__biz=MzAxMjMyMTEwNA==&mid=2660692447&idx=1&sn=3895e03e994 d2f1c98befd9f4beb8eca&chksm (中文)

3. The 17th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Kuching-Sarawak, Malaysia on August 8 - 10, 2018. This year's meeting is going to be organized by the Malaysian Institute of Pharmaceuticals and Nutraceuticals, National Institutes of Biotechnology Malaysia. The meeting provides a platform for regulatory-industrial-academic exchanges and potential research collaborations, on various frontiers of Traditional Chinese Medicine among our worldwide CGCM members and guests. You are cordially invited to attend the meetings and submit abstracts. Preliminary programme and more details will soon be announced on our website. Should you have any enquiries, please feel free to contact the CGCM Central Office: Email: <u>centraloffice@tcmedicine.org</u>; Website: www.tcmedicine.org

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

http://c.eqxiu.com/s/O8xACe2w?eqrcode=1&share_level=4&from_user=a29

<u>4a700-73b5-4d95-9d8b-dc428813e7cd&from_id (中文)</u>

<u>http://mp.weixin.qq.com/s/R5Ao3tYI7Q2UwzaP94ikTw</u>(中文)

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

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

Invitation from Journals

1. World Journal of Traditional Chinese Medicine: Season's greetings, publication of the 3rd issue of 2017 and sincere invitation for submissions. Articles can be submitted via ScholarOne: https://mc03.manuscriptcentral.com/wjtcm, Detailed information about requirements of manuscript and format can be found in "Instruction&Forms" by the above URL, or by accessing WJTCM home page www.wjtcm.org

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 (<u>qihe.xu@kcl.ac.uk</u>), Prof. Pierre Duez (<u>pierre.duez@umons.ac.be</u>) and Prof. Yuan Shiun Chang (<u>yschang0404@gmail.com</u>).

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To welcome the Chinese New Year of the Dog coming in two weeks, we have selected the fine paintings of dogs by Mr. Giuseppe Castiglione (郎世宁, 1688.7.19—1766.7.16) to wish you all a Happy Chinese New Year and a Prosperous Year of the Dog: <u>http://mp.weixin.qq.com/s/SRCiP7HK2svULEJJew9XkA (</u>中文)

