The 1000 Medicinal Plant Genome Project (1KMPG)

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The market share of Traditional Chinese Medicines (TCMs) in the health-care industry has continuously grown inside of China in the past years. The annual sales of all TCMs related products are expected to exceed one trillion RMB in the next few years. Nevertheless, the TCMs have not been well accepted by the Western countries to the levels it is expected. Despite the large investment in the development of TCM drugs, relative few numbers of novel TCM drugs have reached the market comparing with those for small molecule drugs. One of the reasons is the complexity of TCM drugs as a result of the high degree of diversities in the raw materials used to make up of medicines.

In order to tackle the complexity problems of TCMs from the very root, accurate determination of the genetic composition of raw herbal materials is a must. In recent years, several attempts have been made to obtain the complete genome sequences of medicinal fungi and plants. These include *Ganoderma lucidum* [1], *Ganoderma Sinense* [2], *Salvia miltiorrhiza* [3], *Panax notoginseng* [4] and etc. The completion of these work have lifted medicinal plant research and development into a new level. However, these efforts are usually driven by individual research group, a coordinated effort will optimize the resources for effective execution of these projects. To achieve this goal, Institute of Medicinal Plant Development (IMPLAD) from Chinese Academy of Medical Sciences and Illumina Corporation, in March 2017, has initiated the 1000 Medicinal Plant Genome Project (1KMPG), and create the world's first medicinal plant reference genome library.

Medicinal plants are well-known for their high degree of genetic diversity. Furthermore, the genomes of medicinal plants are usually highly heterogeneous, which increases the difficult in obtaining well-assembled genome. As a result, a balance must be made between the overall ambition and the practicality of conducting such a humongous project. Taking these points into consideration, the project is designed to be divided into two phases. First, a reference genome library for 500 medicinal plants is to be established using Next Generation Sequencing (NGS) platform of Illumina. Second, after assessment of the results of the first phase, the strategy would be revised to sequence the remaining 500 medicinal plant species. In particular, IMPLAD and its collaborators will collect and annotate all plant species included in the Chinese Pharmacopoeia 2015, and Illumina will sequence all DNA samples. Afterwards, IMPLAD will assemble and annotate the chloroplast genome with the assistance of Illumina. The project will be completed by the 1KMPG International consortium (under organizing), and Professor Chang Liu of IMPLAD serve as project contact person.

At present, IMPLAD and its collaborators has collected more than 350 medicinal plant samples, in which 150 species have been submitted to Illumina's core sequencing lab for sequencing. As an intermediate goal, the complete chloroplast genome of 40 species has been obtained. The plastid genome are small enough to be sequenced and assembled completely, and at the same time, contain a wealth of genetic information for the development of markers for phylogenetic studies and precision identification.

The potential impact of the successful completion of the 1KMPG is immense, analogous to that of the Human Genome Project, which was launched two decades ago. It would not only to raise the quality of TCM drugs to a new level, but also open up new avenue for the molecular breeding of medicinal plants and industrial production of active components through technologies such as genetic engineering of synthetic biology. Furthermore, 1KMPG will help to setup technological platforms that are ready to be applied to more medicinal plant genomes from around the world, and ultimately to realize the potential of traditional medicines in benefiting human’s health.

References:

**Further reading:** Herbal genomics: Examining the biology of traditional medicines (Chen S et al. Science, 2015, 347:S27-28)

**The project PhytoKat in Lubumbashi, D.R. Congo: Conditions for the integration of traditional medicine in modern healthcare**

Bakari Amuri, Meerts Pierre, Vandenput Sandrine, Okombe Victor, Ngoy Edouard, Ngoy Shutcha Mylor, Kahola Tabu Olivier, Kampembwa Mujinga Florence, Nkulu Fyama Jules, Duez Pierre*

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The D.R. Congo still faces multiple health problems. Notably the access to conventional medicine is limited; as in most Sub-Saharan countries, traditional medicine is the primary, and often the only, source of care for a majority of the population and the WHO advocates its recognition and modernization for primary health care. This pilot project, started in July 2017 for a duration of 5 years, aims to establish the necessary foundation for progress in this direction in Katanga:

- The conditions for the introduction of traditional practices in modern medicine will be evaluated (quality of the practitioners and diagnostics; quality, efficiency, safety of treatments);
- Many plants used in traditional medicine have already been documented in Katanga; certain traditional practices have been validated by the identification of active compounds. The project proposes to deepen the botanical, pharmacological, chemical and agronomic study of these interesting species;
- In the context of regional erosion of plant diversity, excessive harvesting of some vulnerable medicinal species could represent a serious threat; developing a conservation strategy is urgent and requires an inventory of their current distribution.

Through 8 doctoral theses in law, pharmacognosy and biomedical and agronomic sciences, this 500 k€ project aims at correcting the weaknesses identified by the recent Joint Context Analysis developed by Belgian and Congolese experts, at Belgian government initiative, for the domain environment / natural resources: "Lack of information, knowledge and awareness among decision makers and local communities on the benefits of biodiversity-related development".

**Special Features**

1. **Prof. De-an Guo, Past-President of GP-TCM RA, awarded Ho Leung Ho Lee Prize 2017.**

Prof. Guo was awarded the prize thanks to his outstanding national and international contributions to standardisation and quality control of TCM products. The Ho Leung Ho Lee Foundation (HLHL, Chinese: 何梁何利基金) is a Hong Kong-based non-government organisation which annually bestows prizes upon Chinese scientists. It was established on 30 March 1994, with funds donated from the charitable foundations of S. H. Ho (何善衡, He Shanheng), Leung Kau-Kui (梁鶚琚, Liang Qiuju), Ho Tim (何添, He Tian), and Lee Quo-wei (Li Guowei).

http://mp.weixin.qq.com/s/PdUCpG1JRAmCH0ov8yoSRw (中文)

2. **Nobel Prize awarded for discoveries in circadian rhythm.**
Lancet 2017;390:e25. The 2017 Nobel Prize in Physiology or Medicine has been jointly awarded to Jeffrey Hall, Michael Rosbash, and Michael Young for their work in uncovering the mechanism that underpins the circadian rhythm...

http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)32661-2/fulltext?elsca1=etoc

3. Cryo-electron microscopy wins chemistry Nobel. Nature 2017; 550:167 (12 October 2017). Jacques Dubochet, Joachim Frank and Richard Henderson were awarded the prize on 4 October for their work in developing cryo-electron microscopy (cryo-EM), a technique that fires beams of electrons at proteins that have been frozen in solution, to deduce the biomolecules’ structure...


4. The Lancet. WHO launches new leadership, new priorities. Published: 14 October 2017. WHO's Director-General, Dr Tedros, last week launched his new cabinet to widespread acclaim. His mix of deputy and assistant director-generals is made up of nine women (two-thirds of his leadership team) with a geographical spread across 14 countries. India, Brazil, Saudi Arabia, South Africa, and Barbados are all newly represented. The announcement also translated Tedros's verbal promises into structural commitments. New priorities include Universal Health Coverage, climate change, and access to medicines. His cabinet is diverse, talented, and experienced. Now it's all about WHO's actions. A special session of the Executive Board will be convened in November to agree a future global programme of work for the agency. There are important questions to resolve...


http://stm.sciencemag.org/content/9/412/eaan6446.short

Comment 1: Relation between aristolochic acids (AA) and AA-containing herbal remedies and liver carcinoma awaits further studies

http://www.toutiao.com/i6479385018064962062/?tt_from=weixin_moments&utm_campaign (中文)

Comment 2: An implication is only an implication. It cannot be taken as conclusion and it is utterly wrong to use this article as an evidence against the entire TCM.

http://mp.weixin.qq.com/s/WZKKmOSFrM48FFr5iHFVfA (中文)

An eLetter by your Editor Dr Qihe Xu entitled A few potentially fatal problems of this paper and the true value of herbal medicines, submitted to Sci Transl Med on 28th October 2017: The phenomenon reported in this Sci Transl Med paper is of interest but should not have been published until some further clarifications are in place. The paper, as is, unfortunately suffers from a number of potentially fatal problems: (i) it has mistaken A:T>T:A mutations as a unique AA-exposure signature, although it is not. AA-DNA and AA-protein conduct are; (ii) it biasedly blames “an herbal medicine” and Chinese herbal medicines in Mainland China and Taiwan as the cause of AA intoxication, when AA could lead to damages through contaminating food as is the case in Balkan Epidemic Nephropathy; (iii) an implication is made without first ruling out major confounding factors such as viral hepatitis and explaining why these patients do not have well-established AA-induced diseases such as nephropathy and upper urinary tract urothelial or kidney carcinoma. As a nephrologist, may I point out that, based on a report from Taiwan, use of Chinese herbal remedies in chronic kidney disease patients were associated with very significantly reduced progression to end-stage renal failure and mortality. Thus, although legal and rational use is essential, the value of herbal medicines, especially traditional Chinese herbal medicine, deserves further investigation.


6. Horbach SPJM, Halfmann W. The ghosts of HeLa: How cell line misidentification contaminates the scientific literature. PLoS ONE 2017;12(10): e0186281. While problems with cell line misidentification have been known for decades, an unknown number of published papers remains in circulation reporting on the wrong cells without warning or correction. Here we attempt to make a conservative estimate of this ‘contaminated’ literature. We found 32,755 articles reporting on research with misidentified cells, in turn cited by an estimated half a million other papers. The contamination of the literature is not decreasing over time and is anything but restricted to countries in the periphery of global science. The decades-old and often contentious attempts to stop misidentification of cell lines have proven to be insufficient. The contamination of the literature calls for a fair and reasonable notification system, warning users and readers to interpret these papers with appropriate care. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0186281

European Reports


2. EU and India Strengthen Cooperation in Research and Innovation, and ERC Signs Implementing Arrangement with India. During the Fourteenth EU-India Summit in New Delhi, which took place on 6 October, both actors agreed to strengthen cooperation in research and innovation. The ERC have announced an agreement that encourages top Indian researchers to take part in research visits to ERC-funded research teams. https://www.ukro.ac.uk/subscribers/articles/policy/30c94f0e-4286-4585-9f53-e5a69d28a068/2546

3. Commission Clarification for British Applicants to Horizon 2020. The European Commission has added a new item to the Research & Innovation Participant Portal stating: "For British applicants: Please note that until the UK leaves the EU, EU law continues to apply to and within the UK, when it comes to rights and obligations; this includes the eligibility of UK legal entities to fully participate and receive funding in Horizon 2020 actions. Please be aware however that the eligibility criteria must be complied with for the entire duration of the grant. If the United Kingdom withdraws from the EU during the grant period without concluding an agreement with the EU ensuring in particular that British applicants continue to be eligible, you will cease to be eligible to receive EU funding (while continuing, where possible, to participate) or be required to leave the project on the basis of Article 50 of the grant agreement.

The UK Government underwrite for Horizon 2020 remains valid. As stated in the Government’s Horizon 2020 Underwrite Q&A: "The Government’s underwrite commitment guarantees awards where the application is submitted before exit and is subsequently approved after exit. This includes proposals which are informed of their success but, at the point of exit, have not signed a grant agreement, and proposals which have been submitted before exit and that are only informed of their success following exit. We will work with the Commission to ensure payment when funds are awarded."

4. Societal Challenge 2 2018-2020 Work Programme Pre-published. The European Commission has pre-published the draft 2018-2020 Work Programme part for Societal Challenge 2 – 'Food Security, Sustainable Agriculture and Forestry, Marine, Maritime and Inland Water Research and the Bioeconomy'. The Commission has made the document public before its formal adoption to provide potential participants with early information on up-coming calls. As it has not been officially adopted or endorsed by the Commission yet, information and topic descriptions indicated may change in the final version of the document expected to be published in late October, as explained in UKRO’s previous article. Main highlights of the SC2 2018-2020 Work Programme part:

- Move from four calls to three: Sustainable Food Security, Rural Renaissance and Blue Growth;
- The indicative budget for the three calls is €1.3 billion;
- Inclusion of the relevance of the Societal Challenge to UN Sustainable Development Goals (SDG) and the COP 21 Paris Agreement;
- This Work Programme part will also contribute to three of the Horizon 2020 focus areas: Low-Carbon Future, Circular Economy and Digitisation;
- As part of the 'Other Actions' a Circular Bioeconomy Thematic Investment Platform will be introduced.

5. HMPC/EMA monographs on herbal substances at different stages of development

6. Halliday A, Hacker J. Brexit and European science. Science 2017;358:279. "The UK’s vote in favor of leaving the EU has considerable ramifications for science. As the UK negotiates its Brexit, there is recognition that research is crucial to long-term economic success and that Europe needs a strong knowledge and innovation system to compete internationally and tackle challenges such as climate change and improved healthcare. It would be unacceptable to allow Brexit to jeopardize this..." vice-president of the Royal Society and president of the German National Academy of Sciences Leopoldina write.
http://science.sciencemag.org/content/358/6361/279?utm_campaign=toc_sci-mag_2017-10-19&et_rid=33953672&et_cid=1612987

China Reports

1. Chinese science (in a new era). Nature 2017;550:434. China will become "a nation of innovators", according to a speech by the country’s president Xi Jinping on 18 October. Xi laid out the vision as he opened the 19th National Congress of the Chinese Communist Party, an event held every 5 years at which the party shuffles its leadership. It was also a chance for Xi to consolidate his power after five years of heading the party. His support for science and technological innovation, which he says is necessary to build the industrial system needed for “socialism with Chinese characteristics”, has been welcomed by scientists. Xi also boasted of China’s success on environmental issues, and promised to put the country at the forefront of global efforts to combat climate change.
https://www.nature.com/polopoly_fs/1.22883!/menu/main/topColumns/topLeftColumn/pdf/550434a.pdf
2. The Lancet. Xi Jinping's roadmap for China prioritises health. Lancet 2017;390:1928. During the week of Oct 18, General Secretary Xi Jinping presided over the 19th Party Congress of the Communist Party of China. This twice-in-a-decade meeting announces the leadership's ideology and elects the party's top positions. Xi has consolidated power and political will for deeper reform, including establishing the Healthy China initiative for primary health-care services, medical insurance, and modernising hospital management. Xi spoke of the “principal contradiction facing Chinese society”, referring to the tension between unbalanced development and citizens' growing needs for prosperity. Repeatedly, he called on the party to address inadequacies in education, income, health care, housing, and the environment. Three decades of double-digit GDP growth have raised 800 million people out of poverty, but also resulted in uneven development. Since the last Party Congress in 2012, 60 million fewer people live in poverty, lowering the proportion from 10.2% to less than 4%, according to President Xi. By 2020, he vowed, China would eradicate poverty by targeting rural areas. Health-care costs and catastrophic medical expenditure are a major cause of poverty in the country, since the poorest people contribute relatively more for health care. The National Health and Family Planning Commission estimates that 44% of household impoverishment was due to ill health. Among this group, more than 7 million people with chronic diseases will benefit from timely national plans to strengthen community-level general practitioners, improve the medicine supply system, and end the practice of hospitals supplementing their income from the sale of overpriced drugs. Protection from impoverishment due to health-care costs is part of a path towards realising the Chinese Dream of national rejuvenation, and also a fundamental element in the country's pursuit of the Sustainable Development Goals 1 (end poverty in all forms) and 3 (ensure healthy lives). Xi remarked that “a healthy population is a key mark of a prosperous nation and a strong country”. The task now is to turn these laudable visions of the Healthy China initiative into a reality for its 1·4 billion people.

http://mp.weixin.qq.com/s/2o4YuTvSFKaGicBVdlFonA

3. Bai X. Sustainability: China's path to ecotopia. Nature 2017;550:37-38. Xuemei Bai critiques a critique of the country's eco-city initiative (China's Urban Revolution: Understanding Chinese Eco-Cities. Austin Williams Bloomsbury Academic: 2017. ISBN: 978-1350003248). She wrote: “In China's Urban Revolution, architect and writer Austin Williams attempts to do so, probing the country's eco-city experiment against the background of its socio-economic realities. The speed of change in China makes it extremely challenging to grasp what is happening and why: the social and political context can lose relevance rapidly, and so become risky to reference in as little as a decade. Williams should be commended for trying. He promises a nuanced view that is neither sinocentric nor biased towards the West — enticing for those who seek insights beyond blind criticism or blind optimism. Unfortunately, the book falls short of this promise. Williams asserts that it is a “political assessment” of China's eco-urban initiatives, and that his exploration may “give rise to a number of contradictory viewpoints”. His perspectives are indeed often contradictory, sometimes drastically...” and she concluded “China's Urban Revolution is ultimately — as a collection of “contradictory viewpoints” — unsatisfying. But many of the facts presented are fascinating.”

http://www.nature.com/nature/journal/v550/n7674/full/550037a.html?WT.ec_id

4. Normile D. China sprints ahead in CRISPR therapy race. Science 2017; 358:20-21. CRISPR, the wildly popular genome-editing research tool, was invented in the West, but it is speeding toward potential human applications in China. Last week, the Chinese team that sparked a worldwide debate in 2015 when it reported the first use of CRISPR to edit a human embryo's genome notched another first. In early embryos, they showed that a new CRISPR variant, which chemically modifies rather than cuts DNA, can
opportunities
http://www.euro.who.int/en/publications/abstracts/pharmaceutical
pharmacists in China; Traditional Chinese medicine; Hospitals and pharmaceutical policy; Primary care and pharmaceutical policy; Pharmacies and pharmaceutical pricing and reimbursement; Drug quality and supply chain; Irrational prescribing; Inequity in health care and pharmaceutical spending; Affordability and accessibility of pharmaceuticals; Key health issues: ageing, urbanization and noncommunicable diseases; Trends in China: Introduction to Chinese health care reform and pharmaceutical policy; Regulatory structure and drug approval; Key health issues: ageing, urbanization and noncommunicable diseases; Trends in health care and pharmaceutical spending; Affordability and accessibility of pharmaceuticals; Pharmaceutical pricing and reimbursement; Drug quality and supply chain; Irrational prescribing; Hospitals and pharmaceutical policy; Primary care and pharmaceutical policy; Pharmacies and pharmacists in China; Traditional Chinese medicine; Industrial policy; Conclusions and policy recommendations.

China’s National Library opens 175 databases for free to Chinese citizens.

www.gp-tcm.org/news-list/
TCM, Integrative Chinese Medicine and Other Traditional Medicines

1. An illustrated report on progress of TCM in the past 5 years.
http://mp.weixin.qq.com/s/iA4lHakMoltHCHBnAO2z3WZA (中文)

2. CFDA invites feedbacks on draft directory on quality management of TCM medicinal materials (10 月 27 日，中药材生产质量管理规范（修订稿）在 CFDA 官网挂网征求意见)
http://mp.weixin.qq.com/s/cogyq86MxKLTbAqJwQnzA (中文)

3. A must-read on Paozhi, processing of Chinese medicinal materials
http://mp.weixin.qq.com/s?__biz=MzAxODU4NDkzNw==&mid=2650453157&idx=1&sn=50cf41c938abf6d5924e4218a18b96b8&chksm=83da10a3b4ad99b5df011aadad05776e4865b9a89eb3df7649b94d002db39ec09786811aea97e&mpshare=1&scene=5&srcid=021170Zu93IBObH2uc6VUmiu#rd (中文)

4. Melchart D et al. Herbal Traditional Chinese Medicine and suspected liver injury: A prospective study. World J Hepatol 2017; 9:1141-1157. AIM: To analyze liver tests before and following treatment with herbal Traditional Chinese Medicine (TCM) in order to evaluate the frequency of newly detected liver injury. METHODS: Patients with normal values of alanine aminotransferase (ALT) as a diagnostic marker for ruling out pre-existing liver disease were enrolled in a prospective study of a safety program carried out at the First German Hospital of TCM from 1994 to 2015. All patients received herbal products, and their ALT values were reassessed 1-3 d prior to discharge. To verify or exclude causality for suspected TCM herbs, the Roussel Uclaf Causality Assessment Method (RUCAM) was used. RESULTS: This report presents for the first time liver injury data derived from a prospective, hospital-based and large-scale study of 21470 patients who had no liver disease prior to treatment with herbal TCM. Among these, ALT ranged from 1 × to < 5 × upper limit normal (ULN) in 844 patients (3.93%) and suggested mild or moderate liver adaptive abnormalities. However, 26 patients (0.12%) experienced higher ALT values of ≥ 5 × ULN (300.0 ± 172.9 U/L, mean ± SD). Causality for TCM herbs was RUCAM-based probable in 8/26 patients, possible in 16/26, and excluded in 2/26 cases. Bupleuri radix and Scutellariae radix were the two TCM herbs most commonly implicated. CONCLUSION: In 26 (0.12%) of 21470 patients treated with herbal TCM, liver injury with ALT values of ≥ 5 × ULN was found, which normalized shortly following treatment cessation, also substantiating causality.
http://mp.weixin.qq.com/s/cgbl1W5LHcdFEgh0-onf7w (中文)

5. Action Plan to Assist the Poor through Developing the TCM Drugs Industry (2017-2020) was jointly published by China’s SATCM, State Council, Ministry of Industry and Information, Ministry of Agriculture, Chinese Bank of Agricultural Development.
http://mp.weixin.qq.com/s/49RiXLNT3vI9V8JHw- MVA (中文)
2. Cohen J. ‘Base editors’ open new way to fix mutations. *Science* 2017;358:432-433. CRISPR has vastly simplified the ability to edit DNA, but there’s one thing this new technology is not particularly good at: fixing what are known as point mutations, the cause of many human genetic diseases. Now, two new papers, one in *Science* and the other in *Nature*, describe a tool called base editing that borrows heavily from CRISPR and excels at correcting the point mutations. CRISPR, adopted from a primitive immune system used by bacteria, cuts the DNA double helix, which is made up of the bases known in shorthand as A, C, T, and G. The cell repair process can then introduce errors that cripple genes. Researchers can also add DNA to CRISPR to, say, change one base to another. But CRISPR doesn’t do this efficiently. Enter base pair editors, which chemically alter one base into another one without cutting the double helix. In the *Science* study, researchers describe a base editor for RNA that effectively changes A to G and the *Nature* paper reports how a DNA base editor does the same swap. About half of the point mutations associated with human diseases are linked to mutant As. The two new base editors add powerful additions to the first DNA base editor that was reported in 2016, which changed Cs in DNA to Ts.

http://science.sciencemag.org/content/358/6362/432?utm_campaign=crispr
http://mp.weixin.qq.com/s/D3J59o6hLKucSUGZAOP0SA (中文)


http://mp.weixin.qq.com/s/fvvIn93c1qtWcHYr4LKusq (中文)


http://science.sciencemag.org/content/early/2017/10/24/science.aaq0180.long

3. Who owns CRISPR: A guide. (Aggie Mika. Flux and Uncertainty in the CRISPR Patent Landscape. *The Scientist*. October 1, 2017). The battle for the control of the intellectual property surrounding CRISPR-Cas9 is as storied and nuanced as the technology itself. In May 2012, the University of California, Berkeley, filed a patent application for biochemist Jennifer Doudna and the University of Vienna’s Emmanuelle Charpentier, then of Umeå University in Sweden, based on their seminal observation that the bacterial CRISPR-Cas9 gene-editing system can be used to target different sequences of DNA by reprogramming the system’s small homing guide RNAs. The Broad Institute of MIT and Harvard followed suit that December with applications for bioengineer Feng Zhang and colleagues covering CRISPR’s use in eukaryotic cells. When the US Patent and Trademark Office (USPTO) granted Zhang’s patent in April 2014, thanks to an expedited review process, a now-infamous dispute was born… Currently, according to IPStudies, more than 200 patents have been granted worldwide that cover the components, applications, and delivery of this technology. The U.S. is a leader in this space with almost 80 granted patents with CRISPR claims… Please kindly be invited to read how *The Scientist* explains.


4. Trivedi BP. Medicine’s future? *Science* 2017;358:436-440. Over the past 2 years as part of the world’s largest clinical genome sequencing effort, the first available to average Americans as part of standard primary medical care, more than 400 Pennsylvanians have received calls, letters, or electronic messages informing them that they have a disease-linked mutation. Run by the Danville, Pennsylvania–based Geisinger Health System, the effort hopes to ultimately enlist half a million of the nonprofit’s 3.3 million patients. In addition to using the sequencing results to prevent and treat diseases, Geisinger hopes to answer myriad questions, from how primary care physicians with little genetics knowledge cope with advising patients informed of disease mutations, to the challenges of
“cascade testing”—the follow-up with relatives who could also be at risk. The project will inform ongoing debates, including how much people should be told about what their genomes reveal.

http://science.sciencemag.org/content/358/6362/436?utm_campaign

5. Rozenblatt-Rosen O, et al. The Human Cell Atlas: from vision to reality. Nature 2017;550:451-3. As an ambitious project to map all the cells in the human body gets officially under way, Aviv Regev, Sarah Teichmann and colleagues outline some key challenges...


6. Grozhik AV & Jaffrey SR. Epitranscriptomics: Shrinking maps of RNA modifications. Nature doi:10.1038/nature24156; published online on 25 October 2017. The presence of N1 methyl groups on adenine bases was thought to be widespread in messenger RNAs. It now seems that these modifications are much less prevalent, and occur on mRNAs that structurally mimic transfer RNA...

http://www.nature.com/nature/journal/vaop/ncurrent/full/nature24156.html?WT.ec_id

7. Liu Z, et al. Single-cell transcriptomics reconstructs fate conversion from fibroblast to cardiomyocyte. Nature doi:10.1038/nature24454. published online on 25 October 2017. Single-cell transcriptomics analyses of cell intermediates during the reprogramming from fibroblast to cardiomyocyte were used to reconstruct the reprogramming trajectory and to uncover intermediate cell populations, gene pathways and regulators involved in this process...

http://www.nature.com/nature/journal/vaop/ncurrent/full/nature24454.html?WT.ec_id

Other Recommended Readings

1. Tuckson RV, et al. Telehealth. N Engl J Med 2017;377:1585-1592. Burgeoning technology holds the potential to improve the quality and reduce the cost of medical care. However, the evidence base for its use is currently limited. Research is needed to define areas of medicine in which the application of telehealth technology improves outcomes...


2. Mounce R, et al. Ex situ conservation of plant diversity in the world’s botanic gardens. Nature Plants http://dx.doi.org/10.1038/s41477-017-0019-3; 2017. A study published in Nature Plants highlights a survey of 1,116 botanical collections, which shows that they hold representatives from about 30% of the world’s plant species.

https://www.nature.com/articles/s41477-017-0019-3

3. Dance A. Conferences: The secrets of a standout seminar. Nature 2017;550:145-147. Organizing and producing a meeting, no matter the size or length, is a service that faculty members can provide for colleagues in their discipline. Here are some things that you can do to ensure you have the right ingredients for a successful conference.

• Focus on a topic that isn't already getting heavy attention on the meeting circuit.
• Choose an eye-catching title to help stimulate interest and registrations.
• Share the workload. Junior faculty members may want to recruit well-known co-organizers. Senior faculty members within or outside your institution can suggest speakers, and their connections and cachet may come in handy in getting those speakers to accept your invitation.
• Include speakers from many backgrounds, and from locations near and far; and invite researchers from a variety of fields and at different career stages.
• Keep a couple of local scientists on a backup list in case a speaker drops out at the last minute: emergencies happen.
• See if you can get funds, a venue and logistical support from the organization hosting the meeting.
• Apply for grants to offset some of the meeting's production expenses.
• Give yourself at least a year and a half to put the conference together.
• Schedule your meeting at least six months before or after any similar one.
Choose a relatively isolated location. This will stop attendees (and speakers) wandering off for lunch or in search of nightlife, and will encourage them to spend time talking with one another.

http://www.nature.com/naturejobs/science/articles/10.1038/nj7674-145a?WT.ec_id

4. *Nature* editorial. *Science without walls is good for all.* Nature 2017;550:7-8. International mobility and collaboration are linked to stronger research. When it comes to co-authorship, researchers in Europe are the most international. In 1981, only about one in six papers by a European scientist included co-authors from a different country. By 2011, that had risen to one in two. Papers with authors from more than one country also tend to be more highly cited...

http://www.nature.com/news/science-without-walls-is-good-for-all-1.22742?spJobID
http://www.nature.com/news/scientists-have-most-impact-when-they-re-free-to-move-1.22754?WT.ec_id
http://www.nature.com/news/open-countries-have-strong-science-1.22754?WT.ec_id

5. Herman MA, et al. Per-Protocol Analyses of Pragmatic Trials. *N Engl J Med* 2017;377:1391-8. Pragmatic trials are designed to address real-world questions about care options. This article addresses issues that may arise from per-protocol and intention-to-treat analyses of such trials, outlines alternative analytic approaches, and provides guidance on how to choose among them.


6. Mauri L, D'Agostino, Sr. RB. The Changing Face of Clinical Trials: Challenges in the Design and Interpretation of Noninferiority Trials. *N Engl J Med* 2017;377:1357-67. Noninferiority clinical trials have become a major tool for the evaluation of drugs, devices, biologics, and other medical treatments. Treatment with placebo or with a no-treatment control in a study is not ethical when an effective treatment has already been established. Effective medical treatments exist for many medical conditions and are the relevant bar to be surpassed by a new treatment. Although some new treatments offer greater efficacy, others may promise greater safety or convenience, or less expense, while providing similar efficacy. The concept of a good substitute was the original rationale for the design of noninferiority trials (i.e., to evaluate a new treatment for efficacy similar to that of an established treatment). Recently, noninferiority trial methods have also been applied in evaluating whether an effective treatment is safe enough. The number of randomized trials assessing noninferiority increased by a factor of 6 in a decade — in 2005, just under 100 trials were listed in MEDLINE under the general rubric of “noninferiority,” whereas in 2015, there were almost 600 such trials. These trials span multiple medical and surgical disciplines and diverse treatment strategies. In this article, we provide a framework for considering the features, including pitfalls, of noninferiority studies…


7. Wang J, et al. Visualizing the function and fate of neutrophils in sterile injury and repair. Science 2017;358:111-6. Imaging the unforeseen fate of neutrophils. Inflammation that results from insults such as ischemia and reperfusion or trauma in the absence of microorganisms is known as “sterile inflammation.” Neutrophils are recruited in vast numbers during sterile inflammation and have been thought to play a detrimental role. Wang et al. used intravital microscopy to show that neutrophils actually perform helpful tasks such as removing and regenerating thermally damaged blood vessels in the liver (see the Perspective by Garner and de Visser). Moreover, neutrophils neither die nor are phagocytosed. Instead, they return to the circulation in a process called “reverse transmigration,” making a pit stop in the lungs, before ending their lives where they began—in the bone marrow. Thus, a reconsideration of the use of anti-neutrophil therapies after injury may be warranted. [Link to the article]

8. Nature Medicine editorial. Rationalizing combination therapies. Nat Med 2017;23:1113. There are more than 10,000 ongoing clinical trials currently registered in the US alone investigating combination therapies for cancer, infectious diseases, and metabolic, cardiovascular, autoimmune, and neurological disorders. There are even more preclinical-research articles on drug combinations. Yet, these numbers are quite modest relative to all potential combinations that could be tested. This raises the questions of what strategies are best for selecting candidates for combination testing preclinically, and how the success of the results is being judged for transition to the clinic. [Link to the article]

9. 42 pharmacological and toxicological databases online: [Link to the website]

10. The qPCR and dPCR MIQE guidelines – A success story! The MIQE guidelines and the resulting scientific validity will be supported by more and more researchers, biological journals, academic and commercial institutions. Today (20th October 2017) we count around 6,300 citations for the MIQE guidelines applied in qPCR and 250 citations for the digital PCR (dPCR) MIQE guidelines (measured by Google Scholar). Hence the qPCR and dPCR MIQE guidelines are a worldwide full success story which will be driven forward by the scientific community.
   - MIQE & qPCR: How to apply the MIQE guidelines - a visual, interactive and practical qPCR guide. 2nd edition published 26th July 2016. Editors: Afif M. Abdel Nour & Michael W. Pfaffl. Free download via iTunes or in ePub version: [Link to the download]

11. Asher Mullard A. The drug-maker’s guide to the galaxy. Nature 2017;549:445-447. How machine learning and big data are helping chemists search the vast chemical universe for better medicines. [Link to the article]

12. Levin A et al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. Lancet 2017;390:1888–1917. The global nephrology community recognises the need for a cohesive plan to address the problem of chronic kidney disease (CKD). In July, 2016, the International Society of Nephrology hosted a CKD summit of more than 85 people with diverse expertise and professional backgrounds from around the globe. The purpose was to identify and prioritise key activities for the next 5–10 years in the domains of clinical
care, research, and advocacy and to create an action plan and performance framework based on ten themes: strengthen CKD surveillance; tackle major risk factors for CKD; reduce acute kidney injury—a special risk factor for CKD; enhance understanding of the genetic causes of CKD; establish better diagnostic methods in CKD; improve understanding of the natural course of CKD; assess and implement established treatment options in patients with CKD; improve management of symptoms and complications of CKD; develop novel therapeutic interventions to slow CKD progression and reduce CKD complications; and increase the quantity and quality of clinical trials in CKD. Each group produced a prioritised list of goals, activities, and a set of key deliverable objectives for each of the themes. The intended users of this action plan are clinicians, patients, scientists, industry partners, governments, and advocacy organisations. Implementation of this integrated comprehensive plan will benefit people who are at risk for or affected by CKD worldwide.


13. Byler KG, Setzer WN. In-silico screening for anti-zika virus phytochemicals. Planta Med 2016; 82(S 01): S1-S381. Zika virus (ZIKV) is an arbovirus that has infected hundreds of thousands of people and is a rapidly expanding epidemic across Central and South America. ZIKV infection has caused serious, albeit rare, complications including Guillain-Barré syndrome and congenital microcephaly. There are currently no vaccines or antiviral agents to treat or prevent ZIKV infection, but there are several ZIKV non-structural proteins that may serve as promising antiviral drug targets. In this work, we have carried out an in-silico search for potential anti-Zika viral agents from natural sources. We have generated homology models in MOE 2014.09 [1] for ZIKV protease, helicase, methyltransferase, and RNA-dependent RNA polymerase using sequences available in the NCBI database and we have carried out molecular docking analyses of our in-house virtual library of phytochemicals with these protein targets using the Molegro docking package [2]. Overall, 2263 plant-derived secondary metabolites have been docked. Of these, 138 exhibited remarkable docking profiles to one or more of the ZIKV protein targets, and several of these are found in relatively common herbal medicines, suggesting promise for natural and inexpensive antiviral therapy for this emerging tropical disease.


14. Ancient Ink for Cancer Treatment. Photothermal therapy (PTT) is an emerging noninvasive treatment option based on nanomaterials injected to accumulate in cancer cells and heated up by a laser. Nanomaterials are usually expensive, difficult-to-make and toxic. It was found that a traditional Chinese ink, Hu-Kaiwen ink (Hu-ink), carbon-based and stable in water, has similar properties to these nanomaterials. Hu-ink consists of nanoparticles and thin layers of carbon and is non-toxic; interestingly, it is also photocurable to yield cytotoxic effects.

15. Shen C-Y et al. Anti-ageing active ingredients from herbs and nutraceuticals used in traditional Chinese medicine: pharmacological mechanisms and implications for drug discovery. Br J Pharmacol 2017;174:1395-1425. This article summarizes the work performed on TCM natural products that are reported to have anti-ageing effects, over the last two decades: astragoloside, Cistanche tubulosa acteoside, icarin, tetrahydrocurcumin, quercetin, butein, berberine, catechin, curcumin, epigallocatechin gallate, gastrodin, 6-Gingerol, glucarubinone, ginsenoside Rg1, luteolin, icarisid II, naringenin, resveratrol, theaflavin, carnosic acid, catalpol, chrysophanol, cycloastragenol, emodin, galangin, chinacodi, ferulic acid, huperzine, honokiol, isoliensinine, phycocyanin, proanthocyanidins, rosmarinic acid, oxymatrine, piceid, puerarin and salvianolic acid B. The TCMs with anti-ageing function are classified according to their action pathways: the telomerases and telomerase, the sirtuins, the mammalian target of rapamycin, AMP-activated kinase and insulin/insulin-like growth factor-1 signaling pathway, free radicals scavenging and the resistance to DNA damage. http://onlinelibrary.wiley.com/doi/10.1111/bph.13631/full

Reports on Meetings & Events

1. Nobel Laureate Thomas C. Südhof dialogue with TCM scholar Jialing Mao in Chengdu on the 11th May 2017(中医学者对话诺奖得主)
2. The 14th World Congress of World Federation of Chinese Medicine Societies (WFCMS) was held in Bangkok, Thailand, on October 21-22, 2017. Ma Jianzhong, Deputy Commissioner of the China State Administration of TCM, was elected Chairman of WFCMS.

3. Academician Huanming Yang, Chairman and Co-founder of Beijing Genomics Institute (BGI) visited Cambridge in October 2017 and highlighted “Medicinal Plants 4.0 Project”. At the invitation of President Tai-Ping Fan of the GP-TCM Research Association, Academician YANG Huanming 杨焕明, Chairman and Co-founder of Beijing Genomics Institute (BGI) visited Cambridge on 18 and 19 October 2017. In addition to meeting Sir Gregory Winter at Trinity College, Prof. Yang gave a seminar “The Human Genome Project and Future of Man”. This lecture attracted the attention of geneticists Anne Ferguson-Smith, FRS and Richard Durbin; archaeologists Martin Jones and Marie Louise Sørensen, Director of Cambridge Academy of Therapeutic Sciences, Chris Lowe; Associate Director of Metabolic Research Laboratories, Antonio Vidal-Puig; Curator of Cambridge University Botanic Garden, Samuel Brockington, CEO of Dynasty Biotechnology, Simon Hawroth; as well as many Chinese scientists in Cambridge and London. The lecture also highlighted BGI embarking on an ambitious “Medicinal Plants 4.0 Project” in June 2017, with Tai-Ping Fan as its European Coordinator. Together with Guangxi Botanical Garden of Medicinal Plants and several other leading institutes in China and other parts of the world, the project plans establish the world's largest multi-omics databases of medicinal plants, and medicinal plant genome-assisted breeding platform. It is noteworthy that TCM was officially incorporated into the Czech healthcare system in June 2017.
4. Academician Sang Guowei appointed Honorary Dean of School of Integrative Pharmacy, Hangzhou Normal University on the 7th October 2017.

WeChat report in Chinese: 桑国卫院士受聘杭师大整合药学院和整合肿瘤学研究院学术委员会名誉主任 (中文): https://mp.weixin.qq.com/s/sRvP_ySRGpo5veYh1S0S1w

Future Meetings & Events
1. WeChat report on international celebration of the 500 anniversary of Li Shizhen’s birth to be held in Li’s hometown Jichun County, Hubei Province, China, on 26th May, 2018. http://mp.weixin.qq.com/s?__biz=MzAxMjMyMTEwNA==&mid=2660692447&idx=1&sn=3895e03e994d2f1c98be3f9f4b5eb8eca&chksm (中文)

Invitation from Journals
1. Invitation from World Journal of Traditional Chinese Medicine (WJTCM), including special calls on TCM network pharmacology and TCM for cerebral disease. WJTCM, ISSN 2311-8571, a new peer-reviewed journal (quarterly) launched in 2014, is the official journal of the World Federation of Chinese Medicine Societies (WFCMS) and the GP-TCM RA. **Aim & Scope**: Introduce clinical efficacy and mechanism of TCM to doctors and biomedical researchers around the world, so as to provide new ideas and methods for solving the complicated and difficult cases.

   - WJTCM includes reviews and original articles focused on four aspects:
     - Modern Research on Chinese Materia Medica: theories of processing, property, and compatibility of Chinese materia medica; safety of Chinese materia medica; active principles and mechanism and efficacy of crude drugs and Chinese compound formulas
     - Research on TCM Theory: scientific connotation and biological foundation of TCM basic theories
     - TCM clinical Research: disease and syndrome, TCM safety, efficacy evaluation, evidence-based and systematic evaluation
     - Acupuncture and Moxibustion: effect mechanism of acupuncture and moxibustion, specificity of acupoint effect, acupoints compatibility, efficacy evaluation of acupuncture and moxibustion.

   **Submission to the Journal**: All the 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 homepage www.wjtcm.org. All WJTCM articles will be published online via WJTCM website (www.wjtcm.org). PDF articles and electronic/online versions are freely available to global readers.

Sounding Board.
1. 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 Shiuin Chang (yschang0404@gmail.com).

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