

The July/August 2014 Newsletter of The GP-TCM Research Association

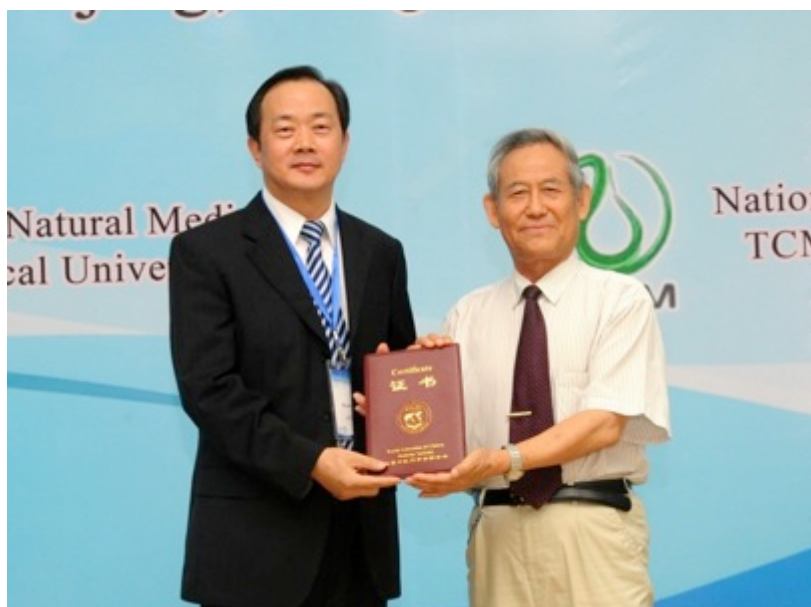


News from the GP-TCM RA:

1. GP-TCM RA President-Elect and BoD Elections

- With the approval of the current GP-TCM RA Board of Directors (BoD), the Secretariat is organising the 2nd GP-TCM RA election for nine BoD members, including President-Elect;
- Based on the Bylaws, Prof. Ian Sutherland of UK's Brunel University, a member who does not run election himself has been approved by BoD to serve as Chairman of the election;
- The new BoD being elected will succeed the current BoD from 1st Jan. 2015 to decide principles and future directions of the GP-TCM RA;
- The new President-Elect will take office on 1st Jan. 2015, when current President-Elect Prof. De-an Guo becomes President and the current President Prof. Rudolf Bauer becomes Past President. The newly elected President-Elect will be member of the BoD and the Executive Council, and will become President of GP-TCM RA on 1st Jan. 2017;
- Details of candidates will be presented at the Association website and the names of the candidates will be sent to every member of the Association in late August;
- Election period: 1 September 2014 until 30 September 2014;
- Announcement of results in October 2014 GP-TCM RA Newsletter;
- Any enquiries please be addressed to membership@gp-tcm.org and secretary-general@gp-tcm.org.

2. Warm congratulations to Prof. De-An Guo, President-Elect of the GP-TCM RA, for being unanimously re-elected President of the Specialty Committee of TCM Pharmaceutical Analysis of the WFCMS at the Council Election during the 5th Annual Conference of the Specialty Committee of TCM Pharmaceutical Analysis of the WFCMS. The GP-TCM RA look forward to the next collaboration with WFCMS in a year's time in Mons, Belgium, i.e. the Joint Conference of 4th GP-TCM RA Annual Meeting, the 6th Annual Meeting of the Specialty Committee of TCM Pharmaceutical Analysis, WFCMS, and the (2015) Annual Meeting of the Specialty Committee of TCM Chemistry, WFCMS.



Prof. De-AN Guo received appointment certificate from Prof. LI Zhenji, Vice Chairman and Secretary-General of WFCMS

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Special feature

Treasurer's Travels

Prof. Peter J Hylands
Treasurer of the GP-TCM RA
Head, Institute of Pharmaceutical Science, King's College London

I had planned to have a really enjoyable, unusually relatively slow-paced visit to various colleagues in southern China in July, culminating in the 4th Board of Directors' face-to-face meeting coinciding with the 3rd Annual Meeting of the GP-TCM RA and the 5th Annual Conference of the TCM Pharmaceutical Analysis Speciality Committee of the WFCMS in Nanjing. Because of pressure of work at King's College London, I could in the end only attend the Nanjing meeting but little did I know what was in store!

I flew KLM as I usually do, and duly took off from Amsterdam on Wednesday 16 July at 17.30 European time. After flying for nearly 5 hours (almost half way to Shanghai) the captain explained that the aircraft had developed a serious electrical problem and rather than land in a remote Siberian airport where it may not have been repairable, he had decided to go back to the Netherlands. So after more than nine hours in the air, we landed again at Amsterdam. The airline put us up in an airport hotel (arriving at 4.30am on Thursday) and after a couple of hours' sleep, I went back to the airport to be told that I had been rebooked on a flight to Shanghai via Beijing. However it turned out that this had been overbooked but they said



'Do not worry' you are on the flight to Guangzhou. That also turned out to be overbooked as well so then they said 'You have a choice'. 'Choice?', I said, 'Sounds good'. The choice was to fly either to Tokyo or Osaka! Since Osaka was less flying time than to Tokyo, I chose Osaka. Bad decision! The plane was 2 hours delayed in taking off so I missed my connection once I arrived in Osaka. Eventually I arrived in Shanghai just before my bag (making its own unaccompanied way from Amsterdam). By then it was too late (it was quite late Friday evening by this time) to travel to Nanjing so I had to stay overnight in Shanghai – I went to the station to buy a ticket to Nanjing. No problem, except the trains were full so I had to wait a few more hours. I finally arrived at the meeting venue in time for tea on Saturday afternoon – about 40 hours late!

Everything worked well for my return on Monday night from Nanjing to Shanghai but on going through Immigration at Pu Dong Airport, the officer told me to wait in a room while they made more enquiries! It turned out that she did not like the look of one of my exit stamps from China (4 years ago), despite my having entered and exited China at least a dozen times since then (and having perfectly readable stamps to prove it).

Anyway they finally let me go. So after a 30,000km round trip, I was able to attend what I could think of a really enjoyable meeting with excellent organisation by De-an.

A journey to remember!

Your jet-lagged Treasurer.

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Meeting reports

1. The 3rd GP-TCM RA Annual Meeting and the 5th Annual Conference of the Specialty Committee of TCM Pharmaceutical Analysis, World Federation of Chinese Medicine Societies (WFCMS) was successfully held in Nanjing, Jiangsu, China, on 18th-20th July 2014. The meeting was hosted by China Pharmaceutical University and was co-chaired by Prof. De-an Guo (Chairman, National Engineering Laboratory for TCM Standardization Technology, Shanghai Institute of Materia Medica, Chinese Academy of Sciences) and Prof. Ping Li (Chairman, State Key Laboratory of Natural Medicines, China Pharmaceutical University) and was attended by over 300 delegates from Australia, Austria, Canada, China, Germany, Hong Kong, the Netherlands, Taiwan, UK and USA. The meeting, accommodating over 50 oral presentations in five sessions and a total of over 150 posters, was kick-started by a whole-day programme featuring the work of the five Interest Groups of the GP-TCM RA and was followed by a workshop focused on scientific writing presented by editors of leading journals in the fields of TCM, natural medicines, ethnomedicines, ethnopharmacology, chemical analysis and separation science. The main meeting programme covered Chemistry & Quality, Pharmacology & Toxicology, Clinical Study and Systems Biology and Regulatory Affairs and Drug Discovery and was intercalated by a bipartite Board of Director meeting of the GP-TCM RA, a Council Election of the Specialty Committee of TCM Pharmaceutical Analysis of the WFCMS and a series of journal editorial board meetings, including the first Editorial Board Meeting of the World Journal of Traditional Chinese Medicine, which is co-edited by Prof. De-an Guo and Prof. Jingyan Han (Chairman, Department of Integration of Chinese and Western Medicine Peking University). The meeting was generously supported by Agilent Technologies Inc., Nanjing Sanhome Pharmaceutical Co. Ltd, State Key Laboratory of Natural Medicines and Chinese Journal of Natural Medicines.

2. The 4th GP-TCM RA BoD Face-to-face Meeting was held in Nanjing as a bipartite meeting. Part A of the meeting was a lunchtime meeting at 12.00pm-1.30pm Beijing Time on 18th July 2014 and was attended by Rudolf Bauer (Chair), De-An Guo, Qihe Xu (Minutes), Tai-Ping Fan, Kelvin Chan, Pierre Duez, Aiping Lu, Nicola Robinson, Rob Verpoort and Vivian Wong; apologies were received from Monique Simmonds and Peter Hylands. Part B of the meeting, a breakfast gathering focused on finance-related issues, was held at 7.25am-8.10am Beijing Time, 20th July 2014. It was attended by Rudolf Bauer (Chair), De-An Guo, Qihe Xu (Minutes), Tai-Ping Fan, Peter Hylands, Pierre Duez, Nicola Robinson, Rob Verpoort and Vivian Wong. Apologies were received from Monique Simmonds, Aiping Lu and Kelvin Chan.

The meeting approved minutes of the 15th BoD teleconference and received reports from President, Vice-Presidents, Secretary-General and Treasurer. It was unanimously agreed that Prof. Aiping Lu (Hong Kong Baptist University), assisted by Prof. Vivian Wong, would host the 2016 Annual Meeting. Great efforts by Prof. De-an Guo, Prof. Ping Li and their local team in organising the Nanjing Meeting were highly appreciated and it was agreed that Professors Nicola Robinson, De-an Guo, Rudolf Bauer and Ping Li would join forces to edit the Nanjing meeting abstracts for publication in the European Journal of Integrative Medicine, due in mid-September 2014. It was updated that the GP-TCM RA had so far 22 Corporate Members and 249 Individual Members. The latter includes 194 Ordinary Members, 25 Student Members, 22 Life Members and 8 Honorary Members. Membership service, fundraising, cash flow and elections were further discussed in detail.

Gallery from the Nanjing Meeting:

The following are a small group of samples from the gallery. For more photos, please visit:

www.gp-tcm.org/

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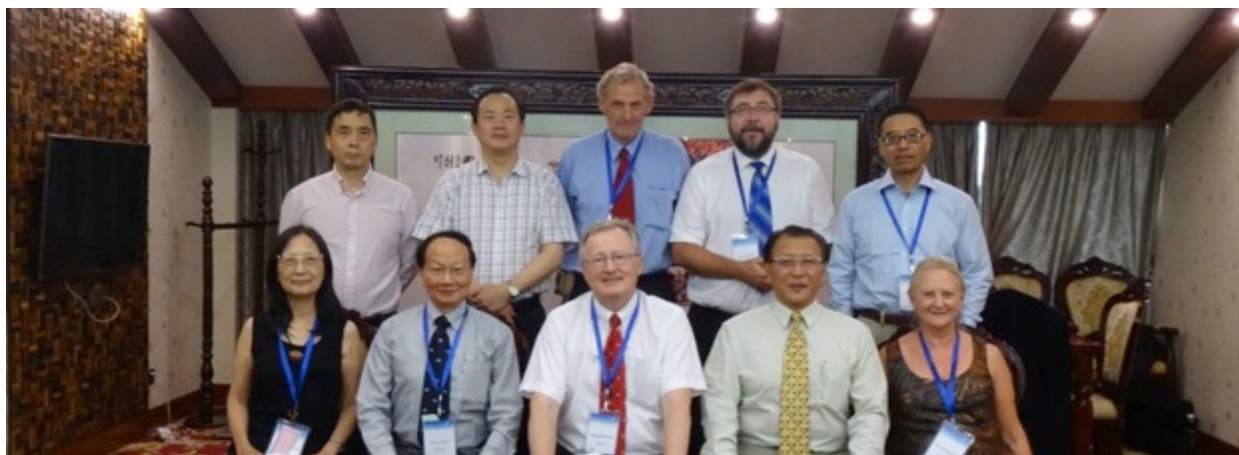


Top & middle: Opening ceremony; **Bottom left:** Meeting Co-Chair Prof. LI Ping, GP-TCM RA President Prof. Rudolf BAUER, President of China Pharmaceutical University Prof. LAI Maode, and Meeting Co-Chair, President of the Specialty Committee of TCM Pharmaceutical Analysis, WFCMS & GP-TCM RA President-Elect Prof. De-An GUO; **Bottom right:** Prof. Gerhard FRANZ received Honorary Membership Award from GP-TCM RA President Professor Rudolf BAUER.

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Left: The GP-TCM Annual General Meeting; **Right:** GP-TCM RA BoD Members Dr. Qihe Xu and Prof. Nicola Robinson stood by a GP-TCM RA poster outside the meeting venue.



Ten GP-TCM RA BoD members attended the 4th BoD Face-to-Face Meeting on 18th July 2014.



GP-TCM RA members met members of the WFCMS.

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Reports from GP-TCM Members:

- 1. Attendees of the Nanjing Meeting from Europe and China loved their Nanjing dishes.**



- 2. Dr Qihe Xu visited Chengdu and Nanning.** At the invitation by Prof. Cheng Peng (Vice President, Chengdu University of Traditional Chinese Medicine, CDUTCM) and Prof. Junguo Duan (President, CDUTCM Affiliated Hospital), Dr. Xu (Vice President, GP-TCM RA; Co-Director of King's Centre for Integrative Chinese Medicine) visited Chengdu on 11th-15th July 2014. He enjoyed interactive discussions with Prof. Peng, Prof. Duan and their team members and delivered three lectures, including one on GP-TCM and GP-TCM RA. This was followed by a successful visit to PuraPharm (Nanning) at the invitation of Mr. Abraham Chan (Chairman of PuraPharm). These visits, together with the Nanjing Meeting on 18th-20th July, were generously sponsored by a Global Partnership Fund award from UK's Department for Business Innovation and Skills.

<http://www.sctcm120.com/zyxy/pages/newsdetail.asp?id=2011>

<http://www.cdutcm.edu.cn/get/2014-07/7796.html>



- 3. Dr Tai-Ping Fan visited Tasly Group, Tianjin University of TCM and Northwest University, Xi'an (21-30 July 2014).** Following the Nanjing Meeting, Dr Tai-Ping Fan visited the state-of-the-art HQ of Tasly Group in the historic and vibrant city of Tianjin. Hosted by Director GUO Zhixin (Center for Global R&D) and Dr. MA Xiaohui (Director of Division of Pharmacology & Toxicology), Tai-Ping gave a lecture. At Tianjin University of TCM, he also had a productive meeting with Academician ZHANG Boli, and gave a seminar which was well attended by Vice-President GAO Xiumei, Prof. FAN Guanwei and many colleagues.

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New R&D center at Tasly Group (Left) and a brief history of Chinese medical science illustrated by stone carvings (Right)



Close-up views of (L) physician Hua Tuo 华佗 (145—208 AD) administering an oral anaesthetic mafeisan 麻沸散 to General Guan Yu 关羽 during an operation to resect necrotic flesh due to Aconitum-poisoned arrow, and (R) LI Shizhen 李时珍 (1518-1593) compiling *BenCao Gang Mu* 本草纲目



A productive meeting with Academician ZHANG Boli.

Relaxing on a river cruise in Tianjin

After intensive meetings at Northwest University in Xi'an, Tai-Ping enjoyed a ride on the High Speed Train with Profs ZHENG Xiaohui and ZHAO Xinfeng back to Beijing, where they met Prof. ZHANG Youyi at the Institute of Vascular Medicine at the 3rd Teaching Hospital of Peking University about consolidating their collaborations on a series of chimeric compounds inspired by Danshen Dripping Pill. At the invitation of Mr MA Jianping of Tong Ren Tang 同仁堂, they visited the flagship shop of this famous TCM company established in 1669.

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Tai-Ping Fan with ZHENG Xiaohui and ZHAO Xinfeng



The flagship dispensary of Beijing Tong Ren Tang

4. Dr Tai-Ping Fan visited the GP-TCM RA Secretariat – AssociAction Enterprises

At the invitation of Stuart Hex (L4) and Alan Ramsay (L6), Directors/Partners of AssociAction Enterprises Ltd, Tai-Ping Fan visited their HQ in Leicester on 14th August 2014. They had extensive discussions on the services provided to date, problems encountered and plan for the future. Tai-Ping also had the opportunity to meet the happy team behind the scene.



Reports from Australia, China and Europe:

1. Latest Newsletter of Australia's National Institute of Complementary Medicine, including Director Professor Alan Bensoussan's comments on the institute's achievements, Australia's regulation of Traditional Chinese Medicine practitioners, his praise of Germany's Kotzting Hospital, and the name change of the NIH's NCCAM to the National Centre for Research on Complementary and Integrative Health.

<http://www.vision6.com.au/em/message/email/view.php?id=1003891&u=66773#director>

2. China considers traditional Chinese medicine legislation: (Xinhua) BEIJING, July 24, 2014 - China's cabinet, the State Council, issued a draft on traditional Chinese medicine (TCM) legislation for public review on Thursday. China will establish a comprehensive TCM medical service system covering both urban and rural areas, the draft said. Local governments above the county level should set up TCM departments in public hospitals and promote TCM service in grassroots clinics, according to the draft. The country encourages private capital to participate in building the TCM system and will guarantee it enjoys the same rights for market entry and medical operations. The Chinese government will enhance the research and development of TCM with

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sound quality control, the draft said. China will also strive to develop and enrich "TCM culture." The central government will include TCM culture in the national culture promotion plan and designate every October 11 as TCM Day.

Now 3. Horizon 2020: Work Programme Update Published on 23rd Jul 2014: The current Horizon 2020 Work Programme covers the period of 2014 and 2015. The European Commission has now published an update to the Work Programme on the Participant Portal.

The previous version of the Work Programme contained a note to the effect that, due to the launching phase of Horizon 2020, parts of the Work Programme relating to 2015 (topics, dates, budget) were provided on an indicative basis only.

The parts that relate to 2015 have, with this revised version, been updated. Potential applicants will find information on the relevant updates for each call under the 'Call update' section of the Participant Portal. For most, though not all, areas of Horizon 2020, the changes are minor and will often relate to the budget allocated to particular parts or be administrative changes.

This version of the Work Programme also brings in two main novelties, namely five inducement prizes (on reducing the mis-use of antibiotics, food-scanner, reduction of air pollution, collaborative sharing of spectrum and breaking the optical transmission barriers) and a new pilot call for Fast Track to Innovation.

For the 2015 round, the value of the Horizon 2020 calls is approximately as follows:

- Excellent Science Pillar: EUR 2.7 billion
- Industrial Leadership: EUR 1.8 billion
- Societal Challenges: EUR 2.3 billion
- Spreading Excellence and Widening Participation, Science with and for Society, Fast Track to Innovation Pilot, Euratom: EUR 0.25 billion

A fuller breakdown can be found in the Commission memo linked below:

http://www.ukro.ac.uk/subscriber/Pages/140723_wp2015_update.aspx

http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/call_updates.html

Now 4. The European Biotechnology Industry Association, EuropaBio, has published its 2013-2014 annual report: EuropaBio has recently published its annual report for 2013-2014. The report reflects on the major developments and achievements for EuropaBio in the three biotechnology sectors it represents, healthcare, industrial and agricultural. Amongst the notable achievements during the period covered by the annual report is the successful nomination of EuropaBio as the most effective trade association in Brussels following a survey of policy makers and key influencers by EurActiv and APCO Insights. The full report can be accessed here:

http://www.europabio.org/sites/default/files/report/europabio_annual_report_2013_2014.pdf

Now 5. A European approach to universal health, technology and environmental questions:

An unmanageable burden of chronic diseases and global failure to mitigate and adapt to climate change are two among 31 major risks concerning individuals across the world. However, where there are risks, there are also opportunities for advancement. The latest issue of *International Innovation* highlights research from prominent European scientists who are seizing these opportunities and creating inventive solutions to health, environmental and technological problems plaguing the globe.

<http://digimag.internationalinnovation.com//launch.aspx?eid=e67260c3-ee02-47d8-842e-d9a3006b9e33>

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Future meetings:

1. The 13th Meeting of Consortium for Globalization of Chinese Medicine (CGCM) will be held in Beijing on 27th-29th August, 2014.

The Meeting is organized by China Academy of Chinese Medical Sciences. It 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 submit abstracts to share your exciting studies with us, also encouraged to forward this message to your colleagues and friends. The abstract submission form has been attached for your information. For more details of the meeting, please refer to the 13th CGCM Meeting website: http://13th_cgcm.icmm.ac.cn/.

Should you have any enquiries, please feel free to contact centraloffice@tcmedicine.org.

2. The Society for Medicinal Plant and Natural Product Research (GA) 62nd Annual Meeting will be held from 31st August to 4th September 2014 in Guimares, Portugal. The Congress will be held at the University of Minho, campus of Azurém, which is located in close vicinity to the medieval city centre of Guimarães, a UNESCO World Heritage Site. The historical city of Guimarães is located in Northern Portugal. The dynamic and colorful Minho Region is famous for its landscape and vineyards where the unique "Vinho Verde" wine is produced. The University of Minho is a leading university in Portugal and offers an excellent setting for the Congress. Plenary lectures by leading scientists, and several workshops will provide insights into various aspects of medicinal plant and natural product research. <http://ga2014.bio.uminho.pt/>

3. The 11th World Congress of Chinese Medicine will be held in St. Petersburg, Russia on 1st-2nd October 2014. Organizer: World Federation of Chinese Medicine Societies; Host: Li'West Company of Russia; Theme: Integrating Eastern and Western Culture, Exploring New Medical Model for Future.

<http://www.gp-tcm.org/wp-content/uploads/2014/06/Introduction-of-Hotels.docx>

<http://www.gp-tcm.org/wp-content/uploads/2014/06/WCCM11-NOTICE-overseas-24th-Feb.pdf>

<http://www.gp-tcm.org/wp-content/uploads/2014/06/WCCM11-REGISTRATION-FORM-overseas.doc>

4. "TCM in Science – Science in TCM" — The 8th International Workshop on Traditional Chinese Medicine in the University City of Porto (Portugal), 3rd – 5th October 2014: Oporto is the second largest city of Portugal and located along River Douro estuary. It is one of the oldest European cities and was registered as a World Heritage Site by UNESCO in 1996. According to the organisers, "The researchers and clinicians invited count to the best in the field of TCM and integrative medicine. They will report on their latest results in basic and clinical TCM research. This workshop will also provide a high-level platform for academic exchange and the establishment of new research networks. The University of Porto ranks high in its international reputation and is the university which hosts the first European TCM Master Programme. Apart from a sophisticated scientific programme we will enjoy the local highlights including Fado, a form of music characterized by mournful tunes and lyrics, the world-famous Port Wine, a cruise on River Douro and the delicious food, to name just a few to make your mouth water. At the beginning of October the weather in Porto usually is very pleasant." Lectures will cover a wide range of TCM. Please download the Registration Form and the Abstract Submission Form from the meeting website: www.dcfg-tcm.com

5. The 8th International Workshop Metabolomics Basics and Applications to Plant Sciences, Leiden, The Netherlands, 13th-17th April, 2015. Please address enquiries to:

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plantsandmetabolomics@gmail.com. Website: www.plantsandmetabolomics.nl

6. The 4th GP-TCM RA Annual Meeting: Joint Meeting of the GP-TCM Research Association, the TCM Chemistry Specialty Committee and the TCM Pharmaceutical Analysis Specialty Committee of the WFCMS will be held in Mons, Belgium, on 13th-15th July 2015.

- Scientific committee: De-An Guo, Rudolf Bauer, Qihe Xu, Peter Hylands, Tai-Ping Fan, Hai-Xue Kuang.
- Local organizing committee:
 - University of Mons: Pierre Duez (Chairman), Blankert Bertrand, Nachtergaele Amandine;
 - ULB: Stévinny Caroline, Bunel Valérian.



Recommended readings:

1. Integrity: reputation in science is everything:

http://www.nature.com/news/research-integrity-cell-induced-stress-1.15507?WT.ec_id=NATURE-20140710

2. Considerations in the Translation of Chinese Medicine

Introduction: <http://newamericamedia.org/2014/07/researchers-address-lost-in-translation-issues-with-chinese-medicine.php>

The document in English: <http://cewm.med.ucla.edu/wp-content/uploads/CM-Considerations-4.10.14-FINAL.pdf>

The document in Chinese (中医文献翻译刍议): <http://cewm.med.ucla.edu/wp-content/uploads/CHINESE-CM-Considerations-4.28.14-FINAL.pdf>

3. Universities: China's rankings rising: China's higher-education star is rising, while Japan's is waning, according to the *Times Higher Education's* Asia University Rankings 2014. Japan dropped two institutions from the top 100, whereas mainland China added four. But Japan still leads the Asian nations with 20 top-100 universities; China is second with 18, and South Korea third with 14. Thomson Reuters, which collates the data, bases the rankings on 13 indicators, including research and technology transfer. China has advanced mostly as a result of increasing its research expenditure, says a Thomas Reuters spokesperson, whereas Japan's research budget has remained flat.

http://www.nature.com/naturejobs/science/articles/10.1038/nj7507-115c?WT.ec_id=NATUREjobs-20140703

4. American Society of Pharmacognosy 2014 Annual Meeting abstracts are available through *Planta Medica* – Held in conjunction with the 14th Annual Oxford International Conference on the Science of Botanicals in Oxford, Mississippi, USA, on 2nd–6th August 2014.

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Chairmen: Larry A. Walker, Ph.D., Ikhlas A. Khan, Ph.D., Issue Editor: Mark O'Neil-Johnson.

<https://www.thieme-connect.com/products/ejournals/issue/10.1055/s-004-27340>

5. Genome sequencing identifies major causes of severe intellectual disability: Intellectual disability is known to be linked to genetic variance but the majority of cases remain undiagnosed. This uses whole-genome sequencing to identify genetic alterations in patients with severe intellectual disability. Sequencing of 50 patients with severe intellectual disability — and with no family history of the condition — produced a conclusive genetic diagnosis in 21 patients. The results suggest that *de novo* copy number variations and single-nucleotide variations affecting the coding region are a major cause of severe intellectual disability.

http://www.nature.com/nature/journal/v511/n7509/full/nature13394.html?WT.ec_id=NATURE-20140717

6. Monsanto's herbicide Roundup is linked to a mysterious fatal kidney disease epidemic that has appeared in Central America, Sri Lanka and India:

<http://www.truth-out.org/news/item/24876-monsantos-herbicide-linked-to-fatal-kidney-disease-epidemic-will-ckdu-topple-monsanto#.U78P4B0IIEI.email>

7. Medicinal herbs in the prevention and treatment of osteoporosis (Chenrui Li et al, *Am. J. Chin. Med.* **42**, 1, 2014) Osteoporosis is a common disease with wide prevalence, especially in the elderly population. Osteoporosis induced fractures not only decrease the patient's life quality, but also cause heavy financial burden to the society. Although current medications for osteoporosis are effective, numerous adverse effects have been observed accompanying their clinical applications. Effective prevention and therapy strategies with high safety are critical, which benefit both individual patients and the whole society. Traditional Chinese medicines have been used for thousands of years to treat bone related diseases in China and a number of modern preparations have been developed that are currently commercially available. In addition, several medicinal herbs demonstrated therapeutic effects against osteoporosis in animal models. This paper reviewed the anti-osteoporotic effects of traditional Chinese formulas, medicinal herbs and bioactive constituents based on clinical trials and *in vivo* animal studies.

http://www.worldscientific.com/doi/abs/10.1142/S0192415X14500013?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

8. Medicinal herbs in the prevention and treatment of osteoporosis

Chenrui Li et al, *Am. J. Chin. Med.* **42**, 1 (2014) Osteoporosis is a common disease with wide prevalence, especially in the elderly population. Osteoporosis induced fractures not only decrease the patient's life quality, but also cause heavy financial burden to the society. Although current medications for osteoporosis are effective, numerous adverse effects have been observed accompanying their clinical applications. Effective prevention and therapy strategies with high safety are critical, which benefit both individual patients and the whole society. Traditional Chinese medicines have been used for thousands of years to treat bone related diseases in China and a number of modern preparations have been developed that are currently commercially available. In addition, several medicinal herbs demonstrated therapeutic effects against osteoporosis in animal models. This paper reviewed the anti-osteoporotic effects of traditional Chinese formulas, medicinal herbs and bioactive constituents based on clinical trials and *in vivo* animal studies.

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9. BREAKING NEWS - Toward Yeast-Based Opioid Production

Synthetic biologists introduce bacterial and poppy plant genes into yeast to manufacture morphine.

By Tracy Vence | August 24, 2014 *The Scientist*

In 2008, a team led by Stanford University's Christina Smolke, then at Caltech, showed in *Nature Chemical Biology* that engineered yeast (*Saccharomyces cerevisiae*) could produce benzyloisoquinoline alkaloid (BIA) metabolites, including the alkaloids from which morphine is derived. Now, in a paper published today (August 24) in the same journal, Smolke's team shows that *S. cerevisiae* engineering to express additional enzymes can be coaxed to synthesize naturally occurring opiates and semisynthetic opioids from BIA precursor molecules. The results represent a step toward engineered yeast-based biomanufacturing of morphine.

"The authors have demonstrated that it is possible to develop a technology platform in yeast that allows the transformation of [the opiate alkaloid] thebaine to a variety of opiate drugs by mixing and matching microbial and plant enzymes," biochemist Neil Bruce from the University of York, U.K., told *The Scientist* in an e-mail. "This is elegant piece of synthetic biology . . . and demonstrates that it may ultimately be possible to generate a [complete] morphinan biosynthetic pathway in yeast."

Smolke and her colleagues have been working to reconstruct this pharmaceutically relevant pathway in yeast for nearly a decade. "When we started this project about 10 years ago, we were interested in plant natural product pathways [and] developing new ways to source these compounds because plants are very difficult to engineer," said Smolke. Around that time, "a lot of genome sequence information was coming out, [along with] advanced informatics and synthetic biology tools, so we could really go in and start to look at reconstructing these complex pathways in yeast."

Altogether, the morphinan biosynthetic pathway involves more than a dozen steps and even more enzymes, so reconstructing it in an organism that doesn't normally produce such metabolites has proven difficult. And when introducing genes from the Opium poppy (*Papaver Somniferum*) and the bacterium *Pseudomonas putida* into the yeast genome, the team encountered an array of engineering challenges. "Getting sufficient activity from those enzymes has been a challenge because every step [of the biosynthetic pathway] is not 100 percent efficient," said Smolke.

Moreover, expressing these enzymes out of their native context opens up the possibility of promiscuous enzymatic activity and unintended byproducts, she added. Indeed, in an early iteration, the researchers found that more than half of their product was diverted away from morphine, instead yielding related molecules neopine and neomorphine.

To circumvent these issues, the researchers devised a strategy to localize and delocalize enzymes within the yeast cells to improve the reaction specificity and, therefore, efficiency. "A particularly elegant aspect of the work is the compartmentalization of one of the enzymes in the endoplasmic reticulum to improve product yields and preventing side reactions," wrote Bruce.

The team's optimized approach was capable of yielding up to 131 milligram of opioid products per liter—a far cry from the titer required for commercial production, but far higher concentration than produced in an engineered microorganism to date.

"I applaud them; they should really keep working on this," said Toni Kutchan, vice president for research at the Donald Danforth Plant Science Center in St. Louis, Missouri. But, she added, the researchers must still piece together the portions of the pathway they've reconstructed in yeast to date.

"This is a long pathway when you string the whole thing together," agreed Smolke, adding that there's more work to be done toward that end. But she has reason to believe an engineered yeast-based approach to morphine production is amenable to industrial scale-up, and suggested that microbial production offers several benefits over agricultural cultivation and processing—chief among them, unlike poppy farming, yeast fermentation doesn't exhibit the same vulnerabilities to

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climate change or affect its surrounding environment, making them a green alternative to poppy farming.

“With microbial fermentation technology,” she said, “there really is an opportunity here to develop a more efficient manufacturing platform, but also one that is more stable, reliable, and easier to secure.”

K. Thodey et al., “A microbial biomanufacturing platform for natural and semisynthetic opioids,” *Nature Chemical Biology*, doi:10.1038/nchembio.1613, 2014.

Acknowledgements

Contributions from Prof. **Rudolf Bauer** (Graz), Prof. **Alan Bensoussan** (Sydney), Prof. **Junguo Duan** (Chengdu), Prof. **Pierre Duez** (Mons), Prof. **De-An Guo** (Shanghai), Dr. **Tai-Ping Fan** (Cambridge), Prof. **Peter Hylands** (London), Prof. **Ping Li** (Nanjing), Prof. **Cheng Peng** (Chengdu), Dr. **Fan Qu** (Hangzhou), Prof. **Nicola Robinson** (London), Prof. **Rob Verpoort** (Leiden), Dr. **Qihe Xu** (London) and Dr. **Hua Yang** (Nanjing) are gratefully acknowledged.