

Inaugural Issue GP-TCM Monthly Newsletter July 2009

Consortium News [Q Xu, London]

1. The 3rd Teleconference of the Coordination Office (CO) was held 12pm-13:30pm, 11 June 2009. Five CO members attended the meeting and reviewed the main events of the past month, including review and approval of 3-year plans of each work package (WP), change of WP6 leadership, the WP5 Kick-off Meeting, website and newsletter editorial board teleconference, etc. The procedures for short-listing and interviewing project manager candidates have been agreed. In particular, The “Deliverables-Central Questions-Labour Division” model has been unanimously agreed as a good model to be recommended to all WPs. It has been agreed that this model is designed to stimulate active thinking and planning, and to promote integration of the whole consortium. The CO has authorised Dr Qihe Xu to call each WP coordinator to introduce this model and answer their questions.

2. Teleconferences between the GP-TCM Coordinator and WP leads: Following the CO teleconference, Qihe has held talks with WP leads of WP1, 3, 6, 7 and 8, as well as co-Chairs of the SOP panel. Agreements on why and how to use the “Deliverables-Central Questions-Labour Division” model to run each work package have been reached. Some misunderstandings and worries have been eliminated and some WP-specific concerns have been identified, addressed or will be addressed in the future.

3. The name of our new Society and the website of the GP-TCM Consortium: As you probably know, the GP-TCM Consortium serves as the organising Committee of a new Society on Chinese medicine research and this new society will be officially launched at the end of our consortium. It has been decided that the name of the new society will be used to name our consortium website. By email, Dr Tai-Ping Fan has asked all newsletter recipients to choose their preferred name of the new society and give comments on the template, features and service providers of our website. If you have responded, please accept our sincere thanks! If not yet, please send your feedback to Dr Fan at your earliest convenience. Dr Fan’s team are striving to finalise the above issues in July, aiming to activate our consortium website in August 2009.

4. Welcome Prof Y. James Kang to join us as a non-beneficiary GP-TCM Consortium Member dedicated to WP3 (Toxicology, led by Prof Xinmin Liu) and WP5 (Animal Studies, led by Prof Javier Lucio-Cazana). James is Professor of Medicine and Professor of Pharmacology and Toxicology, University of Louisville School of Medicine (USA), Honorary Professor and Director, Regenerative Medicine

Research Center, Sichuan University (China) and is Honorary Director of National Key Laboratory of Tissue Engineering based in Chengdu (China). He is not only a well-established toxicologist and pharmacologist, an expert of gene modified animal models, an American Chinese pioneer of TCM research, but also an active organiser of many national and international societies, committees and meetings, and is the recipient of many honours and awards. He is Editor-in-Chief, Cardiovascular Toxicology (2000-); Editor of Methods in Pharmacology and Toxicology Series (2001-); Associate Editor, Experimental Biology and Medicine (2005-) and Associate Editor, Journal of Health Science (2001-), in addition to serving the editorial boards of 7 other journals and book series. Among his over 100 publications, he has published a series of papers investigating Chinese medicine using a herbogenomics approach:

<http://www.ebmonline.org/cgi/reprint/233/9/1059>

<https://louisville.edu/medschool/pharmacology/faculty/joint/y-james-kang>

5. Other important appointments:

5.1. Dr William Weiguo Jia, an existing WP5 member, has also been appointed to WP7 as a member.

5.2. Prof Kenneth Muir and Dr Jin Xu, Acting Coordinator and Local Assistant Coordinator of WP6, have also been appointed to WP8 as members.

6. Recruitment of the GP-TCM Project Manager:

Around 30 applications have been received and the quality of applications is satisfactory. As authorised by the CO, Prof Bruce Hendry, Prof Peter Hylands and Dr Qihe Xu have worked out a shortlist of 7 candidates. Interview will be held on 22nd July and it is expected that appointment of the Project Manager will be announced in the August issue of GP-TCM Newsletter.

Other News

1. Recent news on acupuncture and Chinese herbal medicine from the USA

http://news.xinhuanet.com/english/2009-06/25/content_11596359.htm

2. Have you heard of biological medicine?

<http://www.examiner.com/x-2994-Phoenix-Alternative-Medicine-Examiner-y2009m6d25-Biological-medicine-offers-a-holistic-approach-to-healing>
http://www.marioninstitute.org/matriarch/MultiPiecePage.asp_Q_PageID_E_11_A_PageName_E_BiologicalMedicineNetwork

3. Taiwan and the Mainland collaborate in Chinese medicine industry

<http://taiwanjournal.nat.gov.tw/ct.asp?xItem=53474&ctNode=413>

4. Animal products and endangered species in Chinese medicine?

http://www.thisislocalondon.co.uk/news/4456657.LEE_Animal_products_seized_in_police_raid_at_Chinese_medicine_shop/

5. Worries about alternative medicines by The Editor of Nature Reviews Nephrology:

<http://www.nature.com/nrneph/journal/v5/n7/full/nrneph.2009.96.html>

Special Recommendation:

Chinese Medicine Times: An e-journal covering all aspects of Chinese herbal medicine and acupuncture and being delivered free to over 20,000 practitioners and students worldwide.

<http://www.chinesemedicinetimes.com/>; <http://www.chinesemedicinetimes.com/wiki/CMTpedia>

News & Views

The genetic secrets of younger-looking skin – how about TCM for delaying ageing?[TP Fan, Cambridge]

A recent article in *New Scientist* reported that genetic analyses of human skin are revealing more about what makes us look old. As well as throwing up ways to smooth away wrinkles, the studies may provide a quantifiable way to test claims made for skin products.

[<http://www.newscientist.com/article/mg20227144200-the-genetic-secrets-of-younger-looking-skin.html?DCMP=OTC-rss&nsref=online-news>]

You may ask, “What has it got to do with TCM research?” But we all know *if you look good, then you feel good*. The big question is: *do Chinese herbs have anti-ageing activities like some natural products?*

In the past, cosmetics companies relied on subjective assessments of skin appearance, and changes in its thickness, colour and protein composition, to evaluate the effectiveness of their products and work out the quantities of ingredients needed to get the best results. Now skin researchers are starting to use DNA microarrays, common in the drugs industry, to measure the expression of thousands of genes in skin of different ages. Comparing gene expression in skin samples from the buttocks and forearms of young and older women, scientists found a decrease in the expression of genes involved in cholesterol and fatty acid synthesis in older skin. More surprisingly, the opposite was true for genes associated with inflammation and other components of the immune system, suggesting that the immune system may play a role in ageing.

Treating the older skin with niacinamide, which helps skin retain moisture, damped down expression of genes related to inflammation. “We believe that improving the barrier results in a ‘resignalling’ of key molecular components of the skin,” says Jay Tiesman of P&G. Targeting this inflammation might one day help to keep wrinkles at bay. The findings will appear in the *Journal of Drugs in Dermatology* in July.

Identifying a “genetic signature” of younger skin should also provide a benchmark for testing existing skin products. For example, P&G is measuring the effects on gene expression of a skin cream ingredient called pal-KT. Previous approaches suggested it increased production of structural skin proteins like collagen and laminin. Gene analysis indicates it also affects the expression of genes involved in wound healing.

Skincare products often contain retinol, Coenzyme Q10, and extracts of *Panax ginseng* and/or *Ganoderma lucidum*. In my view, we urgently need to improve our understanding of skin cell senescence, angiogenesis, and the interactions between *intrinsic* and *extrinsic* ageing. With a robust scientific platform, perseverance, imagination and good luck, we might be able to get closer to the Fountain of Youth!



Cantor's picture of Ali Baba, symbolic of predictive medicine

Mexico and China to collaborate on herbal medicine study to fight H1N1 flu [J Jia, Beijing]

Mexican higher education body the National Polytechnic Institute (IPN) will sign an agreement in July with the Beijing-based China Medical University to cooperate in medicinal plants research as part of the efforts to contain the A/H1N1 flu outbreak.

Guillermo Perez Ishiwara, the IPN's head of postgraduate studies and research, said that herbal therapy could work alongside conventional therapy to fight the new flu strain that has killed 83 and infected 4,541 people in Mexico.

IPN is already seeking plant-based anti-viral medicine in a bid to tackle the H1N1 flu virus, Ishiwara said. “We are seeking to find in the two herbal traditions plants that serve as anti-virals. Some of the components of the herbal formulas may stimulate the immune response, which means they could become an alternative in preventing any outbreak that may come in winter,” he said. “This is a virus that will emerge in a recurring manner and not just in the next winter season,” Ishiwara said, urging researchers and scientists from several institutions to work harder and join hands to fight the virus.

Revisiting the principle of *Jun-Chen-Zuo-Shi* (君臣佐使) in Chinese *fufang* (中药复方) [LP Zhao, Shanghai]

Wang, L. et al. (2008). Dissection of mechanisms of Chinese medicinal formula Realgar-Indigo naturalis as an effective treatment for promyelocytic leukemia. PNAS 105, 4826–4831. TCM follows the tenet that a formula should have four major ingredients, each playing its unique role while working together synergistically, to achieve the optimum therapy. The four major ingredients have been described in ancient texts as *Jun* (= emperor), *Chen* (= minister), *Zuo* (= adjuvant) and *Shi* (= courier)¹. However, the molecular basis of such combination therapy has never been explained convincingly at the biochemical level for any known TCM formula. Zhu Chen, Saijuan Chen and their co-workers at Shanghai Jiao Tong University have taken one well-known and clinically tested TCM formula for leukaemia therapy as a model and unveiled the biochemical roles of each ingredient.

The formula, known as Realgar-Indigo naturalis formula (RIF), contains realgar, indigo and *Salvia miltiorrhiza*. Through molecular analyses, the researchers showed that arsenic in realgar works as 'emperor' by directly triggering the degradation of the PML-RAR α oncoprotein in leukaemia cells. Indirubin, the active ingredient in indigo, works as 'adjuvant' by antagonizing the toxicity of arsenic and slowing leukaemia cell growth. Tanshinone IIA, the active ingredient in *S. miltiorrhiza*, acts as 'minister' by partially restoring those pathways that stop leukaemia spreading. Lastly, indirubin and tanshinone IIA work as 'courier'; they can enhance the cellular uptake of arsenic by inducing up-regulation of the transmembrane protein aquaglyceroporin 9.

The study explains the molecular modes and synergistic effects of principal ingredients in a clinically proven TCM formula. This finding will help bridge the gap between TCM and modern medical sciences.

¹Fan TP et al. (2006). Angiogenesis: from plants to blood vessels. *Trends Pharmacol Sci.* 27(6):297-30

Personalized medicine and TCM, a virtuous partnership [A Buriani, Padova]

Personalized Medicine is the concept that managing a patient's health should be based on the individual patient's specific characteristics. Considering that nowadays much of western medical practice is based on "standards of care", this emerging concept could bring meaningful changes in the whole healthcare system.

The term "personalized" was initially coined to indicate the innovative diagnostic application of pharmacogenomics which, through the identification of individual pharmacokinetic and pharmacodynamic genomic profiles, can predict if and how a patient will react to drugs, allowing the prescription of the right drug and the best regimen for the right patient.

The rapidly emerging field of genomic based diagnostics has broadened the meaning of personalized medicine to include all predictive genomic analysis, i.e. the identification of genetic susceptibility to a certain disease (genetic risk factor), and with the same approach will soon include other diagnostic-omic profiles, fast arising from research in other sister disciplines, with proteomics and metabolomics first in the pipeline.

Thanks to such diagnostic profiles, it will be possible to predict the risk of a certain disease, closely monitor it in the preclinical phase and institute measures like lifestyle modifications and increased physician surveillance, improving the chances of disease prevention or decreasing significantly its impact upon the patient. Shifting the focus towards a predictive approach changes the fundamental paradigm of medicine from being reactive, to being pre-emptive and proactive and has the potential to significantly decrease the incidence and prevalence of diseases.

Sustaining the individual's health balance before a disease has developed, has to play a new pivotal role in personalized medicine, but at the same time it highlights a lack of tools and effective strategies in western medicine, mostly built up around the concept of curing the disease.

Maintaining the health balance of the patient and initiate a preventative measure that can be particularly suited, requires a different vision of health and disease, and in this perspective personalized medicine can be envisioned as a modern holistic approach to the patient.

Despite an increasing attention towards preventive measures, when it comes to holistic visions, western medicine is far behind, being strongly anchored to its deterministic approach to disease and therapeutics.

In this perspective, TCM, highly personalized in its approach and with its deep knowledge on preventative strategies, is finding itself at the forefront of a new impulse towards integrative strategies, aimed at bridging together deterministic and holistic medical traditions, an attitude becoming increasingly popular in the scientific and medical community, challenged by the new demands in the path to personalized medicine.

Personalizing medicine: a systems biology perspective [A Dias, Braga]

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2671924>

This editorial deals with a very interesting "systems biology perspective in medicine" that could be helpful to develop a more rational holistic approach to human medicine (and in this sense very useful to study TCM), help to design experiments, and the application of 'omics' to medicine; the references this paper gives are recent ones and very relevant to these topics.

Contamination of Chinese wild mushrooms by nicotine [P Duez, Bruxelles]

A statement has been recently released by the EFSA (European Food Safety Authority) on the potential risks for public health due to the presence of nicotine in wild mushrooms. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902521199.htm?WT.mc_id=EFSAHL01
 The available analytical results (176 samples, mainly cepts, *Boletus edulis* and *Boletus* sp) indicate a level of 0.21 to 9.9 mg/kg dried mushrooms (corresponding to 0.023 - 1.1 mg/kg fresh mushrooms). The highest values were found in samples from China, the lowest in samples from Eastern Europe. A large part of mushrooms on the European market are imported from China, mainly from the province of Yunnan. As Yunnan is an important tobacco center, it is possible that nicotine contamination arises either from its use as insecticide, from the use of tobacco by-products as fuel to dry the mushrooms or from smokers working on mushrooms in confined buildings. No nicotine was found in a fresh *B. edulis* sample, before or after drying; samples of chanterelles, shiitake and some other mushrooms were not contaminated. Data from the highest European consumers (Italy) indicate a likely regular intake of 100 to 250 g fresh mushrooms per person. The exposure levels were accordingly computed by EFSA.

For comparison purposes, a single cigarette yields 4.3 to 24.5 µg nicotine/kg body weight. Clinical signs of nicotine toxicity have been registered at intakes corresponding to 30 - 800 µg/kg body weight. Children accidentally intoxicated with patches yielded symptoms at an estimated dose of 10 µg/kg body weight (nausea, vomiting, diarrhea, abdominal pain, weakness, dizziness, localised rashes).

Exposure	mg nicotine/kg fresh mushrooms	µg nicotine/kg BW/day Adults		µg nicotine/kg BW/day Children	
		Mean	Percentile 95	Mean	Percentile 95
Chronic	0.23	0.03	0.17	0.026	0.28
Acute	0.53 (p95)	0.56	1.67	1.23	3.23
	1.1 (max)	1.17	3.47	2.56	6.71

Meetings

- **8th Consortium for Globalization of Chinese Medicine (26-28 Aug 2009, Nottingham, UK)** <http://www.nottingham.ac.uk/cgcm2009/index.html> for registration and updated information.
- **2nd Shanghai International Conference on Traditional Chinese Medicine and Natural Medicines (S-TCM 2009, 16-18 Oct)** <http://www.phcog.org/ShanghaiTCM-2009.pdf>
- **International Conference & Exposition on Traditional Medicine 2009 (9-11 Nov, Guangzhou, China)** <http://www.ictm.org.cn>
- **WorldPharma2010 in Copenhagen (17-23 July 2010)** 3-day focused conference on **Natural Products: Past and Future**. Contact tpf1000@cam.ac.uk



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