



**Good Practice in Traditional Chinese Medicine Research in
the Post-genomic Era**

GP-TCM

223154

D4.17

Report in the Final Conference



Document description	
Name of document	Report in the Final Conference
Abstract	This document contains the report on the Work Package 4 (In Vitro Studies of Chinese herbal medicine) session at the Final Conference of the FP7 GP-TCM project.
Document identifier	D4.17
Document class	Deliverable
Version	1.0
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Date of creation	22/03/2012
Date of last modification	20/04/2012
Status	Final version
Destination	European Commission
WP number	WP4



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1 REPORT IN THE FINAL CONFERENCE

1.1 Introduction

The Work Package 4 (WP4) of the FP7 GP-TCM consortium specialises in *in-vitro* and *in-silico* studies of Chinese herbal medicine (CHM).

Based on the Technical Annex of the consortium, **the Final Conference** is the final opportunity for WP4 to have intensive discussions on its deliverable reports and other important documents and agree on some major issues through a **face-to-face meeting** among **WP4 members and other consortium members and external experts**.

Thus, it is important to **plan the agenda of the WP4 session** in advance and update it accordingly based on **reviewers' comments and feedback from attendees** of the Final Conference.

1.2 Preface

This report is generated based on **the guidelines** produced by the management team (WP10) and the organisers of the Final Conference (WP9) after a **face-to-face meeting of WP4** members as detailed below:

Attendees: Prof. Peter Hylands (Coordinator), Dr. Alessandro Buriani (Assistant), Dr. David Barlow and Dr. Qihe Xu. The project manager of the consortium, Dr. Halil Uzuner, also attended the meeting and provided invaluable advice.

Venue: King's College London, the Waterloo Campus, London, UK.

Date: 19th-20th March 2012.

1.3 Planned agenda for the WP4 session at the Final Conference

WP4 Session, 15:30-16:45, 12th April 2012

Chair: Prof. Enrica Bosisio, University of Milan

Minutes: Dr. Alessandro Buriani, University of Padova

Presentation session (delivered by: Prof. Peter Hylands, King's College London)

1) Objectives of WP4

The aim was to define and standardise *in-vitro* systems and their use in functional genomics studies of Chinese herbal medicines (CHM), including:

- to develop a general strategy;
- to establish criteria for selection of cell-based models for functional genomics research of CHM;
- to employ these criteria to evaluate the quality of existing data and establish guidelines;
- to obtain a comprehensive database of cell-based CHM studies;



- to establish guidelines for using *in-silico* tools;
- to identify and define the scope, content and quality control procedures required in establishing and maintaining a comprehensive database of the information provided through *in-vitro* studies.

2) WP4 membership and leadership

Members who joined WP4 in the first year of the project (Beneficiary members)

Prof. Peter Hylands (UK), Coordinator
Prof. Verena Dirsch (Austria), Deputy Coordinator
Dr. Alessandro Buriani (Italy), Assistant Coordinator
Dr. Tai-Ping Fan (UK), Beneficiary (Assistant Coordinator before being appointed WP7 Co-ordinator)
Dr. Qihe Xu, (UK), Beneficiary
Dr. David Barlow (UK), Beneficiary
Prof. Bruce Hendry (UK), Beneficiary
Dr. Maria Laura Garcia Bermejo (Spain), Beneficiary
Prof. Jian Zhao Niu (China), Beneficiary
Dr. Hani El-Nezami (China), Beneficiary
Prof. Maria Carrara (Italy), Beneficiary
Prof. Enrica Bosisio (Italy), Beneficiary
Prof. Angelika Vollmar (Germany), Beneficiary
Prof. Monique Simmonds (UK), Beneficiary

Lead organisation: King's College London (**KCL**)

Partner organisations:

University of Vienna (**UV**)
University of Cambridge (**UCAM**)
Beijing University of Chinese Medicine (**BUCM**)
University of Hong Kong (**UHK**)
Ludwig-Maximilians-Universität (University of Munich) (**LMU**)
University of Milan (**UMIL**)
University of Padova (**UP**)
University Hospital Ramón y Cajal-FIBIO (**UHRC**)
Royal Botanic Gardens, Kew (**Kew**).

Members who joined WP4 during the 2nd and the early part of the 3rd year:

Dr. Atanas Atanasov, University of Vienna, beneficiary
Dr. Mario Dell'Agli, University of Milan, Italy, non-beneficiary
Prof. Peter M. Jones, King's College London, UK, non-beneficiary
Prof. Shanta Persaud, King's College London, UK, non-beneficiary
Prof. Thomas Efferth, University of Mainz, Germany, non-beneficiary
Dr. Jue Zhou, Zhejiang Gongshang University, China, non-beneficiary
Prof. Wei-dong Zhang, Second Military Medical University, China, non-beneficiary
Dr. Ivano Eberini, University of Milan, Italy, non-beneficiary
Dr. Thomas Ehrman, King's College London, UK, non-beneficiary
Prof. Hualiang Jiang, Shanghai Institute of Materia Medica, China, non-beneficiary

3) Year 3 WP4 activities

- **3 face-to-face meetings** of certain members of the group were held mainly at King's College London, UK). Activity focussed on the preparation of the deliverables.



- Numerous **teleconferences**.
- Executed 4 **deliverables** (D4.15-D4.18).
- Maintenance of the work package **home page and web database**.
- **Participated in consortium-wide activities**.
- **Participated in discussions leading to creation of the new GP-TCM Research Association**.

4) Year 3 WP4 deliverables

- D4.15- Comprehensive report on the use of functional genomics in *in vitro* research of CHM (month 30)

Finalised in month 35; quality assured by consortium internal reviewers. Abstract: "The use of functional genomics in *in-vitro* research of CHM has been analysed focusing on the use of omics techniques, according to their pros and cons. Several aspects have been considered, among which is their technical and analytical utility and feasibility, as well as their exploitation in the field. Despite a general agreement on their usefulness in CHM research, their use has not yet reached a widespread diffusion in the scientific community due to the difficulties in their introduction in the laboratory. Nevertheless, in the last few years, with the introduction of more user friendly techniques and a deeper understanding of systems biology approaches, there has been an increase in published work on omics techniques in CHM, suggesting new trends towards their dissemination".

- D4.16- Handbook for using functional genomics techniques in *in vitro* CHM research (month 36)

Delivered on time; currently being reviewed by the steering committee. Abstract: "A handbook is presented on the state of the art of the use of functional genomics techniques in CHM research. It represents the culmination of the numerous discussions and deliberations of the WP4 working party of the FP7-funded European consortium, GP-TCM. It provides future perspectives for the use of omics and in-silico approaches in the modernisation and standardisation of TCM, and provides for the first time guidelines for good practice in the application of these methods in CHM research."

This deliverable is built on deliverables D4.8, D4.13 and a new literature search and discussions. Especially it refers to views and main conclusions of the following 6 omics related papers in the GP-TCM J. Ethnopharmacol. Special Issue. The handbook will be published on the website.

- Ouedraogo M, Baudoux T, Stévigny C, Nortier J, Colet JM, Efferth T, Qu F, Zhou J, Chan K, Shaw D, Pelkonen O, Duez P. Review of current and "omics" methods for assessing the toxicity (genotoxicity, teratogenicity and nephrotoxicity) of herbal medicines and mushrooms. J Ethnopharmacol. 2012; 140: 492-512
- Pelkonen O, Pasanen M, Lindon JC, Chan K, Zhao L, Deal G, Xu Q, Fan TP. Omics and its potential impact on R&D and regulation of complex herbal products. J Ethnopharmacol. 2012; 140: 587-593
- Jia J, Yu Y, Deng JH, Robinson N, Bovey M, Cui YH, Liu HR, Ding W, Wu HG, Wang XM. A review of Omics research in acupuncture: The relevance and future prospects for understanding the nature of meridians and acupoints. J Ethnopharmacol. 2012; 140: 594-630
- Uzuner H, Bauer R, Fan TP, Guo DA, Dias A, El-Nezami H, Efferth T, Williamson EM, Heinrich M, Robinson N, Hylands PJ, Hendry BM, Cheng YC, Xu Q. Traditional Chinese medicine research in the post-genomic era: Good practice, priorities, challenges and opportunities. J Ethnopharmacol. 2012; 140: 458-468



- Buriani A, Garcia-Bermejo ML, Bosisio E, Xu Q, Li H, Dong X, Simmonds MS, Carrara M, Tejedor N, Lucio-Cazana J, Hylands PJ. Omic techniques in systems biology approaches to traditional Chinese medicine research: Present and future. *J Ethnopharmacol.* 2012; 140: 535-544
- Barlow DJ, Buriani A, Ehrman T, Bosisio E, Eberini I, Hylands PJ. In-silico studies in Chinese herbal medicines' research: Evaluation of in-silico methodologies and phytochemical data sources, and a review of research to date. *J Ethnopharmacol.* 2012; 140: 526-534
- D4.17- Report in the Final Conference (**month 36**)
Delivered on time; currently being reviewed by the steering committee. Main contents comprise **this WP4 planning document** (omitted here), feedback from review reports by the Steering Committee and the feedback from the participants of the Final Conference. Will be updated and submitted immediately after the Final Conference.
- D4.18- Submission of review papers for publication (**month 36**).

Delivered on month 35; WP4 main publications are:

- **Omic techniques in systems biology approaches to traditional Chinese medicine research: Present and future**, Alessandro Buriani, Maria L. Garcia-Bermejo, Enrica Bosisio, Qihe Xu, Huige Li, Xuebin Dong, Monique S.J. Simmonds, Maria Carrara, Noelia Tejedor, Javier Lucio-Cazana, and Peter J. Hylands, *Journal of Ethnopharmacology*, 2012; 140: 535-544 <http://dx.doi.org/10.1016/j.jep.2012.01.055>.
- **In-silico studies in Chinese herbal medicines' research: Evaluation of in-silico methodologies and phytochemical data sources, and a review of research to date**, DJ Barlow, A Buriani, T Ehrman, E Bosisio, I Eberini, PJ Hylands, *Journal of Ethnopharmacology*, 2012; 140: 526-534
<http://www.sciencedirect.com/science/article/pii/S0378874112000542>

5) Year 3 experiences gained and lessons learnt

- No particular issues were noted but it became increasingly clear that face-to-face meetings are essential to the development of a coherent interaction within the group and represent a unique moment for productivity and high-quality work.
- Interaction between the group members was close and productive.
- The appointment of Dr Buriani as Assistant Coordinator was particularly effective and crucial to the completion of the objectives in a timely manner.
- It seems clear that the appointment of members to more than two (or three) work packages in such a complex consortium is less than productive – a defined limit would allow full participation of members to their allotted tasks.

6) WP4 summary over Years 1-3

- Over the lifetime of the project, management of the project was facilitated by a number of face-to-face meetings, with intermediate individual meetings and telephone conversations. Also, because of overlap of work packages and participants, it was also possible to benefit from a number of joint meetings.
- In total, it was found possible to hold a total of eight face-to-face meetings: in June 2009 in Madrid (joint with WP5), the kick-off meeting in two parts in October 2009 and March 2010, July 2010 (just before the Consortium-wide meeting in Henley-on-Thames, UK), January 2011, March 2011, November 2011 and March 2012.



- Not all members could attend all meetings but it is really considered that even short (one – one and half days) face-to-face meetings are invaluable as a forum for discussion, to maintain interaction and execution of work plans.

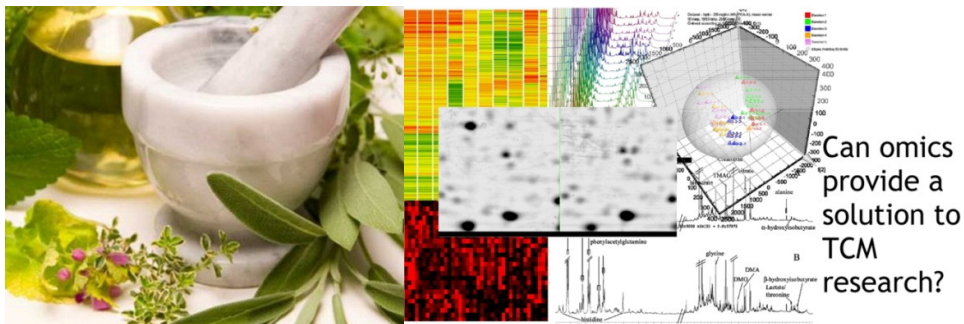
The outputs generated comprised:

- 18 deliverables, including
 - D4.1- Kick-off WP meeting (**month 6**).
 - D4.2- Kick-off meeting report: Agreed schedule of the task assignment of subgroups (**month 6**).
 - D4.3- Website building and maintenance (**month 6**).
 - D4.4- Report of the discussion group on biological target oriented database (**month 12**).
 - D4.5- Biological target oriented database for *in vitro* research on CHM (**month 12**).
 - D4.6- Report on quality criteria and scoring of the CHM database (**month 12**).
 - D4.7- Update of CHM target oriented database with quality scores (**month 12**).
 - D4.8- Handbook on good practice in the reporting of CHM experimental work (**month 18**).
 - D4.9- Discussion group evaluating data about molecular mechanisms of action of CHM (**month 18**).
 - D4.10- Update of the CHM target oriented database with molecular mechanism evaluations (**month 18**).
 - D4.11- Report on existing databases and software for *in silico* studies of phytocomplexes (**month 24**).
 - D4.12- An interdisciplinary consensus meeting on *in silico* tools for CHM research (**month 24**).
 - D4.13- Handbook of guidelines for using *in silico* tools in CHM research (**month 24**).
 - D4.14- Discussion group on use of functional genomic techniques for *in vitro* CHM research (**month 24**).
 - D4.15- Comprehensive report on the use of functional genomics in *in vitro* research of CHM (**month 30**).
 - D4.16- Handbook for using functional genomics techniques in *in vitro* CHM research (**month 36**).
 - D4.17- Report in the Final Conference (**month 36**).
 - D4.18- Submission of review papers for publication (**month 36**).
- These are subcategorised into
 - **3 reports** (D4.4 - Report of the discussion group on biological target oriented database, D4.6 - Report on quality criteria and scoring of the CHM database, and D4.11 - Report on existing databases and software for *in silico* studies of phytocomplexes)
 - **3 handbooks** (D4.8 - Handbook on good practice in the reporting of CHM experimental work, and D4.13- Handbook of guidelines for using *in silico* tools in CHM research, D4.16 - Handbook for using functional genomics techniques in *in vitro* CHM research). These outline handbooks are guides only which will be useful in the generation of more robust and widely applicable reference tools.
 - **A questionnaire survey** on participants' views regarding the value of the application of omic and *in-silico* methods in TCM research
 - **A dedicated webpage on WP4** (*in vitro*) on the GP-TCM website
 - **A searchable database** of critically reviewed and quality scored articles to act as a guideline for future activity (D4.5, D.4.7 and D4.10)
- Main publications of WP4 (D4.18):

The following articles contribute to the Proceedings of the Final Conference and the Leiden Congress in April 2012.

- Omic techniques in systems biology approaches to traditional Chinese medicine research: Present and future, Alessandro Buriani, Maria L. Garcia-Bermejo, Enrica Bosio, Qihe Xu, Huige Li, Xuebin Dong, Monique S.J. Simmonds, Maria Carrara, Noelia Tejedor, Javier Lucio-Cazana, and Peter J. Hylands, *Journal of Ethnopharmacology*, 2012; 140: 535-544 <http://dx.doi.org/10.1016/j.jep.2012.01.055>

Abstract: The available databases that catalogue information on traditional Chinese medicines are reviewed in terms of their content and utility for *in-silico* research on Chinese herbal medicines, as too are the various protein database resources, and the software available for use in such studies. The software available for bioinformatics and 'omics studies of Chinese herbal medicines are summarised, and a critical evaluation given of the various *in-silico* methods applied in screening Chinese herbal medicines, including classification trees, neural networks, support vector machines, docking and inverse docking algorithms. Recommendations are made regarding any future *in-silico* studies of Chinese herbal medicines.



- *In-silico* studies in Chinese herbal medicines' research: Evaluation of *in-silico* methodologies and phytochemical data sources, and a review of research to date, DJ Barlow, A Buriani, T Ehrman, E Bosio, I Eberini, PJ Hylands, *Journal of Ethnopharmacology*, 2012; 140: 526-534 <http://www.sciencedirect.com/science/article/pii/S0378874112000542>

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Another joint article is planned that will focus in detail on the scoring methodology: WP4 produced good practice guidelines on literature review by the development and proposal of a scoring system to help the scientific community to evaluate critically reports and also to serve as a checklist to authors for minimum quality standards in conducting and reporting research involving omic and *in-silico* methods in TCM research and have set of pre-defined rules to do literature reviews, etc.

7) WP plans for future activities towards the extended lifespan of the FP7 GP-TCM project

- Intention to disseminate findings by participation of the CGCM meeting in Macao in August 2012 and the first annual conference of the newly formed GP-TCM Research Association in Shanghai in October 2012.
- Education: PhD courses, Marie Curie Initial Training Network.



- Further related grant applications. As a first initiative an application for the last FP7 call in July 2012 will be taken into consideration

8) WP4 suggestions to the GP-TCM Research Association regarding the future of the area covered by WP4:

- Special Interest Groups (with subjects aligned but not limited to GP-TCM work packages) to be encouraged, for example, omics, *in-silico*, standardisation, etc.
- Membership would be from the Association but not only from the Board of Directors. This could provide a means of engagement for members and also lighten workload on Directors.

9) WP Finances (details of your current WP budget):

The budgetary matters have been efficiently and correctly handled and overseen by the finance Department of King's College London, UK. At the end of the Final Conference, there will be modest positive balance which will be used, if the consortium is extended, to allow selected WP members to attend a conference in China later in 2012.

10) Final Conclusions of your WP:

- WP4 has delivered all deliverables and passed internal quality assurance and the review by the Commission except some most recent deliverables that are currently being quality assured.
- In the past three years, WP4 focused on deliverables and made the best use of the limited funding to organise coordinated actions through a number of face-to-face meetings and other forms of communications.
- All the objectives of the WP have been fulfilled.
- Very strong professional and personal relationships have been formed between members of the work package, which has facilitated its execution.

Discussion session led by Dr. Alessandro Buriani)

- How best to take our outputs and progress into the GP-TCM Research Association?
- Was WP4 too early in the field for TCM focus?
- The very varied quality of work even in good quality journals!
- Authors and Reviewers have insufficient knowledge and/or journals have no criteria?
- The way forward



1.4 Updates based on reviewers' comments and feedback from the Final Conference

During the discussion session, there was a general agreement on the poor quality of the literature available on in vitro research with CHM and that the effort must continue even after the life span of the project to promote good practice in CHM research. This will be one of the objectives of the new Association established by the consortium: *The GP-TCM Research Association*. One more aspect which was agreed upon by many was concerned with the basic criteria for the choice and use of omics techniques in TCM research, which, as presented by WP4 should be applied when clinical or traditional effects of the Chinese Formulae are well consolidated. Also more than one method should always be used (e.g transcriptomics and metabonomics or metabonomics and proteomics). At the end of the discussion, WP4 launched the idea of participating to the next FP7 call with a project on experimental models for proactive prevention with CHM in a personalised medicine perspective.

1.5 Conclusions

The WP4 session of the GP-TCM Final Conference was an invaluable opportunity for the WP to summarise, discuss and conclude on the work of the 3rd year of the WP and the work of the past three years and discuss the achievements with the members of the other work packages.

After this conference, WP4 members will continue to collaborate in the extended life span of the consortium (until end of October 2012) to have the final polishing of its deliverables, to disseminate what has been learnt and to initiate actual laboratory collaborations and new grant applications.