

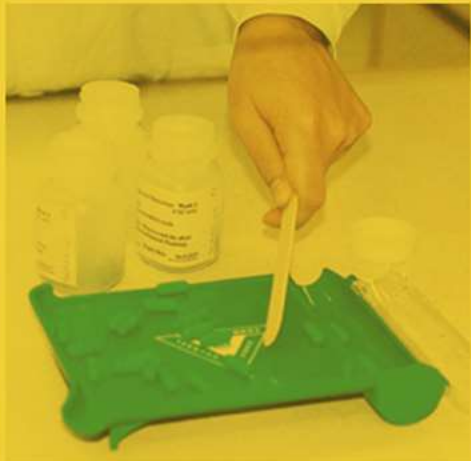


**Clinical Trials Centre**  
**The University of Hong Kong**



# Experience in Clinical Trials of Chinese Medicine

Seminar on Research and Development of Chinese Medicine 2014





# Clinical Trials Centre

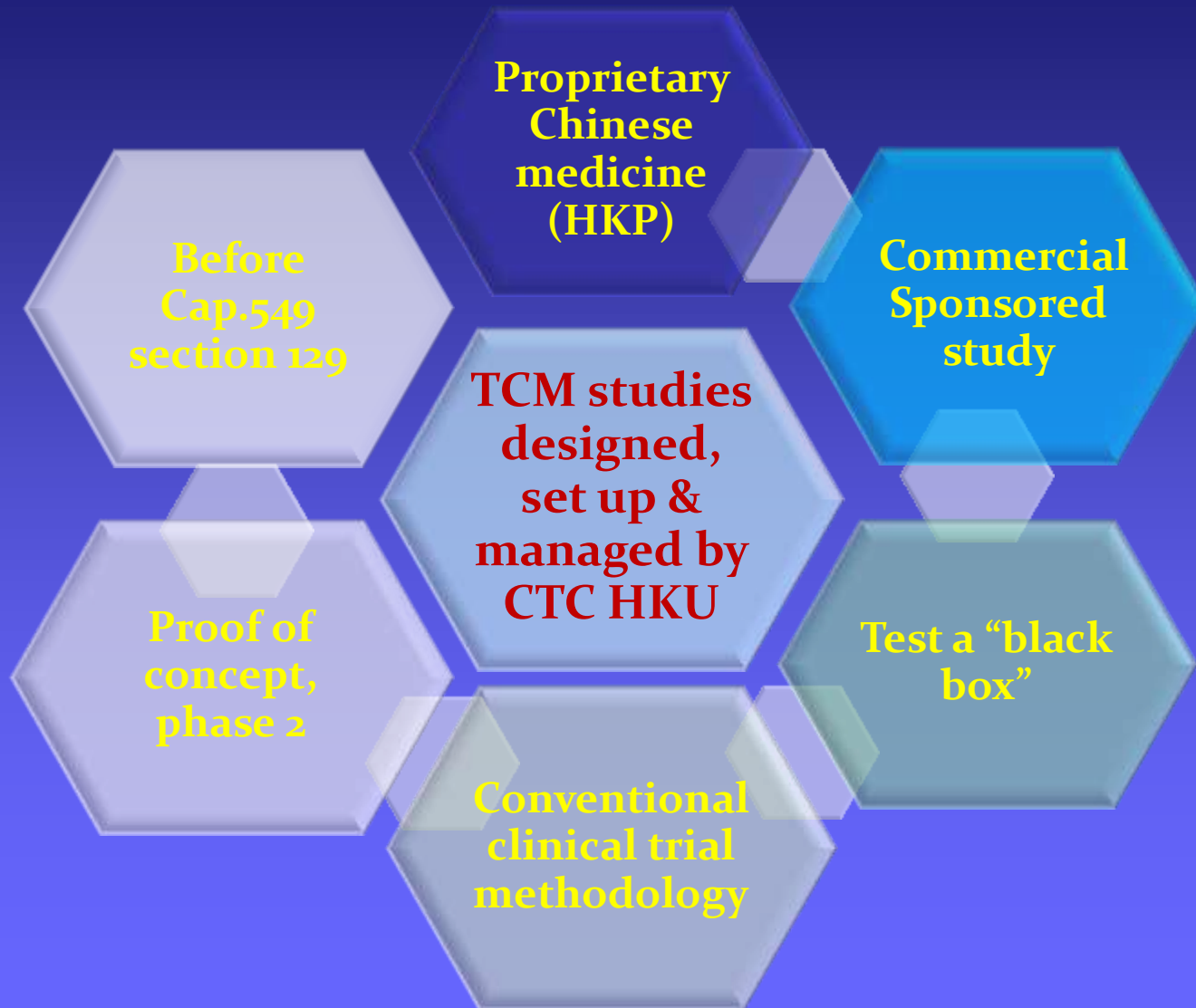
## The University of Hong Kong

<b>6 Functional Units</b>	<b>Major Activities</b>
<b>Corporate Services &amp; Administration</b>	HR, IT Management, Facilities Management
<b>Business &amp; Project Acceleration</b>	Contract & Study Site Financial Management, Project Coordination and Research Ethics Affairs, Study Site Coordination, Specimen & Drug Management
<b>Project Management &amp; Contract Services</b>	Protocol Development, Project Management, Trial Monitoring, Data Management, Med Statistics
<b>QA &amp; Education</b>	Training, Internal Audit, Internal QA
<b>Phase 1 Centre Operation</b>	Phase 1 Trials, BA/BE Studies
<b>PK Lab</b>	Consultation, PK Lab Operations



**What kinds of TCM studies  
have been supported  
by CTC HKU?**

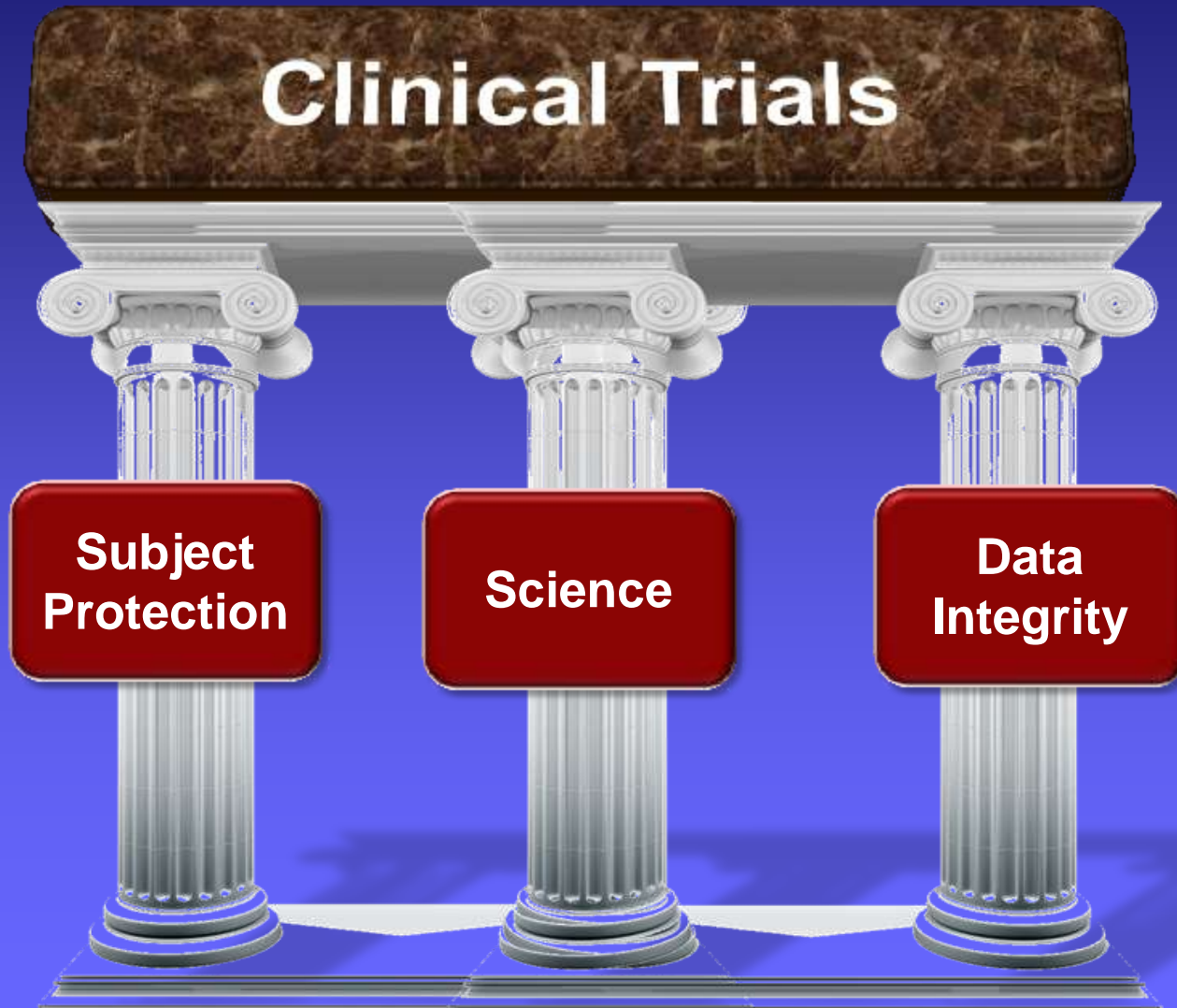
# TCM Clinical Studies Characteristics





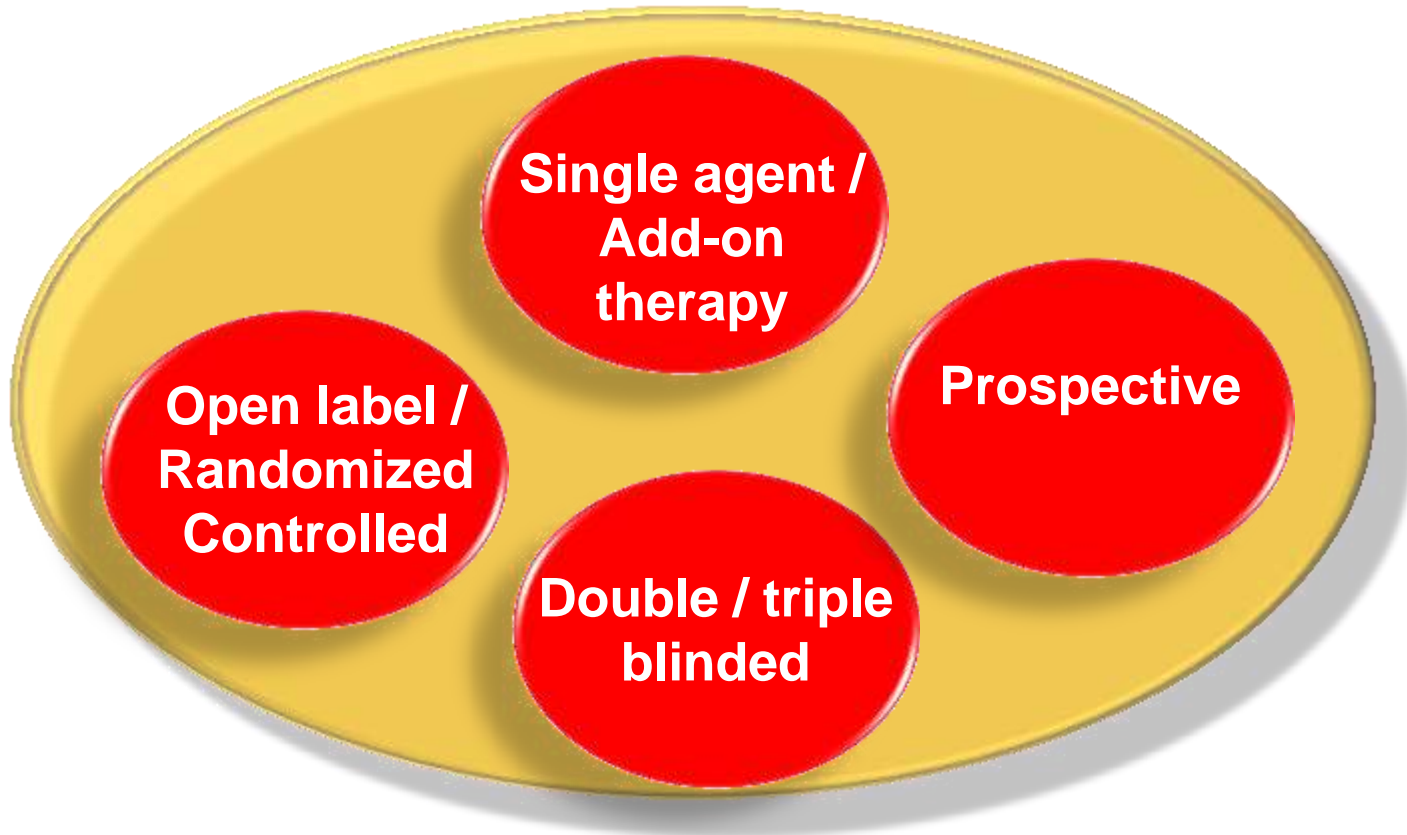
**How we conducted TCM  
clinical studies?**

# Elements Supporting Clinical Trials



# Methodology used

## Conventional Clinical Trial Research Methodology



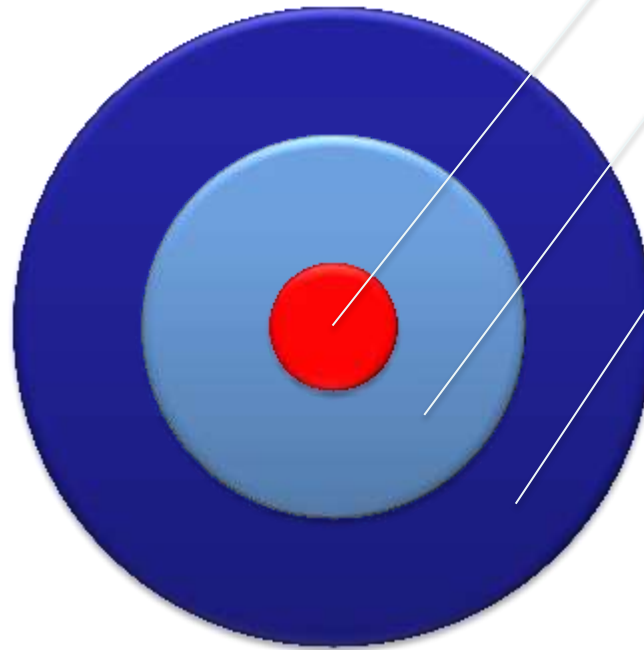
# Methodology Used

Objectives well set - clinically relevant, valid and reliable measure available

**Only *one* primary objective**

**Secondary objective 1**

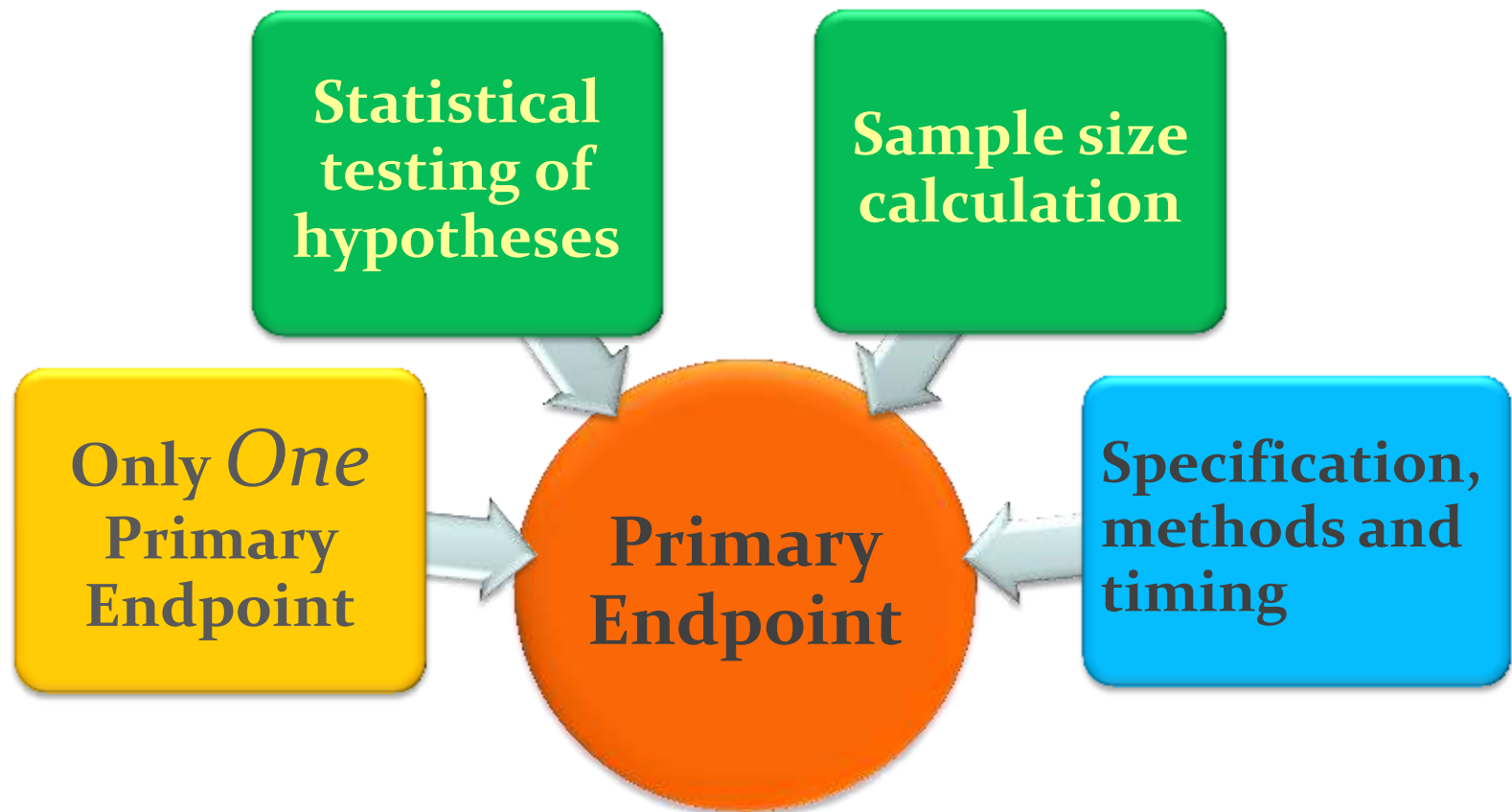
**Secondary objective 2 or more**





## Methodology Used

Primary Endpoint well set - clinically relevant, valid and reliable measure of the primary objective



# Endpoints/Outcome Measures

## *Some examples on measuring efficacy:*

Chronic knee  
Osteoarthritis

- Primary: Pain intensity measured by VAS
- Secondary: Change in WOMAC total score

Decompensated  
cirrhosis

- Primary: Model for End-Stage Liver Disease
- Secondary: Child-Pugh's score, CLDQ, EQ5D, SF36

Parkinson

- Primary: Unified Parkinson's Disease Rating Scale
- Secondary: Modified H & Y Scale, S & England Activities of Daily Living Scale, Total daily dose of levodopa prescribed, daily number of "off" hours

# Endpoints/Outcome Measures

## Safety Outcome Measure:

*Adverse Events* – defined by ICH guideline E2A & E6

Incidence of adverse events by,

- Serious adverse event (SAE)
- Relationship to study intervention
- Expectedness of event
- Severity of event

A safety management plan:

- Safety specification
- Unblinding
- Monitoring
- Reporting

# Safety Measures Used



Common safety assessments:

e.g. physical examinations & vital signs, biochemistry, hematology, urinalysis, ECG / ECHO, pregnancy test

Active detection of adverse events (solicited & non-solicited)

Collect information of any concomitant treatments

For add-on treatment, no co-administration of standard treatment



# Safety Measure Used

**Data Safety Monitoring Committee reviewed safety data of high risk studies**

Independent Members:  
Clinicians/Experts & Statistician

DSMC would recommend  
sponsor to continue/modify/  
terminate the study

Discussion  
via meeting

**Independent  
Review**



# Ethics and Quality Complied

Studies were conducted in accordance with the respective protocols, ICH GCP guidelines, standard operating procedures (SOPs) and applicable regulatory requirements

- Protocol, GCP, SOPs compliance
- Investigational drug accountability
- Site staff training
- Source documentation & data capture
- Site monitoring including source data verification
- Data management
- etc.....





**What were the challenges  
during the studies?**

# Beating the Odds



**pCm placebo without herbal aroma**



- pCm placebo absorbed slight aroma of the pCm when stored in a confined area
- Arranged subjects' visits in different schedule and avoid chance of comparison of trial pCm among subjects



**pCm was accessible from the market. There was a possibility of self-purchase of the trial pCm.**



- Named the trial pCm with code but not the product name
- Informed the trial subjects about the ingredients of the active pCm and manufacturing standards but not the brand name or name of the manufacturer/dealer





**What are the limitations &  
challenges ahead?**

# Limitations & Challenges Ahead



**The dose of trial pCm used may not be appropriate for showing the anticipated effects**

???



**The bioactive compounds that account for the therapeutic effects remain unclear**



**The conventional dose finding phase 1 study i.e. maximum tolerated dose / optimal biologic dose / pharmacokinetic / pharmacodynamic study**

# Limitations & Challenges Ahead



Better understand the efficacy and pharmacological mechanisms

Herbal



OA Alternative Medicine  
Open Access

Review

Integrating transcriptional profiling with network-based methodologies for revealing molecular mechanisms of traditional Chinese medicine

L Huang<sup>1</sup>, L Jiang<sup>1</sup>, Q Kuang<sup>1</sup>, M Li<sup>1</sup>, Z Wen<sup>1,2\*</sup>, L He<sup>3\*</sup>

OPEN ACCESS Freely available online

PLOS ONE

Material Basis of Chinese Herbal Formulas Explored by Combining Pharmacokinetics with Network Pharmacology

Lixia Pei<sup>1,2</sup>, Yuanwu Bao<sup>1,2</sup>, Sheng Liu<sup>1</sup>, Jin Zheng<sup>1</sup>, Xiuping Chen<sup>2\*</sup>

<sup>1</sup>Pharmacology Laboratory of Traditional Chinese Medicine, Longhua Hospital, Shanghai University of Traditional Chinese Medicine, Shanghai, China, <sup>2</sup>State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao, China

# Limitations & Challenges Ahead



The current systematic conventional clinical trial approach may not be a good way to test TCM which works on 'syndromes' rather than 'disease'



- Inclusion of trial subjects based on western diagnosis and also pattern (syndrome) differentiation in TCM i.e. hot, warm, cool and cold
- Involve TCM practitioner in selection of subjects

Rheumatol Int (2012) 32:61–68  
DOI 10.1007/s00296-010-1546-7

ORIGINAL ARTICLE

**Cold and heat pattern of rheumatoid arthritis in traditional Chinese medicine: distinct molecular signatures indentified by microarray expression profiles in CD4-positive T cell**

Cheng Lu · Cheng Xiao · Gao Chen · Miao Jiang ·  
Qinglin Zha · Xiaoping Yan · Weiping Kong · Aiping Lu

## Sum Up



**While we are focusing subject protection, science, data integrity in conducting TCM clinical trials, the pre-clinical development of TCM in identifying bioactive compound and mode of actions is the key.**



**Thank you!**