

Metabonomics-based Research of TCM using Knowledge Engineering (KE) Approaches

应用知识工程手段对中医药的基于代谢组学的研究

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Collaborative partners and the funding

合作各方和基金

- Collaboration between 合作方包括:
Zhejiang Chinese Medicine University (Hangzhou)
浙江中医药大学
Shanghai Institute of Materia Medica,
CAS中科院上海药物研究所
IPI, University of Bradford, UK
IPI制药创新研究院, 英国Bradford大学
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Potential contribution of TCM to development of novel medicines in global market

在全球市场中，中医药对新药开发的潜在贡献

- Long established and successful TCM therapies
长期以来得到证实的中医药成功疗法
- ‘Western’ medicine approaches lack effective, curing therapies for various indications (e.g. Alzheimer’s disease, schizophrenia, diabetes)
西药在很多疾病的治疗上疗效不佳或无法治愈（例如，阿耳茨海默氏病，精神分裂症，糖尿病）
- Opportunities for TCM based novel medicines in global market
基于中医药所开发的新药在全球市场中的机遇

Reconciling Philosophies and Practice of TCM and 'Western' Medicine

将中医和西医的理念和实践调和起来

- Large gaps between TCM and 'modern medicinal chemistry' in philosophy, theories, and practice
在观念、理论和实践上，中药和现代医药化学之间存在鸿沟
- 'Dialectic and holistic' versus 'pure principle' (chemical agent)
“辩证论和整体论”与“单一成份”（化学药）
- To bridge the gaps, need new scientific thinking and approaches in evaluating clinical effects of TCMs and linkages to TCM medicines (e.g. IV/VC, KE/AI tools)
填补鸿沟，需要应用新的科学思路和方法，来找到中药和中药疗效的临床评价之间的关联性（例如，体内外的相关性，知识工程/人工智能技术等）

Recent Data Base and KE Studies

近来的数据库和知识工程技术的应用研究

- Two broad data bases created for constituents of TCMs from the literature – chemical and biological
建立了化学和生物学两大数据库，涵盖了中药组份的文献信息
- Used ‘virtual laboratory’ screening method to link TCM constituents to biological targets and therapeutics
应用“虚拟实验室”筛选方法，将中药组分、生物标靶和临床治疗联系起来
- Computational KE/AI tools – decision trees, random forest models, cluster programs
计算机知识工程/人工智能工具 – 决策树、随机森林模型、组群程序

(Ehrman et al., (2007) J Chem. Inf. & Mol. Modelling, 47, 254-263

Ehrman et al., (2007) J Chem. Inf. & Mol. Modelling, 47, 264-278)

TCM and Modern Biopharmaceutics Theory

中医和现代生物制药学理论

- Apply advanced bioanalytical science to clinical regimens of TCM medicines and treatment
将先进的生物分析技术应用于中医药临床治疗
- Link 'input' and 'output' data using computer based data interrogation technologies
应用基于数据分析手段的计算机技术，将“输入”和“输出”数据关联起来
- Discover determining factors in achieving patient benefit and 'hidden knowledge' using KE/AI tools
应用知识工程/人工智能工具，发现获得疗效的决定性因素和“隐藏的知识”

Metabonomics Theory

代谢组学理论

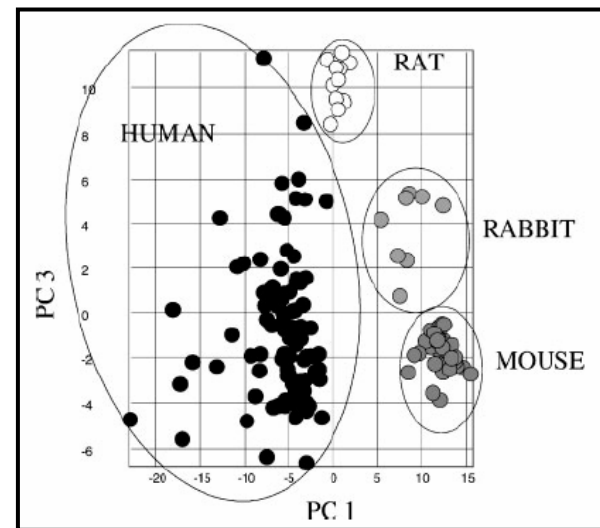
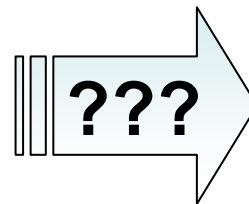
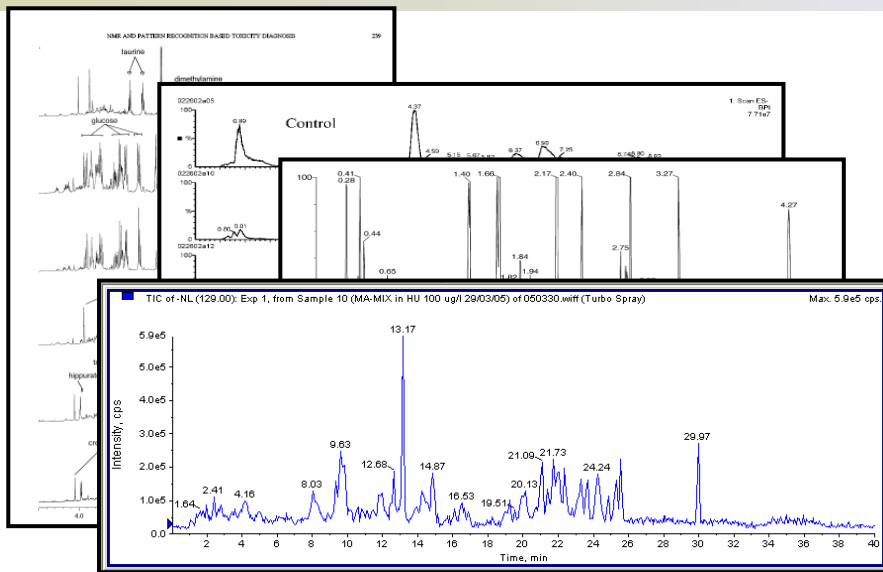
- Metabonomics is the quantitative measurement of the dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modification
代谢组学定量研究生命系统对病理学、基因改变等刺激的动态多参数代谢响应
- Advanced analytical science provides means to determine chemical composition of TCMs, and qualitative and quantitative measurement of dynamic metabolic responses of patients
先进的分析科学提供了测定中药的化学组成和定性、定量测定病人的代谢动力学响应

Metabonomics Process

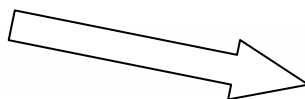
代谢组学过程

- **Analytical methods to capture metabolite signals:**
应用分析手段获取代谢物信号
NMR, LC/MS, GC/MS(TOF)
- **Chemometric and statistical analysis**
化学测定和统计学分析方法
 - **separation of patient groups by dose, time, onset or recovery from disease**
用剂量、时间、疾病的发作或痊愈等因素将病人分为不同群组
 - **determine the pattern(s) of signals that are responsible for association of metabolite profile and 'outcome'**
确定反映代谢物变化特征和“临床结果”的模式
- **Metabolite assignment and biochemical pathway relevance**
代谢物评价和生化过程的相关性

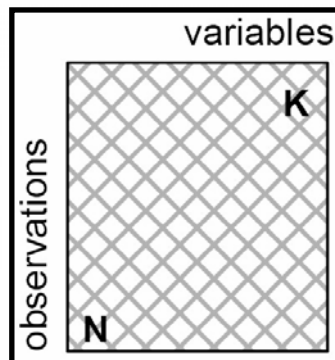
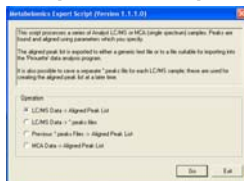
Data \neq Information 数据不等于信息



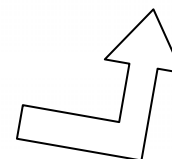
Visualisation



Metabolomics
Export Script



Matrix



SIMCA-P
KE tools

Data Analysis by Computational Methods

应用计算机手段分析数据

- **Results are based on multicomponent, multivariant, non-linear systems with complex interactions**
计算结果基于多组分、多变量、非线性的和存在复杂的相互作用的数据
- **Data interpretation and knowledge discovery will be based on artificial neural networks (ANN) and 'neurofuzzy logic'**
基于人工神经网络和模糊神经网络技术，解释数据和发现新知识
- **Goal is to discover underlying relationships between specific TCM constituents, patient demographics and metabolic responses linked to beneficial or adverse biological effects**
目的是发现中药组份、病人的人口学特征与代谢响应以及相关的正面的和负面的生物效应之间存在的隐含关系

Data Mining plays key role in research of TCM with multiparametric data and their correlation

数据挖掘技术在中药多因素数据及其相关性研究中的重要作用

Chemical Fingerprints

化学指纹

Metabonomic Fingerprint

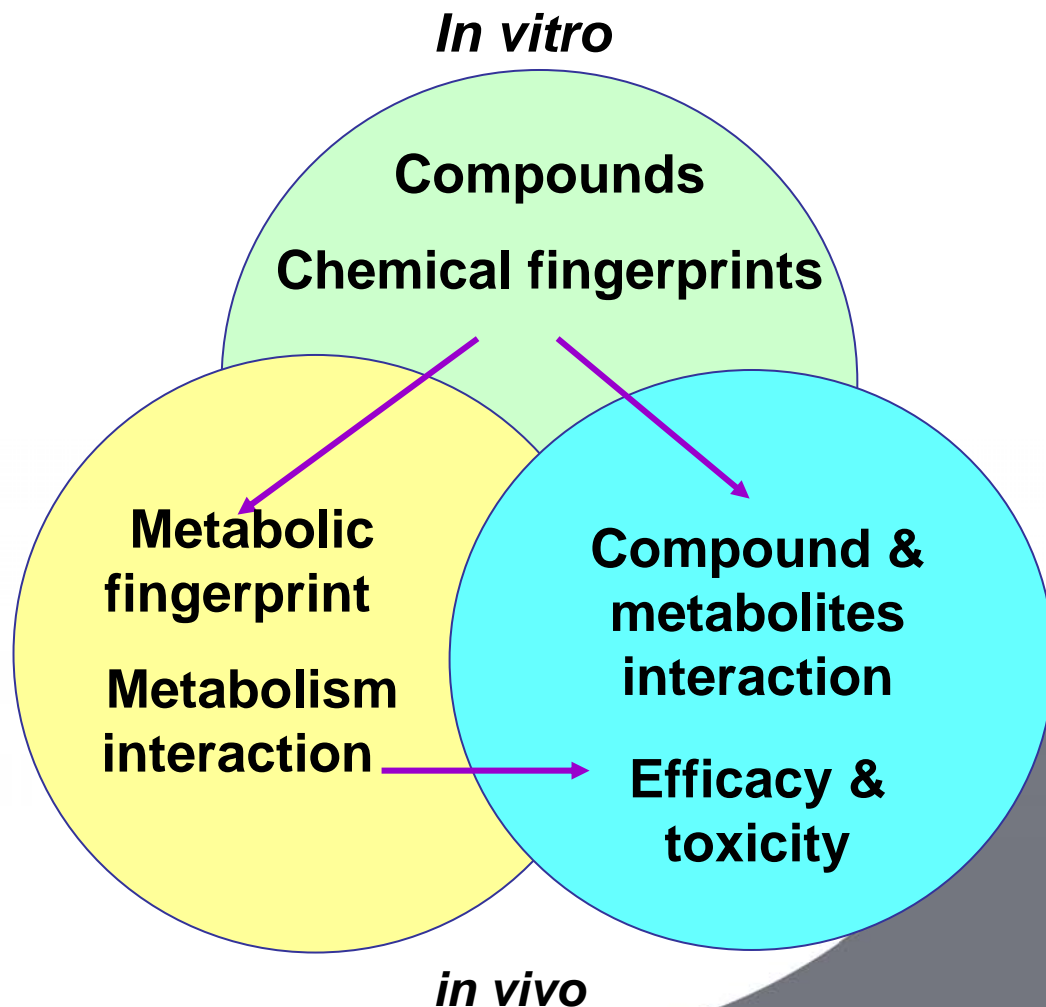
代谢组指纹

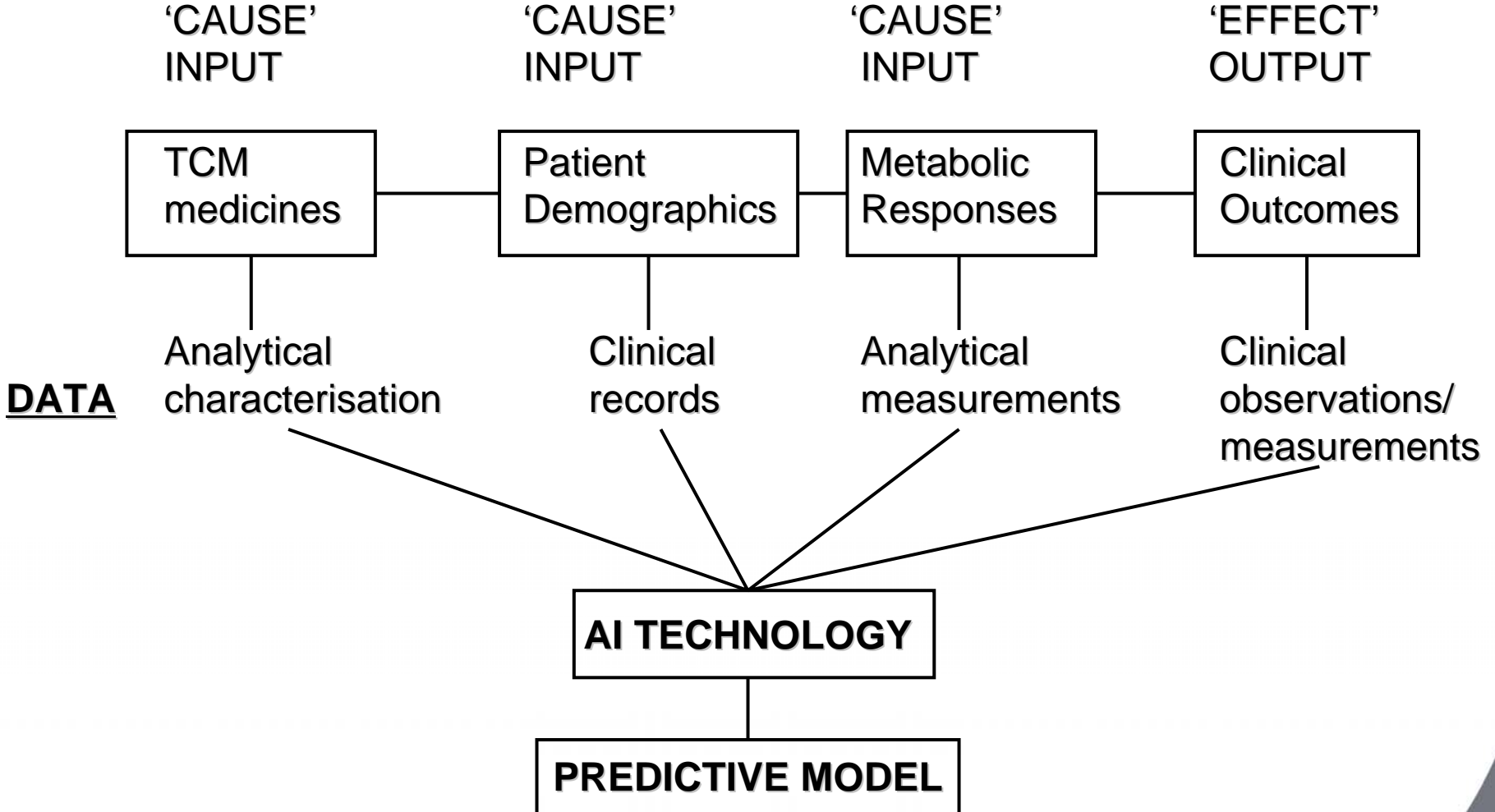
Pharmacodynamic Profile

药效动力学特征

Toxicological Profile

毒理学特征

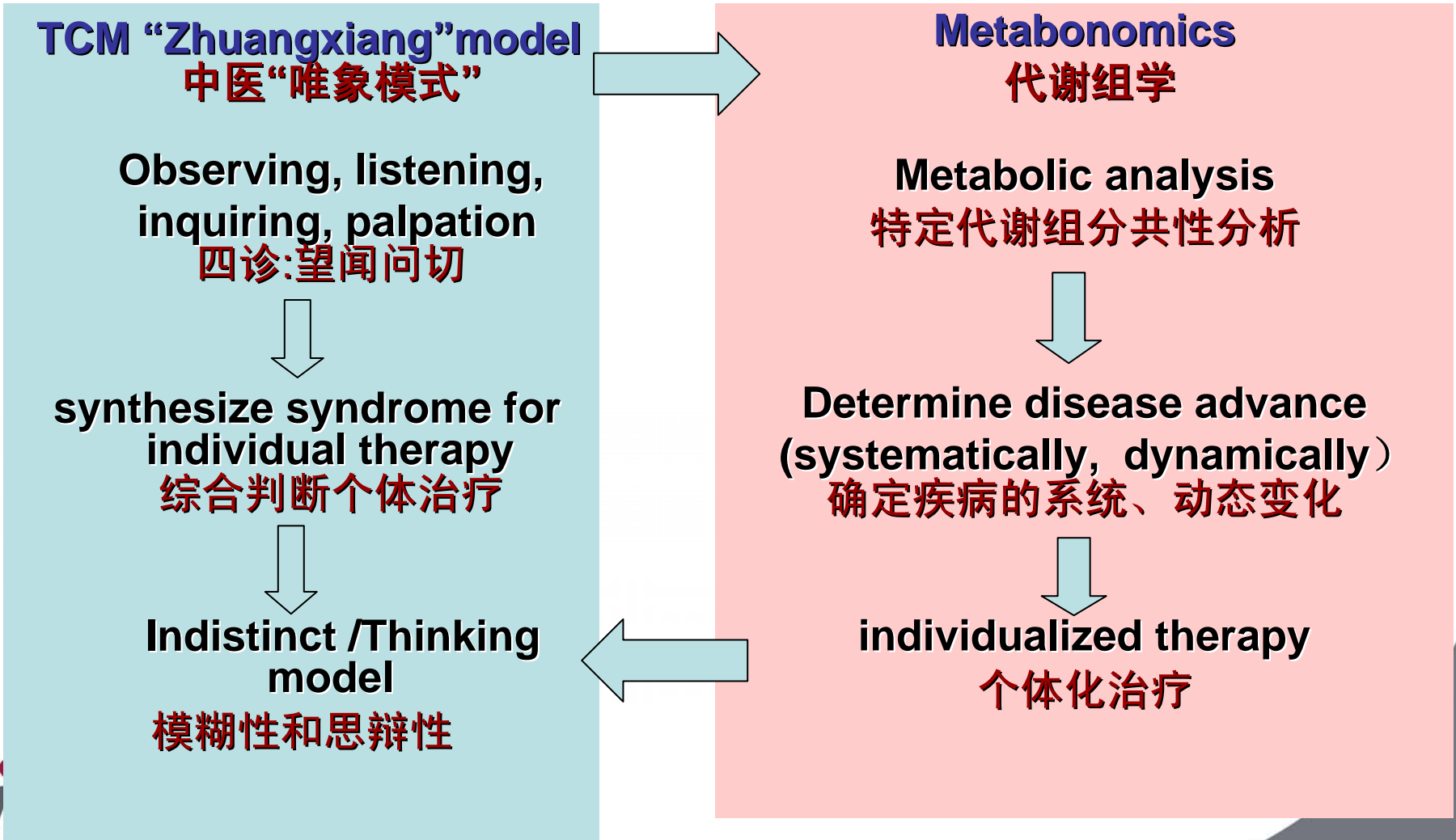




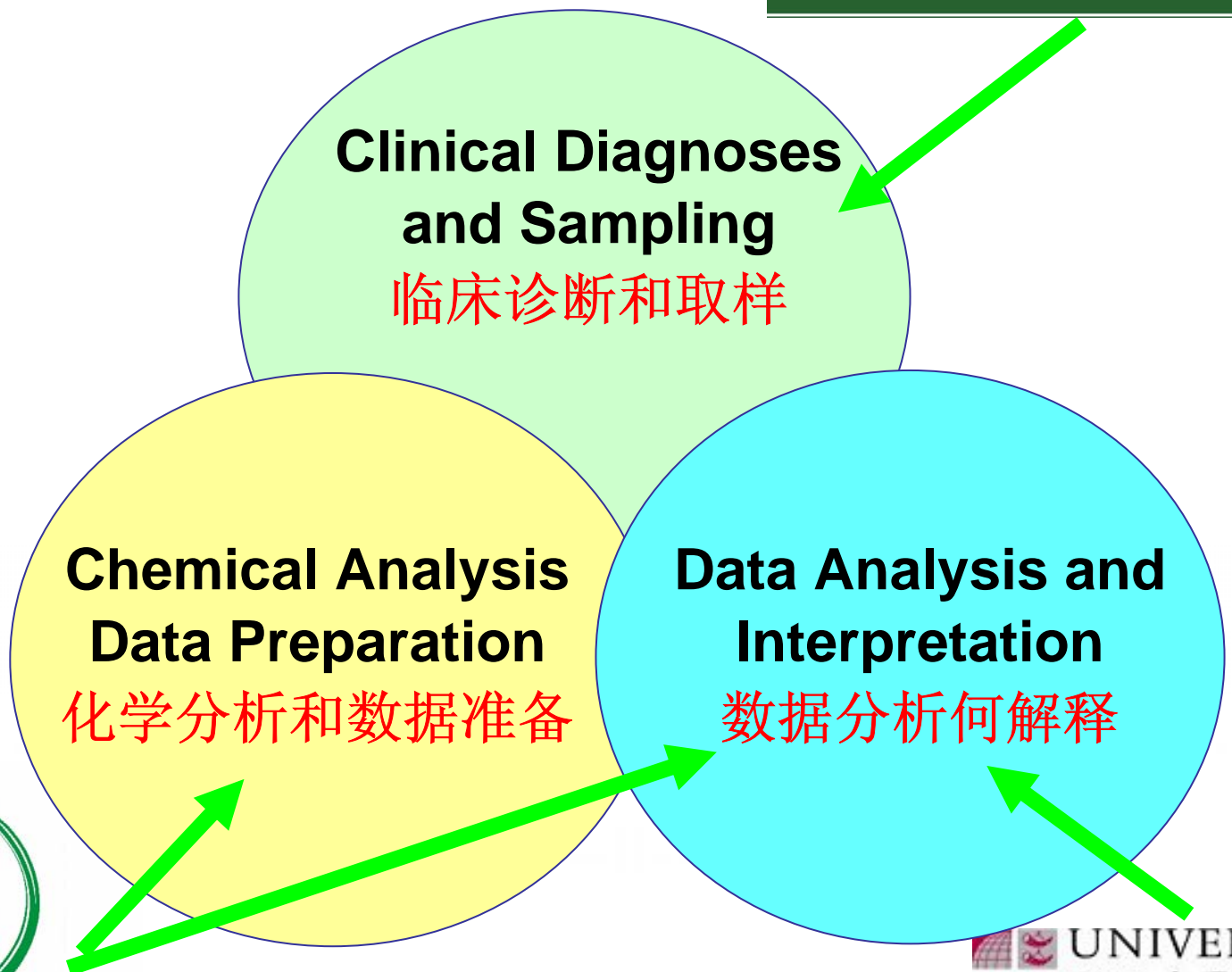
- Apply to diabetes therapy in first instance

Dialectic therapeutic principles vs metabonomics

中医辨证论治与代谢组学



Our roles



Our Goals 我们的目标

- **Provide chemical and biochemical knowledge for explaining clinical outcomes of TCM therapies for diabetes**
为解释中医治疗糖尿病的临床疗效提供化学和生物化学知识
- **Establish principles of metabonomic/KE approach for other TCM therapies**
为其他中医疗法建立代谢组学/知识工程手段的理论基础
- **Use the new knowledge to address the challenges of introducing TCMS into global markets**
应用新知识来应对将中医药推向全球市场所面临的挑战