



Top-down vs. Bottom-up

Gut Microbiota and Whole-body Systems Biology 肠道菌群与人体系统生物学

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中国上海市东川路800号上海交通大学生物楼3-517 赵立平



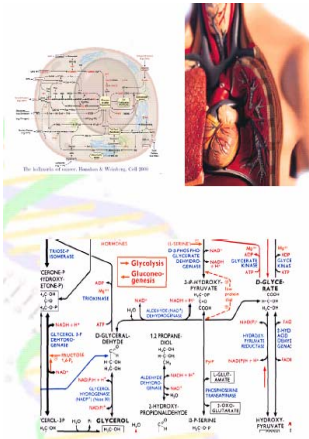
“模糊的”整体

- The four diagnostic techniques “四诊”
 - 望、闻、问、切
- The eight guiding principles for differentiation of syndromes “八纲辨证”
 - 表里
 - 寒热
 - 虚实
 - 阴阳

感官测量 经验判断
Holistic but empirical

从基因的角度解释和防治疾病的分子医学 Gene-centric, molecular medicine

DNA vs. *QI* “氣”



精细的局部
Molecular yet local

- 基因序列多样性与疾病易感性的关系
- 基因序列多样性与药物敏感性的关系
- 基因表达特性与药物代谢机理
- 基因表达特性与疾病发展过程
-

定量测定 模式识别
Molecular detail at cellular level
but fragmentary
at whole body level

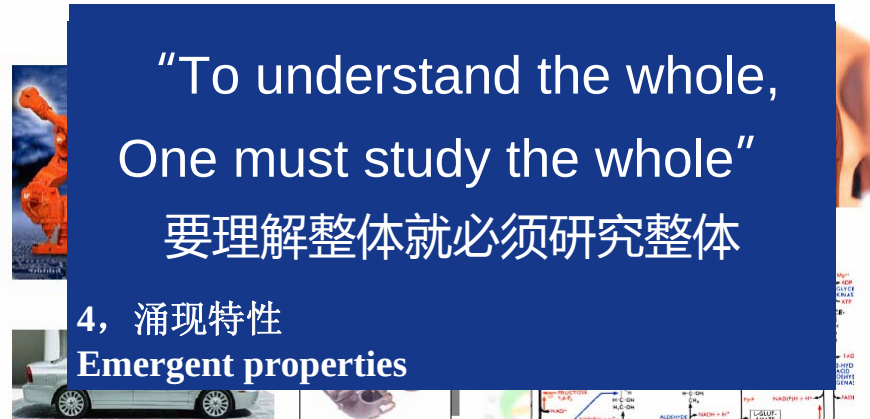
- TCM vs. Western Medicine
 - Diseased man vs. man's disease
 - 病的人与人的病
 - Stratification of patients vs. classification of diseases
 - 病人分类与疾病分型
 - Top-down vs. bottom-up
 - 自上而下与自下而上
 - Global vs. local
 - 整体到局部与局部到整体
 - Intact person vs. Genes
 - 完整的人体与基因





Engineering paradigm and TCM 工程学思维模式与中医理论

Tools for understanding complex engineering systems can be applied in biomedicine

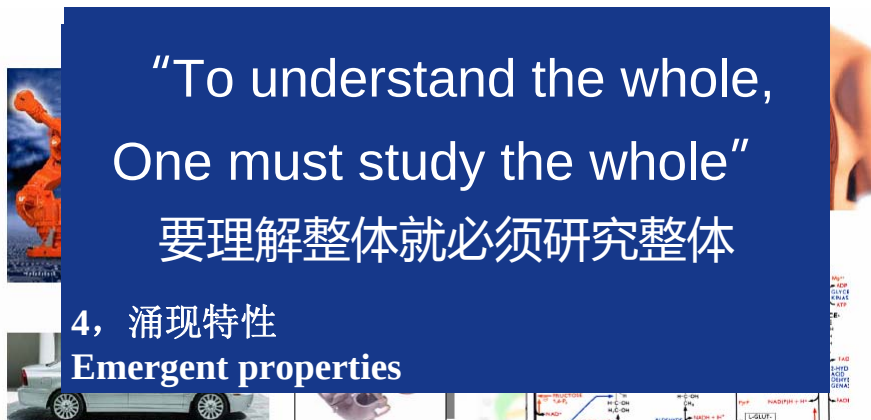


"To understand the whole,
One must study the whole"
要理解整体就必须研究整体

4, 涌现特性 Emergent properties

Engineering paradigm and TCM 工程学思维模式与中医理论

Tools for understanding complex engineering systems can be applied in biomedicine



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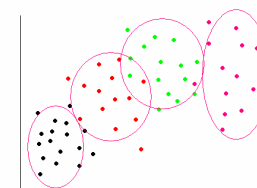
4, 涌现特性 Emergent properties

Engineering paradigm and TCM 工程学思维模式与中医理论

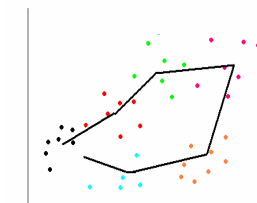
Tools for understanding complex engineering systems can be applied in biomedicine

涌现特性测量与复杂系统分类和监测 Classification and monitoring of complex systems based on measurements of emergent functions

- Systems states and state space models
 - Structural state 结构状态
 - Functional state 功能状态
- System trajectory analysis
 - Attractors 吸引子
 - Initial conditions 起始条件
 - Disturbances 扰动



State space model
状态空间模型



System trajectory analysis
系统轨迹分析



结构健康监测 Structural Health Monitoring



Classification and identification of complex systems based on the measurement of their emergent functions 基于涌现特性测量的复杂系统的 精细分类与鉴定

Classification in an unsupervised learning mode
with no prior knowledge required
无监督的学习分类模式

Changes in vibration, noise and exhaust gas for engine health monitoring

AIAA 1st Intelligent Systems Technical Conference
20 - 22 September 2004, Chicago, Illinois

AIAA 2004-6461

Development of an Information Fusion System for Engine Diagnostics and Health Management

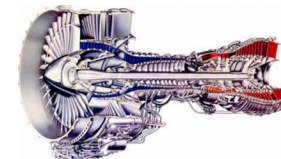
Allan J Volponi
Pratt & Whitney, East Hartford, CT 06108

Tom Brotherton
Intelligent Automation Corp., Poway, CA 92064

Robert Luppold
Luppold & Associates, West Newton, PA 15089

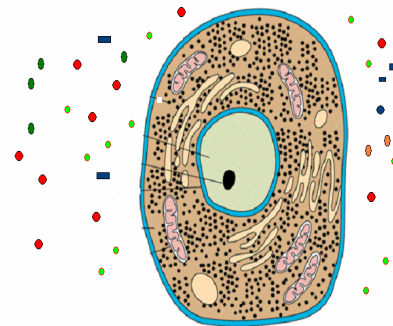


Figure 1 C-17 Globemaster



振动、噪声和尾气的模式变化与发动机健康监测

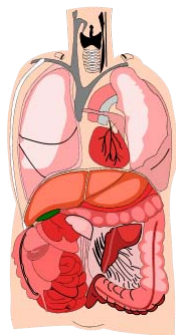
Emergent functions of the cell 细胞的涌现特性



- Secretome-extracellular proteins
- 分泌组 - 胞外蛋白质全谱
- Metabonome-extracellular metabolites
- 代谢组 - 胞外代谢物全谱

- Vibration 振动
- Noise 噪声
- Exhaust Gas 尾气

Nicholson 2004



Metabonome
代谢组
Metagenome
元基因组
Secretome
分泌组



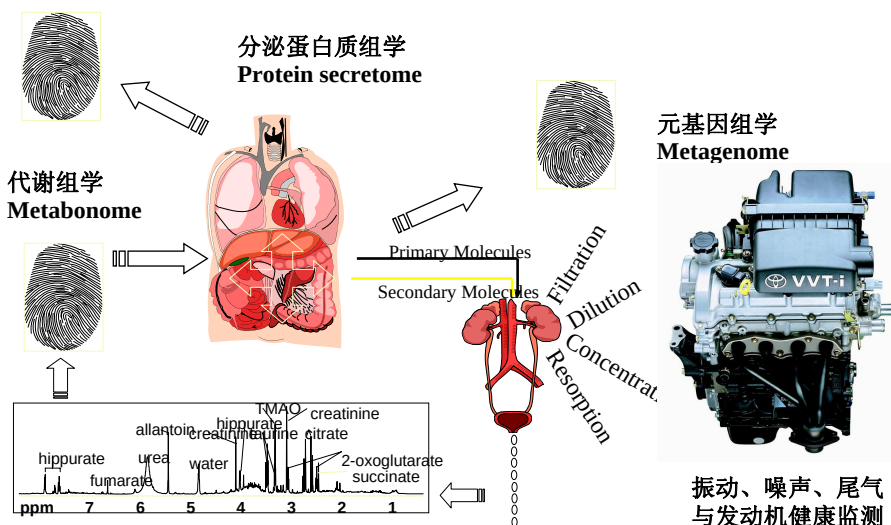
- Urine-metabolites
尿液代谢物谱
- Feces-bacteria
粪便细菌谱
- Blood-proteins
血液蛋白质谱

- Vibration 振动
- Noise 噪声
- Exhaust Gas 尾气

- 人体系统生物学通过在人体水平测定基因与环境互作的结果来准确评估和监测人体的健康
- Health assessment and monitoring based on measurements of results of gene-environment interactions at the whole-body level
- 具有下列特征 Essential criteria:
 - 非破坏性测量，可直接用于人体
 - Non-invasive
 - 整体测量，反映全身的健康状况
 - Global
 - 高通量、低成本可实现大样本人群的动态监控
 - Dynamic, low-cost, high throughput
 - 以核酸、蛋白和代谢物等生物分子为测定对象
 - Molecular-based
 - 非靶向测定，通过“全谱扫描”和“盲分类”可以监测任何类型的健康变化
 - Non-targeted
 - 数字化测量，可实现高度信息化
 - Digital, quantitative, highly reproducible

人体健康的分子测量

Molecular assessment of human health at the whole-body level
——人体健康状况的多参数、多指标评估



Systems approaches for quantitative assessment and monitoring of human health

用系统定量的方法进行人体健康状况的评价与监测

Molecular Profiling and Covariation Analysis
全谱分子扫描技术与模式识别



Gut Microbiota and Whole-body Systems Biology

Liping Zhao
Shanghai Center for Systems Biomedicine
School of Life Science and Biotechnology
Shanghai Jiao Tong University

New view on human body The Superorganism Concept *

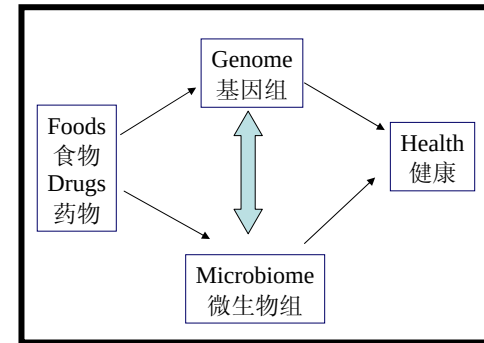
Cell composition of human body

- 10% human cells
- 90% bacterial cells

Gene composition of human body

- Human genome (25,000 genes)
 - Karyome
 - Mitochondrome
- Microbiome
 - 1000 species
 - 1 million genes
 - Diverse and active metabolism

*Joshua Lederberg



Human microbiome-
the second genome acquired after birth
微生物组—人后天获得的第二个基因组

New view on human body The Superorganism Concept *

Cell composition of human body

*Joshua Lederberg

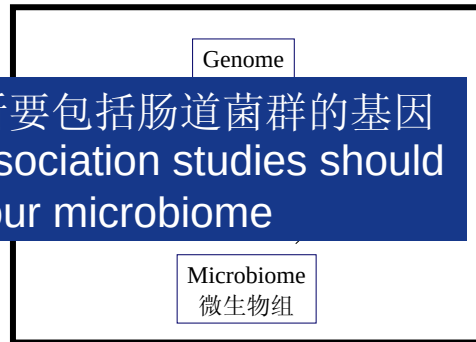
- 10% human cells
- 90% bacterial cells

Gene composition of

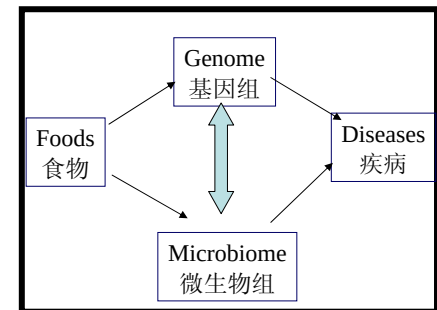
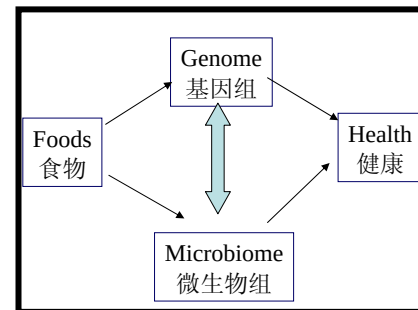
全基因组关联分析要包括肠道菌群的基因
Whole-genome association studies should
Include our microbiome

- Microbiome
 - 1000 species
 - 1 million genes
 - Diverse and active metabolism

Human microbiome-
the second genome acquired after birth
微生物组—人后天获得的第二个基因组



Modulation of the second genome in the Superorganism



Partner for health or Pathogen for diseases?

TCM works primarily via modulation of gut microbiota

肠道菌群其实一直都是中医药的主要作用靶点

PERSPECTIVES

OPINION

Gut microbiota: a potential new territory for drug targeting

Wei Jia, Houkai Li, Liping Zhao and Jeremy K. Nicholson

Abstract | The significant involvement of the gut microbiota in human health and disease suggests that manipulation of commensal microbial composition through combinations of antibiotics, probiotics and prebiotics could be a novel therapeutic approach. A systems perspective is needed to help understand the complex host-bacteria interactions and their association with pathophysiological phenotypes so that alterations in the composition of the gut microbiota in disease states can be reversed. In this article, we describe the therapeutic rationale and potential for targeting the gut microbiota, and discuss strategies and systems-oriented technologies for achieving this goal.

Most current searches for new drugs are generating new insights and opportunities

A microbial organ

The human intestine is more densely populated with microorganisms than any other organ, and is a site where they exert strong influences on human biology. With this in mind, the entire system of the human gut microbiota can be pictured as a 'microbial organ' within the intestine, which contributes to diverse mammalian processes including protective functions against pathogens and immune-system modulation, the metabolic function of fermenting non-digestible dietary fibre, and the anaerobic metabolism of peptides and proteins, which results in the recovery of metabolic energy for the host¹⁰⁻¹².

The intestinal mucosa is the main interface between the immune system and external environment and therefore has an important role in the host-flora interaction. The commensal microbiota profoundly influences the development of humoral com-

strategies for prove the protital industry, uge investments urrets and drug ccess so far. icle provides eutic and of diseases and gut microbiota, gut microbiota-

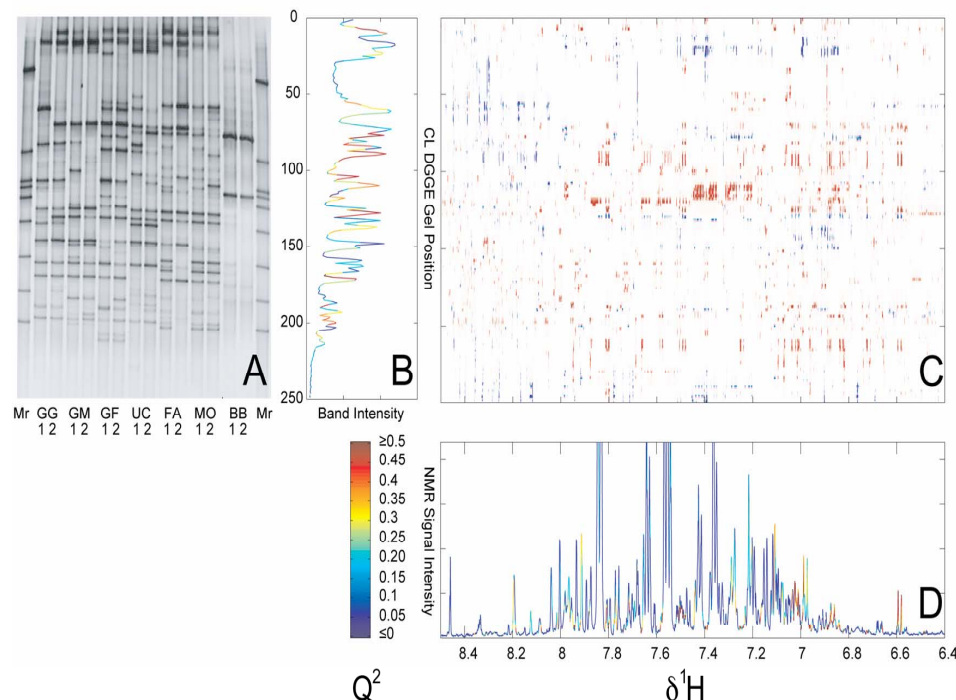
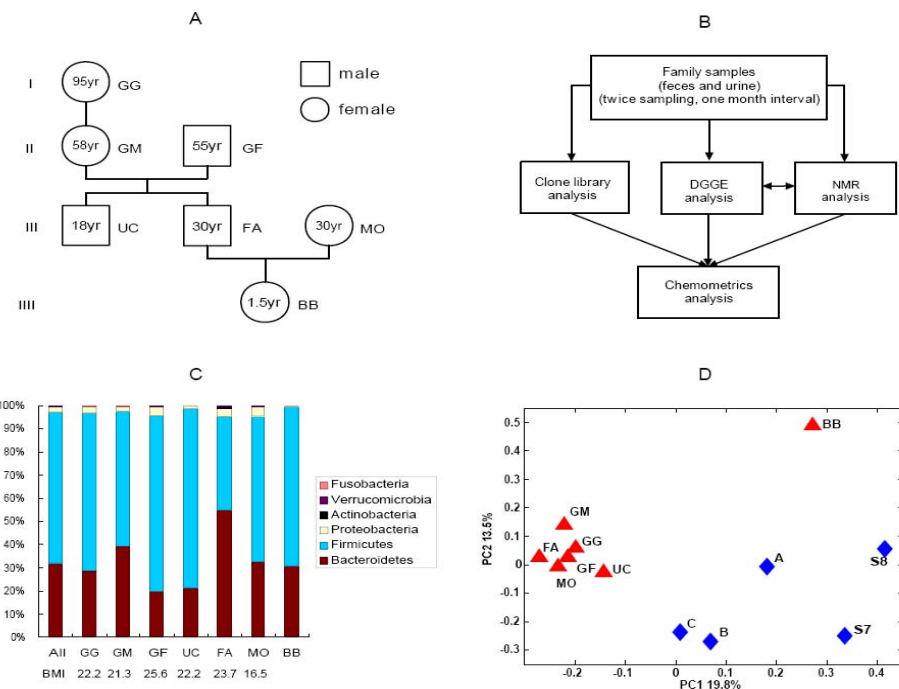
NATURE REVIEWS | DRUG DISCOVERY



Functional analysis of gut microbiota

-Co-variation analysis between host global metabolism and gut microbiota

Li et al., PNAS





http://www.upi.com/NewsTrack/Science/2008/02/06/study_maps_gut_microflora/6812/

Study maps gut microflora

Published: Feb. 6, 2008 at 10:24 AM
LONDON, Feb. 6 (UPI) -- A British-Chinese study has mapped the bacteria living in seven members of a Chinese family to determine the role of gut microbes in bodily processes.

The researchers from Imperial College London and China's Jiao Tong University said the makeup of each person's gut microflora influences their health, with abnormalities in gut microbes linked to diseases such as diabetes and obesity.

However, the relationship between different species of bacteria and different processes has previously been defined only at a broad level, the scientists said, noting that prior to their study, only five people had had their gut microflora profiled in depth, with that data being published.

"Now we have developed a new way of exploring the connections between bugs and man we can hope to find a 'Rosetta Stone' to translate the functional properties of the bugs and so improve therapies to treat disorders of the gut and related conditions," said Imperial College London Professor Jeremy Nicholson, lead author of the study.

The research, led by Professor Liping Zhao of Jiao Tong University in Shanghai, appears in the Proceedings of the National Academy of Science.

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http://www.upi.com/NewsTrack/Science/2008/02/06/study_maps_gut_microflora/6812/

 上海交通大学
Highlighted by Nature Review Microbiology

Symbiosis: Who does what in the microbiome? : Article : Nature Reviews Microbiolo... Page 1 of 1

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- 37 Min Li, Baohong Wang, Menghui Zhang, Mattias Rantalainen, Shengyue Wang, Haokui Zhou, Yan Zhang, Jian Shen, Xiaoyan Pang, Meiling Zhang, Hua Wei, Yu Chen, Haifeng Lu, Jian Zuo, Mingming Su, Yunping Qiu, Wei Jia, Chaoni Xiao, Leon M. Smith, Shengli Yang, Elaine Holmes, Huiru Tang, Guoping Zhao, Jeremy K. Nicholson, Lanjuan Li, Liping Zhao
Symbiotic gut microbes modulate human metabolic phenotypes
Proc. Natl. Acad. Sci. USA Feb 12, 2008; 105: 2117-2122.
(In "Microbiology") [Abstract] [Full Text] [PDF]

nature
REVIEWS MICROBIOLOGY
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Research Highlight

Nature Reviews Microbiology 6, 256-257 (April 2008) | doi:10.1038/nrmicro1880

Symbiosis: Who does what in the microbiome?
Susan Jones

Recent studies have shown that the complement of gut bacteria varies among individuals, but specific data linking the bacteria present to their functions in human physiology have been lacking. In a recent report, Min Li and colleagues describe a multidisciplinary approach to link the functions of the trillions of microbial gut bacteria – the human microbiome – to host metabolic phenotypes. Importantly, they pinpoint specific microorganisms that have defined roles in human metabolism using a functional genomics approach.



A four-generation Chinese family volunteered for the study. Faeces and urine were sampled on two separate occasions and analysed by molecular and spectroscopic techniques. Then, multivariate data analysis was used to identify relationships between individual bacterial species and metabolites. Sequencing of a faecal clone library revealed that all

人源菌群微型猪模型可用于分子机理研究 Human-flora associated pig model for molecular mechanistic studies



ORIGINAL ARTICLE

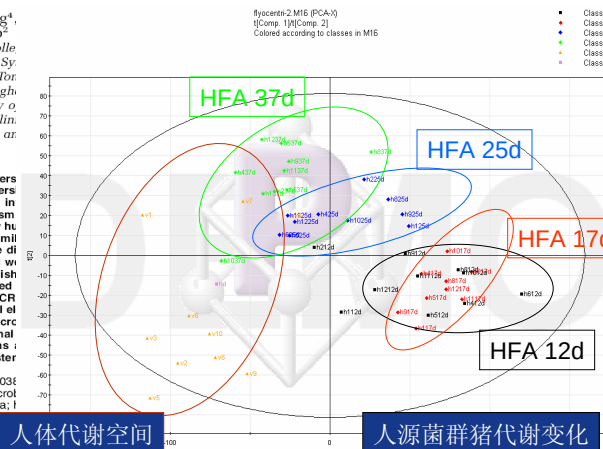
Inter-species transplantation of gut microbiota from human to pigs

Xiaoyan Pang^{1,2}, Xiguang Hua³, Qian Yang⁴, Wei Jia⁵, Peter Bucheli⁷ and Liping Zhao²

¹Department of Bioscience and Biotechnology, College of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, China; ²Key Laboratory of Systems Biomedicine, Shanghai Jiao Tong University, Shanghai, China; ³College of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, China; ⁴College of Animal Physiology and Biochemistry, Ministry of Agriculture, Nanjing, China; ⁵Tyco Clin Shanghai Jiao Tong University, Shanghai, China



Microbiota for unders to its vast divers gut microbiota in logy, metabolism humans. A new he e of the high simil tabolism of the dier system and w boy. The establish ed and compar us sequence-PCR ure gradient gel el ation of gut micr nity with minimal free piglets was i ly improved syste



人体代谢空间

人源菌群猪代谢变化

赵立平组、华修国组

Gut Microbiota and Diet-induced Metabolic Syndrome

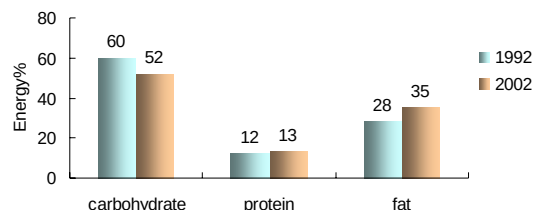
Liping Zhao
Shanghai Center for Systems Biomedicine
Shanghai Jiao Tong University

Nutritional Transition

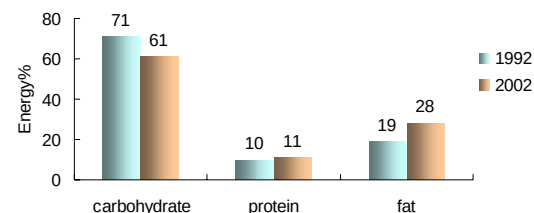
Prevalence of Obesity

Change of Energy Sources (1992 -2002)

Urban



Rural



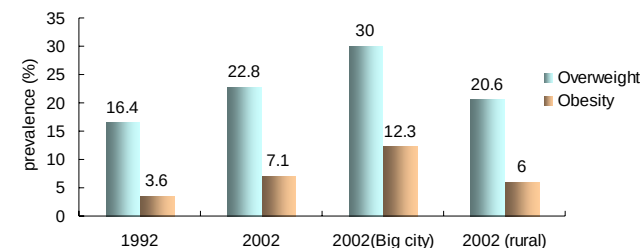
National Nutrition Survey, 2002

Worldwide (WHO)

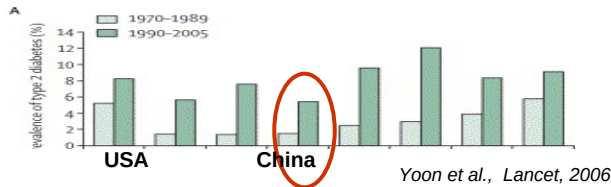
Overweight : 1,200,000,000
Obese: 300,000,000

China (National Nutrition Survey, 2002)

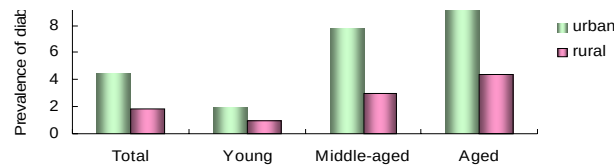
Chinese Adults (≥18 yrs)



Prevalence of Type 2 Diabetes

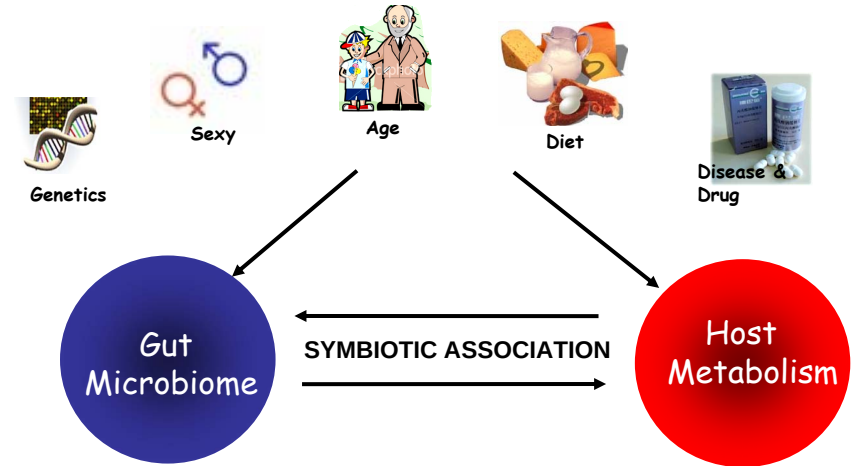


Prevalence of Type 2 Diabetes in Different Countries



Prevalence of Type 2 Diabetes in Chinese (≥18 yrs)

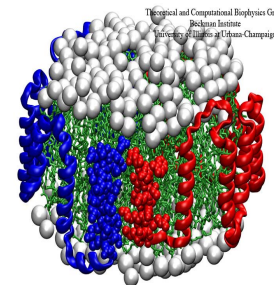
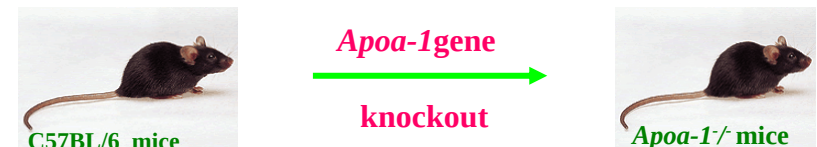
China National Nutrition Survey, 2002



Interactions between gut microbiota, diet and host genotype for host health
食物、基因型和菌群互作影响宿主的健康

赵立平组、陈雁组
ZHAO Lab, CHEN Lab

Apoa-1 gene Knockout Mice Apoa-1基因敲除小鼠



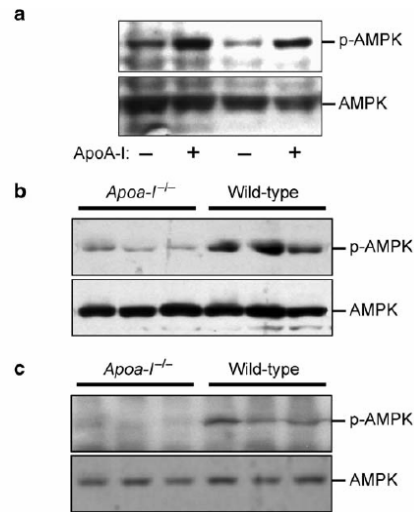
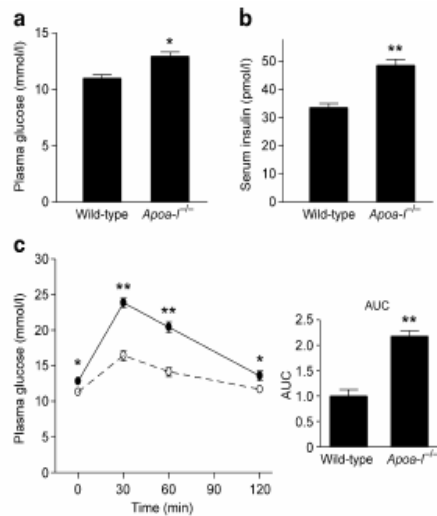
Apolipoprotein A- I

- Reduced HDL-cholesterol levels
- Susceptibility to high-fat dietary-induced atherosclerosis
- Insulin resistance and early symptoms of diabetes

Strategy for targeting the mouse ApoA-I gene.
(Williamson, 1992, PNAS)



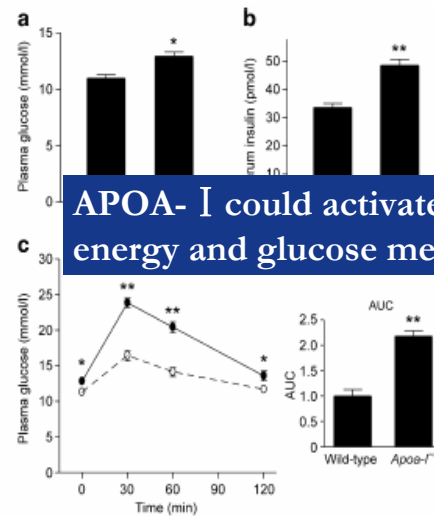
Apolipoprotein A- I and 2 type Diabetes



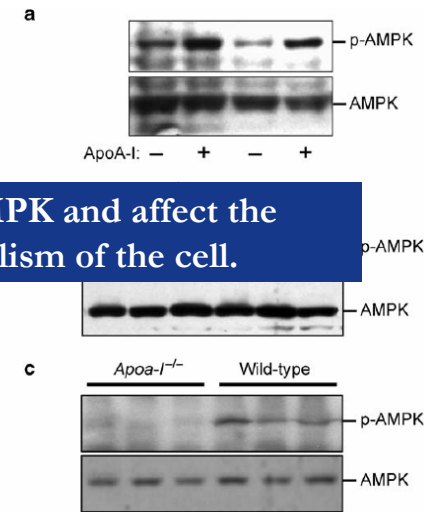
Chen lab, 2007



Apolipoprotein A- I and 2 type Diabetes



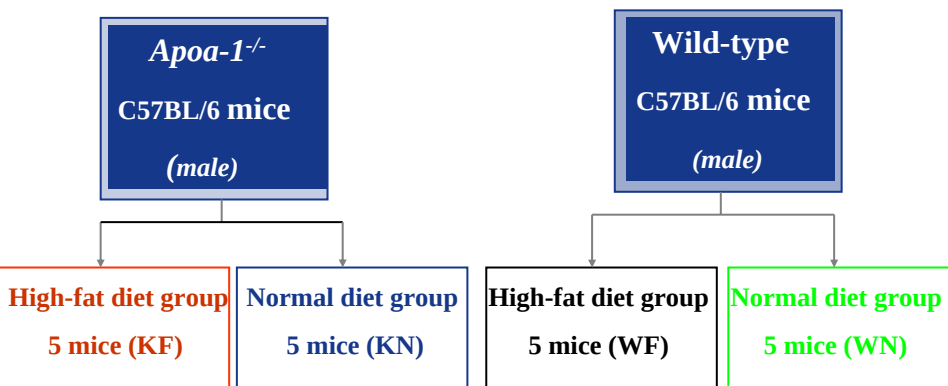
APOA- I could activate AMPK and affect the energy and glucose metabolism of the cell.



Chen lab, 2007

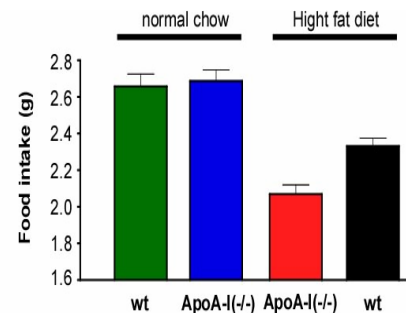


Animal trial scheme

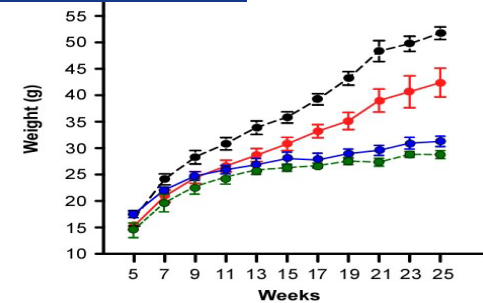


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Shanghai Jiao Tong University

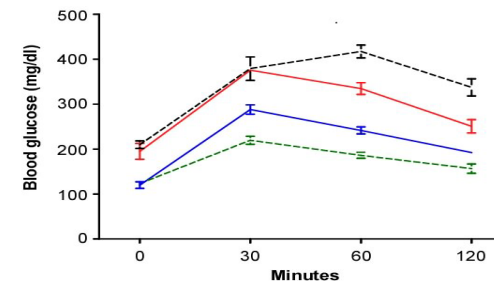
Food intake



Growth Curve

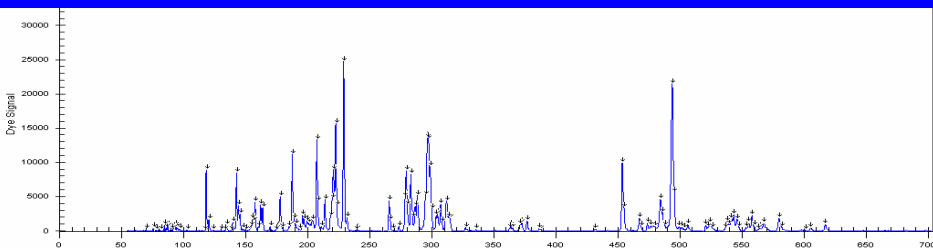
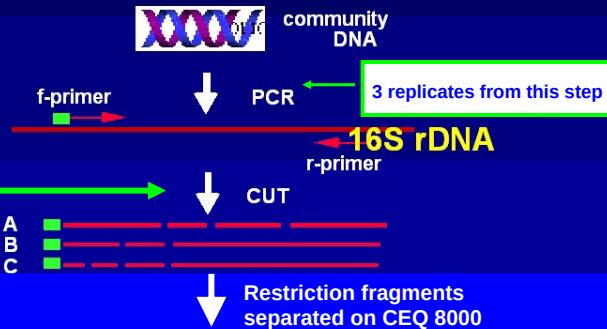


Glucose Tolerance Test

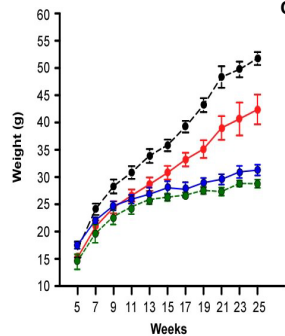


Terminal Restriction Fragment Length Polymorphism (T-RFLP)

- a. *Alu I*
- b. *HaeIII*
- c. *Hha I*
- d. *Msp I*
- e. *Csp6 I*

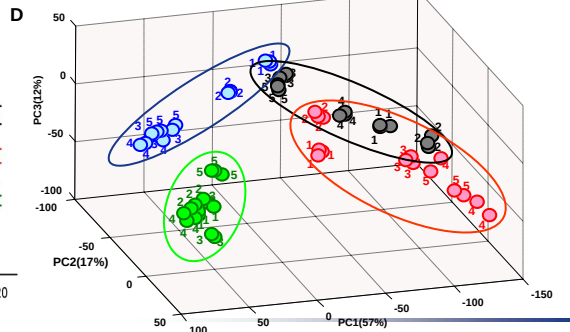
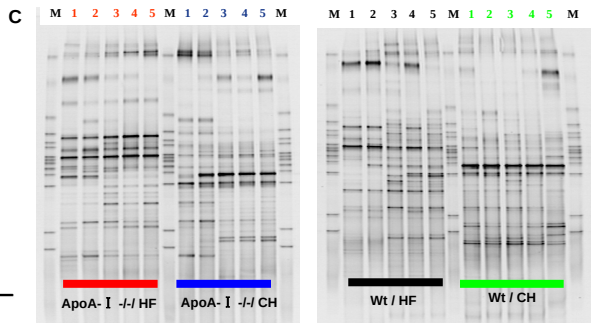
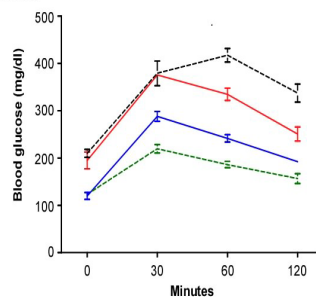


A Growth Curve

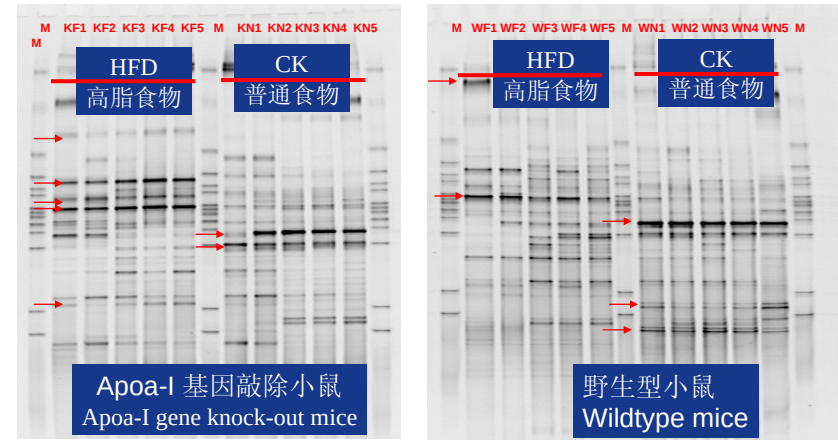


B

Glucose Tolerance Test



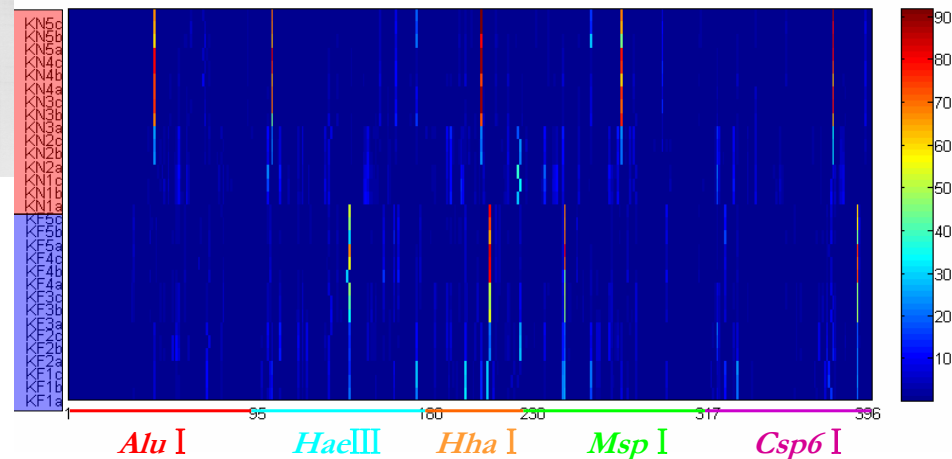
PCR-DGGE Fingerprinting



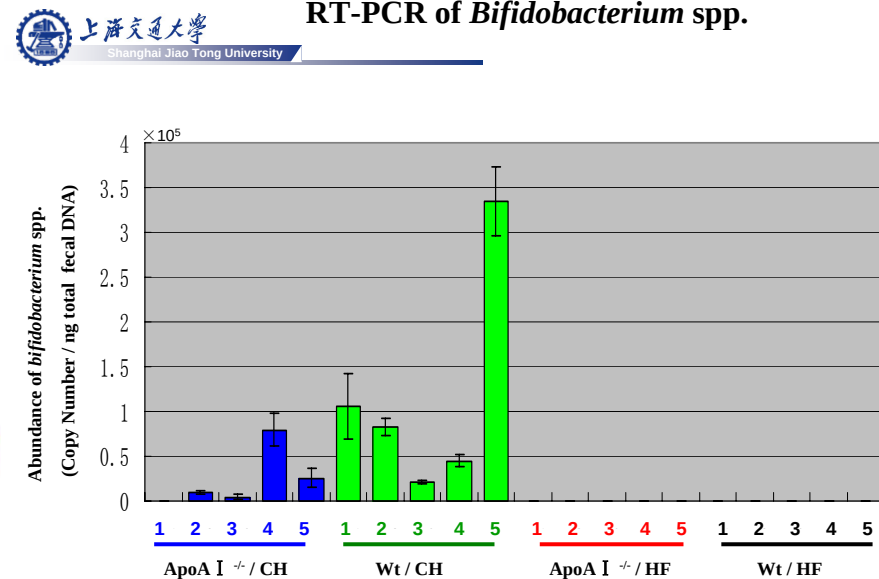
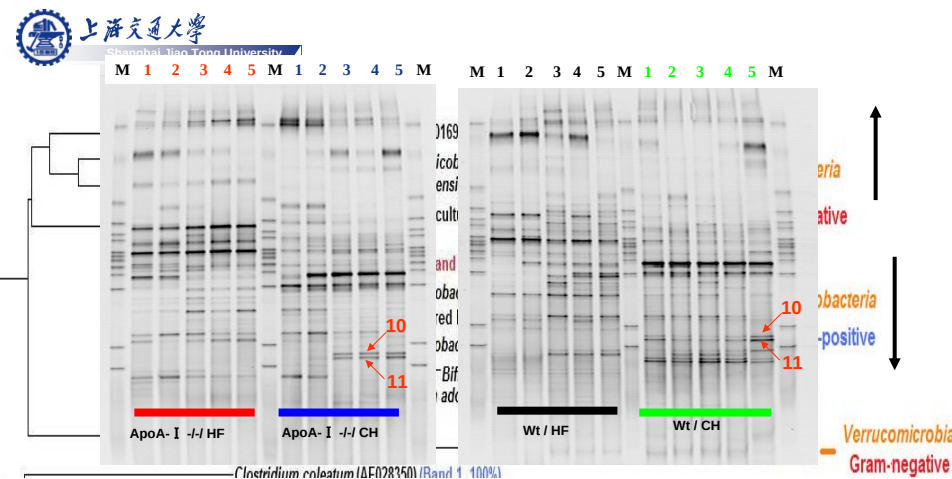
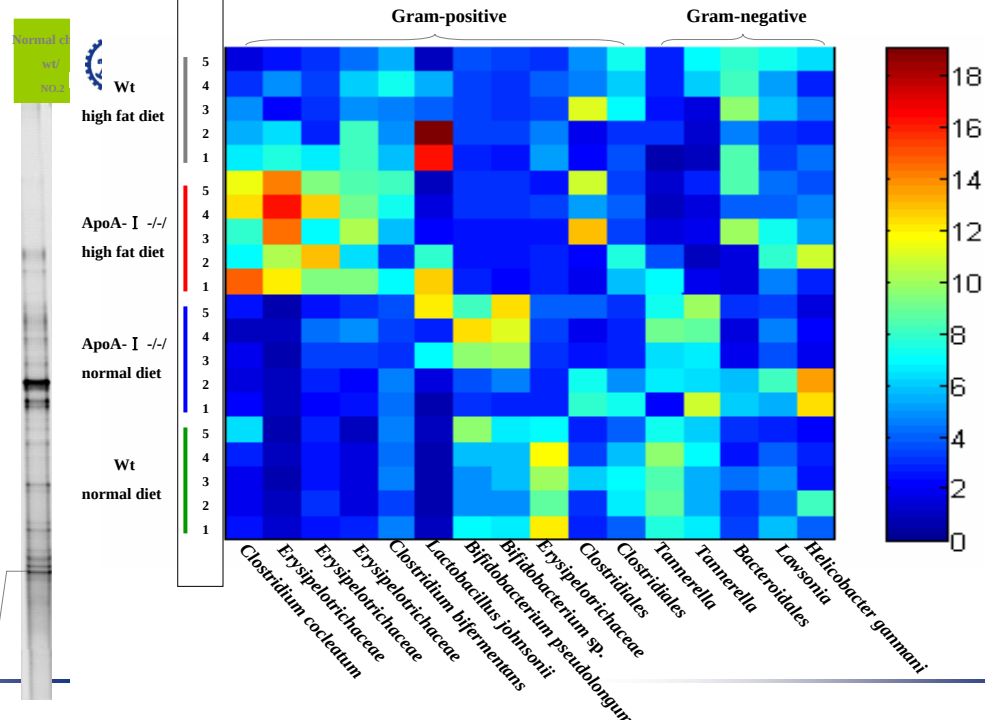
肠道菌群结构可以反映高脂食物和宿主基因型作用下的健康特征
Gut microbiota structure reflecting host health status



TRFs of KF and KN groups



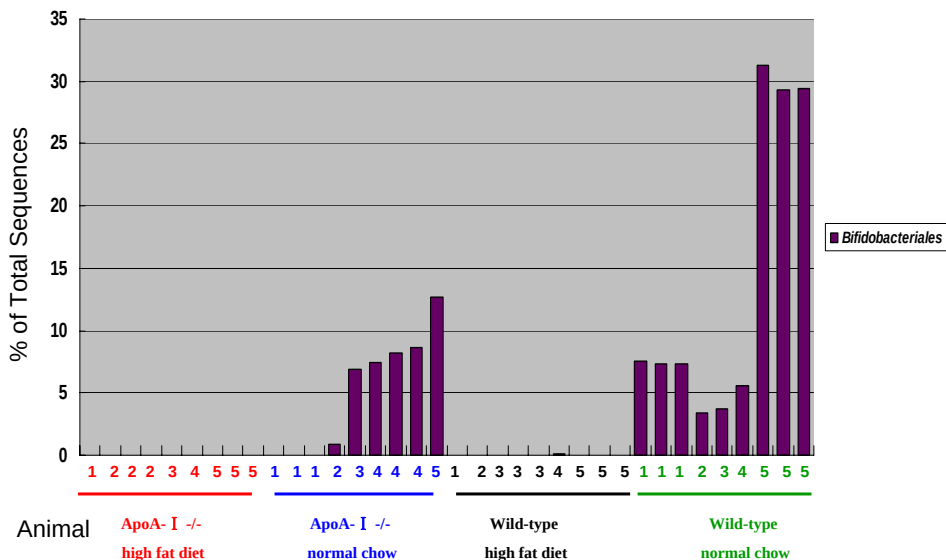
Information of Closed Relatives			
Similarity	Organism (Accession no.)	Phylogenetic affiliation	
8	100	<i>Lactobacillus johnsonii</i> (AB186343)	Firmicutes, Bacilli, Lactobacillales, Lactobacillaceae, Lactobacillus
15	100	<i>Helicobacter ganmani</i> (T) (AF000221)	Proteobacteria, Epsilonproteobacteria, Campylobacteriales, Helicobacteraceae, Helicobacter
6	98	uncultured bacterium (DQ815337)	Bacteroidetes, Bacteroidetes, Bacteroidales, Porphyromonadaceae, Tannerella
	80	<i>Porphyromonas gulae</i> (ATCC51700)	Bacteroidetes, Bacteroidetes, Bacteroidales, Porphyromonadaceae, Porphyromonas
7	99	uncultured bacterium (DQ815337)	Bacteroidetes, Bacteroidetes, Bacteroidales, Porphyromonadaceae, Tannerella
	81	<i>Porphyromonas circumdentaria</i>	Bacteroidetes, Bacteroidetes, Bacteroidales, Porphyromonadaceae, Porphyromonas
10	100	<i>Bifidobacterium pseudolongum</i> subsp. <i>Pseudolongum</i> (AB186304)	Actinobacteria, Actinobacteridae, Bifidobacteriales, Bifidobacteriaceae, Bifidobacterium
11	100	uncultured bacterium (EU511073)	
	98	<i>Bifidobacterium animalis</i> subsp. <i>Animalis</i> (AB186294)	Actinobacteria, Actinobacteridae, Bifidobacteriales, Bifidobacteriaceae, Bifidobacterium
16	99	uncultured bacterium (EF098678)	Firmicutes
	93	<i>Bryantella formatexigens</i> (T) (AJ318527)	Firmicutes, Clostridia, Clostridiales, Clostridiaceae, Bryantella
12	99	uncultured bacterium (EF099100)	Firmicutes, Mollicutes, Incertae sedis 8, Erysipelotrichaceae
	86	<i>Eubacterium cylindroides</i> (L34617)	Firmicutes, Clostridia, Clostridiales, Eubacteriaceae, Eubacterium



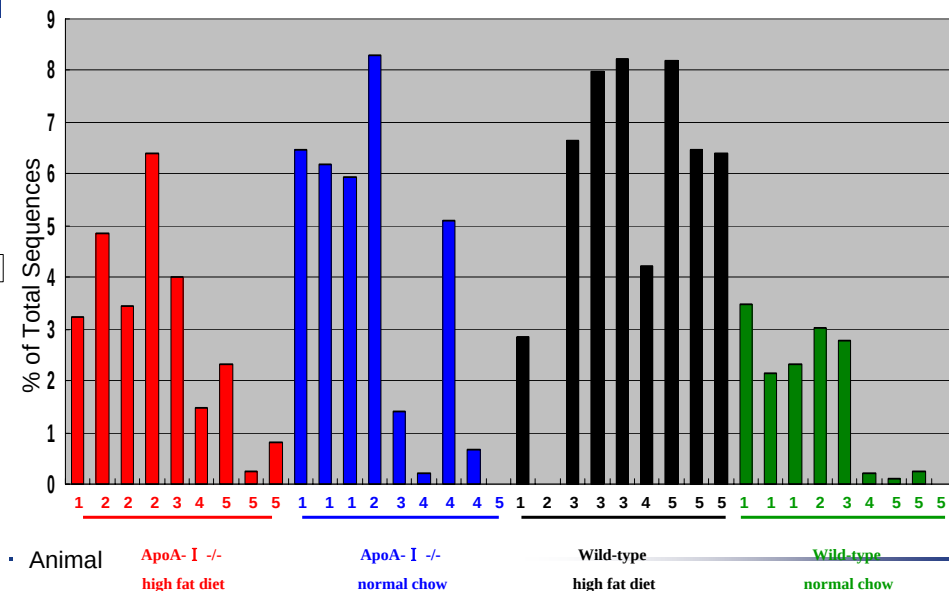
Band10 and Band 11 were *Bifidobacterium* spp.



Abundance distribution of Bifidobacteria based on 454 sequencing

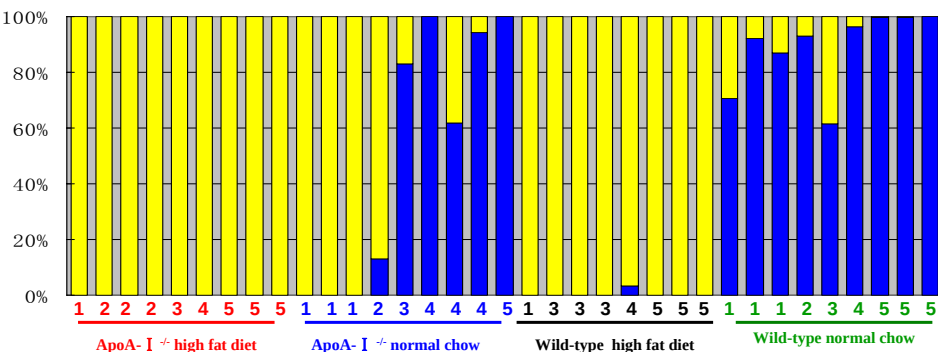


Proteobacteria



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Bifidobacteriales vs. Desulfovibrionales



Bifidobacteriales -protecting gut barrier integrity
Desulfovibrionales -producing endotoxin (LPS)



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肠道菌群结构“分离分析”与 宿主健康动态监测 Structural segregation analysis of gut microbiota and host health monitoring

高脂食物、菌群变化与肥胖的发展
 High fat diet, gut microbiota and obesity

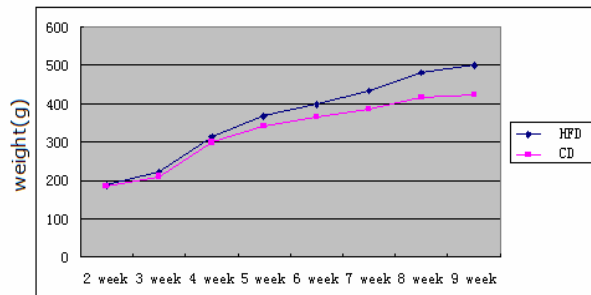
ZHAO lab, JIA lab
 赵立平组, 贾伟组

Progression of high fat diet induced obesity

高脂食物诱发的肥胖的发展

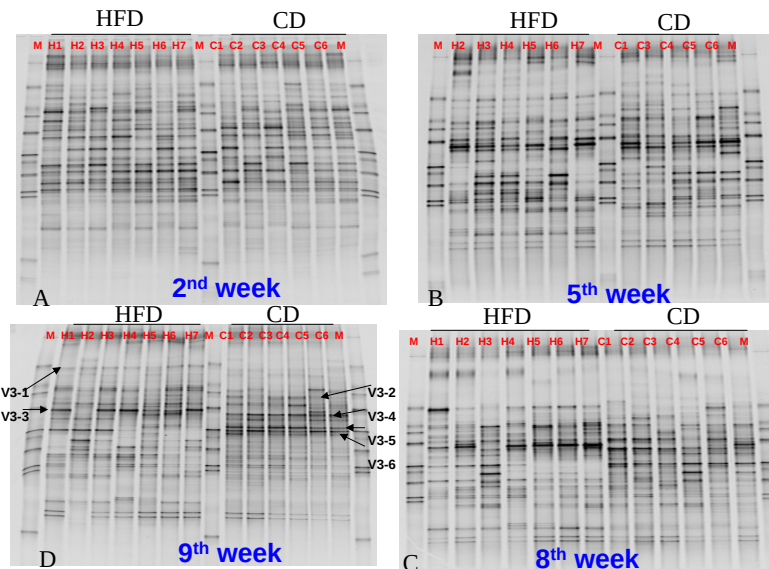
week	2 nd week*	3 rd week*	4 th week*	5 th week*	6 th week*	7 th week**	8 th week***	9 th Week***
group								
HFD	187±2	225±12	315±17	368±20	399±21	437±24	485±31	502±32
CD	185±3	212±7	299±21	344±30	365±38	386±41	416±47	424±48

*P>0.05



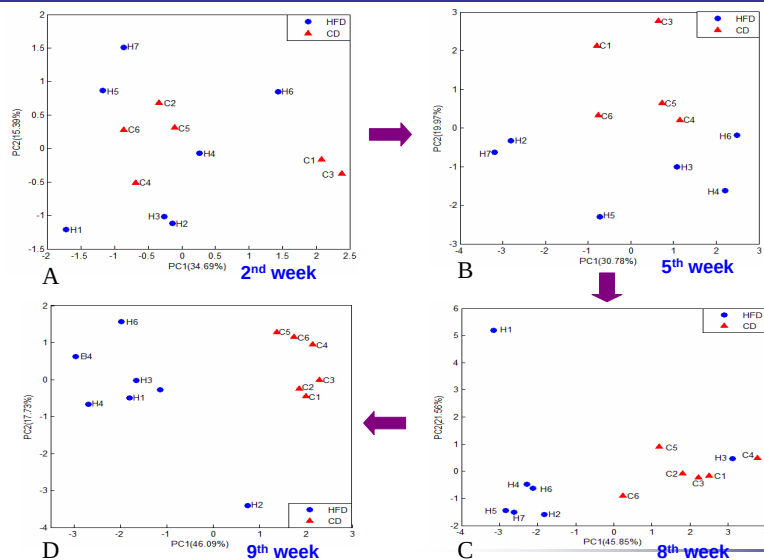
Structural segregation of gut microbiota during obesity progression

肠道菌群结构随肥胖发展而变化

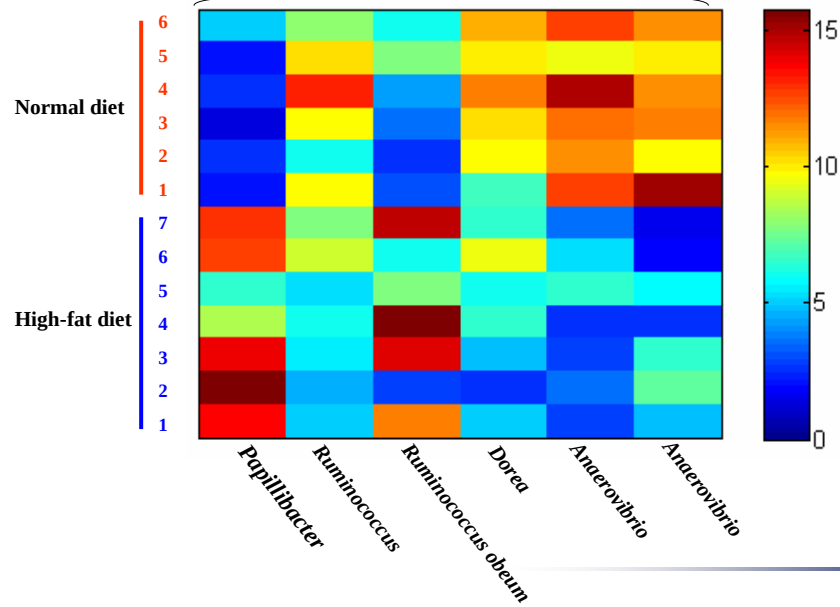


Structural segregation of gut microbiota during obesity progression

肠道菌群结构随肥胖发展而变化



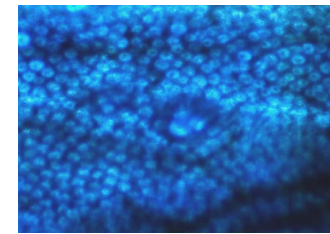
Gram-positive



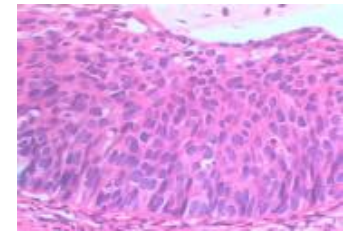


Structural shifts of gut microbiota induced by carcinogen during precancerous lesion development 致癌剂诱导癌前病变过程中肠道菌群结构的动态变化

Development of Colorectal cancer



ACF under a light microscopy ($\times 40$)



Dysplasia



polypoid adenoma



adenocarcinoma

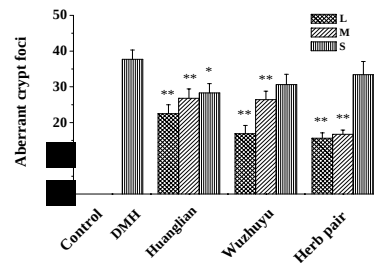
结肠癌的癌前病变模型

Precancerous lesion of colon cancer

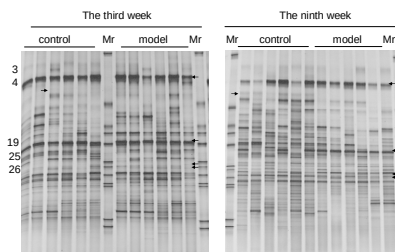
肠道菌群与宿主代谢的监测 Monitoring of host metabolism and gut microbiota



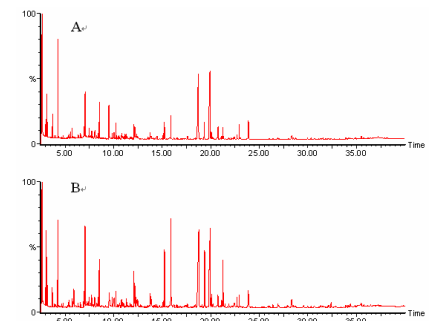
Aberrant crypt foci (ACF) induced by 1,2-dimethylhydrazine (DMH)



Reduction of ACF formation by TCM herbal extracts



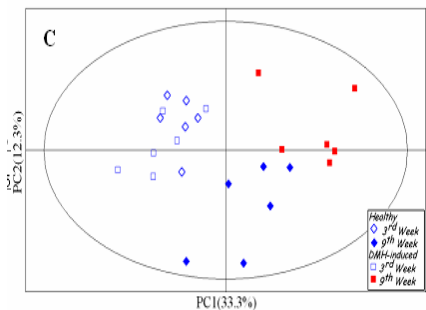
DNA fingerprinting of gut microbiota



GC/MS profiling of host metabolism

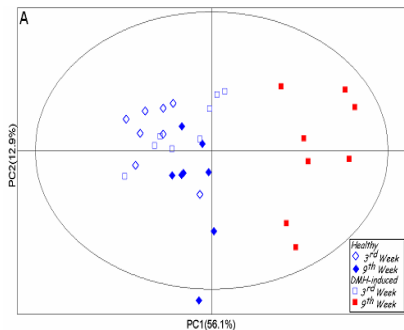
癌前病变动物菌群结构和整体代谢特征的变化

区别癌前病变动物和健康动物的关键代谢物
Key metabolites for differentiation between healthy and precancerous animals



菌群结构变化

Gut microbiota structure



整体代谢变化

Global metabolism

Concomitant shifts of gut microbiota and host global metabolism

away from healthy control during precancerous lesion formation in DMH treated group

- Increased urinary excretion
 - citrate,
 - 4-hydroxy-benzeneacetic acid,
 - 4-hydroxyphenyl-propionic acid,
- Decreased endogenous metabolites
 - butanedioic acid,
 - benzeneacetic acid,
 - glycine,
 - 4-methyl-phenol,
 - hippuric acid,
 - phenylacetyl-glycine.

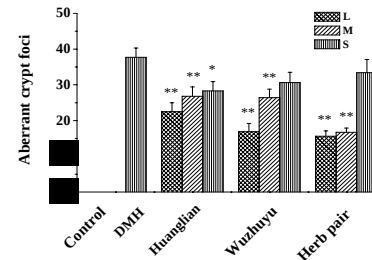
区别癌前病变动物和健康动物的关键细菌
Key gut bacteria for differentiation between healthy and precancerous animals

结肠癌的癌前病变模型 Precancerous lesion of colon cancer

Band		Closest relative	
No.	Similarity (%)	Organism (Accession no.)	Phylogenetic affiliation
19	98	Ruminococcus obeum (AY169419)	Firmicutes; Clostridia; Lachnospiraceae
25	95	Allobaculum stercoricanis (AJ417075)	Firmicutes; Mollicutes; Allobaculum.
26	97	uncultured bacterium (AY986052)	Bacteroidetes; Porphyromonadaceae
	93	Allobaculum stercoricanis (AJ417075)	Firmicutes; Mollicutes; Allobaculum.



Aberrant crypt foci (ACF) induced by 1,2-dimethylhydrazine (DMH)



Reduction of ACF formation by TCM herbal extracts

Wu group, Jia group, Zhao group

Coptidis rhizoma, Evodia rutaecarpa herbal pair

Coptidis Rhizoma



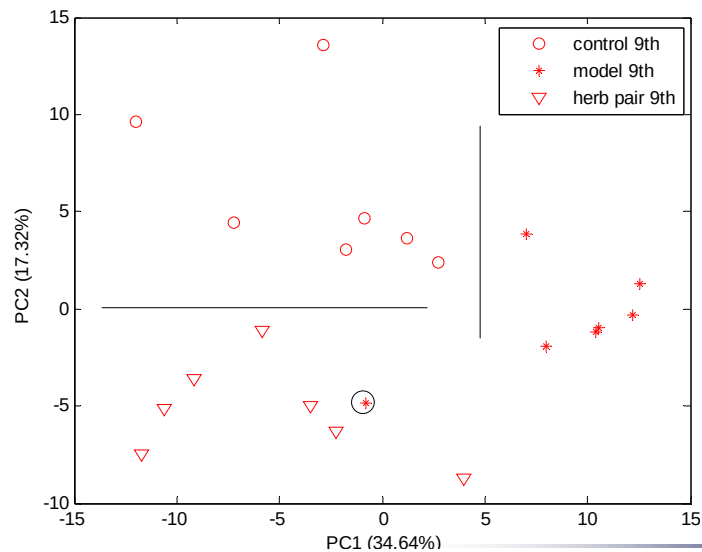
Major component: Berberine, palmatine, jatrorrhizine, coptisine

Evodiae Fructus

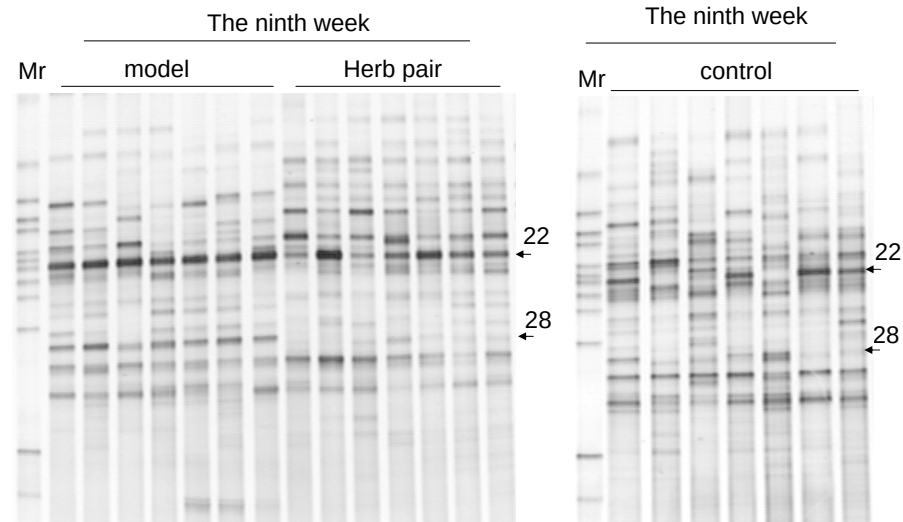


Major component: evodiamine, rutaecarpine, hydroxy-evodiamine, limonin, synephrine, evodente

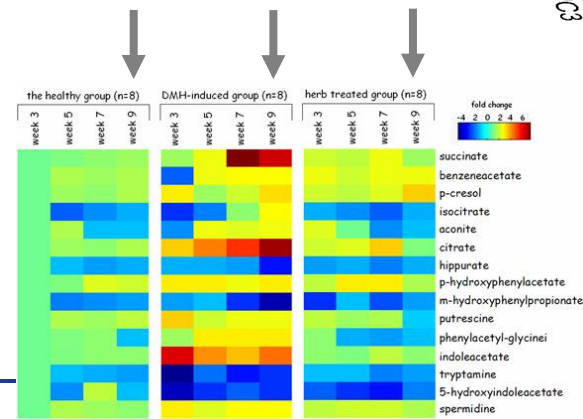
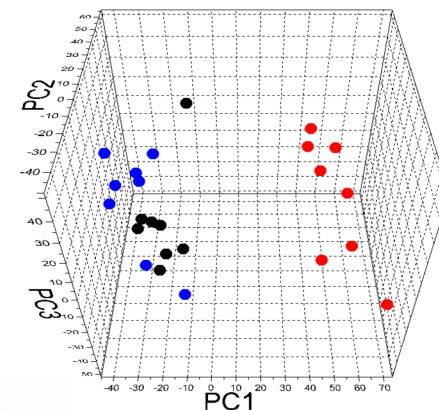
PCA scores plot of the 16S rRNA gene V3 region DGGE profiles of different groups



16S rRNA gene V3 fragment DGGE profiles



A 3D-PCA scores plot of GC/MS spectral data from the three group rats at the 9th week (n=8 per group; DMH-induced, red dots; healthy, blue dots; herb treated, black dots; each dot denotes an individual rat)



Time-dependent mean fold changes of those differential metabolites of healthy group, DMH-induced group and herb treated group at 3rd, 5th, 7th, and 9th week.

METABONOMICS代谢组学

Quantitative measurement of multivariate metabolic responses of multicellular systems to pathophysiological stimuli or genetic modification

多细胞系统在受到病理生理刺激或者遗传修饰后，其代谢反应的多参数定量测定

AIMS TO MODEL HUMAN GLOBAL METABOLIC REGULATION

-THE BASIC HOLISTIC PHILOSOPHY IS IN HARMONY WITH THEORY OF TRADITIONAL CHINESE MEDICINES

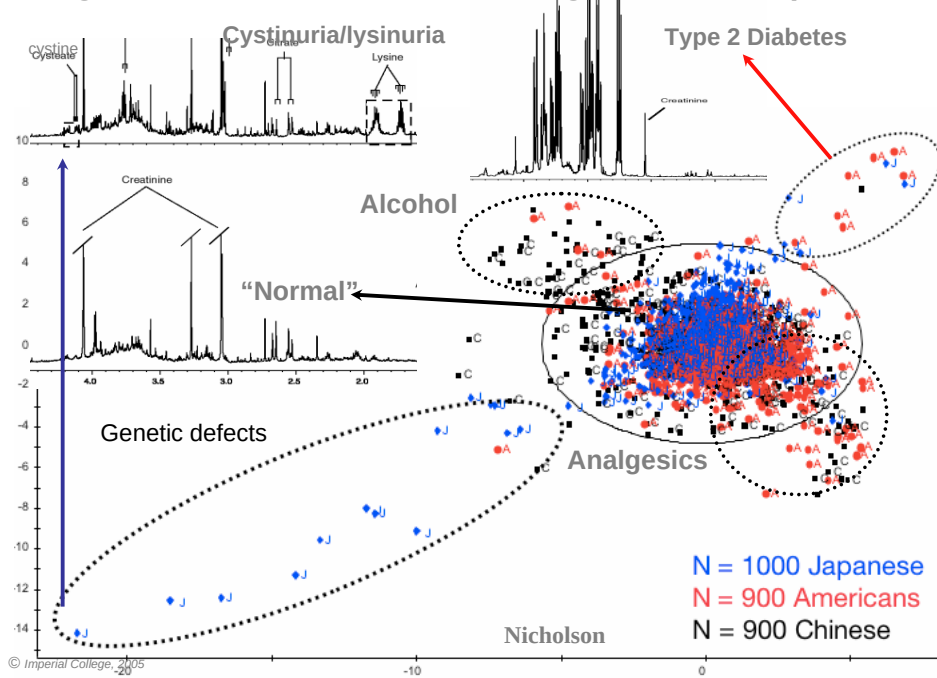
目标是人体整体代谢调控的建模，其基本哲学思想与中医是一致的

GLOBAL SYSTEMS BIOLOGY IS THE TOP-DOWN INTEGRATION OF MULTI-OMICS DATA TO DECIPHER GENE-ENVIRONMENT INTERACTIONS IN RELATION TO DISEASE DEVELOPMENT.

人体系统生物学是用自上而下的策略进行多种组学数据的整合，来解析疾病发展过程中基因与环境的互作关系

Nicholson

Large Scale Metabonomic Screening of Human Populations



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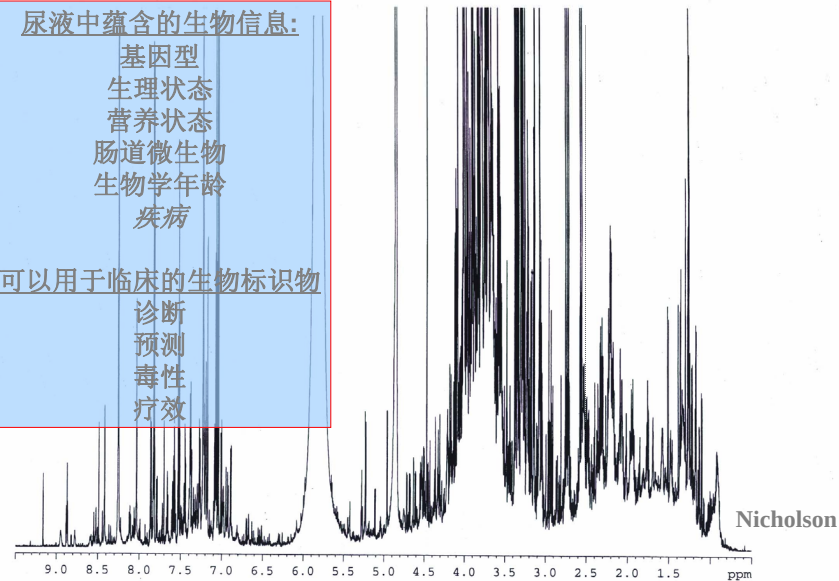
尿液的900 MHz ^1H 核磁共振谱

尿液中蕴含的生物信息:

基因型
生理状态
营养状态
肠道微生物
生物学年龄
疾病

可以用于临床的生物标识物

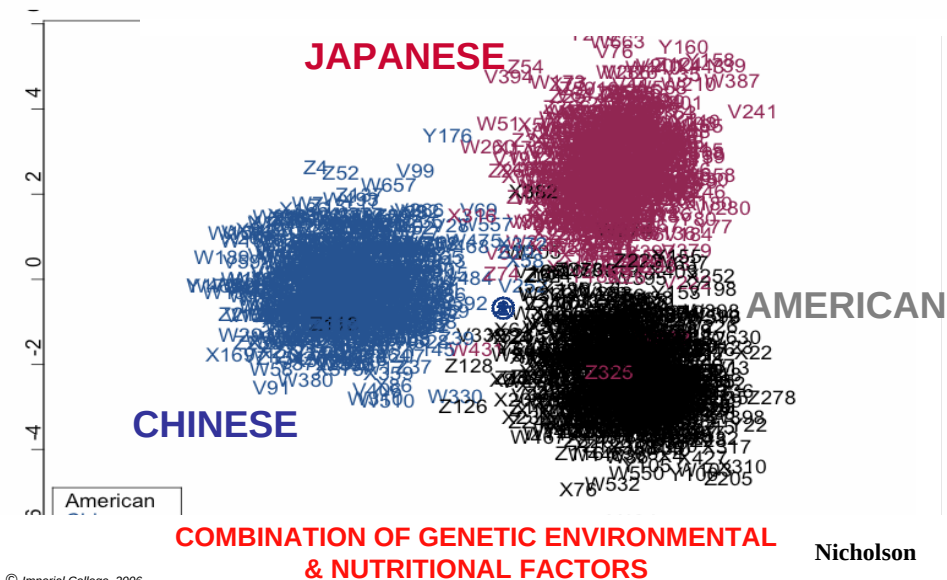
诊断
预测
毒性
疗效



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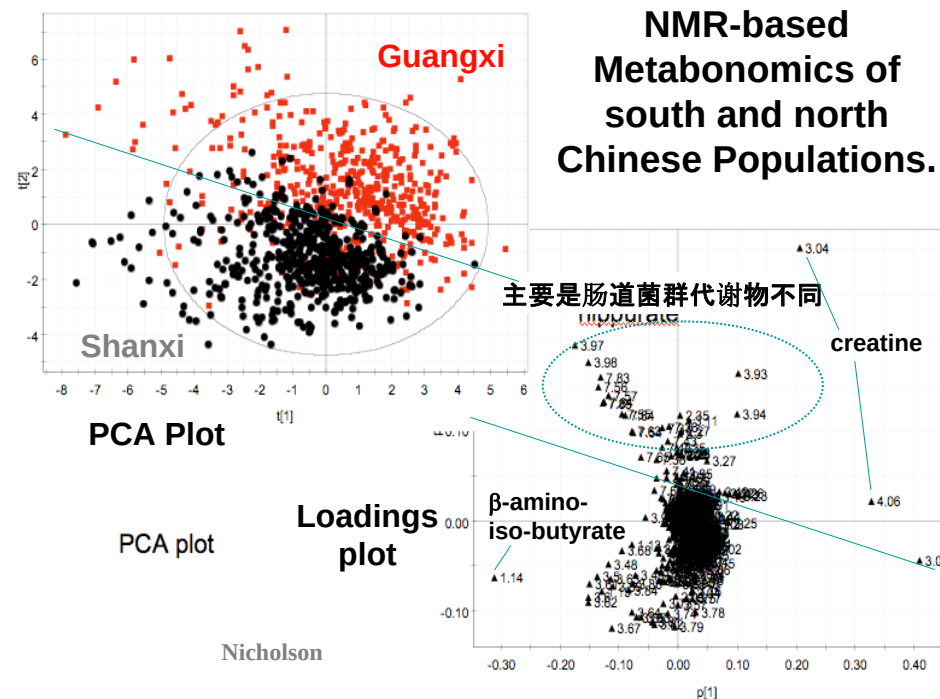
FUNDAMENTAL METABOTYPE DIFFERENCES

PCA-DA of population data (disease outliers removed)

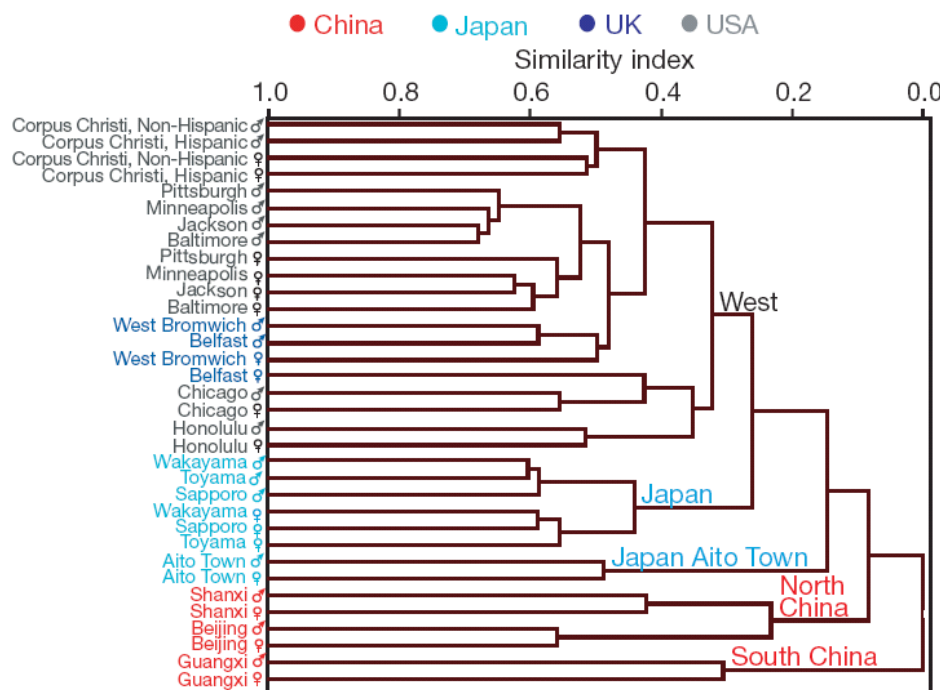
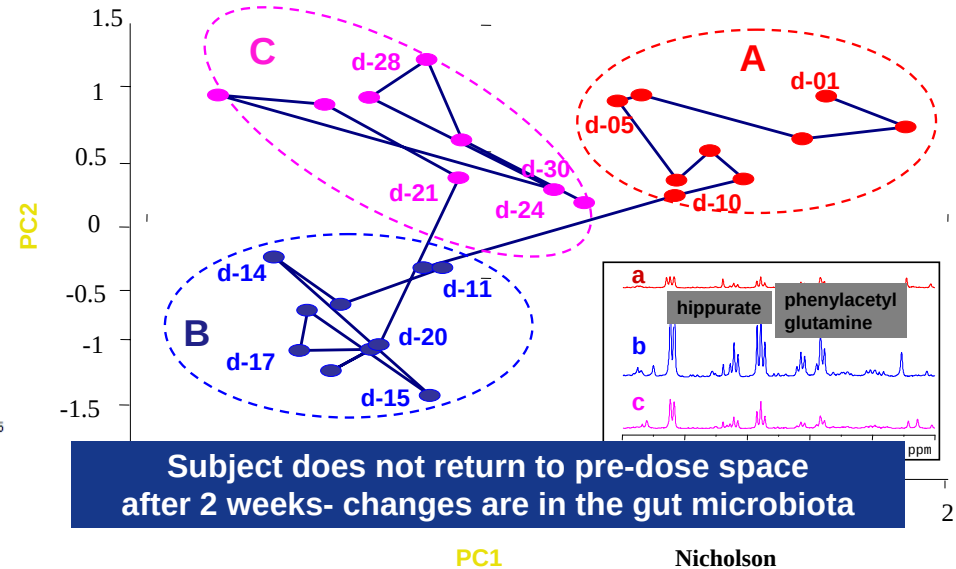


COMBINATION OF GENETIC ENVIRONMENTAL
& NUTRITIONAL FACTORS

Nicholson



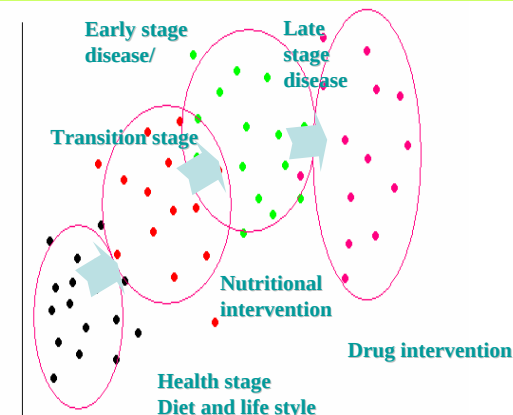
Trajectory plot of OSC-PLS model for individual subject pre and post exposure to chamomile tea



Meta-GUT: Overall Project Aim

Gut Microbiota-based Biomarker Discovery for Preventive Management of Metabolic Diseases via Nutritional Modulation

- ① Nutrition, gut microbiota, host immunity and metabolism, and their interactions in the development of obesity and related metabolic diseases
- ② Opening novel avenues to combat these conditions in a predictive, preventive and personalized manner



Population-based Case-Control Study

Study design:

500 pairs of age, sex and lifestyle matched overweight/obese and non-obese individuals

- **Case:** BMI ≥ 26 kg/m²
- **Control:** $18 \leq \text{BMI} \leq 23$ kg/m²

Inclusion criteria:

- Urban residents in Shanghai
- Residence ≥ 10 yrs
- Age: 35-54, male > 40%
- Without currently participating other study
- Without physical disabilities and mental disorder

Data Collection



Dietary Pattern	FFQ & 24-hr recall
Demographic Information	Name, Gender, Age, Household members, Ethnicity, Marital status, Education level, Occupation, Income
Lifestyle & Health Status	Self-reported health status, Health behavior, Medication, Family history of diseases, Smoking status, Alcohol Drinking
Physical Activities	Frequency, Duration and Level (IPAQ-short form)
Mental Health	CES-D questionnaire
Anthropometrics Body Composition	Height, Weight, Blood pressure, Waist circumferences, Hip circumferences DEXA: Fat, lean mass and bone density, % body fat, % trunk fat

Laboratory Assays



Category	Biomarker
Lipid profile	Total cholesterol, HDL, LDL, triglyceride;
Glucose	Fasting plasma glucose
Hormone	Fasting Insulin
Adipocytokines	Adiponectin, Resistin, PAI-1, RBP4
Inflammatory factors	CRP, TNF α -R1,R2, IL-6
Gene variants	HNF4A, PPARG, PCK1, G6PC, PPARGC1A, NR3C1, ESRRA, ADIPOQ, RBP4, ENPP1,etc.
Others	Ferritin, HbA1C

Laboratory Assays



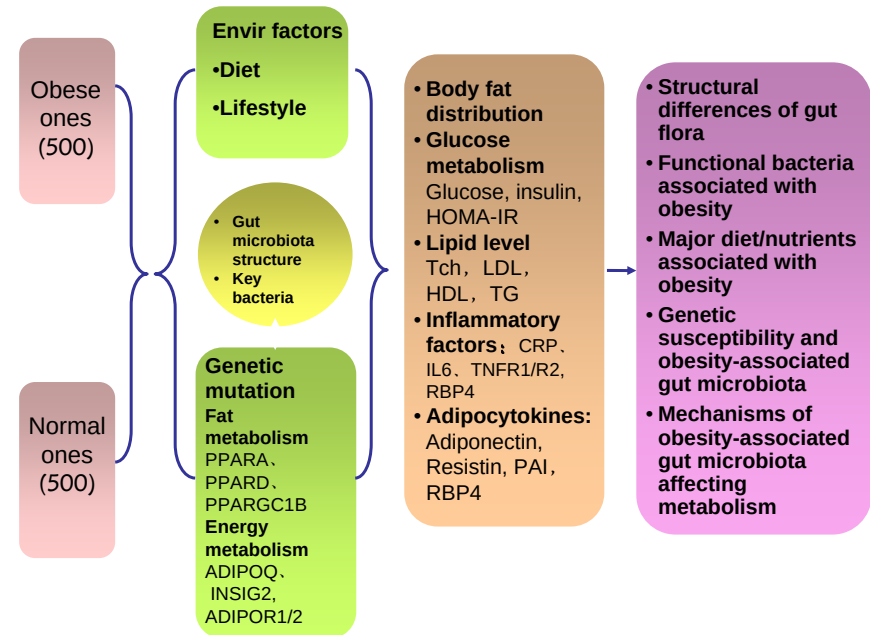
Samples	Analysis
Blood	Protein profiling Metabolic profiling
Urine	NMR spectroscopic profiling MS-based profiling
Fecal matters	Metabolic profiling-fecal water Fragment-based profiling Sequence-based profiling Metagenomic sequencing
Pattern recognition	Unsupervised classification Supervised classification Co-variation analysis

粪、尿液采集情况汇总 Fecal and urine samples

	受试者人数 Number of Participants	合格粪样数量 Fecal samples	合格夜尿数量 Night Urine samples	合格晨尿数量 Morning urine samples
卢湾 Luwan	596	590	581	578
闸北 Zhabei	579	571	568	564
合计 Total	1175	1167	1149	1142

粪尿样均合格者共**1131**人，卢湾**574**人，闸北**557**人

Study Overview



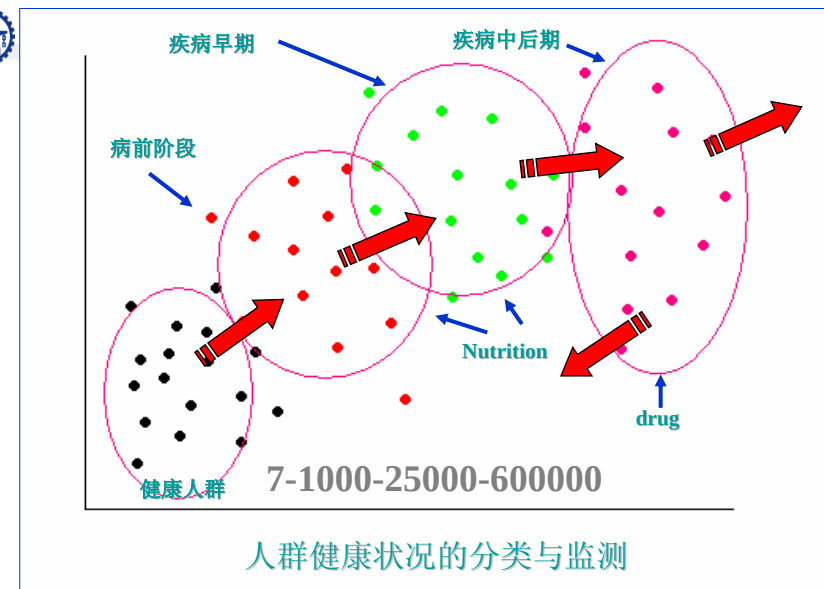
Specific Aims

Scientific

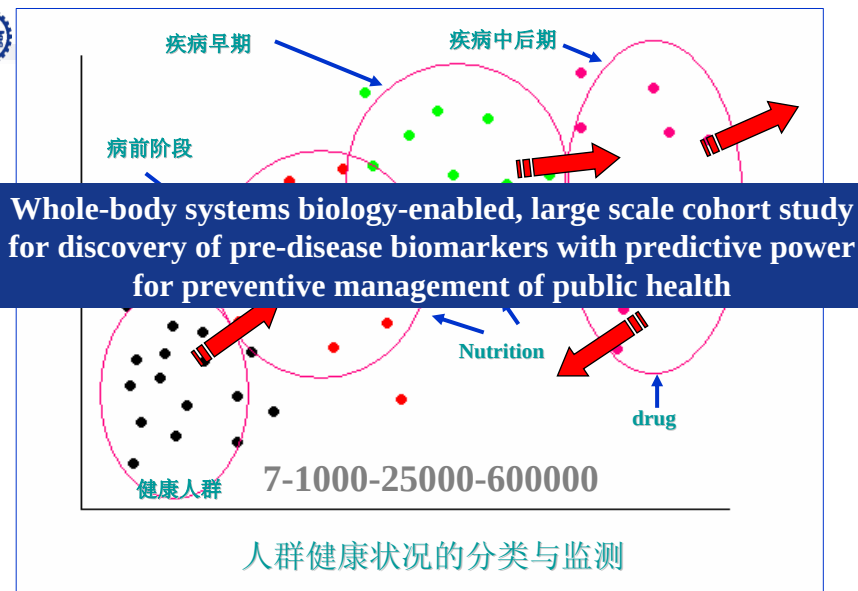
- Build a reference database
- Develop high-throughput methodologies
- Define the pattern of nutritional transition
- Identify and understand host-microbe metabolic interactions

Products for Personalized nutrition

- Health risk assessment
 - Databases and kits
- Diet-based prevention of metabolic diseases
 - The beverage or additive that works just for you



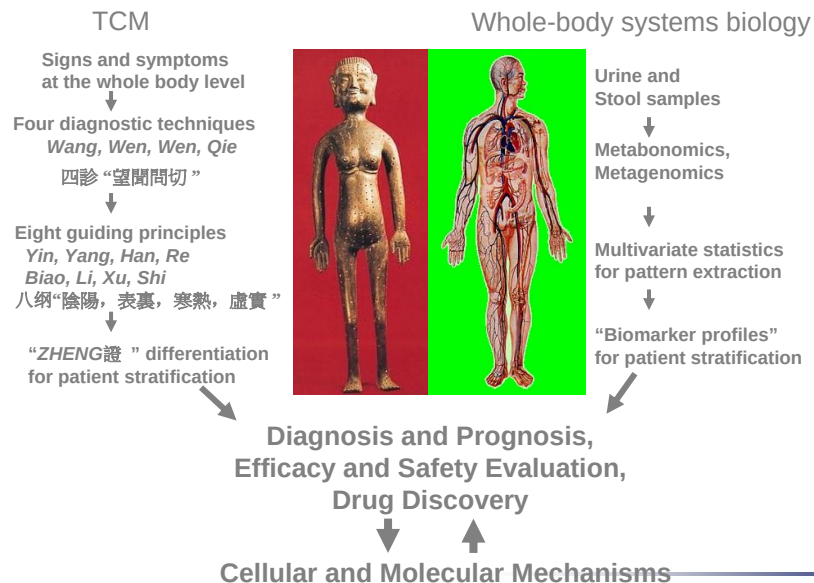
基于人体分子测量的病人分型与健康监测



基于人体分子测量的病人分型与健康监测



Understanding how TCM works



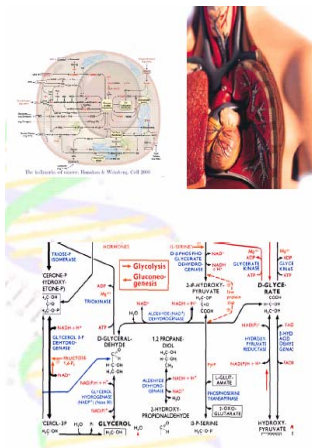
Emerging of New Medicine 东西方医学的汇聚与新医学模式的出现

Traditional medicine



Holistic but empirical
传统医学—模糊的整体

Western medicine



Molecular-based but fragmentary
西方医学—精细的局部

New medicine



Molecular-based and holistic
新医学—精细的整体