

# Phenomics

动物遗传育种分子生物学实验室

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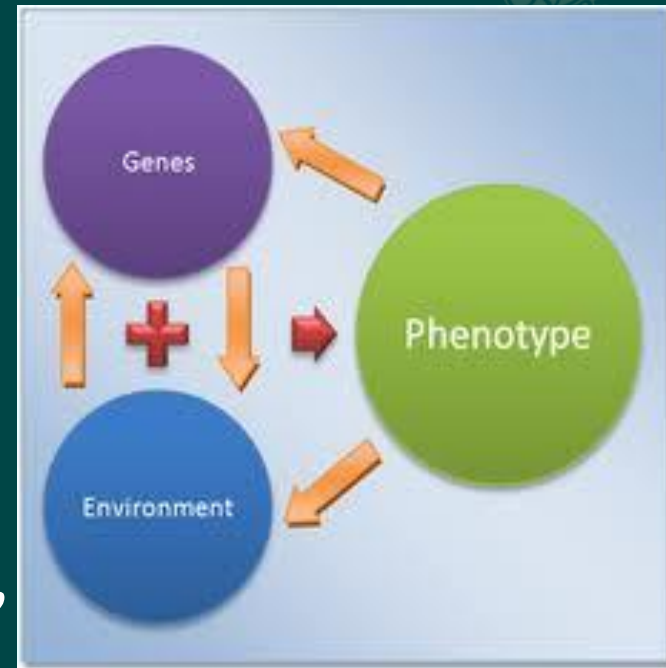
# 表型组学的概念和产生背景

◆ **表型**（Phenotypes）  
又称表现型，对于一个生物而言，表示它某一特定的物理外观或成分。例如一个人是否有耳珠、植物的高度、人的血型、蛾的颜色。



贝壳的不同纹理

- ◆ 表型主要受生物的基因型和环境影响。
- ◆ 表型可分为连续变异或不连续变异。前者较易受环境因素等影响，基因型上则会受多个等位基因影响，如体重、智力和身高；后者仅受几个等位基因影响，而且很少会被环境改变，如血型、眼睛颜色和卷舌的能力。



bessie4.blogspot.com

表型由微观到宏观还可以分为细胞表型、组织表型、器官表型以及整体表型。

# 表型组 (Phenome)

- ◆ 表型组：在遗传和环境因素的影响下，生物体表现型主要信息的集合。（ Varki , Altheide, 2005 ）
- ◆ 生物体在细胞、组织、器官、生物体或种属水平上表现出的所有表型的组合。（维基百科）

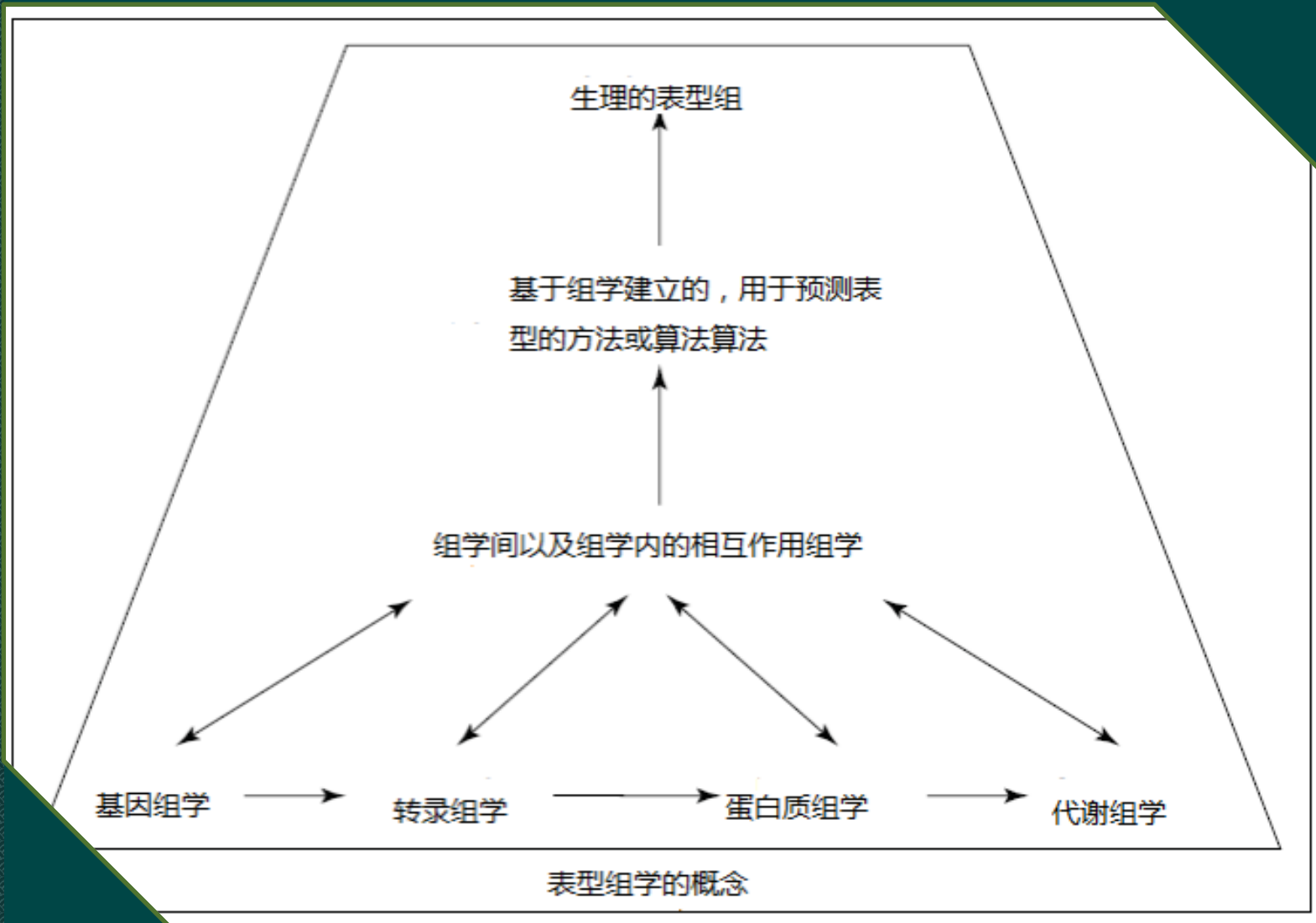
# Background

- ◆ 自20世纪90年代初以来，生命科学领域出现了最为引人注目的“组学(omics)”新概念和新学科，如基因组学(genomics)、转录组(transcriptomics)、蛋白质组学(proteomics)和代谢组学(metabolomics)等。伴随各种“组学”的不断兴起和发展，90年代末，人们提出了表型组(phenome)和表型组学(phenomics)的概念。
- ◆ 1996年，衰老研究中心(The Aging Research Centre (ARC))主任Steven A. Garan在加拿大滑铁卢大学的客座演讲中首次提出“phenomics”这一概念。

# Phenomics

- ◆ 表型组学是联系表现型与基因型的桥梁，并以一体化的形式联系着遗传学与功能基因组学。（Kelsoe and Niculescu ,2002）
- ◆ 表型组学是一门在基因组水平上系统研究表型的学科。（Bilder , 2009）
- ◆ 从表型组角度而言，表型组学是一个与表型鉴定研究相关的领域，并结合基因(基因组)或蛋白(蛋白组)的研究来探究表型的本质及它们之间的相互作用关系的学科。（维基百科）
- ◆ 表型组学可定义为一门在基因组水平上系统研究某一生物或细胞在各种不同环境条件下所有表型的学科。
- ◆ 表型组学是系统生物学组学平台的终端，通过基因组学、转录组学、蛋白质组学、代谢组学、互作组学到表型组学完成了由基因序列到基本生命活动的全过程。（杨胜利）

# 表型组学图解





# 重要的研究机构

表型组学主要的研究机构及其网址

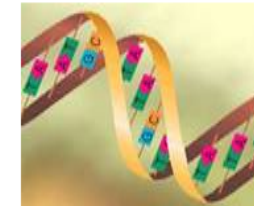
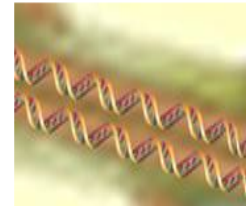
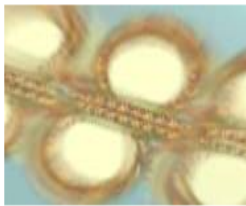
机构名称	网址
CropDesign corporation	<a href="http://www.cropdesign.com/general.php">http://www.cropdesign.com/general.php</a>
The Australian Plant Phenomics Facility (APPE)	<a href="http://www.plantphenomics.org.au/">http://www.plantphenomics.org.au/</a>
The Plant Phenomics Platform	<a href="http://www.lemnatec.com/scanalyzer_g_h.htm">http://www.lemnatec.com/scanalyzer_g_h.htm</a>
The Laboratory of Neurophenomics	<a href="http://www.neurophenomics.info/index.php">http://www.neurophenomics.info/index.php</a>
UCLA Consortium for Neuropsychiatric Phenomics	<a href="http://www.phenomics.ucla.edu/">http://www.phenomics.ucla.edu/</a>
The Aging Research Centre (ARC)	<a href="http://www.arclab.org/">http://www.arclab.org/</a>
Australian Phenomics Facility	<a href="http://www.apf.edu.au/index.shtml">http://www.apf.edu.au/index.shtml</a>

## Aust. Phenomics Fac.

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### What is the APF?

The APF is a National node for promoting interactions across disciplines and the pipeline of Australian research and development, and foster international collaborations aimed at maintaining Australian R&D expertise in health, agriculture and biotechnology at the international cutting edge.

The APF is dedicated to providing the national and international academic and commercial scientific community access to genome scale collections of mice with informative point mutations.

The services provided are used by APF customers to rapidly advance the identification of genes and their function as an early step in the process of identifying potential drug targets and animal models of human disease, understanding cellular functions and biochemical process.

The APF differentiates itself from competing methodologies by offering a unique service to Australian research groups. This comes in the form of major scientific discoveries. A spectacular endorsement of the APF capabilities was demonstrated very early in the APF's existence by the major discovery of a novel molecule associated with an autoimmune syndrome. This discovery was elegantly highlighted in May 2005 in an Article in the journal *Nature* by Dr Carola Vinuesa at The Australian National University and her collaborators in Australia and Oxford, using the APF's technology and services to discover an entirely new health mechanism.

[Download the Australian Phenomics Facility Brochure](#) 



<http://www.apf.edu.au/index.shtml>

澳大利亚澳洲表型组学设施(Australian Phenomics Facility), 是最早将“Phenomics”这一术语用于命名的设施, 同时用于描述鼠类繁殖中不同基因在它们的发育过程中所表现出的效应。

# The Australian Plant Phenomics Facility

## A new era in plant biology in Australia

Plant Scientists have gained vast knowledge about the genetics of various crop species during recent years. It has become increasingly easier and cheaper to sequence and map genomes, giving scientists access to information unimaginable just a few decades ago. However, a bottleneck has developed in capitalising on this information. The Australian Plant Phenomics Facility (APPF) has been developed to alleviate this 'phenotyping bottleneck'.

For Further information on the Australian Plant Phenomics Facility contact the **Plant Accelerator** and the **High Resolution Plant Phenomics Facility** (HRPPC).

## The Plant Accelerator



## The High Resolution Plant Phenomics Centre



<http://www.plantphenomics.org.au>

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创建于2008年的澳大利亚植物表型组学实验室，该实验室可以利用可见光、近红外、远红外和荧光成像，并提供高通量的成像系统；同时有能力及设备，运用现代技术根据植物生长及特性提供综合、持续的表型分析。

About CropDesign  
News & Communication

## Technology

About the technology platform

→ TraitMill - Platform and Process

Biofactories

Product development in rice

Product development in corn

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## Traitmill - Platform and Process

① 2 3 4 5 6 7 →

The TraitMill™ comprises proprietary bioinformatics tools, **high throughput** gene engineering systems, **efficient methods** for plant transformation, and a unique set up for **automated high resolution phenotypic evaluation** of crop performance.

CropDesign has the ability and capacity to modulate the expression of hundreds of genes and evaluate their effect in planta through automated screening methods. TraitMill™ has been developed to work in real crops and is currently running in a high throughput mode for rice.

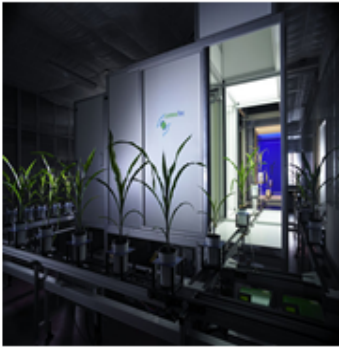
With the TraitMill™, CropDesign has the **largest corporate program** for high-throughput agronomic trait identification in cereals. Leads identified by CropDesign in the TraitMill™ are introduced into elite cereal germplasm to fast-track product development.

成立于1998年的比利时CropDesign公司，可能是最早着手研发可大规模开发转基因和植物性状评价的高通量技术平台的机构，2005年开发了称之为“性状工厂” (TraitMill)的可大规模自动化分析全生育期植物表型的技术设施。

# Scanalyzer 3D Plant Phenotyping



## Accelerating plant phenomics- breeding by design -



LemnaTec scanalyzer3D systems open new prospects for the quantitative, non-destructive analysis of different crops or model plants under high-throughput conditions. Each plant is imaged sequentially in multiple scanalyzer3D camera units, employing different wavelengths that reach far beyond human vision. The result is an unprecedented number of reproducible and significant data points on any aspect of plant development.

Data will be collected continuously and recorded in one snapshot per run through the -scanalyzer3D, thus routinely producing 15 or

more images and several hundred data points per plant and run. Plants are imaged in multiple runs throughout their entire life cycle. All data is available in the database within minutes of imaging – for unparalleled monitoring of dynamic plant development. Comprehensive quantitative representation of plants in datasets generates special data for physiological and genetic plant modeling to identify and quantify the concealed parameters that really control plant development. Such deep insights into plant biology accelerate phenomics and enable plant breeding to deal with the challenges of the 21st century.

### Measured parameters

- Leaf area
- Chlorophyll content

### Application sheets

- High throughput Arabidopsis Phenotyping
- Arabidopsis assessment in time
- Arabidopsis phenotype grouping
- Cereal NIR/SWIR phenotyping
- Corn morphology leaf rolling
- Fluorescence imaging and analysis
- GFP plant assessment
- High throughput phenotyping personnel
- Influence of alignment on biovolume
- LemnaTec roots in 2D and in pots
- LemnaTec weight and pump module
- Lettuce water dynamics NIR imaging
- MovingField concept
- MovingField watering
- Plant engineering and systems biology
- Plant Scanalyzer - the benchtop Scanalyzer
- Plant testing for OECD
- Poplar phenotype assessment
- Randomisation scheme and layouts
- Relation dry weight image leaf area

德国的研究机构LemnaTec 构建了一种新型的表型组学研究平台，能够提供高通量、高容量和全自动化的表型分析系统，并且该系统成功用于玉米和拟南芥形态上的三维结构成像及分析，能够进一步明确植物表型与植物生理功能间关系，最终达到快速的定向育种。

# The Consortium for Neuropsychiatric Phenomics (CNP)

## 神经精神病表型组学协会

<http://www.phenomics.ucla.edu/>

**UCLA Semel Institute**  
Consortium for Neuropsychiatric Phenomics

Tennenbaum Center for the Biology of Creativity | PubAtlas | PubGraph | PubBrain | PhenoWiki

# Welcome to CNP

Investigating neuropsychological phenotypes and mechanisms on a genome-wide scale

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**CNP Virtual Home**

The Consortium for Neuropsychiatric Phenomics (CNP) advances the NIH Roadmap Initiative by assembling a transdisciplinary "research team of the future" to address major unsolved challenges in research on neuropsychiatric disorders. The CNP leverages the new discipline of phenomics - the systematic study of phenotypes on a genome-wide scale - by integrating basic, clinical and information sciences. Neuropsychiatric disorders have enormous public health significance, and there is currently a

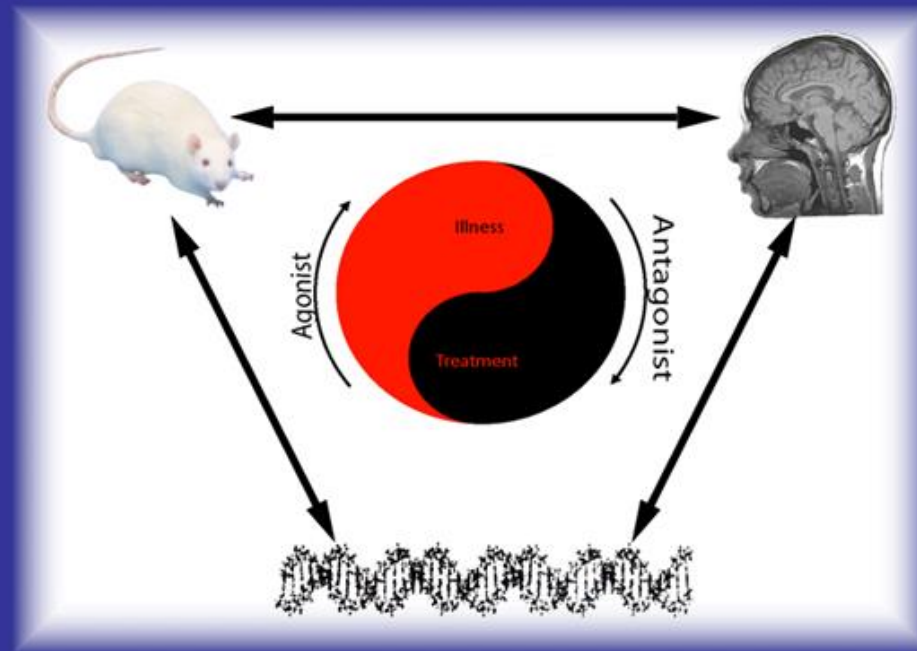


Vertical 7-Level Schema for the Consortium for Neuropsychiatric Phenomics

# The Laboratory of Neurophenomics

## 神经精神医学表型组学实验室

### Laboratory of Neurophenomics



**Our Mission: Personalized Psychiatry.**

Our work points in a translational fashion to the issues of complexity, heterogeneity, overlap and interdependence of major psychiatric syndromes as currently defined by DSM. While some of this overlap might be due to limitations in precision of diagnostic ascertainment in humans and limitations in specificity to a disorder in animal model studies, **an alternative and more compelling explanation is that the genetic and neurobiological structure of psychiatric**

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- TASS: Total Affective State Scale (PDF file)
- Semantic Web Primer (PDF file)
- INBRAIN

<http://www.neurophenomics.info/index.php>

# 学术交流会议



- ◆ 国际植物表型组学研究网络 (I P P N)
- ◆ 2009 年4 月，第一届国际植物表型组学专题讨论会在澳大利亚首都堪培拉召开，128 名业内人士参加了该会议。
- ◆ 用于加强对该领域的信息交流(如表型分析工具的协调)及项目合作，同时制定了该领域研究的相应国际质量标准，该会议最终目的是通过植物表型组学与功能基因组学的研究来提高的作物品质、产量。



# 主要刊物

- ◇ Nature Biotechnology
- ◇ Current Opinion in Biotechnology
- ◇ Bioinformatics
- ◇ Nature Genetics
- ◇ Trends in Genetics
- ◇ Biological Psychiatry (生物精神病学)
- ◇ Neuroscience (神经科学)

# 经典论文

- ◆ Ideker, T. (2001). "Integrated Genomic and Proteomic Analyses of a Systematically Perturbed Metabolic Network." Science **292**(5518): 929–934.
- ◆ Fong, S. S. and B. Ø. Palsson (2004). "Metabolic gene-deletion strains of *Escherichia coli* evolve to computationally predicted growth phenotypes." Nature Genetics **36**(10): 1056–1058.
- ◆ Butte, A. J. and I. S. Kohane (2006). "Creation and implications of a phenome-genome network." Nature Biotechnology **24**(1): 55–62.
- ◆ Niculescu, A. B., L. L. Lulow, et al. (2006). "PhenoChipping of psychotic disorders: A novel approach for deconstructing and quantitating psychiatric phenotypes." American Journal of Medical Genetics Part B: Neuropsychiatric Genetics **141B**(6): 653–662.
- ◆ Salazar-Ciudad, I. and J. Jernvall (2010). "A computational model of tooth and the developmental origin of

# 大肠杆菌代谢基因缺失株预测生长表型

## BRIEF COMMUNICATION

*Nature Genetics* 36, 1056 - 1058 (2004)

Published online: 26 September 2004; | doi:10.1038/ng1432

## **Metabolic gene-deletion strains of *Escherichia coli* evolve to computationally predicted growth phenotypes**

Stephen S Fong & Bernhard Ø Palsson


Department of Bioengineering, University of California, San Diego, 9500 Gilman Drive, La Jolla, California 92093-0412, USA.

# 主要内容

- ◆ 研究者将一群分别携带缺失一个代谢基因 (metabolic gene) 的 *E. Coli* 菌株用不同生长条件进行培养，他们经历适应演变后测量各自终点生长点生长速率，结果又78%的菌株生长速率提高了87%。
- ◆ 研究表明，计算模型能预测遗传修饰的最终效果。
- ◆ 在基因组水平上利用代谢模型有望精确描述细胞表型。

# 材料与amp;方法

- ◆ 他们采用的缺失基因包括：*ackA*<sup>-</sup>（乙酸激酶A基因）、*frd*<sup>-</sup>（延胡索酸还原酶基因）、*pck*<sup>-</sup>（磷酸烯醇式丙酮酸羧化激酶基因）、*ppc*<sup>-</sup>（磷酸烯醇式丙酮酸羧化酶基因）、*tip*<sup>-</sup>（磷酸丙糖同工酶基因）、*zwf*<sup>-</sup>（6-磷酸-1-葡萄糖脱氢酶基因）。
- ◆ 不同碳源培养有： $\alpha$ -酮戊二酸(Akg)、葡萄糖(Glu)、甘油(Gly)、乳酸(Lac)、苹果酸(Mal)、核糖(Rib)和琥珀酸(Suc)。
- ◆ 研究者设计了两个试验：

- 
- ◆ 实验一，将预测组合的缺失菌株分别放入一种碳源中培养，分别预测和实验测定生长表型。
  - ◆ 实验二，将预测组合的缺失菌株组合进入9种不同的碳源中培养，分别与非进化菌株和野生型菌株的生长速率进行比较。
  - ◆ 在这些不同培养环境压力下促使菌株适应性演变，作者假想一个适应演变的菌株将有一个适合的表型生长特征，此特征可用代谢流平衡分析法进行计算。
  - ◆ 他们测量了底物和氧吸收比率，并利用它作为计算模拟的输入参数。试验中每个缺失菌株的实验生长速率从开始直到适应演变重点详细记录后与计算预测数字进行对比，结果基本一致。

# 结果 1

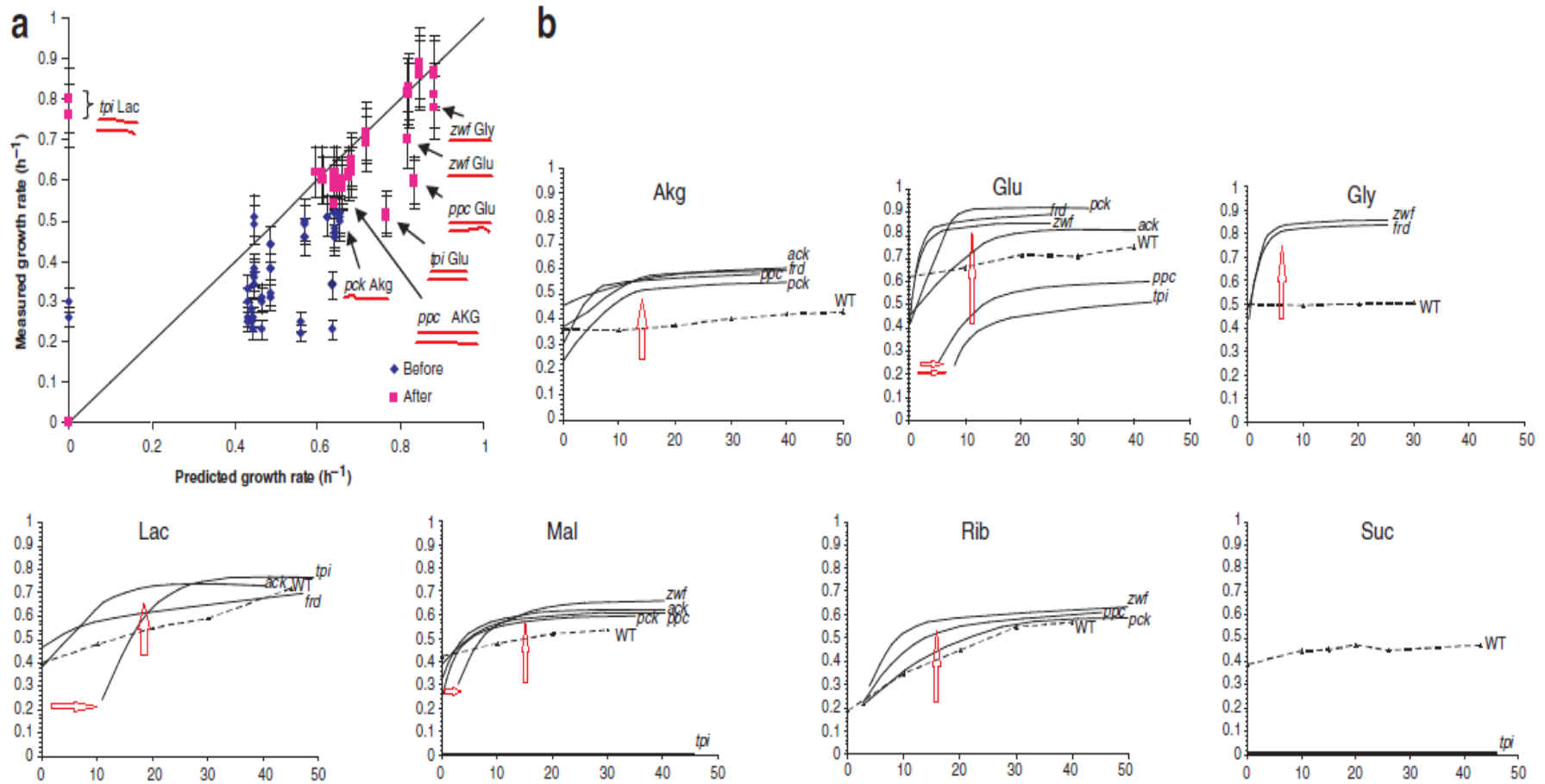



图1. 适应性进化中生长速率的变化。(a) 实验前期、后期预测生长速率和实际测量到的生长速率比较图。(b) 各*E. coli* 在不同碳源培养基中适应性演变中生长速率的变化, 横坐标代表演化天数 (d), 纵坐标代表生长速率 ( $h^{-1}$ ) (Fong et al. ,2004, Nature Genetics 36(10): 1056-1058.)

- 
- ◊ Monitoring the growth-rate changes of each strain throughout evolution yielded two notable observations.
  - ◊ First, each evolved deletion strain showed an increase in growth rate of at least 15% during evolution, the average growth-rate increase was 87%. Several strains showed no observable growth for the first several days of culture, but all recovered to grow at rates 40–50 h<sup>-1</sup> at the end of adaptive evolution.





- ◆ We also observed that the rate of growth adaptation varied greatly between deletion strains. Several deletion strains showed gradual increases in growth rate over the first 20 or more days of evolution, whereas other strains showed rapid increases in growth within the first several days of evolution.
- ◆ In most cases , the rate of adaptation for the deletion strains occurred much more rapidly than is observed for adaptive evolution of wild-type *E. coli*.

# 结果 2

	Evolution on $\alpha$ -ketoglutarate								Evolution on glucose								Evolution on glycerol								
	ack1	ack2	frd1	frd2	pck1	pck2	pck3	ppc1	ppc2	ack1	ack2	frd1	frd2	pck1	pck2	ppc1	ppc2	tpi1	tpi2	zwf1	zwf2	frd1	frd2	zwf1	zwf2
Akg	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲
Glu	—	—	—	—	—	▼	—	—	—	—	—	—	—	▲	▲	▼	▼	▼	▼	—	▲	▲	—	▲	—
Lac	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲
Gly	▲	▲	▲	▲	▲	—	▲	▲	▲	▲	▲	▲	▲	▲	▲	▼	▼	▼	▼	▲	▲	▲	▲	▲	▲
Pyr	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▼	▼	▼	▼	▲	▲	▲	▲	▲	▲
Suc	▲	—	▲	▲	—	—	—	—	—	—	—	▼	—	—	—	—	—	—	—	▼	▼	▲	—	▼	▼
Mal	▲	—	—	—	▲	—	▲	—	—	—	▼	▼	—	▼	▼	—	—	—	—	▼	▼	—	—	▼	▼
Rib	—	▲	▲	▲	▲	▼	▼	▲	▲	—	—	—	—	▲	▲	—	—	▲	▲	—	▼	▲	▲	—	—
Ace	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	—	▲	—	▲	—	▼	▲	▲	▲	▲	▲	▲

	Evolution on lactate						Evolution on malate						Evolution on ribose				Vs. unevolved strain						
	ack1	ack2	frd1	frd2	tpi1	tpi2	ack1	ack2	pck1	pck2	pck3	ppc1	ppc2	zwf1	zwf2	pck1		pck2	ppc1	ppc2	zwf1	zwf2	
Akg	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	—	—	▲	▼	▲	—	▲	Increase 41.5
Glu	▲	▲	▲	▲	▲	▲	▲	▲	—	—	—	—	—	▲	▲	—	—	—	▲	▲	▲	▲	Decrease 26.8
Lac	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	—	—	▲	▲	▲	▲	▲	▲	▲	▲	▲	No growth 4.8
Gly	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	—	—	—	▲	▲	—	▲	▲	▲	▲	▲	▲	No change 26.8
Pyr	▲	▲	▲	▲	▲	▲	▲	—	—	▲	▼	▼	—	▲	▲	▲	▲	▲	▲	▲	▲	▲	
Suc	—	—	▲	—	—	—	▲	▲	—	▲	▲	▲	—	▲	▲	▼	▼	▼	▼	—	—	▲	Vs. wild-type
Mal	▼	—	—	—	—	—	▲	▲	▲	▲	▲	▲	—	▲	▲	—	▼	—	▼	▲	▼	▲	▲ Increase 64.0
Rib	—	—	▲	▲	—	▲	▲	▲	▲	▲	—	—	—	—	▲	▲	▲	▲	▲	▲	▲	▼	▼ Decrease 18.4
Ace	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	—	▲	▲	▲	▲	▲	▲	▲	▲	—	— No change 17.6

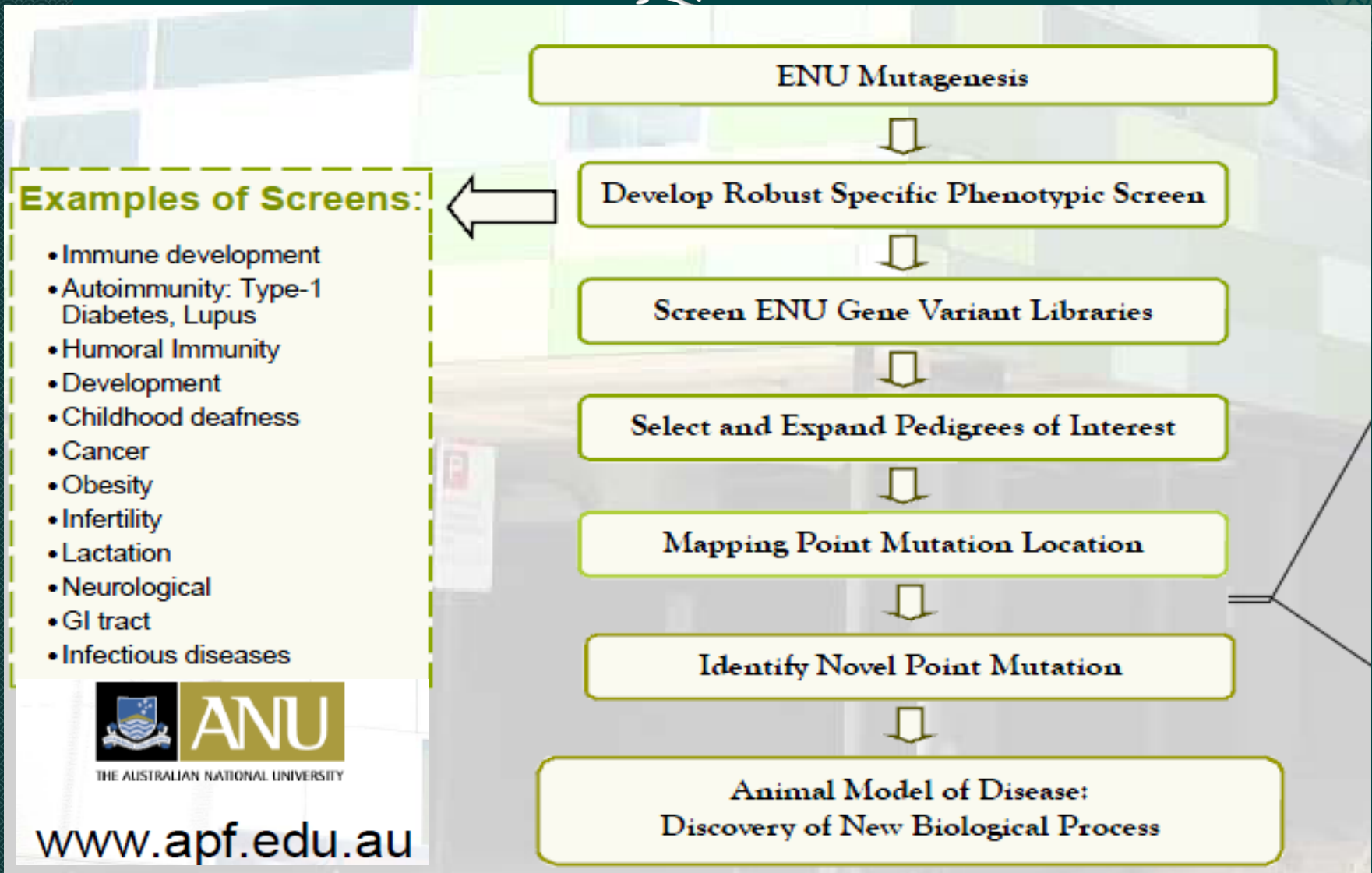
图2. 所有确实菌株在不同碳源培养基上生长速率的定性结果。纵坐标代表不同碳源，横坐标代放在不同碳源中进化的缺失菌株。

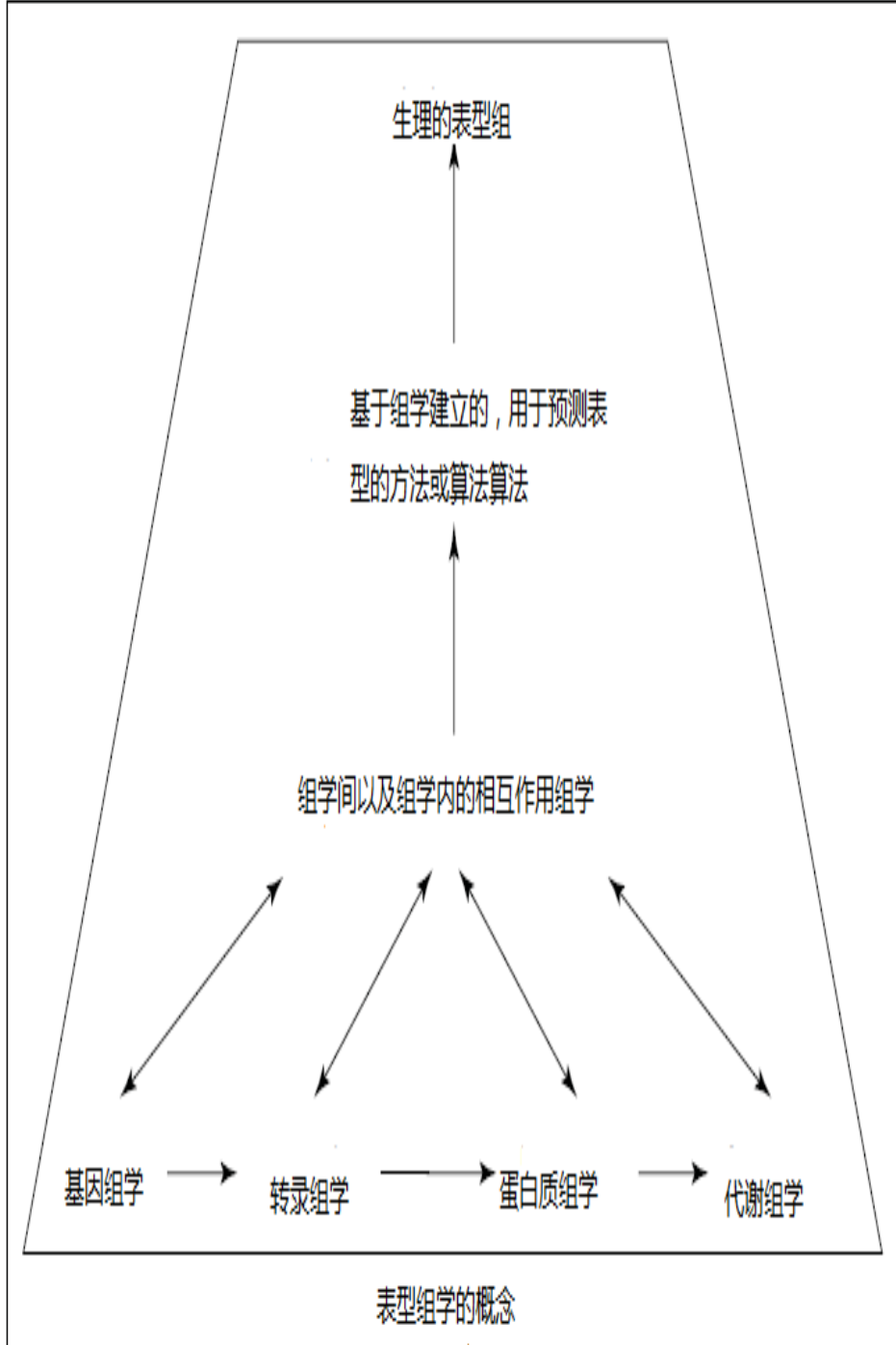
方框内不同的颜色代表与非进化菌株生长速率的比较，方框内符号代表与野生型菌株生长速率的比较。(Fong et al., 2004) *Nature Genetics* 36(10): 1056-1059.



- ◊ Comparison with the wild-type strain showed that nearly two-thirds of the strains resulted in increased growth on nonevolutionary carbon sources, indicating that evolution on one substrate led to concurrent growth improvements on other substrates.
- ◊ Notably, we also observed variation between strains evolved in parallel.

# 重要的前沿课题~尚待解决的问题





- ◆ 表型数据的收集
- ◆ 表型组对象的发展
- ◆ 怎样综合利用基因组学、转录组学、蛋白质组学、代谢组学以及互作组学的信息解释表型
- ◆ 算法以及方法的发展



◆ Thank you!