Special Seminar

Wen-Hsiung Li
Academician of Academia Sinica

Biodiversity Research Center, Academia Sinica, (Taiwan)
Distinguished Research Fellow, Brown University, Providence, RI, USA Ph.D.

EDUCATION AND POSITIONS HELD:

- Ph.D., Applied Mathematics, Brown University, Providence, RI, 1972
- Postdoctoral Fellow, Genetics, University of Wisconsin, 1972–1973
- Assistant Professor, University of Texas Health Science Center-Houston, 1973
- Associate Professor, University of Texas Health Science Center-Houston, 1978
- Professor, University of Texas Health Science Center-Houston, 1984
- Betty Wheless Trotter Professor in Medical Sciences, University of Texas Health Science Center-Houston, 1996–1998
- George Beadle Professor, University of Chicago, 1999–2004
- James D. Watson Professor, University of Chicago, 2004-present.

Honors:

- Member, National Academy of Sciences, 2003
- Fellow, American Academy of Arts and Sciences, 1999
- Academician, Academia Sinica, Taiwan, 1998
- Balzan Prize 2003 for Genetics and Evolution
- President, Society for Molecular Biology and Evolution, 2000
- Horace Mann Medal, 2004
- Cockerham Lecture, 2007

Bioinformatic methods and tools for functional and evolutionary genomics

First, we are developing methods and computer software packages for inferring regulatory modules from gene expression data. Regulatory modules are sets of genes co-regulated to respond to different conditions. Our aim is to be able to infer the genes on each specific module, the regulators of the module, and the conditions under which the regulation occurs. Second, we are also developing methods for studying the evolution of gene regulation and regulatory modules. Third, we shall apply the new and existing methods to analyze data to address the above two issues.

Organization and evolution of the yeast regulatory network

We are using yeast as a model organism to pursue the following broad issues. First, we want to infer important regulatory modules in the yeast genome, including the genes in each specific module, its regulators, and the conditions under which the regulation occurs. Second, we shall study the relative importance (roles) of cis- and trans-acting elements in regulatory evolution. Third, we shall construct a database that contains our own results and the results synthesized from public domains.

Wen-Hsiung Li[1], Jui-Jen Chang[2], Yu-Ju Lin[1,3], Hao-Yeh Lin[1], Caroline Thia[1], Yi-Ying Kao[1], Hong-Wei Pi[1], Ming-Hsuan Lee[1] and Chieh-Chen Huang[3]

[1]Biodiversity Research Center, Academia Sinica, Taipei, Taiwan; [2]Department of Medical Research, China Medical University Hospital, China Medical University, Taichung, Taiwan; [3]Department of Life Sciences, National Chung Hsing University, Taichung, Taiwan

Selecting superb microbial hosts for producing metabolites and peptides

Introduction:

Microbes provide an extremely rich resource for biotechnology. In particular, they can serve as hosts for producing valuable metabolites or peptides. However, we have learned a big lesson in that we chose *Saccharomyces cerevisiae* as the host for bioethanol production --- we found that many genes transformed into the *S. cerevisiae* genome had no function. This is because *S. cerevisiae* has the problem of over-glycosylation. Thus, selecting a suitable microbe as the host for a cell factory is a crucial step.

Selecting a yeast as a super host for metabolite or peptide production.

Many fungi have been employed in industry. For example, *S. cerevisiae* has been heavily used in wine/beer production. However, we found *Kluyveromyces marxianus* to be a much better host for many other purposes. Compared to traditional yeasts, *K. marxianus* has the following advantages: (1) It has a rapid growth rate --- it can achieve a doubling time of 45 minutes, which is comparable or even faster than some bacteria. (2) Its glycosylation is weak. (3) It has a broad substrate spectrum, including glycerol, xylose, lactose, mannose, inulin, and cellobiose. (4) It is toxin-tolerant and has a broad pH tolerance (2.5~9). (5) It can survive up to 46^{o}C. We have indeed successfully used it as the host to produce astaxanthin, which has 14-fold higher antioxidant activity than vitamin E. We are now engineering it to be a humanized yeast for producing human glycoproteins, including therapeutic proteins.

Selecting a host that can live in sea water.

Rhodotorula glutinis, an oleaginous microorganism, contains up to 70% oil of dry cell weight, a potential bioenergy source. *R. glutinis* is an attractive candidate to serve as industrial host because of its ability to utilize various cheap substrates such as molasses and peat extract. Remarkably, it can be cultured in sea water to develop a sustainable industry for saving fresh water. *R. glutinis* is a well-known β-carotene producer in the industry, a valuable compound for healthcare including anti-carcinogenic and antioxidant properties. We have established a synthetic biology platform to improve the carotenoids yield of *R. glutinis*. And a bio-process is being developing for an oil biorefinery and β-carotene production.

Conclusion:

A good host for cell factories should have many desirable features such as a rapid growth rate and simple genetic manipulation. Microbial diversity provides a good opportunity to select a desirable host for any particular purpose. Here Ww have provided 2 examples.