Wen-Hsiung Li

2003 Balzan Prize for Genetics and Evolution

Wen-Hsiung Li has made seminal contributions to the field of evolutionary molecular genetics. He has developed widely used methods for inferring phylogenetic relationships and has made important discoveries about the rate of genetic change in different groups of animals.

Evolution of Gene Regulation and Regulatory Modules in Yeast

The University of Chicago

Adviser for the General Balzan Committee: John Krebs

The purpose of Li's project is to study how the regulation of yeast genes has evolved over time. However, instead of looking at one gene at one time, Li's group has looked at a group of genes, or regulatory module, that are subject to the same or similar regulation at the same time. The fruit of this research is the following two publications:
- A. Prachumwat and W.-H. Li. (2006) *Protein Function, Connectivity, and Duplicability in Yeast*. Mol. Biol. Evol., 23:30-39. Summary: Protein-protein interaction networks have evolved mainly through connectivity rewiring and gene duplication. However, how protein function influences these processes and how a network grows in time have not been well studied. Using protein-protein interaction data and genomic data from the budding yeast, we first examined whether there is a correlation between the age and connectivity of yeast proteins. A steady increase in connectivity with protein age is observed for yeast proteins except for those that can be traced back to bacteria. Second, we investigated whether protein connectivity and duplicability vary with gene function. We found a higher average gene duplicability for proteins interacting with external environments than for proteins localized within intracellular compartments. For example, proteins that function in the cell periphery (mainly transporters) show a high duplicability but are lowly connected. Conversely, proteins that function within the nucleus (e.g., transcription, RNA and DNA metabolisms, and ribosome biogenesis and assembly) are highly connected but have a low duplicability. Finally, we found a negative correlation between protein connectivity and duplicability.
- Marland, E., A. Prachumwat, N. Maltsev, Z. Gu, and W.-H, Li. (2004) *Higher gene duplicabilities for metabolic proteins than for non-metabolic proteins in yeast and E. coli*. J. Mol. Evol. 59:806-814. Summary: Gene duplication produces an extra copy that, free to evolve in function, is the primary source of genetic novelties. The re-

searchers involved found strong support for the view that metabolic proteins tend to have higher gene duplicability than non-metabolic proteins. Moreover, a detailed analysis of metabolic pathways in these two organisms revealed that genes in the central metabolic pathways and the catabolic pathways have, on average, higher gene duplicability than do other genes.
An on-going project on Evolution of Yeast Non-Fermentative Regulatory Network has also been started in order to (1) identify the major genes that control the transition from fermentative to non-fermentative growth (i.e., key regulators) and also their downstream genes, and (2) study how these genes and their regulatory pathways have evolved.

Further publication:
- Li Wen-Hsiung, Chang Ya-Wen, Liu Fu-Guo Robert, Yu Ning, Sung Huang-Mo, Yang Peggy Wang Daryi, Huang Chih-Jen, Shih Ming-Che (2008), *Roles of cis- and trans-changes in the regulatory evolution of genes in the gluconeogenic pathway in yeast,* Mol. Biol. Evol. 25(9).

Statement by the Prizewinner: *I tremendously enjoy doing science and find it a fulfilling life. The Balzan Prize gives me great encouragement and financial support for pursuing my interests further.* Wen-Hsiung Li (Berne, 07.11.2003)