No. 20

New era for network biology of Escherichia coli

Hirotada Mori[1, 2]
([1] Graduate School of Biological Sciences, Nara Institute of Science and Technology
[2]Advanced Institute of Biosciences, Keio University, Tsuruoka, Yamagata, Japan)
e-mail: hmori@gtc.naist.jp

There is not any cellular system, which has ever been elucidated its structure and regulation of the whole physiological network system. Even though the subset of them, such as glycolysis and TCA cycle metabolic pathway network, there is little to have been cleared.

After the completion of genome project of *E. coli* in the beginning of 1997, the post genomic approaches had been launched. The genome projects of *E. coli* were started in 1989 in Japan for W3110(1) and 1990 in Wisconsin University in US for MG1655(2) respectively. In 1990s, technology innovation was remarkable and genomic and post-genomic analyses were expanding rapidly than we expected when started. DNA microarray, which was one of the symbolic development in omics field, was first developed in 1995 by Shcena et al.(3) and it has opened the gate to systematic quantitative analysis with global aspect, so-called omics analyses.

During 1990s, many comprehensive resources were started to be constructed, such as cDNA, ORF clone, deletion strain libraries etc. Especially the society of *Saccharomyces cerevisiae* has been showing outstanding resources and their scientific applications using those resources. And this is one of the leading organisms in the systems biology in the beginning of 21st century.(4)

On the other hand in the *E. coli* society, we also has kept efforts for constructing the comprehensive resources, such as ORF clones(5, 6) and deletion collection (7). Those resources have accelerated *E. coli* science not only individual target researches but post-genomic systems analyses. Such comprehensive resources with systematic approaches are now openning the gates to the new biology to understand whole cell as systems level.

In modern biology, uni-cellular model organisms, such as *E. coli* and Yeast, have emerged as important research target because of the accumulation of biological knowledge and advanced tools to analyze. And most importantly, such uni-cellular organisms have entire cellular function in a single cell.

As Nobel Prize winner in 1965, Dr. Jacques Monod said “What is true for *E. coli* is true for the elephant.” Last 50 years, the concept of genes has been established using *E. coli* and I believe the concept of cellular system will be build up using uni-cellular model organism, such as *E. coli*, in the next 50 years.

According to this concept, my group has long been focusing on *E. coli* systems analyses after the the genome project.

First we constructed the comprehensive ORF plasmid libraries(5, 6) and we also established single gene deletion library, so-called Keio collection as the second resource.(7) Transcriptome analysis using DNA microarray(8, 9) and comprehensive protein-protein interaction analysis(10) were fruitful application using those resources.

Recently we developed the new resources and tools to clear genetic interaction network, which is one of the

approaches to clear the molecular mechanisms of "Robustness".(11, 12) The basic concept is systematic survey of the compensatory gene combination by comprehensive double knockout strain construction. The method to make double knockout is to combine two single gene deletion mutations by conjugation. As Boone and his colleagues has already reported the global picture of cellular network in *S. cerevisiae*, it is promising approach to access the global structure of physiological network system in a cell.(13)
I will introduce our current research project and would like to discuss for the future.

1. Yura T, *et al.* (1992) Systematic sequencing of the Escherichia coli genome: analysis of the 0-2.4 min region. *Nucleic Acids Res* 20(13):3305-3308.
2. Daniels DL, Plunkett G, 3rd, Burland V, & Blattner FR (1992) Analysis of the Escherichia coli genome: DNA sequence of the region from 84.5 to 86.5 minutes. (Translated from eng) *Science* 257(5071):771-778 (in eng).
3. Schena M, Shalon D, Davis RW, & Brown PO (1995) Quantitative monitoring of gene expression patterns with a complementary DNA microarray. (Translated from eng) *Science* 270(5235):467-470 (in eng).
4. Kitano H (2001) *Foundations of systems biology* (MIT Press, Cambridge, Mass. ; London) pp xv, 297.
5. Kitagawa M, *et al.* (2005) Complete set of ORF clones of Escherichia coli ASKA library (A Complete Set of E. coli K-12 ORF Archive): Unique Resources for Biological Research. *DNA Res* 12:291-299.
6. Saka K, *et al.* (2005) A complete set of Escherichia coli open reading frames in mobile plasmids facilitating genetic studies. *DNA Res* 12(1):63-68.
7. Baba T, *et al.* (2006) Construction of Escherichia coli K-12 in-frame, single-gene knockout mutants: the Keio collection. *Mol Syst Biol* 2:2006 0008.
8. Oshima T, *et al.* (2002) Transcriptome analysis of all two-component regulatory system mutants of Escherichia coli K-12. *Mol Microbiol* 46(1):281-291.
9. Oshima T, *et al.* (2002) Genome-wide analysis of deoxyadenosine methyltransferase-mediated control of gene expression in Escherichia coli. *Mol Microbiol* 45(3):673-695.
10. Arifuzzaman M, *et al.* (2006) Large-scale identification of protein-protein interaction of Escherichia coli K-12. *Genome Res* 16(5):686-691.
11. Typas A, *et al.* (2008) High-throughput, quantitative analyses of genetic interactions in E. coli. (Translated from Eng) *Nat Methods* (in Eng).
12. Butland G, *et al.* (2008) eSGA: E. coli synthetic genetic array analysis. (Translated from Eng) *Nat Methods* (in Eng).
13. Costanzo M, *et al.* (2010) The genetic landscape of a cell. (Translated from eng) *Science* 327(5964):425-431 (in eng).