The systematical analysis of gene expression and regulation in response to phosphate starvation in *Escherichia coli*

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Phosphate is the essential cellular element as major building blocks of various biomolecules. Its metabolism and uptake system is closely related with diverse metabolic pathways including energy and central carbon metabolism. In *Escherichia coli*, PhoR-PhoB two-component regulatory system detect and properly response to environmental phosphate concentration. During the growth of *E. coli* W3110 strain under phosphate limiting condition, the global gene expression changes were investigated by using DNA microarray. Expectedly, the expressions of some genes relating to phosphate uptake and metabolism were increased as phosphate was exhausted, whereas the expressions of some genes relating to ribosomal protein or amino acid biosynthesis and metabolism were decreased. Especially, the expression of *pho*B peaked just after phosphate exhaustion and decreased after that during stationary phase, suggesting that the high stability of PhoB. At the *pho*B peak point, the *pho*B- and/or *pho*R-dependent regulation was also investigated by comparing the gene expression levels among the wild type and *pho*B and/or *pho*R knock out mutant strains. Roughly, it seems that *pho*B mutation was epistatic to *pho*R mutation. And it was revealed that the genes for phosphonate or glycerol phosphate metabolism were under *pho*B- and *pho*R-dependent up-regulation and the genes for high-affinity phosphate transport system were under *pho*B-dependent up-regulation. Surprisingly, some genes such as *xas*A (acid sensitive protein, putative transporter), *yib*D (putative regulator), and *ytf*K (hypothetical protein) also showed *pho*B- and *pho*R-dependent up-regulation and had putative pho box; *amn* (AMP nucleosidase) and *tkt*B (transketolase) gene were also up-regulated in *pho*B-dependent manner and had also putative pho box and *ici*A (replication initiation inhibitor) was under *pho*R-dependent down-regulation. This indicates that some genes, which are not directly related with phosphate uptake and metabolism, are controlled by pho regulon. This

shows the roles of PhoB and/or PhoR as global regulators. Additionally, these findings may offer the clue for metabolic engineering for efficient productions of some metabolites or the study of DNA and/or protein interactions.

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1. Hoffer, S. M., H. V. Westerhoff, K. J. Hellingwerf, P. W. Postma, and J. Tommassen, Autoamplification of a two-component regulatory system results in "learning" behavior (2001), J. Bacteriol., 183, 4914-4917.
2. Wanner, B. L., Phosphorus assimilation and control of the phosphate regulon (1996), p. 1357-1381. In F. C. Neidhardt, R. Curtiss III, J. L. Ingraham, E. C. C. Lin, K. B. Low, B. Magasanik. W. S. Reznikoff, M. Riley, M. Schaechter, and H. E. Umbarger (ed.), *Escherichia coli* and *Salmonella*: cellular and molecular biology, 2nd ed. ASM Press, Washington, D.C.