On the Construction of a Model Signaling System with Structural Information: Structural Studies of *Bacillus subtilis* Stress Response Regulators

Tomonori Kaneko,* Hiroyuki Koyama, Nobuo Tanaka and Takashi Kumasaka, *Dept. of Life Science, Tokyo Institute of Technology, Japan*. E-mail: tokaneko@bio.titech.ac.jp

Keywords: network; σ^B; sporulation

A large number of biological macromolecules interact with one another to work inside, outside or on the boundary of cells. Integrating such interactions results in a construction of a network. Here, each macromolecule, usually a protein, is a device of the network. The nature of this network is expected to be very different from that of other networks such as the Internet or brain/neural networks. The features of these networks are that they are composed of simple devices, although the output of their resulting networks can be complicated. On the other hand, in a macromolecular network, each device itself is a complex matter. Can we understand such type of networks at the molecular level? Can we predict their outputs as *in vivo* events? We propose here a model system to analyze a signaling pathway based on the structural information of each component. Once a *Bacillus subtilis* cell suffers from a stress, it stimulates signal regulator proteins that finally induce sporulation in the cell. Nutritional stress signal is transmitted from a putative hydrolase RsbQ to a transcription factor σ^B, through a phosphatase RsbP, an anti-anti-σ^B protein RsbV, and an anti-σ^B kinase RsbW. As the first stage, we have been trying to solve these structures. The structure of RsbQ has already been solved. This putative hydrolase has been proposed to activate the down-stream phosphatase RsbP by modifying it in an unknown way. Although RsbP has a PAS domain, the function as well as its ligand has yet to be elucidated. Some of our recent results about them will be shown.