Molecular Imaging Probes with Tunable Chemical Switches

Kazuya Kikuchi[1,2]

Graduate School of Engineering,[1] Immunology Frontier Research Center,[2] Osaka University, Japan

One of the great challenges in the post-genome era is to clarify the biological significance of intracellular molecules directly in living cells. If we can visualize a molecule in action, it is possible to acquire biological information, which is unavailable if we deal with cell homogenates. One possible approach is to design and synthesize chemical probes that can convert biological information to chemical output.

Protein fluorescent labeling provides an attractive approach to study the localization and function of proteins in living cells. Recently, a specific pair of a protein tag and its ligand has been utilized to visualize a protein of interest (POI). In this method, a POI is fused with a protein tag and the tag is labeled with the ligand connected to a fluorescent molecule. The advantage of this protein labeling system is that a variety of fluorescent molecules are potentially available as labeling reagents, and that the protein tag is conditionally labeled with its fluorescent ligand. However, in the existing labeling systems, there are some problems with the size of a protein tag, the specificity of the labeling or fluorogenicity of labeling reagents. Protein tags for labeling proteins of interest (POIs) with small molecule based probes have become important technique as practical alternatives to the fluorescent proteins (FPs) for live cell imaging. We have designed a protein labeling system that allows fluorophores to be linked to POI. The protein tag (BL-tag) is a mutant class A β-lactamase (TEM-1) modified to be covalently bound to the designed specific labeling probes and the labeling probes is consisted with a β-lactam ring (ampicillin, cephalosporin) attached to various fluorophores. A fluorogenetic labeling system can be designed using the unique property of cephalosporin, which release leaving group by subsequent reaction after opening the lactam ring. For further sophisticated application, multicolor imaging was done by adopting the colorful fluorophores.

Kazuya Kikuchi Professor, Graduate School of Engineering and Immunology and Frontier Research Center (double appointments), Osaka University; B.S. 1988, University of Tokyo; Ph.D. 1994, University of Tokyo (advisor: Masaaki Hirobe); Postdoctoral Training, 1994-1995, University of California, San Diego (advisor: Roger Y. Tsien) 1995-1996, the Scripps Research Institute (advisor: Donald Hilvert); *Chemical biology*; *Design, synthesis and biological application of molecular imaging probes;* Tel: 81-6-6879-7924, Fax: 81-6-6879-7875, E-mail: kkikuchi@mls.osaka-u.ac.jp