# Kazuya KIKUCHI, Professor

Department of Material and Life Science,
Graduate School of Engineering, Osaka University
Immunology Frontier Research Center, WPI-Osaka University (Double Appointment)
Suita, Osaka 565-0871, Japan
Tel: 81(Japan)-6-6879-7924, FAX 81-6-6879-7875
E-mail: kkikuchi@mls.eng.osaka-u.ac.jp

## Education

Ph. D. (March, 1993), M. Pharm. Sci. (March, 1990), B. Pharm. Sci. (March, 1988): The University of Tokyo

## Academic Carrier

1994 (July)-1995 (June): Post-doctoral fellow, Department of Pharmacology, University of California, San Diego (supervisor: Prof. Roger Y. Tsien)
1995 (July)-1996 (December): Post-doctoral fellow, Department of Chemistry, The Scripps Research Institute (supervisor: Prof. Donald Hilvert)
1997 (Jnauary): Assistant Professor, Graduate School of Pharmaceutical Sciences, The University of Tokyo
2000 (December): Associate Professor, Graduate School of Pharmaceutical Sciences, The University of Tokyo
2005 (July)-: Professor, Department of Material and Life Science, Graduate School of Engineering, Osaka University
2009 (July)-: Professor, Immunology Frontier Research Center, WPI-Osaka University, (Double Appointment)

## Awards and Honors

Young Investigator Award, Japanese Pharmaceutical Society (2002), IBM Science Award (2008), Chem Soc Rev Emerging Investigator Award, Royal Society of Chemistry (2008), Japanese Society of Promotion of Science Prize (2010), The Osaka University Award for Research and Education (2011).

## Total Publications

(SCI: 110), Citation (SCI): 5,842 (2011, August), Average Citation: 53.11 (2011, August), h-index: 41

## Recent Papers

1) S. Mizukami, T. Yamamoto, A. Yoshimura, S. Watanabe & K. Kikuchi, “Covalent Protein Labeling with a Lanthanide Complex and its Application to Photoluminescence Lifetime-based Multicolor Bioimaging”, *Angew. Chem. Int. Ed.*, **50,** in press (2011).
2) S. Watanabe, S. Mizukami, Y. Akimoto, Y. Hori & K. Kikuchi, “Intracellular Protein Labeling with Prodrug-Like Probes Based on Mutant β-Lactamase-Tag”, *Chem. Eur. J.*, **17,** 8342-8349 (2011).
3) S. Mizukami, M. Hosoda, T. Satake, S. Okada, Y. Hori, T. Furuta & K. Kikuchi, “Photocontrolled Compound Release System Using Caged Antimicrobial Peptide”, *J. Am. Chem. Soc.*, **132,** 9524-9525 (2010).

# Design, Synthesis and Biological Application of in Vivo Imaging Probes with Tunable Chemical Switches

Kazuya Kikuchi

*Graduate School of Engineering, Osaka University, Immunology Frontier Research Center, Osaka University 2-1 Yamada-oka, Suita City 565-0871, Osaka Japan*
*Phone: +81-6-6879-7924, Fax: +81-6-6879-7875*
e-mail: kkikuchi@mls.eng.osaka-u.ac.jp / http://www-molpro.mls.eng.osaka-u.ac.jp/

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.

Magnetic resonance imaging (MRI) is an imaging modality adequate for *in vivo* studies. Therefore, many scientists are interested in the development of MRI probes capable of detecting enzyme activities *in vivo*. Because background signal is hardly detectable, $^{19}$F-MRI probes are promising for *in vivo* imaging. A novel design strategy for $^{19}$F-MRI probes to detect protease activities is proposed. The design principle is based on the paramagnetic relaxation effect from $Gd^{3+}$ to $^{19}$F. A peptide was synthesized, Gd-DOTA-DEVD-Tfb, attached to a $Gd^{3+}$ complex at the N-terminus and a $^{19}$F-containing group at the C-terminus. The $^{19}$F-NMR transverse relaxation time ($T_2$) of the compound was largely shortened by the paramagnetic effect of intramolecular $Gd^{3+}$. The peptide was designed to have a sequence cleaved by an apoptotic protease, caspase-3. When the peptide was incubated with caspase-3, the peptide was cleaved and subsequently the $Gd^{3+}$ complex and the $^{19}$F-containing group were separated from each other. $T_2$, after cleavage, was extended to cancel the intramolecular paramagnetic interaction. $T_2$ is a parameter that can be used to generate contrasts in MR images. Using this probe as a positive contrast agent, the probe could detect caspase-3 activity spatially using $^{19}$F MRI.[1,2]

**Reference**

[1] Mizukami, S.; Takikawa, R.; Sugihara, F.; Shirakawa, M.; Kikuchi, K. *Angew. Chem. Int. Ed*. **2009,** *48,* 3641-3643.
[2] Mizukami, S.; Takikawa, R.; Sugihara, F.; Hori, Y.; Tochio, H.; Wälchli, M.; Shirakawa, M.; Kikuchi, K. *J. Am. Chem. Soc.* **2008,** *130,* 794-795.