【Grant-in-Aid for Scientific Research(S)】

Integrated Disciplines (Complex systems)

Title of Project : Design, Synthesis and Biological Application of in vivo Imaging Probes

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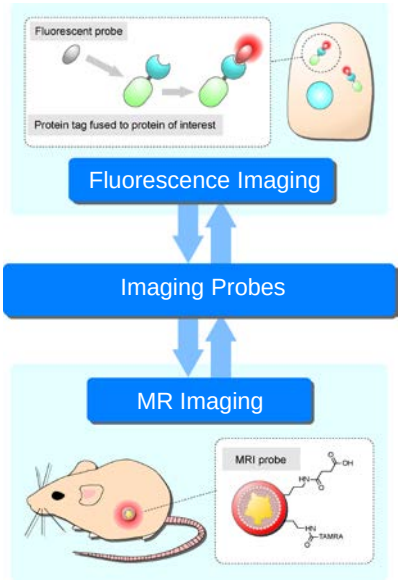
Research Area : Chemical Biology
Keyword : Molecular Imaging, in vivo Imaging

【Purpose and Background of the Research】

One of the great challenges in the post-genome era is to clarify the biological significance of intracellular molecules directly in living systems. 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. In this research, in vivo imaging probe will be developed.

【Research Methods】

Real-time imaging of enzyme activities in vivo offers valuable information in understanding living systems and in the possibility to develop medicine to treat various forms of diseases. Magnetic resonance imaging (MRI) is an imaging modality adequate for in vivo studies. 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. Using this probe as a positive contrast agent, the probe could detect enzyme activity spatially from an image using ^{19}F MRI. I this current research, highly sensitive detection should be possible by using nanoparticle with fluorine compound.



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. 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. A protein tag (BL-tag), a mutant β-lactamase, modified to be covalently bound to the designed labeling probes was developed. Multicolor labeling for intracellular protein will be developed.

【Expected Research Achievements and Scientific Significance】

Current limit of the application of chemical probes on the molecular imaging is in vivo application. The successful application of the chemical probes in this research should prove the significance of interdisciplinary research in the imaging research.

【Publications Relevant to the Project】

・S. Mizukami, R. Takikawa, F. Sugihara, Y. Hori, H. Tochio, M. Wälchli, M. Shirakawa & K. Kikuchi, "Paramagnetic Relaxation-based ^{19}F MRI Probe to Detect Protease Activity", *J. Am. Chem. Soc.*, **130,** 794-795 (2008).
・S. Mizukami, S. Watanabe, Y. Akimoto & K. Kikuchi, "No-Wash Protein Labeling with Designed Fluorogenic Probes and Application to Real-Time Pulse-Chase Analysis", *J. Am. Chem. Soc.,* **134,** 1623-1629 (2012).

【Term of Project】 FY2013-2017

【Budget Allocation】 168, 400 Thousand Yen

【Homepage Address and Other Contact Information】

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