## *Laboratory of Chemical Biology*

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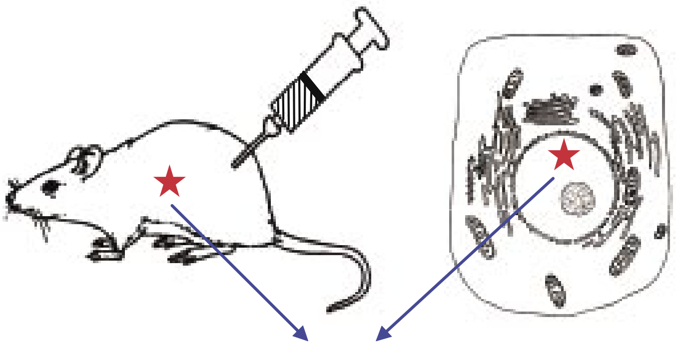
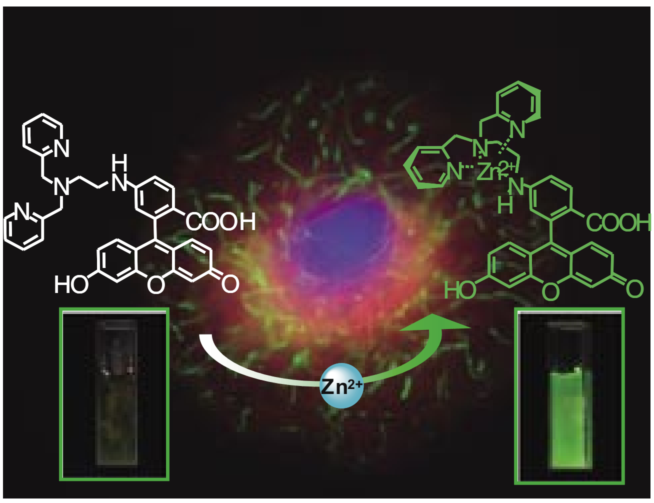
One of the great challenges in the post-genome era is to clarify the biological significance of intracellular molecules directly in living cells. If we can visualize a molecule in action, then it is possible to acquire biological information that is unavailable if we deal only with cell homogenates. One possible approach is to design and synthesize chemical sensor molecules that can convert biological information into chemical outputs that can then be easily monitored. For this purpose, Prof. Kikuchi has developed fluorescent sensor molecules for intracellular messengers and has successfully applied



**Visualize Molecular Action Directly in Living Systems**



them to living cells. The fusion of research involving both chemistry and biology has become a hot topic in the functional clarification of biological molecules in living systems. A most important breakthrough, achieved by Prof. Kikuchi, has been the design and synthesis of chemical compounds which actually work in brain slices, which is a more challenging goal than simply producing chemicals that work *in vitro* as a chemical proof of principle.

One example of this work is low affinity $Zn^{2+}$ sensors. Changes in the ligand structure were designed in order to lower the affinity of $Zn^{2+}$, without changing the selectivity against other cations, and the results were published in *J. Am. Chem. Soc.*, **127,** 10197 (2005). This paper was so well received that it was selected as one of the “100 Current Hot Papers” by the American Chemical Society. The reason for the extensive citation of this paper is that the sensor molecules developed by Prof. Kikuchi have the potential to uncover new biological functions of $Zn^{2+}$. The design of these sensors meets the criteria for cellular application in terms of sensitivity, selectivity and stability in the cell, the key aspect of the design is the application of physical-chemical principles to modulate fluorescence intensity, proving that chemical bases can be quite useful for biological studies.

Thus, his research can be cordially combined together in this research group by providing the chemical tools needed to observe, to modulate and to quantify the biological responses.

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