Plenary 18

Development of Novel Fluorescence Probes Based on Rational Design Strategies: Real-Time Visualization of Various Cellular Responses and in Vivo Tumor Imaging

Yasuteru Urano

Graduate School of Pharmaceutical Sciences, University of Tokyo, Japan

Fluorescence imaging is one of the most powerful techniques currently available for continuous observation of dynamic intracellular processes in living cells. Suitable fluorescence probes are naturally of critical importance for fluorescence imaging, but only a very limited range of biomolecules can currently be visualized because of the lack of flexible design strategies for fluorescence probes. Recently, we demonstrated that the fluorescence properties of most visible light-excitable fluorophores could be controlled and predicted precisely by using the concept of intramolecular photoinduced electron transfer (PeT) [1,2]. Based on these photo-physical findings, we succeeded to construct several totally rational design strategies for novel fluorescence probes, and to develop a wide variety of novel fluorescence probes [2-8].

Further, very recently, we achieved highly specific *in vivo* cancer visualization by employing a newly-designed targeted "activatable" fluorescent imaging probe [9]. This agent is activated after cellular internalization by sensing the pH change in the lysosome. Novel acidic pH-activatable probes based on the BODIPY fluorophore were synthesized, and then conjugated to a cancer-targeting monoclonal antibody. As proof of concept, *ex* and *in vivo* imaging of HER2-positive lung cancer cells in mice were performed. The probe was highly specific for tumors with minimal background signal. Furthermore, because the acidic pH in lysosomes is maintained by the energy-consuming proton pump, only viable cancer cells were successfully visualized. So, these probe conjugates can be a useful clinical tool for cancer detection and real-time monitoring of therapy.

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