Molecular design of activatable Raman probes

Mako Kamiya*
Department of Life Science and Technology, Tokyo Institute of Technology, Yokohama 226-8501, Japan
E-mail: kamiya.m.ad@m.titech.ac.jp

Raman probes based on alkyne or nitrile tags hold promise for highly multiplexed imaging. In order to functionalize the Raman probes to be responsive to biological phenomena in live cells, we have established a general strategy to control Raman signals intensity based on the resonant Raman effect, and prepared activatable Raman probes that show enhanced stimulated Raman scattering (SRS) signals upon reaction with enzymes under physiological conditions. By optimizing xanthene derivative bearing a nitrile group at 9th position, we identified 9CN-JCP as a scaffold dye, and synthesized four activatable Raman probes for different enzymes with different vibrational frequencies by isotope editing of the nitrile group. We validated the activation of the Raman signals of these probes by the target enzymes and succeeded in simultaneous imaging of these enzyme activities in live cells[1]. However, specific visualization of cells with target enzyme activities in tissue was difficult due to leakage of the hydrolysis products from the target cells after activation.Therefore, we recently expanded our molecular design strategy by combining the resonant Raman effect and aggregate formation to develop new series of activatable Raman probes. We focused on a rhodol detivative bearing a nitrile group at 9th position, 9CN-JCR, which shows increased SRS signal intensity and high aggregate-forming ability after probe activation, resulting in good retention in target cells. By using isotope-edited 9CN-JCR-based probes, we could simultaneously detect three ensyme activities in live cultured cells, and distinguish cell regions expressing target enzyme activity in live Drosophila wing disc and fat body ex vivo[2].

Further, we recently developed 9CN-TeP derivatives having a tellurium atom at the 10th position of xanthene as a reaction point of photooxidation. These derivatives show a bathochromic shift in the absorption spectrum and enhanced SRS signal after red light irradiation, thus function as red-light-activatable Raman probes[3].

In this conference, I would like to introduce our molecular design strategy for developing activatable Raman probes and their application to live cells and tissues.

References

[1] Fujioka, H. et. al. *J. Am. Chem. Soc.* **2020**, *142*, 20701–20707.

[2] Fujioka, H. et. al. *J. Am. Chem. Soc.* **2023**, *in press.*

[3] Kawatani, M. et. al. *Chem. Asian J.* **2023**, *18*, e202201086.

Mako Kamiya. The University of Tokyo (BS, 2003), The University of Tokyo (MS, 2005), The University of Tokyo (Ph.D., 2008, Prof. Tetsuo Nagano's lab), EPFL (Postdoc, 2008-2010, Prof. Kai Johnsson), The University of Tokyo (Assistant Professor, Lecturer, Associate Professor, 2010-2022), Tokyo Institute of Technology (Professor, 2022-present). You can add more information on your career hear. [Feld of research] Chemical Biology and Molecular Imaging.