Mono-chromophore Design Strategy for Tetrazine-based Colorful Bioorthogonal Probes with a Single Fluorescent Core Skeleton

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Bioorthogonal chemistry has revolutionized the field of chemical biology by providing powerful chemical tools including metabolite analogous tracking, activity-based protein profiling, target-guided synthesis of enzyme inhibitors, and imaging small molecules in living cells/animals. Among 20 different bioorthogonal reactions, tetrazine ligation has been spotlighted as the most advanced bioorthogonal chemistry because of their extremely faster kinetics and higher specificity than others. Therefore, the iEDDA cycloaddition reaction has emerged as a state-of-the-art approach for selective bio-conjugation in live cells and became an inevitable molecular tool for chemical biologists. One of the interesting features of tetrazine in terms of imaging is the fluorescence quenching effect. In other words, tetrazine moiety serves as a reactive group for the iEDDA reaction and a fluorescence quencher at the same time. Consequently, tetrazine probes can generally serve as a fluorogenic probe during the iEDDA reaction. Many strategies have been pursued to develop tetrazine probes and there are two different representative types of tetrazine probes, FRET or TBET based probes, have been developed. Despite the remarkable fluorogenic property of the probes, however, mechanistic explanation is still controversial and development of tetrazine probes covering full visible color range is still challenging. In this seminar, rational development of super-dark rainbow tetrazine probes will be discussed.

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