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Ligand-directed chemistry for endogenous protein labeling in live cells.

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Traditionally, analysis of proteins function has been conducted under the purified dilute aqueous conditions in most cases. However, it is recently being recognized that structure and functions of natural proteins in live systems are rather different from those in such pure conditions, and thus the protein analysis should be conducted in vivo for deep understanding of these biomolecules. For such objectives, development of chemical methods to selectively label, image and regulate a target protein under live cell conditions is now highly desired in the recent chemical biology research. I describe here our recent progress in chemistry-based methods for specific labeling of proteins driven by coupling of selective molecular recognition and reaction, so-called ligand-directed chemistry (LDchem), under live cell conditions. In LDchem, a reactive and cleavable linker is designed to connect a ligand for selective recognition to a protein-of-interest (POI) with a probe to be tethered to the protein surface. LDchem allows for the protein selective and site selective labeling driven by the proximity effect, in live cells, as well as cell lysates and a pure sample of test tubes. The target proteins are now extended from membrane-bound proteins such as folate receptor, GPCR and neurotransmitter receptors, to intracellular proteins. My group believes that such a new chemistry may facilitate various aspects of fundamental chemical researches, in addition to diagnostic or pharmaceutical applications.

References

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