Development and application of bond-cleavage reactions in bioorthogonal chemistry

With the support from the National Natural Science Foundation of China and the Ministry of Science and Technology of China, a research team led by Prof. Chen Peng (**陈鹏**) at the Department of Chemical Biology, College of Chemistry and Molecular Engineering (CCME), Peking University, developed some novel bioorthogonal bond-cleavage chemistries in recent years and most recently, they were invited to summarize and prospect this new field of "Bioorthogonal Chemistry" in *Nature Chemical Biology* (2016, 12: 129—137).

The concept of bioorthogonal chemistry has drawn an explosion of interest since its first appearance in 2003, which has strengthened the ability to dissect life processes with exogenous chemistry. Traditionally, bioorthogonal chemistry has been largely viewed as a two-component "ligation" reaction in which the inert, stable, and biocompatible reaction pairs react under physiological conditions. However, in recent years, in an opposite direction from the well-established "bond formation" reactions, a panel of bioorthogonal "bond cleavage" reactions, deprotection reactions in particular (also termed bioorthogonal-triggered release), have been rapidly emerging.

In this perspective, Chen and Li summarized the reaction types and highlighted the development and applications of these bioorthogonal cleavage reactions. These reactions have expanded the bioorthogonal chemistry repertoire, enabling an array of exciting new biological applications that range from the chemically controlled spatial and temporal activation of intracellular proteins and small-molecule drugs, to the direct manipulation of intact cells under physiological conditions. Most importantly, they lay out challenges and propose future directions along this appealing avenue of research. This timely Perspective paper in *Nature Chemical Biology* would help to figure out the direction of this filed and strengthen the real purpose of developing new bioorthogonal chemistry.

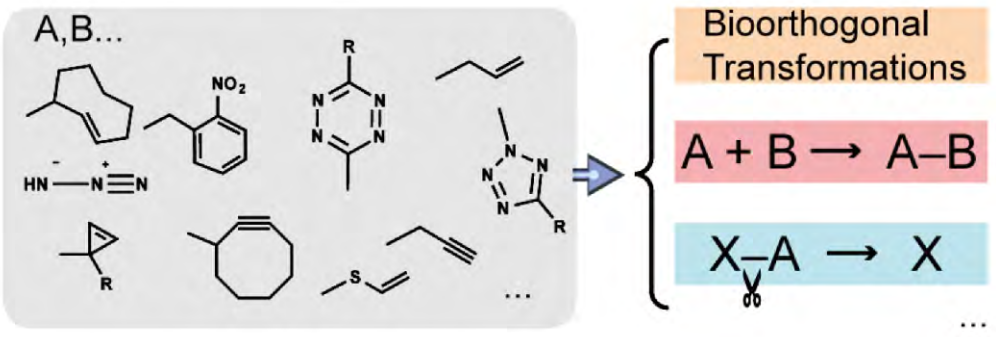

Figure Bioorthogonal reactions beyond ligation.