**Bioorthogonal Cleavage Reactions in Living Systems**

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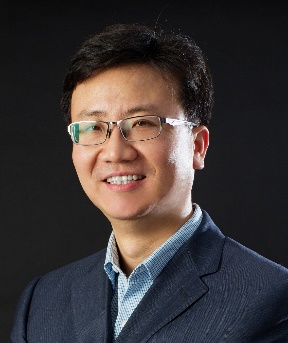
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Employing small molecules or chemical reagents to modulate the function of an intracellular protein of interest, particularly in a gain-of-function fashion, remains a challenge. In this talk, I will introduce a “chemical decaging” strategy that relies on our developed Bioorthogonal Elimination Reactions to control protein activation in living cells. These reactions exhibited high efficiency and low toxicity for chemical decaging of the masked-lysine residue on intracellular proteins, which is complementary to the previously used photo-decaging reactions. In certain applications, particularly within live animals, small-molecule mediated chemical decaging is highly desired and advantageous. We are currently employing this method to block specific kinase’s activity in living cells, which allowed the subsequent gain-of-function study of each kinase within the intracellular signaling transduction network. Together, our strategy expanded the view of Bioorthogonal chemistry beyond ligation reactions, which may be generally applicable for chemically rescue of a given protein, thus manipulating its activity within a native cellular context.

**References**

1. Li J, Chen P. “Development and application of bond-cleavage reactions in bioorthogonal chemistry” *Nat. Chem. Biol****.*** **2016,** *12*, 129-37.
2. Zhang G, Li J, Xie R, Fan X, Liu Y, Zheng S, Ge Y, Chen P. “Bioorthogonal chemical activation of kinases in living systems”, *ACS Cent. Sci*. **2016**, *2*, 325-31.
3. Wang J, Zheng S, Liu Y, Zhang Z, Lin Z, Li J, Zhang G, Wang X, Li J, Chen P. “Palladium-triggered chemical rescue of intracellular proteins via genetically encoded allene-caged tyrosine”, *J. Am. Chem. Soc.* **2016**, *138*, 15118-21.
4. Li J, Jia S, Chen P “Diels-Alder reaction-triggered bioorthogonal protein activation in living cells”, *Nat. Chem. Biol****.,*** **2014**, *10*, 1003-5.
5. Li J, Yu J, Zhao J, Wang J, Zheng S, Lin S, Chen L, Yang M, Jia S, Zhang X, Chen P. “Palladium-triggered deprotection chemistry for protein activation in living cells”, *Nat. Chem.***2014**, *6*, 352-61.

**Biography**

Professor Peng Chen is now the Chairman of Department of Chemical Biology at Peking University. He obtained BS degree in Chemistry at Peking University in 2002 and Ph.D in Chemistry at The University of Chicago in 2007. After postdoctoral training at The Scripps Research Institute, he started his independent career as an Investigator at Peking University in July 2009 and was promoted to Full Professor with tenure in 2014. His research focuses on developing and applying novel chemistry tools to investigate protein-based interactions and activities in living cells. His lab is best known for the creation of versatile genetically encoded photocrosslinkers for studying protein-protein interactions, as well as for the development of bioorthogonal cleavage reactions for protein activation in living systems. He has received many awards including NSFC Distinguished Young Scholar Award (2012), RSC Chemical Society Review Emerging Investigator lectureship (2014), The Chemical Society of Japan Distinguished Lectureship Award (2015), Young Scientist Award from Ministry of Education in China (2016), Tan Kah Kee Young Scientist Award (2016), and Society of Biological Inorganic Chemistry Early Career Award (SBIC award, 2017).